Toward Optimized Practice

CERVICAL CANCER SCREENING

Clinical Practice Guideline | May 2016

OBJECTIVE

Alberta clinicians will understand the recent evidence, offer age and risk-appropriate cervical cancer screening, and follow up on abnormal screen results.

TARGET POPULATION

Consider all women 21-69 years of age who are or have ever been sexually active. Include transgender people with a cervix.

EXCLUSIONS

Women who have never been sexually active

Women with symptoms such as vaginal spotting or bleeding need investigation but not screening

RECOMMENDATIONS

SCREEN

- ✓ Asymptomatic average risk women who are or have ever been sexually active* (see Table 1)
- ✓ Start after three years from onset of sexual activity* or age 25, whichever is later.

**Sexual activity includes intercourse as well as digital or oral sexual activity involving the genital area with a partner of any gender.*

Age Range	21-24	25-29	30-69	≥70
Screen	? Optional screening	✓ Initiate routine screening	✓ Routine screening	✓ Screen If unscreened/under-screened (i.e., not screened regularly at three year intervals)
Interval	Every three years	Every three years	Every three years	Until three consecutive negative Pap tests (collected at least one year apart) within 10 years
Evidence	Harm is likely greater than benefit (moderate evidence)	Benefit is likely greater than harm (moderate evidence)	Benefit is likely greater than harm (strong evidence)	Less evidence, but biologically plausible that the risk of disease is high/continues. Screening may reduce morbidity and mortality.

Table 1: Cervical Cancer Screening Algorithm

PRACTICE POINT

Regular screening should be emphasized for women 25-69 and older (if under/unscreened), but all women 21 and older should be given a choice.

The decision to start or stop screening should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin screening between the ages of 21-24 and some women may choose to continue with screening beyond the age of 69.

To assist with the discussion and patient decision-making see the FAQ resource.

DO NOT SCREEN WOMEN

- X **Less than 21 years of age**
- X Greater than or 70 years of age who have been adequately screened and choose to stop screening
- X With a limited life expectancy and no benefit from screening
- X With a total hysterectomy for benign disease with no cervical abnormalities
- X Who have never been sexually active

> **PRACTICE POINT**
>
> *A Papanicolaou (Pap) test is a screening test for use in an **asymptomatic population** with no apparent signs of neoplasia.*
>
> *If the woman is **symptomatic** she should be investigated regardless of age. See http://sogc.org/guidelines/abnormal-uterine-bleeding-in-pre-menopausal-women-replaces-no-106-aug-2001/.*

CONSIDERATIONS FOR SCREENING PREGNANT WOMEN

- ✓ Screen pregnant women according to the recommendations for screening non-pregnant women.
- X DO NOT repeat the Pap test until six months post-partum if ASC-US or LSIL is detected during pregnancy. All other findings, especially more advanced lesions, should be managed according to Management of Abnormal Pap Test Results.
- X DO NOT over-screen. There is no need to perform Pap test during pre-natal and post-partum visits unless the woman is otherwise due for screening.

CHECKLIST FOR PROVIDING OPTIMAL PAP TESTING

See Appendix A.

KEY MESSAGES TO GUIDE PERSONAL DECISION-MAKING

See Appendix B.

OFFER ADDITIONAL SCREENING INFORMATION

- ✓ Refer women to the following resources** available from the Alberta Cervical Cancer Screening Program (ACCSP):
  - Cervical Screening: Do I Really Need a Pap Test?
  - Cervical Screening: Making Sense of Abnormal Pap Test Results
  - Cervical Screening: Human Papillomavirus (HPV) - What You Need to Know and Do

***Resources can be ordered at no charge: http://www.screeningforlife.ca/healthcareproviders/order-resources or toll free 1.866.727.3926.*

IMPLEMENTATION APPROACHES

- Initiate opportunistic discussion when women present for other health concerns. Outreach and preventive health screening checklists also increase the likelihood of engaging women to make informed decisions about cervical cancer screening.
- Use electronic medical records (EMRs) to track and flag patients due/overdue for screening in order to offer screening opportunistically.
- Utilize the support and services offered by the ACCSP to improve appropriate screening and increase screening rates for those un/under-screened.

INCREASED RISK SURVEILLANCE[ǂ]

For women who have ever had:	Surveillance Recommendations
• Biopsy confirmed high-grade squamous intra epithelial lesions (HSIL) • Adenocarcinoma in situ (AIS) • Invasive cervical cancer	✓ Suggest annual screening with Pap for life.[**]
• Total hysterectomy with previous HSIL, AIS or invasive cervical cancer	✓ Suggest annual vault smears for life.[**]
For women who have been sexually active with immunosuppression from:	
• Human immunodeficiency virus (HIV/AIDS) • Lymphoproliferative disorders • Organ transplantation • Use of long-term oral corticosteroids. • Common/long term use of immunosuppressant, tumor necrosis factor inhibitors	? Evidence is limited/non-existent regarding need for increased frequency (i.e., annual) screening in this cohort of women. ✓ Some women may benefit from annual surveillance. ✓ Assess on case-by-case basis. ✓ Use clinical judgement.
[*]Provide the history to the lab with the specimen. [**]Based on expert opinion/consensus. Consider patient choice.	

