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NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

Screening for Anal Dysplasia and Cancer in Adults With HIV

Updates, Authorship, and Related Guidelines

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Highlights of changes, additions, and updates in the February 25, 2025 edition	• Global: – Discussion and citations added of 2024 consensus guidelines on anal cancer screening published by the International Anal Neoplasia Society and U.S. Department of Health and Human Services – Epidemiologic data and citations updated • Screening for Anal Disease section: – Recommendations on the timing of anal cancer screening by age and population revised – Table 1 added to outline acceptable anal cancer screening strategies, their specificity and sensitivity, and their benefits and limitations • Follow-Up of Abnormal Anal Cancer Screening Results section: Figure 1 revised to include algorithms detailing appropriate follow-up for all anal cancer screening strategies • Treatment and Follow-Up section: Recommendation on follow-up of patients with a history of high-grade squamous intraepithelial lesions revised
Intended users	New York State clinicians who provide primary care to individuals with HIV who are at risk of developing anal dysplasia and cancer
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Purpose of This Guideline

This guideline on screening for anal cancer and dysplasia in individuals with HIV was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) to inform clinicians in New York State who provide primary care to individuals with HIV about human papillomavirus (HPV)-related anal disease and assist them in identifying opportunities for its prevention, screening, and treatment. Accordingly, this guideline addresses HPV transmission, prevention, and screening and the diagnosis, follow-up, and treatment of HPV-related anal disease.

The goal of this guideline is to provide standards for clinicians in New York State to identify HPV-related anal disease in individuals with HIV and provide currently available treatment and follow-up and to:

- Increase the numbers of New York State residents with HIV who are screened and effectively treated for HPV-related anal and perianal dysplasia.
- Support the NYSDOH Prevention Agenda 2019-2024 by educating care providers on the importance of HPV vaccination and increasing the rate of 3-dose HPV immunization among individuals with HIV.
- Reduce the morbidity and mortality associated with HPV-related anal and perianal disease in individuals with HIV through early identification and treatment of potentially precancerous and cancerous lesions, when treatment is most likely to be effective.

Because data on screening and management of anal dysplasia are limited and conflicting, many of the recommendations included here are based on the expert opinions of experienced clinicians. Results from the Anal Cancer HSIL Outcomes Research (ANCHOR) study have provided additional evidence supporting early identification and treatment of HPV-related anal disease. In the ANCHOR study, progression to anal cancer was significantly reduced in participants who received treatment for high-grade squamous intraepithelial lesions compared with those in the study observation arm [Palefsky, et al. 2022]. Additionally, consensus guidelines on risk-based anal cancer screening were published in 2024 by the International Anal Neoplasia Society [Stier, et al. 2024] and the U.S. Department of Health and Human Services [DHHS 2024]. See guideline section Screening for Anal Disease > Approaches to Screening for further discussion.

HPV-Related Anal Disease in Individuals With HIV

The American Cancer Society estimates there will be 10,930 new cases of anal cancer in 2025 among the general population in the United States: 7,370 in women and 3,560 in men [ACS 2025]. These numbers represent increases since 2024 in cases among women (7,180) and men (3,360) [ACS 2024]. Human papillomavirus (HPV)-associated cancers occur more often among individuals with HIV than in the general population [Thompson, et al. 2018; Jemal, et al. 2013].

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 (MSM), regardless of their HIV status; and among men and women with HIV [Islami, et al. 2017; Palefsky 2017; Hessol, et al. 2013]. Incidence of squamous cell carcinoma of the anus (SCCA) is also rising in the United States in both men and women; distant-stage SCCA incidence tripled and regional-stage SCCA incidence nearly doubled from 2001 to 2015 [Deshmukh, et al. 2020]. HIV seropositivity is associated with an increased incidence of anal cancer in men (hazard ratio [HR], 20.73; 95% confidence interval [CI], 15.60-27.56) and women (HR, 12.88; 95% CI, 8.69-19.07) [Michaud, et al. 2020]. Current incidence rates of SCCA among MSM with HIV are higher than the rates of cervical cancer that prompted the adoption of universal screening of women for cervical dysplasia [Machalek, et al. 2012; Silverberg, et al. 2012; Gustafsson, et al. 1997]. Anal cancer burden is projected to decrease in future years in the United States, with the majority of cases occurring in people with HIV [Deshmukh, et al. 2024].

→ KEY POINTS

- Lower rates of anal cancer screening for people of color have been described and represent inequities in health care [Gillis, et al. 2020].
- Missed opportunities for screening and prevention have been documented in 44% of individuals with anal cancer [Ye, et al. 2021].
- **Resource:** NYSDOH AI Health Equity Competencies for Health Care Providers

HPV Type and Anal Dysplasia

The relationship between specific HPV types and HPV-related anal disease is still being studied. It has been estimated that HPV infection is responsible for approximately 91% of anal cancers, including anal and rectal SCC [CDC(a) 2024]. A wide range and high prevalence of HPV types responsible for oncogenic and nononcogenic HPV-related anal disease has been documented in individuals with HIV [Liu, et al. 2018; Kojic, et al. 2011; Clifford, et al. 2006]. HPV type 16 is the most common high-risk type among individuals with or without HIV [Lin, et al. 2018]. However, among MSM with HIV, many other HPV types are found [AIDSmap 2018]. High-risk HPV types other than type 16 are more common and are more frequently associated with anal cancer among MSM with HIV than MSM without HIV [Poynten, et al. 2021]. Infection with more than 1

HPV type occurs more frequently among individuals with HIV, putting them at risk for cervical, vulvar, perianal, or anal squamous intraepithelial lesions (SILs) and cancer [Castilho, et al. 2015; Clifford, et al. 2006].

→ KEY POINT

- Infection with more than 1 HPV type occurs more frequently among individuals with HIV, and such individuals can be at risk for cervical, vulvar, and perianal or anal SILs.

HIV and Anal Cancer Risk

HIV infection is an independent risk factor for anal high-grade SILs (HSILs) [Sobhani, et al. 2004; Sobhani, et al. 2001] and confers additional risk for the development of anal cancer [Michaud, et al. 2020; Hessol, et al. 2018; Piketty, et al. 2012; Chaturvedi, et al. 2009; Shiels, et al. 2009]. Higher rates of HSILs have been documented among men and women with HIV than among the general population [Darwich, et al. 2013; Mallari, et al. 2012; Silverberg, et al. 2012].

Other risk factors associated with anal dysplasia include hepatitis B virus in MSM with HIV [Aldersley, et al. 2019], lower CD4 cell count [Baranoski, et al. 2012; Tandon, et al. 2010], and cigarette smoking [Poljak, et al. 2017; Bertisch, et al. 2013]. Some data suggest that immune reconstitution due to antiretroviral therapy reduces but does not eliminate the risk of anal cancer [Kelly, et al. 2020; Palefsky 2017; van der Snoek, et al. 2012].

