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Screening for Cervical Dysplasia and Cancer in Adults With HIV

Updates, Authorship, and Related Guidelines

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Purpose of This Guideline

Purpose: This guideline on cervical cancer screening for adults with HIV was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) to inform primary care providers and other practitioners in New York State about screening for cervical dysplasia in patients with HIV. The goal of cervical screening is to identify and treat precancerous lesions to prevent cervical cancer. Comprehensive primary care for adults with HIV includes access to antiretroviral therapy (ART) and screening, diagnosis, and treatment of gynecologic comorbidities, especially cervical dysplasia and cancer.

Screening for cervical and anogenital tract cancer is appropriate for all adult patients; this guideline provides standards of care for cervical, vaginal, and genital screening for patients with HIV. Inclusive and culturally sensitive healthcare that acknowledges the needs of transgender, transmasculine, transfeminine, and nonbinary patients should include an anatomical inventory that identifies which organs are present and absent to determine and meet the screening and healthcare needs of each patient regardless of their gender expression.

Goals: This guideline addresses the prevention of, screening methods for, and diagnosis of genital dysplasia in patients with HIV to achieve the following:

- Increase the number of New York State residents with HIV who are screened for and receive effective medical management of cervical, vaginal, or vulvar dysplasia.
- Emphasize the role of ART-associated viral suppression in improving clearance or suppression of human papillomavirus (HPV), preventing cervical dysplasia, and reducing cervical cancer in individuals with HIV.
- Reduce the incident morbidity and mortality associated with genital HPV disease in individuals with HIV through vaccination against HPV and identification and treatment of precancerous lesions, when treatment is most successful, and cancerous lesions.
- Support the NYSDOH Prevention Agenda 2019-2024, which aims to increase cervical cancer screening by 5% among individuals who are 21 to 65 years old and have an annual income below $25,000.
- Integrate current evidence-based clinical recommendations into the healthcare-related implementation strategies of the New York State Ending the Epidemic initiative.

HPV-Associated Cervical Disease

The American Cancer Society estimates that in the United States in 2022, approximately 14,100 new cases of invasive cervical cancer will be diagnosed, and approximately 4,280 individuals will die from cervical cancer [ACS 2022]. In 2018, there were 792 new cases of cervical cancer among all women in New York State, with 233 deaths from the disease [CDC(d) 2021]. Nearly 100% of cases of cervical cancer are associated with HPV infection [CDC(a) 2021; CDC(b) 2021; Chaturvedi, et al. 2011; Winer, et al. 2006]. Individuals with HIV are at increased risk of human papillomavirus (HPV) infection and related disease and are 5 times more likely than those without HIV to be diagnosed with cervical cancer [Liu, et al. 2018; Grulich, et al. 2007]. Cervical cancer is an AIDS-defining illness.

In the general population, the HPV subtypes most commonly associated with cervical cancer are 16 and 18 [CDC(a) 2021], and infection with multiple HPV subtypes has been associated with benign condylomata acuminata (genital warts), squamous intraepithelial lesions (SILs), vulvar and anal dysplasia, and anogenital carcinoma [NCI SEER 2018]. In individuals with HIV, a broader range of HPV oncogenic subtypes are associated with cervical dysplasia [Orlando, et al. 2017].

HPV-related cervical cell abnormalities: Persistent HPV infection is necessary for the development of cervical SILs, which arise at the junction of the cervical squamous and columnar epithelium around the cervical os, the transformation zone. SILs are the most common type of precancerous cervical lesions, preceding nearly 80% of cervical cancers [ICESCC 2007]. Glandular carcinomas are the second most common type of cervical cancer [ICESCC 2007]. SILs occur more frequently in individuals with HIV than in those without HIV [Liu, et al. 2018; Maiman, et al. 1993].

Cervical cell abnormalities can be categorized as high risk (cancer causing) or low risk (benign warts) based on oncogenic potential. High-risk HPV types that are related to anogenital cancers include types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, and 82 [Guan, et al. 2012; Hariri, et al. 2012]. Although high-risk HPV types are detected in 99% of cervical cancers, types 16 and 18 are the most oncogenic [Clifford, et al. 2017; Keller, et al. 2015] and account for nearly 70% of all cervical cancers in the general population [CDC(a) 2021].

Among individuals with HIV, cancer is associated with types 16 and 18 and high-risk types 51, 52, 53, 56, 58, and 59 [McKenzie, et al. 2010], and low-risk types 6 and 11 are most commonly associated with benign disease (genital warts) [McKenzie, et al. 2010]. Identifying the presence of high-risk HPV types is central to managing abnormal cytology results in individuals with and without HIV [Perkins, et al. 2020; Hariri, et al. 2012].

Higher risk of cervical disease associated with HIV: The risk of HPV-related cervical disease is increased in individuals with HIV [McClymont, et al. 2020; Grabar, et al. 2019; Liu, et al. 2018; Konopnicki, et al. 2013]. Cervical cancer has historically been a leading cause of cancer death among individuals with HIV [Dryden-Peterson, et al. 2016], which may be related to the increased prevalence and persistence of HPV in this population [Kojic, et al. 2014; Moscicki, et al. 2004].

HPV Prevention

☑ RECOMMENDATION

HPV Prevention

- Given the increased lifetime risk of persistent human papillomavirus (HPV) infection and increased prevalence of HPV-related cancers, clinicians should recommend the 9-valent HPV vaccine 3-dose series at 0, 2, and 6 months to all individuals with HIV who are 9 to 45 years old regardless of CD4 cell count, prior cervical or anal screening results, HPV test results, HPV-related cytologic changes, or other history of HPV-related lesions. (A3)

HPV Vaccine

In 2006, the U.S. Food and Drug Administration (FDA) approved a 9-valent vaccine that protects against nononcogenic HPV types 6 and 11 and oncogenic HPV types 16, 18, 31, 33, 45, 52, and 58 (Gardasil 9). Because it offers broader coverage of HPV types than other approved bivalent vaccines, the 9-valent vaccine is the only HPV vaccine available in the United States (see CDC: Supplemental information and guidance for vaccination providers regarding use of 9-valent HPV for more information). The HPV vaccine is approved by the FDA for preventive but not therapeutic use.

Extrapolating data from the demonstrated effectiveness of the quadrivalent HPV vaccine in older individuals [Wilkin, et al. 2018], the FDA expanded the age range for approved use of the HPV vaccine in the United States from ages 9 to 26 years to ages 9 to 45 years [FDA 2020]. There is no specific mention of HIV infection in the updated FDA approval. Although 1 study demonstrated lower efficacy of the quadrivalent vaccine in individuals with HIV [Wilkin, et al. 2018], other research has linked HIV viral suppression to vaccine efficacy [Money, et al. 2016]. Given the increased lifetime burden of persistent HPV infection, disease, and morbidity, proactive vaccination among individuals with HIV is a strategic means of primary prevention and potential disease mitigation that should be strongly considered and encouraged [Di Donato, et al. 2021; Karimi-Zarchi, et al. 2020; Lichter, et al. 2020].

