Screening and Treatment of HPV Lesions to Reduce Anal Cancer: Part 1

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Disclosures

HSK: No conflicts of interest or relationship to disclose

JS: No conflicts of interest or relationship to disclose

We will discuss off-label product uses

Outline

March 24, 2022

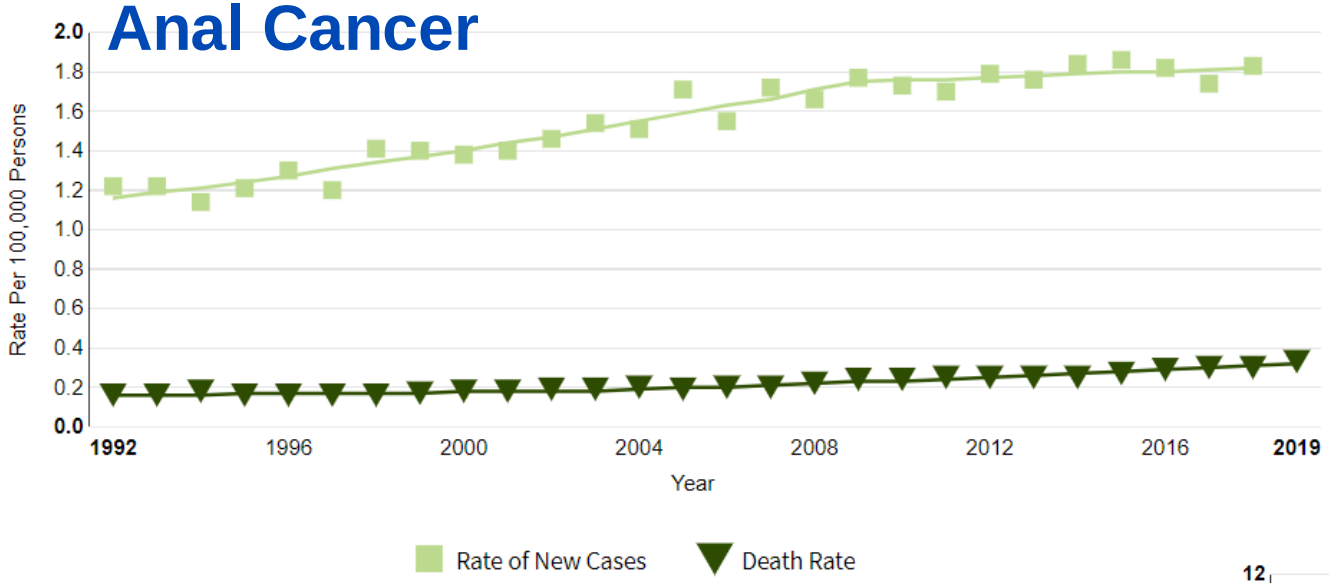
- Overview of HPV and anal cancer risks
- Contemporary terminology
- Design, endpoints, results, and implications of the ANCHOR study

March 31, 2022

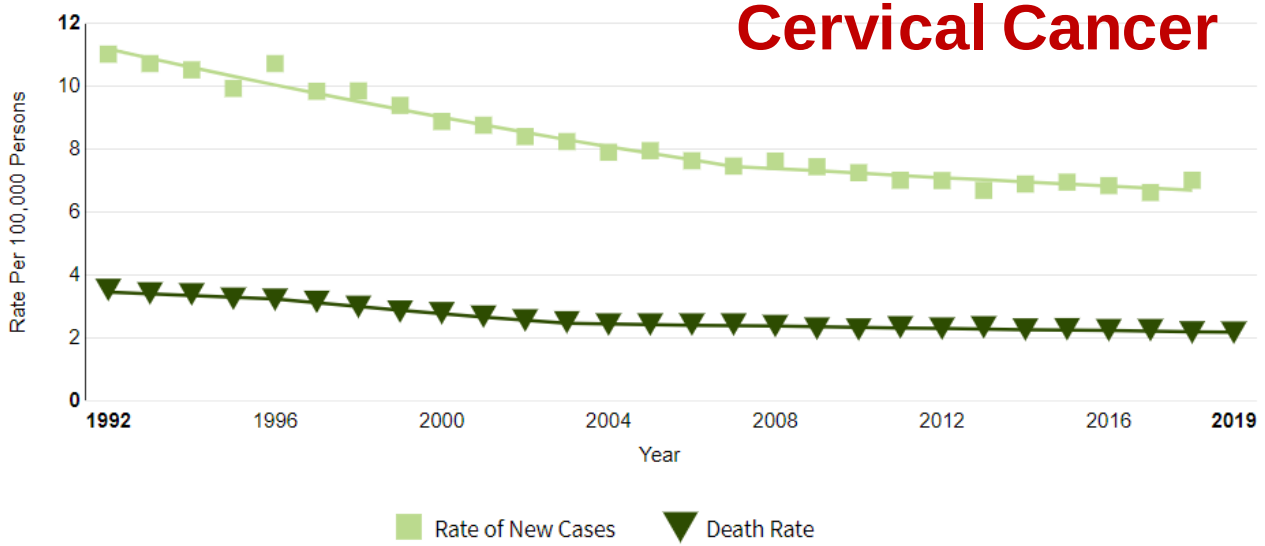
- High-resolution anoscopy (HRA) and anal dysplasia treatment
- Current challenges