Table 2: Increased Risk Surveillance

MANAGEMENT OF ABNORMAL PAP TEST RESULT

As per laboratory and colposcopy guidelines. See table below.

MANAGEMENT OF ABNORMAL PAP TEST RESULT

Return to routine screening: Patient returns to three-year interval Pap testing and is defined as from the date of the last NILM [negative for intraepithelial lesion or malignancy] specimen regardless of age and/or any previous testing interval.

Unsatisfactory: Repeat Pap but not before three months.

Transformational zone absent (SNTZ) is a lab code (now modified): Absence of endocervical glandular cells/ transformation zone component. *Specimen still considered satisfactory for evaluation and does not require repeat*.

Atypical squamous cells of undetermined significance(ASC-US)

Patients ≤24 years: If screened, with ASC-US result, repeat Pap test every 12 months for two years (two tests):

- At 12 months: ONLY high-grade lesions refer for colposcopy.
- At 24 months: Negative → return to routine screening.
  ASC-US or greater → refer for colposcopy no later than three years after initial ASC-US result date; otherwise Pap test must be repeated.

Patients 25-29 years: Repeat Pap test every six months for one year (two tests). These tests must be at least six months apart.

- If both repeat results are negative → follow up is routine screening (every three years).
- If either repeat result is ASC-US or greater → refer for colposcopy no later than three years after initial ASC-US result date; otherwise Pap test must be repeated.

Patients > 30 years: (*The lab will automatically perform HPV reflex testing*)

- HPV Negative* → risk level equivalent to NILM. Follow-up is routine screening
- HPV Positive → refer for colposcopy no later than three years after initial ASCUS result date; otherwise Pap test must be repeated.
- HPV Indeterminate → manage as per lab instructions.

Low-grade squamous intraepithelial lesion (LSIL)

Patients ≤24 years: If screened with LSIL result: Repeat Pap test every 12 months for two years (two tests):

- At 12 months: ONLY high-grade lesions refer for colposcopy
- At 24 months: Negative → follow up is routine screening
  ASC-US or greater→refer for colposcopy no later than three years after initial LSIL result date; otherwise Pap test must be repeated.

Patients 25-49 years: Repeat Pap test every six months for one year (two tests). These tests must be at least six months apart.

- If both repeat results are negative → follow up is routine screening.
- If any either repeat is ASC-US or greater → refer for colposcopy no later than three years after initial LSIL result date; otherwise Pap test must be repeated.

Patients >50 years: *(The lab will automatically perform HPV reflex testing)*

- HPV Negative* → risk level is equivalent to NILM. Follow-up is routine screening.
- HPV Positive → refer for colposcopy no later than three years after initial LSIL result date; otherwise Pap test must be repeated.
- HPV Indeterminate → manage as per lab instructions.

**The risk of CIN3+ over three years is virtually the same for HPV negative patients as for patients with negative cytology in the absence of HPV testing.*

High-grade squamous intraepithelial lesion (HSIL)	ASC-H	Atypical glandular cells (AGC), adenocarcinoma in situ	Squamous carcinoma, adenocarcinoma, other malignancy
Refer all ages for colposcopy.			Refer all ages to specialist

Patients with cytologically benign endometrial cells

Endometrial sampling is required if there is abnormal bleeding, the woman is asymptomatic and post-menopausal. Also consider endometrial sampling if the woman is asymptomatic, pre-menopausal and at increased risk for endometrial cancer due to chronic unopposed estrogen stimulation.

BACKGROUND

INTRODUCTION

These revised cervical cancer screening recommendations are based on a review of the evidence regarding cervical cancer screening and epidemiologic data since the last published TOP clinical practice guideline (CPG) in 2011.[1] The recommendations reflect the Canadian Task Force on Preventive Health Care (CTFPHC) guidelines published in 2013[2] as well as cervical cancer screening approaches in other jurisdictions across Canada and elsewhere. This background section provides a summary of evidence for cervical cancer screening recommendations, and also provides an update on the status of HPV reflex testing and HPV vaccinations in Alberta as they affect cervical cancer screening.

NATURAL HISTORY

Squamous cell carcinoma accounts for 80-90% of cervical malignancies and the remainder are mostly adenocarcinomas. Persistent infection with one of the carcinogenic types of human Papillomavirus (HPV) is a necessary but not sufficient cause of both squamous and glandular malignancy.[3] Both types arise from a four-step progression as depicted in Figure 1[4]:

1. HPV infection of metaplastic epithelium at the cervical transformation zone
2. HPV persistence
3. Development of pre-cancer in persistently infected cells
4. Invasive cervical cancer

HPV infection is very common in young women in their first decade of sexual activity. The lifetime cumulative prevalence of high-risk infection approaches 80%.[5] More than 90% of these infections are cleared spontaneously through cell-mediated immunity within two years of infection.[6]