When to Vaccinate

HPV vaccination for all individuals may be scheduled at the same time as standard adolescent vaccines offered at ages 9 to 12 years. If possible, the HPV vaccine series should begin at age 9 years [Glidden, et al. 2016]. The 3-dose vaccine is recommended for all patients with HIV who are 9 to 45 years old. The 9-valent HPV vaccine should be administered according to the CDC standard schedule for immunocompromised adults, children, and adolescents (a 3-dose regimen over a 6-month period at 0, 2, and 6 months) and should be offered regardless of CD4 cell count.

HPV vaccination provides high levels of neutralizing antibodies for at least 5 years and is protective in individuals ≤26 years old who do not have HIV, regardless of history of sexual activity; however, the full length of its protection has not been established. In an observational study conducted in England that examined the effectiveness of a national HPV immunization program, the reduction in cervical cancer was greatest in individuals who received the vaccine at ages 12 to 13 years [Falcaro, et al. 2021]. Although data are limited, the immunogenicity of the quadrivalent HPV vaccine has been demonstrated in individuals with HIV [Wilkin, et al. 2018; Kojic, et al. 2014].

HPV testing and vaccination: HPV testing is not recommended before vaccine administration. It is unlikely that an individual will have been infected with all the HPV types covered by the 9-valent vaccine; therefore, it is expected that the 9-valent HPV vaccine will be effective against any of the 9 HPV types or any HPV types to which the individual has not yet been exposed. There also may be beneficial prevention due to cross-reactivity with other HPV types not included in the 9-valent vaccine [Wheeler, et al. 2012].

Revaccination with the 9-valent HPV vaccine is not currently recommended for individuals previously immunized with the bivalent or quadrivalent HPV vaccine [ACOG 2020; Petrosky, et al. 2015]. Vaccination with the quadrivalent HPV vaccine has demonstrated cross-protection against other oncogenic HPV types [Kemp, et al. 2011]. There is no maximum interval between vaccine doses; as long as all 3 doses are given, there is no need to repeat doses if a scheduled vaccination is not given on schedule [CDC(c) 2021].

→ KEY POINTS

- HPV vaccination status does not change the schedule of cervical cancer screening.
- HPV testing is not recommended before administration of the HPV vaccine.

Other Forms of HPV Prevention

HPV infection is the most common sexually transmitted infection (STI) in the United States, and many individuals become infected with multiple types of HPV during their lives [CDC 2022]. Most HPV infections resolve, become latent, or are not detectable on clinical assays within a few years of exposure and infection [Ho, et al. 1998; Moscicki, et al. 1998; Evander, et al. 1995]. HPV is transmitted via skin-to-skin contact, so barrier protection, such as male/insertive and female/receptive condoms, offers some but not full protection. Because prior identification of HPV infection in a sexual partner is unlikely, limiting the number of sexual partners may reduce but not eliminate an individual's exposure to HPV [Workowski, et al. 2021].

→ KEY POINTS

- Inform patients with HIV about the risk of acquiring HPV and other STIs from close physical contact with the external genitalia, anus, cervix, vagina, urethra, mouth and oral cavity, or any other location where HPV lesions are present.
- Consistent and correct condom use remains an effective way to reduce the risk of transmission of most STIs, including HPV. However, inform patients that barrier protection such as condoms and dental dams may not fully protect against HPV.

Cervical Cancer Prevention

☑ RECOMMENDATIONS

Cervical Cancer Prevention

- In providing comprehensive primary care for adults with HIV, clinicians should ensure that patients at risk of cervical cancer receive age- and risk-appropriate screening (A3) and provide education about harm reduction measures that may reduce the risk, including:
  - HPV vaccination (A2)
  - ART to suppress HIV viral load (A2)
  - Tobacco use cessation (A2)
  - Sexual exposure prevention strategies, including using barrier protection (A3) and reducing the number of sex partners and associated sexual networks when possible (A3)
- Clinicians should establish a schedule for routine cervical screening based on a patient's medical history, anatomical inventory, age, and risk profile. (A2)

Abbreviations: ART, antiretroviral therapy; HPV, human papillomavirus.

Information on tobacco use and cessation: NYSDOH: Information about Tobacco Use, Smoking and Secondhand Smoke; American Academy of Family Physicians: FDA-Approved Medications for Smoking Cessation

HPV vaccination, sustained access to and adherence to effective ART, and compliance with recommended screening intervals, treatment schedules, and overall sexual and preventive healthcare are critical aspects of preventing cervical cancer in people with HIV. Minimizing gaps in care or refusal of care, with the goal of identifying treatable precancerous lesions (cervical intraepithelial neoplasia [CIN] 3 or greater), coupled with treatment and follow-up is a powerful strategy to decrease the incidence of HPV-related cancers in individuals with HIV [USPSTF, et al. 2018; Massad, et al. 2017; Thorsteinsson, et al. 2016].

The 2019 American Society for Colposcopy and Cervical Pathology (ASCCP) Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors and ASCCP Management Guidelines App Quick Start Guide provide extensive discussion of risk and an app for calculating risk. Factors that increase the risk of cervical cancer include older age, HPV type 16 infection, persistent HPV infection, a cytology result of high-grade squamous intraepithelial lesions, a history of CIN 3, or previous cervical cancer.

ART as prevention: Early in the epidemic, women with HIV presented with cervical cancer at later stages, when treatment was less successful [Maiman, et al. 1993]. Risk of incident cervical cancer for individuals with HIV has declined significantly

over the last 20 years [Hernandez-Ramirez, et al. 2017; Robbins, et al. 2017]. ART has been found to reduce HPV acquisition, improve regression, and decrease rates of cervical disease progression [Carlander, et al. 2018; Kelly, et al. 2018; Liu, et al. 2018; Ghebre, et al. 2017; Adler, et al. 2012]. Rates of cervical dysplasia in women with HIV who are virally suppressed on ART and have a CD4 count ≥500 cells/mm^3 are comparable to rates in women without HIV [Silverberg, et al. 2018; Aho, et al. 2017; Massad, et al. 2017]. Cervical disease pathogenesis is the same in women with HIV who are virally suppressed and have a CD4 count ≥500 cells/mm^3 as for women who do not have HIV [Davies, et al. 2015; Kim, et al. 2013; Konopnicki, et al. 2013; Harris, et al. 2005].

Screening: Countries with a national screening program have lower rates of cervical cancer among women with HIV, and some U.S. cohorts have demonstrated comparable rates of invasive cervical cancer in people with or without HIV [Massad, et al. 2009]. Cervical cancer screening and prompt referral for treatment of precancerous lesions and invasive cervical cancer are most effective when integrated into routine HIV services, ideally within HIV clinics [McCormick Viens, et al. 2023]. Universal access to comprehensive HIV treatment, health care maintenance, and HPV prevention and cancer screening are critical for reducing the burden of HPV-related cancers in people with HIV [Ghebre, et al. 2017].

Tobacco use cessation: Tobacco use is associated with development of genital HPV lesions and disease [Gallaway, et al. 2018], and cigarette smoking potentiates the risk for acquisition of high-grade CIN in individuals with HIV [Massad(a), et al. 2012]. Clinicians should inform patients of the risks of tobacco use and encourage reduction or cessation of use of all tobacco products as a component of prevention of genital HPV disease. For more information on addressing tobacco use with your patients, see the NYSDOH AI guideline Substance Use Screening, Risk Assessment, and Use Disorder Diagnosis in Adults > Patient Engagement and Interventions and NYSDOH resources at TalkToYourPatients.ny.gov.

