

Screening and treatment of HPV lesions to reduce anal cancer: ANCHOR results and implications

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Disclosures

No conflicts of interest or relationship to disclose.

I will discuss off-label product uses.

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Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.



To Learn More:

<https://www.cdc.gov/minorityhealth/racism-disparities>

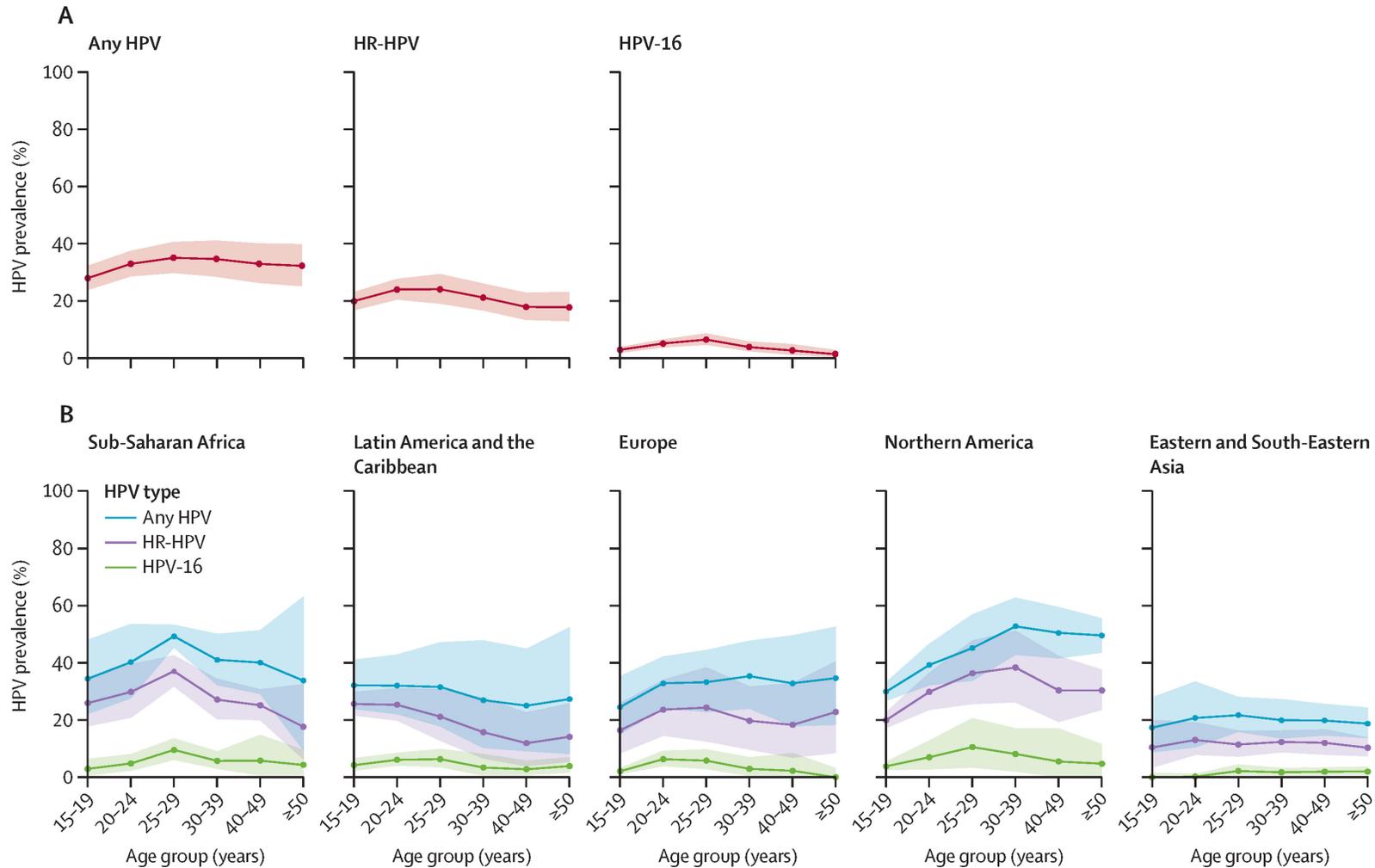
Outline

- Overview of HPV and anal cancer risks
- Contemporary terminology
- Digital anorectal exam (DARE)
- The high resolution anoscopy (HRA) exam
- Design, endpoints, results, and implications of the ANCHOR study
- Possible screening algorithms
- Implementation challenges

HPV infection is very common

- Almost *one in three men* worldwide are infected with at least one genital HPV type and around *one in five men* are infected with one or more HR-HPV types.
- HPV prevalence is high in men over the age of 15 years and support that sexually active men, regardless of age, are an important reservoir of HPV genital infection.
- These estimates emphasise the importance of incorporating men in comprehensive HPV prevention strategies to reduce HPV-related morbidity and mortality in men and ultimately achieve elimination of cervical cancer and other HPV-related diseases.

Age-specific prevalence of genital HPV infection in men



HPV prevalence in women is impacted by HPV vaccination

This study measured whether HPV vaccination has been associated with reduced infection rates among recently born vaccinated women (vaccine-mediated immunity) and unvaccinated women (herd protection), HPV prevalence was compared in the 1980s vs the 1990s birth cohorts and a prevaccination period vs a recent period.

This cross-sectional study analyzed data from 2 cycles (2005-2006 and 2015-2016) of the National Health and Nutritional Examination Survey (NHANES)—a stratified multistage probability sample of the civilian population in the US.

Demographic characteristics, including immunization history and race and ethnicity were self-reported and collected by trained interviewers during a home interview.

Participants provided self-collected cervicovaginal swab specimens that were evaluated by a polymerase chain reaction test and followed by type-specific hybridization.

HPV prevalence in women is impacted by HPV vaccination

Study findings suggest that HPV vaccination was associated with a reduction in HPV-16/18 infection prevalence among a *recent* birth cohort of vaccinated and unvaccinated 18- to 26-year-old women.

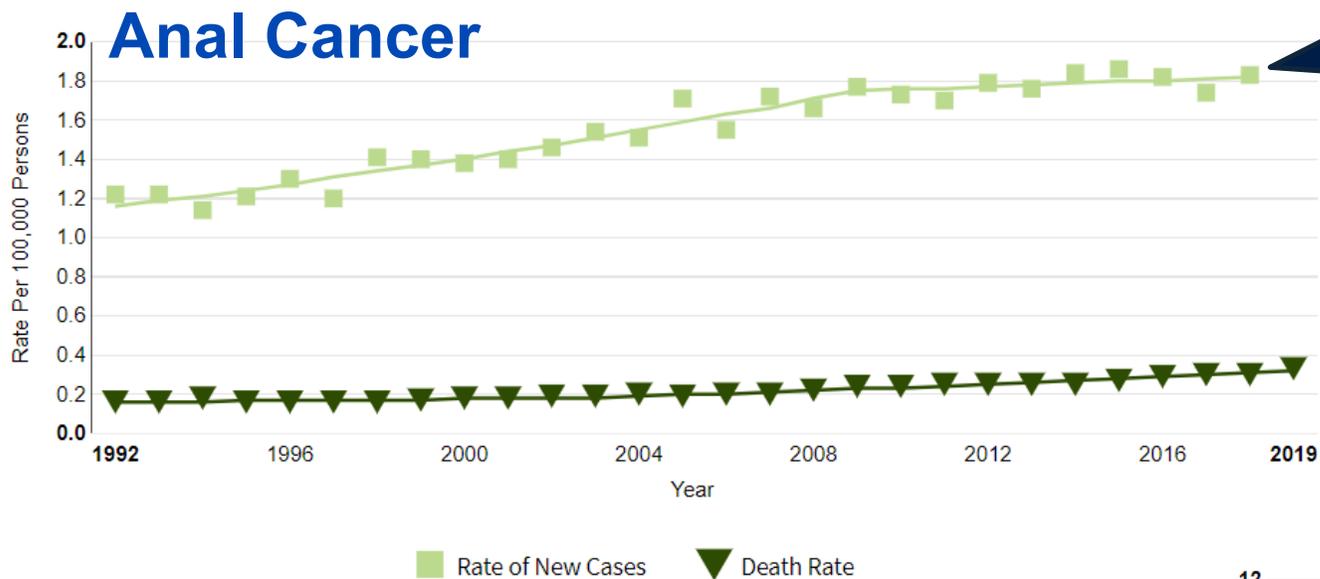
A larger decline in the prevalence of HPV-16/18 infection among 18- to 20-year-old women during the 2015–2016 time period may reflect *greater direct and herd protection* from broader HPV vaccination coverage.

Furthermore, this study provides a birth cohort perspective and suggests a change in the age distribution of HPV-16/18 prevalence.

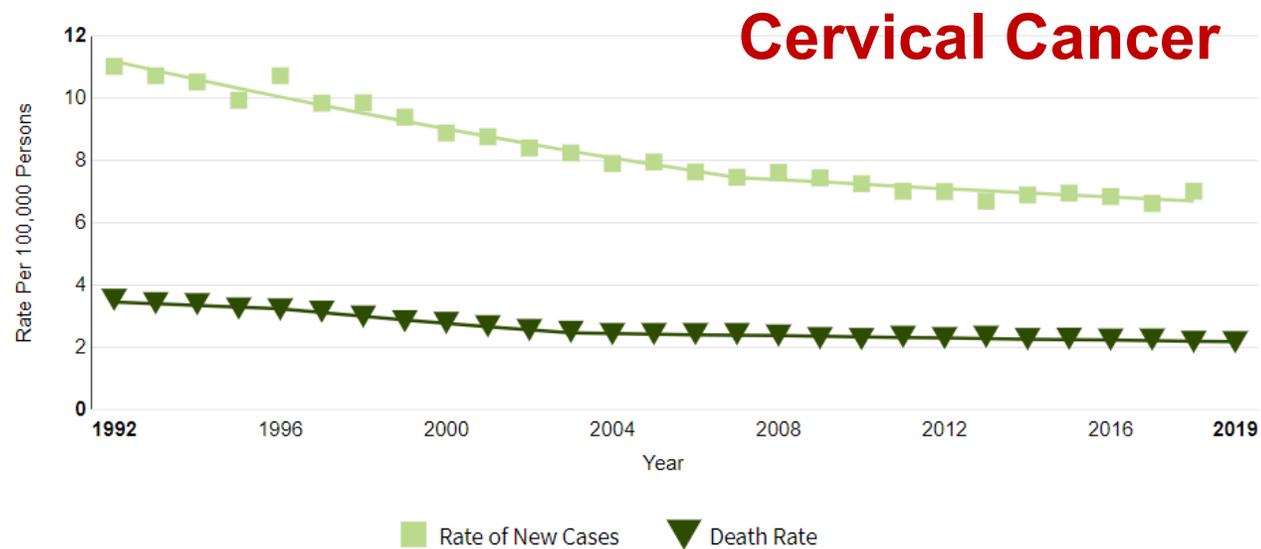
Study limitations are the use of self-reported HPV vaccination status and exclusion of HPV types not covered by the vaccine.

Historically in the US, HPV infection prevalence among women has followed a log-normal distribution pattern, with the peak observed among young age groups. This foundational concept may need to be reevaluated for HPV-16/18 infection, given the recent peak shift that was observed.

Incidence of invasive anal and cervical cancer in the U.S.

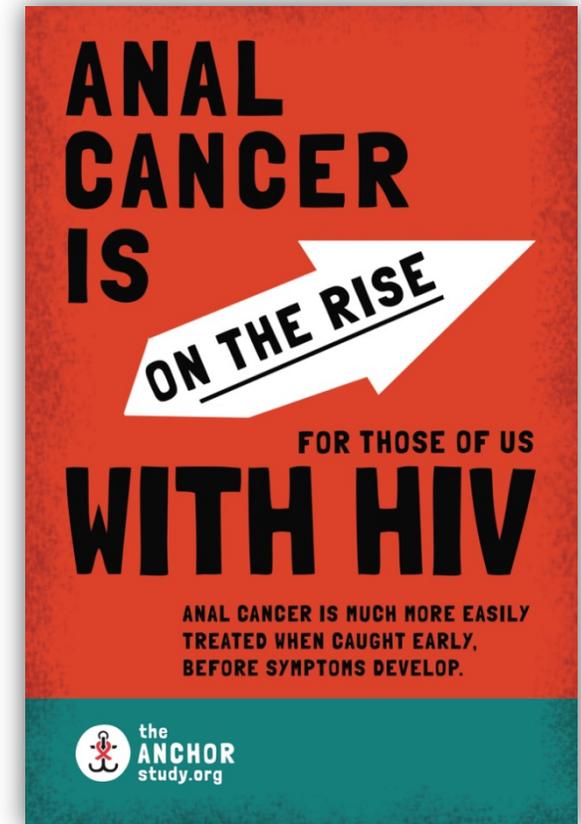


Incidence has not decreased with improved HIV viral suppression.

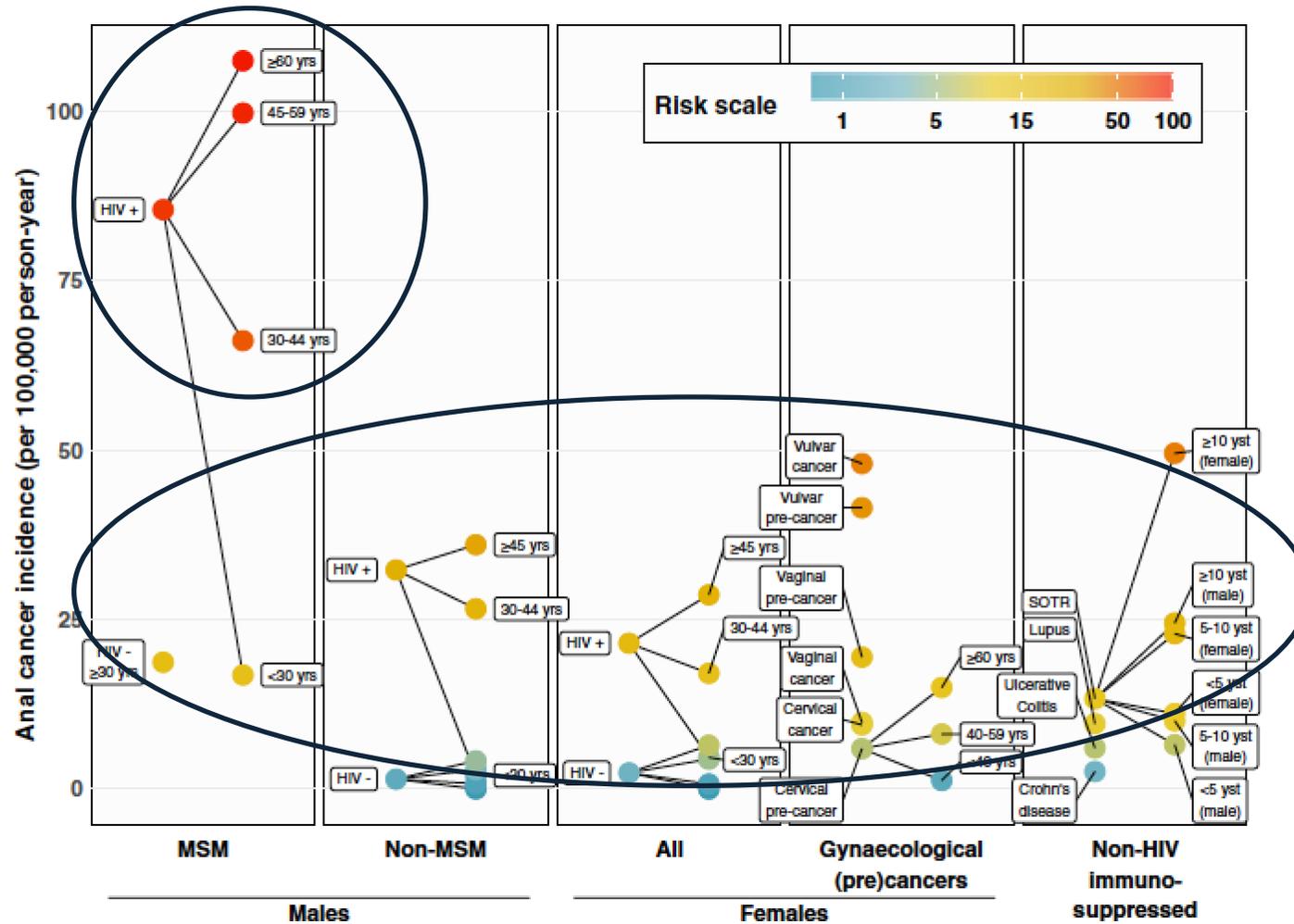


What We Know About Anal Cancer

- Anal cancer is more frequent among HIV+ men and women than the general population.
- Men who have sex with men (MSM) are 35 times more likely to develop anal cancer.
- HIV+ men who have sex with men (MSM) are 80-130 times more likely to develop anal cancer than HIV- men.
- Anal cancer incidence is rising among HIV+ men and women despite HAART.
- Anal cancer is preceded by precancerous cells called "high-grade squamous intraepithelial lesions" = HSIL



