What was NOT explained in the ANCHOR trial?

Barcelona HPV Course
September 16, 2024

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Disclosures

Merck - Consultant/Honorarium Recipient
Vir Biotechnologies - Consultant/Honorarium Recipient
Virion Therapeutics - Consultant/Stock Shareholder
Roche Diagnostics - Consultant/Honorarium Recipient
Spotlight Therapeutics - Consultant/Honorarium Recipient
Abbott - Consultant/Honorarium Recipient
GSK- Consultant/Honorarium Recipient
Asieris Pharmaceuticals- Consultant/Honorarium Recipient

Objectives

1. Summary of what the ANCHOR trial DID tell us
2. Gaps in knowledge in screening and treatment of anal high-grade squamous intraepithelial lesions that ANCHOR can help address
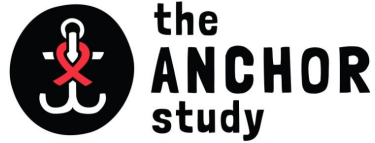3. Gaps in knowledge of pathogenesis of anal cancer

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

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
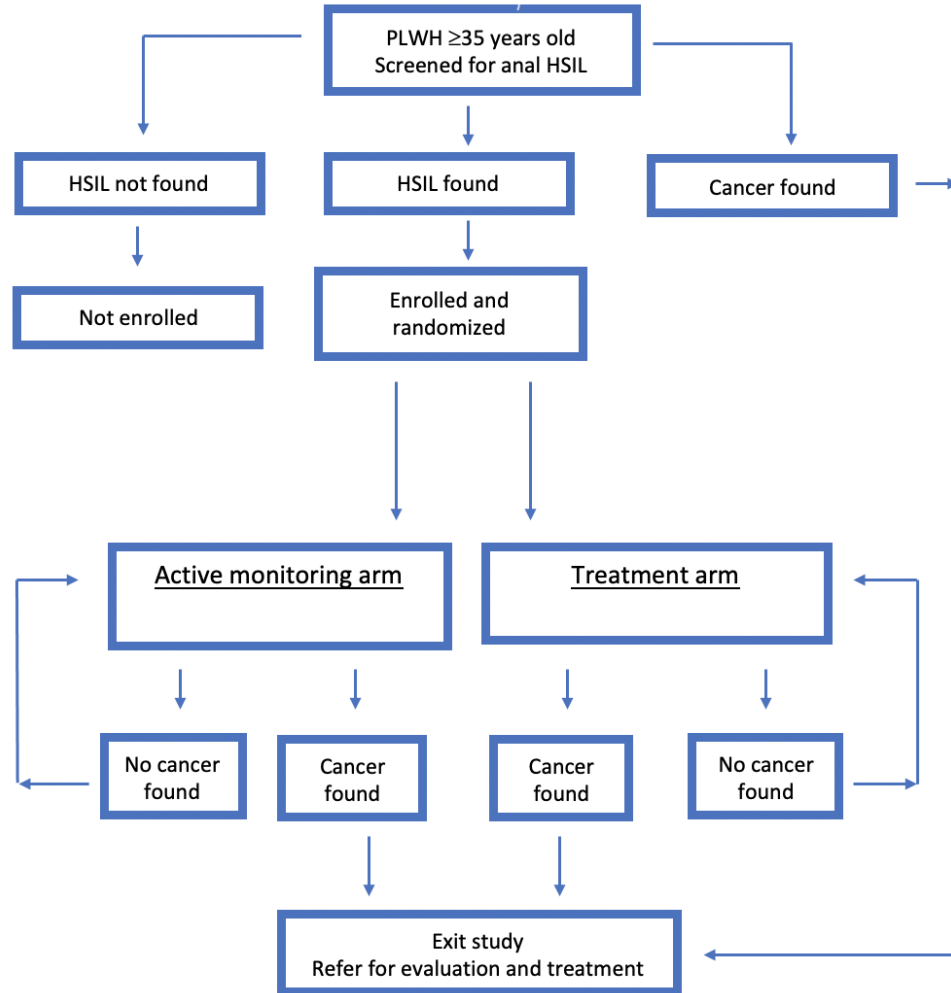
Results