HPV and Anal Dysplasia in Men

Cisgender men: Cisgender men living with HIV, particularly MSM, have higher rates of anal HPV disease than other populations. In a multicenter cohort study, the incidence of anal cancer was higher among MSM with HIV (131/100,000 person-years) than among other men with HIV (46/100,000 person-years) and men who did not have HIV (2/100,000 person-years) [Silverberg, et al. 2012]. A meta-analysis of anal cancer incidence rates in various risk groups found a higher incidence among MSM with HIV (85/100,000 person-years) than among men with HIV who were not MSM (32/100,000 person-years) [Clifford, et al. 2021]. In MSM with HIV, receptive anal intercourse is the most common risk factor for anal cancer, likely reflecting concurrent HPV infection.

As observed in the multicenter cohort study noted above, HIV is also associated with a higher risk of anal cancer among men who have sex with women (MSW), although the risk is lower than for MSM. In a single-center, retrospective cohort study of 221 individuals with HIV, 28% of MSW had abnormal anal cytology results, compared with 48% of MSM [Gandra, et al. 2015]. In that report, most abnormalities were atypical squamous cells of undetermined significance. Among those with abnormal anal cytology or high-risk HPV who underwent high-resolution anoscopy, 39% of MSM, 25% of women, and 12% of MSW had high-grade anal intraepithelial neoplasia, representing 16%, 5%, and 2%, respectively, of the total numbers screened. However, because populations based on sexual practices were not prospectively screened, these data cannot be used to estimate the prevalence of HPV disease to guide a general screening recommendation.

Currently, there are no prevalence data available on anal cancer in transgender MSM with HIV.

HPV and Anal Dysplasia in Women

Cisgender women: Cisgender women with HIV have a higher incidence of anal cancer than cisgender women without HIV. A multicenter study that included 8,842 women with HIV and 11,653 women without HIV reported an anal cancer incidence of 30 per 100,000 person-years among women with HIV and no cases among those without [Silverberg, et al. 2012]. Women with HIV are significantly more likely to have abnormal anal cytology or histology results than women without HIV, with the rates in some studies similar to those reported among men with HIV [Gandra, et al. 2015; Stier, et al. 2015; Baranoski, et al. 2012; Tandon, et al. 2010; Dal Maso, et al. 2009; Hessol, et al. 2009; Frisch, et al. 2000]. A multicenter trial reported a 27% prevalence of anal HSILs among women with HIV [Stier(b), et al. 2020].

Although abnormal cervical cytology results are a risk factor for abnormal anal cytology results, women may have anal dysplasia without concomitant cervical disease. In some studies, the prevalence of HPV-related anal disease was higher than HPV-related cervical disease in women [Liu, et al. 2020; Gaisa, et al. 2017; Kojic, et al. 2011], supporting the recommendation to screen all cisgender women aged ≥45 years with HIV for HPV-related anal disease regardless of cervical cytology (Pap test) results (for discussion of age-based screening, see guideline section Screening for Anal Disease > Approaches to Screening).

Data are inconsistent regarding the role of anal intercourse as a risk factor for anal dysplasia in women with HIV [Stier(b), et al. 2020; Gaisa, et al. 2017; Kojic, et al. 2011; Weis, et al. 2011; Goodman, et al. 2010; Hessol, et al. 2009; Park, et al. 2009; Piketty, et al. 2003; Palefsky, et al. 2001]. Vulvar cancer is associated with an increased risk of anal cancer. In the meta-analysis discussed above, anal cancer incidence was 48 per 100,000 person-years among women diagnosed with vulvar cancer [Clifford, et al. 2021].

→ KEY POINTS

- The absence of HPV-related cervical disease in the genital tract does not eliminate the need to screen for anal dysplasia in cisgender women aged ≥45 years with HIV.
- For individuals diagnosed with vulvar cancer, initiate anal cancer screening with review of symptoms, digital anorectal examination, and anal Pap testing.

Transgender women: Transgender women with HIV also have an increased risk of developing HPV-associated anal disease. Although specific data are not available in this population, screening transgender women at age ≥35 years is warranted, given the similar risks observed among cisgender MSM with HIV. In a study evaluating the anal cytology samples of 62 transgender women, 69% of whom had HIV, 47% had anal dysplasia and 74% had high-risk HPV [Harfouch, et al. 2023].

Progression From Anal Dysplasia to Anal Carcinoma

Progression from anal dysplasia to anal cancer is slower than the progression from cervical dysplasia to cervical cancer [Stewart, et al. 2018; Roberts, et al. 2017; Machalek, et al. 2012]. However, similar to the natural history of cervical cancer, it is generally accepted that anal dysplasia is the precursor to invasive anal carcinoma.

Data supporting the notion of a stepwise progression from low-grade SILs (LSILs) to HSILs to invasive carcinoma are limited, but 2 studies documented a progression to HSILs at the same site as the initial LSILs [Liu, et al. 2018; Berry, et al. 2014]. In a prospective study, 41% of individuals with HIV who had LSILs at baseline developed HSILs during the 20-month follow-up period. The majority (84%) of HSILs were situated at the site of the baseline LSILs [Liu, et al. 2018]. In a retrospective study, anal cancers were documented at the site of previously biopsied HSILs; the average time for progression from diagnosis of HSILs to anal cancer was 5 years [Berry, et al. 2014].

Spontaneous regression of anal dysplasia, including HSILs, has also been described. In a randomized clinical trial, HSILs resolved among nearly one-third of participants in the active monitoring group that did not receive treatment [Goldstone, et al. 2019]. In a retrospective study, HSILs spontaneously regressed in 20% of participants with HIV [Tong, et al. 2013]. Currently, there are no data to guide the assessment of lesions to determine which ones will progress, persist, or regress.

HPV Prevention

☑ RECOMMENDATIONS

HPV Prevention

- Given the increased lifetime risk of persistent human papillomavirus (HPV) infection and increased prevalence of HPV-related cancers, clinicians should recommend the 3-dose nonavalent HPV vaccine series (0, 1–2, and 6 months) to all individuals with HIV aged 9 to 45 years 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)
- Clinicians should promote smoking cessation, optimal virologic control with antiretroviral therapy, and condom use for all patients with HIV, especially those at increased risk for anal cancer. (A3)

HPV Vaccine

The U.S. Food and Drug Administration (FDA) approved a quadrivalent HPV vaccine in 2006 and a nonavalent vaccine (Gardasil 9) in 2014. Because it offers broader coverage of HPV types, the nonavalent vaccine is the only HPV vaccine currently available in the United States (see Centers for Disease Control and Prevention HPV Vaccination Recommendations 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 previously available 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 2024]. There is no specific mention of HIV infection in the updated FDA approval. Although a study demonstrated lower efficacy of the quadrivalent vaccine in individuals with HIV [Wilkin, et al. 2018], other research linked HIV viral suppression to vaccine efficacy [Money, et al. 2016].

