Anal Cancer Screening

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Disclosures

No conflicts of interest to disclose

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Case

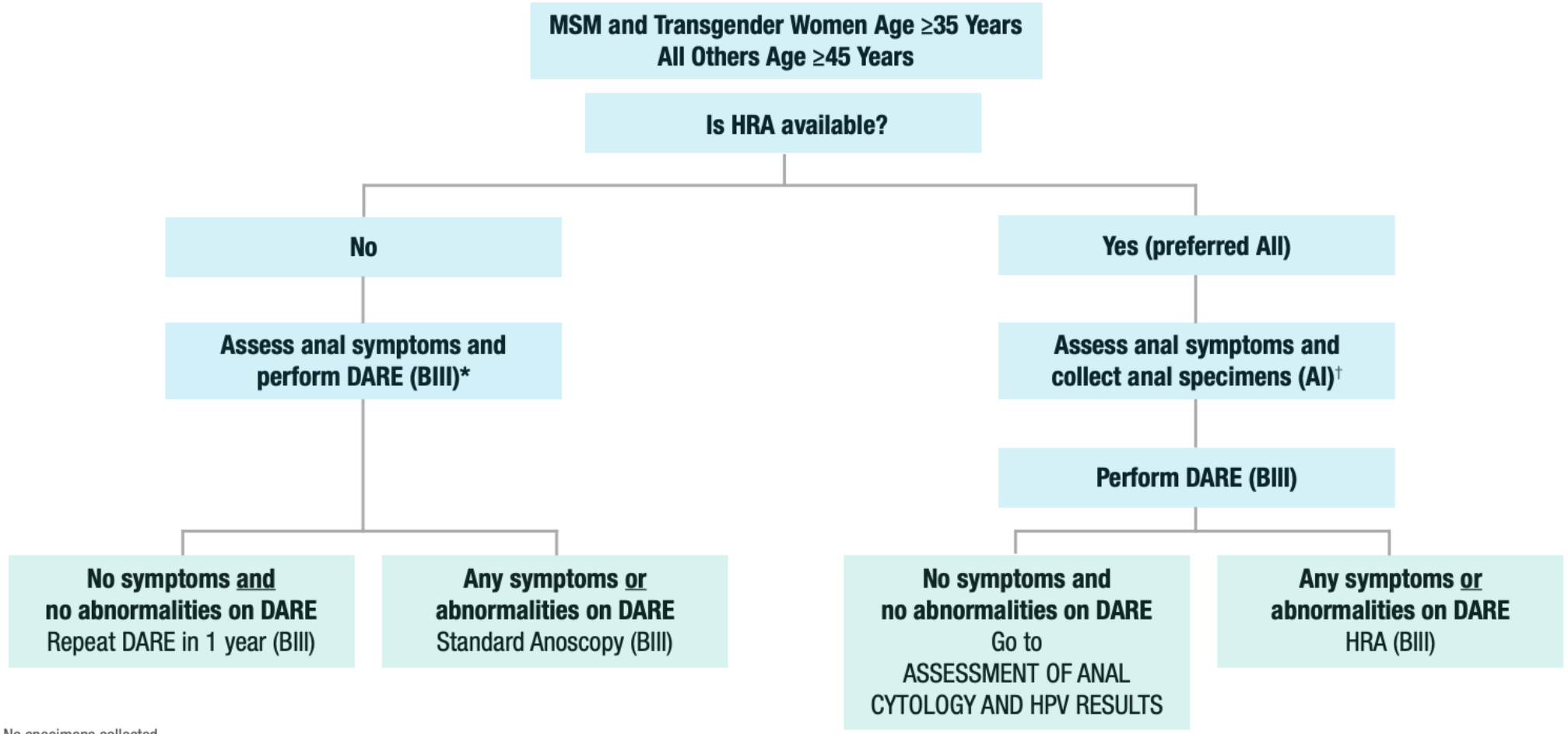
47 year old man presents for routine HIV care. He was diagnosed with HIV at age 30 and has been undetectable since starting ART shortly after diagnosis. He has no comorbidities. In addition to screening for anal symptoms, which of the following is most appropriate with regards to anal cancer screening:

1. He does not need screening as he is under 50
2. He does not need screening as he is asymptomatic
3. Digital anal rectal exam (DARE) is indicated
4. Anal cytology (anal Pap) and DARE are indicated

Anal Cancer Screening

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

SCREENING ALGORITHM FOR ANAL CANCER IN ASYMPTOMATIC PEOPLE WITH HIV



* No specimens collected

† Collect any specimens either for cytology or for cytology with HPV co-testing prior to DARE. HPV testing without cytology is not recommended (BIII)

Key: DARE = digital anorectal exam; HPV = human papillomavirus; hr-HPV = high-risk HPV; HRA = high-resolution anoscopy; MSM = men who have sex with men

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Anal Cancer Screening

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV

Was hr-HPV co-testing performed?

No

Cytology Normal
Repeat cytology in 1 year (BIII)

Normal x 3 consecutive years
Repeat cytology in 3 years (BIII)

Cytology ≥ ASC-US
HRA (BIII)

Yes

Cytology Normal
Assess hr-HPV results

hr-HPV Negative	Repeat cytology and hr-HPV in 3 years (BIII)
hr-HPV Positive, No HPV typing	Repeat cytology and hr-HPV in 6 months† (BIII)
hr-HPV Positive, HPV 16 and 18 negative	Repeat cytology and hr-HPV in 1 year† (BIII)
hr-HPV Positive, HPV 16 or 18 positive	HRA (BIII)

Cytology ASC-US
Assess hr-HPV results

hr-HPV Negative	Repeat cytology and hr-HPV in 1 year† (BIII)
hr-HPV Positive	HRA (BIII)

Cytology ≥ LSIL
HRA (BIII)

† If at repeat testing either cytology is ≥ ASC-US or any hr-HPV is detected, refer for HRA (BIII)

Key: ASC-US = atypical squamous cells of undetermined significance; HPV = human papillomavirus; hr-HPV = high-risk HPV; HRA = high-resolution anoscopy; LSIL = low-grade squamous intraepithelial lesion

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Anal Cancer Screening Guidelines

	NIH OAR Adult and Adolescent OI Guidelines	IANS Guidelines
Primary anal HPV testing alone without cytology as screening option	No	Yes
High-priority patients if HRA availability limited (no priority order specified in either guideline)	• Higher grade of cytologic abnormality • HPV16 on HPV testing • Smokers • >60 years of age • Longer known duration of HIV • History of AIDS	• Higher grade of cytologic abnormality • HPV16 on HPV testing