Persistent infection and development to pre-cancer occur in less than 10% of these infections within 5-10 years.[7] Regression from persistent HPV infection and from pre-cancer is also common.[6]

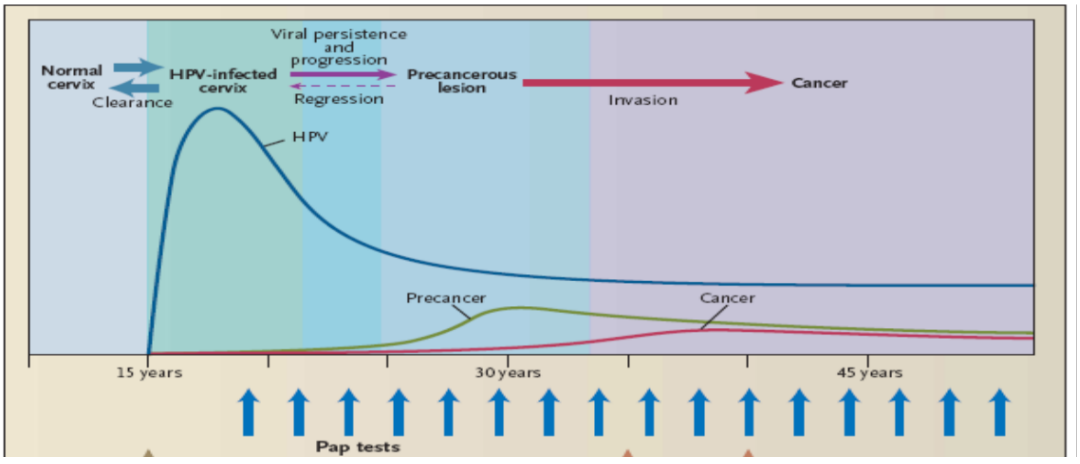

Figure 1: Image modified from: Schiffman et al.2007.[4] Reproduced with permission.

Invasive cancer arises over many years, even decades, in a minority of women with pre-cancer. Early detection and treatment during this lengthy precancerous stage can prevent the vast majority of invasive cervical cancers.

Premalignant squamous lesions are classified as either low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL). The majority of LSIL clear spontaneously and only infrequently progress to invasive carcinoma, however approximately 13% of untreated HSIL will progress over time to invasive carcinoma.[8]

A very few cancers develop rapidly, progress to invasion, or metastasize before detection. However, the screening process is not effective for improving clinical outcomes when these rare cases occur.

EPIDEMIOLOGY

Prior to screening, the incidence of cervical cancer in Canada was more than 1 in 70 women, and mortality about 1 in 100 women.[9] Cervical cancer incidence and mortality have decreased substantially in the past 50 years.[9] It is now the 13th most commonly diagnosed cancer among Canadian women.[10] In comparison, cervical cancer is the second most commonly diagnosed cancer among women in less developed countries, where screening is not established.[11] Thus many immigrant women from those locations are at higher risk.

In 2015, it is estimated that 1,500 women will be diagnosed with cervical cancer and 380 women will die from it in Canada. The probability of developing or dying from cervical cancer, based on 2010 estimates, is about 1 in 152 Canadian women expected to develop cervical cancer during her lifetime, and 1 in 475 who will die from it.[10] Most advanced cervical cancer (with consequent mortality) occurs among women who have not undergone screening or who have had a long interval between Pap tests.[12] Consequently the greatest value comes from helping these women to participate.

Invasive cervical cancer is rare among women younger than 21 because progression from HPV infection to pre-cancer typically takes 5 to 10 years, and the development of invasive cancer mostly takes several additional years. Since widespread cervical screening throughout Canada, incidence has dropped slightly in young women, rates have dropped to 1/3 for most women over 40 years of age (see Figure 2). However, the highest incidence of cervical cancer still occurs in middle age. A study of incidence in Alberta showed similar reductions at older ages, but none for women under 35 years.[13] Although over time mortality has also dropped among older women, there is still a steady increase in mortality with age.[9]

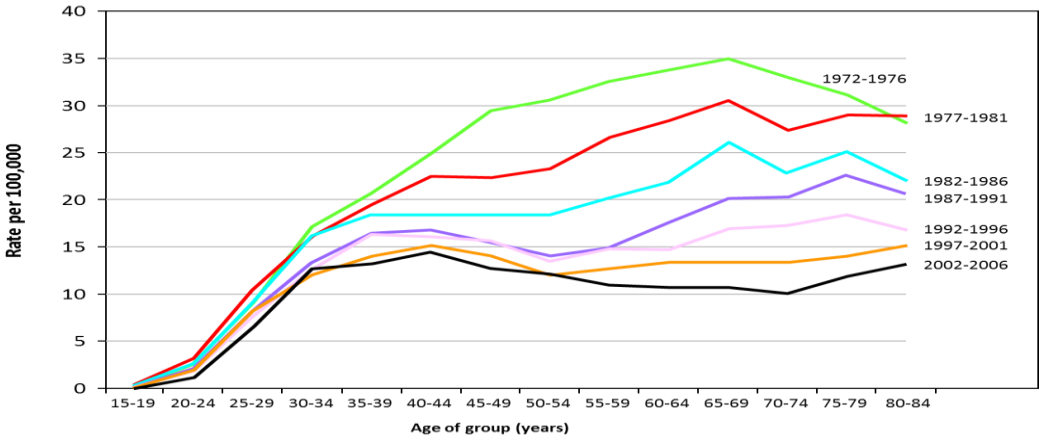

Figure 2: Age-specific Incidence of Invasive Cervical Cancer in Canada, 1972-2006[9]