Screening for Cervical Abnormalities

☑ RECOMMENDATIONS

Screening for Cervical Abnormalities

- Clinicians should perform an anatomical inventory to identify patients eligible for screening. (A*)
- Clinicians should perform screening for cervical and genital tract dysplasia and cancer in patients with HIV who have or have had a cervix and meet the below criteria for age-based screening. (A2)
- Clinicians should perform physical examinations of the vulva, vagina, and anogenital perineum at least annually and at the time of cervical cytology and to assess interval complaints. (A3) Abnormal cytology results may reflect vaginal, vulvar, or anogenital dysplasia in the absence of cervical dysplasia.

Age-Based Screening

- For patients <30 years old, testing for HPV is not recommended (A2†). For these patients, clinicians should perform cervical cytology within at least 2 years of the onset of receptive sexual activity or by age 21 years, regardless of the mode of HIV acquisition (A2), and if cytology results are normal, repeat testing every 3 years. (A2)
- For patients ≥30 years old, clinicians should perform cytology/HPV cotesting within 3 years of previous testing. (A2) If the baseline cytology and HPV test results are negative, clinicians should repeat both tests every 3 years thereafter. (A2)
- Clinicians should repeat cervical cytology after 2 months but within 4 months after a result of "insufficient specimen for analysis" has been reported. (A3)
- Clinicians should continue cervical cancer screening for patients ≥65 years old; however, factors such as a patient's life expectancy and risk of developing cervical cancer should inform shared decision-making regarding continued screening. (A3)

Concomitant Screening for Anal Cancer and STIs

- Clinicians should perform concomitant anal cytology. If appropriate follow-up of abnormal results is not available within the clinician's institution, a referral plan should be in place.
- Regardless of a patient's cervical cytology results, clinicians should perform routine STI screening.

☑ RECOMMENDATIONS

Post-Hysterectomy Cancer Screening

- In patients with an intact cervix, clinicians should perform cervical cytology as above [a]. (A*)
- In patients with HIV who have undergone total hysterectomy (uterus and cervix removed), clinicians should screen for vaginal intraepithelial neoplasia by performing *vaginal* cytology with HPV cotesting and manage as noted under "age-based screening" above. (A2†)
- If a patient's hysterectomy was performed to treat HSILs, CIN 2 or CIN 3, or AIS [a], clinicians should perform 3 consecutive annual HPV tests, after which long-term surveillance should be initiated, with HPV testing every 3 years for 25 years. (A3)

Post-Cervical Excision HPV Testing

- After a patient has undergone cervical excision, clinicians should perform cervical cytology with HPV testing as follows: at 6 months post-excision, annually until 3 sequential negative test results have been obtained, and every 3 years thereafter for at least 25 years. (A3)

Abbreviations: AIS, adenocarcinoma in situ; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; STI, sexually transmitted infection.

Note:

a. Every possible effort should be made to determine the reason for a patient's hysterectomy and to obtain the pathology report.

Purpose of Screening

The primary goal of cervical cytology is to identify and treat precancerous lesions—defined as CIN 3, AIS, and in rare cases, invasive cervical cancer [Perkins, et al. 2020]. Cervical cancer is a relatively rare finding in the United States; nevertheless, identification and treatment are essential and may include more frequent testing, referral for colposcopy and directed biopsy, and subsequent treatment of biopsy-proven histologic abnormalities. CIN 2 has appreciable regression rates [Perkins, et al. 2020].

A histology result of CIN 3 or higher is the established surrogate for cancer risk. CIN 3 is a finding of severely atypical cellular changes that encompass greater than two-thirds of the epithelial thickness and include full-thickness lesions. Previous terms for CIN 3 were "severe dysplasia" and "carcinoma in situ." CIN 3 was chosen instead of CIN 2 because it is a more pathologically reproducible diagnosis [Perkins, et al. 2020]. The HPV type distribution in CIN 3 lesions more closely approximates that of invasive cervical cancer.

How cervical cytology results are reported: Cervical cytology currently uses the Bethesda Classification System as standard nomenclature to describe abnormal results that may require further follow-up [CPBG 2016; Massad, et al. 2013]. The Bethesda Classification System (see Box 1, below) also describes the degree of neoplastic change found on biopsy. These naming conventions are not interchangeable (see guideline section Follow-Up of Abnormal Cervical Cytology Results).

Box 1: Cytologic and Histologic Classifications of Cervical Dysplasia [a]

Bethesda Classification System (describes cervical cytology results):

- Negative for intraepithelial lesion or malignancy (NILM)
- Atypical squamous cells of undetermined significance (ASC-US)
- Atypical squamous cells, high-grade squamous intraepithelial lesion cannot be excluded (ASC-H)
- Atypical glandular cells (AGC): endocervical cells, endometrial cells, or glandular cells
- Atypical glandular cells not otherwise specified (AGC-NOS)
- Atypical glandular cells favoring neoplasia (AGC-FN)
- Low-grade squamous intraepithelial lesions (LSIL)
- High-grade squamous intraepithelial lesions (HSIL)
- Squamous cell carcinoma
- Cancer

Box 1: Cytologic and Histologic Classifications of Cervical Dysplasia [a]

Cervical intraepithelial lesion or neoplasia (describes histology obtained at biopsy):

- Atypia
- Low-grade cervical intraepithelial neoplasia (CIN 1)
- Moderate-grade cervical intraepithelial neoplasia; may be a low-grade or high-grade lesion (CIN 2)
- High-grade cervical intraepithelial neoplasia (CIN 3)
- Carcinoma in situ (CIS)
- Endocervical carcinoma in situ
- Cancer

Note:

a. Adapted from [Nayar and Wilbur 2015].

Who to Screen

Cervical dysplasia is caused by genital HPV, an STI. Consistent with American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines [Perkins, et al. 2020], cervical cancer screening in patients <30 years old with HIV who have a cervix should begin within at least 2 years of first receptive sexual activity or by age 21 years [Keller, et al. 2012].

Patients ≥65 years old: HIV has been associated with an increased lifetime risk of cervical cancer; therefore, the ASCCP guidelines recommend continued screening in this population beyond age 65 years [Perkins, et al. 2020]. However, patients and their clinicians may decide to discontinue screening after a shared decision-making assessment of the risks and benefits, possible mitigating factors involved with ongoing risk for HPV infection, and the purpose of screening. Factors to consider include HPV status and risk of acquisition, history of screening results and risk of cervical cancer, the burden of screening and associated follow-up, viral suppression status, comorbidities, and life expectancy [DHHS 2021; Massad, et al. 2021; Aserlind, et al. 2017].

