BREACH
BELGIAN RESEARCH AIDS&HIV CONSORTIUM

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Anal cancer screening: PROs

Dr Deborah Konopnicki, MD, PhD

deborah.konopnicki@stpierre-bru.be

CHU Saint-Pierre
UMC Sint-Pieter

MiA
MALADIES INFECTIEU-SES-ZE AANDOENINGEN

Service de Maladies Infectieuses
Centre Reference VIH

Agenda

1. **Why should we screen for anal cancer?**
2. Who should we screen for anal cancer?
3. How should we screen for anal cancer?
4. Is anal cancer screening cost-effective?
5. Is anal cancer screening recommended?

- High Incidence
- Morbidity and Mortality
- Treating precursor lesions decreases anal cancer incidence

Anal cancer

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CANCER EPIDEMIOLOGY

A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale

Gary M. Clifford[1] | Damien Georges[1] | Meredith S. Shiels[2] | Eric A. Engels[2] | Andreia Albuquerque[3,4] | Isobel Mary Poynten[5] | Alexandra de Pokomandy[6] | Alexandra M. Easson[7] | Elizabeth A. Stier[8]

Threshold for colorectal cancer screening in ≥ 50 years

Threshold for cervical cancer screening in ≥ 35 years

General population
Incidence of anal cancer: 1-2/100.000 person-year

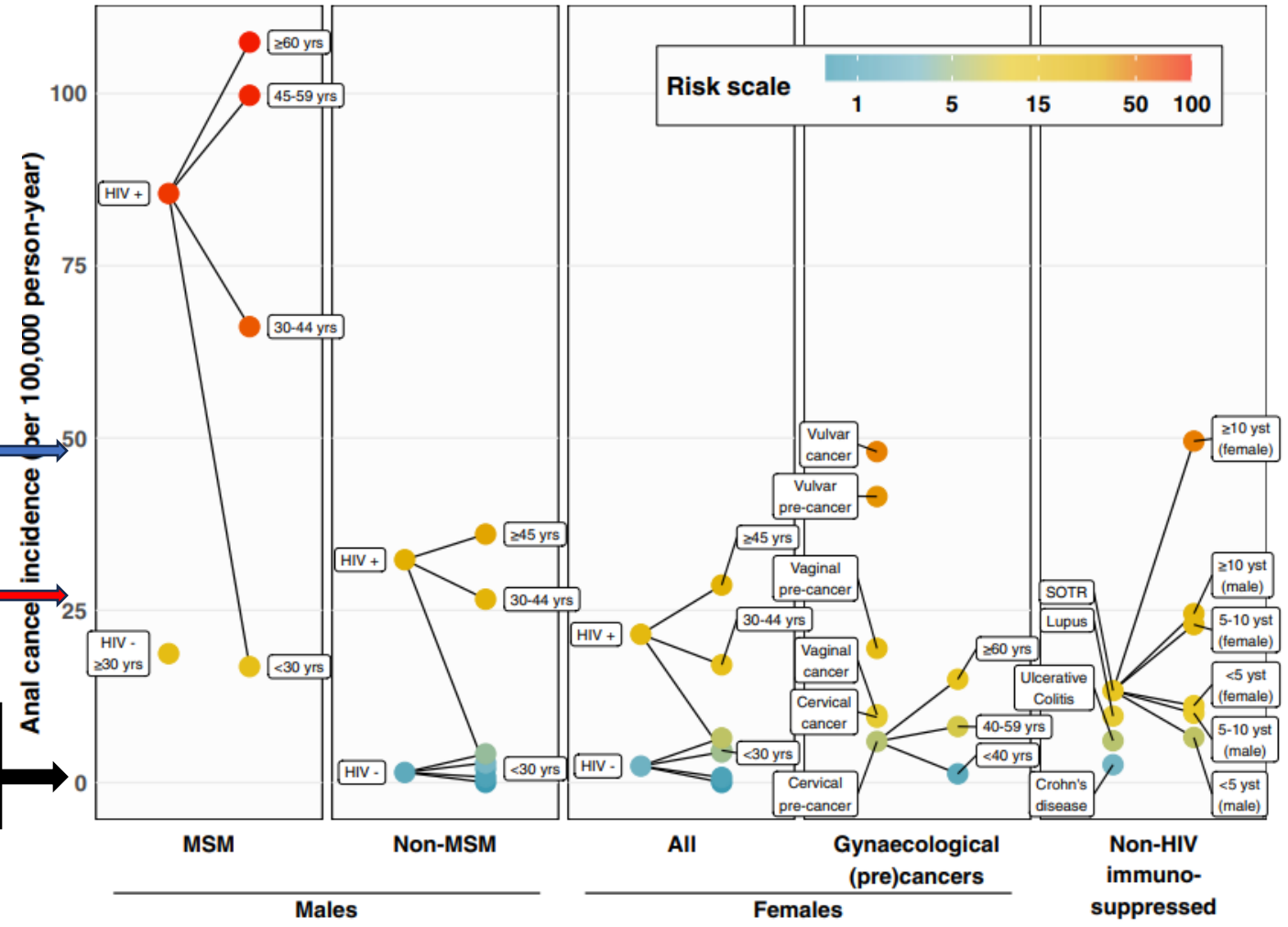

FIGURE 5 Anal cancer risk scale. 95% CIs around the point estimates can be found in the relevant Figures 1-4 and Tables S1 and S2. Estimates for HIV-negative men and men are shown, without labels, for age-groups <30, 30 to 44, 45 to 59, and ≥60 years (see Section 3). CI, confidence interval; MSM, men who have sex with men; MSW, men who have sex with women. yrs, years old; yst, years since transplant

Anal Cancer and HIV: mortality and screening

Effect of the introduction of screening for cancer precursor lesions on anal cancer incidence over time in people living with HIV: a nationwide cohort study

2023

Ramon P van der Zee, Ferdinand W N M Wit*, Olivier Richel, Marc van der Valk, Peter Reiss, Henry J C de Vries, Jan M Prins, on behalf of the ATHENA national observational HIV cohort†*

Summary

Background Incidence of anal cancer is high in people living with HIV, particularly in men who have sex with men (MSM). Screening for and treatment of precursor lesions might prevent progression to anal cancer in people living with HIV. We examined trends in incidence of and mortality after anal cancer diagnosis in people living with HIV, including the effect of screening from 2007 onwards, in the Netherlands.

Lancet HIV 2023; 10: e97–106
Published Online January 11, 2023
https://doi.org/10.1016/S2352-3018(22)00368-X

- Athena Cohort 1996-2020: 28.175 PWH (60% MSM, 19% women)
- Screening since 2007 in MSM

- **Incidence** decreases over time for MSM, not for other groups

- Risk factors changed overtime
  - Less smoking
  - Less cumulative exposure to CD4 <200/µL and HIV RNA > 1.000 cp/ml

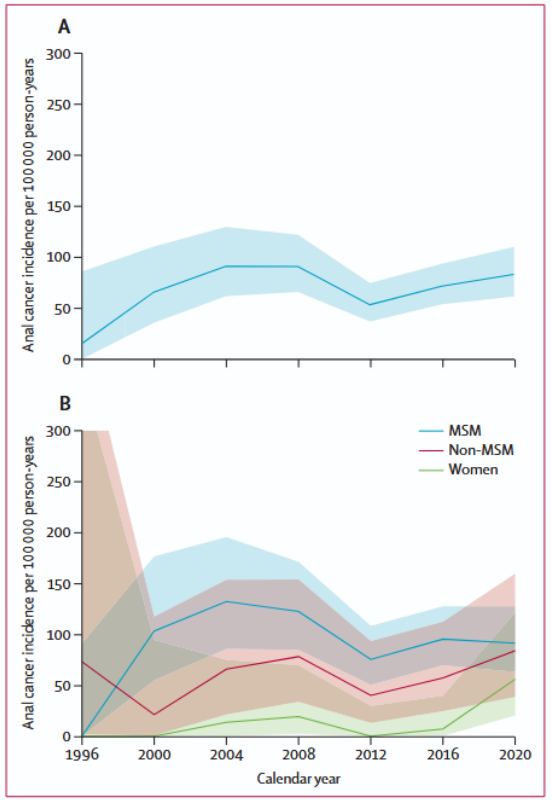

Figure 1: **Crude anal cancer incidence in the Netherlands per 100 000 person-years (95% CIs), 1996–2020**
(A) Total group of people living with HIV. (B) MSM, non-MSM, and women separately. Calendar year represents the middle of a 4-year block. MSM=men who have sex with men. Non-MSM=men who do not have sex with men.

	Men who have sex with men		Men who do not have sex with men		Women	
	Incidence per 100 000 person-years (95% CI)	Age-adjusted rate ratio* (95% CI)	Incidence per 100 000 person-years (95% CI)	Age-adjusted rate ratio* (95% CI)	Incidence per 100 000 person-years (95% CI)	Age-adjusted rate ratio* (95% CI)
1996–2005	107·00 (75·73–146·88)	1 (ref)	51·08 (20·54–105·25)	1 (ref)	8·09 (0·20–45·06)	1 (ref)
2006–12	95·22 (71·33–124·55)	0·75 (0·49–1·14)	56·64 (28·27–101·34)	0·98 (0·38–2·55)	10·22 (1·24–36·92)	1·03 (0·09–11·53)
2013–20	93·71 (75·26–115·32)	0·62 (0·41–0·92)	67·82 (40·83–105·91)	1·03 (0·42–2·55)	24·95 (10·03–51·40)	1·94 (0·22–16·98)

*Rate ratios are derived from multivariable Poisson models, adjusted for age.