When to Vaccinate

HPV vaccination may be scheduled at the same time as standard adolescent vaccines offered at ages 9 to 12 years [CDC(b) 2024]. If possible, the HPV vaccine series should begin at age 9 years. The 3-dose vaccine is recommended for all patients aged 9 to 45 years with HIV. The nonavalent HPV vaccine should be administered according to the CDC standard schedule for immunocompromised adults, children, and adolescents (a 3-dose series at 0, 1–2, 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 aged ≤26 years 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]. In a study conducted in Italy, HPV vaccination after onset of sexual activity in men who have sex with men (MSM) aged <45 years with or without HIV was associated with significantly decreased rates of squamous intraepithelial lesions (SILs). Among vaccinated participants, 54.5% with HIV and 33.3% without HIV had SILs detected, compared with 81.8% and 63.1%, respectively, of unvaccinated participants [Cavallari, et al. 2023].

Vaccination is not expected to change the course of established HPV infection but may prevent infection from other strains that are part of a polyvalent vaccine.

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 nonavalent vaccine; therefore, it is expected that the nonavalent HPV vaccine will be effective against any of the 9 HPV types or any HPV types to which the individual has not been exposed. There may also be beneficial prevention due to cross-reactivity with other HPV types not included in the nonavalent vaccine [Wheeler, et al. 2012].

Revaccination with the nonavalent HPV vaccine is not currently recommended for individuals who previously received the bivalent or quadrivalent HPV vaccine [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 3 doses are given, so there is no need to repeat doses if a scheduled vaccination is missed [CDC(b) 2024].

Other Forms of HPV Prevention

HPV infection is the most common sexually transmitted infection (STI) in the United States, and approximately 85% of people will be infected with at least 1 HPV type during their lifetime [CDC(b) 2024; CDC(c) 2024]. 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 sex partner is unlikely, limiting the number of sex partners may reduce but not eliminate an individual's exposure to HPV [Workowski and Bolan 2015].

→ KEY POINTS

- It is important that clinicians 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, it is important that clinicians inform patients that barrier protection, such as condoms and dental dams, may not fully protect against HPV.

Screening for Anal Disease

☑ RECOMMENDATIONS

Anal Cancer Screening, With Evaluation of Anal Symptoms, Digital Anorectal Examination, and Anal Pap Testing

- For all patients aged ≥35 years with HIV, regardless of HPV vaccination status, clinicians should:
  - Inquire annually about anal symptoms, such as itching, bleeding, palpable masses or nodules, pain, tenesmus, or a feeling of rectal fullness. (A2)
  - Perform a visual inspection of the perianal [a] region. (A3)
  - Provide information about anal cancer screening and engage the patient in shared decision-making regarding screening, including anal cytology before DARE. (A3)
  - Perform DARE annually and whenever anal symptoms are present. (A*)
- Clinicians should evaluate any patient aged <35 years with HIV who presents with signs or symptoms that suggest anal dysplasia. (A3)
- For adults aged ≥35 years who have HIV and are cisgender men who have ever had sex with men (A3), are transgender women (A3), or are transgender men who have sex with men (B3), clinicians should perform or recommend annual (A3) anal cancer screening to identify dysplasia and precancerous and malignant lesions [b].
  - See the NYSDOH AI GOALS Framework for Sexual History Taking in Primary Care.
- For individuals who have been diagnosed with vulvar cancer or vulvar intraepithelial neoplasia grade 3, clinicians should initiate annual anal cancer screening within 1 year of diagnosis to identify dysplasia and precancerous and malignant lesions. (B1)
- For adults aged ≥45 years who have HIV and are cisgender women or are cisgender men or transgender men who have never had sex with men, clinicians should perform or recommend annual anal cancer screening to identify dysplasia and precancerous and malignant lesions. (A3)
  - See Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy for management of abnormal screening test results.
- For individuals with HIV who have undergone solid organ transplant and have no other indication for earlier screening, clinicians should initiate anal cancer screening 10 years after transplant (as recommended for solid organ transplant recipients without HIV; see text) if that occurs earlier than the recommended age for screening. (A3)
- Clinicians should engage in shared decision-making regarding discontinuing screening for anal cancer in individuals whose life expectancy is less than 10 years. (B3)
- For individuals who have 2 consecutive anal screenings that are negative for both high-risk HPV and high-grade dysplasia on cytology, clinicians should perform anal cancer screening every 3 years. (B3)

Abbreviations: DARE, digital anorectal examination; HPV, human papillomavirus.

Notes:

a. The perianal area is a 5 cm radius from the anal verge. In women, the vulvar and perianal areas overlap.
b. Data for some populations, such as nonbinary individuals, are limited.

Approaches to Screening

Anal cancer screening and assessment are modeled after cervical cancer screening: early identification of squamous intraepithelial lesions (SILs), follow-up to monitor for disease progression, and interventions to prevent disease progression and cancer. Based on the available epidemiologic evidence and the benefits of the analogous cervical screening, this committee has recommended anal screening for specific subpopulations of individuals with HIV since 2007.

The Anal Cancer HSIL Outcomes Research (ANCHOR) study, which compared treatment of high-grade SILs (HSILs) with active monitoring of lesions (no treatment) in individuals aged ≥35 years with HIV, found that treatment reduced the rate of progression to anal cancer by nearly 60% [Palefsky, et al. 2022]. These findings confirm the importance of identifying and treating HSILs in patients with HIV. See guideline section Treatment and Follow-Up for further discussion.

Consensus guidelines published by the International Anal Neoplasia Society (IANS) reviewed anal cancer incidence rates by risk category and advocate for screening in groups with incidence rates more than 10-fold that of the general population [Stier, et al. 2024]. As a result, this committee recommends anal cytology screening for individuals aged ≥35 years with HIV who are cisgender men who have ever had sex with men, are transgender women, or are transgender men who have sex with men. Additionally, individuals with HIV who have been diagnosed with vulvar cancer or vulvar intraepithelial neoplasia grade 3 should initiate screening with anal cytology within 1 year of diagnosis. Solid organ transplant recipients should be screened 10 years after transplant if that occurs earlier than the recommended screening age, as recommended for transplant recipients without HIV by the American Society of Transplantation Infectious Diseases Community of Practice [Chin-Hong, et al. 2019]. Adults who have HIV and are cisgender women, cisgender men, or transgender men who have never had sex with men should be screened beginning at age ≥45 years. However, because of stigma, some cisgender men may not disclose having had sex with men; screening some cisgender men who do not report previous sex with men beginning at age 35 years may be considered based on history of sexually transmitted infections and the clinician's assessment of risk.

Specific tests used for anal cancer screening may differ based on the clinician's assessment and access to available testing modalities. Different screening strategies for high-grade anal dysplasia were assessed in 1,620 individuals with HIV [Liu, et al. 2024]; these findings, outlined in Table 1, below, include the sensitivity, specificity, benefits, and limitations of these strategies. Any of the below strategies are acceptable anal cancer screening methods.