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

Anal Cancer



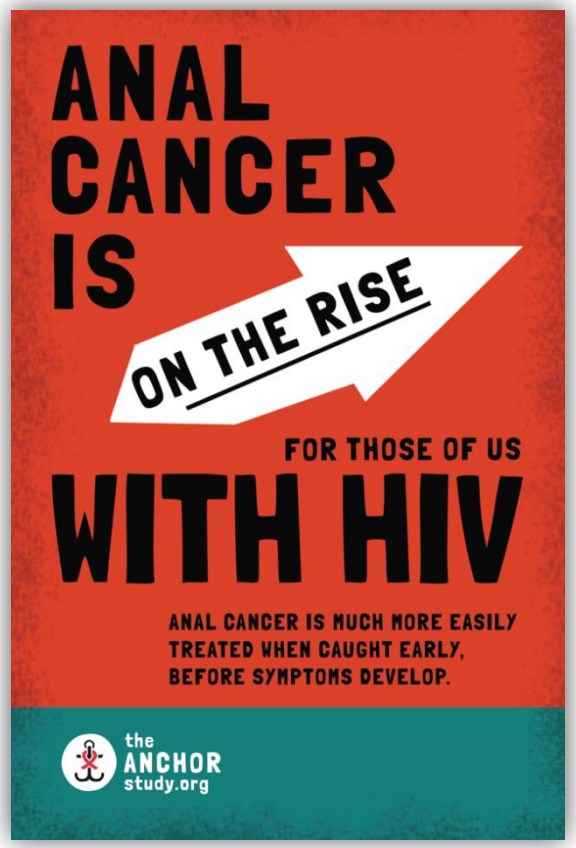
Cervical Cancer



SEER/NCI

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



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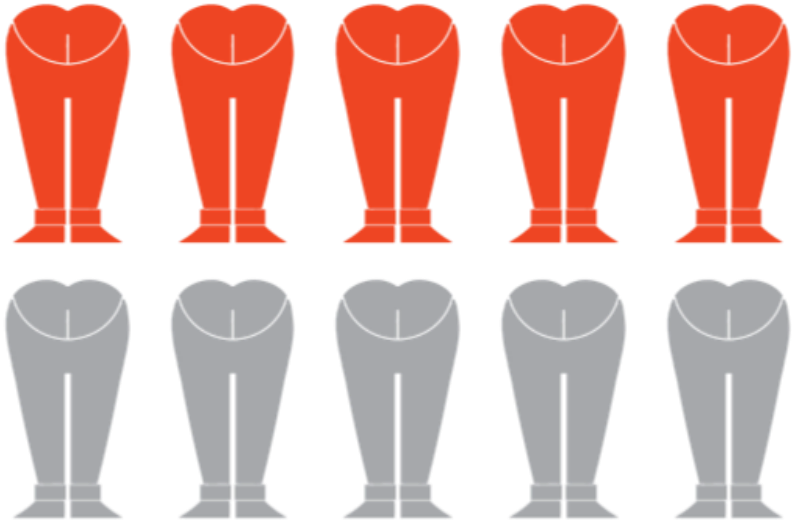
Among HIV+ MSM,
5 Out of 10 Asymptomatic Men Have Anal HSIL



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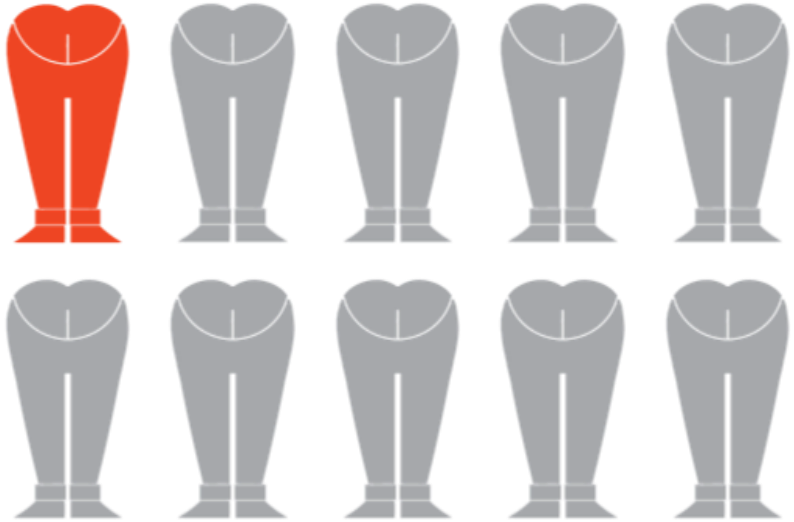
It Is Estimated That 1 In 10 HIV+ MSM Will Get Anal Cancer Over Their Lifetime