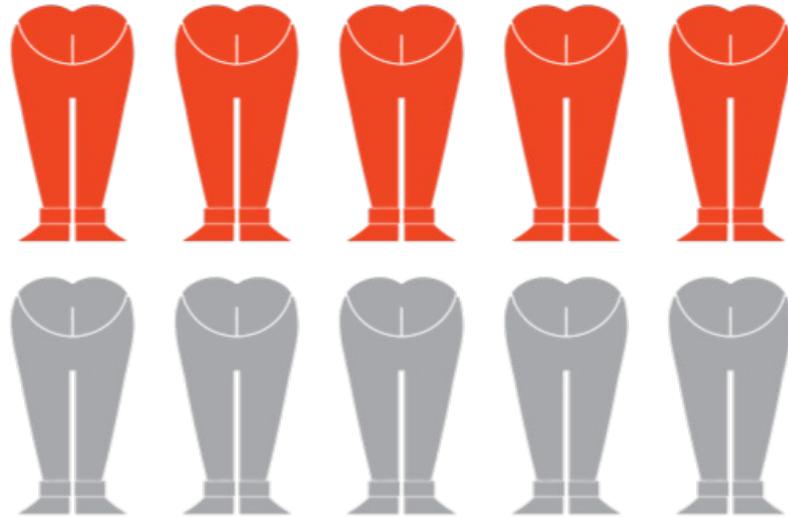
Anal cancer risk scale



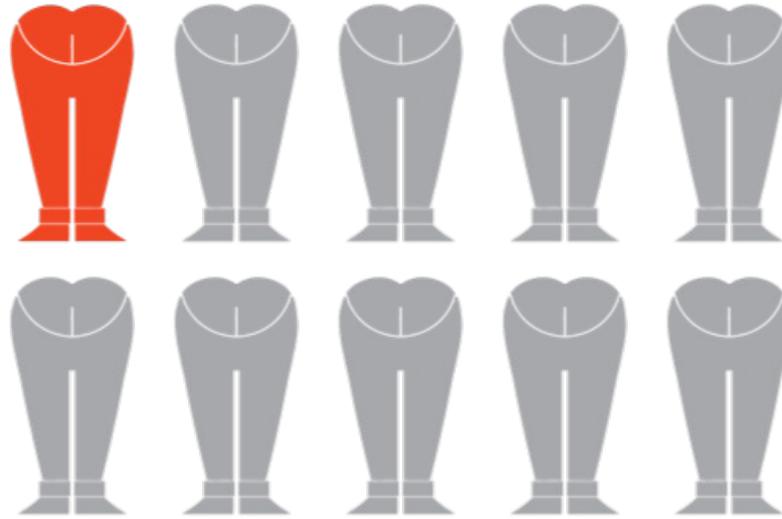
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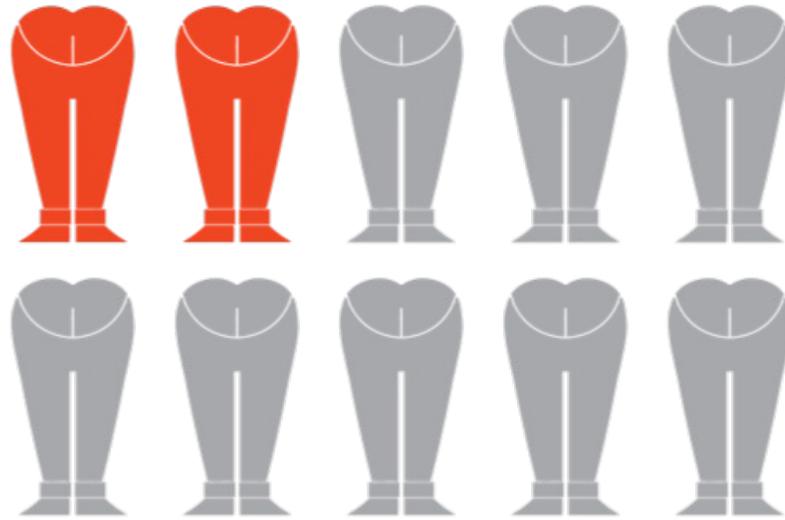
Among HIV+ MSM, 5 Out of 10 Asymptomatic Men Have Anal HSIL



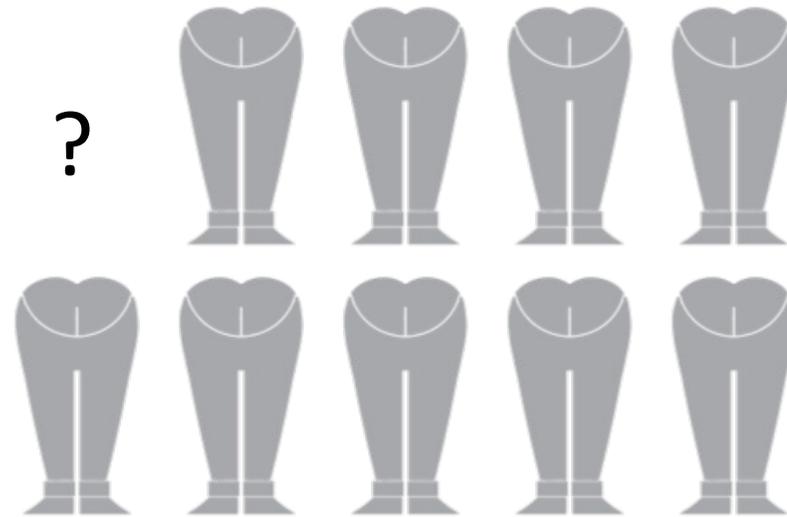
It Is Estimated That 1 In 10 HIV+ MSM Will Get Anal Cancer Over Their Lifetime



Among HIV+ Women, It Is Estimated That 2 Out of 10 Have Anal HSIL

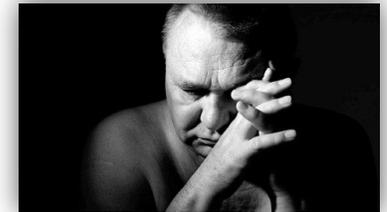
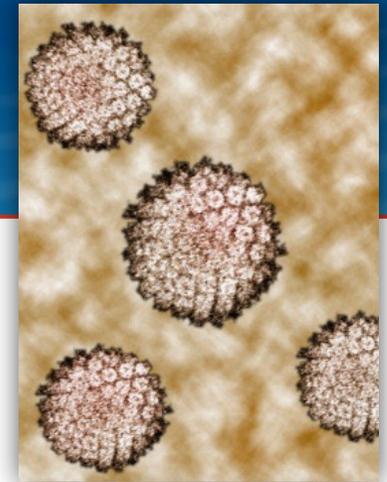


It is Not Known How Many HIV+ Women Will Get Anal Cancer

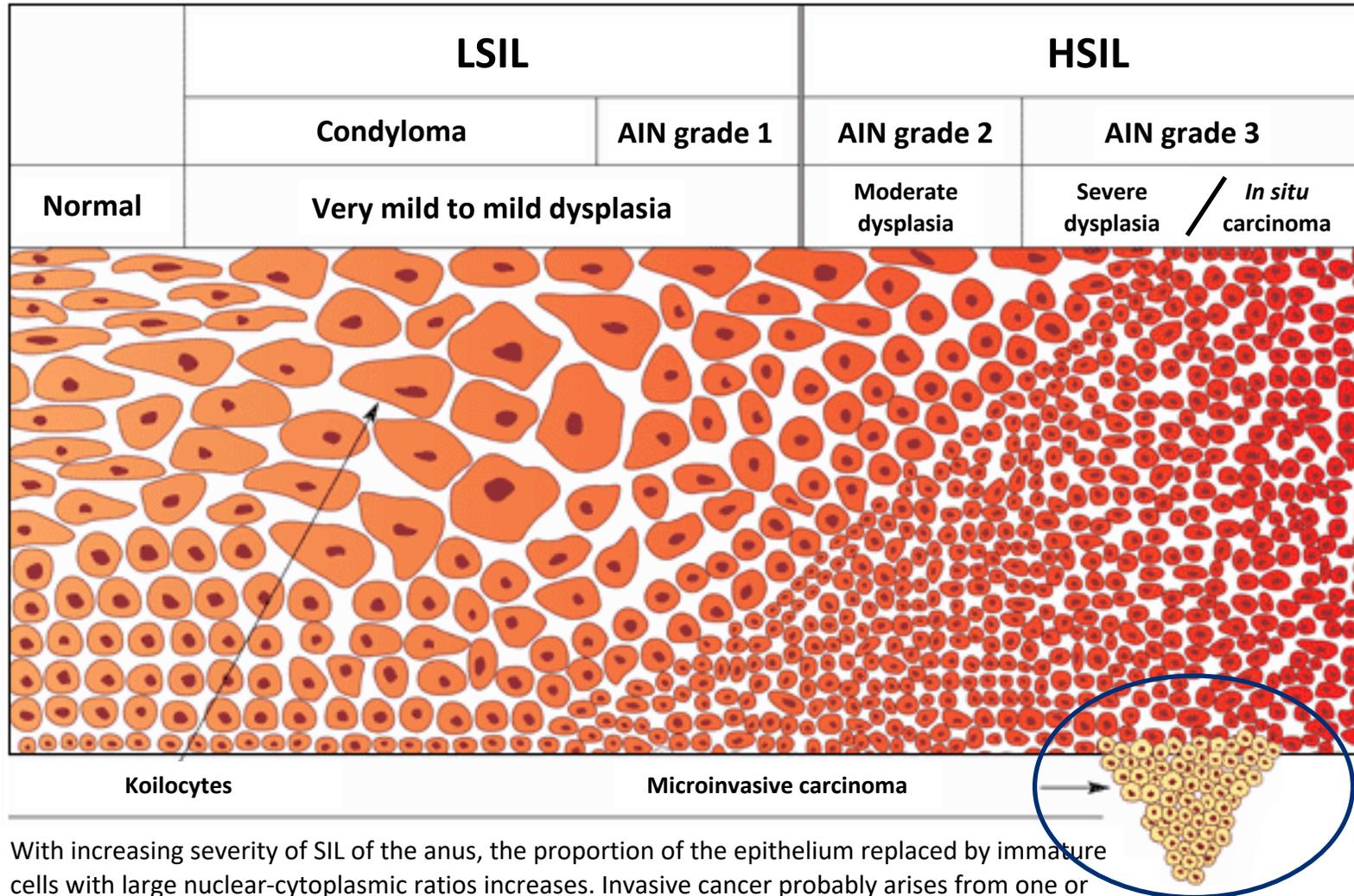


Known Risk Factors for Anal Cancer

- Infection with oncogenic strains of HPV (i.e., HPV 16 and 18)
- Older age
- History of having a low CD4+ cell count (nadir CD4)
- Smoking
- Cervical and vulvar HSIL and cancers
- History of genital warts



Continuum of HPV Neoplasia



With increasing severity of SIL of the anus, the proportion of the epithelium replaced by immature cells with large nuclear-cytoplasmic ratios increases. Invasive cancer probably arises from one or more foci of HSIL, as depicted in the drawing by epithelial cells crossing the basement membrane below the region of HSIL.

Digital Anorectal Exam (DARE)

WHAT IS A DARE?

A DARE is an extension of DRE. However, unlike a DRE, a DARE also includes palpation of the entire anal canal and visualization/palpation of the anal margin (defined as 5 cm distal to the anal verge). In addition to the situations listed hereinafter, consideration should also be given to performing DARE whenever DRE is routinely performed.

TABLE 1. Groups Who May Potentially Benefit From DARE, With Proposed Frequencies

Group	Minimum ^a proposed DARE frequency
Those with symptoms suggesting anal cancer such as: bleeding, anal/perianal mass, tenesmus, pain, altered bowel habit (read, Read et al., 2013) ³⁸	Immediately, with referral for anoscopy, HRA, or to a colorectal specialist if the initial DARE is negative
HIV-positive MSM	At least annually in men ≥ 35 y
Those with demonstrated cytologic or histologic anal HSIL	At least annually
Those with a history of treated anal squamous cell carcinoma	Every 4 mo after completion of radiation for first 2 y, then every 6 mo for the next 3 y, then at least annually (Wright et al., 2010) ³⁹
Other immunosuppressed populations, such as other groups with HIV infection and recipients of solid organ transplants	At least annually in those ≥ 50 y
HIV-negative MSM	Every 2 to 5 y in those ≥ 50 y
Women with a history of cervical, vulvar or vaginal neoplasia or cancer	Every 2 to 5 y, depending on further risk assessment (Moscicki et al., ¹⁵ 2015)

Colonoscopy may miss anal canal lesions and performing a DARE potentially provides an opportunity to assess the anal canal while the patient is sedated.

^aFrequency may increase, depending on risk assessment, such as anal history, degree of immunosuppression, age, and smoking status.

High-Resolution Anoscopy (HRA): Examination

- Thorough exam with biopsies, 15-20 minutes
- Areas to be examined:
 - SCJ
 - AnTZ
 - Anal Canal
 - Anal Verge
 - Perianal Skin

Satisfactory exam = ALL aspects viewed completely

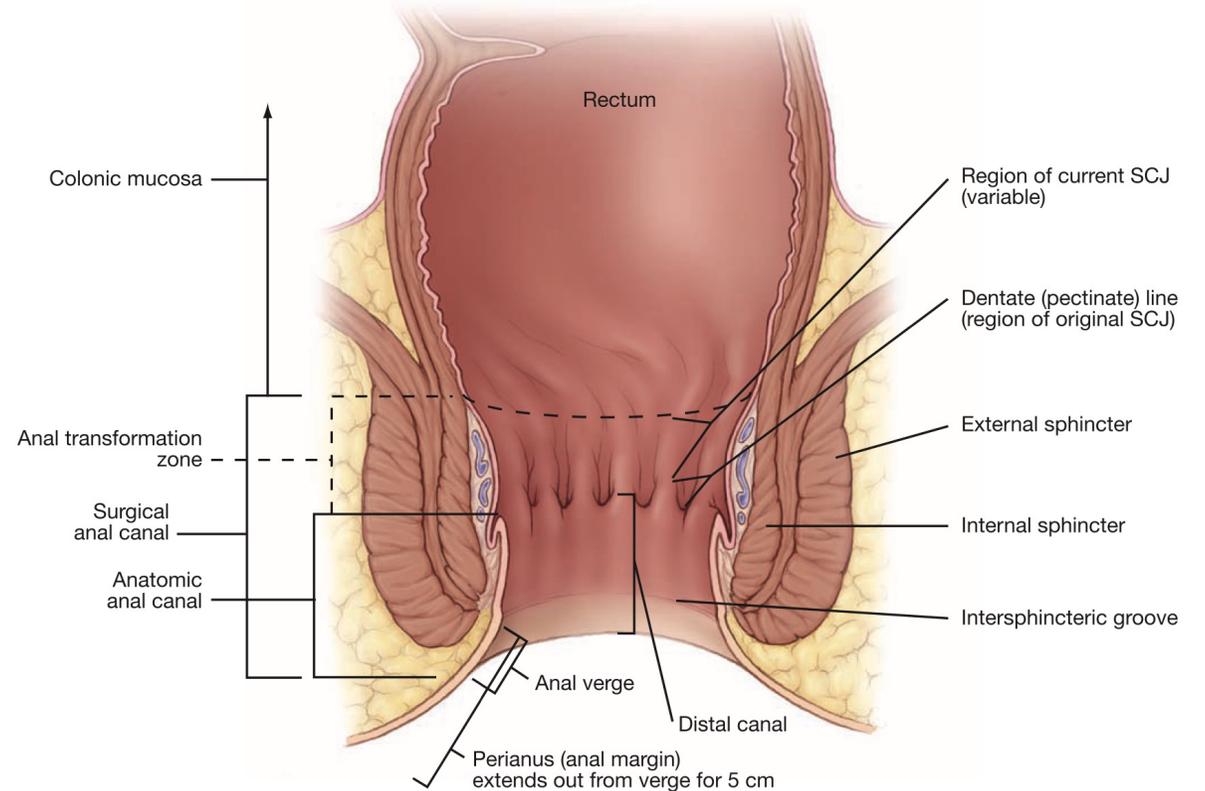
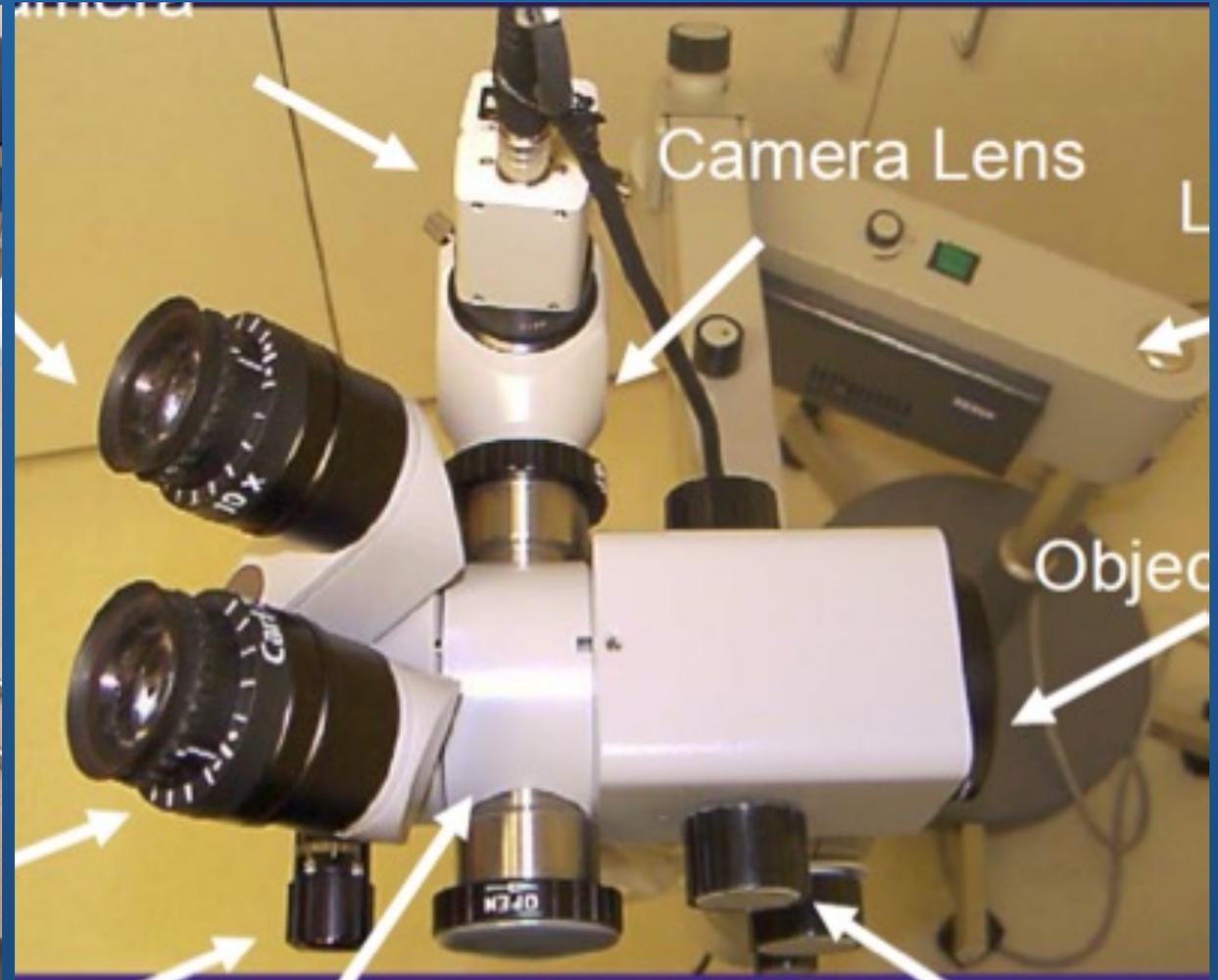