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

Palefsky JM et al. New Engl J Med 2022; 386: 2273-82

Results

Anal cancer at screening

- 17 individuals diagnosed with anal cancer
- 6 more found - 214/100,000

Palefsky JM et al. New Engl J Med 2022; 386: 2273-82

Treatments used in the ANCHOR Study

Over the course of the study: most participants had only one treatment modality (86%)= electrocautery (office-based hyfrecation)
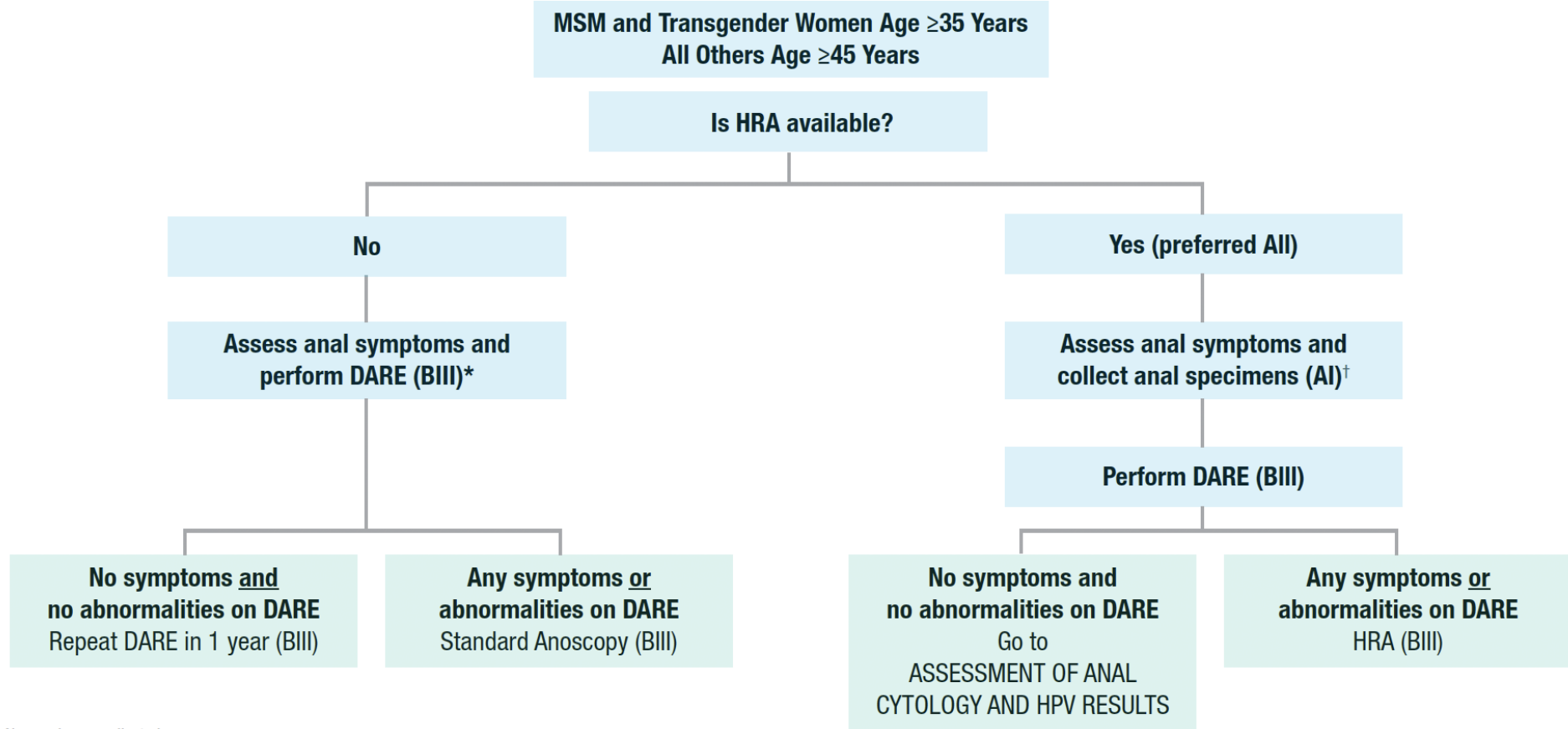
Palefsky JM et al. New Engl J Med 2022; 386: 2273-82

SCREENING ALGORITHM FOR ANAL CANCER IN ASYMPTOMATIC PEOPLE WITH HIV

MSM and Transgender Women Age ≥35 Years
All Others Age ≥45 Years

Is HRA available?