Table 1: Anal Cancer Screening Strategies [a]

Screening Strategy	Sensitivity [b]	Specificity [b]	Benefits and Limitations
Anal cytology alone	88% (95% CI, 85–90)	30% (95% CI, 27–33)	Has a high sensitivity but relatively low specificity and generates a large number of HRA referrals
Anal cytology with hrHPV triage	85% (95% CI, 82–88)	47% (95% CI, 44–50)	Generates fewer unnecessary HRAs than some other strategies but includes the second step of hrHPV determination
hrHPV alone	96% (95% CI, 95–97)	27% (95% CI, 25–30)	Has the highest sensitivity but lowest specificity and triggers the most HRA referrals
hrHPV with anal cytology triage	85% (95% CI, 82–88)	48% (95% CI, 44–51)	Generates fewer unnecessary HRAs than some other strategies but includes the second step of cytology
Anal cytology with hrHPV cotesting	89% (95% CI, 86–91)	40% (95% CI, 37–44)	An efficient strategy but requires coordination with laboratory services

Abbreviations: ASC-US, atypical squamous cells of undetermined significance; CI, confidence interval; HRA, high-resolution anoscopy; hrHPV, high-risk human papillomavirus.

Notes:

a. Adapted from [Liu, et al. 2024].
b. For predicting anal high-grade squamous intraepithelial lesions.

Clinicians may perform anal cancer screening for any patient with HIV who has rectal symptoms or who requests it. If clinicians have previously adopted screening for anal cancer, including anal cytology, HRA, and treatment in younger individuals, they may engage their patients in shared decision-making regarding ongoing screening or deferral until indicated age. Considerations that may be weighed in the discussion include cytology results; high-risk HPV status; previously identified HSILs or atypical squamous cells, cannot exclude HSIL (ASC-H); and previous treatment.

Although this committee recommends referral to HRA experts when indicated, the difficulty of the procedure and the training and practice required to develop expertise limit the availability of care providers for referral [Hillman(b), et al. 2016].

→ KEY POINTS

- All anal cancer screening strategies are acceptable, based on resources and available testing.
- Inform patients about the objective of anal cancer screening and risk prevention. It is important to discuss the specifics of the screening procedure and identify patient preferences to support informed decision-making about screening [Schneiderman and Lopetegui-Lia 2020].

Rationale for screening: Anal dysplasia and invasive carcinoma are often asymptomatic. Perianal warts are a risk marker for HPV type 16 infection and abnormal cytology [Cerejeira, et al. 2020]. Five-year survival rates for early stage anal cancer are much higher than for late-stage disseminated disease (84.5% vs. 36.3%) [NCI SEER 2024]. Screening and close follow-up of individuals with HIV and HSILs can detect preneoplastic lesions and cancers early, before clinical presentation of symptoms, and, with appropriate treatment, reduce mortality [Revollo, et al. 2020; Cajas-Monson, et al. 2018; Stewart, et al. 2018]. As noted above, the ANCHOR study showed that treatment of HSILs significantly reduced anal cancer risk among people with HIV [Palefsky, et al. 2022]. A prospective study found that more than half of men who have sex with men (MSM) with HIV reported at least 1 anal symptom, but there was no association between anal symptoms and the presence of HSILs [Goddard, et al. 2019]. In another prospective study of MSM with HIV and HSILs, nearly half of those who developed anal cancer were asymptomatic [Berry, et al. 2014].

The reported rate of anal cancer among individuals with HIV is currently higher than the rate of cervical cancer before the adoption of universal screening programs. Incidence rates of anal cancer among MSM (85/100,000 person-years) and women (22/100,000 person-years) with HIV are comparable to those estimated for colon cancer among individuals aged ≥50 years (50/100,000 person-years) and cervical cancer before Pap screening among women aged ≥35 years (30–40 per 100,000 person-years) [Clifford, et al. 2021]. HIV infection is recognized as an independent risk factor for anal HSILs and progression to anal cancer among MSM and women (see guideline section HPV-Related Anal Disease in Individuals With HIV). It should be noted that anal dysplasia and cancer can develop even in the absence of anal sex or cervical disease; therefore, screening is recommended regardless of additional risk factors.

HPV typing: HPV typing has been used to stratify the risk of cervical cancer and follow-up in women with low-grade cervical disease and post-treatment for high-grade disease. High-risk HPV infection was associated with anal HSILs in several studies [Malagon, et al. 2024; Stier, et al. 2024; Clarke, et al. 2019; Lin, et al. 2018; Machalek, et al. 2016]; among HPV types, HPV16 is strongly associated with higher risk.

A meta-analysis from the National Cancer Institute found overall high sensitivity but low specificity of HPV testing for anal cancer screening, especially in studies limited to MSM with HIV [Clarke and Wentzensen 2018]. A large study conducted mostly in MSM (44% with HIV) found that screening with anal cytology plus high-risk HPV testing significantly improved the sensitivity and negative predictive value beyond cytology alone [Sambursky, et al. 2018]. In a large retrospective analysis, the negative predictive value for high-risk HPV testing was 91% among MSM with and without HIV and women with HIV [Gaisa, et al. 2021].

A prospective study from Brazil confirmed the low rate of HSILs when an anal cytology result of ASC-US was associated with negative high-risk HPV, although the numbers in each subgroup limited statistical power. HSILs were present in 2 of 23 participants (8.7%) with a cytology result of ASC-US who were negative for high-risk HPV, compared with 3 of 9 participants (33.3%) with a cytology result of ASC-US and HPV type 16 or 18 [Kimura, et al. 2021]. Testing for high-risk HPV can reduce the number of HRA referrals for the cytology result of ASC-US.

Currently, HPV testing for anal cancer is not approved by the U.S. Food and Drug Administration and may require laboratory validation; therefore, it may not be available to all care providers.

→ KEY POINT

- The absence of high-risk HPV in the anal canal is associated with a low risk of high-grade dysplasia and anal cancer.

Safety: Screening for anal cancer does have some negative effects but is generally safe. Anal cytology testing is both safe and well tolerated. HRA and biopsy are safe but may be less well tolerated because of discomfort during the procedure and pain and potential bleeding after biopsy. Patients may experience anxiety while waiting for or learning their test results. Careful patient education and explanation of the benefits and nature of the procedures and the meaning of results may help alleviate anxiety and improve tolerability [Russo, et al. 2018]. Some studies have reported higher levels of discomfort or anxiety among some subpopulations, specifically younger MSM and women [De-Masi, et al. 2018; Lam, et al. 2018; Ong, et al. 2018; Leeds and Fang 2016; Steele, et al. 2012].

Cervical screening: Clinicians should follow the recommendations for cervical screening presented in the NYSDOH AI guideline Screening for Cervical Dysplasia and Cancer in Adults With HIV.

When to Conduct Screening

Delayed diagnosis of anal cancer is common [Chiu, et al. 2015; Ristvedt, et al. 2005]; MSM may have benign conditions such as fissures or sexually transmitted infections (STIs) that can mask the diagnosis. The average age at which anal cancer is diagnosed in the general population is in the early 60s. Anal cancer is diagnosed at younger ages (age 40–49 years) in individuals with HIV than in those without HIV [Chiao, et al. 2008; Piketty, et al. 2008]. Because of the low incidence and low pretest probability of anal cancer in people younger than 35 years [Deshmukh, et al. 2017; Brickman and Palefsky 2015], this committee recommends initiating routine anal cancer screening at age 35 years in individuals with HIV who are cisgender men who have ever had sex with men, are transgender women, or are transgender men who have had sex with men, and at age 45 years for those who are cisgender women or are cisgender men who have never had sex with men. The higher incidence of and younger age at anal cancer diagnosis in individuals with HIV, the lack of knowledge about HPV pathogenesis in the anus, and the morbidity associated with delayed diagnosis warrant screening at this younger age to detect abnormalities before progression to cancer.