Table 2: **Crude incidence and age-adjusted incidence ratios of anal cancer over time**

Anal Cancer and HIV: mortality and screening

Effect of the introduction of screening for cancer precursor lesions on anal cancer incidence over time in people living with HIV: a nationwide cohort study

2023

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Lancet HIV 2023; 10: e97–106
Published Online January 11, 2023
https://doi.org/10.1016/S2352-3018(22)00368-X

Anal cancer-related **mortality** at 5 year after diagnosis of anal cancer: decreased from **30,4%** (1996-2005) to **18,3%** (2013-2020) in MSM

- 3,7% in screened
- 24% in non screened

In multivariate analysis:
-Participation in a screening program
-reduced exposure to CD4 <200/µL

Earlier diagnosis in screened persons

In women anal cancer-related mortality at 5 year :
62,5% with more advanced stage cancer at time of diagnosis

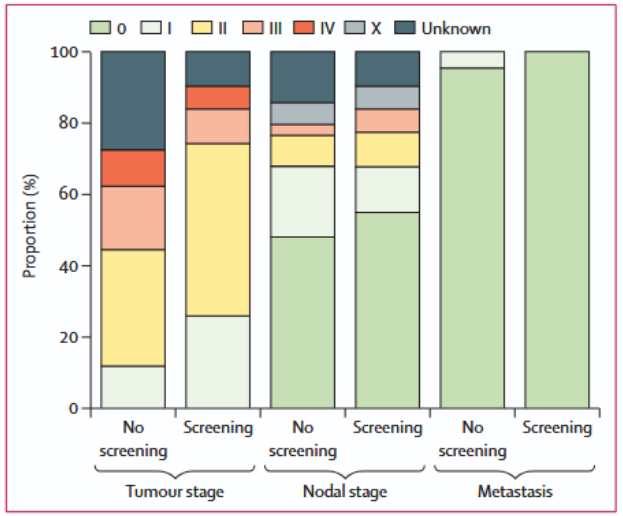
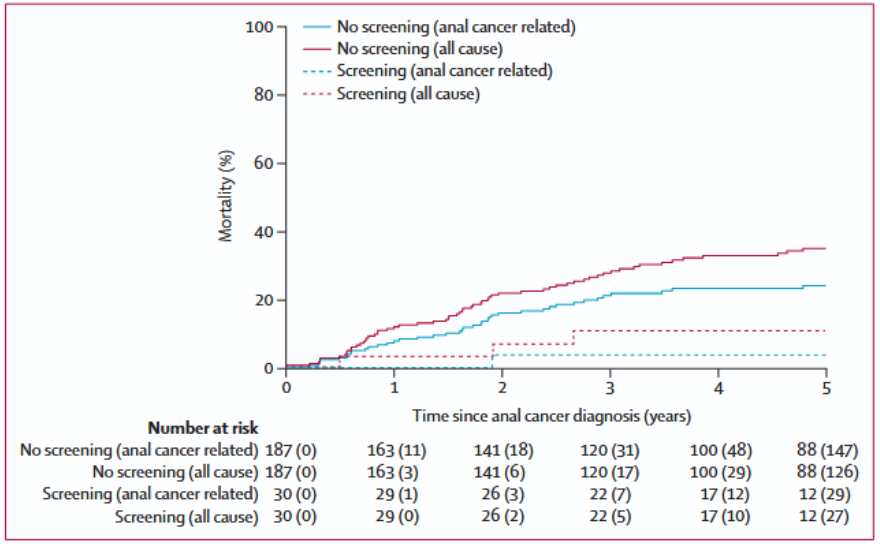


Figure 2: **TNM stage at the moment of anal cancer diagnosis, stratified by participation in an anal cancer screening programme**
TNM=tumour, nodal, and metastatic stages.[21] Unknown=missing. X=could not be assessed.



Anal Cancer and HIV: mortality

Survival by sex and HIV status in patients with anal cancer in the USA between 2001 and 2019: a retrospective cohort study

2024

Jaimie Z Shing, Eric A Engels, April A Austin, Megan A Clarke, Jennifer H Hayes, Aimée R Kreimer, Analise Monterosso, Marie-Josèphe Horner, Karen S Pawlish, Qianlai Luo, Elizabeth R Zhang, Aimee J Koestler, Ruth M Pfeiffer, Meredith S Shiels

Summary

Background The risk of anal cancer is increased among people with HIV, particularly men who have sex with men. Estimating survival by HIV status and sex and identifying groups at high risk is crucial for documenting prognostic

Lancet HIV 2024; 11: e31–41

Published Online

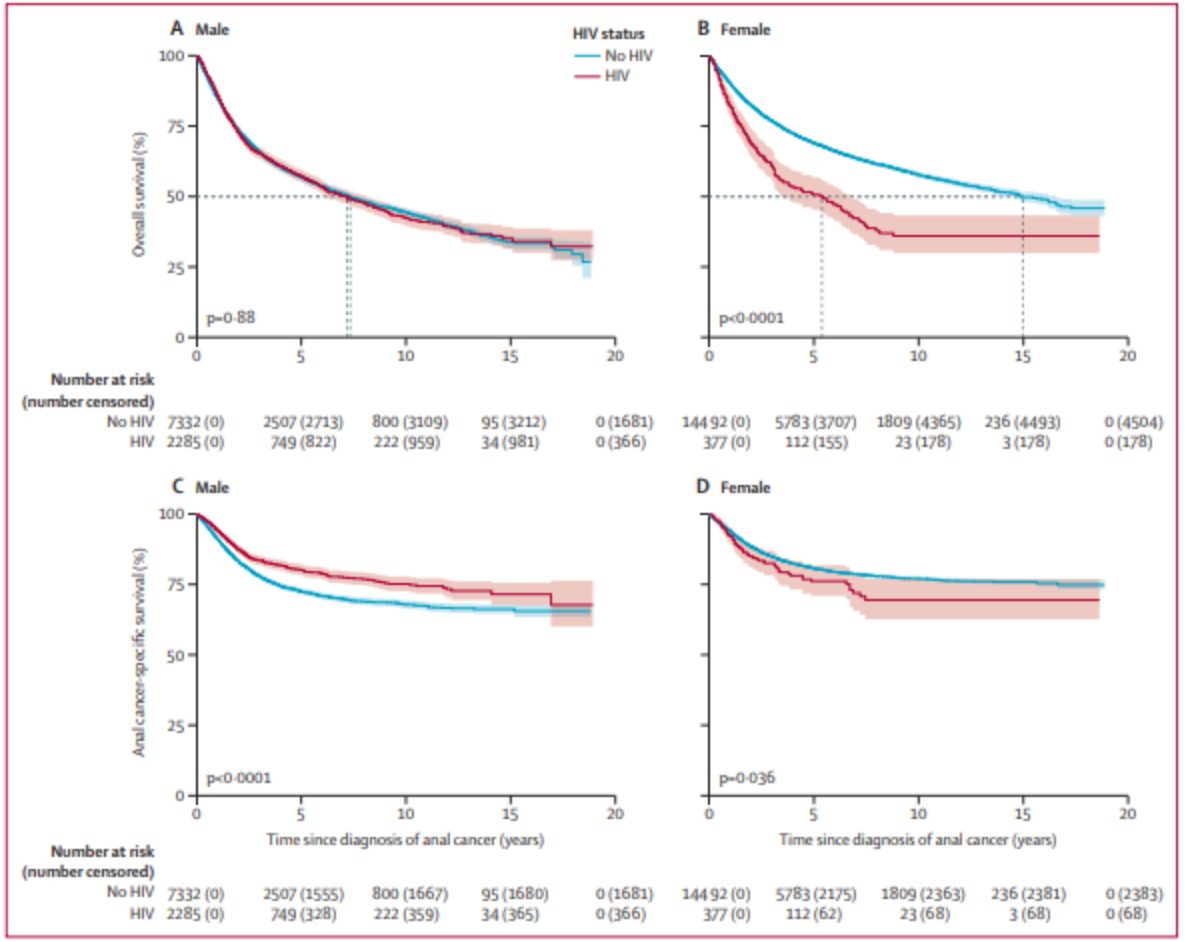


Figure 1: **Overall and anal cancer-specific survival by HIV status and sex**

Kaplan-Meier curves of overall survival (A, B) and anal cancer-specific survival (C, D) in male and female patients with anal cancer. Dashed lines indicate median survival.