Key: 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

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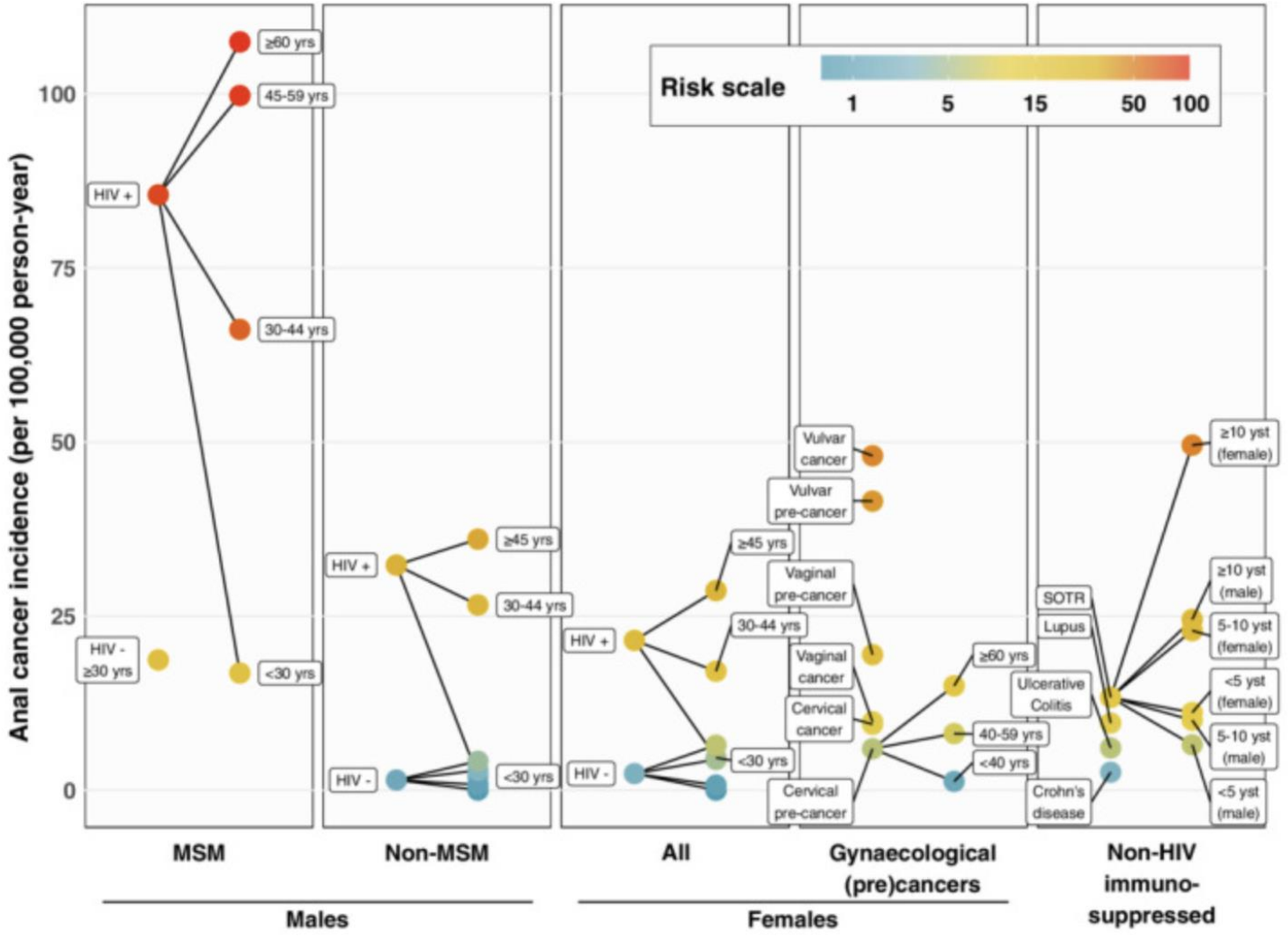
Rationale for Anal Cancer Screening

Screening and treatment for anal HSIL are recommended for PWH based on age given:

- high incidence of anal cancer in people with HIV
- high prevalence of anal HSIL in people with HIV
- the high progression rate of anal HSIL to anal cancer in the absence of treatment
- efficacy in treating anal HSIL to reduce progression to anal cancer



Source: PMID: 32621759; linicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections

ORIGINAL ARTICLE

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

Authors: Joel M. Palefsky, M.D., C.M., Jeannette Y. Lee, Ph.D., Naomi Jay, R.N., Ph.D., Stephen E. Goldstone, M.D., Teresa M. Darragh, M.D., Hillary A. Dunlevy, M.D., Isabella Rosa-Cunha, M.D., +26, for the ANCHOR Investigators Group* Author Info & Affiliations

The NEW ENGLAND JOURNAL of MEDICINE

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- Phase 3 trial at 25 US sites
- Participants: PWH ≥ 35+ years old who had biopsy-proven anal HSIL randomized to treatment vs active monitoring
- Primary outcome: progression to anal cancer
- All participants underwent HRA every 6 months