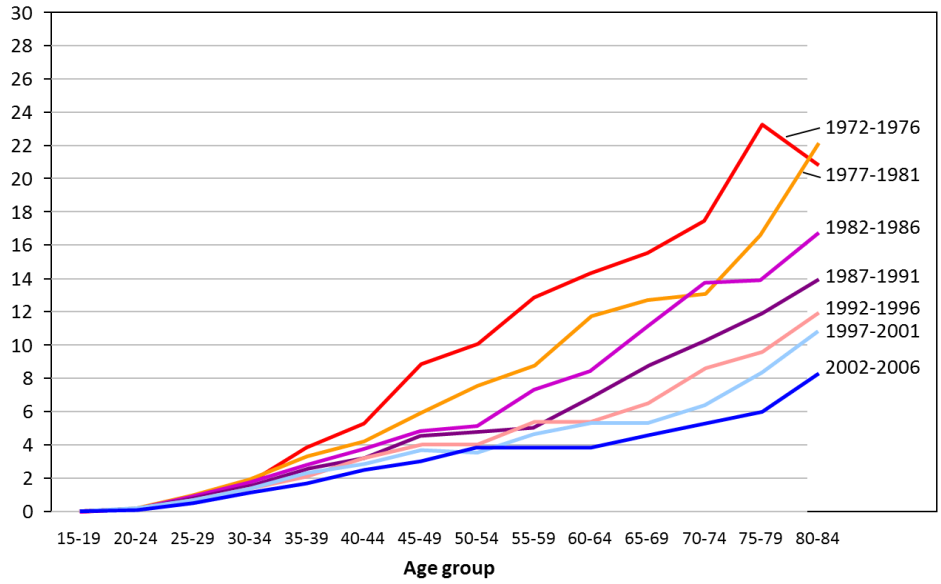

Figure 3: Mortality from Invasive Cervical Cancer in Canada from 1972 to 2006[9]

In 2012 there were 135 new cases of cervical cancer in Alberta, 35 deaths attributable to the disease and1090 potential years of life were lost due to cervical cancer. The five-year relative survival ratio for cervical cancer in Alberta is approximately 81% based on 2008 and 2010 data. In 2015, approximately 180 cases of cervical cancer are expected to be diagnosed.[14,15]

Balancing Risks and Benefits

The benefits of screening to reduce the incidence of invasive disease and death due to cervical cancer have been consistently shown in cohort and case-control studies. Most advanced cervical cancer (with consequent mortality) occurs among women who have not undergone screening or who have had a long interval between Pap tests.[12] Conversely initiating screening when the risk is very low and/or screening too frequently can produce more harm than benefit.[16]

Younger women have more abnormal results but these results are much less likely to represent a serious abnormality, putting these young women at risk of over-diagnosis and over-treatment. Furthermore, harms have not been measured as well as benefits until recently. Such harms include:

1. Inconvenience, discomfort and embarrassment that women feel from attending for Pap tests, and having uncomfortable bimanual examinations
2. Physical and psychological impact of being informed about an abnormal test, and according to the abnormality, being asked to undergo repeat testing, referral for colposcopy, biopsy and return for results, or having treatment with LEEP or other procedure
3. The risk for pregnancy loss for those women who had a LEEP or cone biopsy rises from 0.6% to 1.8% (increase of 1.2 %) primarily in the second trimester.[17,18]

Younger women have more abnormal results but these results are much less likely to represent a serious abnormality, putting these young women at risk of over diagnosis and overtreatment[12] (see Table 3). When these women are referred, the colposcopist may biopsy the cervix. If the biopsy shows cervical intra-epithelial neoplasia, the colposcopist may treat the cervix by removing the transformation zone using various methods. These procedures cause short-term pain, bleeding and discharge[19] but could lead to early loss of future pregnancies or premature labour.[17,18] This risk is more serious in younger women who are less likely to have started or completed their families, and many can be considered "overtreatment" since few of these lesions would progress to cancer.[20-22] Although at the time of the procedure, it is not possible to know which ones will progress and those that are indolent. Colposcopists have become more cautious in recent years about the extent of excisions, so there are fewer large excisions.

