

# **An Introduction to Anal Cancer and Anal Dysplasia Screening**

**Ami Multani, MD**

**Medical Director of Infectious Disease, HIV and Anal Dysplasia -  
Fenway Health**

**Clinical Instructor of Medicine and Infectious Disease - Harvard  
Medical School**

**10/1/24**



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## Fenway Health

- Independent 501(c)(3) FQHC
- Founded 1971
- Mission: To enhance the wellbeing of the LGBTQIA+ community as well as people in our neighborhoods and beyond through access to the highest quality health care, education, research, and advocacy
- Integrated primary care model, including HIV and transgender health services

## The Fenway Institute

- Research, Education, Policy



# The National LGBTQIA+ Health Education Center

- Training and Technical Assistance
- Grand Rounds
- Online Learning
  - CE and HEI Credit
- Environmental Influences On Child Health Outcomes (ECHO) Programs
- Publications and Resources



Learning Module



Publication



Toolkit



Video



Webinar

# Advancing Excellence in Transgender Health Conference

- What: Designed to train the whole health care team in providing skilled and confident gender-affirming health care, grounded in research evidence and best clinical practices
- Who: All members of health care teams, including physicians, behavioral health care providers, physician assistants, nurses and other staff
- Where: Hyatt Regency Boston on 1 Ave de Lafayette in Boston, MA
- When: October 25-27, 2024



<https://cmecatalog.hms.harvard.edu/advancing-excellence-transgender-health>

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<b>Other Health Professionals</b>	Confirm equivalency of credits with relevant licensing body.



# Learning Objectives

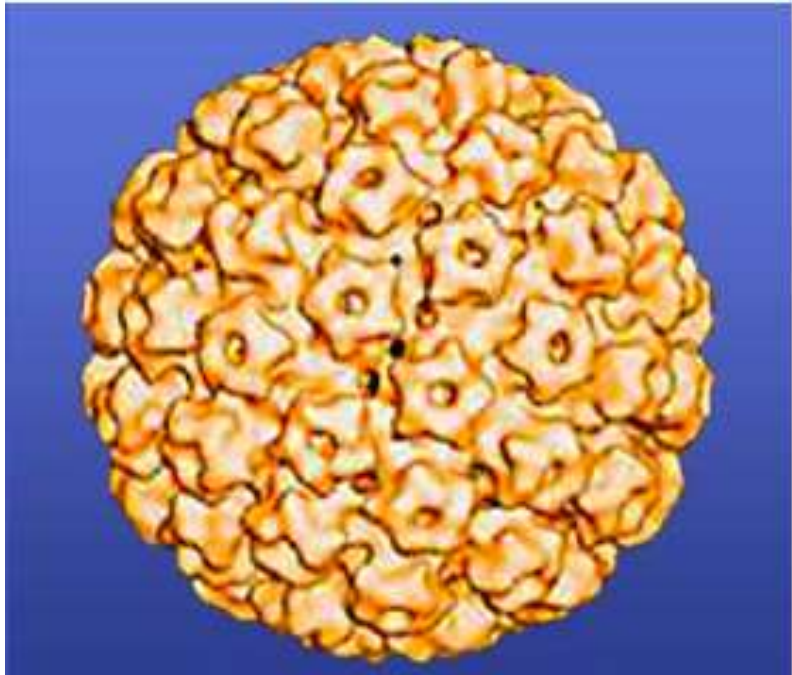
- Why do we screen for anal dysplasia and anal cancer?
- Who should we be screening for anal dysplasia and anal cancer?
- How do I perform an anal pap smear?
- How do I interpret anal pap smear results?





# Human Papilloma Virus (HPV)

- Non-enveloped double stranded DNA virus
- Papilloma Virus Family



- >120 types identified
- 40-50 ano-genital
  - 15-20 oncogenic types including 16, 18, 31, 33, 35, 39, 45, 51, 52, 58
    - HPV 16 (54%) and HPV 18 (13%) account for the majority of worldwide cervical cancers
    - High risk HPV types incorporate virus into host genome
  - Non-oncogenic types include 6, 11, 40, 42, 43, 44, 54
    - HPV 6 and 11 are most often associated with external anogenital warts
    - Low risk strains remain separate from host DNA and replicate separately

Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. Fields Virology. 4th ed. Philadelphia, PA: Lipencott-Raven; 2001: 2197-2229

Schiffman M, Castle, PE. Arch Pathol Lab Med. 2003; 127: 930-934.

Wiley DJ, Douglas J, Beutner K, et al. Clin Infect Dis 2002; 35 (suppl 2): S210-S224.

Munoz N, Bosch FX, de Sanjose S; et al. N Engl J Med 2003; 348: 518-527.

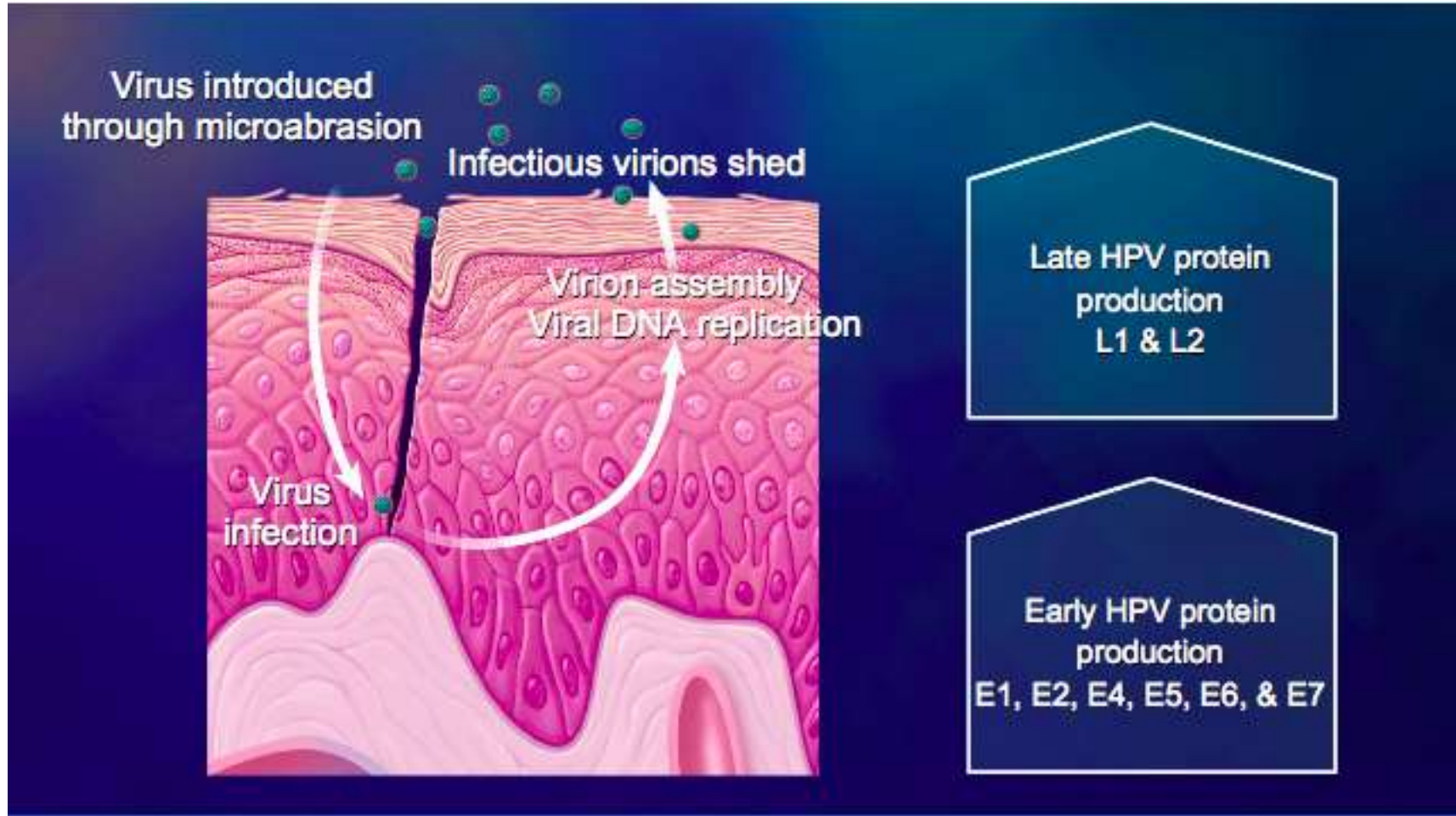
Clifford GM, Smith JS, Aguado T, Franceschi S. Br J Cancer 2003: 89; 101-105.