FIGURE 17.16. Anatomy of the anal canal.

Anoscope with Image Capture



Essential Equipment for Procedures

- Proper exam table (usually done in left lateral decubitus position- some do it in the prone position)
- Dacron or polyester swabs
- Cytology Thinprep fixative, formalin
- Anoscopes (disposable)
- 5% Acetic acid, Lugol's & Monsel's solutions, 80% trichloroacetic acid
- K-Y Jelly, 4-5% lidocaine gel
- Non-sterile scopettes, Q-tips, gauze
- Forceps: Baby or Baby Tischlers, flexible endoscope forceps, ENT forceps
- 1-2% injectable lidocaine with epinephrine, 8.4% sodium bicarbonate, 0.25% bupivacaine, 27-gauge straight needles, 1-3cc syringes

Procedures



Cytology Collection

Digital Anorectal Exam

High Resolution Anoscopy

Biopsy

How to Perform an Anal Cytology (Pap Smear)

1. Prior to the DARE- gently spread the buttocks and insert tap water (or sterile water) moistened Dracon swab until it bypasses the internal sphincter and abuts the distal wall of the rectum.



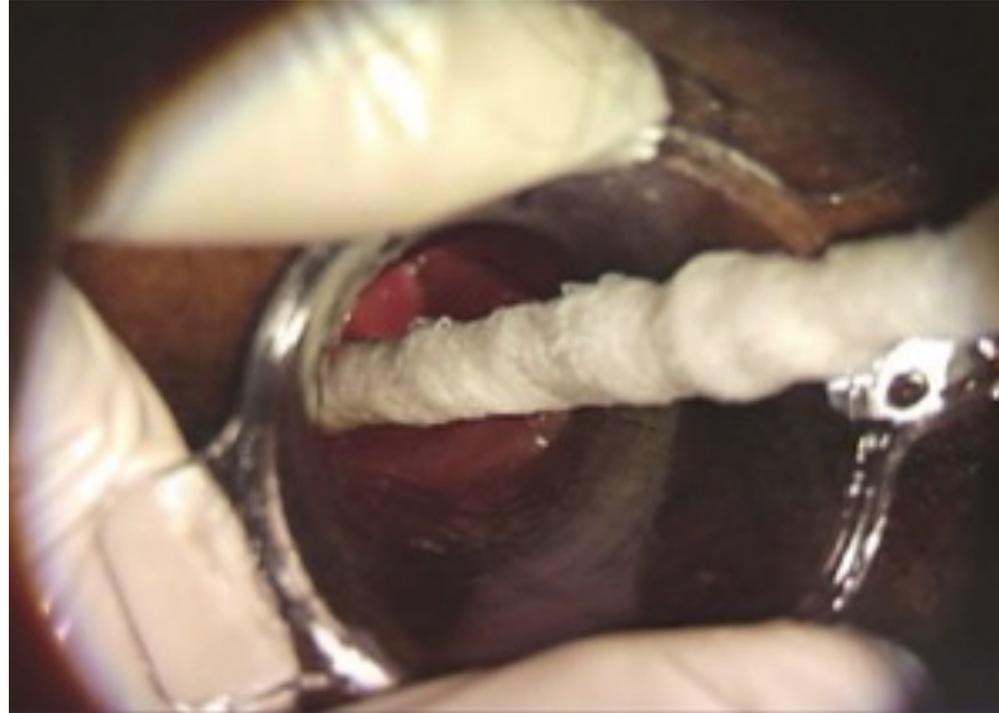
Anal Cytology (con't)

2. Sweep in a circular fashion as the swab is withdrawn in order to sample cells from all aspects of anal canal. Count to 10 as withdrawn-sweeping the sides of the anal canal. Vigorously shake in the Thinprep solution for 20 seconds. Discard the swab. (*Order non-Gyn cytology and select anal swab.*)



HRA (con't)

6. After the DARE insert Q-tip wrapped in gauze soaked in acetic acid through anoscope.



HRA (con't)

7. Remove anoscope leaving the gauze & Q-tip inside. Also place an ascetic acid-soaked gauze at the anal verge. Soak for 1-2 minutes.



HRA (con't)

8. Remove gauze and exam the perianal skin and anal verge thoroughly through the colposcope (10-16 power) with the patient holding the right buttock up. Then re-insert anoscope.
9. Observe through colposcope (16 to 25 power) slowly withdrawing the anoscope until the SCJ starts to come into focus.



Standard terminology for lesion locations- also relative to the SCJ and distance from the SCJ to the anal verge (Not by the clock)

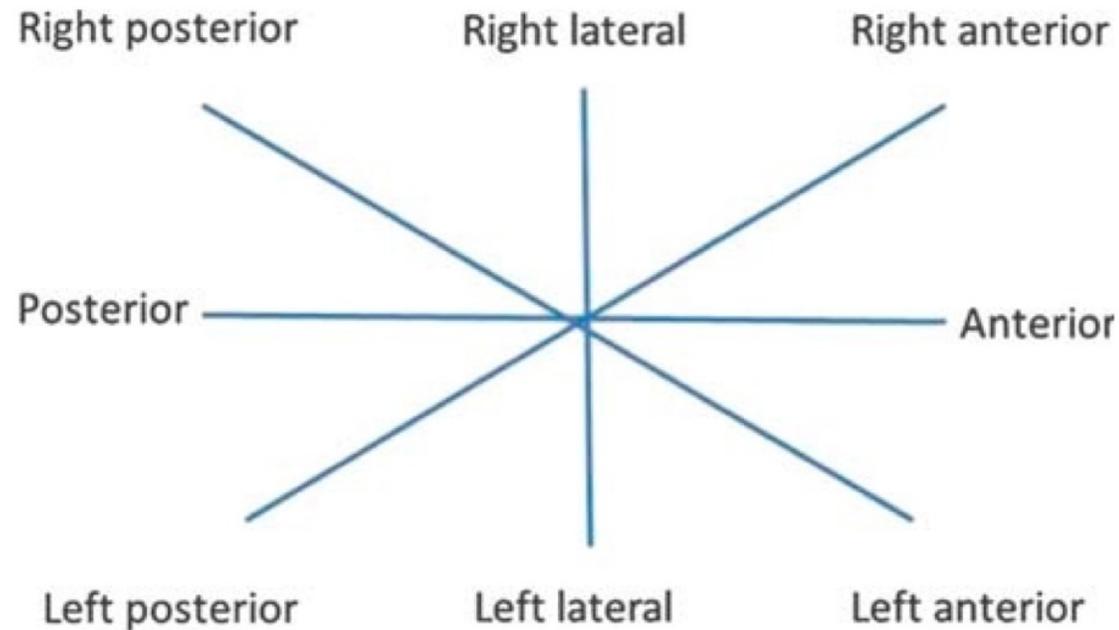


FIGURE 2. Location descriptors (for patient in the left lateral position). Note: The location of these descriptors are markedly different if the patient is in a prone or lithotomy position.

SCJ and the Transformation Zone

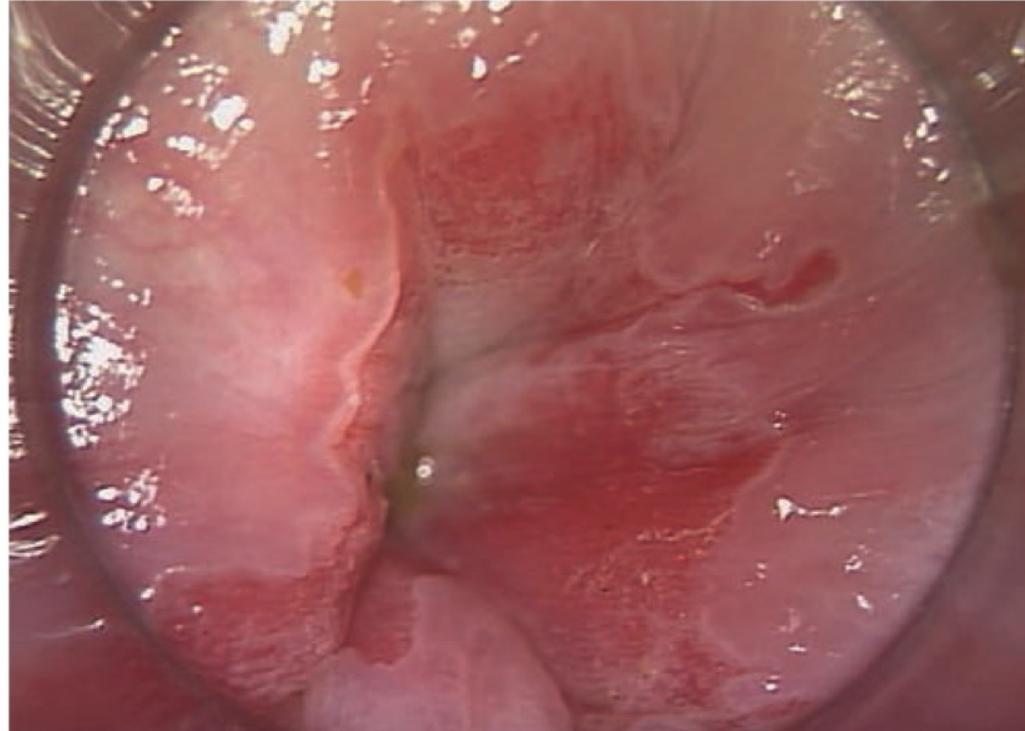
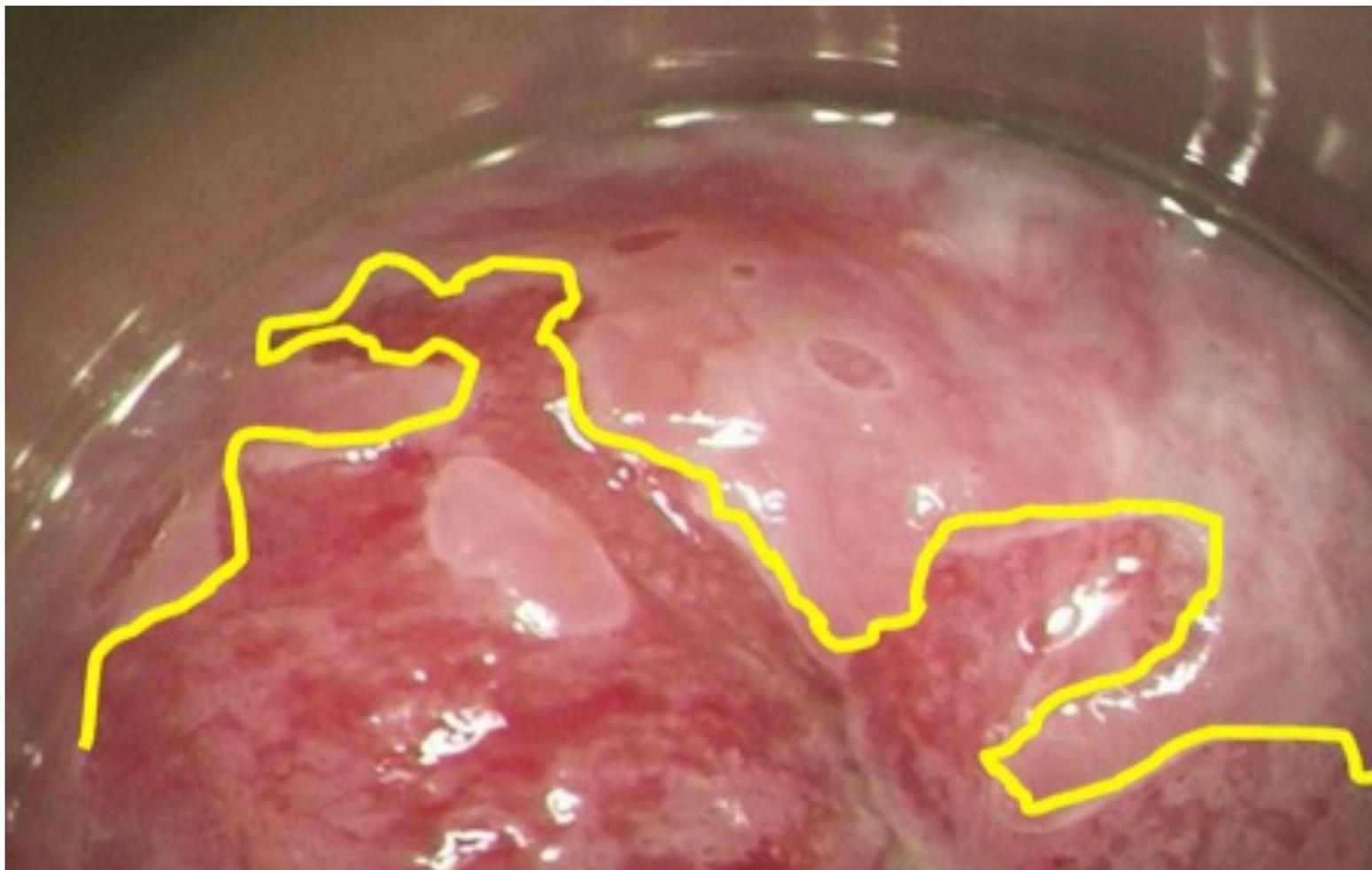


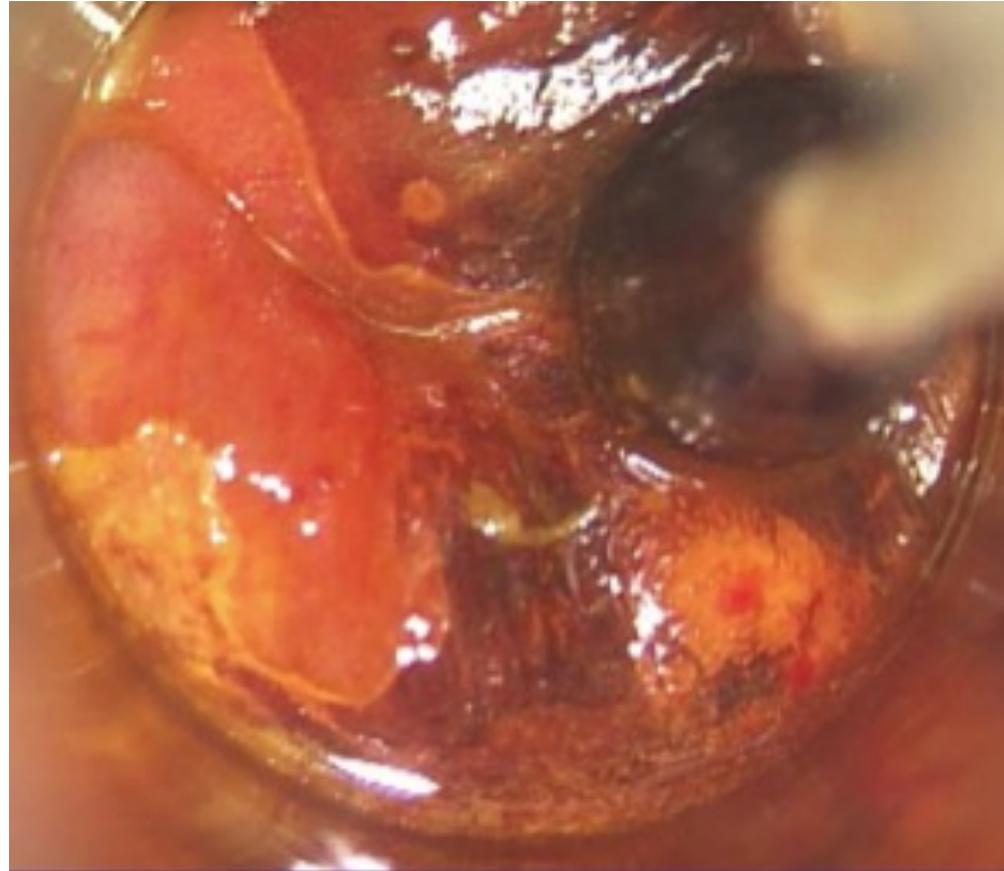
FIGURE 17.22. Rectal columnar epithelium and anal squamous epithelium abut at the SCJ. Note that the rectal mucosa is dark red compared to the lighter pink color of the anal epithelium. The AntZ here is seen as a thin, white line of metaplasia.