No

Assess anal symptoms and perform DARE (BIII)*

No symptoms and no abnormalities on DARE
Repeat DARE in 1 year (BIII)

Any symptoms or abnormalities on DARE
Standard Anoscopy (BIII)

Yes (preferred AII)

Assess anal symptoms and collect anal specimens (AI)†

Perform DARE (BIII)

No symptoms and no abnormalities on DARE
Go to
ASSESSMENT OF ANAL
CYTOLOGY AND HPV RESULTS

Any symptoms or abnormalities on DARE
HRA (BIII)
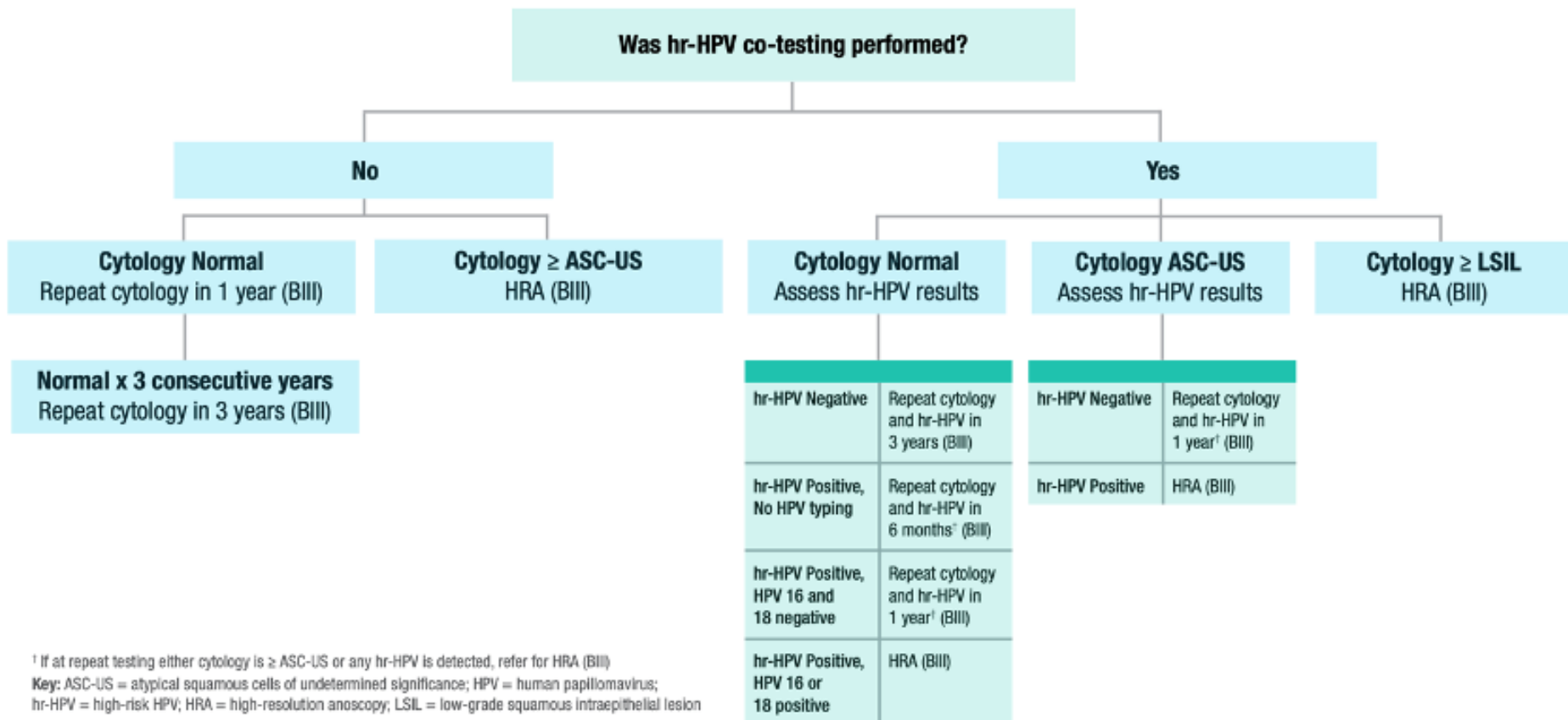
* No specimens collected
† Collect any specimens either for cytology or for cytology with HPV co-testing prior to DARE. HPV testing without cytology is not recommended (BIII)
Key: ASC-US = atypical squamous cells of undetermined significance; DARE = digital anorectal exam; HPV = human papillomavirus; hr-HPV = high-risk HPV; HRA = high-resolution anoscopy; MSM = men who have sex with men

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)