All-cause mortality:
HIV was associated with
1·35 times (95% CI 1·24–1·47) increase in males
2·47 times (2·10–2·90) increase in females
Anal cancer-specific mortality
HIV was associated with
1·52 times (1·18–1·97) in female

Anal Cancer screening in WLWH in Europe

Online survey on guidelines and practice on anal screening in WLWH

- 240 health care workers
- from 25 countries in WHO European region

Women are often not included in national guidelines for anal cancer screening in Europe

BMJ Group

Krankowska DC, *et al*. *Sex Transm Infect* 2025;**0**:1–6. doi:10.1136/sextrans-2025-056687

Original research

Missed opportunities for anal cancer (AC) screening in women living with HIV: results from a survey across the European region

Dagny Clea Krankowska [1,2] Maria Mazzitelli,[3,4] Deborah Konopnicki [5] Eva Orviz [6] Hazal Albayrak Ucak [7] Konstantinos Protopapas [8] Harriet Mortimer,[9,10] Elena Barzizza,[11] Alessandro Fanesi,[12] Yvonne Gilleece,[9,10] Karoline Aebi-Popp[13,14]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/sextrans-2025-056687).

For numbered affiliations see end of article.

Correspondence to
Dr Dagny Clea Krankowska; d.krankowska@gmail.com

YG and KA-P contributed equally.

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Accepted 2 November 2025

ABSTRACT

Objective The incidence of anal cancer (AC) is higher in women with HIV than in women without HIV due to immunosuppression and persistence of human papilloma virus (HPV). Since 2024, the International Anal Neoplasia Society's and European AIDS Clinical Society (EACS) guidelines recommend annual AC screening of cisgender women (CW) of ≥45 years old, transgender women (TW) of ≥35 years old and women with previous vulvar high-grade squamous intraepithelial lesion (HSIL)/cancer regardless of age. This study describes current clinical practices and protocols for AC screening in women with HIV within healthcare settings across WHO European Region (WER).

Methods Between November 2024 and January 2025, an anonymous online survey on AC screening and prevention in persons with HIV was disseminated among healthcare

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Treatment of high-grade squamous intraepithelial lesion (HSIL) decreases the risk of anal cancer (AC), therefore screening for precancerous lesions is an important part of prevention. Women with HIV have a higher risk of developing AC than women without HIV.

WHAT THIS STUDY ADDS

⇒ Women with HIV are often not included in European national guidelines on screening for AC, and healthcare workers do not routinely perform digital anal rectal examination in this population. Access to anal cytology or high-resolution anoscopy is still limited in many

Anal cancer morbidity

ARTICLE IN PRESS

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO GASTROINTESTINAL ONCOLOGY

2025

REVIEW

Patients' perspective in anal cancer

S. Manfrida[1], L. Dinapoli[2*], V. De Luca[1], G. Chiloiro[1], A. Romano[1], D. P. R. Chieffo[2,3], E. Segelov[4,5], P. Franco[6,7] & M. A. Gambacorta[1,8]

[1]Department of Radiology and Radiation Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome; [2]Clinical Psychology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome; [3]Department of Women, Children and Public Health, Università Cattolica del Sacro Cuore, Rome, Italy; [4]Department of Clinical Research, Faculty of Medicine, University of Bern, Bern; [5]Department of Radiation Oncology, Inselspital, University of Bern, Bern, Switzerland; [6]Department of Radiation Oncology, "Maggiore della Carità" University Hospital, Novara; [7]Department of Translational Medicine (DIMET), University of Eastern Piedmont, Novara; [8]Università Cattolica Del Sacro Cuore, Rome, Italy

Available online XXX

Table 2. Toxicities presentation and management

Late effects	Clinical presentation	Clinical management
Bowel dysfunction	Frequency, urgency, flatulence, painful defecation, diarrhea, constipation	Dietary modifications, antidiarrheal medications, bile acid sequestrants, sucralfate enemas, advanced intervention (argon plasma coagulation, APC) or formalin treatment[44]
Sexual dysfunction	Erectile dysfunction in men, painful intercourse, decreased sexual enjoyment, vaginal narrowing, dryness	Vaginal dilators, topical hormone therapy, sexual counseling[45]
Urinary symptoms	Urgency, incontinence, nocturia	Bladder training, fluid regulation, pelvic floor therapy, antimuscarinic medications, beta-3 agonists, hyaluronic acid bladder instillations[46]
Pelvic floor symptoms	Urinary and fecal incontinence, pelvic pain, dyspareunia, muscle weakness	Pelvic floor therapy, biofeedback, electrical stimulation, manual techniques, targeted exercises[47]
Accelerated bone degeneration	Pelvic insufficiency fractures, pain, reduced mobility	Pain management, physiotherapy, weight-bearing exercises, calcium and vitamin D supplements, bisphosphonates or denosumab[48]

Treating precursors lesions (HSIL) decreases anal cancer

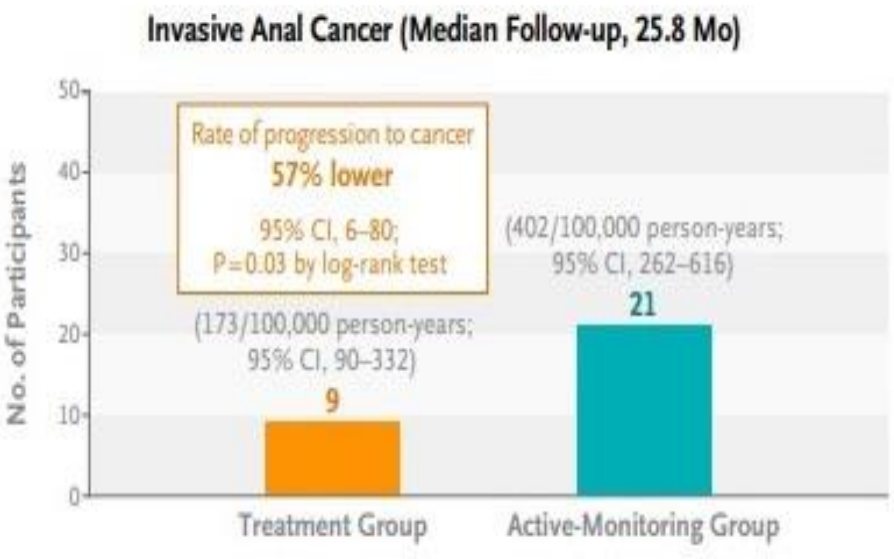
The NEW ENGLAND JOURNAL of MEDICINE

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*

2022



Rate of progression to cancer according to HSIL size:

>50%: 1047/ 100,000 person-years

≤50%: 185/ 100,000 person-years

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Treatment Group (N=2227)	Active-Monitoring Group (N=2219)
Median age (IQR) — yr	51 (44–57)	51 (44–57)
Median time since HIV diagnosis (IQR) — yr	17 (10–24)	17 (10–25)
Median follow-up (IQR) — mo	25.3 (11.7–42.0)	27.2 (12.0–42.1)
Gender identity — no. (%)		
Male	1793 (80.5)	1782 (80.3)
Female	346 (15.5)	365 (16.4)
Transgender	85 (3.8)	68 (3.1)
Nonbinary	2 (0.1)	2 (0.1)
Declined to answer	1 (<0.1)	2 (0.1)
Race or ethnic group — no. (%)†		
Black	935 (42.0)	939 (42.3)
Non-Hispanic White	695 (31.2)	737 (33.2)
Non-Black Hispanic	381 (17.1)	339 (15.3)
Asian or Pacific Islander	27 (1.2)	29 (1.3)
Other or unknown	189 (8.5)	175 (7.9)
CDC criterion for risk of HIV infection — no. (%)‡		
Male-to-male sexual contact	1716 (77.1)	1717 (77.4)
Heterosexual	532 (23.9)	510 (23.0)
Injection-drug use	152 (6.8)	177 (8.0)
Transfusion	53 (2.4)	47 (2.1)
Hemophilia	2 (0.1)	4 (0.2)
Other	34 (1.5)	27 (1.2)
Smoking history — no. (%)		
Current smoker	710 (31.9)	743 (33.5)
Smoked >100 cigarettes over lifetime§	1268 (56.9)	1353 (61.0)
History of HSIL treatment ≥6 mo before randomization — no. (%)¶	228 (10.2)	215 (9.7)
Plasma HIV-1 RNA copies/ml — no./total no. (%)		
<50	1853/2213 (83.7)	1800/2201 (81.8)
51–199	155/2213 (7.0)	160/2201 (7.3)
200–1000	83/2213 (3.8)	93/2201 (4.2)
>1000	122/2213 (5.5)	148/2201 (6.7)
Median CD4 count (IQR) — cells/mm³‖	602 (393–827)	607 (410–837)
Nadir CD4 count — no. (%)**		
≤200 cells/mm³	1130 (50.7)	1121 (50.5)
>200 cells/mm³	1097 (49.3)	1098 (49.5)
HSIL size at screening — no. (%)**		
>50% of anal canal or perianal region	285 (12.8)	282 (12.7)
≤50% of anal canal or perianal region	1942 (87.2)	1937 (87.3)

Agenda

1. Why should we screen for anal cancer?
2. **Who should we screen for anal cancer?**
3. How should we screen for anal cancer?
4. Is anal cancer screening cost-effective?
5. Is anal cancer screening recommended?

Screening guidelines: anal cancer

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DOI: 10.1002/ijc.34850

SPECIAL REPORT

IJC INTERNATIONAL JOURNAL of CANCER

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

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

International Journal of cancer, Dec 2023

Who to screen?

TABLE 1 Populations for screening.