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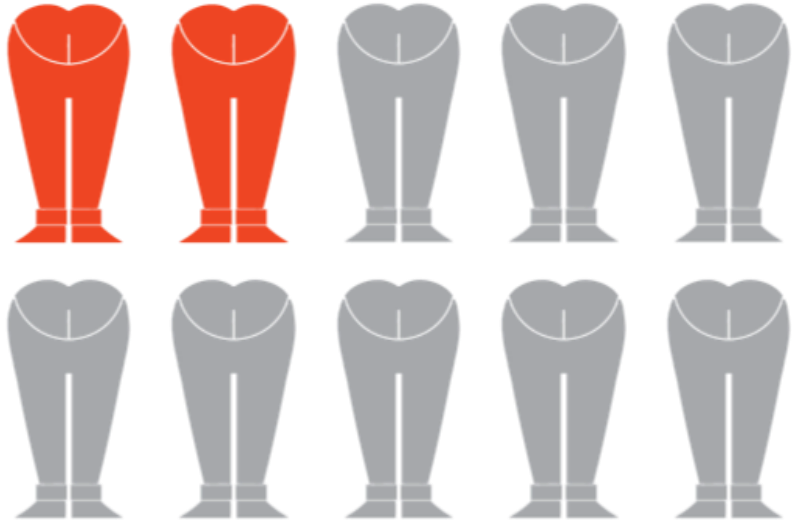
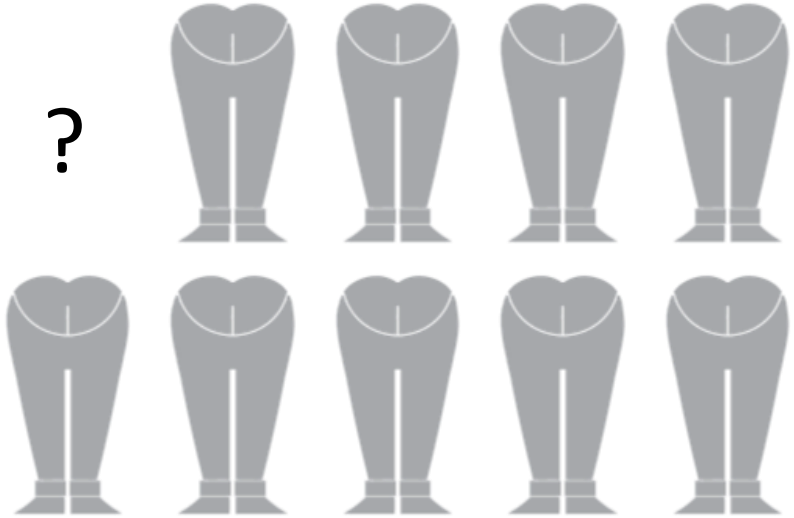
Among HIV+ Women, It Is Estimated That 2 Out of 10 Have Anal HSIL



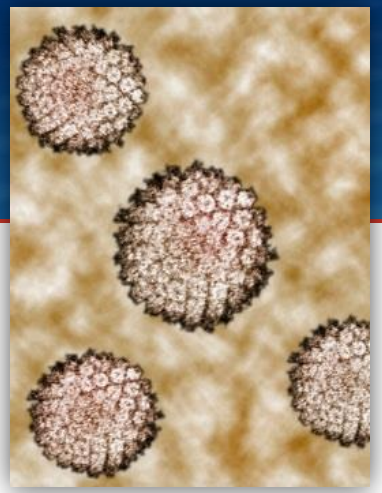
It is Not Known How Many HIV+ Women Will Get Anal Cancer

?



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
- Smoking
- Cervical and vulvar HSIL and cancers
- History of genital warts



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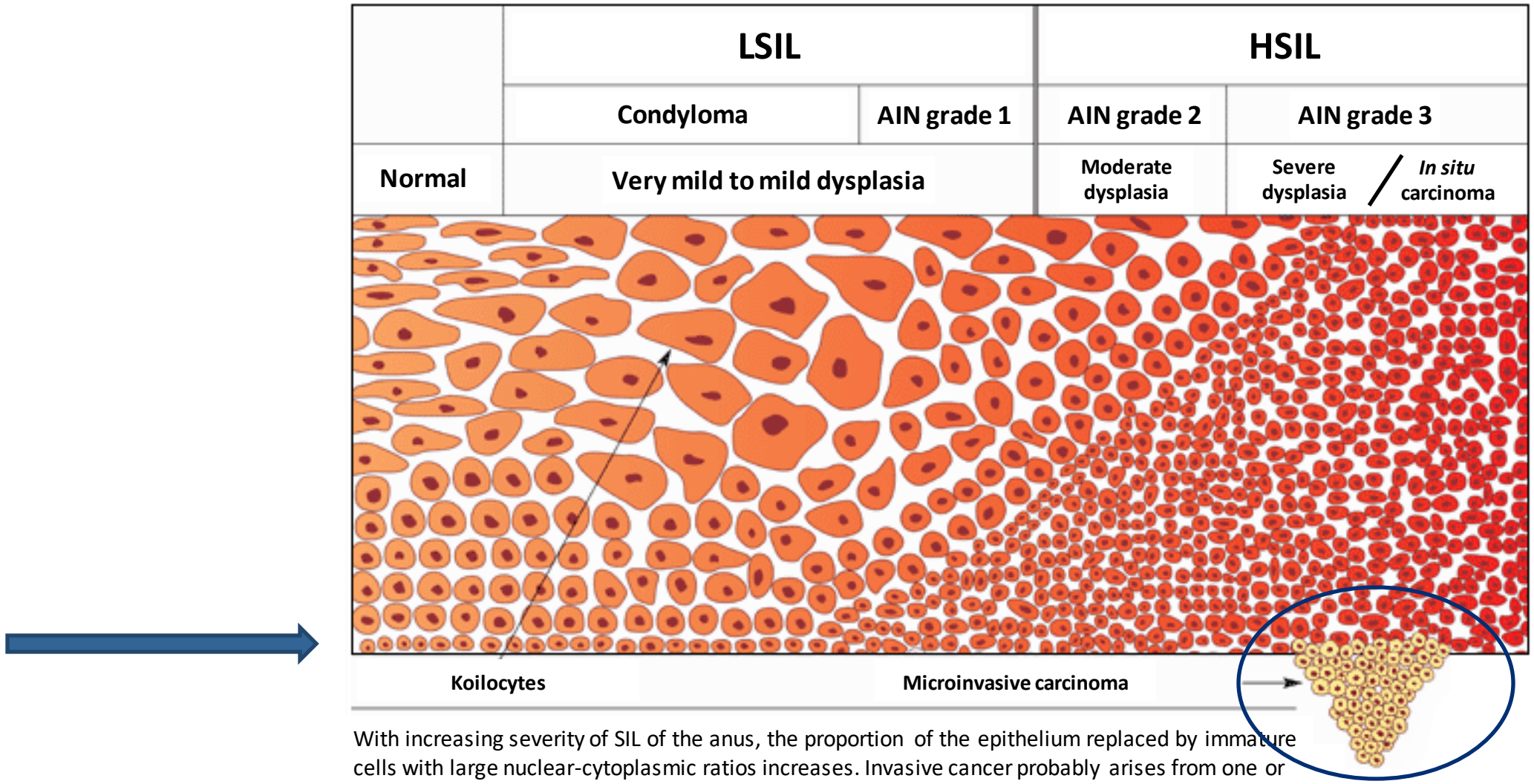
Continuum of HPV Neoplasia