Alberta Cervical Cancer Screening Program Colposcopy Referrals by Age Group			
Age group (years)	**Number screened**	**Number referred for colposcopy**	**% referred colposcopy**
18 - 20	24985	497	2.0%
21 - 29	194499	10655	5.5%
30 - 39	210833	7671	3.6%
40 - 49	173359	3624	2.1%
50 - 59	154986	2412	1.6%
60 - 69	80344	806	1.0%
≥ 70	13705	166	1.2%
Total	852711	25831	3.0%

Table 3: Colposcopy Referrals by Age Group in the Alberta Cervical Cancer Screening Program (ACCSP) 2008-2013

INFORMED DECISION-MAKING

With the evidence presented and subsequent recommendations in this guideline, each woman's values, preferences and beliefs about cervical screening must be taken into consideration when

presenting the information about possible benefits and harms from the screening process. Screening should always be a choice and an informed decision made by the woman.

SCREENING INITIATION

WOMEN YOUNGER THAN 21 YEARS

The 2011 TOP Cervical Cancer Screening clinical practice guideline (CPG) recommended the initiation of screening rise from the start of sexual activity to age 21. This was based on the evidence that cancer is extremely rare under that age. Yet many women under the age of 21 in Alberta continue to be screened – including in 2014 about 40% of women aged 18-20. (ACCSP program data, 2014) This is inappropriate since benefit is almost non-existent.

If Pap tests are performed in this age group and LSIL identified, there is a very high probability these changes will resolve spontaneously.[23] For this reason, recommended follow-up of women younger than 21 years with ASC-US or LSIL is more conservative than for older women. See Management of Abnormal Pap Test Results. HPV DNA testing results can also be misleading for women with ASC-US or LSIL under age 30. Because HPV is so frequent in this age group, HPV testing would result in high rates of colposcopy referrals with a very low probability of cervical carcinoma or progressive disease yet a tendency for overtreatment. Therefore, HPV testing in this age group is strongly discouraged.

WOMEN AGED 21-24 AND 25-29

For women over 21, analysis of national mortality and incidence data show that mortality has dropped substantially in older age groups, but it was always low below the age of 30.[24] Current incidence and mortality in these screened women are similar to data in 1972 to 1976 prior to widespread screening [24] In Alberta from 1994-2013, the annual incidence rate for cervical cancer (Surveillance & Reporting: Information Request Edmonton: Cancer Control Alberta, Alberta Health Services, 2014) was extremely low at age 20 or younger, and remained low to age 25 (see Figure 4). There is a clear increase in incidence after 25 years of age.