Squamocolumnar Junction (SCJ)



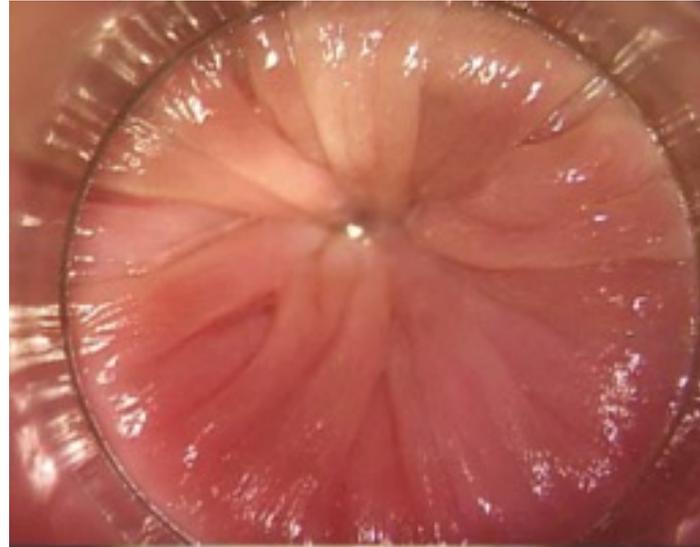
HRA (con't)

11. Apply Lugol's solution after identifying all aspects of AnTZ with acetic acid.



HRA (con't)

13. Observe the distal anal canal and verge as you withdraw the anoscope.



14. Wipe off lube, apply vinegar to perinatal region and examine on lower power.



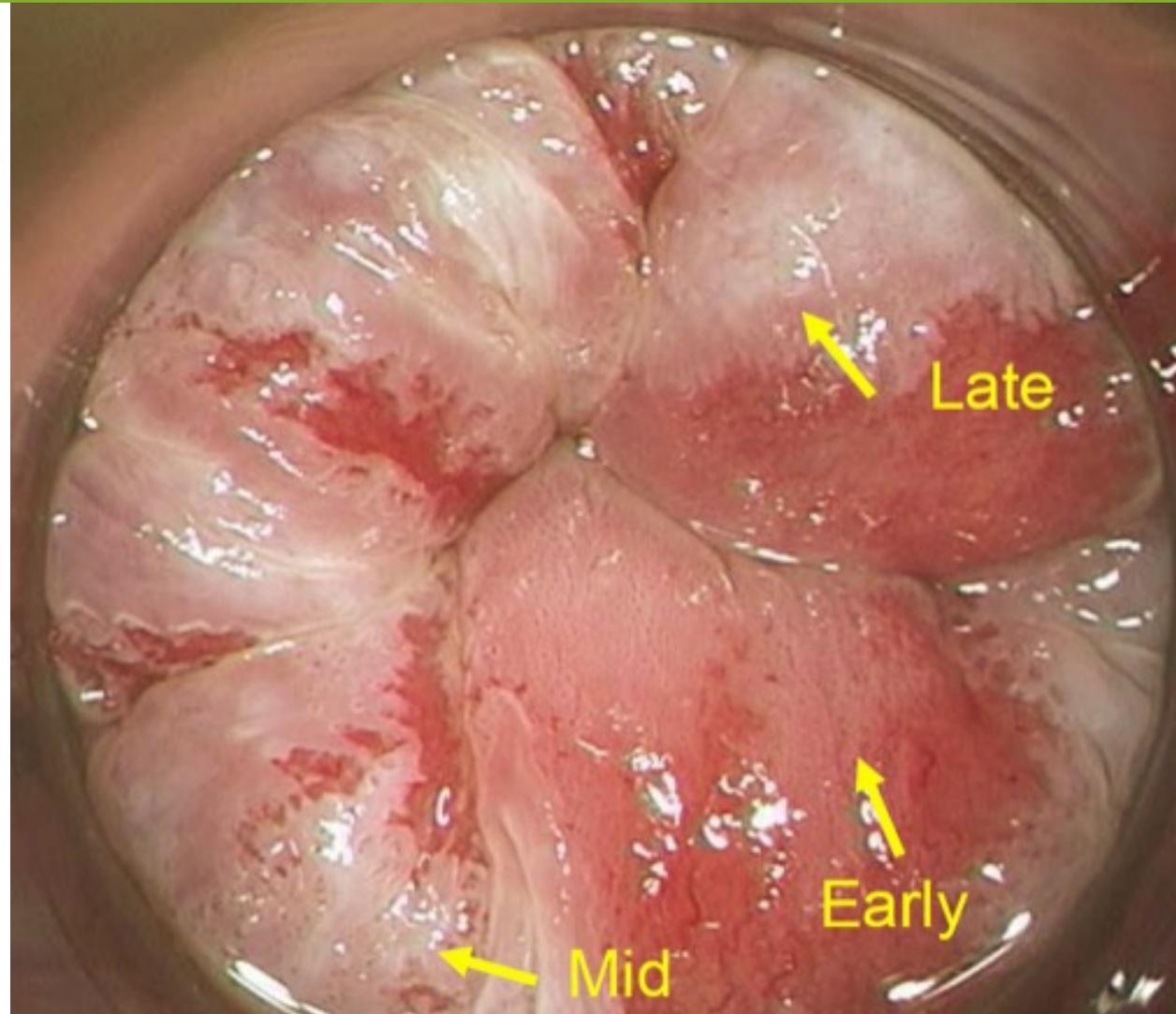
Standard terminology for lesion descriptors

TABLE 3. Description of Lesion Characteristics

Category	Characteristic	Description
Contour	Flat	No elevation or minimal thickening, may be irregular or uneven
	Raised	Exophytic, verrucous, thickened, often in association with papillary changes
Surface patterns	Smooth	Even, without texture
	Granular	Irregular, coarse, or gritty
	Papillae	Thin, finger-like projections, often with warty looped vessels
	Micropapillae	Slightly raised projections, similar to papillae but flattened in comparison, small capillary vessels may be present
Vascularity	Punctuation	End-on view of dilated capillary vessels creating dotted pattern, which maybe fine or coarse
	Mosaic pattern	Tile-like pattern of connected vessels, even or uneven, fine or coarse and thickened
	Warty vessels	Looped capillary vessels often within papillae or verrucous lesions
Margins	Distinct	Well-demarcated borders, sharply defined, may have internal margins
	Regular	Symmetrical, straight, or smooth outline
	Indistinct	Feathery, borders lacking clarity
Lugol stain	Negative	No iodine uptake, yellow
	Partial	Variable iodine uptake, speckled appearance of yellow and brown
	Complete	Mahogany brown coloring, uniform uptake

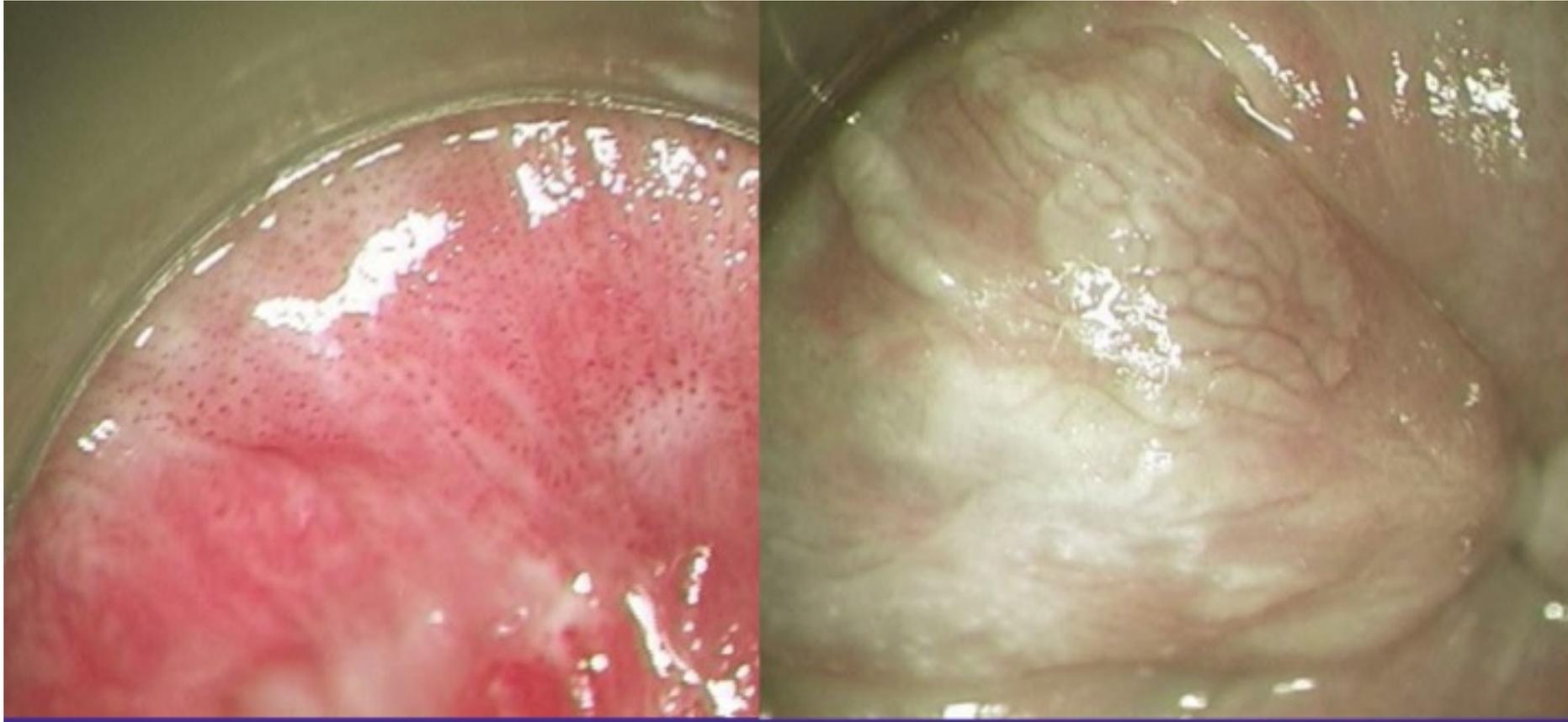
(Adapted from Jay [Jay N, 2015]).

Squamous Metaplasia



Slide from ASCCP HRA Course

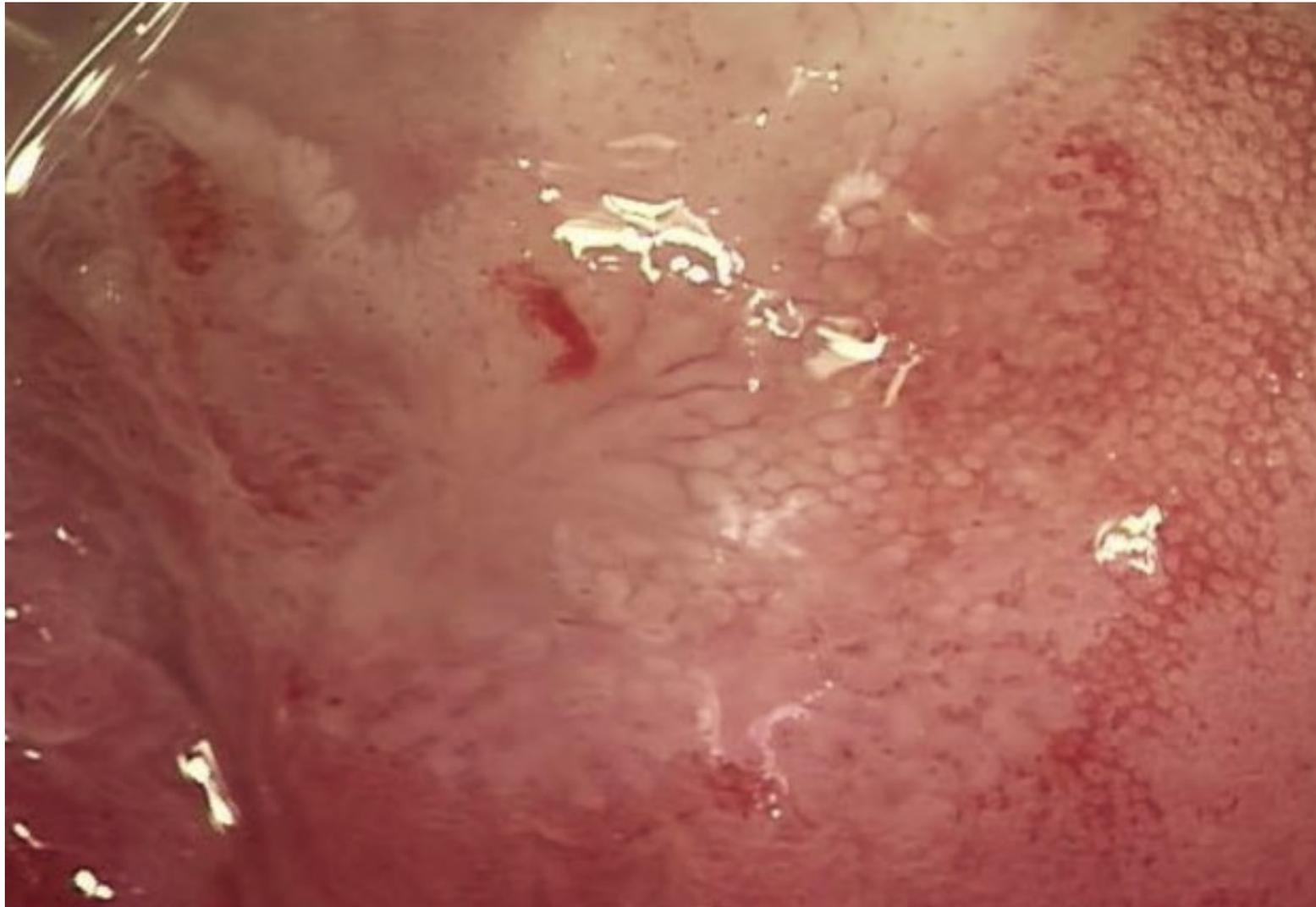
HSIL Vessels



Punctuation

Mosaic Pattern

HGAIN (AIN 3) with Coarse Punctation and Mosaicism



HGAIN (AIN 3) with striated vessels and “lacey metaplasia”