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# HPV Infection and Productive Life Cycle

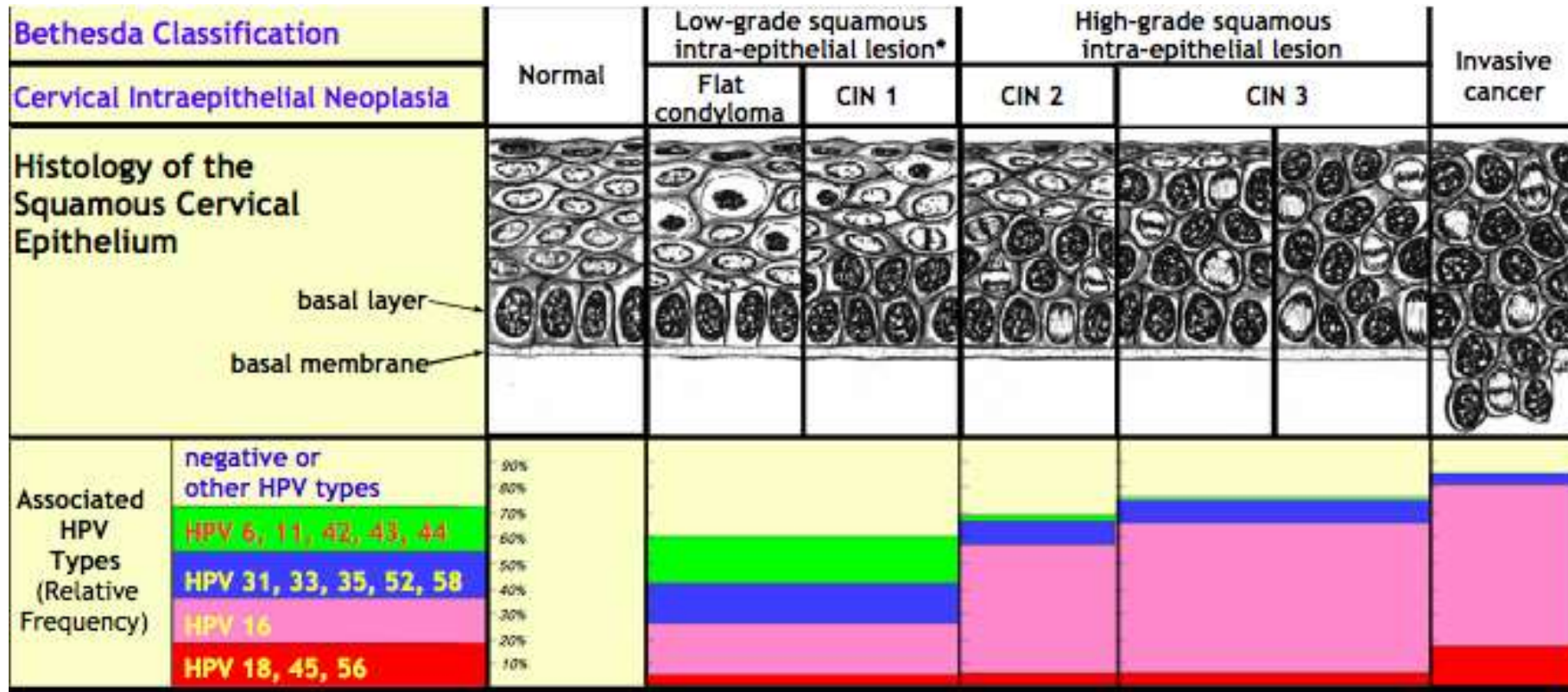


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Adapted from Doorbar J. *J Clin Virol.* 2005;32S:S7-S15.

# Histology of Squamous Intraepithelial Lesions (SIL)



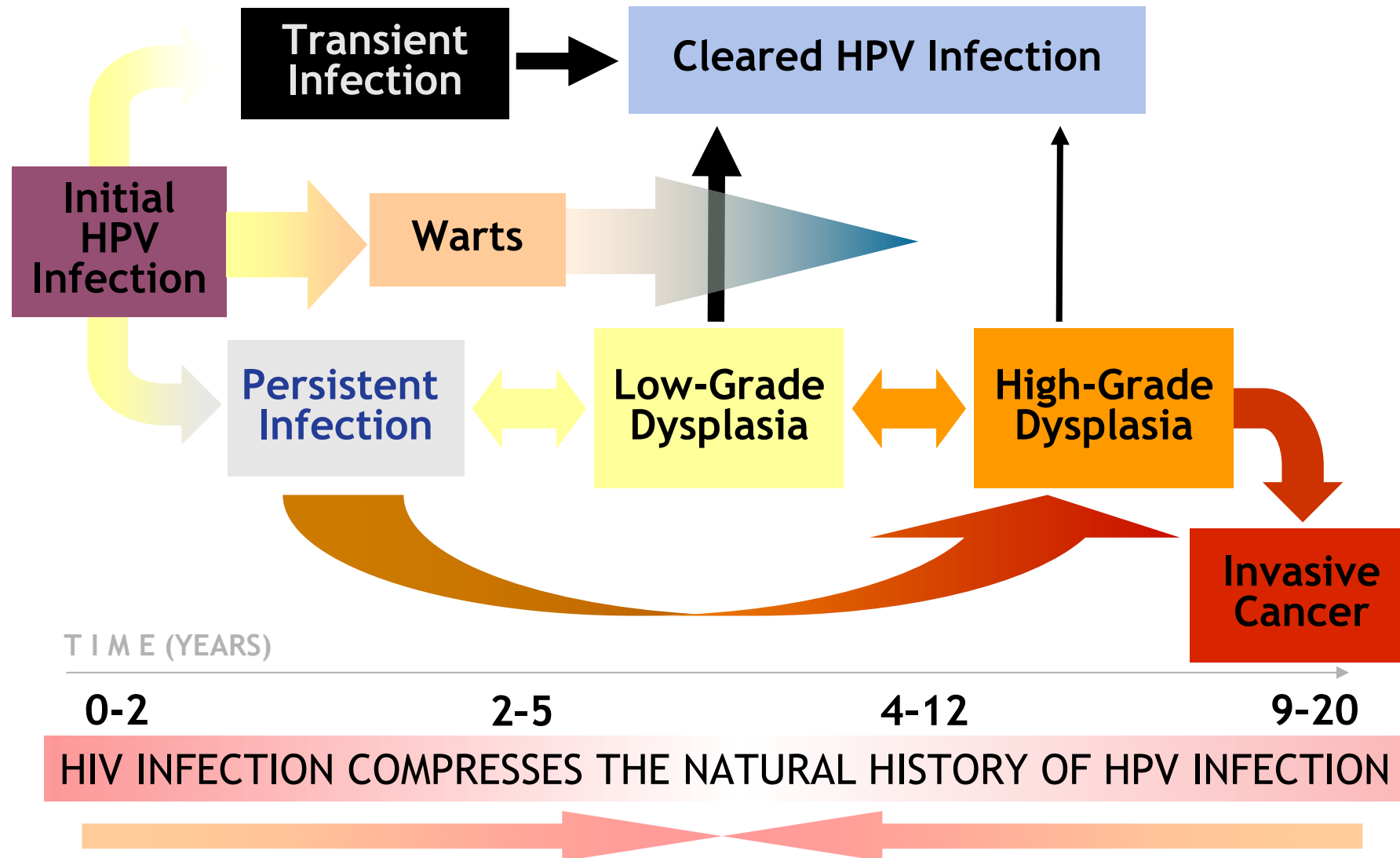
Modified from Bonnez W. Papillomavirus. In: Richman RD et al eds. *Clinical Virology*. 2nd ed. Washington, DC: American Society for Microbiology; 2002:557-596.