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.

The Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions

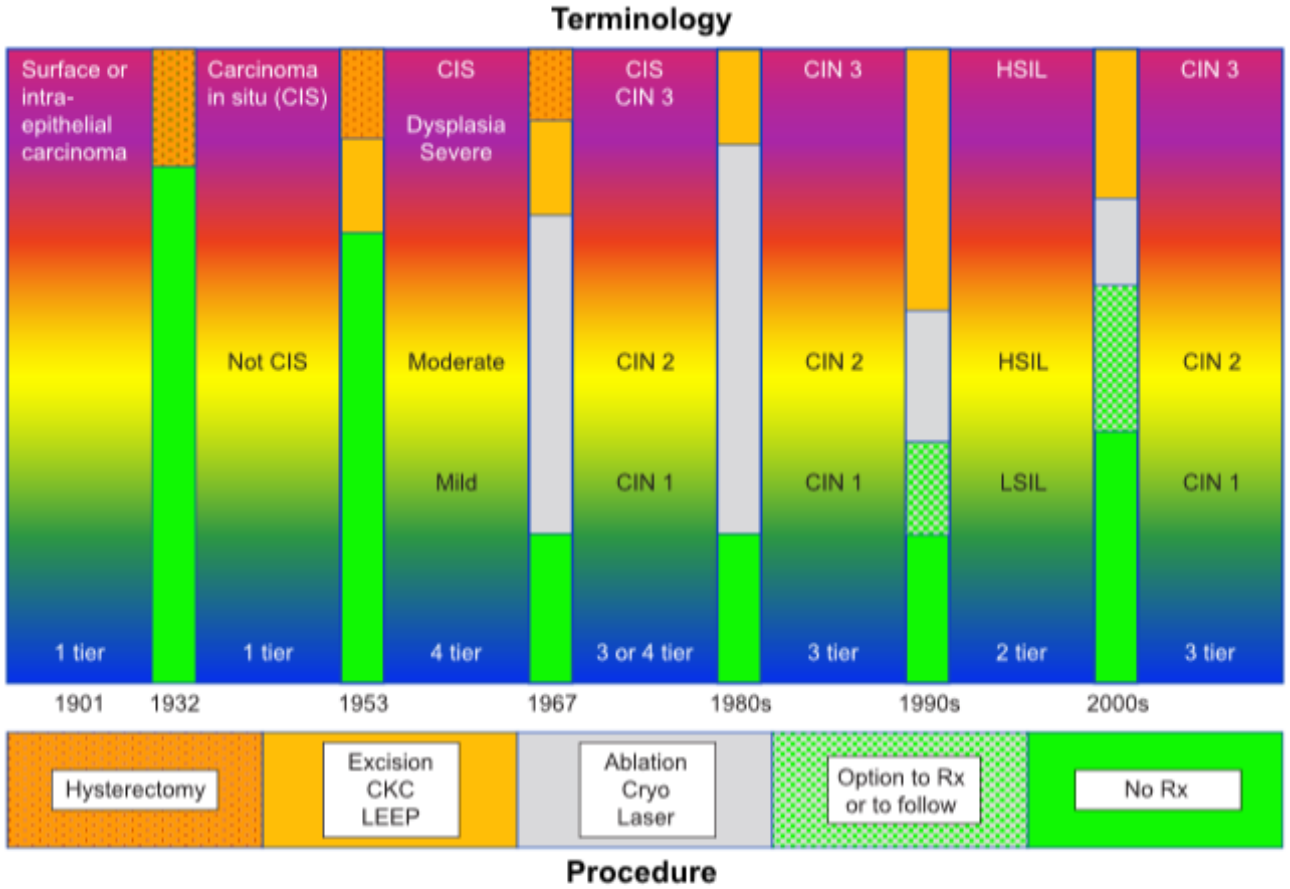


Figure 2. Changes to the terminology and number of tiers used to describe cervical precancer over time with corresponding management options (procedure). See text for additional details. CKC, cold knife conization; Cryo, cryotherapy; RX, treatment. Modified with permission. Courtesy of J. Thomas Cox.

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

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ANCHOR Study

- The **An**al **C**ancer **H**SIL **O**utcomes **R**esearch study is a NIH-funded study with the primary objective of determining whether treating anal high-grade squamous intraepithelial lesions (HSIL) is effective in reducing the incidence of anal cancer in people living with HIV, just as screening for and treating similar lesions in the cervix reduces the incidence of cervical cancer.