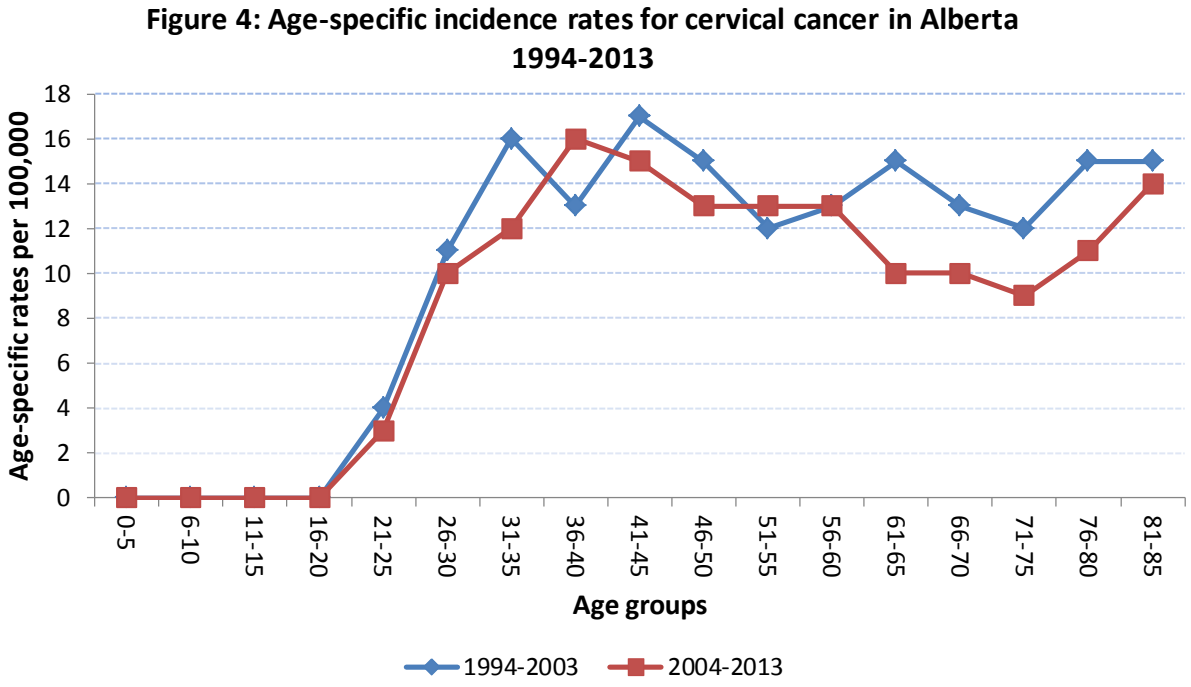

Figure 4: Age-specific incidence Rates for Cervical Cancer in Alberta 1994-2013

There is also uncertainty about the effectiveness of screening for these rare cervical cancers in women under 30 years old. The National Health Services (NHS) cervical cancer screening program in the United Kingdom (UK) investigated this concern and found that the effectiveness of screening improved with age, with odds ratios around 1 (no effect) in women under 25, around 0.5 by age 30, and 0.2 around age 50.[25] Further, they also showed that there was no protective effect against developing cervical cancer in the future from screening below the age of 25.[25] This was supported by data from elsewhere.[26] The UK modified its cervical screening policy to initiate screening at age 25 in 2003, while programs in the Netherlands and Finland start at age 30. The World Health Organization recommends "women under 30 should not be screened for cervical cancer."[27]

Thus current evidence regarding screening initiation for women 21 to 29 years of age shows very low risk but not absence, therefore the small potential benefits of screening must be balanced against the substantial harms. The CTFPHC concluded that the balance of benefit against harm changes in the middle of the decade so screening may be initiated sometime in the years 25-29.[2] Clinicians can offer women a choice to be screened and/or may suggest screening to women who may be at a higher risk and more likely to benefit e.g., early sexual debut, multiple partners (or whose partners have had multiple partners), or not HPV vaccinated. Smoking is also a risk factor,[28] approximately doubling risk.

Screening Interval

The evidence for screening intervals comes from case control studies in several countries showing that there was a small increase in sensitivity between five and three-year intervals but the gain from more frequent intervals was minimal.[29] When compared to the harms and costs to women of more

frequent testing, many groups have recommended three years as a reasonable balance between benefits and harms.

Remembering a three-year interval for cervical cancer screening may be difficult for women and their providers, therefore the ACCSP provides province-wide reminder notifications to women after three years that they are now due for cervical cancer screening.

When to Discontinue Screening

Different countries have different approaches as to when screening should be discontinued; ranging from 60 to 65, or up to 70 years of age. Many guidelines are based on the assumption that the death rate drops in older women. However, in Canada, current mortality rates rise steadily with age (see Figure 3).

Cervical cancer occurs among older women who have never been screened or have not been regularly screened. In addition, it can occur in women who have had abnormalities treated earlier in life that recur in old age.

Based on life expectancy, and provided women 69 years of age and older have had three normal results from screening over the previous 10 years with no other related health problems, screening for cervical cancer can be discontinued. However, the decision to discontinue screening should be a personal one. Women who have a long life expectancy, no other health issues and are aware of the challenges associated with Pap testing in older ages (e.g., estrogen depletion/need for replacement, discomfort/pain, difficulty obtaining sample, false positive tests) may wish to continue with screening.

Screening Test

Pap Test – Liquid-Based Cytology

Traditionally, the conventional Pap test sample was collected using a wooden spatula and brush, smeared on to a glass slide and fixed. Alberta now offers liquid-based cytology (LBC). The specimen is collected from the patient using a plastic spatula and brush then placed into a jar containing a liquid preservative medium. This technology offers several advantages over conventional Pap testing:

1. Immediate preservation of collected cells
2. Entire sample is recovered rather than lost with the discarded spatula/brush.
3. Preservative contains chemicals that lyse blood, mucus and inflammatory cells allowing for a clean specimen and easier identification of abnormal cells.
4. Multiple slides can be prepared.
5. Additional tests such as HPV reflex testing can be performed on the same sample.

Optimal Specimen Collection

Most cervical pre-cancer and cancer develop in the squamo-columnar junction, also called the transformation zone.[30] Because cells in this area of the cervix are always dividing, they are at risk for

incorporation of HR HPV infection with subsequent transformation to abnormal cells. The transformation zone is characterized by columnar cells proximally, squamous metaplastic cells centrally and mature squamous cells distally. The ideal sample has both representation from ectocervical and columnar/metaplastic cells in adequate numbers.

The transformation zone can be identified by a change in colour and texture at visual examination. The squamous epithelium appears pale pink, shiny, and smooth. The columnar epithelium appears reddish with a granular surface. The transformation zone typically recedes into the endocervical canal during menopause, reducing the chance of obtaining a squamocolumnar component in a Pap test specimen.

Obtaining an optimal specimen requires the clinician to clearly visualize the cervix where the collection device is sampling. The spatula must be swept around the full circumference of the cervix, even when the os is irregular in shape. The brush should be inserted most of its depth into the endocervical canal, though this is not always possible in older women. Strict adherence to the sampling technique as recommended by the manufacturer, including minimal use of lubricant, can substantially improve the quality of the specimen.[30] In general, for reproductive age patients, sampling during the mid-cycle is optimal for collection.

During pregnancy the cervix is more vascular and prone to easy bleeding (spotting). This may alarm women. Further, there is a potential concern about inserting a sampling device in the cervical os. The transformation zone is usually everted, so if sampling is required during pregnancy, one can usually sample without having to enter the os at all. Visualizing the transformation zone and swiping the spatula around it should provide an adequate sample. With longer intervals between Pap tests, it is better to time the test so it can be done post-partum to avoid changes related to delivery.