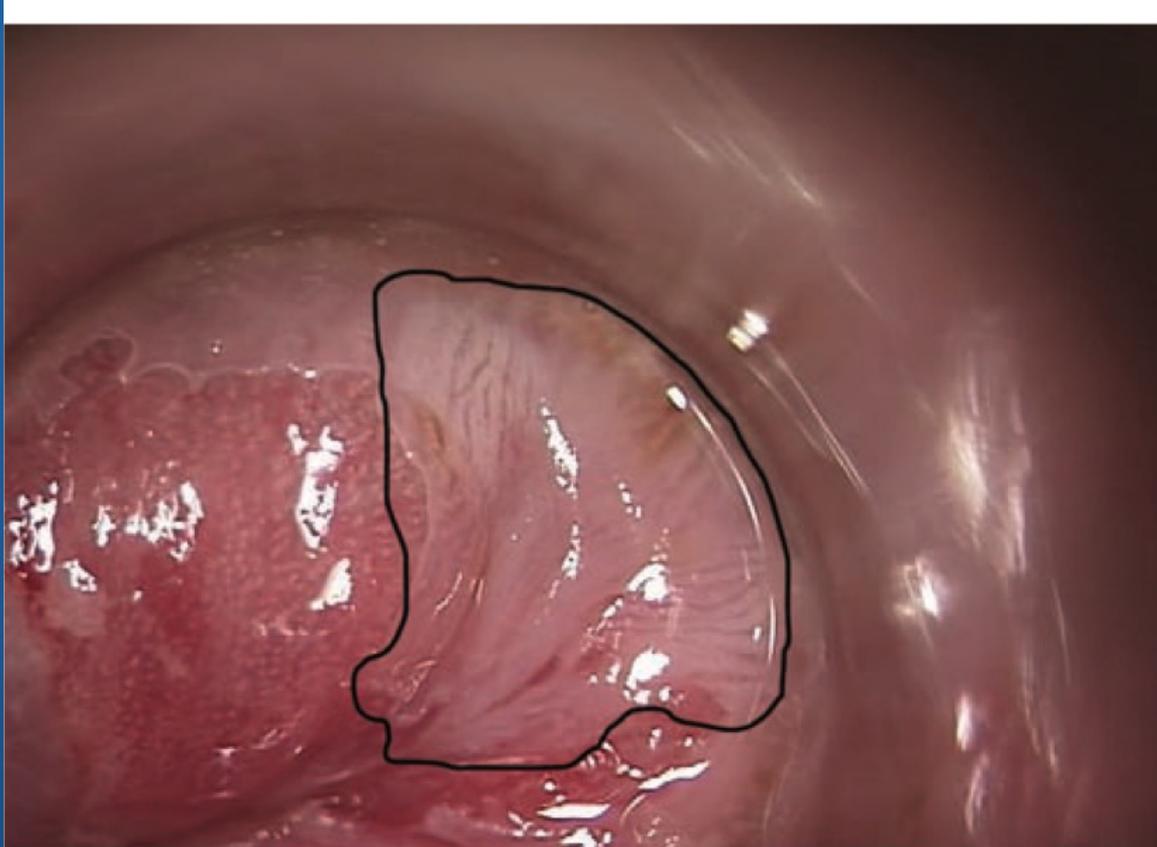


FIGURE 17.37. Striated vessels; biopsy showed HGAIN.

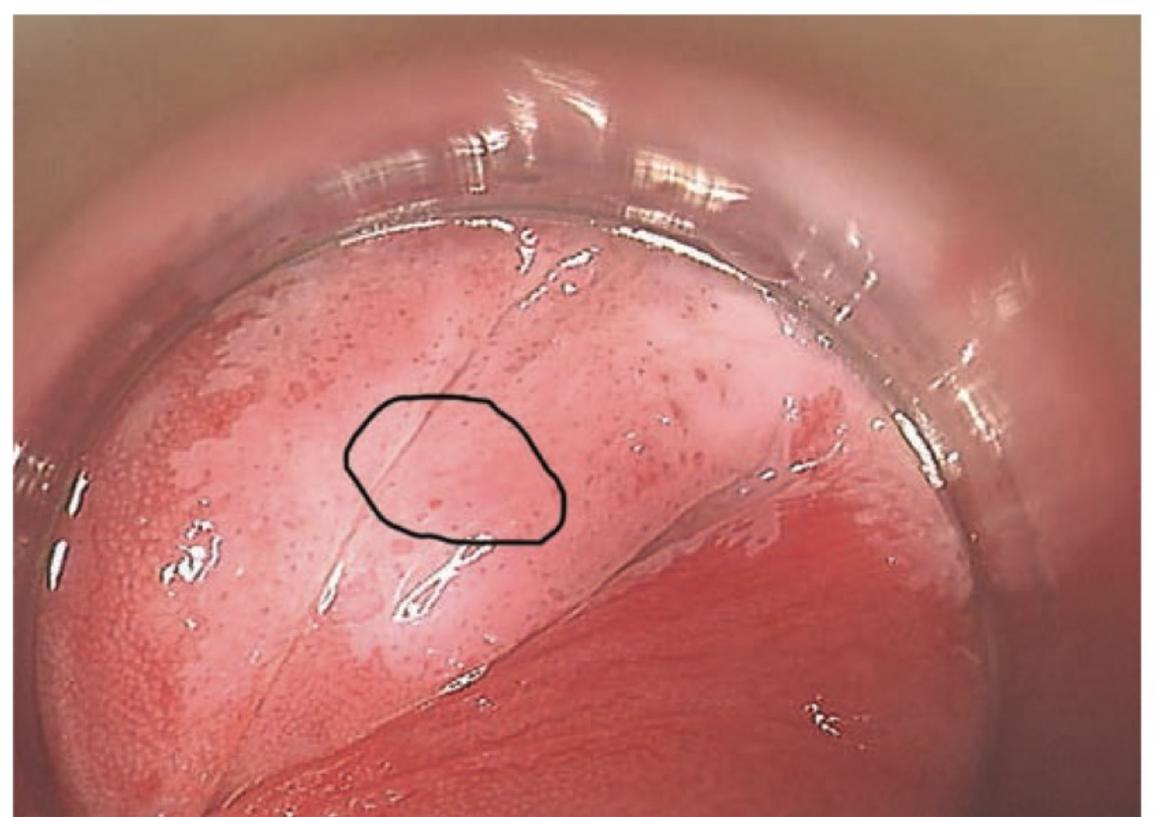


FIGURE 17.44. Atypical metaplasia with ringed glands; biopsy (*designated by circle*) showed HGAIN.

Perianal HSIL



FIGURE 17.90. Perianal HGAIN: acetowhite, flat, granular, and thickened.



FIGURE 17.93. Perianal HGAIN: extensive lesion with flat and slightly raised areas at the base and center, and a raised thickened area with defined margins at the superior aspect of the lesion.

Histology HSIL versus LSIL

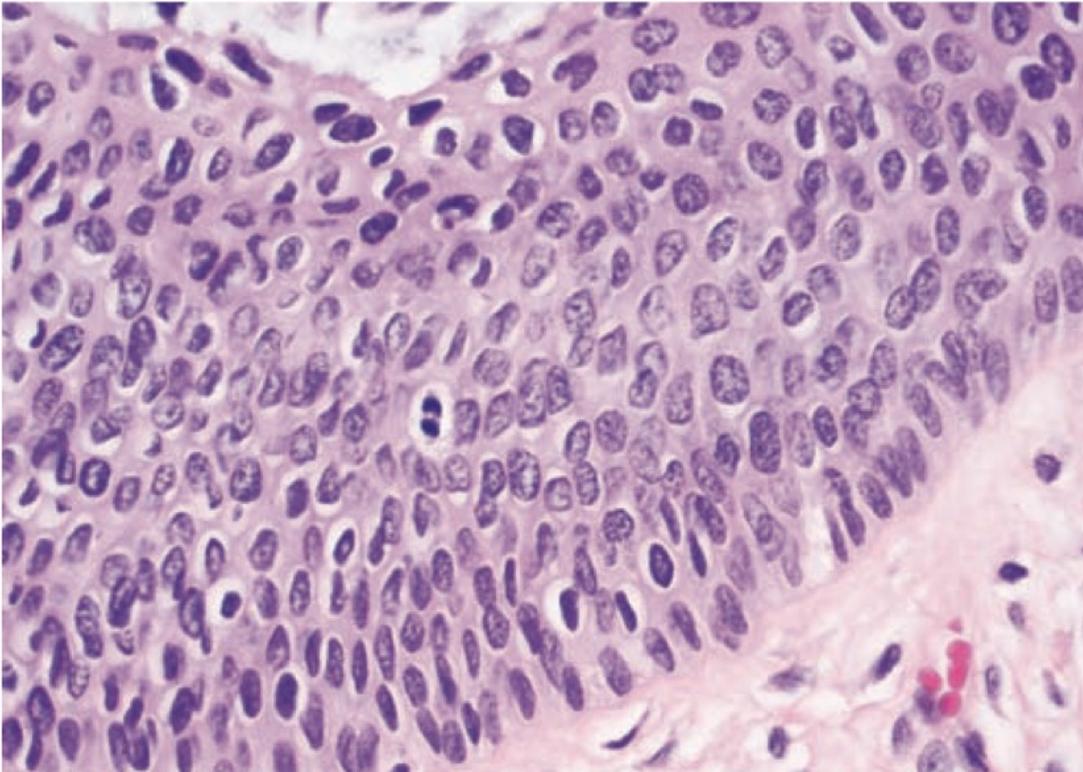


FIGURE 17.12. High-grade AIN. Note the mitotic figure in the midportion of the epithelium, above the basal layer (H&E, medium magnification).

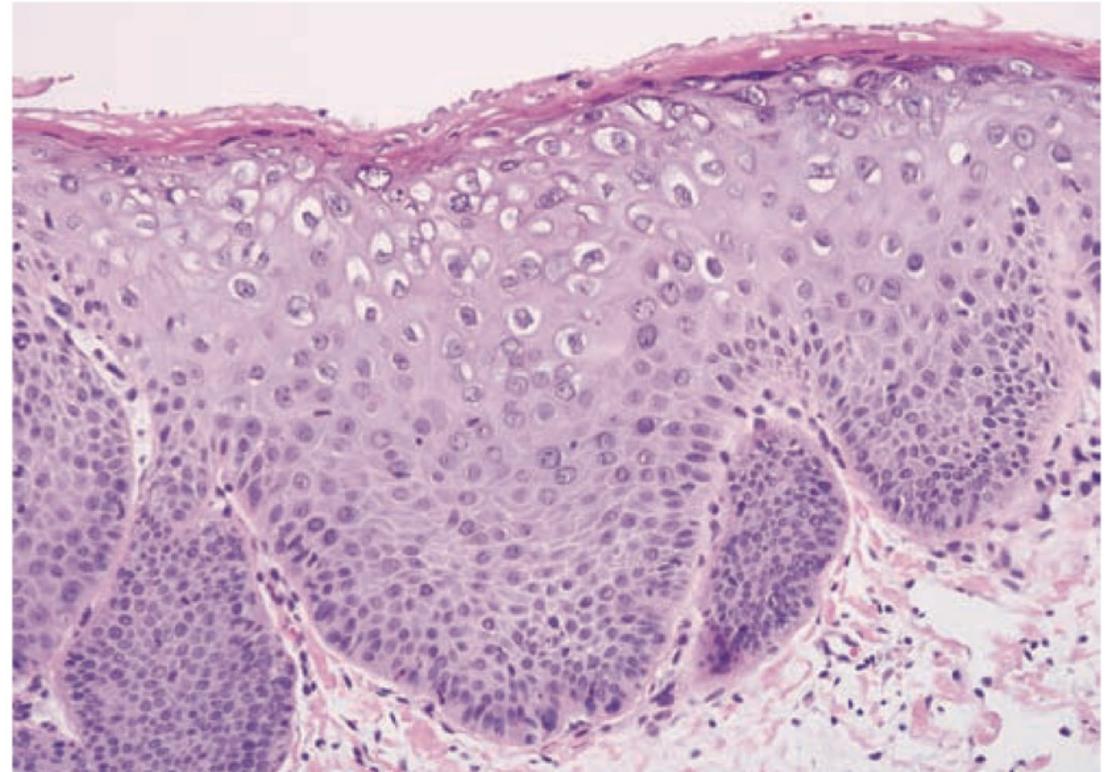
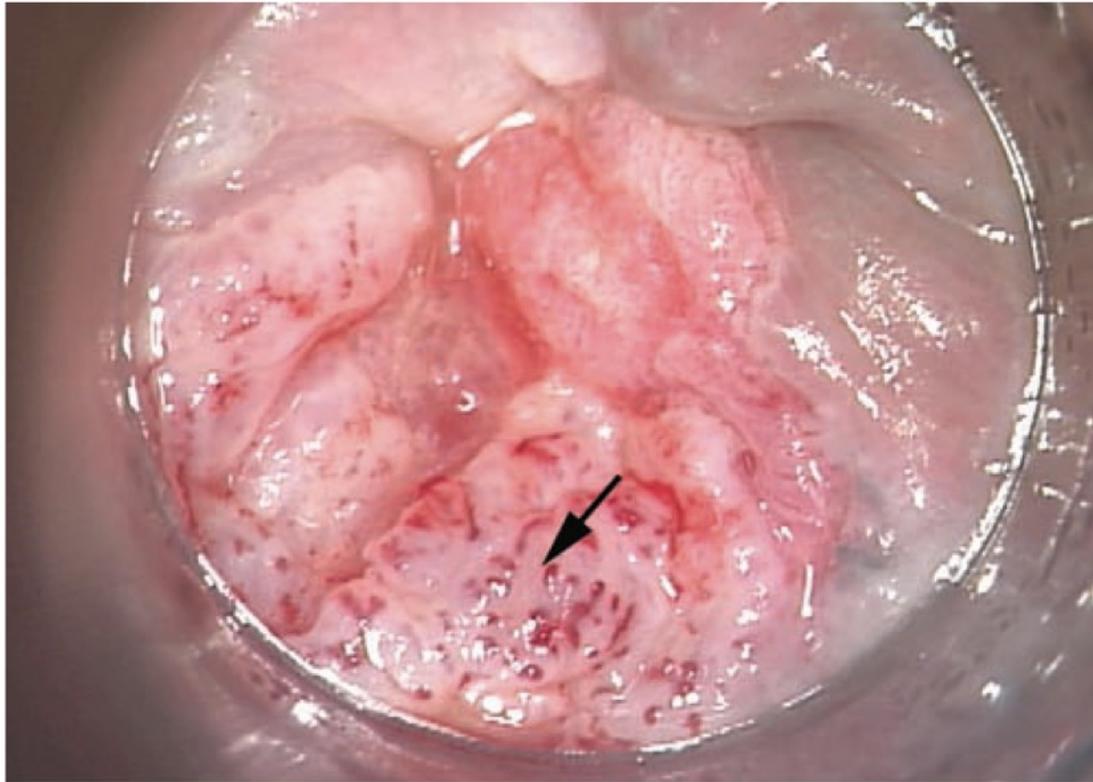
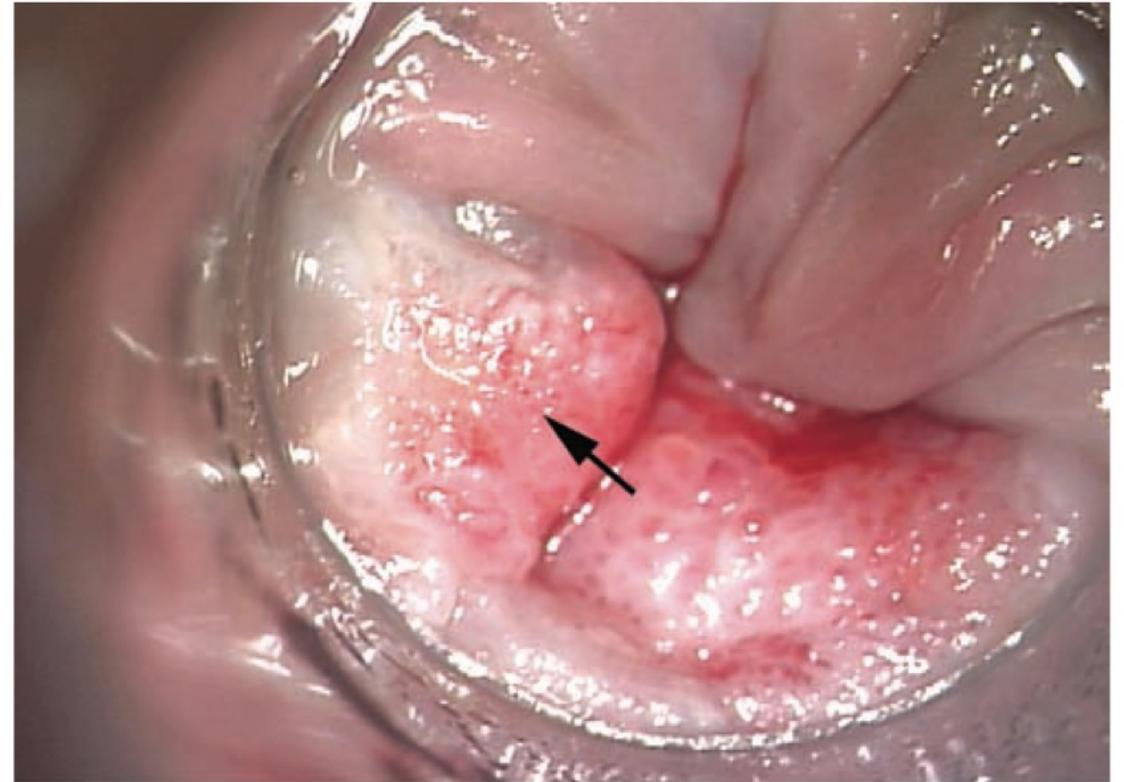


FIGURE 17.14. Low-grade PAIN. Prominent HPV-cytopathic effect is seen (H&E, medium magnification).