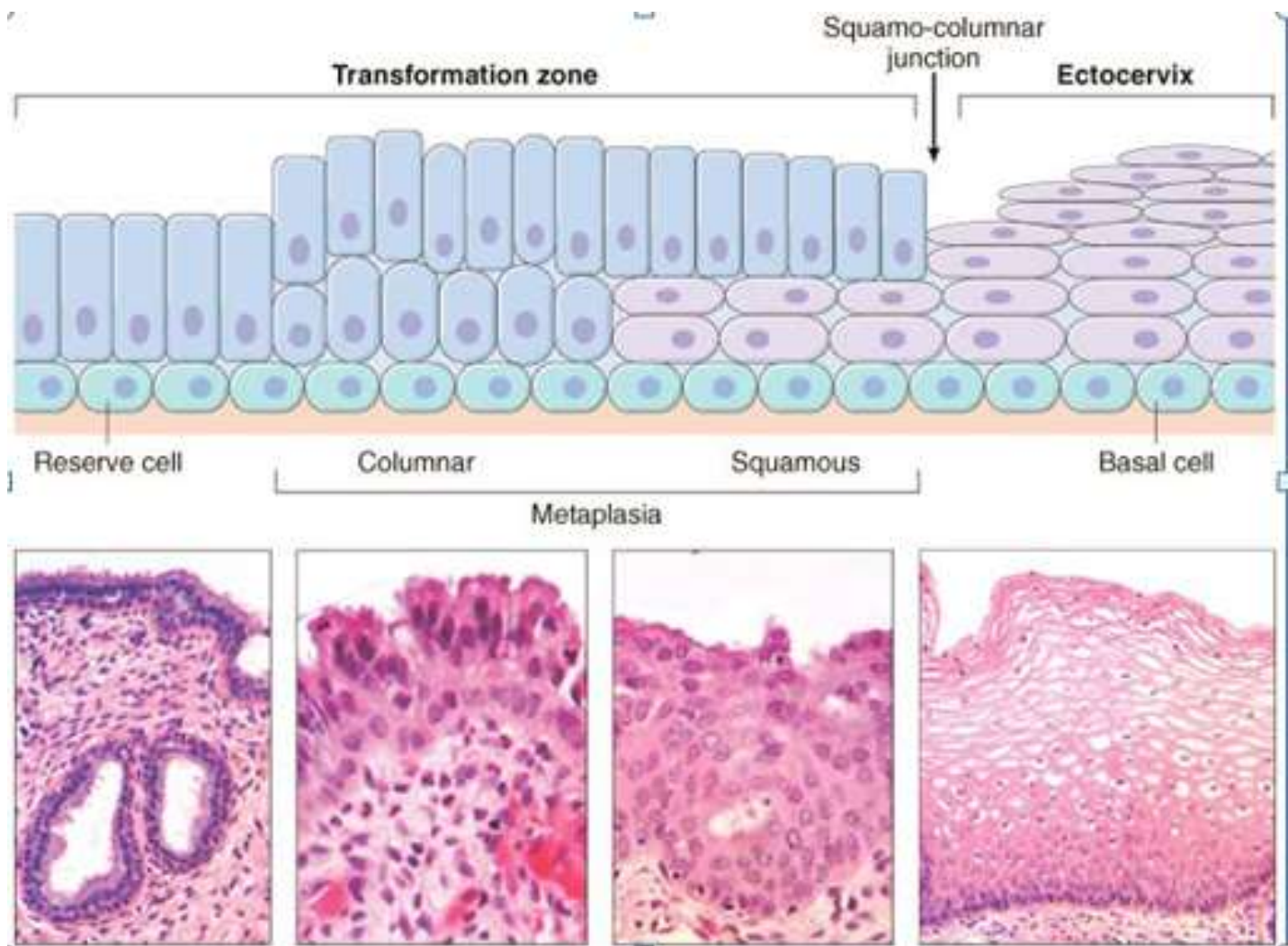
# HPV Clearance and Persistence

- >90% of HPV infections are transient
  - 70% of new HPV infections clear within 1 year, and 91% clear within 2 years
  - Median duration of infection = 8 months
- Persistence of high-risk HPV is crucial for development of high-grade dysplasia and cancer
  - Age at acquisition ( $\geq 30$  years)
  - Immunosuppression
  - Smoking

# Natural History of HPV Infection



# The Transformation Zone



Cervix



Anus



Oropharynx



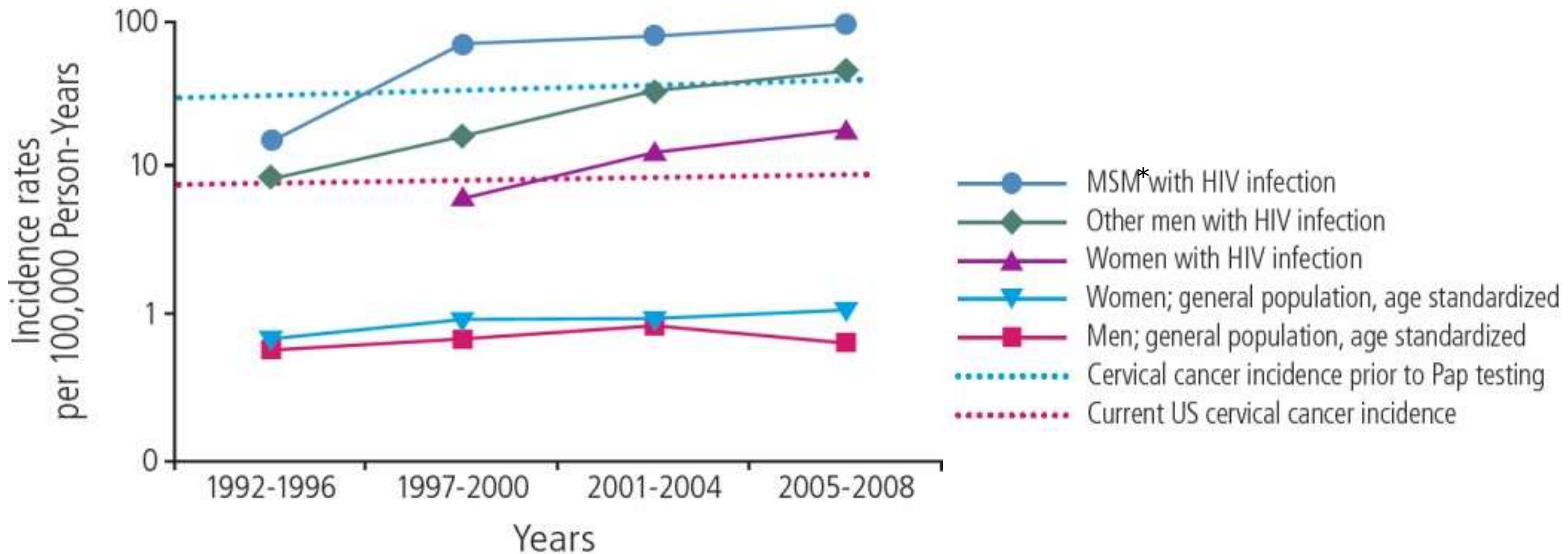
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# HPV in Human Immunodeficiency Virus (HIV) Infection

- Both viruses can induce shift in T helper cell (CD4 cell) profile leading to HPV persistence
- Clinically:
  - HIV infected patients have higher HPV local viral load
  - Decreased clearance
  - Increased rate of HPV reinfection
  - More persistent HPV infection
- Risk of carriage of high risk HPV increases with decreasing CD4 cell count
- Applies to cervical, anal and oral infection