Virally suppressed patients: Patients who are virally suppressed and have demonstrated adherence to HIV care and primary care, who have negative cytology and negative HPV test results, no genital or pelvic complaints, do not use tobacco products, and do not have any other cervical cancer risk factors may benefit from cervical screening every 5 years [Robbins, et al. 2017]. When navigating extended screening intervals or discontinuation of screening based on lifetime prognosis, a compassionate engagement of patient-centered shared decision-making is critical, so that clinician and patient can address lifetime risk of HPV-related disease, goals for screening, cultural and personal values, and benefits of a personalized screening interval that considers each patient's unique risk scenario.

→ KEY POINTS

- Compassionate engagement in shared decision-making is crucial when navigating extended screening intervals or discontinuation of screening based on a patient's lifetime prognosis. When engaging patients in shared decision-making regarding screening intervals, consider duration of HIV infection, viral load and CD4 cell count over time, and history of abnormal Pap test results and anogenital HPV lesions.
- Cervical screening every 5 years may benefit virally suppressed patients adherent to HIV and primary care with negative cytology and negative HPV test results, no genital or pelvic complaints, no tobacco use, and no other cervical cancer risk factors.

Transgender individuals: It is important that care providers and facilities establish a safe and welcoming environment for transgender patients [UCSF(a) 2016]. Approximately one-third of transgender or gender-diverse individuals assigned female sex at birth identify as nonbinary [National Center for Transgender Equality 2017]. Asking patients to provide details about all gender-affirming and gynecologic surgical procedures will help establish the need for screening for HPV-related cancers (for terminology and definitions related to transgender care, see the University of California San Francisco Center of Excellence for Transgender Health).

Currently, there are no published data on cervical cancer screening and treatment in transgender men. Although the recommendations in this guideline are based on data from studies in cisgender women, this committee supports extrapolation of that data to support recommendations for all adults with HIV who are eligible for cervical screening.

Transgender men who have a uterine cervix are at risk for cervical cancer, yet screening rates are lower in this population than in cisgender women, largely because of barriers to inclusive, informed medical care for transgender people. Testosterone use in transgender men causes vaginal atrophy, which is associated with high rates of cytology results that are classified as "insufficient." Notation of testosterone use and amenorrhea, when indicated, will facilitate accurate interpretation of cell morphology in transgender men [Tabaac, et al. 2018; UCSF(b) 2016; Peitzmeier, et al. 2014].

Transgender women may undergo genital reconstruction, or vaginoplasty, to create a neovagina. There are no studies to support cervical or vaginal screening of a neovagina; however, visual examination to assess symptoms or as part of routine screening is appropriate [Fierz, et al. 2019; UCSF(b) 2016; van der Sluis, et al. 2016; Heller 2015].

→ KEY POINTS

- Inclusive and culturally sensitive healthcare includes a safe and welcoming environment that acknowledges the needs of transgender, transmasculine, transfeminine, and nonbinary patients.
- Ask patients to provide details about all gender-affirming and gynecologic surgical procedures they have undergone to help inform screening for HPV-related cancers.
- To facilitate accurate interpretation of cell morphology, note testosterone use and the presence of amenorrhea in the requisition for cervical cytology in transgender men.

HPV Testing

HPV testing: HPV testing is used to assist risk stratification as a primary screening tool. The U.S. Food and Drug Administration (FDA) has approved 2 assays for primary HPV testing to be used for screening individuals ≥25 years old in the general population. Currently, there is limited use of this screening strategy for people with HIV in the United States. Research from a retrospective cohort has suggested that primary HPV screening with reflex to 16/18 genotyping in cervical cancer screening for people with HIV may result in fewer colposcopies over the subsequent 1 to 2 years than cytology with HPV testing [Strickler, et al. 2020].

HPV cotesting: Cervical cytology with HPV cotesting has been used to extend cervical screening intervals to every 5 years in women without HIV [USPSTF, et al. 2018; ACOG 2016; CPBG 2016]. However, cervical cytology with HPV cotesting is not indicated for individuals <30 years old because resolution of HPV infection and cervical dysplasia is likely regardless of HIV status [USPSTF, et al. 2018; Plummer, et al. 2007; Woodman, et al. 2001]. Aggressive treatment of dysplasia from transient HPV infection may damage the cervix, contribute to preterm delivery, and be more harmful than beneficial in this age group [Conner, et al. 2014; Bruinsma and Quinn 2011]. HPV cotesting is a useful adjunct to cervical cytology in individuals with HIV ≥30 years old [Alade, et al. 2017; Castle, et al. 2012; Keller, et al. 2012].

→ KEY POINT

- In individuals ≥30 years old, cytologic surveillance alone is acceptable only if HPV cotesting is unavailable. Cytology is less sensitive than HPV testing for detection of precancer and, therefore, requires testing at shorter, more frequent intervals [Perkins, et al. 2020]. It is recommended that clinicians without access to HPV cotesting offer cytology at a minimum of 3-year intervals.

Concomitant Screening for Anal Cancer and STIs

Diagnoses of anal cancer are on the rise in the United States among women in the general population; among men who have sex with men, regardless of their HIV status; and among men and women with HIV [Islami, et al. 2017; Palefsky 2017; Hessol, et al. 2013]. Anal SILs have been associated with concurrent cervical SILs; however, they can also occur independently. Anal cytology should be performed for all individuals ≥35 years old with HIV, including cisgender women [Gaisa, et al. 2017; Stier, et al. 2015; Hessol, et al. 2013; Kojic, et al. 2011], with or without cervical abnormalities, according to guidelines for adults with HIV. Regardless of cytology results, it is important that screening for STIs is performed routinely in patients who engage in risk behaviors (for more information, see CDC: 2021 Sexually Transmitted Infections Treatment Guidelines).

Post-Hysterectomy Cancer Screening

After a patient who does not have HIV has had a hysterectomy for benign disease, routine screening for vaginal cancer is not generally recommended. However, because HIV and HPV infection increase the risk of vaginal SILs [Bradbury, et al. 2019; Massad(b), et al. 2012], vaginal cytologic testing post-hysterectomy is recommended for patients with HIV [Smeltzer, et al. 2016]. SILs on the vaginal cuff can recur from a latent anogenital HPV infection or as primary disease post-hysterectomy, not related to previous cervical infection [Smeltzer, et al. 2016; Saslow, et al. 2012].

If the indication for hysterectomy in a patient with HIV is not known, screening should be performed as it would be in a patient with an intact cervix. Individuals with HIV who have undergone hysterectomy and have any history of high-grade CIN, AIS, or invasive cervical cancer, regardless of whether the hysterectomy was performed for that disease or subsequently for benign disease, should receive a minimum of 3 consecutive annual HPV tests before long-term surveillance with cervical cytology and HPV testing every 3 years is initiated [Perkins, et al. 2020; Khan, et al. 2016].

The FDA has not approved HPV testing for vaginal samples; however, the sensitivity of HPV-based testing seems superior to cytology alone when screening for high-grade SIL after hysterectomy [Perkins, et al. 2020; Khan, et al. 2016]. Abnormal vaginal screening results should be managed according to colposcopy guidelines for vaginal cytology [Perkins, et al. 2020].