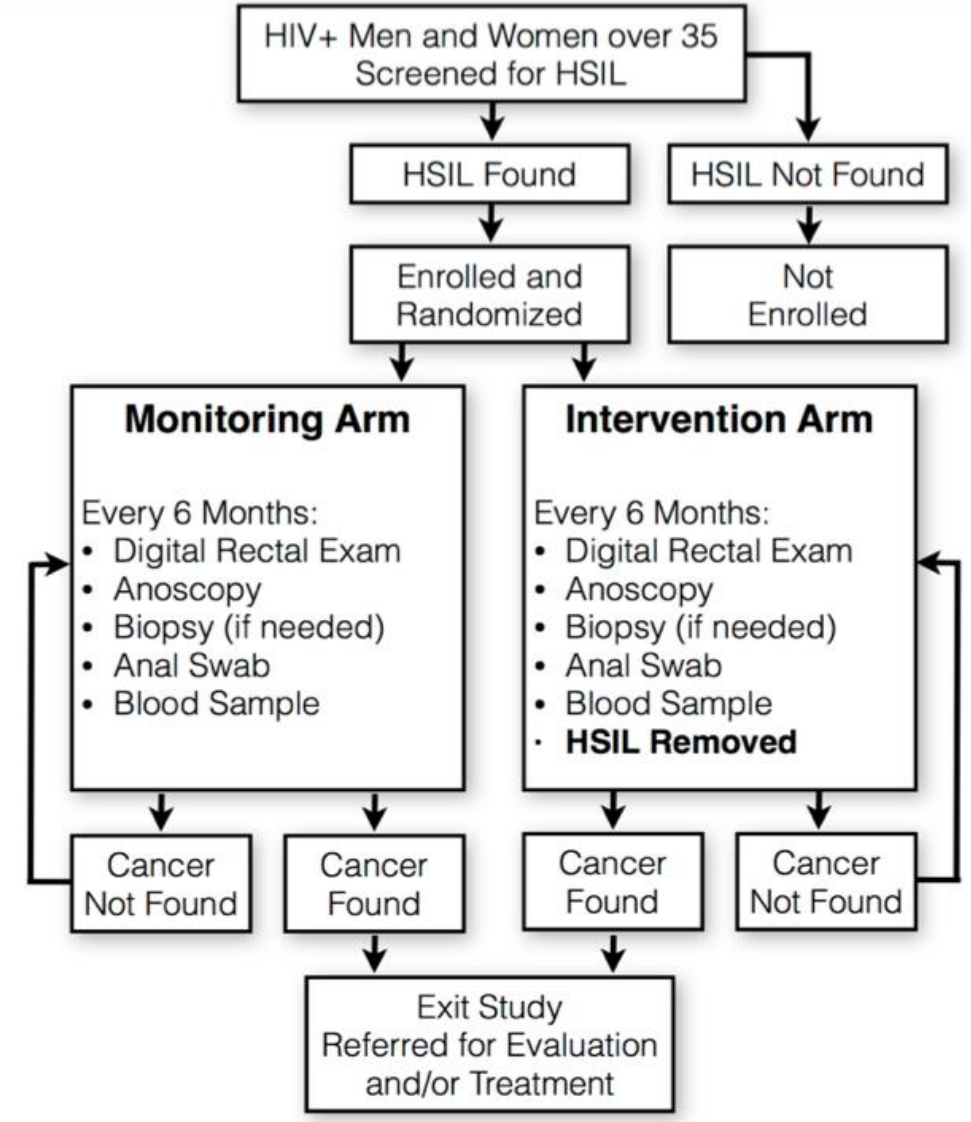
ANCHOR Study: Recruitment Goals and Study Design

Screen > 17,385 volunteers

Enroll 5,058 study volunteers

Retain for 5 years in study

Estimated < 50
people will develop anal cancer



ANCHOR Study Procedures

Over 5 Years

- Every 6 months: blood draw, 3 anal swabs, high resolution anoscopy, anal biopsies as necessary, a questionnaire
- If in Treatment Arm: Additional treatment visits depending on the treatment used and response to treatment
- $100 per visit

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ANCHOR Study Endpoints

- **Primary objective**
  - To determine whether treating anal high-grade intraepithelial neoplasia (HSIL) is effective in reducing the incidence of anal cancer in HIV-infected men and women.

- **Secondary objectives**
  - To determine the safety of infrared coagulation, electrocautery, imiquimod, laser, and 5- fluorouracil treatments for anal HSIL.

- **Exploratory objectives**
  - Collect clinical specimens and data to create a bank of well-annotated specimens that will enable correlative science: a) Identification of viral factors in HSIL progression to cancer; b) identification of host factors in HSIL progression to cancer; c) identification of biomarkers of HSIL progression to cancer and d) identify medical history and behavioral risk factors for HSIL progression to cancer.

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ANCHOR Study Design/Endpoints

The study assumes an incidence rate of anal cancer of 100/100,000 among all HIV-infected men and women, which by definition includes those with and without prevalent anal SIL.

We are assuming that the obligate anal cancer precursor is HSIL, and that all cases of cancer develop from HSIL.

If half of the population develops HSIL, then the incidence of cancer among those with HSIL would be expected to be 200/100,000.

