

ANMC Cervical Cancer Prevention Guideline

Our system for the prevention of cervical cancer in Alaska Native Women requires four elements working together.

1. Maximize uptake of HPV vaccine.
2. Regular Pap screening of women at risk for the disease.
3. Medical evaluation and management of abnormal Pap results.
4. Tracking of Pap results and treatments with patient notification.

After maximizing vaccine uptake, the system that is in place for tracking Pap tests and treatment has worked well. Facilities and providers involved in women's health will need to continue to work together to maintain the integrity of this database that we all rely on to deliver quality care.

HPV Vaccination Recommendations:

Human papilloma virus (HPV) infections, specifically 15 high risk subtypes, are associated with cervical cancer. About 70% of cervical cancers are associated with HPV genotypes 16 and 18 worldwide. ANMC currently offers the 9-valent HPV vaccine, Gardasil 9. Gardasil 9 protects against oncogenic genotypes 16, 18, 31, 33, 45, 52, and 58, as well as 6 and 11 which are associated with condyloma. A review of ANMC colposcopy specimens showed that 95% of CIN 3 involved the Gardasil 9 genotypes.

The Center for Disease Control (CDC) Advisory Committee on Immunization Practices recommends that routine HPV vaccination start at age 11 or 12 years and as early as 9 years old. Vaccination is also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series. Males who have sex with men aged 22 through 26 years may be vaccinated.

In formal studies, the previous quadrivalent vaccine was close to 100% effective in preventing cervical intraepithelial neoplasia CIN 2, CIN 3. The vaccine is most effective when given before the onset of sexual activity, but sexually active girls and women may receive some benefit from vaccination. Protection has been shown to last at least 5 years. The vaccine is not recommended for pregnant women but can be given in breastfeeding women. Vaccination does not replace the need for routine cervical cytology screening with Pap testing. Women with previous CIN or genital warts are still candidates for vaccination but may receive fewer benefits from it. Immunosuppression is not a contraindication but may make the vaccine less effective.

The vaccine is administered IM as three separate 0.5-ml doses. The second dose is given 1-2 months after the first, and the third 6 months after the first. If the schedule is interrupted, give the next dose. The series does not need to be restarted. Revaccination with the 9-valent HPV vaccine is not recommended in those people who have already completed the three-dose series with the quadrivalent or bivalent HPV vaccination. If the series of vaccinations has already been started in a patient, the

series may be completed with any HPV vaccination product. Eligible patients should receive whichever vaccination is immediately available to them.

Pap Screening Recommendations:

The Alaska Native Medical Center has adopted the March 2012 American Cancer Society, the American Society for Colposcopy and Cervical Pathology, US Preventative Services Task Force, and the American Society of Clinical Pathologists recommendations. We will continue to track our age-specific cervix cancer rates and periodically review our guidelines to be sure that no deviation from the national recommendations is still warranted.

The definition of cotesting means both cytology (Pap test) and a high risk HPV test on the same liquid pap specimen.

- Cervical cancer screening should begin at age 21. Women between the ages of 21 to 29 should have a Pap test only every 3 years. They should **not** be tested for high risk HPV even for follow up of an abnormal Pap test unless it is part of the recommended follow up algorithm.
- Women between the ages of 30 and 65 should have both a Pap test and a high risk HPV test every 5 years (cotesting).
- There are special screening recommendations for women who have HIV, a history of DES exposure in utero, or who are immunocompromised. Women who are HIV infected or who are otherwise immunosuppressed, or who were exposed to DES, should start screening at age of initiation of intercourse or by age 21. Cervical cancer screening in women who are infected with HIV should continue throughout a woman’s lifetime. (See [Special Circumstances](#))
- Unsatisfactory Pap results should be repeated in 2 to 4 months. Colposcopy is also recommended when two consecutive Pap tests are unsatisfactory.
- Women with normal cytology but no or insufficient endocervical cells/transformation zone:
Age 21-29 of age, routine screening with cytology in 3 years
Age \geq or equal to 30 years of age, in whom cotesting is preferred, the HPV results guides management:
 - If HPV -, routine screening with cotesting in 5 years
 - If HPV +, then either cotesting in 1 year
 - If HPV testing was not done, then HPV testing is recommended
- Women over age 65 who have had regular screenings with normal results should not be screened for cervical cancer, e. g., if there are 3 normal Pap tests over a 10 year period, or 2 consecutive normal cotests. The most recent test should be within 5 years of stopping screening. When considering exit from screening for women aged 65 or older, HPV-negative with ASC-US results

should be considered abnormal. Repeat cotesting should be done in 3 years. A short course of vaginal estrogen to treat vaginal atrophy prior to follow up cotesting, is a practical option to rule out true dysplasia for patients who have no contraindication to estrogen therapy. (See [Special Circumstances](#))