Pap tests in women without a cervix, but with a previous history of high-grade lesions or malignancy, require scraping of the vaginal vault. Cells from the apex of the vault should be collected using the rounded end of a spatula and transferred according to the liquid based cytology manufacturer's recommendations.

HPV Reflex Testing

High-risk HPV (hr-HPV) types are potentially carcinogenic and may lead to progression of cervical abnormality. There are many hr- HPV types and types 16 and 18 are the most common.[31] The HPV Reflex Test can detect 14 carcinogenic HPV types.[31]

Reflex testing for hr-HPV is automatically performed in Alberta labs when a Pap test result is ASC-US at age 30 and over, and for LSIL results at age 50 and over. This is a triage mechanism to determine if follow-up colposcopy is required for these results in these cohorts.[32]

Treatment of high-grade abnormalities can eliminate a high-risk virus and therefore risk of carcinoma. For women who test negative for a high-risk virus, there is a very low risk for developing cervical cancer and more frequent screening is not required. However, such women who have tested negative for hr-HPV can subsequently acquire the high-risk virus types from a new exposure and therefore do require ongoing routine screening.

For women who are 50 years of age and older, as estrogen levels begin to drop, atrophic cells may be detected on a Pap test. These atrophic cells may mimic intraepithelial abnormalities and may be reported as cytologic abnormalities.[32] Therefore, the lab will conduct routine HPV reflex testing for

women 50 years and older with ASC-US or LSIL Pap test results. If the HPV result is negative, the woman can return to routine screening; if positive, referral to colposcopy is recommended.

Limitations of Screening

Like all screening tests, Pap tests are not 100% accurate. A false negative result occurs when the Pap test fails to detect an abnormality that is present on the cervix at the time of collection. False negative results can occur from cervical sampling limitations. Therefore, providers performing Pap testing must use thoughtful technique to sample the full cervix circumference and the endocervical canal. False negative results can also occur from laboratory factors so laboratories have quality assurance programs to minimize these errors.

False positive screening test results are also of concern. Given the transient nature of many cervical abnormalities, screening detects many abnormalities that are destined to resolve on their own. The current guidelines are intended to minimize the anxiety and potential harms associated with screening while helping to reassure patients that clinically significant cervical changes are identified.

Despite its limitations, the Pap test is the best screening test to date.[33] This test is most effective at reducing squamous cell cancer, and less for adenocarcinoma.[33] To help overcome the false sense of security that can arise from a false negative test result, it is important to advise women to report any symptomatic changes such as unusual vaginal bleeding or discharge including bleeding after intercourse, after menopause, or between menstrual periods.

Other Considerations Regarding Cervical Cancer Screening

Women Who are Pregnant

The first prenatal visit and the six-week postpartum check-up are often used by physicians as “incidental” opportunities for cervical screening. This is appropriate for women who otherwise do not attend for screening, but if done as routine, can produce over-screening. In addition, cervical changes associated with pregnancy and delivery produce Pap tests that are more difficult to interpret. There is no need to perform Pap tests during these visits unless the woman is due for a Pap test or is unlikely to return for screening at an appropriate time, e.g. non-participant in screening.

After Hysterectomy

Women who have had a total hysterectomy for non-malignant pathology with no dysplasia in their cervix require no further Pap testing. Women who have undergone subtotal hysterectomy and retained their cervix should continue with routine screening according to the TOP CPG.

Women with a history of proven biopsy-confirmed high-grade squamous intraepithelial lesion (HSIL), adenocarcinoma in situ (AIS), or invasive cervical cancer should have vault smears annually thereafter as they are at higher risk for vaginal neoplasia.[34]

CONTRACEPTION, STIS AND PELVIC EXAMS

In their policy statement on contraception in adolescents, the American Academy of Pediatrics no longer includes cervical cancer screening as a recommendation when prescribing contraceptives to young women.[35]

There is no evidence supporting use of a Pap test when testing for STIs or to initiate a discussion with a woman regarding STIs. A urine test or vaginal swab (as per your laboratory requisition) for STIs is sufficient.

Pelvic examinations may cause pain, discomfort, fear, anxiety, or embarrassment in about 30% of women, yet no data were found to support the use of pelvic examination in asymptomatic, average-risk women who present for Pap test and/or a well-woman visit.[36,37] Therefore, this additional examination should not be undertaken routinely.

HIGHER RISK SURVEILLANCE

There is a paucity of evidence to support increasing frequency of cervical cancer screening for immunosuppressed women and women taking immunosuppressant medication. It does not appear that, in general, cervical cancer rates are higher or that cervical cancer progresses more rapidly in these women.[38] Some studies, however, suggest that certain immunosuppressant medications such as azathioprine are associated with an increased risk of cervical cancer[38] and some highly immunosuppressed women are at increased risk of HPV infection and cervical dysplasia when compared to the general population.[39] This may indicate a need for increased cervical screening in this cohort of patients.