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]		

Abbreviations: HSIL, high grade squamous intraepithelial lesion; MSM, Men who have sex with men; MSW, Men who have sex with women; TW, Transgender women.

[a]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.

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TABLE 3 Management of screening test results.

Primary screening test	Triage test	Test results	Management	Modification for low HRA capacity[a]
Cytology	None	NILM	Repeat screening 12 months	Repeat 12–24 months
		ASC-US or worse	HRA referral	ASC-US/LSIL—repeat 12 months HSIL and ASC-H—HRA referral
	hrHPV testing of ASC-US or worse	ASC-US/hrHPV negative	Repeat screening 12 months	Repeat 24 months
		LSIL/hrHPV-negative	Provider discretion—either HRA referral or repeat screening in 12 months	Repeat 12 months
		ASC-US or LSIL/hrHPV positive	HRA referral	ASC-US/LSIL/hrHPV positive (non 16)—repeat 12 months hrHPV16 positive (regardless of cytology)—HRA referral
		ASC-H/HSIL (regardless of HPV)	HRA referral	HRA referral
hrHPV testing [HPV16 genotyping]	None	hrHPV negative	Repeat screening 12–24 months	Repeat 24 months
		hrHPV positive	HRA referral	hrHPV positive (non16)- repeat 12 months HPV16 positive—HRA referral
	Cytology of hrHPV positive	NILM/hrHPV positive [hrHPV positive (non16)]	Provider discretion—either HRA referral or repeat screening in 12 months	Repeat 12 months
		ASC-US or worse/hrHPV positive [HPV16 positive/regardless of cytology]	HRA referral	ASC-US/LSIL/hrHPV positive (non16)—repeat 12 months HSIL, ASC-H (regardless of hrHPV)—HRA referral hrHPV16 positive (regardless of cytology)—HRA referral
Cytology/hrHPV co-testing [HPV16 genotyping]	None	NILM/hrHPV negative	Repeat screening 12–24 months	Repeat 24 months
		ASC-US/hrHPV negative	Repeat screening 12 months	ASCUS/hrHPV negative—repeat 24 months
		NILM/hrHPV positive [NILM/hrHPV positive (non16)]	Provider discretion—either HRA referral or repeat screening in 12 months	Repeat 12 months
		LSIL/hrHPV negative	Provider discretion—either HRA referral or repeat screening in 12 months	Repeat 12–24 months
		ASC-US or LSIL/hrHPV positive HSIL, ASC-H (regardless of HPV) [HPV16 positive, regardless of cytology]	HRA referral	ASC-US/LSIL/hrHPV positive (non16)—repeat 12 months HSIL, ASC-H (regardless of hrHPV)—HRA referral hrHPV16 positive (regardless of cytology)—HRA referral

Which one is more sensitive, specific and needs less HRA referral?

Sensitivity and specificity of anal swab testing

Clinical Infectious Diseases

BRIEF REPORT

2024 Anal Cancer Screening Guidelines: Analysis of Clinical Performance and Use of High-Resolution Anoscopy in a Large Cohort of Persons With HIV

Michael Gaisa,[1] Ashish Deshmukh,[2] Keith Sigel,[1] and Yuxin Liu[3]

[1]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA; [2]Department of Public Health Sciences, College of Medicine, Medical University of South Carolina, Charleston, South Carolina, USA; and [3]Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Table 1. Screening Performance of 5 Recommended Strategies in 1223 Persons With Human Immunodeficiency Virus[a]

Screening Strategy	Abnormal Results Triggering HRA Referral	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Youden's Index	PPV, % (95% CI)	NPV, % (95% CI)	HRAs Generated, No. (%)	HSILs Detected, No. (%) (n = 507)	HRA/HSIL Ratio
Cytology alone	ASCUS or worse	86 (83–89)	31 (28–34)	0.17	47 (44–50)	76 (71–81)	933 (76)	438 (86)	2.13
Cytology with hrHPV triage	ASCUS/hrHPV positive; LSIL/hrHPV positive; ASC-H/HSIL regardless of hrHPV; HPV-16 positive	83 (80–86)	49 (45–52)	0.32	53 (50–57)	80 (76–84)	790 (65)	422 (83)	1.87
hrHPV alone	hrHPV positive	96 (94–97)	29 (26–33)	0.25	49 (46–52)	91 (86–94)	994 (81)	486 (96)	2.04
hrHPV with cytology triage	hrHPV positive/ASCUS or worse; HPV-16 positive, regardless of cytology	88 (85–90)	43 (40–47)	0.31	52 (49–56)	83 (79–87)	851 (70)	445 (88)	1.91
Cotesting	NILM/HPV-16 positive; ASCUS/hrHPV positive; LSIL/hrHPV positive; ASC-H/HSIL regardless of hrHPV; HPV-16 positive	88 (85–91)	43 (39–46)	0.30	52 (49–55)	83 (80–87)	856 (70)	445 (88)	1.92

Abbreviations: ASC-H, atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion; ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; HPV, human papillomavirus; HRA, high-resolution anoscopy; hrHPV, high-risk HPV; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; NILM, negative for intraepithelial lesion or malignancy; NPV, negative predictive value; PPV, positive predictive value.

[a]Strategies recommended by 2024 International Anal Neoplasia Society guidelines.

How to screen? Which steps?

1. Detect early stage cancer: 80% are symptomatic

- Without screening: most cancers are detected at ≥30 mm
- When detected at < 20 mm: 80-100% survival
- **Asking for symptoms at the consultation**:
  pain, bleeding, local mechanical symptoms or lesion
- **DARE** digital ano-rectal examination or **self DARE**

The accuracy of anal self- and companion exams among sexual minority men and transgender women: a prospective analysis

Alan G. Nyitray,[a,b,*] Timothy L. McAuliffe,[b] Cameron Liebert,[c] Michael D. Swartz,[d] Ashish A. Deshmukh,[e,f] Elizabeth Y. Chiao,[g] Lou Weaver,[g] Ellen Almirol,[h] Jared Kerman,[h] John A. Schneider,[h] J. Michael Wilkerson,[i] Lu-Yu Hwang,[j] Derek Smith,[k] and Aniruddha Hazra,[h] The Prevent Anal Cancer Palpation Study Team

The Lancet Regional Health - Americas
2024;31: 100704

N=774 patients
clinician provided all education and DAREs
245 lesions detected
median size= 3 mm (1-10 mm)
30% prefered self- or partner- DARE
Easy to perform in 90%

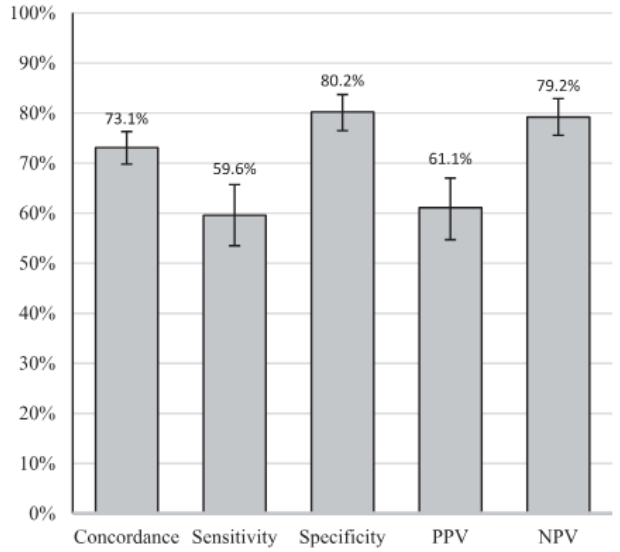


Fig. 1: Agreement and accuracy for lay anal examinations compared with clinician examinations in Chicago, Illinois and Houston, Texas, USA 2020–2022. Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