- Women who have had a hysterectomy, with both their uterus and cervix removed, and have no history of biopsy proven CIN 2, CIN 3, or cancer require no further screening.
- Women who have had a hysterectomy with both their uterus and cervix removed and have a history of proven CIN 2 or higher in the past 20 years or cervical cancer at any point will require Pap tests only every 3 years for routine screening after the initial post treatment surveillance period.
- A woman with a history of CIN 2, CIN3, or adenocarcinoma in situ should continue screening for a total of 20 years after the appropriate management and follow up even if this extends beyond age 65.
- If anything was abnormal at the last exam (Pap test or HPV) then the next exam is in one year (except in the case of ASC-US, HPV negative, which requires follow up screening in 3 years.) If the Pap test and HPV are normal at 1 year, the next exam after that will usually fall 3 years after the first follow exam. Management options and follow up may vary if the woman is age 21-24, ie, follow up with cytology alone may be recommended. Please see ASCCP cervical cancer screening algorithms document for specific recommendations for each clinical scenario. [ASCCP Guidelines](#)
- Women who have had the HPV vaccine should still follow the screening recommendations for their age group.

When to order an HPV test with a Pap Smear:

Your lab should offer two options when ordering a Pap. Pap with HPV and Pap with Reflex HPV testing.

- *Screening Pap under age 30.*
Screening should be done every 3 years starting at age 21. They should not be tested for HPV unless it is tested reflexively after an abnormal Pap test result. These abnormal Pap test results include a reflex HPV test for those with an ASC-US, ASC-H or AGC (atypical glandular cells) result.
- *Screening Pap 30 years and over.*
This would be ordered every 5 years. These should include a Pap test and HPV test for all samples.
- *Follow-up Pap.*
These would be done as follow-up after an abnormal Pap, colposcopy, LEEP

procedure or a positive HPV test. Order an HPV test for all these samples except for management of women ages 21-24 where cotesting is recommended only under certain circumstances such as follow up after CIN 2,3. The ASCCP algorithms will specify when cotesting is recommended. [ASCCP Guidelines](#)

Who Should Evaluate the Abnormal Pap Test:

Basic colposcopy privileges

Granted to providers trained in colposcopy, but not expert in treatment of gynecologic disease. These providers could see patients with ASC-US HPV(+) and LSIL. These two results comprise more than 90% of the patients needing colposcopy. While finding high grade dysplasia in any one of these patients is unlikely, most of the significant dysplasia will come from this group because it is so much larger than the remaining groups. The risk of CIN2/3+ for this group is 6-12%. If the provider recommends a treatment outside the guidelines, then consultation with a provider who has full colposcopy privileges is required.

Full colposcopy privileges

This is limited to providers with training in colposcopy and the treatment of dysplasia and malignancy. All colposcopies for Pap results other than ASC-US and LSIL and all colposcopy for pregnant patients should be with a provider in this group. If the provider recommends a treatment outside the guidelines, then it is required that the provider document the reasons for the plan in the patient's record. We recommend that documentation always be included in the **colposcopy** note from the patient visit. When a patient is scheduled with a gynecologist for a colposcopy, this is a consultation. This indicates that the problem to be addressed requires decisions that cannot be delegated to the Screening and Prevention staff or a provider with basic colposcopy privileges. The provider may or may not do a colposcopy, but the dysplasia history will be reviewed and a plan of care will be prepared.

Colposcopy Responsibilities

- Record a **colposcopic impression**
 - normal/no evidence of dysplasia
 - CIN I
 - CIN II
 - CIN III
 - lesion suspicions for invasive disease
- Record **adequacy of exam**
 - colposcopy satisfactory
 - colposcopy unsatisfactory

A satisfactory colposcopy is defined as visualization of the entire transformation zone, including the squamo-columnar junction, and the limits of any lesion if present. In the setting of an unsatisfactory colposcopy, endocervical sampling is required to complete the evaluation.

- Describe all lesions
 - A diagram can be used.

- List all biopsies taken
- Notify patient and Screening and Prevention of results and plans for treatment or follow up. Documentation of this should be included in the **colposcopy** note from that visit.

Follow-up after colposcopy:

When evaluating Low grade cytology results (LSIL and ASC-US) (this should cover all visits for providers with basic privileges):

- Refer for treatment and gynecologic consultation when CIN 2,3 or High grade dysplasia is found.
- When no lesion or CIN 1 is found on biopsy:
Women older than 24: Cotesting in 1 year followed by age-appropriate retesting in 3 years for normal follow up results.
Women aged 21-24: cytology only at 1 year followed by repeat cytology only at 12 months.