Screening for Cervical Dysplasia During Pregnancy

☑ RECOMMENDATIONS

Screening for Cervical Dysplasia During Pregnancy

- Clinicians should perform cervical cytology screening for pregnant patients with HIV as appropriate for each patient's age. (A2†)
- Clinicians should refer pregnant patients for follow-up with experienced colposcopy providers when the following cervical cytology results are obtained: repeated ASC-US, ASC-US with HPV, negative cytology with persistently positive HPV, ASC-H, or LSIL or greater. (A3)
- When cervical dysplasia is diagnosed, clinicians should ensure that patients understand the potential risks and benefits and engage pregnant patients in shared decision-making regarding treatment. (A3)
- Clinicians should follow up on abnormal cytology or colposcopy results, ideally within 6 weeks postpartum. (A2)

Abbreviations: ASC-H, atypical squamous cells, high-grade squamous intraepithelial lesions cannot be excluded; ASC-US, atypical squamous cells of undetermined significance; HPV, human papillomavirus; LSIL, low-grade squamous intraepithelial lesion.

Pregnant individuals with HIV should undergo cervical cytology and HPV cotesting as appropriate for their age group. Referral to a practitioner skilled and experienced in colposcopy is recommended for all pregnant patients with cervical screening results of persistent ASC-US, ASC-US with HPV, negative cytology with persistently positive HPV, ASC-H, or LSIL or greater.

The natural history, pathogenesis, rate of progression, and prognosis of cervical cancer are not affected by pregnancy. Colposcopy-directed biopsies are generally safe during pregnancy but should be performed only if a lesion appears to be carcinoma in situ or cancer [UpToDate 2023]. Endocervical curettage, endometrial biopsy, and treatment without biopsy are unacceptable practices during pregnancy. Diagnostic excisional procedure or repeat biopsy is recommended only if cancer is suspected based on cytology, colposcopy, or histology results [Perkins, et al. 2020]. Shared decision-making that accounts for a patient's risk of cancer, ongoing monitoring and treatment plan, pregnancy options, and reported values and goals should be applied when managing cervical dysplasia in pregnancy.

Close follow-up of abnormal cytology or colposcopy results is critical in the postpartum period. The colposcopic exam should be performed no earlier than 4 weeks after delivery; however, biopsy during pregnancy should be conducted for any lesions suspicious for cancer to avoid delays in treatment. To prevent loss to follow-up, the clinician can refer for postpartum colposcopy in the antepartum period, making sure to include the provision of ongoing health insurance.

→ KEY POINT

- Although cervical biopsies are not routinely recommended in pregnancy, any lesion suspicious for carcinoma in situ or cancer merits immediate evaluation with biopsy.

Follow-Up of Abnormal Cervical Cytology Results

☑ RECOMMENDATIONS

Follow-Up of Abnormal Cervical Cytology Results

- When a cervical cytology result of ASC-US is returned for a patient <30 years old or for a patient ≥30 years old who did not receive cotesting [a], the clinician should perform reflex [b] HPV testing. (A2)
- If the reflex HPV test result is positive, the clinician should refer the patient for colposcopy. (A2)
- If the reflex HPV test result is negative, the clinician should repeat both the cervical cytology and HPV testing at 1 year. (A2)
  - If at 1 year the cervical cytology and HPV test results are negative, the clinician should resume standard cervical cytology testing every 3 years. (A2)
  - If at 1 year the cervical cytology result indicates ASC-US and the HPV test result is negative, the clinician should repeat cervical cytology and HPV testing 1 year following (A3); alternatively, if the patient has a history of cervical dysplasia or individual risk factors for cervical cancer, the clinician should refer for colposcopy. (A3)
  - If at 1 year the HPV test result is positive, the clinician should refer the patient for colposcopy. (A2)
- When a patient of any age with HIV has a cervical cytology result of LSIL, HSIL, ASC-H, AGC, or AIS, the clinician should refer for colposcopy regardless of the HPV test result. (A2)

Abbreviations: AGC, atypical glandular cells; AIS, adenocarcinoma in situ; ASC-H, atypical squamous cells, HSIL cannot be excluded; ASC-US, atypical squamous cells of undetermined significance; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

Notes:

a. Cervical cytology with concomitant HPV testing (i.e., cotesting) is recommended for patients with HIV who are ≥30 years old.
b. For individuals <30 years old, a reflex HPV test is performed in response to an abnormal cytology result and not concurrently with cervical cytology.

Abnormal cervical cytology and referral for colposcopy: Colposcopy with biopsy is the recommended diagnostic test for cervical dysplasia identified through cervical cytology; colposcopy is not used for primary screening. Colposcopy visually locates specific lesions for directed biopsy and histologic diagnosis and has better sensitivity and specificity for SILs than cytology alone. Abnormal cytology results that require colposcopy include:

- ASC-US with high-risk HPV
- ASC-H
- AGC
- LSILs
- HSILs
- Repeated positive high-risk HPV cotest results in the presence of negative cervical cytology
- Repeated ASC-US cytology, regardless of HPV result (see discussion below)

Figure 1, below, describes appropriate follow-up of abnormal cervical cytology results in patients with HIV.

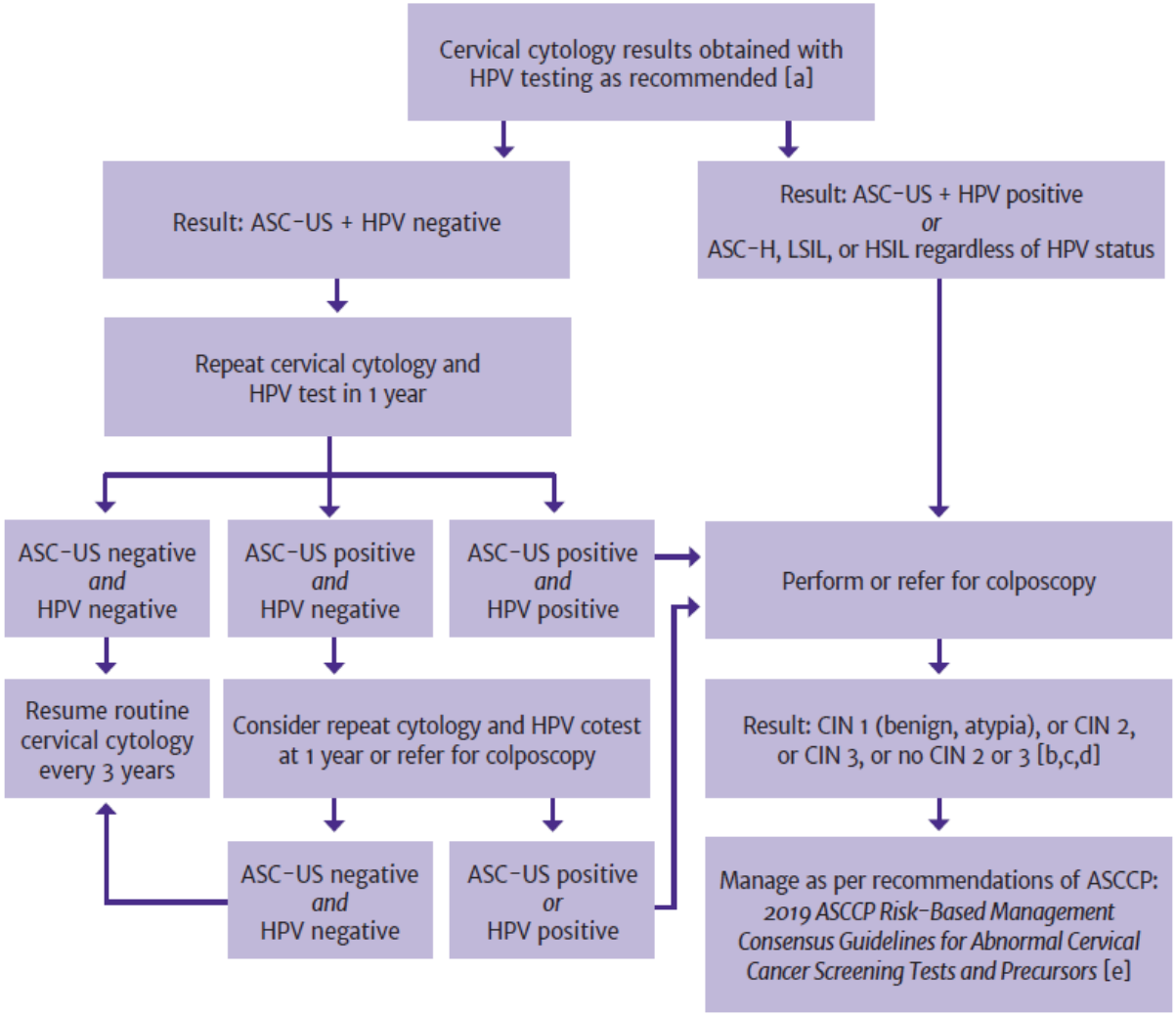
ASC-US: Because a cervical cytology result of ASC-US indicates the inability to determine whether the cellular abnormality is benign or high risk, an HPV test in response to the cytology result (HPV reflex testing) is recommended regardless of a patient's age. The purpose is to identify possible high-risk HPV infection, which, if present, requires follow-up with colposcopy.