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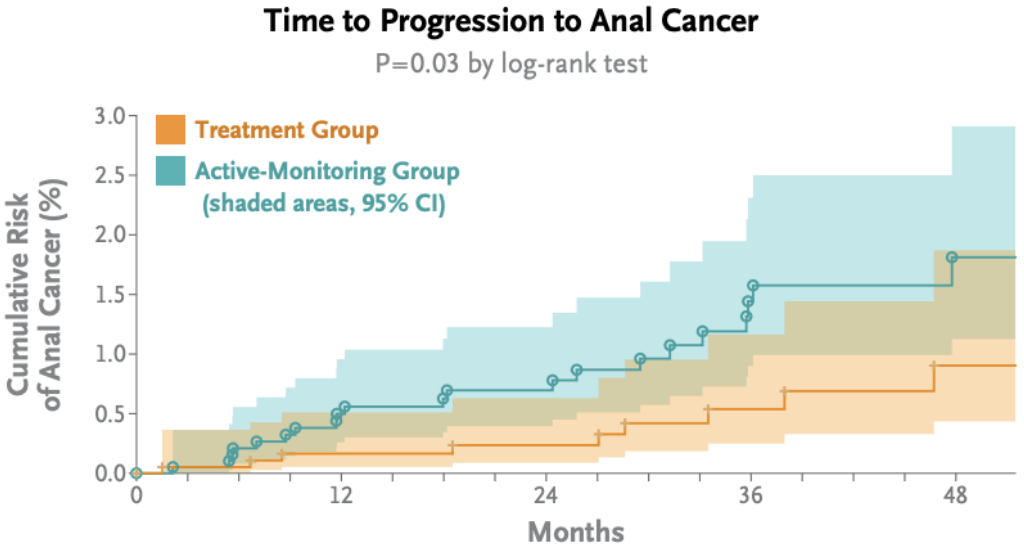
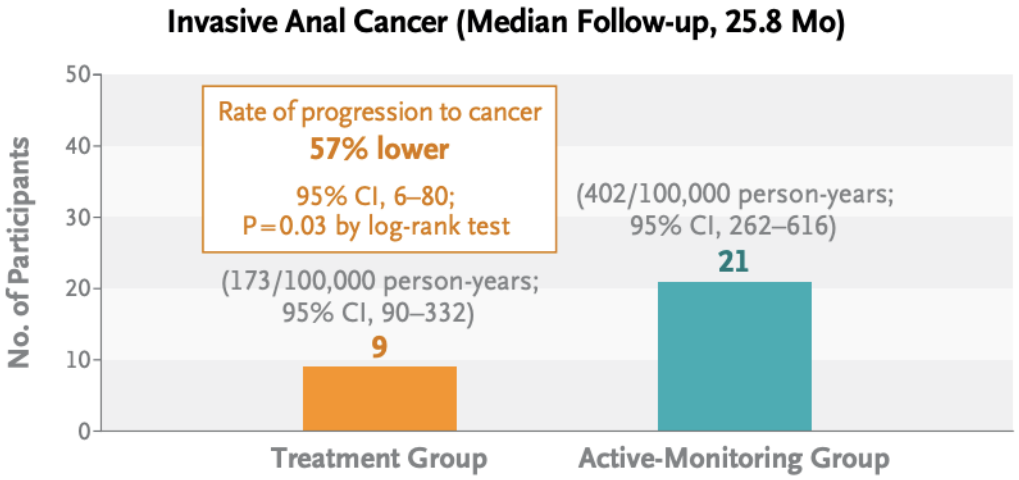
ANCHOR Study Showed that Treatment Can Prevent Anal Cancer!





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ORIGINAL ARTICLE

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

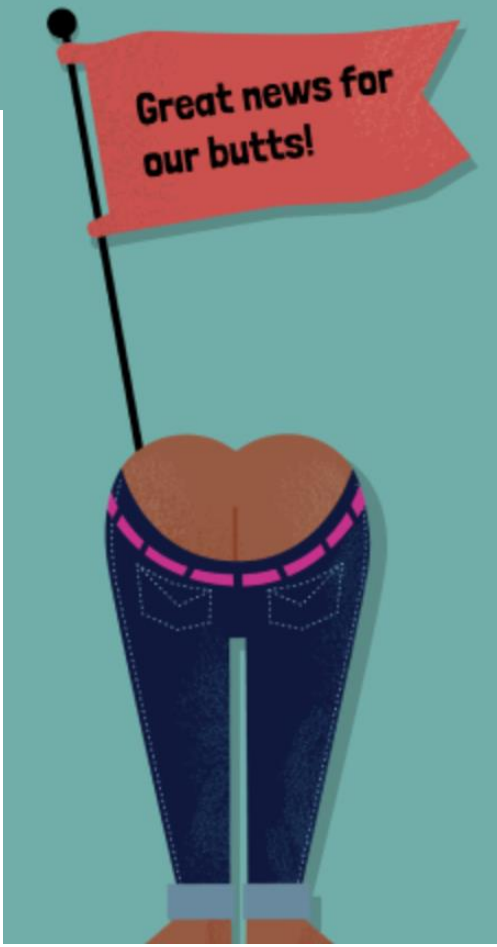
CONCLUSIONS

Among adults living with HIV who had anal HSIL, treatment of HSIL reduced the risk of progression to anal cancer, with a low incidence of serious adverse events.

