Cervical Screening for Dysplasia and Cancer in Patients with HIV
Purpose of the Guideline

• Increase the numbers of NYS residents with HIV infection who are screened for cervical dysplasia and whose care is managed effectively if cervical dysplasia or cancer are diagnosed.

• Support the NYSDOH Prevention Agenda 2013-2018, which aims to increase by 5% the percentage of all females aged 21 to 65 years with an income of <$25,000 who receive cervical cancer screening.

• Reduce the incidence of morbidity and mortality associated with cervical cancer in persons living with HIV infection through early identification and treatment of precancerous and cancerous lesions, when treatment is most successful.
Who to Screen

• Screening for cervical cancer in the setting of HIV should be performed as detailed in this guideline for eligible individuals, including cisgender women, transgender men, and nonbinary individuals assigned female at birth. Transgender men who have an intact vagina or cervix remain at risk of HPV infection, vaginal or cervical dysplasia, and cervical cancer.

• Throughout this guideline, the term *transgender men* refers to individuals assigned female at birth but who identify as males. Approximately one-third of transgender or gender nonconforming individuals who were assigned female at birth identify as neither male nor female (i.e., *nonbinary*).

• This committee encourages care providers to discuss the need for cervical cancer screening with transgender men and nonbinary individuals to help ensure appropriate care for these individuals.
Preventing Cervical Cancer and Precancerous Lesions

✔ RECOMMENDATION

• Clinicians should offer all individuals with HIV infection aged 9 to 26 years the 9-valent HPV vaccine 3-dose series regardless of prior Pap test results or CD4 cell count. (AI)
Rationale for HPV Vaccination

• Nearly 100% of cervical cancers are associated with HPV infections.

• The 9-valent HPV vaccine protects against non-oncogenic HPV subtypes 6 and 11 and oncogenic HPV subtypes 16, 18, 31, 33, 45, 52, and 58.

• Although the HPV infection subtypes most commonly associated with cervical cancer are HPV 16 and HPV 18 in the general population, in females with HIV, a broader range of HPV oncogenic subtypes are associated with cervical dysplasia.

• In females with HIV infection, the risk of HPV-related cervical disease is greater than in those who do not have HIV, and cervical cancer is the leading cause of cancer death among this population.

• HPV vaccination coupled with regular cervical cytologic screening to identify precancerous lesions, treatment, and follow-up is an effective intervention for decreasing the incidence of cervical cancer.
Cervical Pap Tests

**RECOMMENDATIONS**

- Clinicians should perform a cervical Pap test for all individuals who have HIV infection at the following time intervals:
  - Within 2 years of the onset of sexual activity or by age 21 years. (AII)
  - Annually until 2 tests in a row screen negative, then every 3 years. (AII)
  - At 6 months after treatment for an abnormal result, then annually until 2 tests in a row screen negative, then every 3 years. (AIII)
- Clinicians should perform cervical cytologic screening for individuals who have undergone a supracervical hysterectomy (cervix left *in situ*). (AI)
- After total hysterectomy (uterus and cervix removed), clinicians should perform *vaginal* Pap testing at least annually until negative for 2 tests in a row, then every 3 years. (AII)
- Clinicians should repeat cervical cytologic tests after 2 months but within 4 months after a result of “insufficient specimen for analysis.” (AIII)
Routine STI Screening and Annual Physical Exams

KEY POINTS:

- Regardless of Pap test results, it is important that routine screening for STIs continues to be performed to assess for risk behaviors that require repeat or ongoing screening.

- It is important that clinicians continue to perform visualization of the external anogenitalia and a digital pelvic examination as part of the annual physical examination.
Testosterone Use Affects Specimen Adequacy

KEY POINTS:

• Because testosterone use can induce vaginal atrophy and affect specimen adequacy for a cervical Pap test, the Pap test requisition for transgender men should note both testosterone use and the presence of amenorrhea to assist the accurate interpretation of cell morphology.

• Asking patients about all gender-reassignment and gynecologic surgical procedures is essential to determine the need for cervical or vaginal screening.
## Cytological and Histological Classification of Cervical Dysplasia

### Bethesda Classification System (2014)
Describes cytology obtained at cervical Pap.

- **ASC-US:** Atypical squamous cells of undetermined significance
- **ASC-H:** Atypical squamous cells, high-grade squamous intraepithelial lesion (HSIL) cannot be excluded
- **AGC:** Atypical glandular cells
- **AGC-NOS:** Atypical glandular cells not otherwise specified
- **AGC-FN:** Atypical glandular cells favoring neoplasia
- **LSIL:** Low-grade squamous intraepithelial lesion
- **HSIL:** High-grade squamous intraepithelial lesion
- **Cancer:** --

### Cervical Intraepithelial Lesion (or neoplasia [CIN])
Describes histology obtained at biopsy.

- **Atypia:** --
- **CIN I:** Low-grade cervical intraepithelial neoplasia
- **CIN II:** Moderate-grade cervical intraepithelial neoplasia; may be a low-grade or high-grade lesion
- **CIN III:** High-grade cervical intraepithelial neoplasia
- **CIS:** Carcinoma in situ
- **Cancer:** --

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HPV Co-Testing Vs. Reflex Testing

✓ RECOMMENDATION
• Clinicians should perform HPV co-testing (cervical cytologic test with a concurrent HPV test) only for individuals who are 30 years or older. (All)

HPV co-testing is routinely performed at the same time as a cervical Pap test in individuals ≥30 years.