When evaluating high grade cytology results (HSIL/ASC-H):

- For CIN 2,3 or High grade lesion on colposcopy, inadequate colposcopy, recurrent CIN 2,3, or High grade lesion or ECC with CIN 2,3 in women older than age 24 : Excision recommended followed by cotesting at 12 and 24 months. Follow up after that will be repeat cotesting in 3 years. If all follow up is negative, routine screening may resume but should be continued for at least 20 years, even past age 65.
- For CIN 2,3, or high grade lesion on colposcopy in women older than 24 with CIN 2,3 or High grade lesion at the margins or on ECC of an excisional procedure: ECC, cytology, HPV testing, and colposcopy at 6 months with gynecologist. We do not recommend review of Pap test and histology option that ASCCP guidelines offer, because it may delay care.
- For CIN 1 on colposcopy results: Either observation with colposcopy, cytology and HPV testing at 6 month intervals X 1 year or Diagnostic excisional procedure
Observation is only recommended for those women who plan on future pregnancy.
- For CIN 2,3, or High grade lesion in young women \leq age 24: Either treatment or excision if acceptable. If observation only, then colposcopy and cytology recommended at 6 month intervals for 12 months followed by cotesting in 1 year.
- If no CIN 2,3, or High grade lesion in young women \leq age 24: observation with colposcopy and cytology at 6 month intervals for up to 2 years.

The ASCCP algorithms provide additional detailed information for recommended follow up. [ASCCP Guidelines](#)

ASCCP:

ANMC has adopted the ASCCP guidelines in algorithm form as our framework. We strive to limit the number of visits and thereby limit the cost and inconvenience to our patients. By linking our guidelines to the ASCCP, we hope to remain current and to present our process in a familiar format.

Here is where we differ from ASCCP:

- For ASC-US we recommend only the reflex HPV testing pathway even in women ages 21-24.
- We do not recommend HPV DNA typing to HPV 16 or 18 at this time.
- We recommend colposcopy in pregnancy for women over age 24 who have an LSIL Pap test.
- If observation is chosen instead of diagnostic excision for women with no lesion or biopsy-confirmed CIN 1 preceded by ASC-H or HSIL cytology, we recommend observation and visit with gynecologist for colposcopy, cytology, and with or without HPV testing, depending upon age, at 6 month intervals X 1 year. This option can be considered in women who may be planning future pregnancy.
- We do not recommend the review of Pap test, histological, and colposcopic findings option. In our experience it has delayed patient care.
- We recommend merging the two pathways for AGC (atypical glandular cells), and we recommend reflex HPV testing, colposcopy, and consideration of endometrial biopsy at one visit for AGC to reduce the number of steps needed to evaluate the patient.
- We recommend against Cryotherapy.
- We recommend the follow-up of patients treated for High grade dysplasia who have margins positive or ECC with CIN 2,3, or High grade dysplasia to follow up ECC, cytology, HPV testing, and colposcopy with gynecologist at 6 months.

The ASCCP Screening and Management Guideline can be found at:
[ASCCP Guidelines](#)

Special Circumstances: Ambiguous Results

It is not uncommon to have results where there is no specific guideline or evidence based resource to direct care. In these circumstances, it is best to consult a provider with full colposcopy privileges for a plan of care, since that plan may well involve an excisional procedure for diagnosis or a continuity-based follow up plan or a complex discussion of options with the patient. Common examples include:

- An ECC shows dysplasia but the grade is not specified.
- A LEEP procedure has positive margins.

Special circumstances: Young women

- At ANMC, the term young women will mean those less than 25 years old. According to ASCCP the term “young women” also can indicate those who need to be counseled concerning the risk of excisional procedures to pregnancy outcomes, and therefore, no specific age threshold has to be placed on women considering future child bearing. Any deviation from recommended guidelines, should be documented under the provider’s **colposcopy** note and a detailed follow up plan should be included.
- Young women are at virtually no risk for developing cervical cancer and have a very high incidence of transient HPV infection that presents as an abnormal Pap.
- Aggressive management with colposcopy and possible excision or ablative therapy is unlikely to have any benefit and can cause significant harm. Dysplasia when found in a young woman is both less likely to progress and more likely to regress than similar lesions found in an adult.
- Any Pap visit with a young woman should include a review of vaccination history and an offer to start or complete the HPV vaccine series.
- In young women, LSIL and ASC-US results do not result in colposcopy unless the Pap test is abnormal 3 times in a row. We have an obligation to inform the patient and potentially her family about the results, and our recommended follow up and to answer their questions. A plan to “do nothing” after an abnormal test will be unfamiliar to a patient and may not be adequately explained by a letter, so we recommend that these patients be contacted by phone and that the contact be recorded in a chart note. This is another opportunity to consider vaccination.