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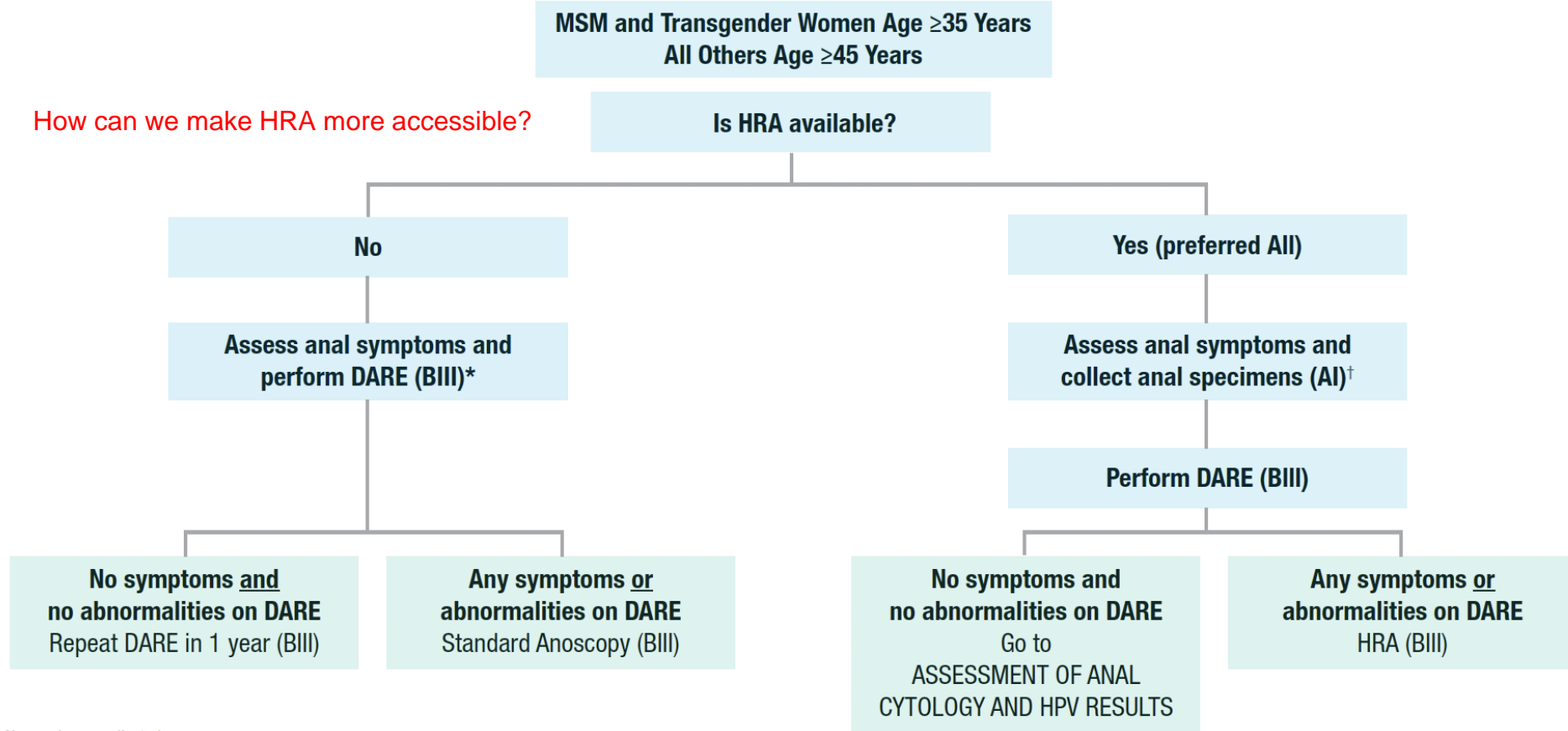|	
hr-HPV Negative	Repeat cytology and hr-HPV in 1 year† (BIII)
hr-HPV Positive	HRA (BIII)

Cytology ≥ LSIL
HRA (BIII)

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How can we make HRA more accessible?