In the absence of conclusive evidence no recommendation can be made with respect to shorter screening intervals i.e., annual screening, for this cohort of women. It is suggested that they be screened every three years until more conclusive evidence is forthcoming. However, depending on the degree of immunosuppression i.e., severe immune deficiency, for whatever reason (e.g., AIDS, certain immunosuppressant medication), clinicians may choose to offer more frequent screening e.g., every one or two years, recognizing that the consequence will be more frequent HPV detection that may produce over-diagnosis and over-treatment. As new evidence emerges on this topic, this guideline will be updated accordingly.

HPV IMMUNIZATION

HPV vaccination continues to be available in Alberta for all girls and boys in grade five. A catch up program is offered to boys in grade nine from September 2014. HPV vaccination programs are offered in all provinces and territories across Canada with some variation in eligibility.

The role of cytology and HPV testing continues to evolve as the cohort of HPV-vaccinated females approaches the age-group recommended for screening. The first vaccinated cohort (grade nine girls vaccinated in 2009/10) reached 21 in 2015. It is important for health care providers to be aware that:

- HPV vaccinated women are also at risk, albeit lower, of developing cervical cancer if they do not receive regular screening. As the current vaccines do not cover all carcinogenic HPV types, women need to avoid a "false sense of security."

- Effectiveness of HPV vaccine for preventing cervical cancer over the long term is unknown.
- Not everyone in the cohort offered vaccination has been vaccinated – there is substantial variation throughout the province.

For more information on HPV immunization refer to:

http://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-hpv-bio-pg-07-240.pdf

http://www.albertahealthservices.ca/services.asp?pid=service&rid=1026220

Future Directions

Cytology continues as the primary screening test for cervical cancer in Alberta. There is interest to use HPV for the primary screening test but more evidence supporting its use is required and further studies are currently underway. HPV testing for screening is more expensive than the current Pap test but screening intervals could potentially be extended as long as there is adequate patient reminder and recall systems are in place.

HPV reflex testing will continue to be used as a triage in Alberta for women over 30 with abnormalities on the pap screen.

The emerging evidence will continue to be monitored and this guideline updated accordingly.

References

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For more information see www.topalbertadoctors.org

GUIDELINE COMMITTEE

The committee consisted of representatives of family medicine, anatomical pathology, community medicine, obstetrics & gynecology and pathology.

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APPENDIX A

CHECKLIST FOR PROVIDING PAP TESTING

GENERAL CONSIDERATIONS

- ✓ Discuss HPV vaccination and sexually transmitted infection (STI) prevention and testing with the woman if relevant.
    - To test for STIs does not require a pelvic exam or Pap test. A urine nucleic acid amplification test (NAAT) or vaginal swab is used for STI testing.
- ✓ Screen women who have received the HPV vaccine.
- ✓ Screen women who have undergone subtotal hysterectomy and have retained their cervix.
- ✓ Resume routine screening with a Pap test once the woman is discharged from colposcopy.
- Atrophic cells and cervical stenosis are common in older postmenopausal women and can result in difficulty obtaining satisfactory samples and test interpretation. Estrogen supplementation may be necessary prior to Pap testing.
- X DO NOT perform a Pap test on women currently being assessed by a colposcopy clinic, including those who did not attend their colposcopy appointments. Encourage these women to go to colposcopy.
- X It is not necessary to perform Pap test or pelvic exam prior to prescribing contraception.
- X DO NOT routinely perform pelvic exams on asymptomatic women with or without Pap testing.

APPENDIX B

KEY MESSAGES TO GUIDE PERSONAL DECISION-MAKING

- ✓ Inform asymptomatic women about the consequences of their decisions to be screened or not to be screened at different ages:
  - Age below 21
    - Cervical cancer incidence and mortality is extremely low.
    - Abnormality rates are high and most HPV infections are cleared by the immune system, so no treatment is required.
    - Discovery of abnormality may lead to harms through unnecessary treatments.
  - Age 21-24
    - There is low incidence of cervical cancer and mortality from cervical cancer is very low
    - High rates of abnormal results, often transient, can lead to unnecessary treatments and therefore harms.
    - Screening benefit is unclear.
  - Age 25-29
    - Screening is potentially beneficial as incidence and mortality of cervical cancer rises in this age group.
    - There are still more false positive tests in this age group compared to older age groups.
    - The balance of benefit and harms is more in favour of screening.
  - Age 30-69
    - Cervical cancer incidence and mortality is high in unscreened women.
    - Evidence is strong for screening effectiveness.
    - Benefit is likely to be greater than harms.
  - Age ≥70
    - Cervical cancer incidence and mortality continue to rise.
    - Evidence is limited for screening effectiveness for those having had regular screening.
    - It is important to screen for cervical cancer in those who are unscreened or inadequately screened.
    - The decision to stop screening should be a personal one based on the woman's life expectancy, quality, personal values and understanding the challenges of screening beyond this age, e.g., estrogen depletion, pain, difficulty obtaining samples, false positive results.

See FAQ resource for additional considerations regarding different age groups.