# Anal Cancer Incidence, By Group

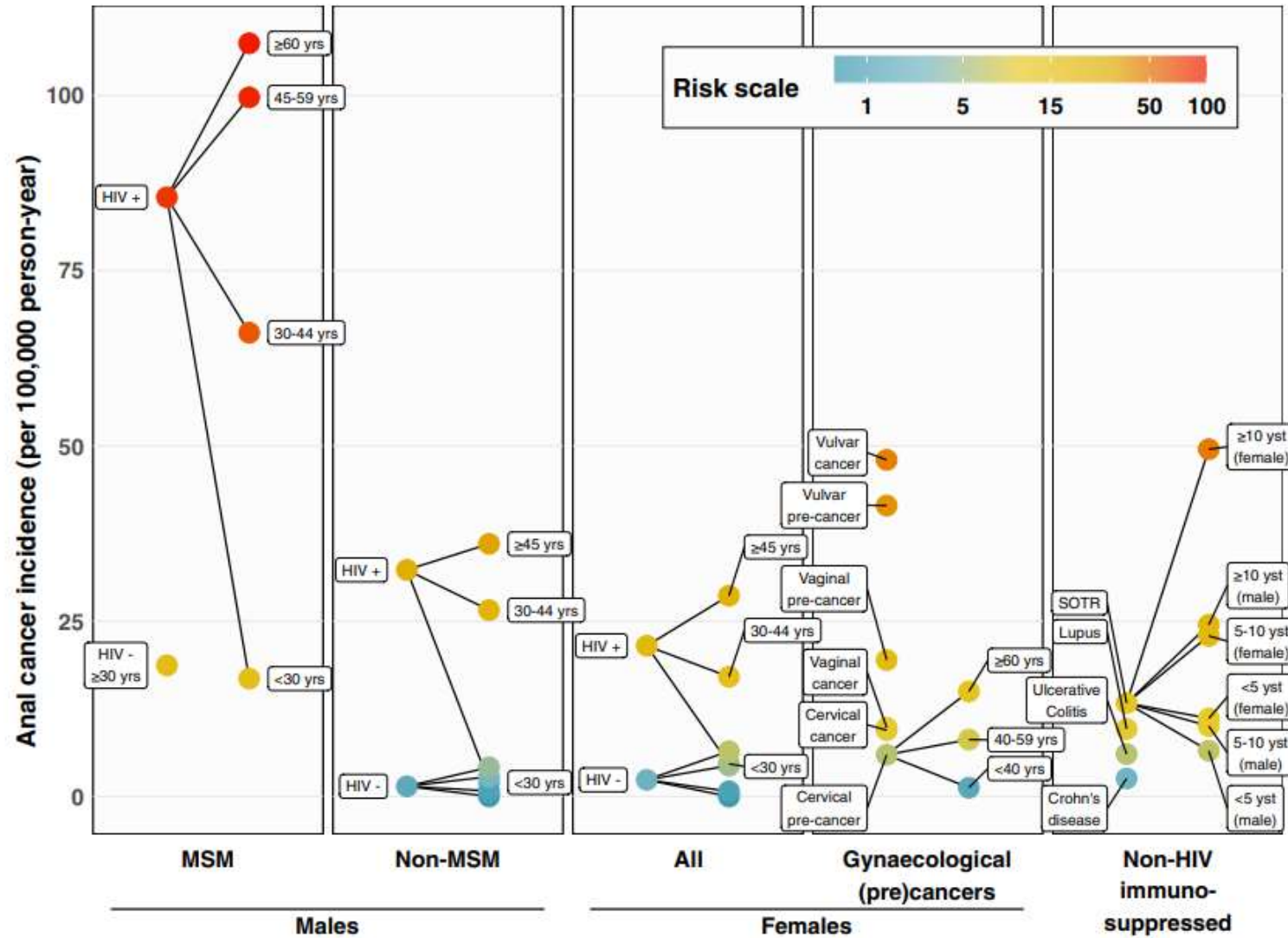


\*men who have sex with men

Wilkin TJ. Human papillomavirus-related malignancies in HIV infection: anal and oropharyngeal cancers. Top Antivir Med. 2018 Sep;26(3):85-88.



# Anal Cancer Risk Scale

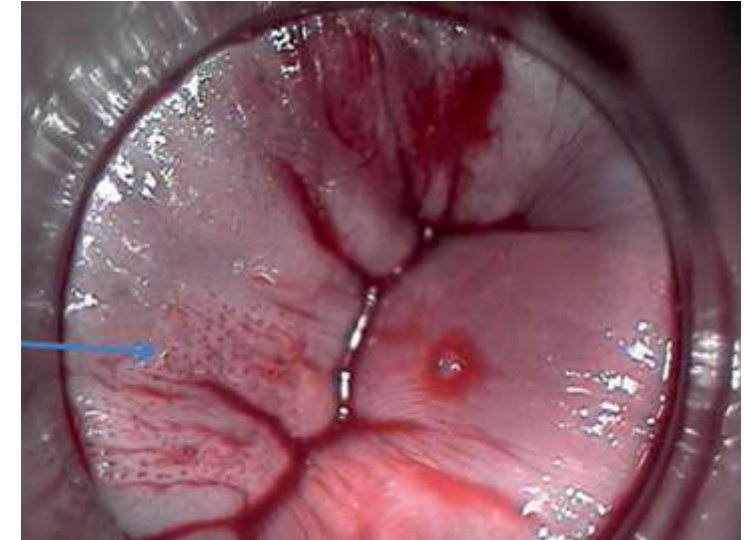


# Anal Cancer

- Patient presentations can be nonspecific
- Most early lesions are silent and symptomatic disease is usually advanced
- Lesions tend to develop in the squamocolumnar joint (SCJ), 2 cm from the anal verge
- Symptoms:
  - Rectal bleeding
  - Pain with defecation
  - Anal pruritis
  - Feeling of rectal fullness
  - Tenesmus
  - Ano-rectal ulcer or mass
- 85% of anal cancers are squamous cells cancers, 15% other cell types
- High-resolution anoscopy (HRA) may be most helpful in identifying anal squamous cell carcinoma (SCC) below dentate line

# Anal Squamous Cell Carcinoma in HIV

- Anal Cancer is preceded by precursor SIL
  - Anal Cancer High-grade SIL (HSIL) Outcomes Research (ANCHOR) Study: HSIL → Anal Cancer, 402/100,000
  - Diagnosis of HSIL to development of anal cancer
    - 9 months – 5 years in HIV + MSM
- Risk increased
  - CD4 <200
  - HIV Viral Load (VL) >100,000
  - Age >50
  - Tobacco use
- Treatment: Chemoradiotherapy (CRT) and chemotherapy
- 3-yr overall survival:
  - HIV + 42%
  - HIV – 76%



Palefsky JM, et al. N Engl J Med. 2022 Jun 16;386(24):2273-2282.  
Kreuter A, et al. Br J Dermatol. 2010 Jun; 162 (6): 1269-1277  
Berry JM et al. Int J Cancer.2014; 134: 1147-1155  
Palefsky JM. Curr opin HIV AIDS. 2017 Jan; 12 (1): 26-30  
Scholefield JH, et al. Br J Surg. 2005 Sep; 92 (9): 1133-6.  
Wang CJ et al. Surg Oncol Clin N Am. 2017 Jan; 26 (1): 17-31  
Grew D, et al. Dis Colon Rectum. 2015 Dec; 58 (12): 1130-6

# Case 1

- You are seeing a 48-year-old male on PrEP and DoxyPEP for follow up sexually transmitted disease (STD) screening
- He remarks that he has heard from a few of his friends that they have had anal HPV screening with their primary care providers
- He asks if he should be screened for anal dysplasia
- How do you respond?





# Prior Anal Dysplasia Screening Guidance

## Preventing Anal Cancer

Some cost-effectiveness evaluations indicate that in HIV-seropositive patients, screening for lesions using anal cytology and treating anal precancerous lesions to reduce risk of anal cancer in HIV-infected patients may provide clinical benefits comparable to measures for prevention of other opportunistic infection.<sup>122-125</sup> AIN lesions are similar in many ways to CIN, but there may be differences in natural history, optimal screening, and treatment approaches to prevent cancer. At this time, no national recommendations exist for routine screening for anal cancer.<sup>70</sup> However, some specialists recommend anal cytologic screening or high resolution anoscopy<sup>125</sup> for HIV-seropositive men and women **(CIII)**. An annual digital anal examination may be useful to detect masses on palpation that could be anal cancer **(BIII)**.<sup>125</sup> Screening for anal cancer with anal cytology should not be done without the availability of referral for high resolution anoscopy. If anal cytology is performed and indicates ASC-US, then ASC cannot rule out ASC-H, LSIL, or high-grade squamous intraepithelial lesion (HSIL), then it should be followed by high-resolution anoscopy **(BIII)**. Visible lesions should be biopsied to determine the level of histologic changes and to rule out invasive cancer **(BIII)** (see section on treatment for details on treating AIN).



## Sexually Transmitted Infections Treatment Guidelines, 2021

CORRECTED PROOF

### Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Melanie A Thompson, Michael A Horberg, Allison L Agwu, Jonathan A Colasanti, Mamta K Jain, William R Short, Tulika Singh, Judith A Aberg Author Notes

*Clinical Infectious Diseases*, ciaa1391, <https://doi.org/10.1093/cid/ciaa1391>

Published: 06 November 2020 Article history



## CLINICAL GUIDELINES PROGRAM

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

## Screening for Anal Dysplasia and Cancer in Adults With HIV

<https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/human-papillomavirus-disease?view=full>

<https://www.cdc.gov/std/treatment-guidelines/hpv-cancer.htm>

Melanie A Thompson et al., Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 73, Issue 11, 1 December 2021, Pages e3572-e3605, <https://doi.org/10.1093/cid/ciaa1391>  
<https://www.hivguidelines.org/guideline/hiv-anal-cancer/>



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the  
**ANCHOR**  
study.org

# The ANCHOR Study

- Followed HIV + patients aged 35+ for anal HSIL
  - Patients were randomized into a monitoring vs intervention arm and followed for 5+ years to study the progression of HSIL into anal cancer