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ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS

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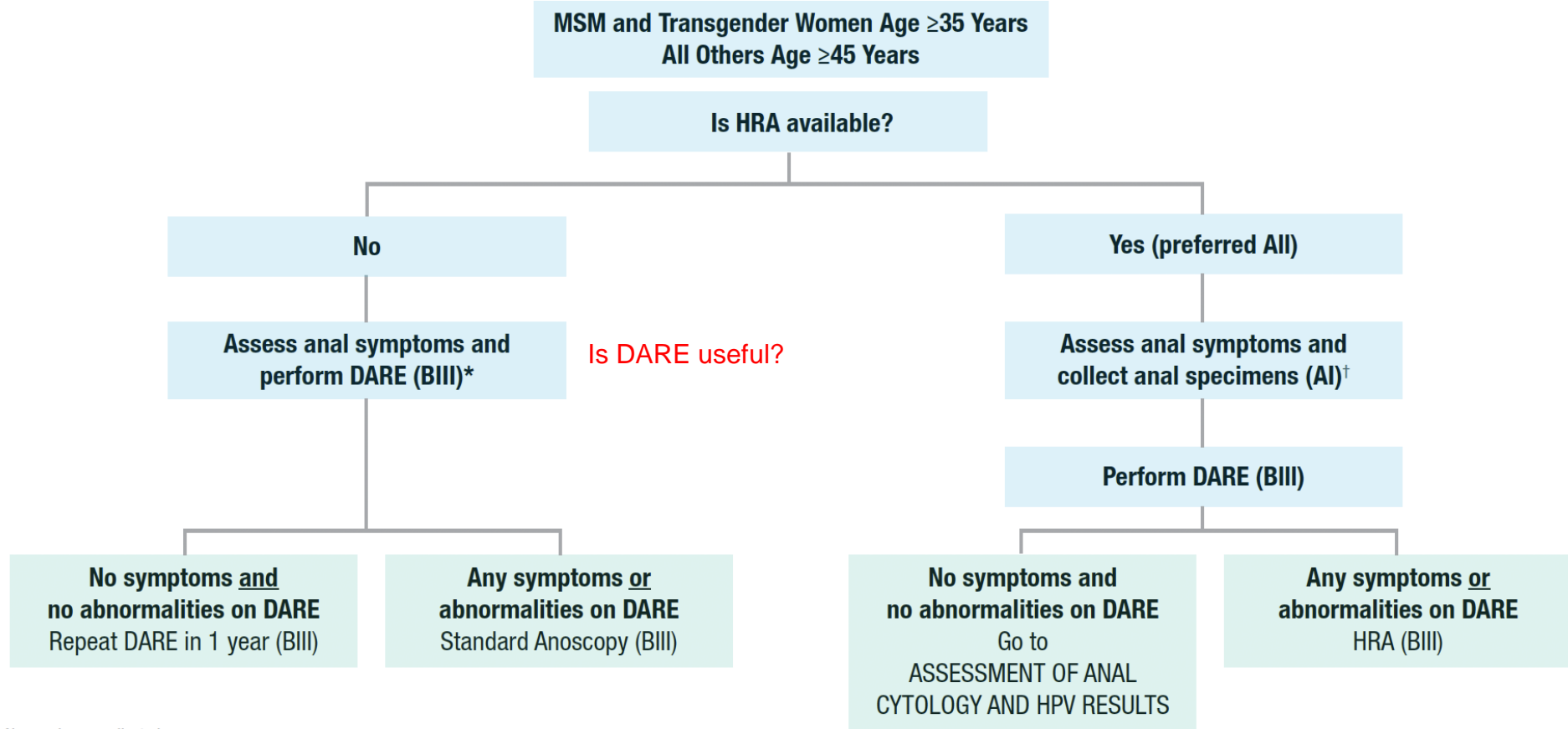HRA (BIII)

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How can we make HRA more accessible?

- ## Scale-up HRA training programs
- >124,000 PWH who need HRA would have no access
- ## Reassess HRA competency metrics
- Consider different tiers of expertise

Rim SH et al. JAMA Network Open 2024; 7(3)3240068

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Is DARE useful?