The upper age limit for anal cancer screening has not been established. Screening for anal cancer can be discontinued based on shared decision-making with the patient when life expectancy is less than 10 years. In individuals with 2 consecutive anal screenings negative for both high-risk HPV and high-grade dysplasia on cytology, screening frequency can be decreased from annually to every 3 years.

Histopathologic Classification of Anal Cytology

Because many parallels exist between cervicovaginal and anorectal screening, the Bethesda Classification System for reporting cervical cytology terminology has been used for reporting anorectal cytology results that may require further follow-up. SILs of the anal squamous mucosa are classified as low grade (LSILs) or high grade (HSILs). An LSIL does not typically progress to cancer, whereas an HSIL (anal intraepithelial neoplasia [AIN] 2/AIN 3) is considered the precursor lesion to invasive carcinoma; however, anal cytology may not correlate closely with histology. Therefore, any abnormal result should prompt the clinician to perform or refer for HRA or histology (via biopsy).

A Pap test result of ASC-US indicates that the lesion cannot be distinguished as low grade or high grade. HPV genotyping is useful to stratify risk. ASC-US lesions require follow-up as described in the guideline section Follow-Up of Abnormal Anal Cancer Screening Results.

Anal Cytology Tests

Baseline and annual anal cytologic screening (i.e., anal Pap testing and clinical assessment) for individuals with HIV have been suggested for many years [Rosa-Cunha, et al. 2011; Conley, et al. 2010; Palefsky, et al. 2005].

Anogenital examination to assess for visible HPV lesions is necessary because HPV can also infect the urethra and the external genitalia [Ehrenpreis and Smith 2018; Leeds and Fang 2016; Tyerman and Aboulafia 2012; Weyers, et al. 2010]. Direct visualization of the perianal skin, anus, and lower rectum (via standard anoscopy) may also reveal lesions.

An anal cytology sample can be obtained by inserting a moistened nylon or polyester swab into the rectum. Cytologic sampling should include the transformation zone [Roberts, et al. 2016]. If anal cytology test results are not adequate for interpretation, for any reason, the test should be repeated. Patients should be advised not to perform an enema or douche before cytologic screening.

Box 1: Performing an Anal Cytology Test

- Perform an anal cytology test *before* using swabs for other sexually transmitted infection testing, using lubricant, or performing digital anorectal examination.
- A moistened nylon or polyester swab may be used to obtain an anal cytology sample according to the laboratory authority's collection instructions (cotton swabs should not be used).
  - For detailed instructions, see University of California San Francisco Anal Neoplasia Clinic, Research and Education Center > Obtaining a specimen for anal cytology.
- Instruct patients to refrain from performing an anal enema or douche, engaging in anal sex, or inserting any objects into the anus for 24 hours before cytologic screening.

Anal cytology testing is a well-validated technique. When compared with anal histology, the sensitivity and specificity of anal cytology are similar to those of cervical cytology [Fox, et al. 2005]. As discussed above, among 1,620 individuals with HIV, anal cytology had a sensitivity of 88% and a specificity of 30% [Liu, et al. 2024]. Studies of self-collected samples for anal cytology are small and demonstrate variable reliability compared with clinician-collected samples [McNeil, et al. 2016; Cranston, et al. 2004]. In a recent study in sub-Saharan Africa, self-collected anal cytology samples were found to be suitable for detecting HPV compared with practitioner-collected samples [Ferré, et al. 2024].

If a rectal swab for anal screening is performed and testing for gonococcal and chlamydial infections is also performed, then swabs can be obtained sequentially, with anal cytologic samples obtained first.

HPV Testing

High-risk HPV is common in individuals with HIV. The absence of high-risk HPV indicates there is no concerning dysplasia. Combining high-risk HPV testing with anal cytology helps identify patients for whom HRA can be deferred. High-risk HPV DNA testing significantly increases sensitivity to detect high-grade dysplasia and cancer when used with anal cytology [Liu, et al. 2024; Gaisa, et al. 2021]. A patient with a cytology result of ASC-US should be assessed for high-risk HPV in the anal canal. If high-risk HPV is present or HPV typing is not available, then HRA is indicated. If high-risk HPV is not found, then HRA can be deferred and annual screening continued [Liu, et al. 2024; Stier, et al. 2024; Gaisa, et al. 2021]. HPV testing alone in lower-risk groups may reduce otherwise unnecessary cytology and HRA referrals.

→ KEY POINT

- For adults aged ≥45 years who have HIV and are cisgender women or are cisgender men or transgender men who have never had sex with men, a tailored and more acceptable approach to screening might be to offer hrHPV 16 testing alone as it has the highest negative predictive value; those who screen negative may repeat hrHPV screening every 2 to 3 years, whereas those who screen positive for HPV 16 would be referred to HRA [Liu, et al. 2024].

Direct Visualization and Biopsy via High-Resolution Anoscopy

Abnormal anal cytology results should be followed by direct visualization via HRA and directed biopsy. As with cervical disease, histology is required to make a diagnosis and guide interventions for anal disease (for a brief description of this procedure, see UCSF Anal Cancer Neoplasia Clinic, Research and Education Center > High Resolution Anoscopy [HRA]).

As with cervical carcinoma, HSILs (the precursors to invasive carcinoma) are generally asymptomatic. Colonoscopy does not screen for anal cancer and is not an acceptable alternative to HRA. Individuals with anal cancer may complain of thickening and irritation of the perianal skin, itching, bleeding, tenesmus, pain with defecation, constipation, change in stool caliber, or pain during receptive anal sex. Anorectal bleeding, the most common presenting symptom of anal cancer, is often mistakenly attributed to hemorrhoids. Only 30% of individuals with anal cancer experience pain or the sensation of an anal mass [Abbas, et al. 2010]. Visual inspection can identify abnormal anal physical findings, such as warts, hypopigmented or hyperpigmented plaques/lesions, or lesions that bleed.

Among individuals with anal warts or other lesions, anal cytology alone may not be adequate to detect HSILs [Papaconstantinou, et al. 2005]. Tissue that has an HSIL may be buried within or under the visible lesion; therefore, it is reasonable to advise HRA for such patients even if cytology is normal, particularly if high-risk HPV is found. Patients with perianal warts may have concurrent intra-anal warts and HSILs. Visual inspection of warts may not correctly predict histologic abnormality. Larger, persistent, or variegated-appearing lesions may require biopsy by trained clinicians to determine histology and exclude HSILs in individuals with HIV.