LIMITATIONS AND REMAINING QUESTIONS

- HSIL treatment did not prevent all cancers, which underscores the need for close follow-up and for more effective treatments.
- The results may not be generalizable to settings in which high-resolution anoscopy and treatment are performed by clinicians with less training and support.
- Additional research is warranted to improve screening algorithms for identifying anal HSIL.

ANCHOR Study Showed that Treatment Can Prevent Anal



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Optimizing Approach to Screening

AIDS 2024 22–26 July

Title

The effectiveness of different anal cancer screening strategies for people living with HIV/AIDS

Presenter

Michael Gaisa

Authors

Y. Liu[1], A. Deshmukh[2], K. Sigel[3], M. Gaisa[3]

Screening Strategy	Results triggering HRA referral	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	# HRAs
Cytology alone	ASCUS or worse	88 (85-90)	30 (27-33)	48 (45-51)	77 (72-81)	1,252 (77%)
hrHPV alone	hrHPV+	96 (95-97)	27 (25-30)	49 (47-52)	92 (88-95)	1,341 (83%)
Cytology with hrHPV triage	ASCUS/hrHPV+ LSIL/hrHPV+ ASC-H/HSIL All HPV16+	85 (82-88)	47 (44-50)	54 (51-57)	81 (78-84)	1,080 (67%)
hrHPV with cytology triage	hrHPV+/ASCUS or worse All HPV16+	85 (82-88)	48 (44-51)	54 (51-57)	81 (78-84)	1,073 (66%)
Cotesting	NILM/hrHPV+ ASCUS/hrHPV+ LSIL/hrHPV+ ASC-H/HSIL All HPV16+	89 (86-91)	40 (37-44)	52 (49-55)	83 (80-87)	1,167 (72%)

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- The approach of hr-HPV with cytology triage, or vice versa, yielded the highest PPV (54%) while hr-HPV alone had the highest NPV (92%).
- The number of HRA referrals triggered by screening was highest for hrHPV alone (83%) followed by cytology alone (77%) and lowest for hr-HPV with cytology triage (66%)

triage	All HPV16+ NILM/hrHPV+ ASCUS/hrHPV+					
Cotesting	LSIL/hrHPV+ ASC-H/HSIL All HPV16+	89 (86-91)	40 (37-44)	52 (49-55)	83 (80-87)	1,167 (72%)

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Addressing Limited HRA Access

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- Combined approach of cytology and hr-HPV testing, whether utilized as cotesting or triage, proves more effective than cytology or hr-HPV testing alone
- The incorporation of hr-HPV testing increases specificity and results in a reduced number of HRA referrals, a critical consideration given the limited HRA capacity, even in high-resource settings