Invasive anal SCCa



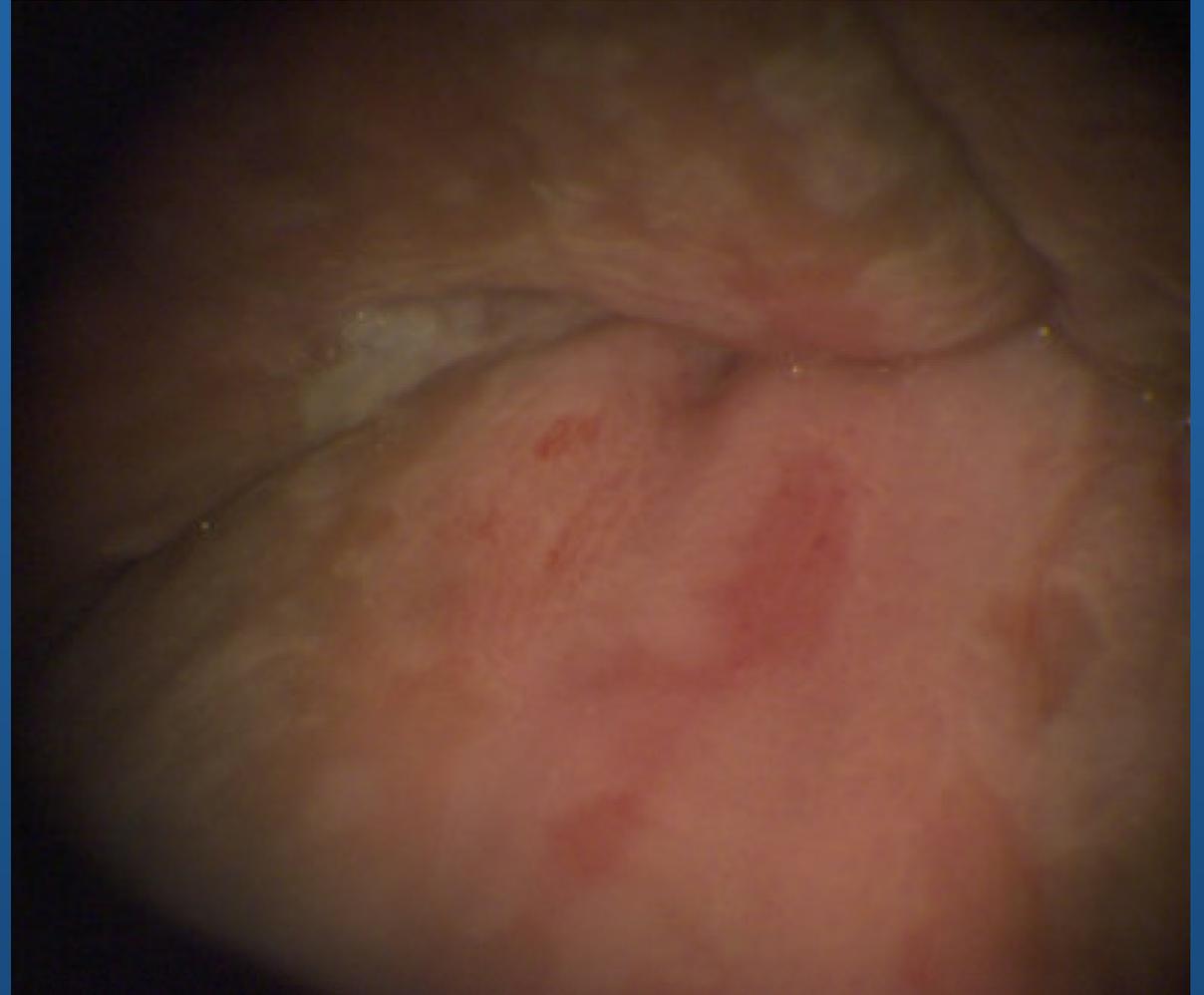
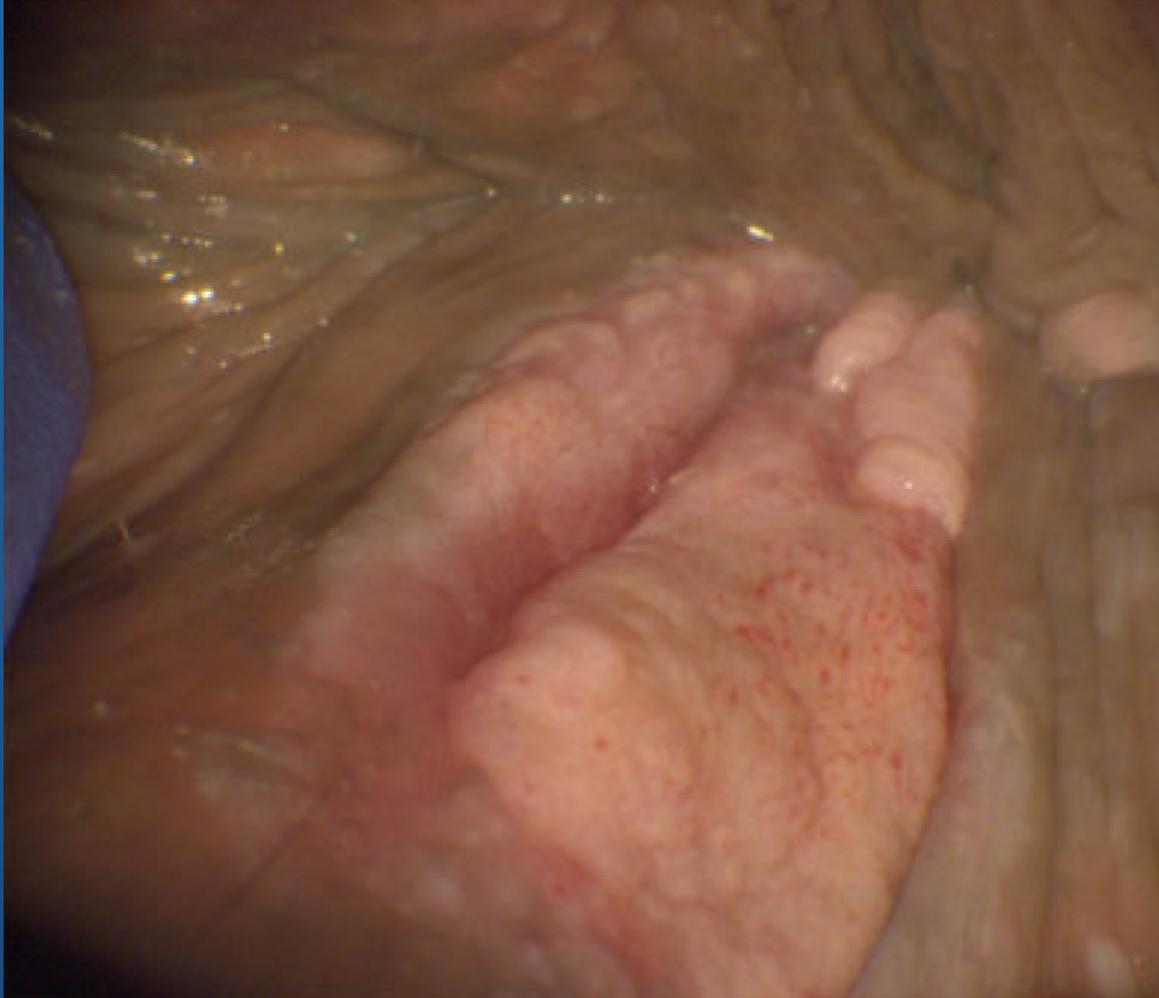
A



B

FIGURE 17.70. Patient had palpable thickening on DARE. HRA showed the mass with atypical vessels consistent with cancer. **A:** At SCJ. **B:** In distal canal, at *dentate line*. Arrows indicate biopsy sites performed in the office; biopsies showed invasive SCC.

Invasive perianal SCCa- pre and post-CMT



Topical Treatments for HSIL and Condylomas

- Podophyllotoxin- only used for perianal condylomas
- **Imiquimod (Aldara)- for immunocompetent patients (TIW at night up to 16 weeks)**
- **5-Fluorouracil (Efudex)- primary choice for extensive HSIL in immunocompromised patients (5 days BID then 9 days off for 8 cycles)**
- Sinecatechins (Veregan)
- Interferon
- Trichloroacetic acid
- Cidofovir (compounded)

Note: some of these are not FDA-approved for treatment of condylomas and none are approved for the treatment of HSIL or intra-anal application.

Treatment with infrared coagulation or hyfrecation



**Smoke-Evac Fusion
4" Preferred Blade**
5/box
Product # 14-1004P (sterile)



**Smoke-Evac Fusion
6" Preferred Blade**
5/box
Product # 14-1006P



**Smoke-Evac Fusion
Hyfrecator Tubing Kit - 8'**
10/box
Product # 14-4010HA (non sterile)

<https://www.zinnantisurgical.com/hra>

Why anal screening and treatment of HSIL might not work

- In many at-risk people lesions are large and multifocal
- Clinicians may miss lesions
- Clinicians may inadequately treat lesions
- New lesions often arise- anal whack-a-mole!



Why try to prevent anal cancer?

- About 50% in the general population present with localized disease, with relatively high survival rate

SEER stage	5-year relative survival rate
Localized	82%
Regional	66%
Distant	34%
All SEER stages combined	69%

Deshmukh A et al. J Natl Cancer Inst, 2020, Vol. 112, No. 8

Howlader N, SEER Cancer Statistics Review, 1975-2017, https://seer.cancer.gov/csr/1975_2017, posted to the SEER web site, April 2020.



Why try to prevent anal cancer?

- Survival rate is lower for more advanced disease
- Among those who do survive, there is substantial morbidity associated with standard treatment, primarily due to radiation therapy



the
ANCHOR
study

The ANCHOR Investigators Group
Protocol A01 of the AIDS Malignancy Consortium
UM1CA121947

ORIGINAL ARTICLE

Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

J.M. Palefsky, J.Y. Lee, N. Jay, S.E. Goldstone, T.M. Darragh, H.A. Dunlevy, I. Rosa-Cunha, A. Arons, J.C. Pugliese, D. Vena, J.A. Sparano, T.J. Wilkin, G. Bucher, E.A. Stier, M. Tirado Gomez, L. Flowers, L.F. Barroso, R.T. Mitsuyasu, S.Y. Lensing, J. Logan, D.M. Aboulafia, J.T. Schouten, J. de la Ossa, R. Levine, J.D. Korman, M. Hagensee, T.M. Atkinson, M.H. Einstein, B.M. Cracchiolo, D. Wiley, G.B. Ellsworth, C. Brickman, and J.M. Berry-Lawhorn, for the ANCHOR Investigators Group*

ABSTRACT

BACKGROUND

The incidence of anal cancer is substantially higher among persons living with the human immunodeficiency virus (HIV) than in the general population. Similar to cervical cancer, anal cancer is preceded by high-grade squamous intraepithelial lesions (HSILs). Treatment for cervical HSIL reduces progression to cervical cancer; however, data from prospective studies of treatment for anal HSIL to prevent anal cancer are lacking.

METHODS

We conducted a phase 3 trial at 25 U.S. sites. Persons living with HIV who were 35 years of age or older and who had biopsy-proven anal HSIL were randomly assigned, in a 1:1 ratio, to receive either HSIL treatment or active monitoring without treatment. Treatment included office-based ablative procedures, ablation or excision

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Palefsky can be contacted at joel.palefsky@ucsf.edu or at the University of California, San Francisco, 513 Parnassus Ave., Rm. S420, Box 0654, San Francisco, CA 94143.

*The members of the ANCHOR Investigators Group are listed in the Supplementary Appendix, available at NEJM.org.

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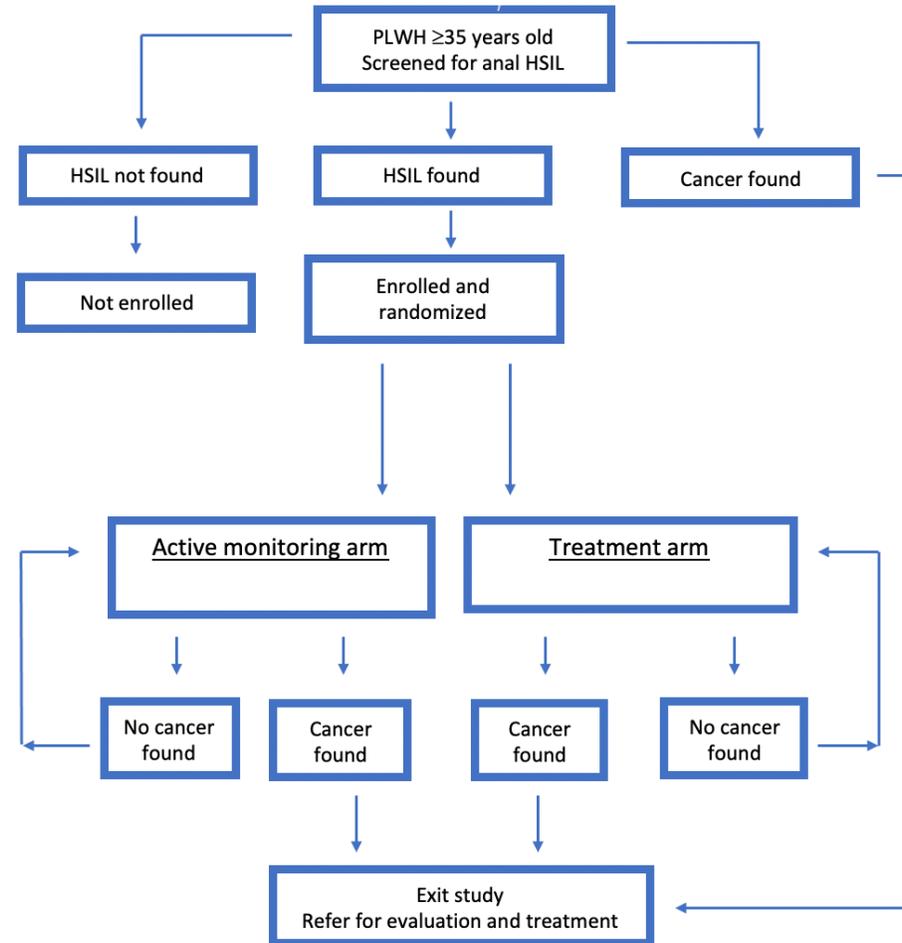
- .
- **Aim 1:** To determine whether treating anal high-grade squamous intraepithelial lesions (HSIL) is effective in reducing the incidence of anal cancer in PLWH
- **Aim 2:** To determine the safety of treatment for anal HSIL
- .