Digital Anorectal Examination

DARE is recommended as a companion to anal cytology for anal cancer screening. The IANS has developed practice guidelines for DARE [Hillman, et al. 2019]. DARE enables clinicians to feel for masses that may not be evident with direct visualization during anoscopy or HRA. Conversely, a normal DARE result does not rule out anal cancer because it does not provide information about cytologic abnormalities, especially for superficially invasive squamous cell carcinomas (SISCCAs). In a prospective study among MSM with HIV, a palpable mass, area of induration, or ulcer was present in 85% of new cases of anal cancer; the remaining cases were SISCCAs detected solely by HRA visualization and biopsy of vascular changes [Berry, et al. 2014]. For individuals assigned male sex at birth, prostate size and the presence of any nodules should be noted.

Visual examination of perianal skin and DARE are important parts of screening. Changes in sphincter tone or irregularities of the mucosa can indicate potential lesions that may require biopsy. All adults aged ≥35 years with HIV should receive an annual DARE; DARE may be useful for diagnosing intra-anal warts in younger individuals with HIV, but anal cancer is rarely observed in these individuals. Patients with a mass felt on DARE should be referred to an experienced clinician for anoscopy and biopsy.

→ KEY POINTS

- In individuals with HIV, assessment for visible anogenital HPV lesions is part of the annual physical examination.
- If a DARE is performed with anal cytology or HRA, clinicians should obtain the cytologic sample before introducing lubrication into the anal canal. Lubrication may affect the ability to obtain an adequate cytologic sample. DARE may also cause bleeding, which can contaminate the cytologic sample.

Follow-Up of Abnormal Anal Cancer Screening Results

☑ RECOMMENDATIONS

Follow-Up of Abnormal Anal Cancer Screening Results

- Clinicians should refer patients with abnormal anal cancer screening results to a care provider with experience performing high-resolution anoscopy (HRA) and follow up as indicated in Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy. (A3)
- Clinicians should refer patients with suspected anal cancer determined by digital anorectal examination or histology to an experienced specialist for evaluation and management. (A3)
- Clinicians should perform cervical cancer screening for any individual who is not up to date with current cervical screening guidelines. (A3)

The sensitivity, specificity, benefits, and limitations of different anal cancer screening strategies are outlined in Table 1: Anal Cancer Screening Strategies. Unlike cervical cytology, a cytologic diagnosis of anal atypical squamous cells of undetermined significance (ASC-US) with high-risk human papillomavirus (HPV) and low-grade SILs may have a significant risk (60% to 91%) of anal HSILs at biopsy [Darragh and Winkler 2011]. Patients with ASC-US who do not have high-risk HPV do not require HRA, and annual follow-up with anal cytology is appropriate for these individuals. Although the appropriate follow-up for abnormal anal cancer screening results remains an active area of investigation, Figure 1, below, provides a straightforward evaluative approach. Note that if the assay used does not differentiate HPV subtypes 16 and 18, HRA should be performed. Clinicians may elect to use cytology screening or high-risk HPV screening alone and refer all abnormal results, including ASC-US, for HRA.

Abnormal anal cytology test results should prompt repeat cytologic testing or HRA, if available, at 1 year to determine whether abnormal tissue is present that corresponds to the prior screening. Because cervical and anal HPV-related dysplasia may occur simultaneously, cervical cytology should be performed in individuals with HIV who have abnormal anal cytology [Gaisa, et al. 2017; Kojic, et al. 2011].

HRA applies the techniques of standard cervical colposcopy to the examination of the anal mucosa and perianal area and is the preferred method for visualization of the anal canal in otherwise asymptomatic individuals [Berry, et al. 2004; Panther, et al. 2004]. HRA is used to obtain tissue for diagnosis.

Anal cancer screening is a standard of care in New York State for all individuals with HIV. Clinicians and clinical sites that do not provide HRA services should establish a relationship with an experienced HRA practitioner to whom patients may be referred for follow-up. As with colposcopy, HRA is best performed by clinicians who regularly perform the procedure and understand how to evaluate abnormalities. Until a clinician develops the expertise to fully evaluate patients for abnormal anogenital physical findings, referral to an expert is indicated.

Identifying care providers to whom patients can be referred for follow-up HRA-directed biopsy and care may be challenging. Few primary care clinicians currently have expertise in HRA, although the techniques and tools are available in many obstetric, gynecologic, colorectal, and gastrointestinal clinics, practices, and training programs. The International Anal Neoplasia Society offers virtual HRA courses and has developed practice guidelines for the detection of anal cancer precursors [Hillman(a), et al. 2016]. Alternatively, gynecologists, nurse practitioners, and physician assistants who have experience performing cervical colposcopy can learn the techniques necessary to perform the procedure in the anus. Clinicians experienced in HRA can also train other interested clinicians outside of a formal course. The procedure should be performed regularly to maintain expertise.

Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy [a]