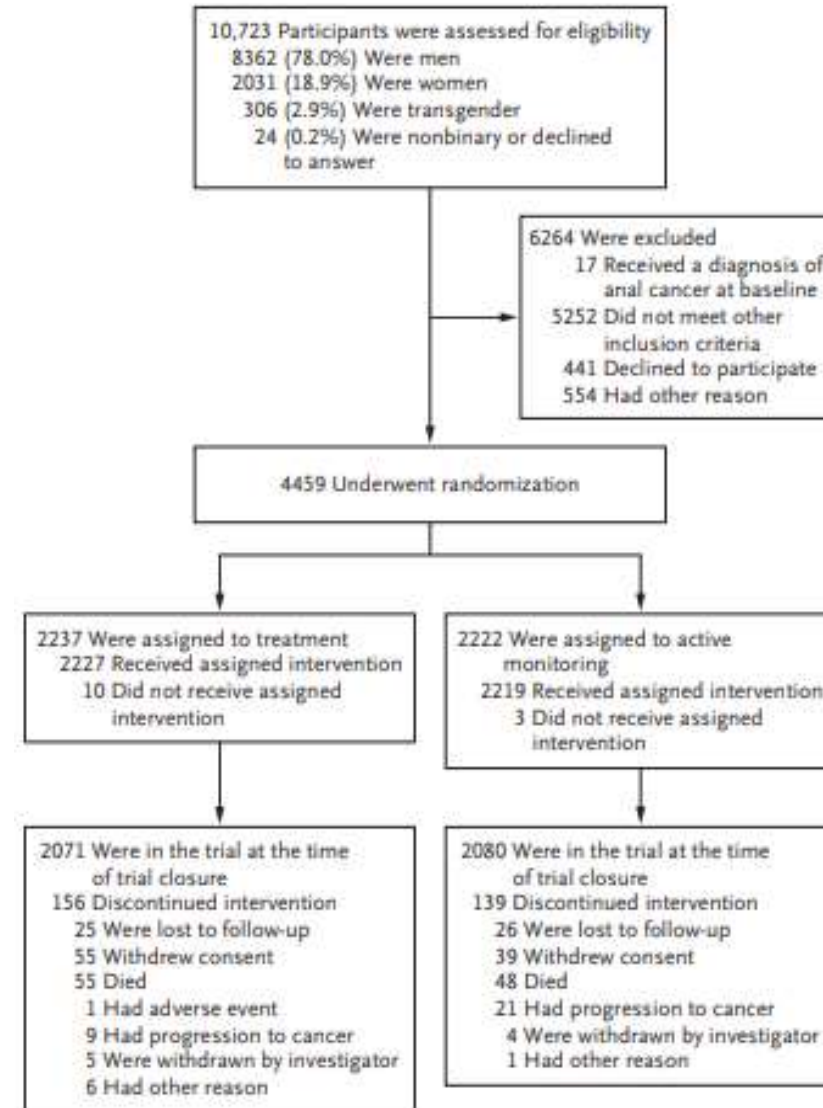


AIDS Malignancy Consortium (AMC)  
Protocol A01  
Funded by the National Cancer Institute  
Joel Palefsky, MD, Nat'l Principal  
Investigator



# The ANCHOR Study

- Phase 3 Randomized control trial with 4,446 participants enrolled
  - 25 clinical sites across US
  - People living with HIV (PLWH) age 35+ with biopsy proven anal HSIL followed longitudinally for 5+ years (2014-2021)





# ANCHOR Study

## Treatment Arm

- Followed according to treatment algorithm
- Biopsied if suspicion for HSIL, re-treated as needed
- Examined every six months once treatment complete
- Seen every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer

## Active Monitoring Arm

- Examined every six months
- Biopsied annually to confirm persistent HSIL
- Seen every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer



# Anal HSIL and Cancer at Screening

- 10,723 PLWH screened from 9/24/14 to 8/5/21
  - 53.3% of men screened found to have anal HSIL
  - 47.2% women screened found to have anal HSIL
  - 67.1% transgender individuals screened found to have anal HSIL
  - 17 individuals (0.16%, 160/100,000) were diagnosed with anal cancer at baseline

# Results

- Data and Safety Monitoring Board recommended stopping the study for efficacy
- Recommendation made to treat all individuals in the monitoring arm
- ANCHOR continues to follow all individuals who wish to be treated and/or followed

ORIGINAL ARTICLE

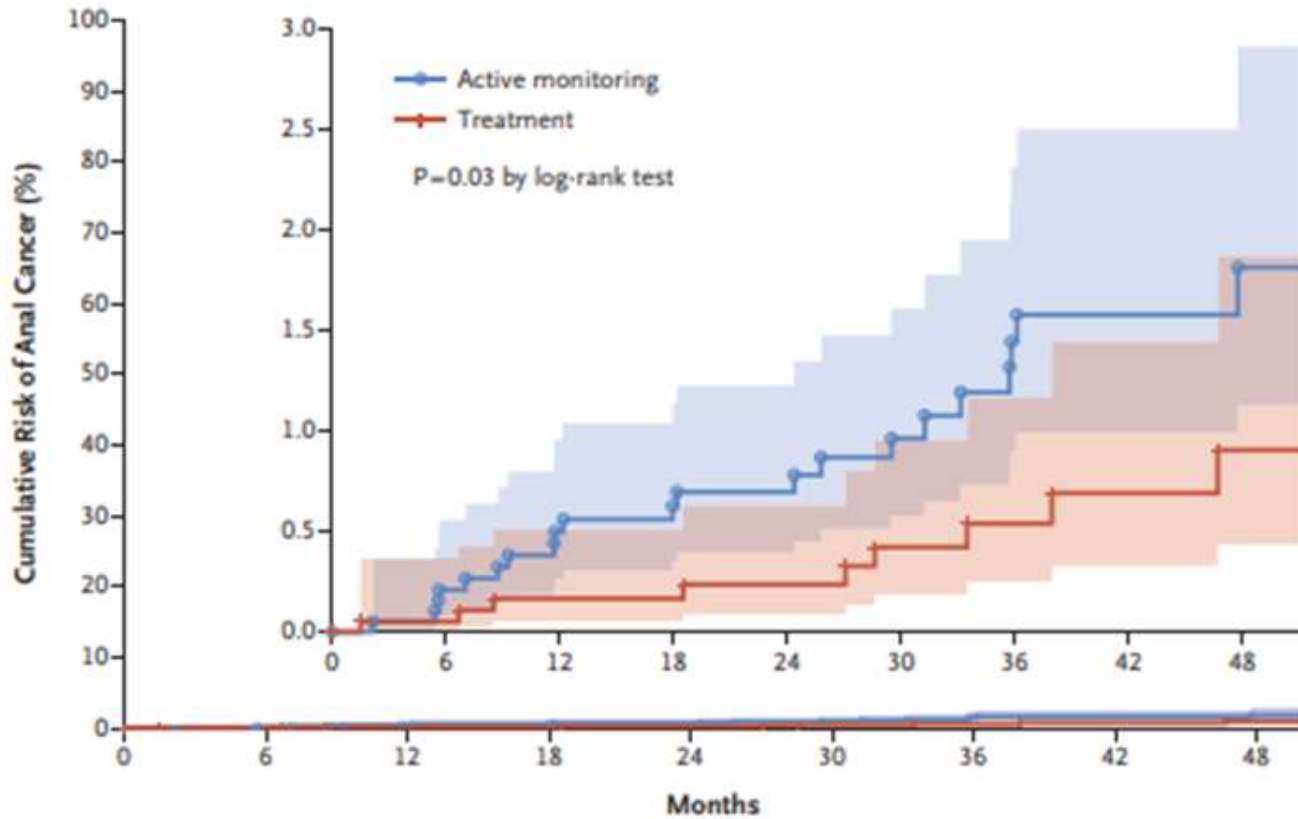
## Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

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\*

- Of 4459 randomized participants, 4446 (99.7%) were included in the analysis of time to progression to anal cancer
  - 9 cases anal cancer diagnosed in the treatment group (173/100,000 person years; 95% confidence interval (CI) 90 to 332)
  - 21 cases anal cancer diagnosed in the active monitoring group (402/100,000 person years; 95% CI 262 to 616)
- Rate of progression to anal cancer was lower in treatment group than in the active monitoring group by 57%
- **Among participants with biopsy proven anal HSIL, the risk of anal cancer was significantly lower with treatment for anal HSIL than with active monitoring**



# Anchor Study Results: Time to Progression to Anal Cancer



- Cumulative progression to cancer at 48 months was 0.9% in the treatment arm and 1.8% in the monitoring arm
- 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)



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Palefsky et al. Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer. N Engl J Med. 2022 Jun 16;386(24):2273-2282. doi: 10.1056/NEJMoa2201048. PMID: 35704479.

# Additional Conclusions

- The incidence of anal cancer is higher among males living with HIV than females living with HIV
  - There are few data on the incidence of anal cancer among transgender persons living with HIV
- Those reporting male-to-male sexual contact are at higher risk of anal cancer than men living with HIV who do not report male-to-male sexual contact
- The incidence of anal cancer increases with age among people living with HIV
- White people living with HIV are at higher risk than Black or Hispanic people living with HIV

# Anchor Take Aways

- “Our data provide support for the use of screening and treatment for anal HSIL as the standard of care for persons living with HIV who are 35 years of age or older”
- Rate of progression from anal HSIL to cancer is high
- Treatment of anal HSIL is effective in reducing the incidence of anal cancer
- These data are being used to recommend screening and treating anal HSIL as standard of care



**SPECIAL REPORT**



# International Anal Neoplasia Society's consensus guidelines for anal cancer screening

Elizabeth A. Stier<sup>1</sup>  | Megan A. Clarke<sup>2</sup>  | Ashish A. Deshmukh<sup>3,4</sup>  |  
Nicolas Wentzensen<sup>2</sup>  | Yuxin Liu<sup>5</sup>  | I. Mary Poynten<sup>6</sup>  |  
Eugenio Nelson Cavallari<sup>7</sup> | Valeria Fink<sup>8</sup> | Luis F. Barroso<sup>9</sup> |  
Gary M. Clifford<sup>10</sup>  | Tamzin Cuming<sup>11</sup> | Stephen E. Goldstone<sup>12</sup> |  
Richard J. Hillman<sup>6,13</sup> | Isabela Rosa-Cunha<sup>14</sup> | Luciana La Rosa<sup>15,16</sup> |  
Joel M. Palefsky<sup>17</sup> | Rosalyn Plotzker<sup>18</sup> | Jennifer M. Roberts<sup>19</sup>  | Naomi Jay<sup>17</sup>