Vaginal or cervical infections (e.g., trichomonas, herpes simplex virus, gonorrhea, chlamydia, or bacterial vaginosis) or age-related atrophic changes may be associated with inflammation and abnormal cytology results. In addition to considering an individual's history of dysplasia, clinicians should consider, screen for, and treat inflammatory conditions in all patients, especially those with a cytology result of ASC-US and a negative HPV test result. After a patient's inflammatory condition(s) have been treated, clinicians may repeat cytology and HPV cotesting before referring to colposcopy.

ASC-H: Cervical cytology results may be described as ASC-US when the lesion cannot be determined to be high grade; however, a result of ASC-H suggests that a lesion is precancerous, and colposcopy is indicated regardless of the HPV cotest result.

LSILs: A cytology result of LSIL indicates early cell changes associated with HPV infection. In women who do not have HIV, LSILs tend to be associated with transient changes that regress over time [UpToDate 2023; Solomon, et al. 2002]. Data on women with HIV indicate higher rates of recurrence and progression of LSILs than observed among those without HIV [Zeier, et al. 2012; Nappi, et al. 2005; Robinson, et al. 2003]. Individuals with HIV and LSIL on cytology should be referred for colposcopy.

Figure 1: Follow-Up for Abnormal Cervical Cytology Results in Patients With HIV



Abbreviations: ASC-H, atypical squamous cells, high-grade squamous intraepithelial lesion cannot be excluded; ASC-US, atypical squamous cells of undetermined significance; ASCCP, American Society for Colposcopy and Cervical Pathology; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

Notes:

a. In patients <30 years old, HPV reflex testing should be performed in patients with a positive cervical cytology result; in patients ≥30 years old, HPV cotesting is recommended.
b. If cotesting was not performed, then HPV reflex testing is indicated following an abnormal cytology result.
c. For non–high-grade CIN, refer to ASCCP recommendations for management of LSIL (CIN 1) preceded by ASC-H or HSIL cytology.
d. In patients <25 years old, immediate excision is not recommended; in nonpregnant patients ≥25 years old, the decision regarding expedited treatment versus colposcopy with biopsy should be based on shared decision-making between the patient and clinician.
e. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2020;24(2):102-131. [PMID: 32243307]

HSILs: A cytology result of HSILs suggests that a lesion is more likely to be precancerous. HSILs are associated with high-risk types of HPV and have a high risk of progression to cervical intraepithelial neoplasia (CIN) or cancer [UpToDate 2023]. In individuals with HIV, both LSILs and HSILs require close follow-up and referral for colposcopy.

For nonpregnant individuals ≥25 years old with HSILs, current American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines for the general population recommend consideration of immediate treatment—destruction or excision of precancerous lesions—in cases in which the risk of CIN 3 or higher is ≥25% [Perkins, et al. 2020]. Treatment without colposcopy removes an intermediate step for those at highest risk for CIN 3 or higher. In cases in which the risk of CIN 3 or higher exceeds 60%, expedited treatment is preferred. Reasons for consideration of expedited treatment will vary and may include limited access to healthcare. Immediate treatment without histologic confirmation is not recommended for individuals <25 years old. The age cutoff of 25 years balances the benefits and harms related to very low cervical cancer rates and high rates of HSIL regression in individuals <25 years old [Perkins, et al. 2020]. Because individuals with HIV are known to have an elevated risk of cervical cancer, a thorough discussion with patients of the risks and benefits of treatment of cervical dysplasia is crucial to ensuring shared decision-making.

CIN: As described in the guideline section Screening for Cervical Abnormalities, SILs are cytologic findings and CIN is a histologic finding found on biopsy performed at the time of colposcopy.

CIN 1 is used to describe a low-grade lesion and refers to mildly atypical cellular changes in the lower third of the epithelium; HPV cytopathic effect (koilocytotic atypia) is often present.

CIN 2 (formerly called moderate dysplasia) describes a high-grade lesion and refers to atypical cellular changes confined to the basal two-thirds of the epithelium with preservation of epithelial maturation. However, CIN 2 has poor reproducibility and is likely a heterogeneous mix that includes lesions that could be called CIN 1 or 3. CIN 2 is stratified according to p16 immunostaining to identify precancerous lesions. Specimens that are p16 negative are referred to as LSILs and those that are p16 positive are referred to as HSILs. Because of the poor reproducibility of CIN 2, CIN 2 and 3 are often classified together as "CIN 2/3."

CIN 3 (formerly called severe dysplasia or carcinoma in situ) describes a high-grade lesion and refers to severely atypical cellular changes encompassing greater than two-thirds of the epithelial thickness and includes full-thickness lesions [UpToDate 2023].

Indications for expedited treatment: ASCCP guidelines urge consideration of diagnostic excision and treatment without the intermediary step of colposcopy in cases in which risk of CIN 3 exceeds 25%; expedited treatment is preferred when risk exceeds 60% [Perkins, et al. 2020]. The ASCCP guidelines do not specifically address individuals with HIV (for discussion of risk calculation, see the 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors).

AGC: Any cervical cytology result of AGC requires immediate follow-up with colposcopy and further evaluation (see Figure 2, below). Treatment decisions are based on the resulting tissue diagnosis.