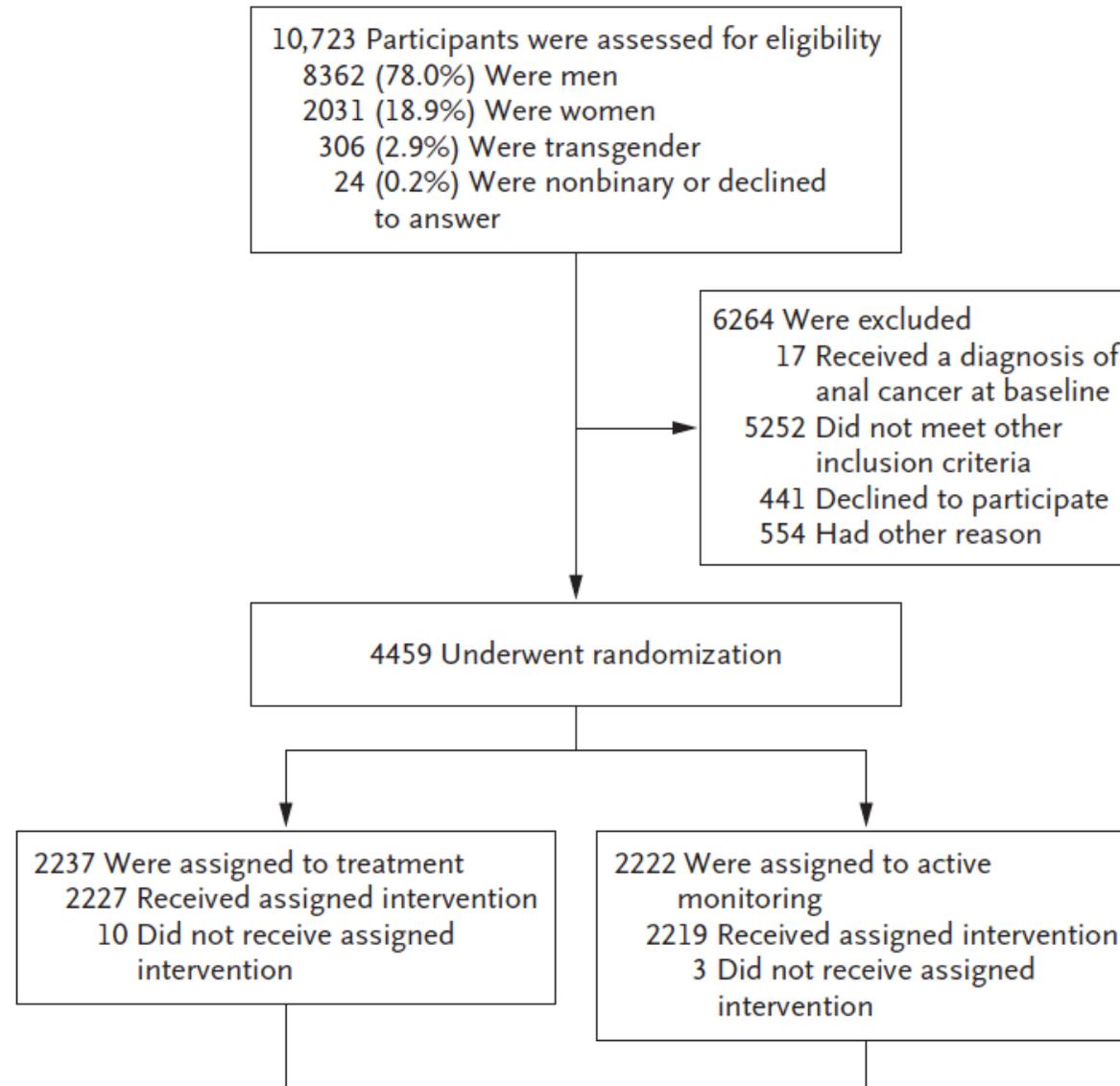
- **Aim 3:** To develop and implement an instrument to measure the impact of ANCHOR procedures on QoL (ANCHOR Health-Related Symptom Index (A-HRSI))
- **Aim 4:** Collect clinical specimens and data to create a bank of well-annotated specimens that will enable correlative science:
 - Identify host and viral factors in HSIL progression to cancer
 - Identify host and viral biomarkers of progression from HSIL to cancer

Study schema

Approximately 17,385 participants who provide informed consent for study participation will be screened to identify 5,058 eligible participants with previously untreated HSIL.



Study screening and randomization

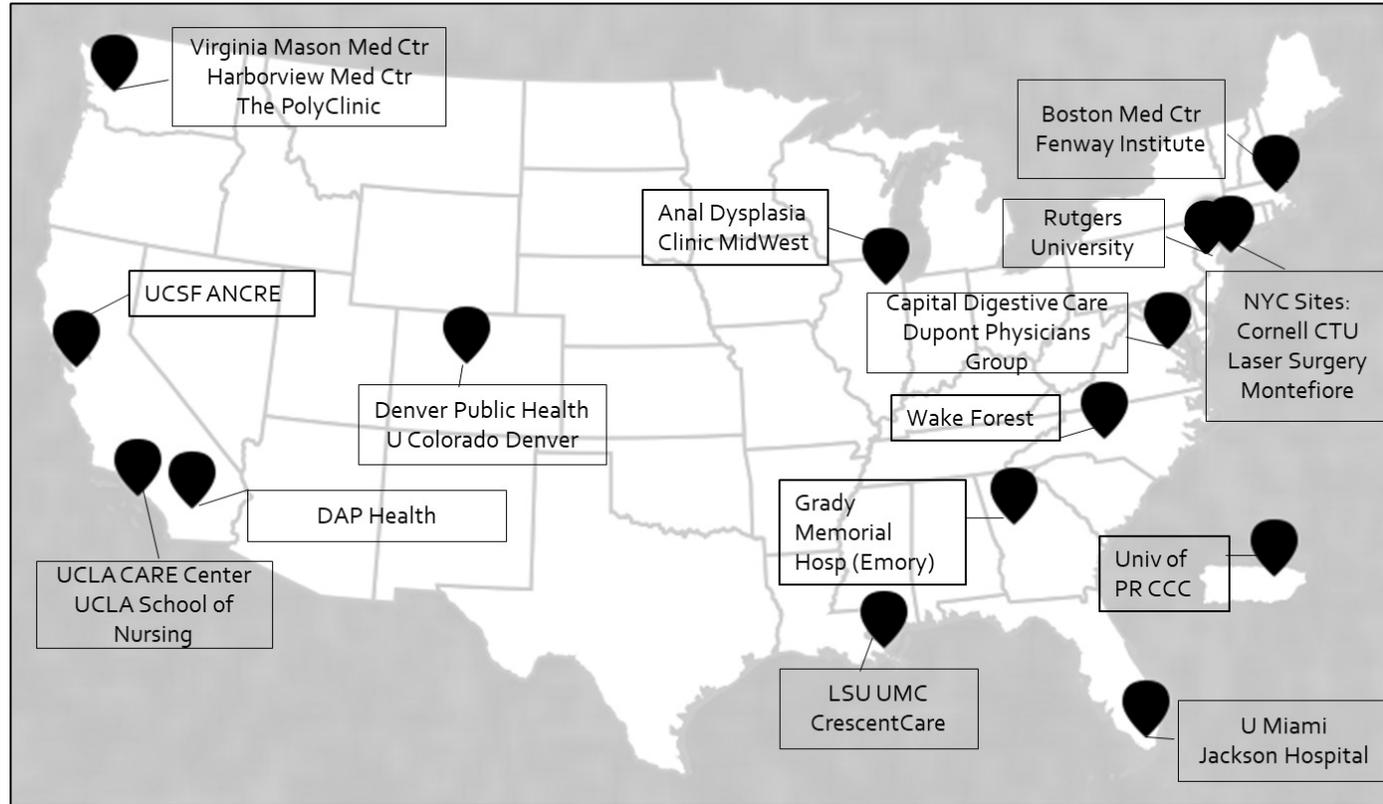


Methods

- Powered to detect difference between 50/100,000 PY in the treatment arm and 200/100,000 PY in the AM arm at the two-sided 0.05 significance level with power of 0.90
- Event-driven analysis, primary outcome= time-to-cancer
- N=2,529 per arm (total 5,058) to detect 31 anal cancers



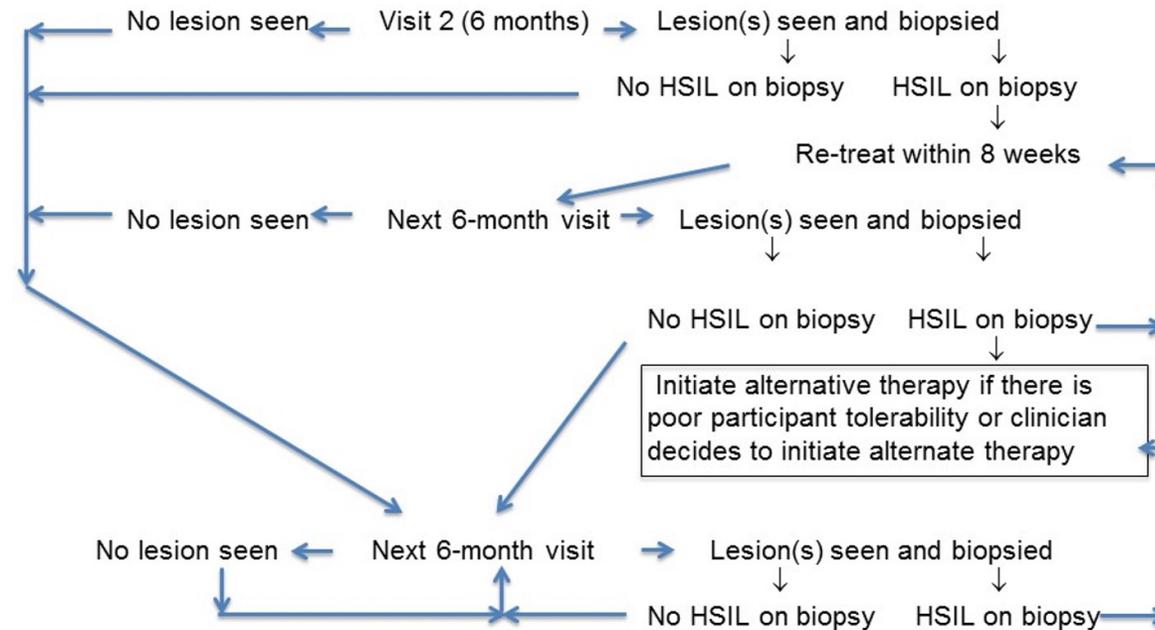
ANCHOR sites



Treatment arm

- Treated immediately- hyfrecation, IRC, 5-FU, imiquimod

Figure 4-B: IRC, hyfrecation, or electrocautery performed at visit 1 (randomization visit)



If no lesions are seen, participant will return for HRA at the next 6 month visit. If HSIL is found, alternative treatment is initiated per guidelines

Treatment arm

- Followed according to treatment algorithm
- Biopsied if suspicion for HSIL
- Anal cytology, swabs, HRA, blood every 6 months after HSIL cleared
- Every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer

Active monitoring arm

- Anal cytology, swabs, HRA, blood every 6 months
- Biopsied annually to confirm persistent HSIL
- Every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer

Screening

- 10,723 PLWH from 9/24/2014 to 8/5/2021
 - 53.3% of men
 - 47.2% of women
 - 67.1% of transgender individuals
- 17 individuals (0.16%, 160/100,000) were diagnosed with anal cancer (prevalent cases)



Demographics of randomized population (1)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Median age at randomization (years, IQR)	51.0 (44.0-57.0)	51.0 (44.0-57.0)	0.79
Median years at randomization since HIV diagnosis (years, IQR)	17.0 (10.0-24.0)	17.0 (10.0-25.0)	0.96
Months of follow-up (median, IQR)	25.3 (11.7 – 42.0)	27.2 (12.0 – 42.1)	0.77
Gender identity N (%)			0.30 ²
Male	1793 (80.5)	1782 (80.3)	
Female	346 (15.5)	365 (16.5)	
Transgender	85 (3.8)	68 (3.1)	
Neither male nor female	2 (0.1)	2 (0.1)	
Decline to answer	1 (0.0)	2(0.1)	

Demographics of randomized population (2)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Race/ethnicity N (%)			
Non-Hispanic White	695 (31.2)	737 (33.2)	0.37
African-American	935 (42.0)	939 (42.3)	
Hispanic, non-African-American	381 (17.1)	339 (15.3)	
Asian/Pacific Islander	27 (1.2)	29 (1.3)	
Other/Unknown	189 (8.5)	175 (7.9)	
CDC HIV risk group N (%)			
Homosexual	1738 (78.0)	1742 (78.5)	0.74
Heterosexual	532 (23.9)	510 (23.0)	0.48
Injection drug use	152 (6.8)	177 (8.0)	0.14
Transfusion	53 (2.4)	47 (2.1)	0.56
Hemophilia	2 (0.1)	4 (0.2)	0.41
Other high-risk group	34 (1.5)	27 (1.2)	0.37

Demographics of randomized population (3)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Current smoker N (%)	710 (31.9)	743 (33.5)	0.26
Plasma HIV-1 RNA copies/mL at randomization N (%)			0.27
<50	1852 (83.7)	1800 (81.8)	
51-199	155 (7.0)	160 (7.3)	
200-1000	83 (3.8)	93 (4.2)	
>1000	122 (5.5)	148 (6.7)	
CD4 cells/uL at randomization (median, IQR)	602 (393-827)	607 (410-837)	0.32

Demographics of randomized population (4)

	Randomized population N=4,446		P value ¹
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Stratification factors at randomization N (%)			
Nadir CD4 cells/uL			0.88
≤200 cells/uL	1130 (50.7)	1121 (50.5)	
>200 cells/uL	1097 (49.3)	1098 (49.5)	
HSIL size at screening			0.93 ⁸
>50% of anal canal/perianal region	285 (12.8)	282 (12.7)	
≤50% of anal canal/perianal region	1942 (87.2)	1937(87.3)	

Results

- For the participants in the treatment arm, initial treatment:
 - Office-based electrocautery ablation (86.2%)
 - Infrared coagulation (4.8%)
 - TUA (2.3%)
 - Topical 5-fluorouracil cream (4.5%)
 - Topical imiquimod (0.5%)

- Over the course of the study:
 - 1921 (86.0%) with therapeutic modality
 - 233 (10.4%) with two modalities
 - 33 (1.5%) with three modalities
 - 1 (<0.1%) with four modalities

ANCHOR Results

- DSMB notified when 32 cancers diagnosed (incident cases)
 - final analysis based on 30 cases
- 9 participants were diagnosed with invasive anal cancer in the treatment arm and 21 in the AM arm
- Median follow-up of 25.8 months, 57% reduction in anal cancer (95% CI 6% to 80%, chi-squared = 4.74, P=.029)
- Cancer incidence in the treatment arm was 173/100,000 PY of follow-up, compared with 402/100,000 PY in the AM arm

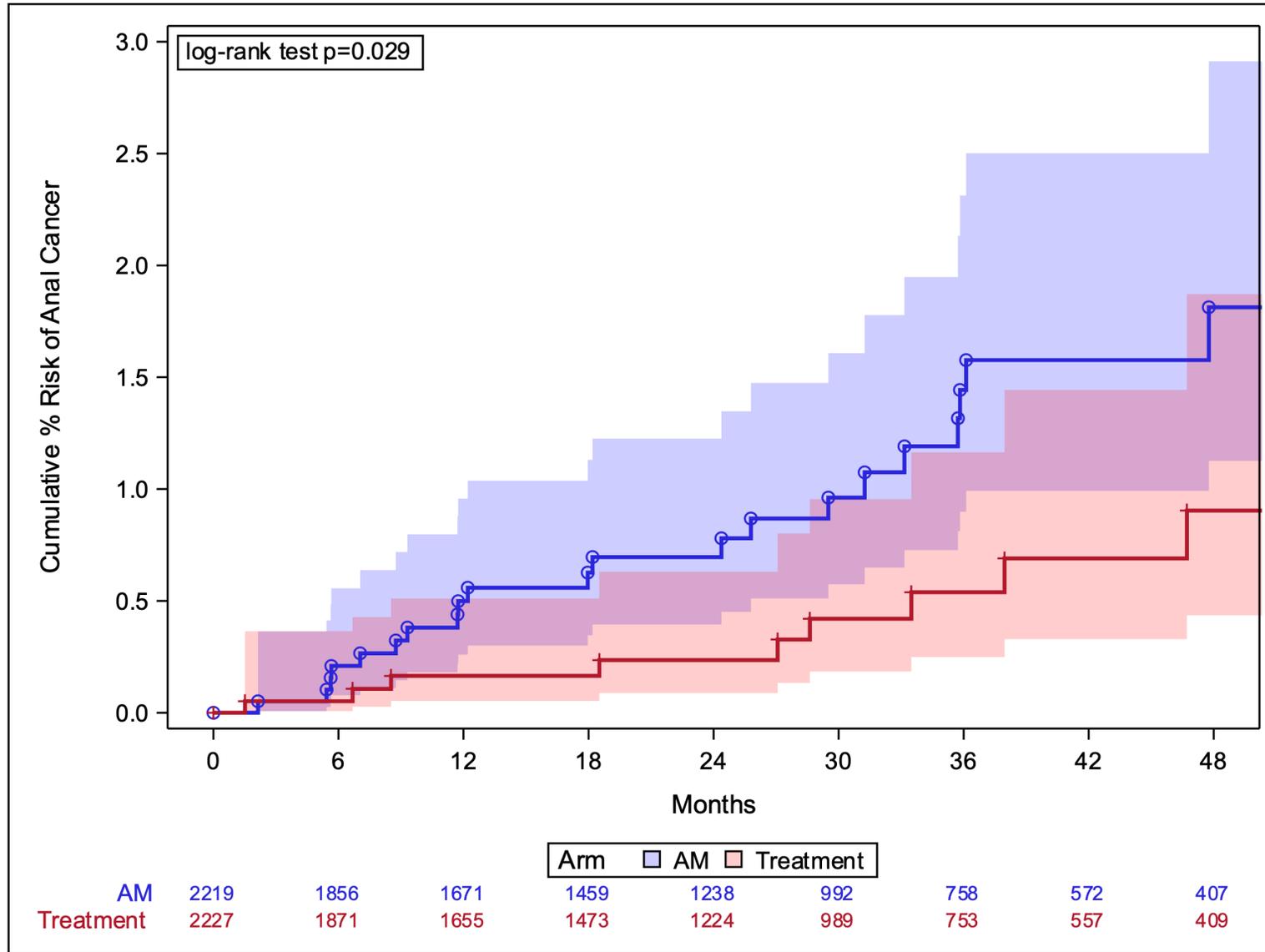
Reminder: Methods

Cancer incidence in the treatment arm was 173/100,000 PY of follow-up, compared with 402/100,000 PY in the AM arm