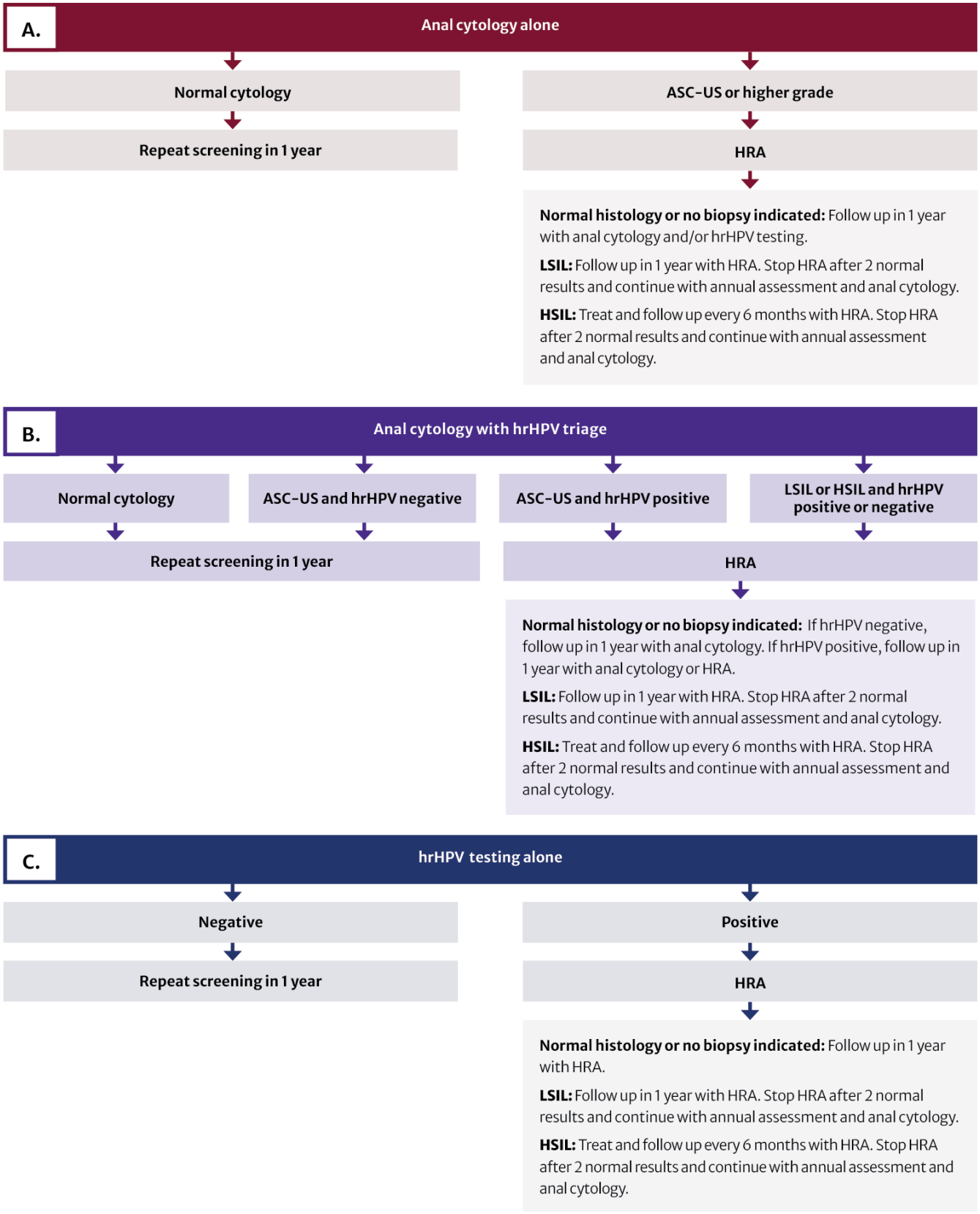
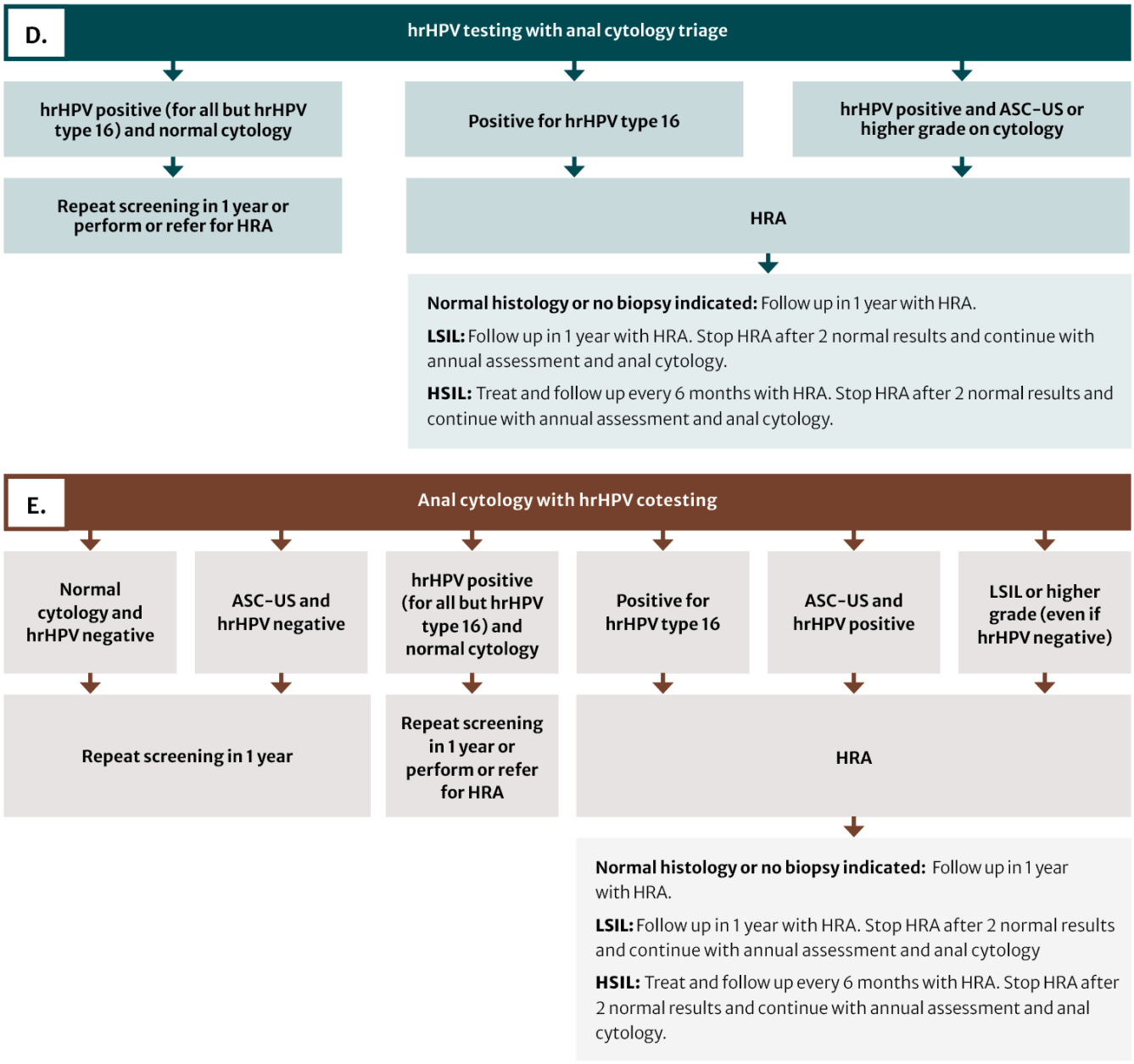


Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy [a], *continued*



Abbreviations: ASC-US, atypical squamous cells of undetermined significance; hrHPV, high-risk human papillomavirus; HRA, high-resolution anoscopy, HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

Note:

a. Adapted from International Anal Neoplasia Society guidelines [Stier, et al. 2024].

Treatment and Follow-Up

☑ RECOMMENDATIONS

Anal HSILs

- Clinicians should perform or refer for post-treatment follow-up with repeat HRA at 6 months in patients who have been successfully treated for anal HSILs. (A3)
- Clinicians should base follow-up after a patient's first post-treatment HRA and biopsy on the most recent histopathology findings (see Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy). (A3)
- For patients with a history of HSILs, clinicians should continue annual HRA or annual anal cancer screening, with referral for HRA if screening results are abnormal, as long as life expectancy exceeds 10 years (A3), until 2 consecutive anal screenings are negative for both high-risk HPV and high-grade dysplasia on cytology, after which clinical assessment and anal cancer screening should be performed every 3 years. (B3)

Anal Cancer

- Clinicians should immediately refer patients diagnosed with anal cancer to an oncologist or surgeon trained in the management of anal cancer. (A2)
- Clinicians should closely monitor patients with anal cancer in collaboration with the oncologist after definitive treatment for cancer. (A3)

Abbreviations: HRA, high-resolution anoscopy; HPV, human papillomavirus; HSILs, high-grade squamous intraepithelial lesions.