## Populations to screen

**Risk Category A**  
Cancer incidence >17/100,000

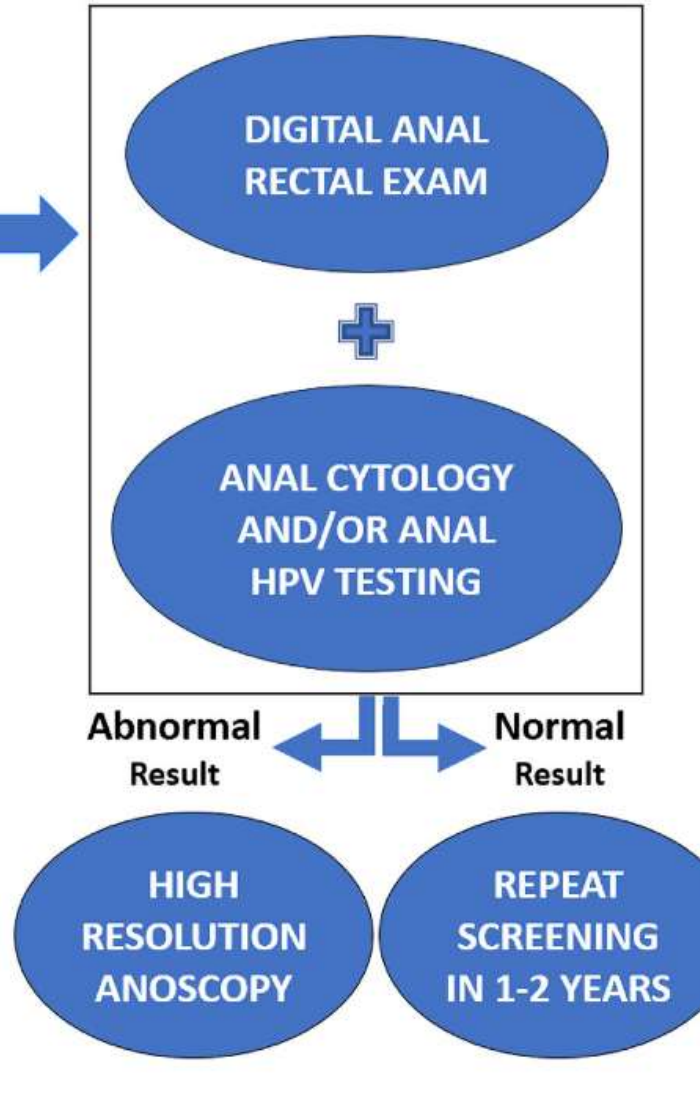
<b>Persons with HIV</b> <ul style="list-style-type: none"> <li>Men who have sex with men (MSM) age 35+</li> <li>Transgender women (TW) age 35+</li> <li>Men (not MSM) age 45+</li> <li>Women age 45+</li> </ul>	Vulva Dysplasia or Vulva Cancer
	MSM without HIV age 45+ TW without HIV age 45+
	Solid organ transplant recipients 10 years post transplant

**Risk Category B**  
Cancer incidence <10/100,000

Shared Decision-Making Age 45+  
with history of:

<ul style="list-style-type: none"> <li>Cervical/Vaginal HSIL or Cervical/Vaginal Cancer</li> <li>Perianal Warts</li> </ul>	<ul style="list-style-type: none"> <li>Persistent Cervical HPV 16+</li> <li>Other immunosuppression or on chronic systemic steroid therapy</li> </ul>
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## How to screen



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Stier EA, Clarke MA, Deshmukh AA, Wentzensen N, Liu Y, Poynten IM, Cavallari EN, Fink V, Barroso LF, Clifford GM, Cuming T, Goldstone SE, Hillman RJ, Rosa-Cunha I, La Rosa L, Palefsky JM, Plotzker R, Roberts JM, Jay N. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. *Int J Cancer*. 2024 Jan 31. doi: 10.1002/ijc.34850. Epub ahead of print. PMID: 38297406.





# HIV Clinical Guidelines Now Recommend High Resolution Anoscopy as Part of Anal Cancer Screening Program for People with HIV

**Content From:** [NIH Office of AIDS Research](#) • **Published:** July 10, 2024 • ⌚ 3 min read

Topics [People with HIV](#) [Treatment](#)



Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America. Year. Available at <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection>. Accessed (9/11/24) [Screening for Anal Cancer]

## • **Recommendations:**

- Assess all adults living with HIV at least once a year for anal abnormalities (anal pain, burning, masses) and perform a Digital ano-rectal examination (DARE)
- PLWH <35 who are symptomatic or show signs of anal cancer (visual or palpable abnormalities) should undergo standard anoscopy
- HIV + MSM and Transgender women  $\geq 35$  AND all other PLWH  $\geq 45$ 
  - Assess anal symptoms and collect anal specimens (anal cytology +/- HR HPV co-testing) and perform DARE



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## Case 2

- You are seeing a 53-year-old non-binary, assigned female at birth (AFAB) patient for their annual complete physical exam (CPE) and cervical pap smear
- They have a known history of cervical intraepithelial neoplasia 3 (CIN 3) status post loop electrosurgical excision procedure (LEEP) 4 years ago
- Would you recommend anal dysplasia screening in addition to cervical dysplasia screening?



# Who should we be screening for anal cancer?

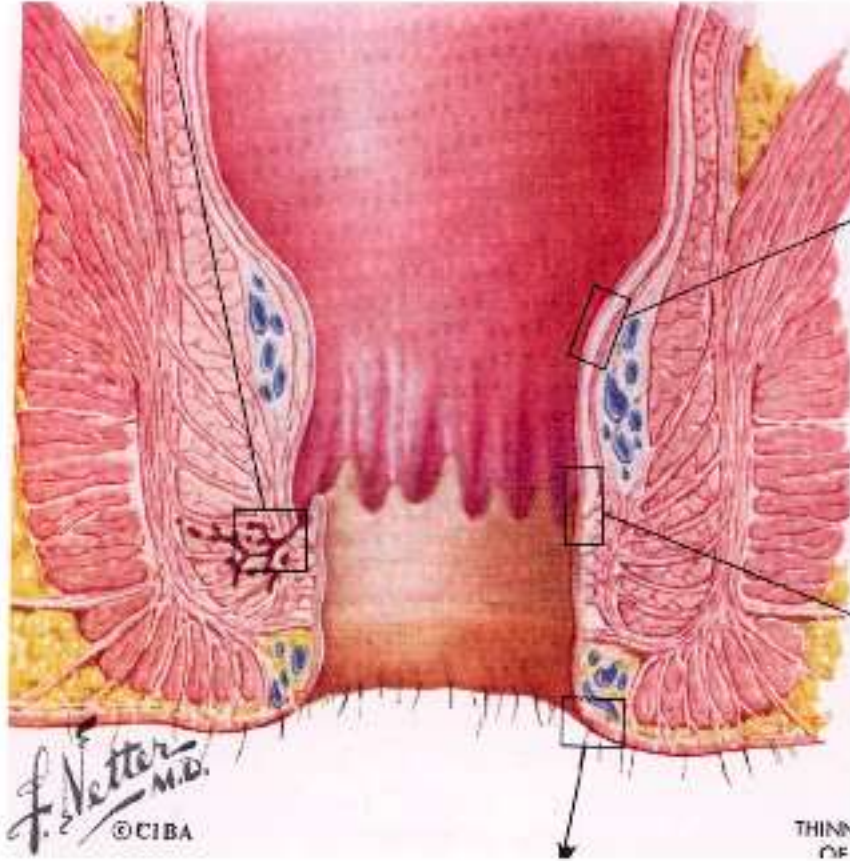
Population – Risk category	When	Anal cancer incidence <sup>2,5</sup> per 100,000 person-years
<b>Risk Category A (Incidence ≥10-fold compared to the general population)</b>		
MSM and TW with HIV	Age 35	>70/100,000 age 30-44 >100/100,000 age 45+
Women with HIV	Age 45	>25/100,000 age 45+
MSW with HIV	Age 45	>40/100,000 age 45+
MSM and TW not with HIV	Age 45	>18/100,000 age 45-59 >34/100,000 age 60+
History of vulvar HSIL or cancer	Within 1 year of diagnosis	>40/100,000
Solid organ transplant recipient	10 years post-transplant	>25/100,000
<b>Risk Category B (Incidence up to 10-fold higher compared to the general population)</b>		
Cervical/Vaginal Cancer	*Shared decision age 45	9/100,000
Cervical/Vaginal HSIL	*Shared decision age 45	8/100,000
Perianal warts (male or female)	*Shared decision age 45	unknown
Persistent cervical HPV 16 (>1 yr)	*Shared decision age 45	unknown
Other immunosuppression (e.g., Rheumatoid arthritis, Lupus, Crohn's, Ulcerative colitis, on systemic steroid therapy )	*Shared decision age 45	6/100,000
<b>Incidence among the general population: 1.7 per 100,000<sup>8</sup></b>		
Abbreviations: MSM, Men who have sex with men; TW, Transgender women; MSW, Men who have sex with women; HSIL, high grade squamous intraepithelial lesion *Shared decision-making is defined as the process in which a health care provider and patient work together to make a health care decision. The optimal decision considers evidence-based information regarding available options, the provider's knowledge and experience, and the patient's values and preferences.		