Special Circumstances: Menopause/ Atrophy

- ASC-US or LSIL in a postmenopausal woman is often due to the effect of estrogen loss on the epithelium (atrophy), rather than HPV infection.
- If the HPV testing is negative, it is recommended that the LSIL Pap result be attributed to the cytologic effect of atrophy and no further diagnostic testing for dysplasia is needed (don’t schedule a colposcopy). The Pap and HPV should be repeated in 1 year.
- A diagnosis of atrophic vaginitis should be made by history and exam, including a visual exam of the vagina and a wet mount looking for squamous maturation (parabasal cells). Treatment should be offered, based on symptom relief goals.
- A short course of vaginal estrogen to treat vaginal atrophy prior to follow up cotesting is a practical option to rule out true dysplasia for patients who have no contraindication to estrogen therapy. Rx: Conjugated estrogen cream (Premarin) 1gm vaginally qHS X 3wks then repeat cytology (Pap) in 1wk. If the follow up Pap test and/or HPV test are abnormal, then colposcopy is recommended.

Special circumstances: HIV, women who are immunocompromised, DES

- While cervical cancer is a diagnostic criterion for AIDS and cervical cancer is

more common in HIV-positive women it is rarely a cause of death for these patients.

- Women who are younger than 30 infected with HIV should have Pap testing (cytology only) at the time of initial diagnosis with HIV. Cotesting is not recommended for HIV-infected women younger than 30. If the initial cytology screening result is normal, the next screening should be in 12 months. If three consecutive annual screenings are normal, follow-up cervical cytology should be every 3 years.
- Women who are 30 years and older should be screened with cotesting. Women infected with HIV who have one negative cotest result (normal cytology and negative HPV) can have their next cervical screening in 3 years.
- Women with HIV infection are managed as per the ASCCP guidelines.
- No studies or major society recommendations exist to guide cervical cancer screening in women who are not HIV-infected but have other reasons to be immunocompromised. It is reasonable to use the HIV recommendations for women in this group and to start screening at age 21.
- Women who have been exposed to diethylstilbestrol should have annual cytology annually.

Special circumstances: Pregnancy

- The indications for colposcopy are not changed by pregnancy.
- We recommend that only providers with full colposcopy privileges evaluate pregnant patients.
- Cervical biopsies are safe in pregnancy and should be done for lesions suspicious for high-grade disease or invasion. Endocervical sampling or curettage should not be done.
- Since unsatisfactory colposcopy may become satisfactory as the pregnancy progresses, it is recommended that women with an unsatisfactory colposcopy undergo a repeat exam in 6-12 weeks.
- The increased vascularity of the cervix in pregnancy may accentuate colposcopic findings.
- For Pap results including ASC-US and LSIL a single colposcopic exam that rules out a high-grade lesion is sufficient evaluation during pregnancy.
- For patients with HSIL cytology or colposcopic findings of high-grade dysplasia found early in pregnancy a second evaluation can be done later in pregnancy.
- If the abnormal Pap was not completely evaluated during the pregnancy or high grade dysplasia was suspected then a colposcopy should be scheduled for the 6wk post-partum visit. Otherwise the patient can follow normal follow up intervals.

Limitations of Pap Screening:

Alaska Native women at one time had higher rates of cervix cancer than the general population. More recent evaluations show cervix cancer occurring no more frequently than in Non-Native women.

A single cytology exam (Pap test) when done correctly has a limited sensitivity (30-

87%). Therefore we will often use a negative HPV test to reassure us that the risk of cancer is low and additional treatment or testing is unnecessary. We are not currently using or recommending the FDA-approved primary HPV screening test that can be considered as an alternative to current cytology-based screening methods. Cytology alone and cotesting remain what current major society guidelines recommend.

Patients with a new diagnosis of cervical cancer often have not had a Pap in many years representing a missed opportunity for prevention. Adenocarcinoma does not have the same long pre-invasive period as squamous cell disease and it can arise high in the endocervical canal beyond the view of colposcopy. This means that our screening program does not have the same reliability (negative predictive value) in excluding adenocarcinoma.

Vulvar and vaginal cancers can be detected by cytology but their low incidence does not warrant regular screening without specific history or physical findings. Gynecologic malignancies other than cancer of the cervix are sometimes discovered in evaluating a patient for an abnormal Pap test. The Pap test is not a useful test for these malignancies and a normal Pap in no way excludes these conditions. Surveillance for these malignancies will not be addressed by this guideline.

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- The impact of human papillomavirus vaccination on cervical cancer prevention efforts (Gynecologic Oncology)
- ACOG Committee Opinion: Human Papillomavirus Vaccination
- 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors (Green Journal)

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