- Powered to detect difference between 50/100,000 PY in the treatment arm and 200/100,000 PY in the AM arm at the two-sided 0.05 significance level with power of 0.90
- Event-driven analysis, primary outcome= time-to-cancer
- N=2,529 per arm (total 5,058) to detect 31 anal cancers



Kaplan-Meier curve of time-to-confirmed cancer cases



Adverse events

	Treatment arm	Active monitoring arm
Adverse events (N)	683	635
Deaths	55	48
Serious adverse events (N)	586	568
Study-related adverse events (N)	43	4
Study-related serious adverse events (N)	7	1
Skin ulceration due to 5-fluorouracil	1	0
Anal abscess due to electrocautery	1	0
Pain due to electrocautery	1	0
Pain due to treatment under anesthesia	1	0
Pain due to infrared coagulation	1	0
Infection or abscess due to anal biopsy	2	1

Results

- DSMB recommended stopping the study for efficacy in October 2021
- Recommendation made to treat all individuals in the monitoring arm
- We continue to follow all individuals who wish to be treated and/or followed until September 2024



Progression to Cancer

- Cumulative progression to cancer at 48 months was 0.9% in the treatment arm and 1.8% in the monitoring arm
- The cancer risk was 185/100,000 PY (95% CI: 115-298) and 1047/100,000 PY (95% CI: 608-1803) for those with lesions $\leq 50\%$ and $>50\%$ of the anal/perianal canal, respectively (hazard ratio 5.26, 95% CI: 2.54-10.87)

Implications of the ANCHOR study findings

- Rate of progression from anal HSIL to cancer is high
- Treatment of anal HSIL is effective in reducing the incidence of anal cancer
- There is room for improvement in treatment of anal HSIL
- There is a need for biomarkers for HSIL progression or regression
- There is a need for optimization of screening algorithms for HSIL
- There is a need for a large scale-up of HRA training programs
- These data should be included in an overall assessment for inclusion of screening for and treating anal HSIL as standard of care
- Extrapolation of our results to other immunosuppressed groups at high risk of anal cancer

What to do in the short term

- DARE on all PLWH annually
- Screen PLWH IF you do HRA and treatment or you can refer to someone trained in HRA and treatment

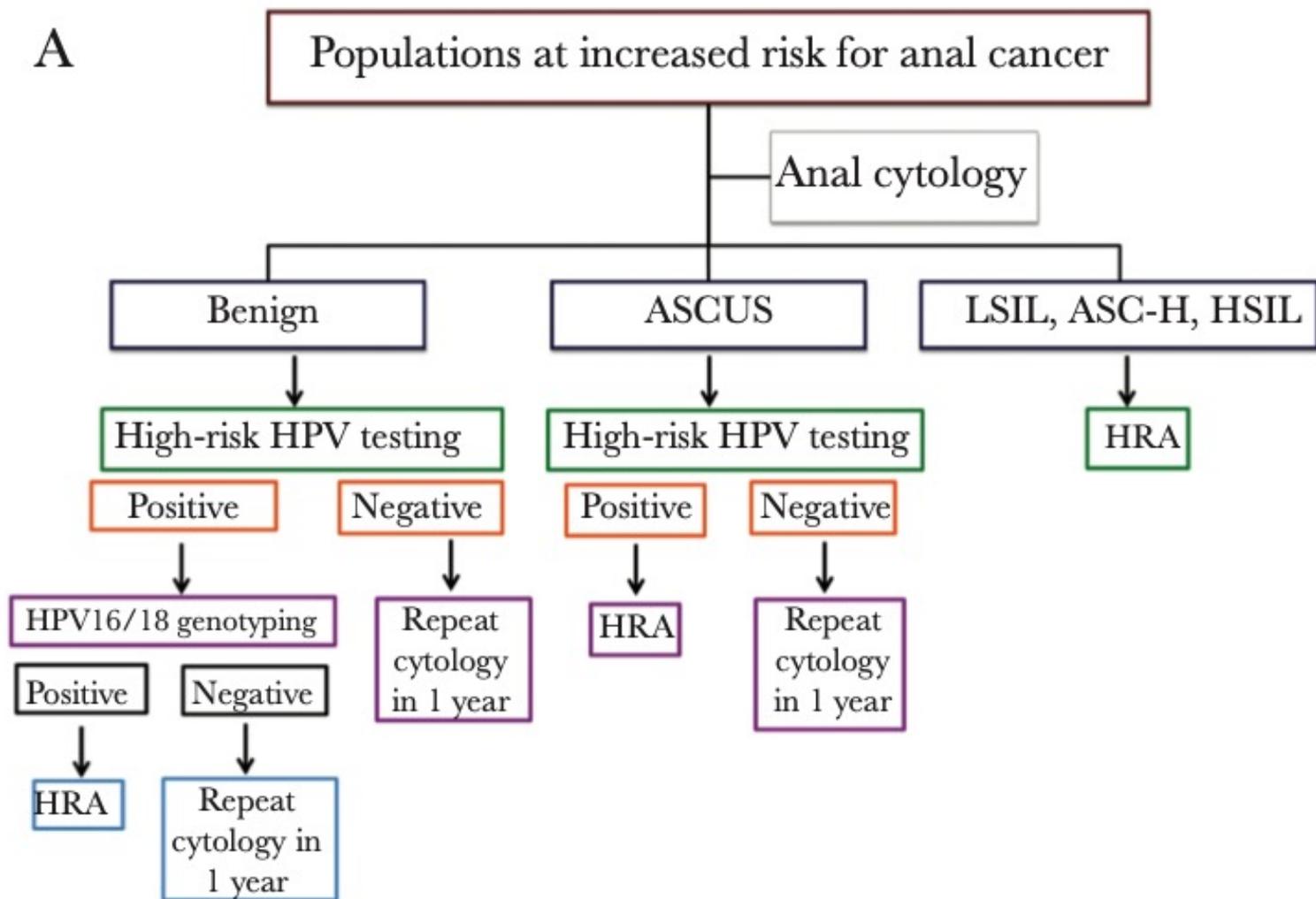


With deep gratitude to:

- ANCHOR Investigators Group and the study staffs at all of the ANCHOR sites
- Study participants
- ANCHOR Community Advisory Board
- AIDS Malignancy Consortium
- Emmes Corporation
- NCI/Office of HIV and AIDS Malignancies

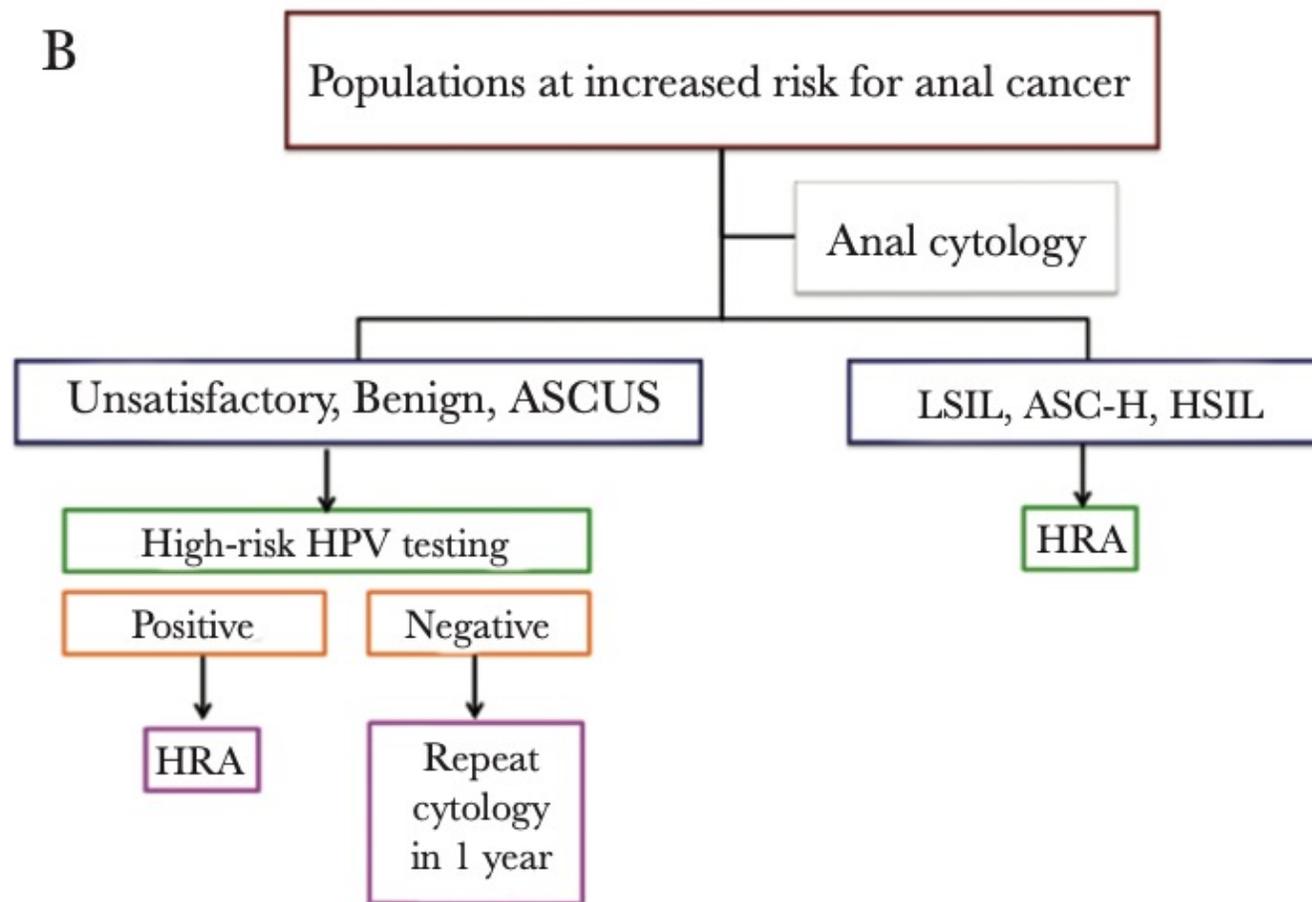


Possible screening algorithms



Anal cytology, hrHPV DNA testing, and HRA-guided biopsy results were analyzed from 1837 participants (1504 HIV-infected men who have sex with men (MSM), 155 HIV-uninfected MSM, and 178 HIV-infected women).

Possible screening algorithms



Possible screening algorithms

- Histological HSIL/cancer was detected in 756 (41%) participants.
- Cytology had the lowest sensitivity (0.76–0.89) but highest specificity (0.33–0.36) overall and for each subgroup.
- Algorithm B was the most sensitive strategy overall (0.97) and for MSM (HIV-infected 0.97; HIV-uninfected 1.00).
- For women, hrHPV testing and both algorithms yielded higher sensitivity than cytology (0.96, 0.98, and 0.96).
- Specificity was low for all strategies/subgroups (range, 0.16–0.36).
- Conclusions. Screening algorithms that incorporate cytology and hrHPV testing significantly increased sensitivity but decreased specificity to detect anal precancer/cancer among high-risk populations.

AMC 084

Two-Year Incidence and Cumulative Risk and Predictors of Anal High-Grade Squamous Intraepithelial Lesions (anal precancer) among Women with HIV

Stier et al., 2023 | *Clinical Infectious Diseases*



BACKGROUND: Detection and treatment of anal histologic high-grade squamous intraepithelial lesions (hHSIL) prevents anal cancer. However, anal hHSIL incidence among women living with HIV (WLHIV) remains unknown. Performance of anal high-risk (hr)HPV, anal cytology (anal-cyt), and both for hHSIL detection longitudinally over 2 years also remains undetermined



METHODS: 229 WLHIV followed annually for 2 years with high resolution anoscopy with directed biopsy for anal HSIL. incident and 2-year cumulative anal HSIL was estimated.



RESULTS: Anal hrHPV or abnormal anal-cyt was associated with an increased risk of incident anal hHSIL at 2 years (18.9/100py [95% CI 11.4-31.3] and 13.4/100py [95% CI 8.0-22.7] respectively) compared with no detection of anal HPV or negative cytology (2.8/100py [95% CI 1.1-7.4] and 4.2 [95% CI, 1.8-10.2])



CONCLUSION: Detection of anal hrHPV or abnormal anal cytology are comparable predictors for 2-y-CR of anal hHSIL. The absence of anal hrHPV combined with negative cytology was predictive of a lower (but measurable) risk of developing anal hHSIL.

Resources



Welcome to IANS

We are the world's first professional society devoted to the prevention and treatment of AIN (anal intraepithelial neoplasia) and anal cancer.

Our mission is to provide a forum for individuals with a broad spectrum of backgrounds, viewpoints and geographic origin, an exchange of ideas and dissemination of knowledge regarding the pathogenesis, diagnosis, treatment and prevention of anal neoplasia.



IANS Podcast



WebRounds

WEBROUNDS - TREATING SISCCA REVIEW AND SISCCA CASE DISCUSSIONS
Tuesday, October 10, 2023 8:30 PM (EDT) • Online Webinar

WEBROUNDS - JOURNAL CLUB
Tuesday, November 28, 2023 12:00 PM (EST) • Online Webinar

Courses

IANS VIRTUAL STANDARD HRA COURSE 2023
Wednesday, March 01, 2023 (UTC) • Online

IANS Scientific Meeting 2023

In-Person Event



IANS Europe Corner

New! European Task Force Monthly Meetings

Join the committee the first Thursday on the month starting in October at 17:00 CET

Join the Task Force Meeting

Watch Recording

Upcoming Courses

In the News



IANS is now a Project ECHO Hub



IANS Virtual Standard HRA Course 2023

Start **Wednesday, March 01, 2023 (UTC)**

End **Thursday, November 30, 2023 (UTC)**

Location **Online**

Registration

- **Member – \$400.00**
Discount registration for members
- **Member (Low/Middle income or Trainee) – \$225.00**
Discount registration for members
- **Non-Member – \$700.00**
- **Non-Member (Low/Middle income or Trainee) – \$300.00**
Check country status here: <https://data.worldbank.org/income-level/low-and-middle-income>



IANS Virtual Standard HRA Course 2023
Detailed instructions in the confirmation email

Registration closes on November 16, 2023

<https://www.iansoc.org>



IANS HRA Guidelines and Practice Standards

2016 IANS International Guidelines for Practice Standards in the Detection of Anal Cancer Precursors

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These guidelines propose initial minimum competencies for the clinical practice of HRA, against which professionals can judge themselves and providers can evaluate the effectiveness of training. Once standards have been agreed upon and validated, it may be possible to develop certification methods for individual practitioners and accreditation of sites.

From Novice to Expert

- Long learning curve
- *Not* – observe one, do one, teach one
- Observe 25, do 100, work 5 years, then teach
- Lesions can be subtle, don't settle for the obvious especially in high-risk populations
- Biggest pitfall for novices is missing some lesions; or extent of disease – causes inadequate diagnosis and treatment

Major Challenges Remain

- Training and procurement of equipment and space. High resolution anoscope, high-res digital camera, image capture software (i.e., Second Opinion). Total >\$20,000.
- A high resolution anoscope is not a colposcope- different focal length, no center post, need 16 and 25 power magnification.
- No show rates are relatively high.
- Working with cytologists and pathologists to understand procedure and standardize diagnosis with LAST recommendations. (Including P16 and Ki67 staining for intermediate lesions (AIN 2)) *
- Establishing a relationship with surgeon for referral of cases that need surgical evaluation and/or treatment.
- Still need better treatments for anal HSIL.
- Best approach to screening for anal HSIL- HR-HPV co-testing, methylation markers??
- Anal HR-HPV testing is not yet FDA approved.
- Awaiting revisions of the CDC HIV OI Treatment Guidelines
- [USPSTF Proposed framework](#)- anal cancer screening- initial comments were due January 11, 2023.
- Prepare for the lack of HRA capacity.
- How applicable are the ANCHOR results to other immunocompromised individuals?

* Journal of Lower Genital Tract Disease, Volume 16, Number 3, 2012, 205-242

CDC HPV Vaccine Recommendations

- HPV vaccine is recommended for routine vaccination at age 11 or 12 years. (Vaccination can be started at age 9.)
- ACIP also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger. HPV vaccination is given as a series of either two or three doses, depending on age at initial vaccination.
- Vaccination is not recommended for everyone older than age 26 years. Some adults ages 27 through 45 years might decide to get the HPV vaccine based on discussion with their clinician, if they did not get adequately vaccinated when they were younger. HPV vaccination of people in this age range provides less benefit, for several reasons, including that more people in this age range have already been exposed to HPV.
- For adults ages 27 through 45 years, clinicians can consider discussing HPV vaccination with people who are most likely to benefit. HPV vaccination does not need to be discussed with most adults over age 26 years. See ACIP's [shared clinical decision-making FAQs](#).

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The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, HRSA, HHS, or the U.S. Government.