Glandular carcinoma of the cervix may be preceded by a negative cytology result or a test result indicating the presence of AGC [Moukarzel, et al. 2017]. A cytology result of AGC may indicate a precursor lesion for a glandular cell cervical cancer, although this is rare. AGC may be related to HPV infection or may be a contaminant from endometrial or fallopian tube cancer.

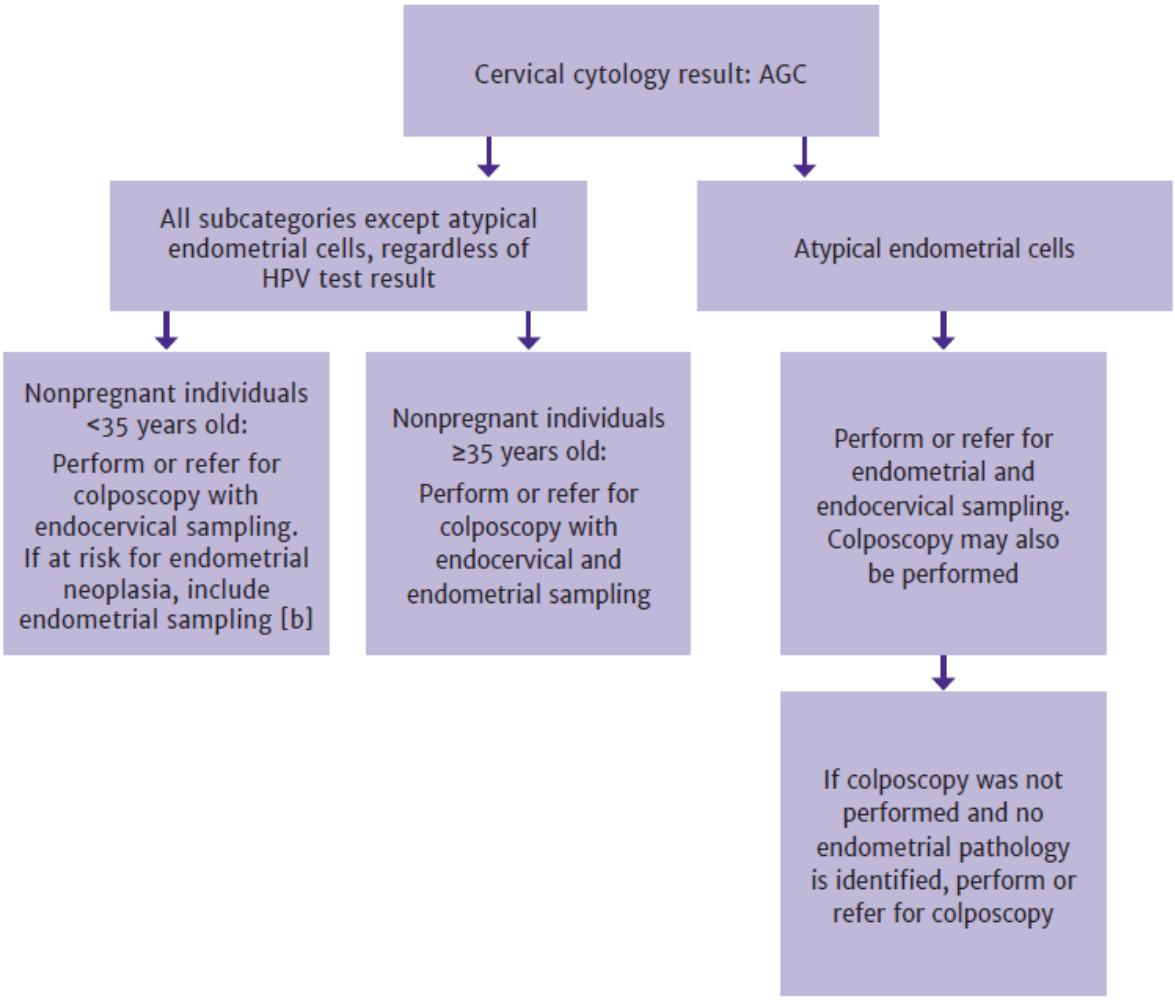
→ KEY POINTS

- Any cervical cytology result of AGC requires immediate follow-up with colposcopy and further evaluation.
- This committee strongly encourages all facilities that provide medical care for patients with HIV to develop a clinical pathway for the screening, diagnosis, and treatment of abnormal anal cytology results.

◊ RESOURCES

- ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors
- ASCCP Management Guidelines App Quick Start Guide
- Department of Health and Human Services Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

Figure 2: Follow-Up for Cervical Cytology Results of AGC in Patients With HIV [a]



Abbreviations: AGC, atypical glandular cells; ASCCP, American Society for Colposcopy and Cervical Pathology; HPV, human papillomavirus.

Notes:

a. Adapted with permission from the ASCCP. See Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2020;24(2):102-131. [PMID: 32243307]

b. Conditions that increase risk for endometrial neoplasia include abnormal uterine bleeding, obesity, or conditions suggesting chronic anovulation.

Management of Cervical Cancer

☑ RECOMMENDATIONS

Management of Cervical Cancer

- Clinicians should *immediately* refer patients with HIV and a diagnosis of cervical cancer to a gynecologic oncologist or surgeon trained in the management of cervical cancer. (A*)
- Clinicians should closely monitor patients with a history of cervical cancer with possible consultation with a gynecologic oncologist after definitive treatment for cancer, which may include surgery, radiation, and chemotherapy. (A3)

Individuals with cervical cancer may have few and nonspecific symptoms; when they do present with symptoms, more advanced disease is often found. Vaginal bleeding and postcoital bleeding are the most common symptoms. Malodorous vaginal discharge, pelvic pain, back pain, and lower abdominal pain are also common. Weight loss, leg pain, edema, and obstructive uropathy indicate advanced disease [ACS 2020]. Patients with a diagnosis of cervical cancer, with or without symptoms, should be referred immediately for assessment and management of their disease. Support services often facilitate patient engagement and maintenance in cancer treatment and care.

The standard therapeutic approach to treating cervical cancer in individuals with HIV is the same for individuals without HIV. Treatment by high-volume surgeons at high-volume hospitals with higher rates of guideline-based care is associated with better cervical cancer survival outcomes [Bonte, et al. 2019; Liu, et al. 2018; Uppal, et al. 2017; ACOG 2016; Showalter, et al. 2016]. Appropriate staging, management, and therapy for cervical cancer should be determined by a gynecologic oncologist or a clinician with similar training and experience. Although the effect of treatment by gynecologic oncology specialists has not been studied among patients with cervical cancer, research suggests that patients with other gynecologic cancers experience better survival outcomes, especially when treated at National Cancer Institute Comprehensive Cancer Centers [Bonte, et al. 2019; Wright, et al. 2017; Bristow, et al. 2015; Minig, et al. 2015; Mercado, et al. 2010].

Management and therapy should be based on the stage of disease. Treatment may include cone biopsy/loop electrosurgical excision, total hysterectomy, radical hysterectomy, radiation therapy, chemotherapy, and combined modality therapy with surgery, radiation, and chemotherapy. The increased risk of treatment failure and high recurrence rate in individuals with HIV demand close follow-up by a multidisciplinary team of clinicians even after definitive treatment for cervical cancer.