ANCHOR STUDY SITES

Seattle Consortium PI:

- David Aboulafia, MD

Seattle Site co-PIs:

- Jeffrey Schouten, MD (Harborview/Virginia Mason)
- Helen Stankiewicz Karita, MD (Harborview)
- Juan de La Ossa, MD (Polyclinic)
- Teresa Vasicej, PA-C (Virginia Mason)

Funded by the National Cancer Institute

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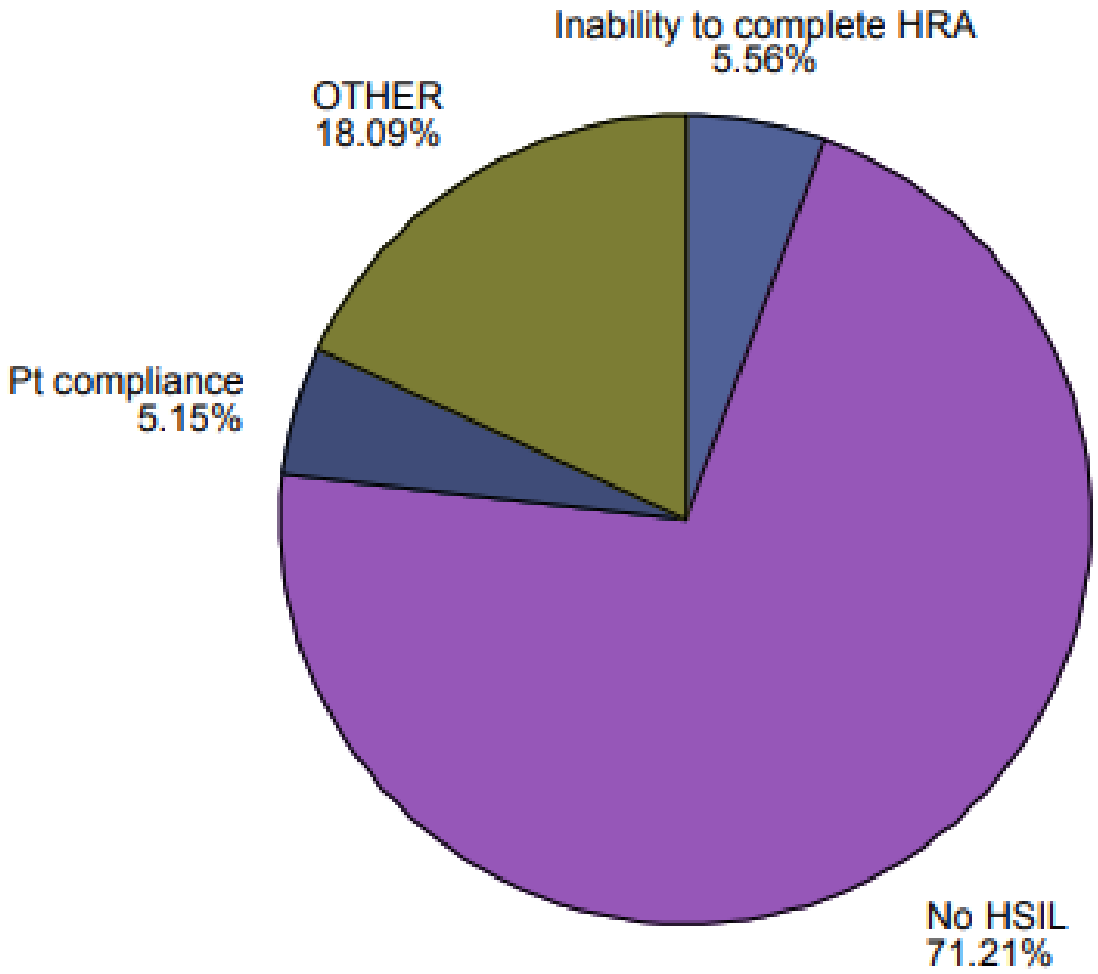
ANCHOR Accrual (as of March 2022)

	Screened	Enrolled/ Randomized
National	10,885	4,535 (5,058)
HMC	153	63
VMMC	178	87
Polyclinic	50	9



Demographics of randomized population

	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 (cont.)