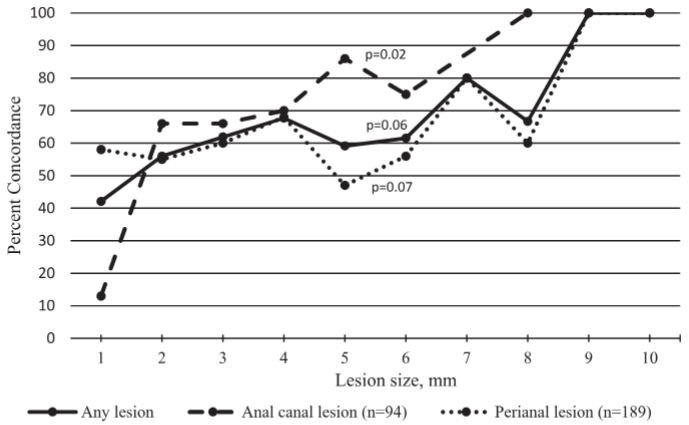
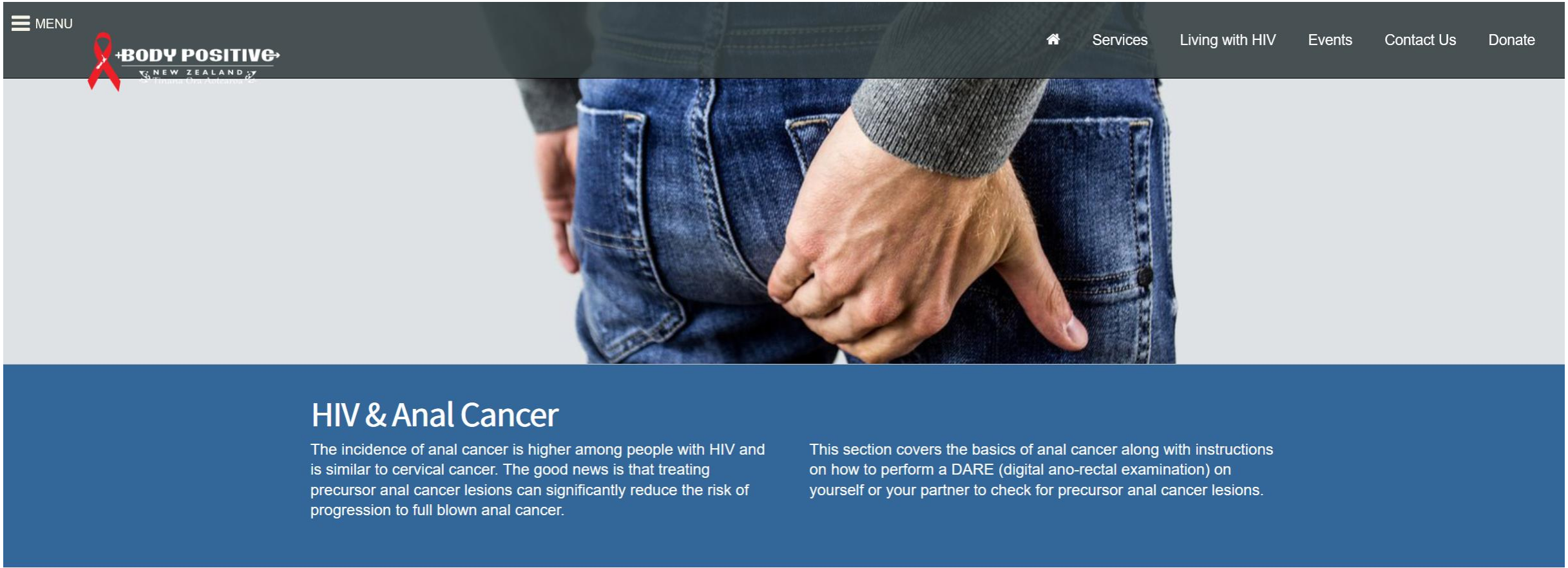


Fig. 2: Concordance by lesion size between lay and clinician anal examinations stratified by anatomic site in Chicago, Illinois and Houston, Texas USA 2020–2022. p value is derived from the Cochrane-Armitage test for trend. Size and number of lesions; 1 mm (n = 19), 2 mm (n = 84) 3 mm (n = 63), 4 mm (n = 31), 5 mm (n = 22), 6 mm (n = 13), 7 mm (n = 5), 8 mm (n = 6), 9 mm (n = 1), 10 mm (n = 1).

➢ Refer to proctogist

https://bodypositive.org.nz



How to screen? Which steps?

2. Detect HSIL= high grade squamous intraepithelial lesions

- Anal swab
  - Cytology
  - HPV DNA
  - Other markers of cellular proliferation (p16/Ki67, E6/E7 mRNA,…)

➢ Anoscopy

➢ Referal to **High resolution anoscopy (HRA)**

(*J Low Genit Tract Dis* 2016;20: 283–291)

CONSENSUS TERMINOLOGY

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

Richard John Hillman, MD, PhD,[1,2] Tamzin Cuming, MD,[3] Teresa Darragh, MD,[4] Mayura Nathan, MBBS, FRCP,[5] Michael Berry-Lawthorn, MD,[6] Stephen Goldstone, MD,[7] Carmella Law, MB, BS, FAChSHM, MBA,[8] Joel Palefsky, MD,[9] Luis F. Barroso, MD,[10] Elizabeth A. Stier, MD,[11] Céline Bouchard, MD,[12] Justine Almada, BA,[13] and Naomi Jay, PhD, RN[14]

- Need well-trained physician
- Timely, costly
- Not always reimbursed
- May cause pain, bleeding and infection
- How to prioritize patients?

Availibility High resolution anoscopy (HRA) in Belgium

- UZ Antwerpen
- UZ Gent
- UZ Ghent
- UZ Leuven
- CHU St-Pierre
- UZ Brussel
- Université de Liège

How to reduce HRA referal and over treatment?

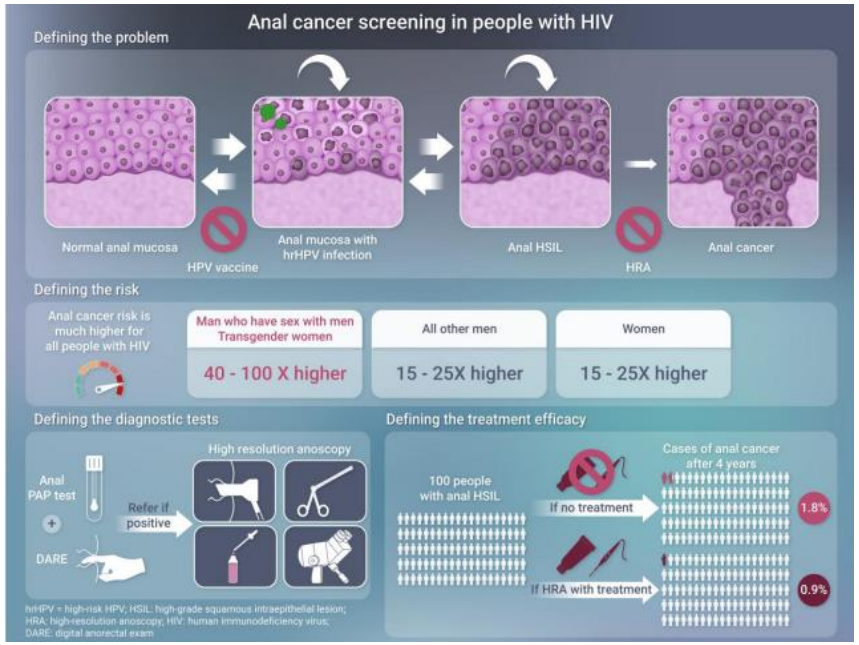
- Alternative to HRA
- Prioritize/optimize candidates for HRA
- Need to distinguish between LSIL and HSIL

Clinical Infectious Diseases
STATE-OF-THE-ART REVIEW
IDSA OXFORD

State-of-the-Art Review: Anal Cancer Screening in People With HIV

Hayden S. Andrews,[1,2,©] Meena Murthy,[3] and Benjamin T. Davis[3]
[1]Division of Infectious Diseases and Geographic Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA; [2]Parkland Health, Dallas, Texas, USA; and [3]Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, USA

CID 2025:80 (15 June)



Alternative to HRA

SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY
2024, VOL. 59, NO. 2, 232–238
https://doi.org/10.1080/00365521.2023.2268229

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Endoscopic underwater detection and resection of anal squamous intraepithelial lesions in non-anesthetized patients – a feasibility study and comparison with standard surgical treatment

Peter Borch-Johnsen[a,b], Jonas Nygren[c,d] and Peter T. Schmidt[b]

[a]Department of Medicine, Ersta Hospital, Stockholm, Sweden; [b]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [c]Department of Surgery, Ersta Hospital, Stockholm, Sweden; [d]Karolinska Institutet (KIDS), Stockholm, Sweden

Retrospective comparison between

- new endoscopic technique to detect and remove ASILs in non-anesthetized patients with a diathermia snare after local injection of xylocaine/adrenaline: n=37 (less invasive than surgery and more available than HRA)
- standard surgical treatment n=43
- Comparable in term of bleeding post procedure
- Need more endoscopy procedures to reach treatment of all lesions

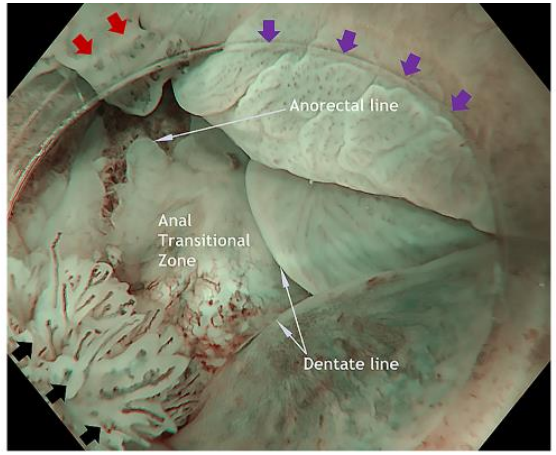


Figure 1. Landmarks in the anal canal seen under water: anorectal line, dentate line and the area between, the anal transitional zone. Purple arrowheads show a flat, slightly raised ASIL (anal squamous intraepithelial lesions) with widened and irregular IPCL (intra papillary capillary loops). Black arrowheads show an exophytic villous ASIL and the red arrowheads show an exophytic non-villous ASIL.