HPV reflex testing is performed in response to an abnormal cervical Pap test result in individuals <30 years, and in individuals ≥30 years who did not receive an HPV co-test at the time of their cervical Pap test.
HPV Co-Testing Vs. Reflex Testing

HPV co-testing has been found to be a useful adjunct to cervical cytology screening in females with HIV infection who are 30 years or older.

- If HPV/cervical cytologic co-testing is performed in an individual with HIV infection and results are positive for high-risk HPV but negative for abnormal cytology, clinicians should consider repeating the Pap test at a shorter time interval and/or colposcopy for further evaluation for abnormal cells that may have been missed on the initial screen.

- Females with HIV infection, a normal Pap test, and a positive high-risk HPV test result have four times the risk of having an abnormal finding on colposcopy.

HPV co-testing is not indicated for individuals younger than 30 years.

- Spontaneous clearance of HPV infection and cervical neoplasia often occurs in younger females regardless of HIV status.

- Aggressive treatment of dysplasia from transient HPV infection may damage the cervix and could be more harmful than beneficial in this age group.
Follow-Up of Abnormal Pap Test Results in Patients <30 Years

✔ RECOMMENDATIONS

• For individuals < 30 years with a Pap test result of atypical squamous cells of ASC-US, clinicians should ensure that a reflex HPV test is performed. (A reflex HPV test is performed in response to, not concurrent with, an abnormal Pap test.)
  o If the reflex HPV test result is positive, clinicians should refer the patient for colposcopy. (AII)
  o If the reflex HPV test is negative, clinicians should perform both a repeat Pap test and an HPV test at 1 year. (AII)
    ▪ If both tests are negative at 1 year, then the clinician should resume standard Pap testing (every 3 years). (AII)
Follow-Up of Abnormal Pap Test Results in Patients ≥30 Years

**RECOMMENDATIONS**

- For individual ≥30 years, an HPV co-test is routinely performed along with a Pap test; however, if an HPV co-test was not performed in a patient with a Pap test result of ASC-US, clinicians should perform HPV reflex testing.
  - If the HPV test result is positive, clinicians should refer the patient for colposcopy. (AII)
  - If the HPV test result is negative, clinicians should perform both a repeat Pap test and an HPV test at 1 year:
    - If either test result is positive, clinicians should refer the patient for colposcopy. (AII)
    - If both test results are negative, then the clinician should resume standard Pap testing (every 3 years). (AII)
Follow-Up of Abnormal Pap Test Results in All Patients

✅ RECOMMENDATIONS

- For individuals of all ages, clinicians should refer for or perform colposcopy in response to the following Pap test results:
  - Atypical squamous cells, HSIL cannot be excluded (ASC-H). (AI)
  - Low-grade squamous intraepithelial lesion (LSIL). (AI)
  - High-grade squamous intraepithelial lesion (HSIL). (AI)
  - Any result of atypical glandular cells (AGC). (AI)
- Colposcopy is not indicated as an initial screening test. Clinicians should limit colposcopy for use as a follow-up to abnormal screening on either Pap test or high-risk HPV test. (AII)
- After a patient has completed treatment for an abnormal cervical biopsy test, clinicians should repeat cytologic tests at 6 months, then annually until 2 tests in a row screen negative, then every 3 years. (AIII)
FIGURE 1. Follow-Up for Cervical Pap Test Result Atypical Squamous Cells of Undetermined Significance (ASC-US) in Individuals with HIV Infection

- Individuals <30 years
  - HPV reflex test is performed*
  - Negative HPV Test
    - Repeat cervical Pap and HPV test in 1 year
      - Negative cervical Pap test and negative HPV test
      - Resume standard cervical Pap testing every 3 years
    - Positive HPV Test
      - Perform or refer for colposcopy
      - Cervical Pap or HPV test is positive
        - Repeat cervical Pap and HPV test in 1 year
  - Negative HPV Test
    - Repeat cervical Pap and HPV test in 1 year
      - Negative cervical Pap test and negative HPV test

- Individuals ≥30 years
  - HPV co-test or reflex test performed*
  - Negative HPV Test
    - Repeat cervical Pap and HPV test in 1 year
      - Negative cervical Pap test and negative HPV test
    - Positive HPV Test
      - Perform or refer for colposcopy
      - Cervical Pap or HPV test is positive
        - Repeat cervical Pap and HPV test in 1 year
Diagnosed Cervical Cancer

KEY POINT: The standard therapeutic approach to treating cervical cancer in individual with HIV is the same as that for those who do not have HIV; however, the increased risk of treatment failure and high recurrence rate warrant close follow-up by a multidisciplinary team of clinicians even after definitive treatment for cervical cancer.

✓ RECOMMENDATIONS

• Clinicians should *immediately* refer patients with HIV infection and a diagnosis of cervical cancer to a gynecologic oncologist or surgeon trained in the management of cervical cancer. (AII)

• Clinicians should closely monitor patients with cervical cancer in close collaboration with the gynecologic oncologist after definitive treatment for cancer. (AIII)