Once an HSIL has been identified, ablation is indicated. As previously noted, findings of the Anal Cancer HSIL Outcomes Research (ANCHOR) study confirm that expectant management of HSILs is no longer appropriate and all HSILs should be treated. The ANCHOR study, a randomized clinical trial that included 4,446 participants, compared treatment of HSILs with active monitoring of lesions (no treatment) in individuals aged ≥35 years with HIV [Palefsky, et al. 2022]. The study was stopped early because of the "public health importance of the findings" [ANCHOR 2021], and the investigators found that treatment of HSILs significantly reduced the rate of progression to anal cancer by nearly 60%, with a median follow-up of 25.8 months; two-thirds of cancers were at stage 1 or 2 in trial participants [Palefsky, et al. 2022].

Treatment and ablation of anal HSILs: Treatment of HSILs may include topical medications (e.g., topical trichloroacetic acid, imiquimod, and fluorouracil), local destruction with infrared coagulation or electrocautery ablation (hyfrecation), and surgical excision, which should be performed by a clinician with expertise in managing anal dysplasia. Hyfrecation is generally preferred in practice. The effectiveness of treatment to prevent recurrence or disease progression remains uncertain. Follow-up with repeat HRA is recommended at 6 months after treatment. After the initial post-treatment HRA, subsequent follow-up should be based on histopathologic findings, especially those of the most recent HRA. The most appropriate follow-up is repeat HRA with biopsy, with or without anal cytology.

Some studies have shown high rates of persistence or recurrence of HSILs after treatment with HRA and ablation [Gaisa, et al. 2020; Stier(a), et al. 2020; Goldstone, et al. 2011; Pineda, et al. 2008; Chang, et al. 2002]. However, the sole available randomized clinical trial that compared infrared coagulation ablation with active monitoring (no treatment) of HSILs among adults with HIV reported a significantly higher rate of complete or partial clearance of HSILs in the treatment group (82% vs. 47%) [Goldstone, et al. 2019]. No cases of anal carcinoma were reported among participants, possibly because of the relatively short (1-year) follow-up period.

Treatment for anal cancer: Treatment modalities for anal cancer may include radiation therapy, chemotherapy, excision, or combined modalities. Evidence-based recommendations on the management of anal cancer, including staging, choice of treatment, and surgical intervention, are beyond the scope of this guideline. An oncologist experienced in the management of anal cancer in individuals with HIV can address specific approaches to treatment of tumors based on size [Touboul, et al. 1994; Schlienger, et al. 1989; Boman, et al. 1984], invasiveness, and presence of residual or recurrent disease [Allal, et al. 1999; Pocard, et al. 1998; Bartelink, et al. 1997].

All Recommendations

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

HPV Prevention

- Given the increased lifetime risk of persistent HPV infection and increased prevalence of HPV-related cancers, clinicians should recommend the 3-dose nonavalent HPV vaccine series (0, 1–2, and 6 months) to all individuals with HIV aged 9 to 45 years 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)
- Clinicians should promote smoking cessation, optimal virologic control with antiretroviral therapy, and condom use for all patients with HIV, especially those at increased risk for anal cancer. (A3)

Anal Cancer Screening, With Evaluation of Anal Symptoms, Digital Anorectal Examination, and Anal Pap Testing

- For all patients aged ≥35 years with HIV, regardless of HPV vaccination status, clinicians should:
  - Inquire annually about anal symptoms, such as itching, bleeding, palpable masses or nodules, pain, tenesmus, or a feeling of rectal fullness. (A2)
  - Perform a visual inspection of the perianal [a] region. (A3)
  - Provide information about anal cancer screening and engage the patient in shared decision-making regarding screening, including anal cytology before DARE. (A3)
  - Perform DARE annually and whenever anal symptoms are present. (A*)
- Clinicians should evaluate any patient aged <35 years with HIV who presents with signs or symptoms that suggest anal dysplasia. (A3)
- For adults aged ≥35 years who have HIV and are cisgender men who have ever had sex with men (A3), are transgender women (A3), or are transgender men who have sex with men (B3), clinicians should perform or recommend annual (A3) anal cancer screening to identify dysplasia and precancerous and malignant lesions [b].
  - See the NYSDOH AI GOALS Framework for Sexual History Taking in Primary Care.
- For individuals who have been diagnosed with vulvar cancer or vulvar intraepithelial neoplasia grade 3, clinicians should initiate annual anal cancer screening within 1 year of diagnosis to identify dysplasia and precancerous and malignant lesions. (B1)
- For adults aged ≥45 years who have HIV and are cisgender women or are cisgender men or transgender men who have never had sex with men, clinicians should perform or recommend annual anal cancer screening to identify dysplasia and precancerous and malignant lesions. (A3)
  - See Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy for management of abnormal screening test results.
- For individuals with HIV who have undergone solid organ transplant and have no other indication for earlier screening, clinicians should initiate anal cancer screening 10 years after transplant (as recommended for solid organ transplant recipients without HIV; see text) if that occurs earlier than the recommended age for screening. (A3)
- Clinicians should engage in shared decision-making regarding discontinuing screening for anal cancer in individuals whose life expectancy is less than 10 years. (B3)
- For individuals who have 2 consecutive anal screenings that are negative for both high-risk HPV and high-grade dysplasia on cytology, clinicians should perform anal cancer screening every 3 years. (B3)

Follow-Up of Abnormal Anal Cancer Screening Results

- Clinicians should refer patients with abnormal anal cancer screening results to a care provider with experience performing HRA and follow up as indicated in Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy. (A3)
- Clinicians should refer patients with suspected anal cancer determined by digital anorectal examination or histology to an experienced specialist for evaluation and management. (A3)
- Clinicians should perform cervical cancer screening for any individual who is not up to date with current cervical screening guidelines. (A3)

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

Anal HSILs

- Clinicians should perform or refer for post-treatment follow-up with repeat HRA at 6 months in patients who have been successfully treated for anal HSILs. (A3)
- Clinicians should base follow-up after a patient's first post-treatment HRA and biopsy on the most recent histopathology findings (see Figure 1: Follow-Up of Anal Cancer Screening Results, by Screening Strategy). (A3)
- For patients with a history of HSILs, clinicians should continue annual HRA or annual anal cancer screening, with referral for HRA if screening results are abnormal, as long as life expectancy exceeds 10 years (A3), until 2 consecutive anal screenings are negative for both high-risk HPV and high-grade dysplasia on cytology, after which clinical assessment and anal cancer screening should be performed every 3 years. (B3)

Anal Cancer

- Clinicians should immediately refer patients diagnosed with anal cancer to an oncologist or surgeon trained in the management of anal cancer. (A2)
- Clinicians should closely monitor patients with anal cancer in collaboration with the oncologist after definitive treatment for cancer. (A3)

Abbreviations: DARE, digital anorectal examination; HRA, high-resolution anoscopy; HPV, human papillomavirus; HSILs, high-grade squamous intraepithelial lesions.

Notes:

a. The perianal area is a 5 cm radius from the anal verge. In women, the vulvar and perianal areas overlap.
b. Data for some populations, such as nonbinary individuals, are limited.

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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.
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.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
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.