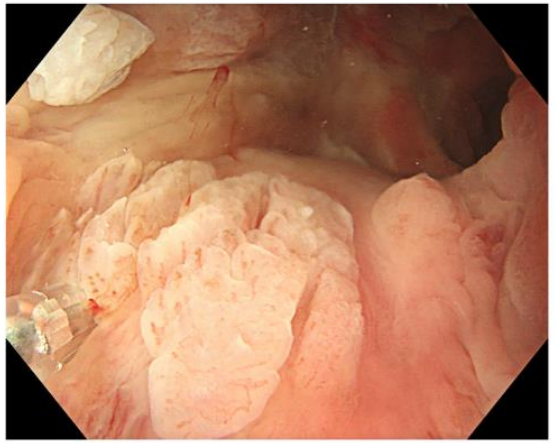


Figure 2. Creating a submucosal cushion under the lesion and also providing local anesthesia. Proximal and on the left side of the lesion is the mucosa paler after the previous injection. At 11 o'clock is an exophytic whitish non-villous exophytic ASIL.

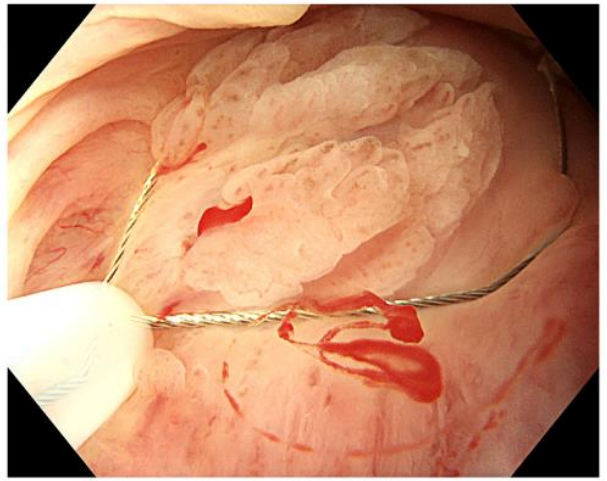


Figure 3. Placing the snare with a slight pressure. At the tip of the casing is a small non-villous exophytic ASIL.

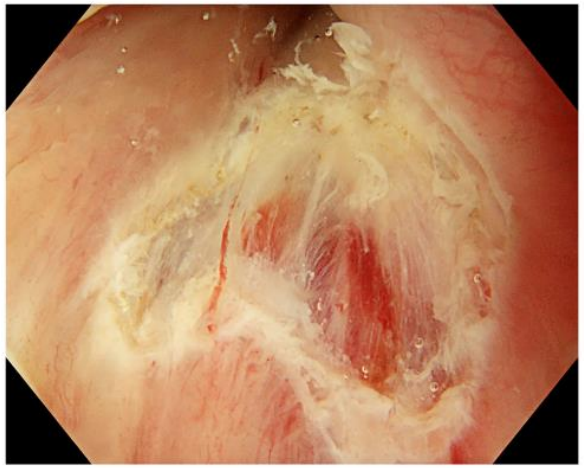


Figure 4. Resection of the lesion. The lesion is retrieved and sent for histopathology. Minor bleeding can be coagulated with the top of the snare. In case of uncertainty about radical resection, the edges can also be coagulated.

Prioritizing patients?

Identifying risk factors for anal cancer in people with HIV in Spain: a multicentre retrospective cohort study nested in the PISCIS cohort

*Josep M Llibre, Boris Revollo, Jordi Aceiton, Yesika Díaz, Pere Domingo, Joaquim Burgos, Patricia Sorni, Maria Saumoy, Hernando Knobel, Marta Navarro, Elena Leon, Amat Orti, Laia Arbonés, Arantxa Mera, Elisabet Deig, Guillem Sirera, Josep M Miró, Jordi Casabona, Raquel Martin-Iguacel, on behalf of the PISCIS Cohort Study Group**

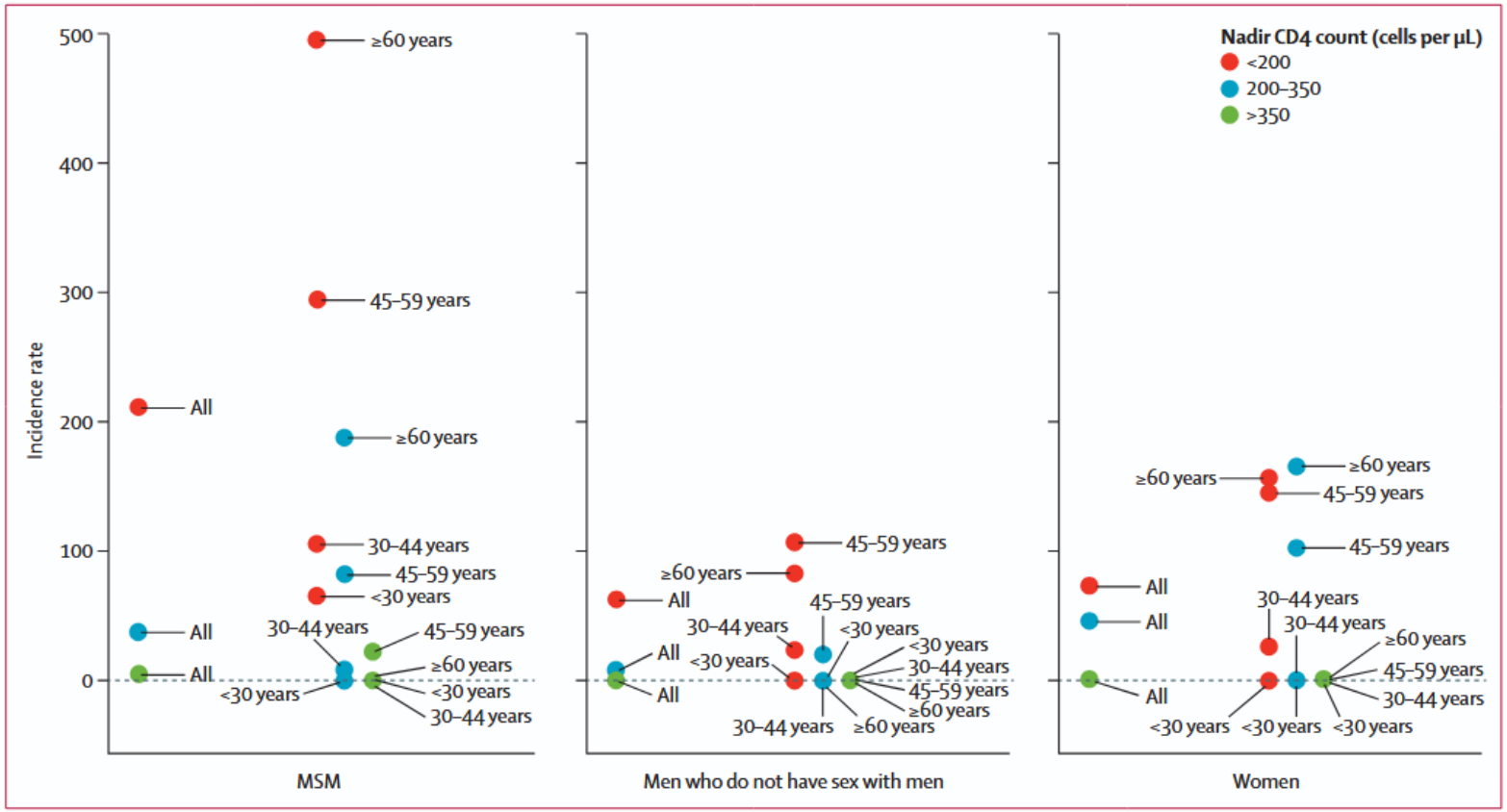


Figure 1: **Incidence rates for anal cancer in people with HIV**
Point estimates are shown for MSM, men who do not have sex with men, and women for the following (time-updated) age groups: younger than 30 years, 30–44 years, 45–59 years, and 60 years and older. MSM=men who have sex with men.

Highest risk at Saint-Pierre HIV reference centre

	N=	65% HRA	
• MSM and transgender women > 35 years	1136	738	
• MSM and transgender women > 35 years and CD4 nadir < 350/µL	568	370	-50%
• MSM and transgender women > 35 years and CD4 nadir < 200/µL	260	169	-50%
• Women with previous vulvar or cervical cancer	7	5	
• Women with previous vulvar or cervical HSIL	178	116	

CHU Saint-Pierre
UMC Sint-Pieter

New surrogate markers

Alone or in combination

- **Distinguish between LSIL and HSIL**
- **Distinguish which HSIL will become cancer**

  - Dual staining by p16 and Ki-67
  - HPV E6/E7 mRNA
  - DNA Methylation of human genes

DNA high-risk HPV, mRNA HPV and P16 tests for diagnosis of anal cancer and precursor lesions: a systematic review and meta-analysis

Ana Cristina Macedo,[a] Antônio José Grande,[b,c] Tatiana Figueiredo,[a] Tamy Colonetti,[a] João Carlos Gonçalves,[a] Eduardo Testoni,[a] and Maria Inês da Rosa[a,*]

[a]Laboratory of Translational Medicine, Postgraduate Program in Health Sciences at the University of Extremo Sul Catarinense, Criciúma, SC, Brazil
[b]Laboratory of Evidence-based Pratice, State University of Mato Grosso do Sul, Campo Grande, MS, Brazil
[c]Post-graduate Program in Infectious Disease and Parasites, Federal University of Mato Grosso do Sul, Campo Grande, MS, Brazil

eClinicalMedicine 2023;62: 102128

Summary

Background Anal cancer prevention has two critical points: the incidence rate is several fold higher for some groups,