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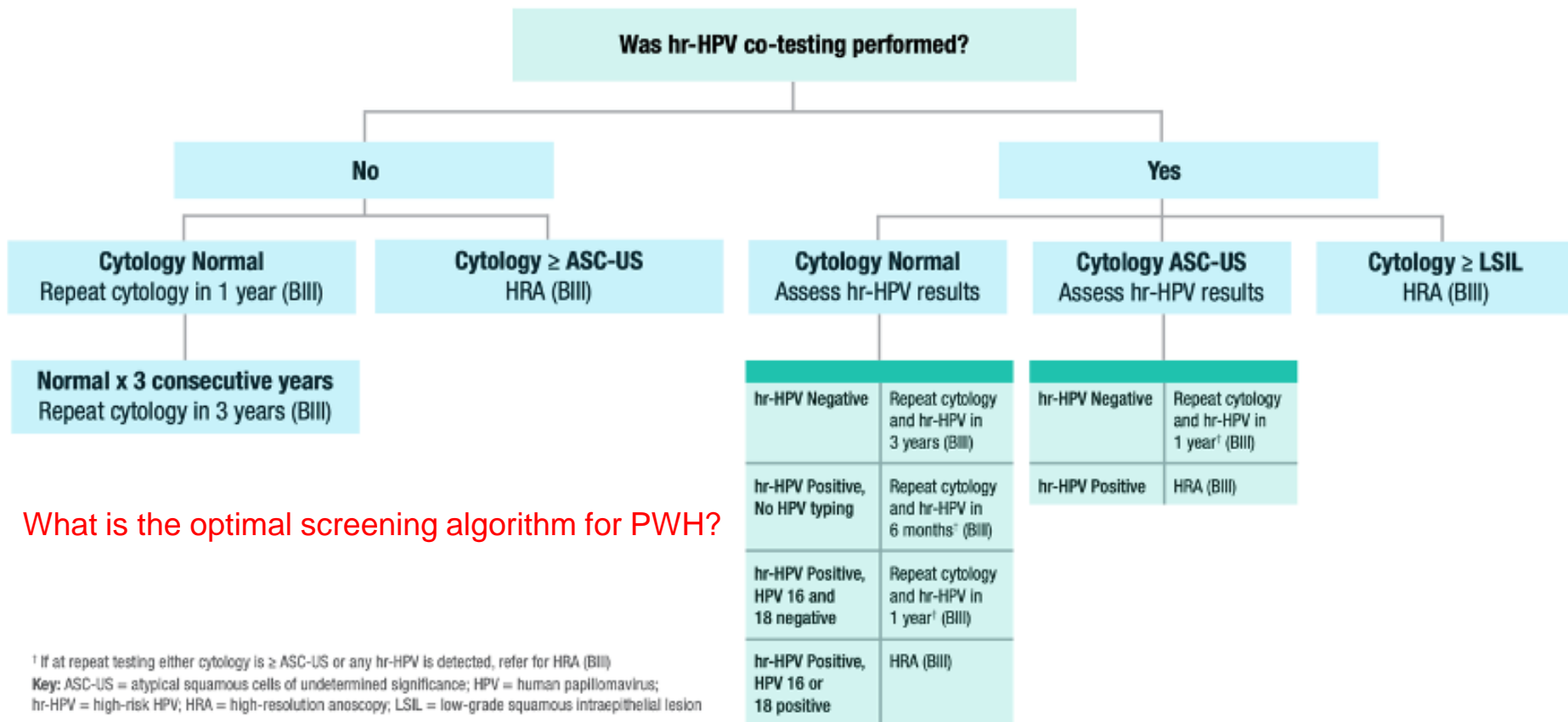HRA (BIII)

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Is DARE useful?

- DARE has good sensitivity-82%
- Has reasonable specificity-87%
- Has very low PPV

Dunlevy H et al, manuscript in preparation

ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV

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What is the optimal screening algorithm for PWH?