All Recommendations

☑ ALL RECOMMENDATIONS: SCREENING FOR CERVICAL DYSPLASIA AND CANCER IN ADULTS WITH HIV

HPV Prevention

- Given the increased lifetime risk of persistent human papillomavirus (HPV) infection and increased prevalence of HPV-related cancers, clinicians should recommend the 9-valent HPV vaccine 3-dose series at 0, 2, and 6 months to all individuals with HIV who are 9 to 45 years old regardless of CD4 cell count, prior cervical or anal screening results, HPV test results, HPV-related cytologic changes, or other history of HPV-related lesions. (A3)

Cervical Cancer Prevention

- In providing comprehensive primary care for adults with HIV, clinicians should ensure that patients at risk of cervical cancer receive age- and risk-appropriate screening (A3) and provide education about harm reduction measures that may reduce the risk, including:
  - HPV vaccination (A2)
  - ART to suppress HIV viral load (A2)
  - Tobacco use cessation (A2)
  - Sexual exposure prevention strategies, including using barrier protection (A3) and reducing the number of sex partners and associated sexual networks when possible (A3)
- Clinicians should establish a schedule for routine cervical screening based on a patient's medical history, anatomical inventory, age, and risk profile. (A2)

Screening for Cervical Abnormalities

- Clinicians should perform an anatomical inventory to identify patients eligible for screening. (A*)
- Clinicians should perform screening for cervical and genital tract dysplasia and cancer in patients with HIV who have or have had a cervix and meet the below criteria for age-based screening. (A2)
- Clinicians should perform physical examinations of the vulva, vagina, and anogenital perineum at least annually and at the time of cervical cytology and to assess interval complaints. (A3) Abnormal cytology results may reflect vaginal, vulvar, or anogenital dysplasia in the absence of cervical dysplasia.

Age-Based Screening

- For patients <30 years old, testing for HPV is not recommended (A2†). For these patients, clinicians should perform cervical cytology within at least 2 years of the onset of receptive sexual activity or by age 21 years, regardless of the mode of HIV acquisition (A2), and if cytology results are normal, repeat testing every 3 years. (A2)
- For patients ≥30 years old, clinicians should perform cytology/HPV cotesting within 3 years of previous testing. (A2) If the baseline cytology and HPV test results are negative, clinicians should repeat both tests every 3 years thereafter. (A2)
- Clinicians should repeat cervical cytology after 2 months but within 4 months after a result of "insufficient specimen for analysis" has been reported. (A3)
- Clinicians should continue cervical cancer screening for patients ≥65 years old; however, factors such as a patient's life expectancy and risk of developing cervical cancer should inform shared decision-making regarding continued screening. (A3)

Concomitant Screening for Anal Cancer and STIs

- Clinicians should perform concomitant anal cytology. If appropriate follow-up of abnormal results is not available within the clinician's institution, a referral plan should be in place.
- Regardless of a patient's cervical cytology results, clinicians should perform routine STI screening.

Post-Hysterectomy Cancer Screening

- In patients with an intact cervix, clinicians should perform cervical cytology as above [a]. (A*)
- In patients with HIV who have undergone total hysterectomy (uterus and cervix removed), clinicians should screen for vaginal intraepithelial neoplasia by performing *vaginal* cytology with HPV cotesting and manage as noted under "age-based screening" above. (A2†)
- If a patient's hysterectomy was performed to treat HSILs, CIN 2 or CIN 3, or AIS [a], clinicians should perform 3 consecutive annual HPV tests, after which long-term surveillance should be initiated, with HPV testing every 3 years for 25 years. (A3)

☑ ALL RECOMMENDATIONS: SCREENING FOR CERVICAL DYSPLASIA AND CANCER IN ADULTS WITH HIV

Post-Cervical Excision HPV Testing

- After a patient has undergone cervical excision, clinicians should perform cervical cytology with HPV testing as follows: at 6 months post-excision, annually until 3 sequential negative test results have been obtained, and every 3 years thereafter for at least 25 years. (A3)

Screening for Cervical Dysplasia During Pregnancy

- Clinicians should perform cervical cytology screening for pregnant patients with HIV as appropriate for each patient's age. (A2†)
- Clinicians should refer pregnant patients for follow-up with experienced colposcopy providers when the following cervical cytology results are obtained: repeated ASC-US, ASC-US with HPV, negative cytology with persistently positive HPV, ASC-H, or LSIL or greater. (A3)
- When cervical dysplasia is diagnosed, clinicians should ensure that patients understand the potential risks and benefits and engage pregnant patients in shared decision-making regarding treatment. (A3)
- Clinicians should follow up on abnormal cytology or colposcopy results, ideally within 6 weeks postpartum. (A2)

Follow-Up of Abnormal Cervical Cytology Results

- When a cervical cytology result of ASC-US is returned for a patient <30 years old or for a patient ≥30 years old who did not receive cotesting [b], the clinician should perform reflex [c] HPV testing. (A2)
- If the reflex HPV test result is positive, the clinician should refer the patient for colposcopy. (A2)
- If the reflex HPV test result is negative, the clinician should repeat both the cervical cytology and HPV testing at 1 year. (A2)
  - If at 1 year the cervical cytology and HPV test results are negative, the clinician should resume standard cervical cytology testing every 3 years. (A2)
  - If at 1 year the cervical cytology result indicates ASC-US and the HPV test result is negative, the clinician should repeat cervical cytology and HPV testing 1 year following (A3); alternatively, if the patient has a history of cervical dysplasia or individual risk factors for cervical cancer, the clinician should refer for colposcopy. (A3)
  - If at 1 year the HPV test result is positive, the clinician should refer the patient for colposcopy. (A2)
- When a patient of any age with HIV has a cervical cytology result of LSIL, HSIL, ASC-H, AGC, or AIS, the clinician should refer for colposcopy regardless of the HPV test result. (A2)

Management of Cervical Cancer

- Clinicians should *immediately* refer patients with HIV and a diagnosis of cervical cancer to a gynecologic oncologist or surgeon trained in the management of cervical cancer. (A*)
- Clinicians should closely monitor patients with a history of cervical cancer with possible consultation with a gynecologic oncologist after definitive treatment for cancer, which may include surgery, radiation, and chemotherapy. (A3)

Abbreviations: AGC, atypical glandular cells; AIS, adenocarcinoma in situ; ART, antiretroviral therapy; ASC-H, atypical squamous cells, high-grade squamous intraepithelial lesions cannot be excluded; ASC-US, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; STI, sexually transmitted infection.

Information on tobacco use and cessation: NYSDOH: Information about Tobacco Use, Smoking and Secondhand Smoke; American Academy of Family Physicians: FDA-Approved Medications for Smoking Cessation

Note:

a. Every possible effort should be made to determine the reason for a patient's hysterectomy and to obtain the pathology report.
b. Cervical cytology with concomitant HPV testing (i.e., cotesting) is recommended for patients with HIV who are ≥30 years old.
c. For individuals <30 years old, a reflex HPV test is performed in response to an abnormal cytology result and not concurrently with cervical cytology.

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Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B. Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.