Primary Screening Test	Triage test	Level of Evidence	Special Considerations
Cytology	None	BII	Anal cytology is the most widely used and evaluated test for anal cancer screening. Providers may consider using different thresholds for referral to HRA depending on capacity (see table 3).
	hrHPV (with or without genotyping)	CII	hrHPV testing to triage ASC-US cytology (or other results, see table 3) could be used to reduce HRA referral rates. This strategy has not been widely evaluated in the literature.
hrHPV (with or without genotyping)	None	BII	<p>The efficiency of primary testing with a pooled hrHPV test is limited in populations with high HPV prevalence (e.g., MSM with HIV). This strategy could be considered in settings with no cytology infrastructure, or to reduce HRA (for patients testing hrHPV negative) in practices providing HRA on all patients. In most settings, additional triage will be needed for individuals who test hrHPV positive.</p> <p>Use of hrHPV genotyping, specifically for HPV16, may help identify patients with high risk of HSIL or cancer. Performance does not seem to improve with the addition of HPV18.<sup>4</sup></p> <p>hrHPV testing may not be available in many settings.</p>
	Cytology	CII	Triage of hrHPV-positive results with cytology (e.g., at an ASC-US or worse threshold) can improve specificity of hrHPV-testing and reduce HRA referral. However, observational data on this approach are lacking in the literature.
Cytology/hrHPV co-test (with or without genotyping)	None	BII	Current available data suggest that anal co-testing does not provide any benefit over primary hrHPV testing for anal HSIL. However, anal co-testing may be especially beneficial for its negative predictive value. Co-testing may be less efficient in populations with high hrHPV prevalence.
Digital Anal Rectal Exam (DARE)	None	BII	All populations at-risk for anal cancer receive DARE at time of screening tests (or in lieu of screening tests in absence of HRA availability).

Abbreviations: hr, high risk; ASC-US, atypical squamous cells of undetermined significance; MSM, men who have sex with men; HSIL, high grade squamous intraepithelial lesion; HRA, high resolution anoscopy



# Anal Cytology: Goal



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- Sample entire anal canal
- Anal transition zone
  - Analogous to cervical transformation zone
  - Squamous metaplasia
- Non keratinized squamous mucosa
- Keratinized squamous mucosa



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# How to Do an Anal Pap

1. Wet dacron/ rayon/ polyester swab (NOT cotton swab) under tap
2. Insert  $\sim 1\frac{1}{2}$ " into canal
  - No prior douching, enemas or K-Y
- 3 Process just as you would a cervical Pap

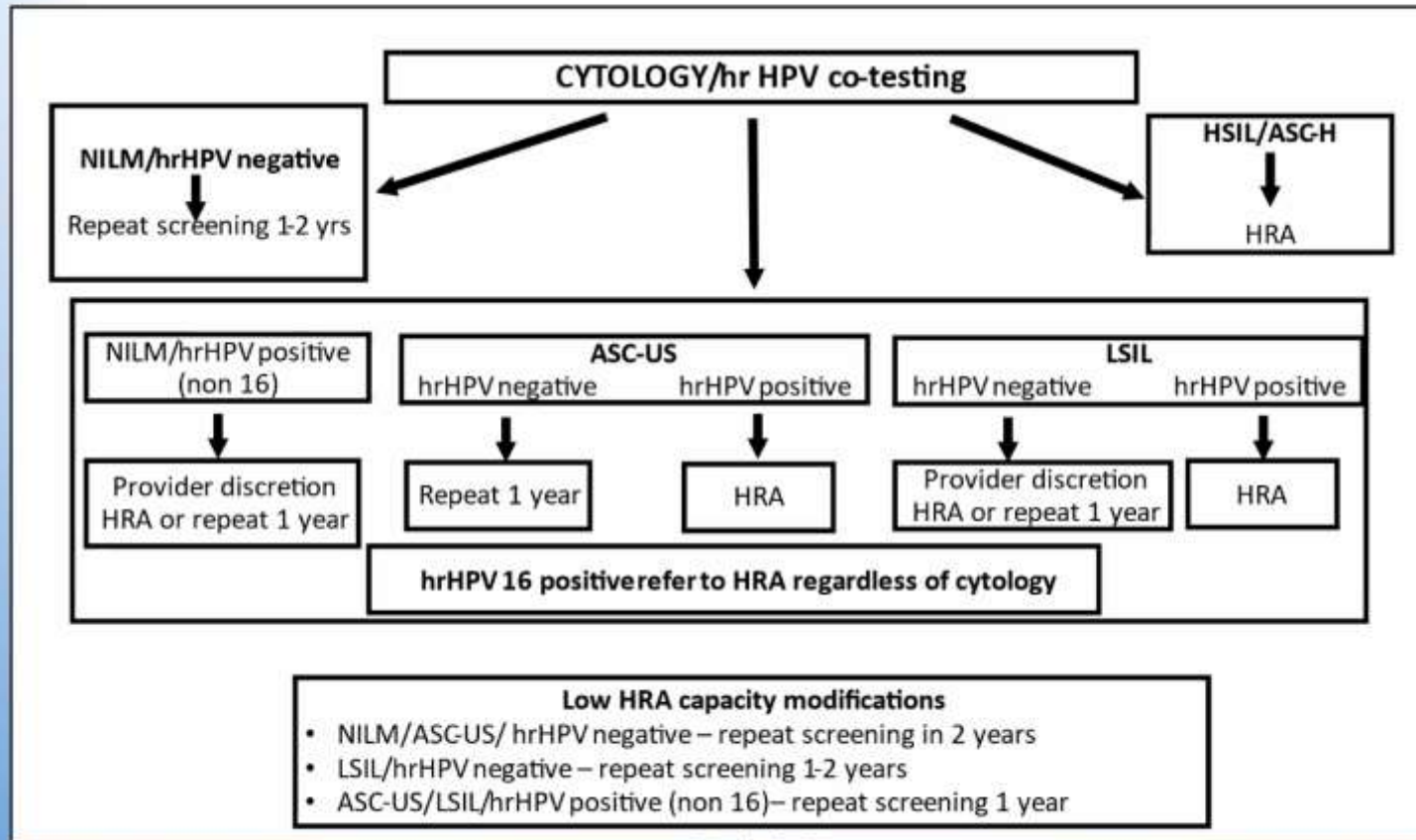


## Case 3

- You recently saw a 37-year-old HIV + cisgender male for HIV follow up and annual CPE
- You opted to complete STD screening, HIV follow up labs and his annual screening anal pap smear
- His anal pap smear returned with low-grade SIL, cannot exclude HSIL (LSIL-H), + high-risk (HR) HPV 16
- What does this mean? How do you counsel this patient?