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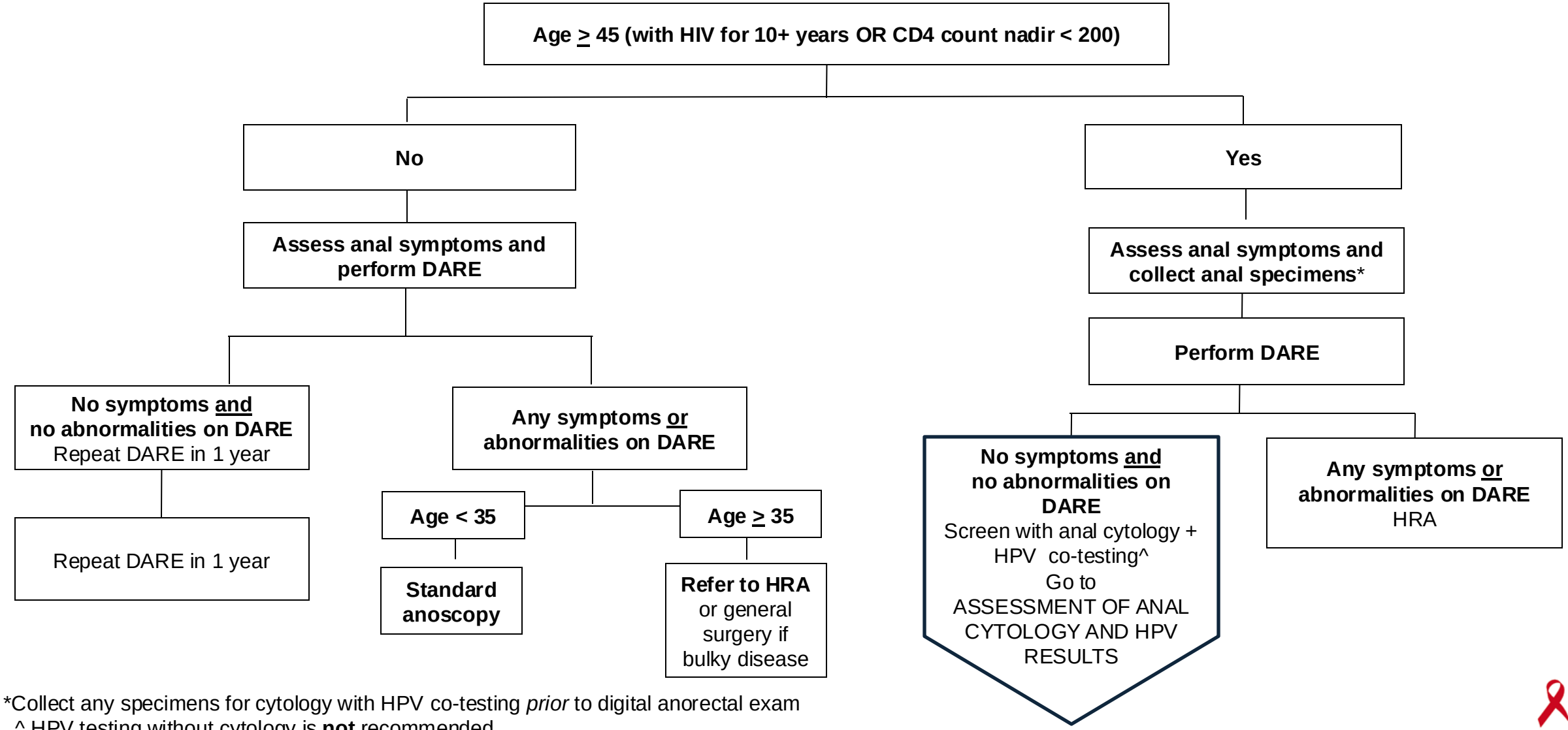
Madison Clinic Approach

- Modified from DHHS guidance due to limited HRA availability

SCREENING ALGORITHM FOR ANAL CANCER IN PEOPLE WITH HIV AT MADISON

Screen age ≥45 years (with HIV for 10+ years OR CD4 count nadir < 200).
All adults with HIV should undergo anal symptom assessment and digital anorectal exam, or DARE, annually



*Collect any specimens for cytology with HPV co-testing *prior* to digital anorectal exam
^ HPV testing without cytology is **not** recommended

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ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV

Perform anal cytology with reflex HPV testing (EPIC order – "Anal Cytology Reflexive HPV")

Cytology Normal
Assess hr-HPV results

hr-HPV Negative	Repeat cytology & HR-HPV in 3 years
hr-HPV Positive, HPV 16 and 18 negative	Repeat cytology & HR-HPV in 1 year†
hr-HPV Positive, HPV 16 or 18 positive	HRA

Cytology ASC-US or unsatisfactory
Assess hr-HPV results

hr-HPV Negative	Repeat cytology & HR-HPV in 1 year
hr-HPV Positive, HPV 16 and 18 negative	Repeat cytology & HR-HPV in 1 year†
hr-HPV Positive, HPV 16 or 18 positive	HRA

Cytology > ASC-US
Refer for HRA

† If at repeat testing either cytology is ≥ASCUS or any HR- HPV is detected, refer for HRA (BIII)

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Summary

- Anal screening is now recommended
- HRA access is limited to non-existent in some areas, and screening approaches will need to be modified
- Guidelines likely to evolve with additional data

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