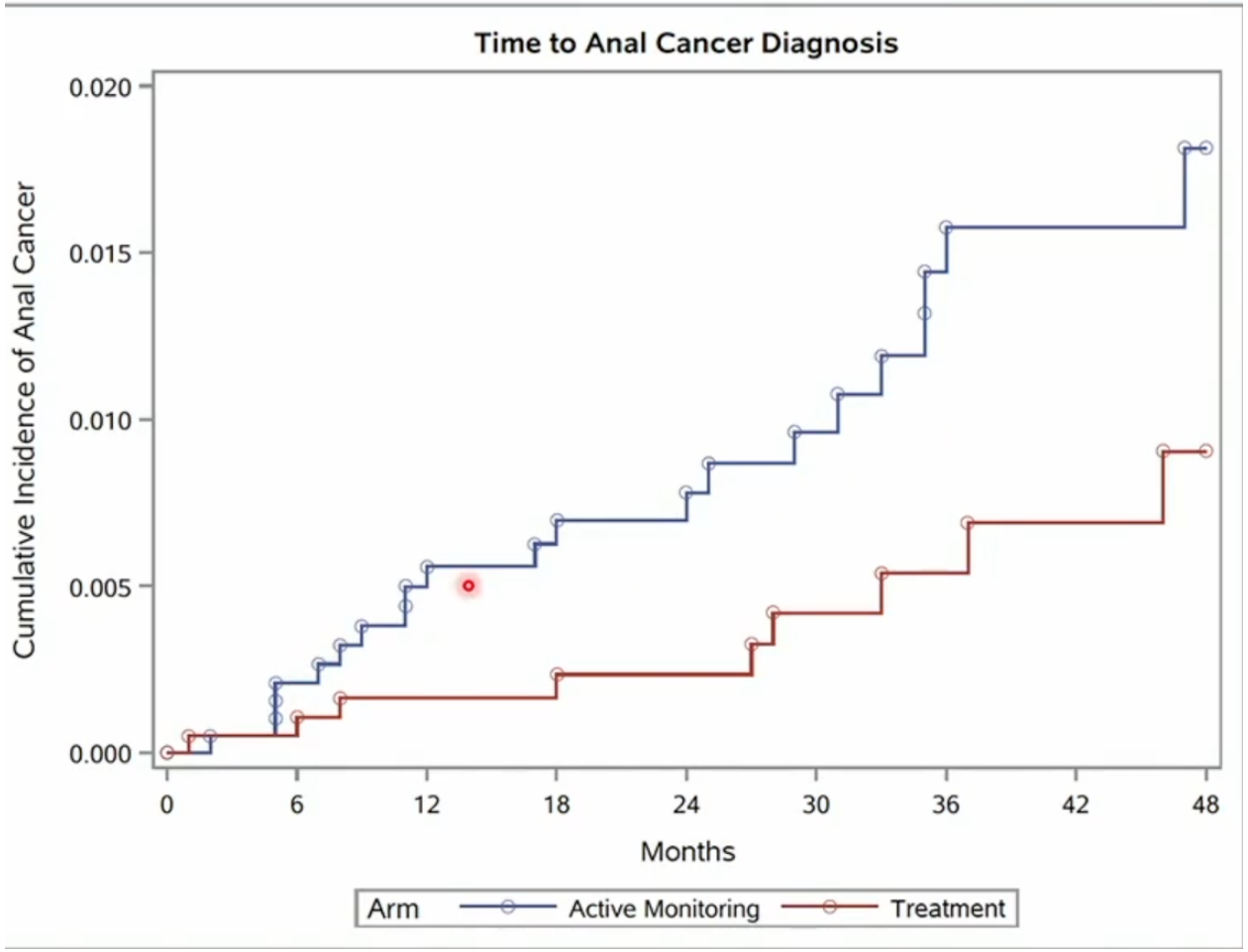
	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Race/ethnicity N (%)			
Non-Hispanic White	695 (31.2)	737 (33.2)	0.37
African-American	935 (42.0)	939 (42.3)	
Hispanic, non-African-American	381 (17.1)	339 (15.3)	
Asian/Pacific Islander	27 (1.2)	29 (1.3)	
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 (cont)

	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

- DSMB notified when 32 cancers diagnosed
- 9 participants were diagnosed with invasive anal cancer in the tx arm and 21 in the AM arm
- Cancer incidence in the tx arm 173/100,000 PY of f-u, compared with 402/100,000 PY in the AM arm



Median f-u of 25.8 months, **57% reduction in anal cancer** (95% CI 6-80%, p= 0.029)

Results

- DSMB recommended stopping enrollment in the study due to efficacy
- Recommendation made to treat all individuals in the monitoring arm
- We will continue to follow all individuals who wish to be treated and/or followed