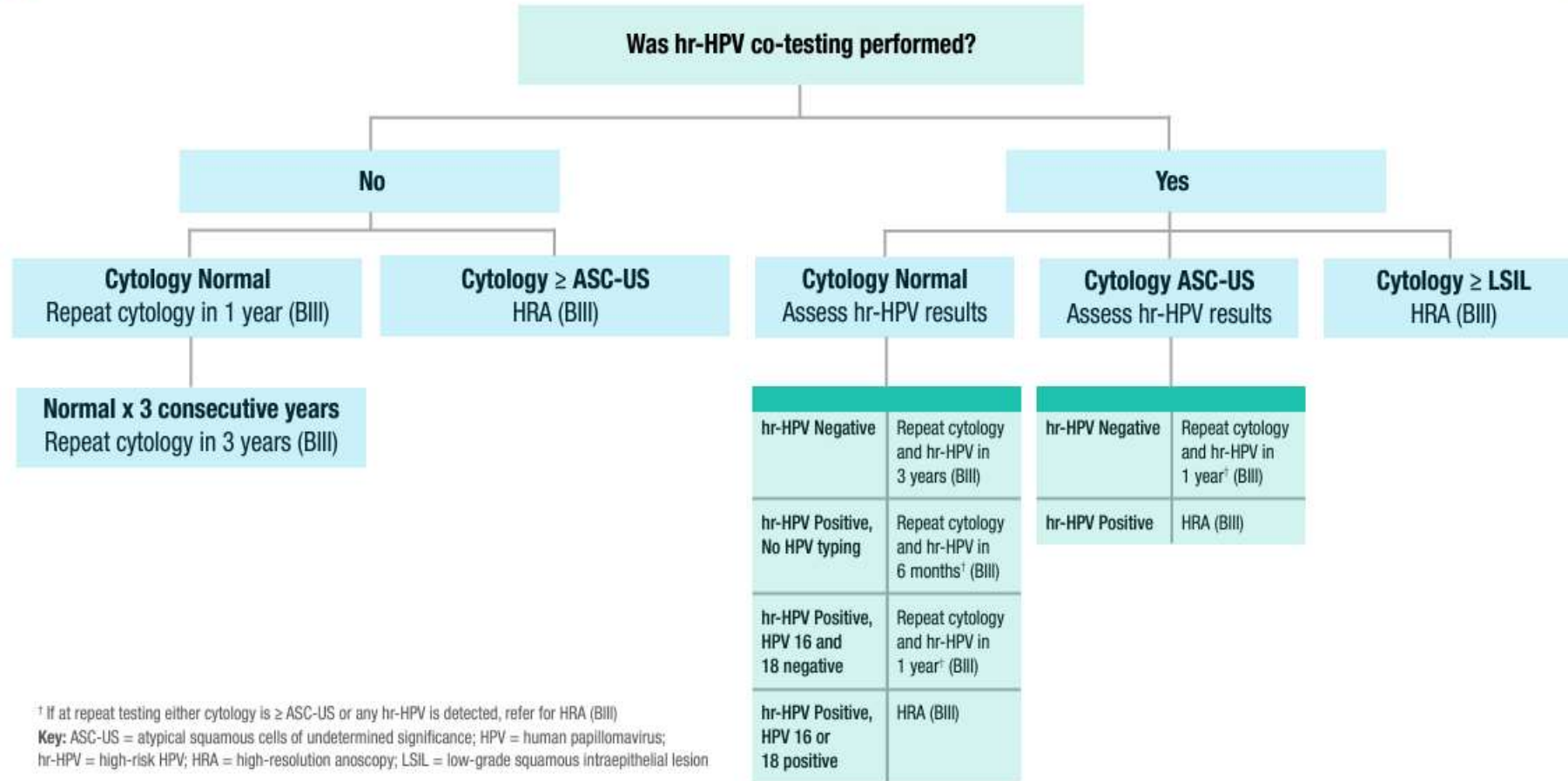
# MANAGEMENT OF SCREENING RESULTS: CYTOLOGY AND HRHPV CO-TESTING



**Key:** NILM=negative for intraepithelial lesions; ASC-US=atypical squamous cells of undetermined significance



## ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV



Overview of Anal Cancer Screening Guidelines in People With HIV		
	NIH OAR Adult and Adolescent OI Guidelines	IANS Guidelines
<b>Primary anal HPV testing alone without cytology as screening option</b>	No	Yes
<b>High-priority patients if HRA availability limited (no priority order specified in either guideline)</b>	<ul style="list-style-type: none"> <li>• Higher grade of cytologic abnormality</li> <li>• HPV16 on HPV testing</li> <li>• Smokers</li> <li>• &gt;60 years of age</li> <li>• Longer known duration of HIV</li> <li>• History of AIDS</li> </ul>	<ul style="list-style-type: none"> <li>• Higher grade of cytologic abnormality</li> <li>• HPV16 on HPV testing</li> </ul>
<p><b>Key:</b> HPV = human papillomavirus; HRA = high-resolution anoscopy; IANS = International Anal Neoplasia Society; NIH OAR = National Institutes of Health Office of AIDS Research; OI = opportunistic infection</p>		

# Fenway Health Management of Anal Dysplasia Screening Results

Cytology	HR HPV	HIV Positive	HIV Negative
NILM	- HR HPV	Repeat pap in 12 months **	Repeat pap in 24 months
ASCUS	- HR HPV	Repeat pap in 12 months	Repeat pap in 12-24 months
NILM	+ HR HPV (18,45)	Repeat pap in 6 months	Repeat pap in 12 months
ASCUS	+ HR HPV (16,18,45)	HRA referral	HRA referral
LSIL	+/- HR HPV	HRA referral	HRA referral
ASC-H	+/- HR HPV	HRA referral	HRA referral
LSIL-H	+/- HR HPV	HRA referral	HRA referral
HSIL	+/- HR HPV	HRA referral	HRA referral
Any result	+ HPV 16	HRA referral	HRA referral

\*\*Conservative recommendation based on IANS consensus guidelines

Adapted from Stier EA, et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702. doi: 10.1002/ijc.34850. Epub 2024 Jan 31. PMID: 38297406

Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America. Year. Available at <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection>. Accessed (9/11/24) [Screening for Anal Cancer]



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# What do we still need to learn?

- There is room for improvement in the 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
- Should we start screening earlier than 35 for HIV + MSM and HIV + transgender women?



# Case 4

- You are seeing a 50-year-old HIV + cisgender female for HIV follow up and perform her annual screening anal pap smear
- Her anal pap returns with ASCUS, - HR HPV co-testing
  - When would you complete her pap smear again?
  - What if her pap smear returned with no malignant cells but + HR HPV 16
  - What would you recommend?



# How Well Do Anal Pap Smear Results Correlate to Anal Precancer?

Type of pap smear	Sensitivity to detect HSIL	Specificity to detect HSIL
Cervical	55.4%	96.8%
Anal	55-89%	40-67%

- Multiple studies report anal specificity for diagnosing the correct degree of dysplasia was poor
- False negative cytology has been reported as high as 23% in MSM and 45% in HIV + patients

Clarke MA, Wentzensen N. Strategies for screening and early detection of anal cancers: A narrative and systematic review and meta-analysis of cytology, HPV testing, and other biomarkers. *Cancer Cytopathol.* 2018 Jul;126(7):447-460

Salit IE, Lytwyn A, Raboud J, Sano M, Chong S, Diong C, Chapman W, Mahony JB, Tinmouth J. The role of cytology (Pap tests) and human papillomavirus testing in anal cancer screening. *AIDS.* 2010 Jun 1;24(9):1307-13.

McCutcheon T, et al. The correlation Between anal pap cytology and histologic outcomes in HIV-Positive males. *Am J Surg.* 2022 Apr;223(4):759-763.

# Prevention

- HPV Vaccine:
  - FDA approved for prevention of:
    - Cervical, vulvar, vaginal and anal cancer caused by HPV types 16, 18, 31, 33, 45, 52 and 58.
    - Genital warts caused by HPV types 6 and 11
    - Cervical and anal precancerous lesions due to HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in people ages 9 – 26 y.o.
    - 2018 – approved use for those aged 27-45 with shared clinical decision-making
    - 2020 – expanded to include prevention of oropharyngeal cancer
- HPV Vaccine Dosing Schedule **in HIV**:
  - The Advisory Committee on Immunization Practices (ACIP) recommends vaccination with 3-dose schedule (NOT 2-dose schedule) at 0,1-2, 6 months for patients with HIV
  - Safe to administer regardless of CD4 count
  - Newer data suggests all MSM with HIV may benefit from vaccination

# HPV Vaccine Efficacy

- 9 valent (9v) HPV vaccine efficacy was 96.7% in preventing infection and disease related to HPV 31, 33, 45, 52 and 58 and generated an antibody response to HPV 6, 11, 16, and 18
- 4v HPV vaccine efficacy against anal intraepithelial neoplasia (AIN) associated with HPV types 6, 11, 16, or 18 was 90.4%
  - 89.4% efficacy against external anogenital warts in males aged 16-26

# SUMMARY

- HPV infection is common, easily transmitted and usually asymptomatic
- High risk HPV infection underlies most genital epithelial cancers
- Some groups of people are at a higher risk of developing anal dysplasia and subsequently anal cancer
- There are new anal cancer screening guidelines available for the general population and specifically for people living with HIV
- Please perform anal paps on your eligible patients and ensure they are up to date with their anal dysplasia screening!





# THANK YOU!

The National LGBTQIA+ Health Education Center provides educational programs, resources, and consultation to health care organizations with the goal of optimizing quality, cost-effective health care for lesbian, gay, bisexual, transgender, queer, intersex, asexual, and all sexual and gender minority (LGBTQIA+) people.

The Education Center is part of The Fenway Institute, the research, training, and health policy division of Fenway Health, a Federally Qualified Health Center, and one of the world's largest LGBTQIA+ focused health centers.

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 617.927.6354

 [education@fenwayhealth.org](mailto:education@fenwayhealth.org)

 [www.lgbtqiahealtheducation.org](http://www.lgbtqiahealtheducation.org)

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