Biopsies

Test All	DNA HR HPV% (IC 95%)	mRNA HPV% (IC 95%)	HPV 16% (IC 95%)	p16% (IC 95%)
Sensitivity	92.4 (84.2–96.5)	77.3 (73.2–80.9)	53.3 (35.4–70.3)	68.8 (47.9–84.1)
Specificity	41.7 (33.9–44.9)	61.9 (56.6–66.9)	71.7 (55.3–83.8)	64.1 (51.0–75.4)
DOR	8.7 (4.6–16.2)	5.52 (4.2–7.1)	2.88 (1.28–4.48)	3.93 (1.12–6.74)
AUC	0.67 (0.63–0.71)	0.78 (0.74–0.82)	0.69 (0.64–0.72)	0.74 (0.70–0.77)
TP	1768	466	230	448
FP	3172	544	649	597
FN	144	142	205	138
TN	1724	898	1394	849
N total	**6798**	**2050**	**2478**	**2032**
Studies	**20**	**7**	**6**	**8**
MSM HIV+				
Sensitivity	96.8 (89.2–99.1)	79.0 (74.0–83.0)	60.0 (54.0–65.0)	76.0 (49.0–91.0)
Specificity	32.1 (26.3–38.6)	59.0 (52.0–65.0)	67.0 (54.0–79.0)	65.0 (52.0–76.0)
DOR	14.13 (4.34–45.95)	5.0 (4.0–8.0)	3.0 (2.0–6.0)	6.0 (2.0–17.0)
AUC	0.55 (0.51–0.60)	0.80 (0.76–0.83)	0.62 (0.57–0.67)	0.73 (0.69–0.77)
TP	1315	269	191	249
FP	2550	350	574	405
FN	68	72	131	87
TN	1105	509	940	575
N total	**5038**	**1200**	**1836**	**1316**
Studies	**12**	**5**	**5**	**5**

MSM (Men Sex Men); HIV: human immunodeficiency virus; AIN: anal intraepithelial neoplasia; CI: Confidence interval; DOR: diagnostic odds ratio; AUC: area under the curve; TP: true positive; FP: false positive; FN: false negative; TN: true negative. Outcomes: AN1- vs. AIN2+.

Table 2: **Accuracy of DNA HR HPV, mRNA HPV, DNA HPV16 and p16 for detection of Anal Intraepithelial Neoplasia (AIN2+) in histopathological, Pooled and discerning by subgroup.**

New surrogate markers

Distinguish between LSIL and HSIL on anal swabs:
MAL methylation was significantly (p = 0.002) increased in HSIL compared with LSIL in HIV positive participants with **79.8%** correctly indicated as **HSIL**.

scientific reports

OPEN

Gene methylation of *CADM1 and MAL* identified as a biomarker of high grade anal intraepithelial neoplasia

Samuel Phillips[1,2,3,9✉], Kahli Cassells[1,9], Suzanne M. Garland[1,2,3], Dorothy A. Machalek[2,4], Jennifer M. Roberts[5], David J. Templeton[4,6,7], Fengyi Jin[4], I. Mary Poynten[4], Richard J. Hillman[4,8], Andrew E. Grulich[4], Gerald L. Murray[1,2,3], Sepehr N. Tabrizi[1,2,3], Monica Molano[2,10], Alyssa M. Cornall[1,2,3,10] & SPANC team

New surrogate markers

DNA Methylation of human genes on

- Anal biopsies
- **Anal swabs**

The Journal of Infectious Diseases
MAJOR ARTICLE
2025
IDSA OXFORD

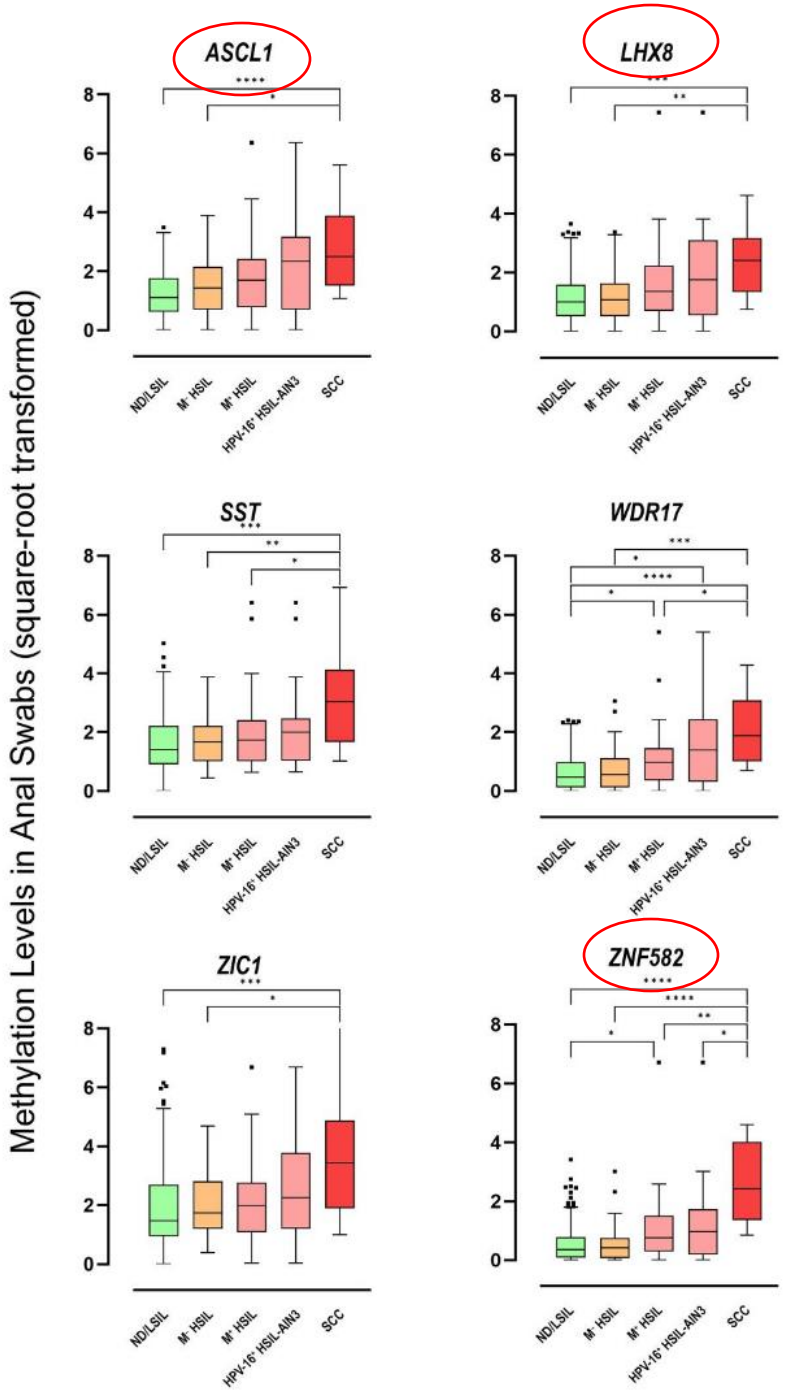
DNA Methylation Analysis on Anal Swabs for Anal Cancer Screening in People Living With Human Immunodeficiency Virus

Fernando Dias Gonçalves Lima,[1,2,3,4,a,©] Kirsten Rozemeijer,[1,2,a,©] Ramon P. van der Zee,[1,2,4,5,a,©] Stéfanie Dick,[1,2,5,©] Timo J. ter Braak,[1,2,©] Debby E. Geijsen,[6,©] Philip Meijnen,[7,©] Birgit I. Lissenberg-Witte,[8,©] Carel J. M. van Noesel,[9,©] Henry J. C. de Vries,[3,4,10,©] Jan M. Prins,[4,5,©] and Renske D. M. Steenbergen[1,2,©]

[1]Department of Pathology, Amsterdam UMC, location Vrije Universiteit Amsterdam; [2]Imaging and Biomarkers, Cancer Center Amsterdam; [3]Department of Dermatology, Amsterdam UMC, location University of Amsterdam; [4]Amsterdam Institute for Infection and Immunity; [5]Division of Infectious Diseases, Department of Internal Medicine; [6]Department of Radiation Oncology, Amsterdam UMC, location University of Amsterdam; [7]Department of Radiation Oncology, Amsterdam UMC, location Vrije Universiteit Amsterdam; [8]Department of Epidemiology and Data Science, Amsterdam UMC, location Vrije Universiteit Amsterdam; [9]Department of Pathology, Amsterdam UMC, location University of Amsterdam; and [10]Department of Infectious Diseases, Sexually Transmitted Infection Outpatient Clinic, Public Health Service of Amsterdam, The Netherlands

Decrease HRA by 43%

while detecting all cancers and the majority of HSIL



New surrogate markers

Cytology and reflex biomarkers **decreases HRA**

Open Forum Infectious Diseases

MAJOR ARTICLE

Using Anal Cytology and Human Papillomavirus DNA and E6/E7 mRNA Detection to Optimize High-Resolution Anoscopy Referrals in Men Who Have Sex With Men With HIV