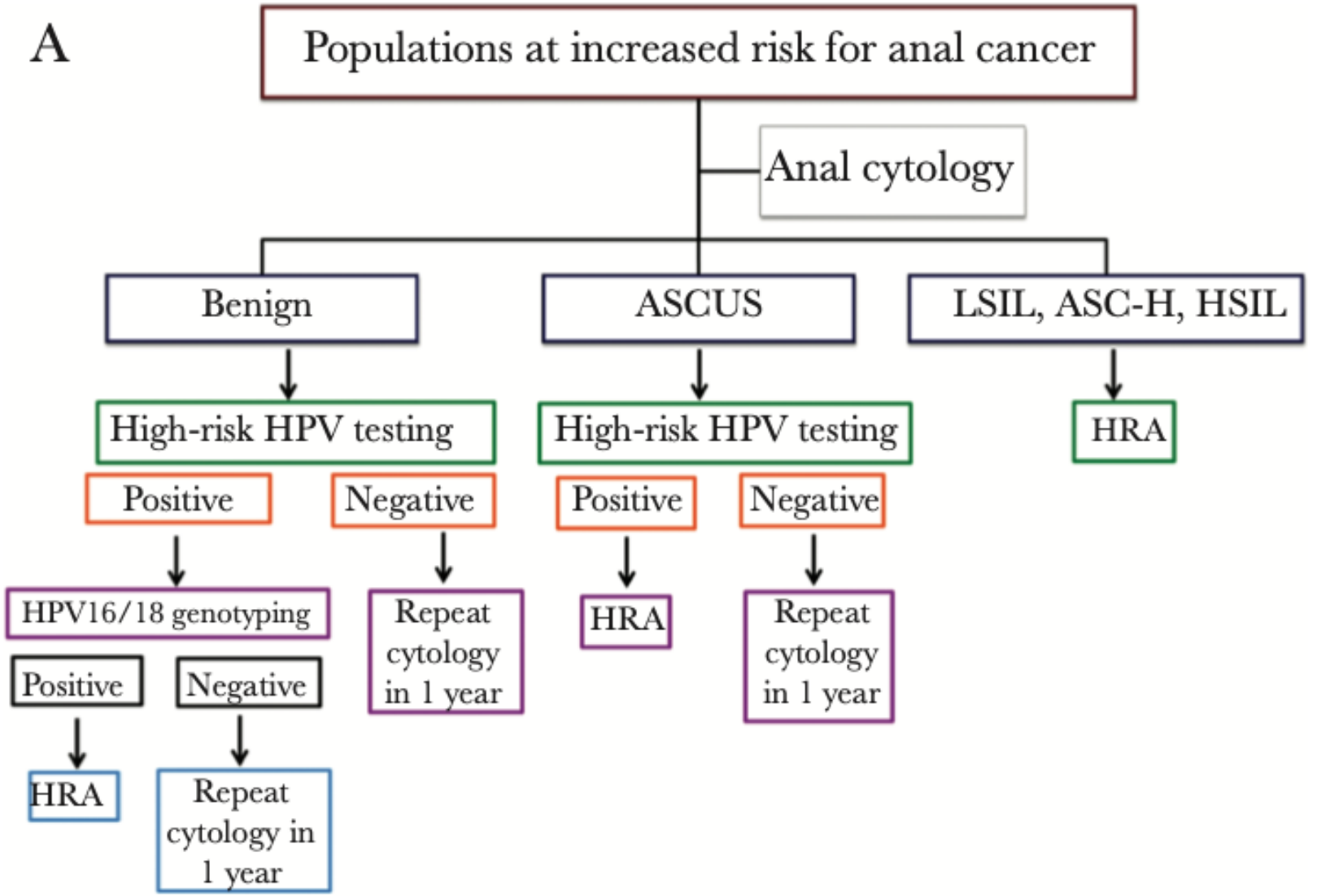
Adverse events

	Treatment arm	Active monitoring arm
Adverse events (N)	683	635
Deaths	54	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

Implications of the ANCHOR study findings

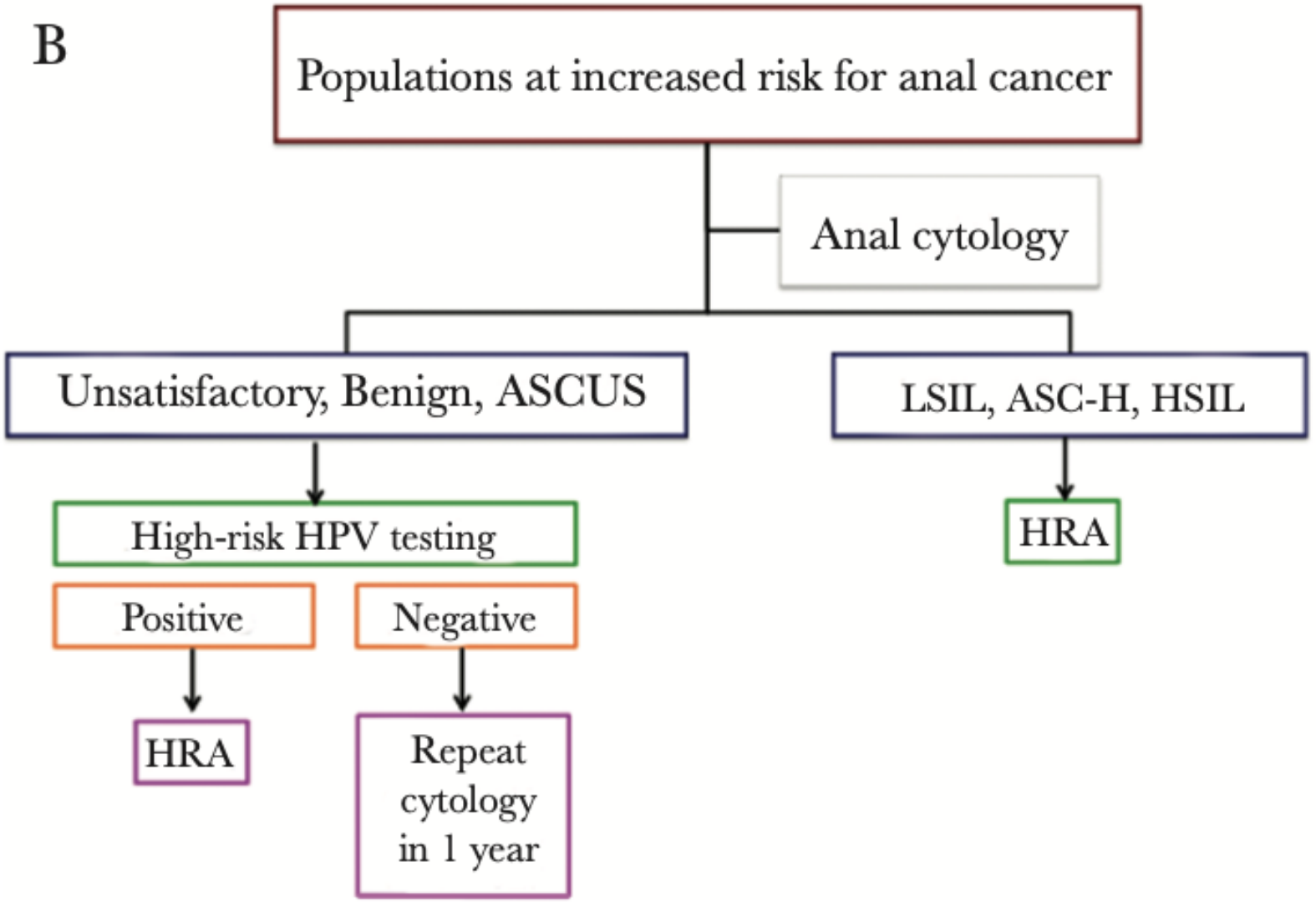
- Treatment of anal HSIL is effective in reducing the incidence of anal cancer
- These data should be included in an overall assessment for inclusion of screening for and treating anal HSIL as standard of care
- There is a need for optimization of screening algorithms for HSIL
- There is a need for a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

Possible screening algorithm



JID 2021; 224(5)881-888

Possible screening algorithm



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AETC AIDS Education & Training Center Program Mountain West