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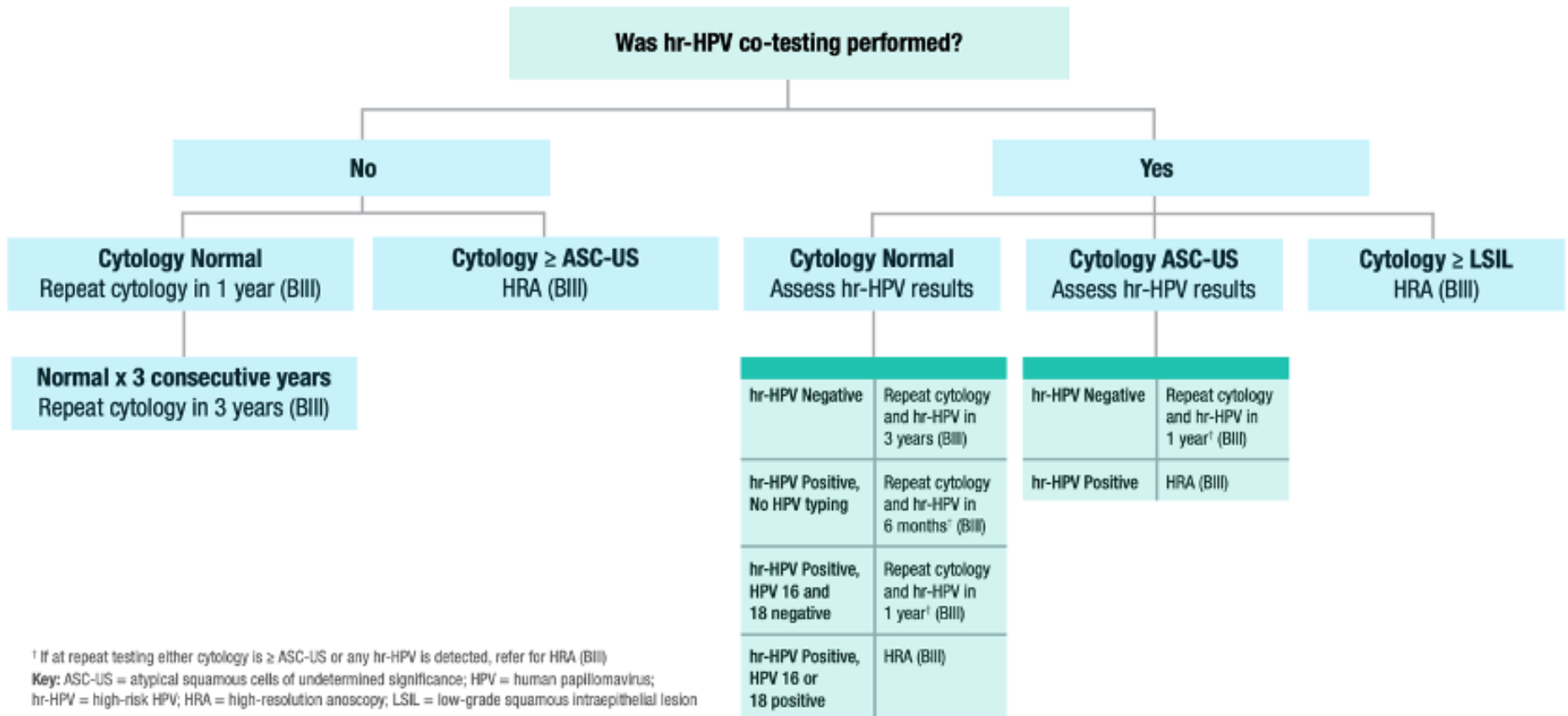# What is the optimal screening algorithm for PWH?

- ANCHOR will provide robust data for cytology, HPV typing by age, racial/ethnic background, sex at birth
  - Cytology alone is not very helpful
  - HPV testing as a primary screen is probably not very helpful
  - HPV 16 testing alone may not be sufficient

- Samples will be looked at to determine utility of triage testing- methylation, CINTec Plus, ctDNA, HPV seropositivity, others

- When can we stop screening?

Darragh T et al, manuscript in preparation

International Anal Neoplasia Society screening guidelines

Population—Risk category	When	Anal cancer incidence[2,5] per 100,000 person-years
Risk Category A (incidence ≥ 10-fold compared to the general population)		
MSM and TW with HIV	Age 35	>70/100,000 age 30–44 >100/100,000 age 45+
Women with HIV	Age 45	>25/100,00 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
Risk Category B (incidence up to 10-fold higher compared to the general population)		
Cervical/vaginal cancer	Shared decision age 45[a]	9/100,000
Cervical/vaginal HSIL	Shared decision age 45[a]	8/100,000
Perianal warts (male or female)	Shared decision age 45[a]	Unknown
Persistent cervical HPV 16 (>1 year)	Shared decision age 45[a]	Unknown
Other immunosuppression (e.g., Rheumatoid arthritis, Lupus, Crohn's, Ulcerative colitis, on systemic steroid therapy)	Shared decision age 45[a]	6/100,000
Incidence among the general population: 1.7 per 100,000[8]		

Stier E et al. In J Cancer 2024;1–9

ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV

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How do the algorithms need to be modified for people not living with HIV?