Ana C. Silva-Klug,[1,©] Sònia Paytubi,[2,3] Montserrat Torres,[2,3,a] Loris Trenti,[4] Nuria Baixeras,[5] Monica Sanchez-Llamas,[1] Miquel A. Pavon,[2,3] Silvia De Sanjose,[7] Isabel Catala,[5] August Vidal,[5] Mario Poljak,[6] Laia Alemany,[2,3] Daniel Podzamczer,[1,b] Sebastian Videla,[8] and Maria Saumoy[1]

[1]HIV and STD Unit, Infectious Diseases Department, Bellvitge University Hospital/Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, Barcelona, Spain, [2]Infection and Cancer Laboratory, Cancer Epidemiology Research Program, Catalan Institute of Oncology/Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, Barcelona, Spain, [3]Centro de investigación Biomédica en Red en Epidemiología y Salud Pública, Ministerio de Ciencia e Innovación en Epidemiología y Salud Pública, Madrid, Spain, [4]Colorectal Unit, General and Digestive Surgery Department, Bellvitge University Hospital/Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, Barcelona, Spain, [5]Pathology Unit, Bellvitge University Hospital/Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, Barcelona, Spain, [6]Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [7]Viral and Bacterial Infections Worldwide Program, Barcelona Institute for Global Health, Barcelona, Spain, and [8]Clinical Research Support Area, Department of Clinical Pharmacology, Germans Trias i Pujol University Hospital, Badalona, Spain

Table 4. Participants Referred for HRA, Biopsy-Proven HSILs, and NND vs aLBC of the 18 Screening Strategies

	Biomarker Alone		Cytology and Biomarker in All		Cytology and Reflex Biomarkers	
	Biopsy-Proven HSIL Detection (n = 75)	NND	Biopsy-Proven HSIL Detection (n = 75)	NND	Biopsy-Proven HSIL Detection (n = 75)	NND
aLBC	60	2.7	…	…	…	…
LA	73 (97.3)[a]	5.3	74 (98.7)[a]	6.21	59 (78.7)	2.2
LA 14 HR-HPV	68 (90.7)	3.5	73 (97.3)[a]	4.31	57 (76)	2.1
LA HPV-16	34 (57.3)	3.4	63 (84)	2.7	40 (53.3)	2.3
HC2	58 (77.3)	2.4	67 (89.3)	3	54 (72)	2
E6/E7 mRNA	62 (82.7)	2.9	70 (93.3)[a]	3.1	55 (73.3)	2.2
E6/E7 mRNA HPV-16	31 (41.3)	3.6	62 (82.6)	2.6	38 (50.7)	2.7

Data are presented as No. (%). Only *P* values showing significant differences in favor of the screening strategy vs aLBC are notated; otherwise, differences are nonsignificant.

Abbreviations: aLBC, anal liquid-based cytology; E6/E7 mRNA, E6/E7 mRNA detection for all 14 high-risk genotypes in the test; E6/E7 mRNA HPV-16, E6/E7 mRNA detection for HPV-16; HC2, Hybrid Capture 2 HPV DNA test; HRA, high-resolution anoscopy; HSIL, high-grade squamous intraepithelial lesion; LA, Linear Array HPV DNA test for all 37 genotypes in the test; LA 14 HR-HPV, Linear Array HPV DNA test for the 14 most important high-risk genotypes; LA HPV-16, Linear Array HPV DNA test for HPV-16; NND, number needed to diagnose.

[a]$P < .001$.

Agenda

1. Why should we screen for anal cancer?
2. Who should we screen for anal cancer?
3. How should we screen for anal cancer?
4. **Is anal cancer screening cost-effective?**
5. Is anal cancer screening recommended?

Annals of Internal Medicine 2025 ORIGINAL RESEARCH

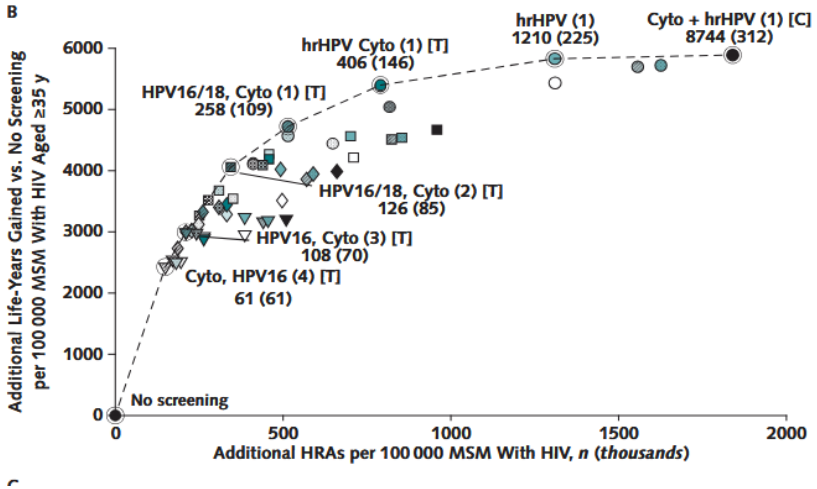
Screening for Anal Cancer Among Men Who Have Sex With Men With HIV: Benefits, Harms, and Cost-Effectiveness Analyses

Ashish A. Deshmukh, PhD, MPH; Haluk Damgacioglu, PhD; Keith Sigel, MD, PhD, MPH; Joel M. Palefsky, MD; Megan A. Clarke, PhD, MHS; Nicolas Wentzensen, MD, PhD, MS; Alan G. Nyitray, PhD; Ana Patricia Ortiz, PhD, MPH; Yueh-Yun Lin, PhD; Elizabeth Y. Chiao, MD; Elizabeth Stier, MD; Naomi Jay, NP, PhD; Michael Gaisa, MD, PhD; Yuxin Liu, MD, PhD; Eric G. Meissner, MD, PhD; Gweneth Lazenby, MD; Anna R. Giuliano, PhD; Stephen E. Goldstone, MD; Gary M. Clifford, PhD; Kalyani Sonawane, PhD*; and Jagpreet Chhatwal, PhD*

- Harm to benefit analysis
- Cost effectivness of different screening strategies including no screening

  ➢ 100.000 **MSM** ≥ 35 years with HIV during lifetime:

  In absence of screening, 4064 cancers and 680 deaths



➢ Annual cytology in MSM ≥35 years: reduce mortality by 65%

Screening starting at 35 years-old with cytology is more cost-effective than at 40-45 years

➢ Best interval?

- **Triennial cytology** yields optimal values
- …but less unnecessary HRA and overtreatment with **triage**

Most efficient triage:

1. Quadrennial cytology with HPV16 triage
2. Triennial HPV16 with cytology triage
3. Biennial HPV16/18 with cytology triage
4. Annual HPV16/18 with cytology triage
5. Annual HR HPV with cytology triage

Agenda

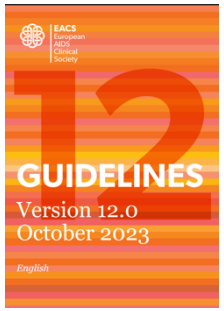
1. Why should we screen for anal cancer?
2. Who should we screen for anal cancer?
3. How should we screen for anal cancer?
4. Is anal cancer screening cost-effective?
5. **Is anal cancer screening recommended?**

Anal cancer screening is recommended

- IANS International Anal Neoplasia Society (Stier 2024)
- DHHS 2025
- EACS Oct 2025

Cancer: Screening Methods[1]

Problem	Persons	Procedure	Evidence of benefit	Screening interval	Additional comments
Anal cancer	MSM and persons with HPV-associated dysplasia[30]	Digital rectal exam, high resolution anoscopy & anal cytology	Reduces incidence of anal cancer	1-3 years	Ongoing research may identify at risk groups for screening
Breast cancer	Women 50-74 years[41]	Mammography	↓ Breast cancer mortality	1-3 years	
Cervical cancer	Women > 21 years	PAP smear or liquid based cervical cytology test	↓ Cervical cancer mortality	1-3 years	HPV genotype testing may aid PAP/liquid based cervical screening



Person:
MSM and TW age >35 y, all others > 45 y.
Vulvar HSIL or cancer regardless of age within one year of diagnosis.

Procedure:
symptoms review, digital rectal examination and co-testing cytology plus HR HPV on anal swab if a follow-up system is in place .
Refer to high resolution anoscopy, but if not available, proctoscopy +/- biopsy if:
-presence of **symptoms** or **abnormal digital anal rectal examination**
-or **any dysplasia** (LSIL, ASCUS, ASCH, HSIL) on cytology (if co-testing available with any positive HR HPV)
-or **positive HPV 16 once** or **positive HR HPV non 16 confirmed after 6 to 12 months** (even if cytology normal)

Conclusion

Anal cancer screening should be performed in **persons living with HIV** because of

- High incidence, morbidity and mortality of anal cancer
- First steps (asking for symptoms, self- DARE) are easy but need patients and health care workers education and new care bundles
- Anal cytology combined with HPV detection and other biomarkers in development could reduce the number of patient that need HRA
- Screening decreases mortality, is cost-effective and is recommended by several health authorities