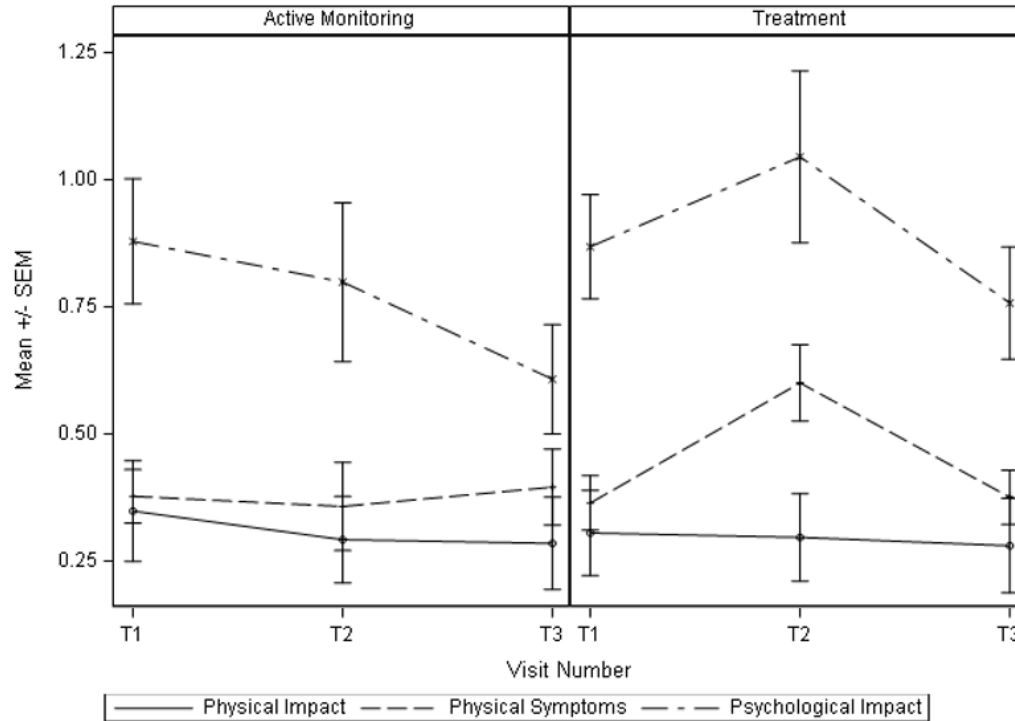# What is the cost-effectiveness of screening and treatment ?

- Screening and treating MSMLWH not cost-effective in the Australian setting
- Cost-effective in US setting
- ANCHOR data will be used

What is the effect of treatment on quality of life?

Cheng Q et al Lancet Reg Health West Pac 2023 Jan 10:32:100676

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

Palefsky JM et al. New Engl J Med 2022; 386: 2273-82

Effect of treatment on quality of life

Atkinson T et al, manuscript in preparation

What is the best treatment for anal HSIL?

- Better treatment is needed
- Systemic treatment is needed
- HPV-targeted therapy is needed

# What is the best follow-up algorithm after treatment for anal HSIL?

Can we develop biomarkers of disease progression or regression?

- Serum, anal swab or tissue biomarkers
- Optimize HRA utilization

What is the molecular pathogenesis of progression or regression?

- Gene expression libraries
- Proteomics
- Metabolomics
- Immunopathogenesis

- Targets for new therapies?
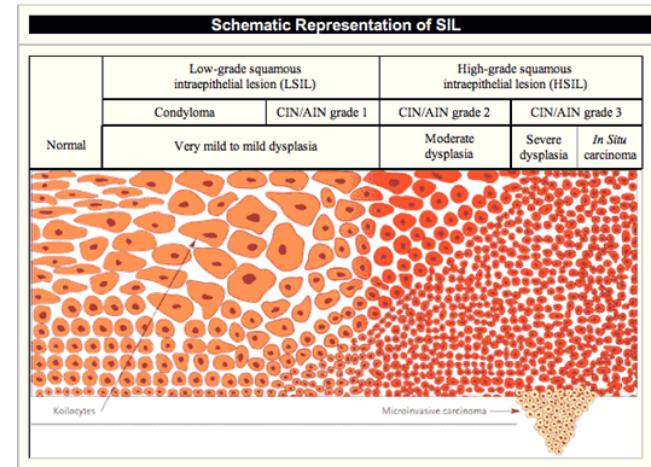
Gaps in knowledge

- Optimal screening algorithms for PWH and for other demographics
- Markers of prevalent anal cancer during screening
- Optimal follow-up algorithms after treatment
- Biomarkers of risk of HSIL progression or regression
- How to scale up treatment programs and train more people in HRA more quickly
- Cost-effectiveness data
- Better treatment methods

Muchas gracias!