



Advances in Anal Cancer Prevention in People with HIV

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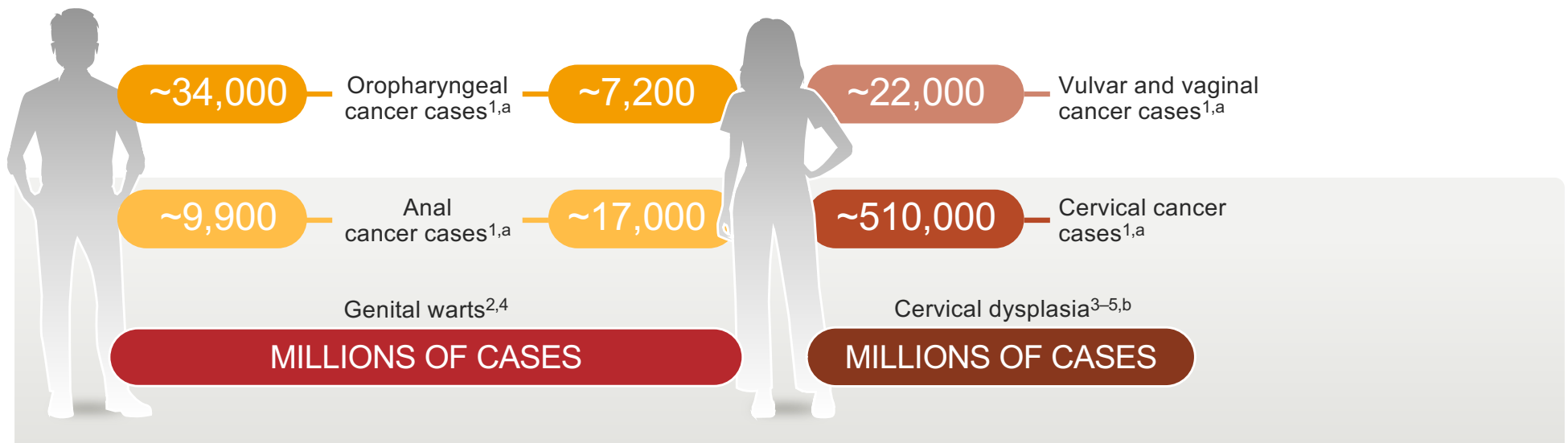
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Objectives

- 1. Understand the current epidemiology of anal cancer in people living with HIV
- 2. Be aware of the results of the ANCHOR study
- 3. Be aware of HPV vaccination recommendations and new screening guidelines for anal cancer prevention in people living with HIV
- 4. Understand gaps in knowledge in screening and treatment of anal high-grade squamous intraepithelial lesions

Estimated Annual Global Incidence of HPV-related Cancers and Diseases in Males and Females^{1–3}



GCO = Global Cancer Observatory; HPV = human papillomavirus; OPC = oropharyngeal cancer.

^aIncidence estimates derived from 2018 GCO data¹; ^bIncludes data from 31 European countries.³

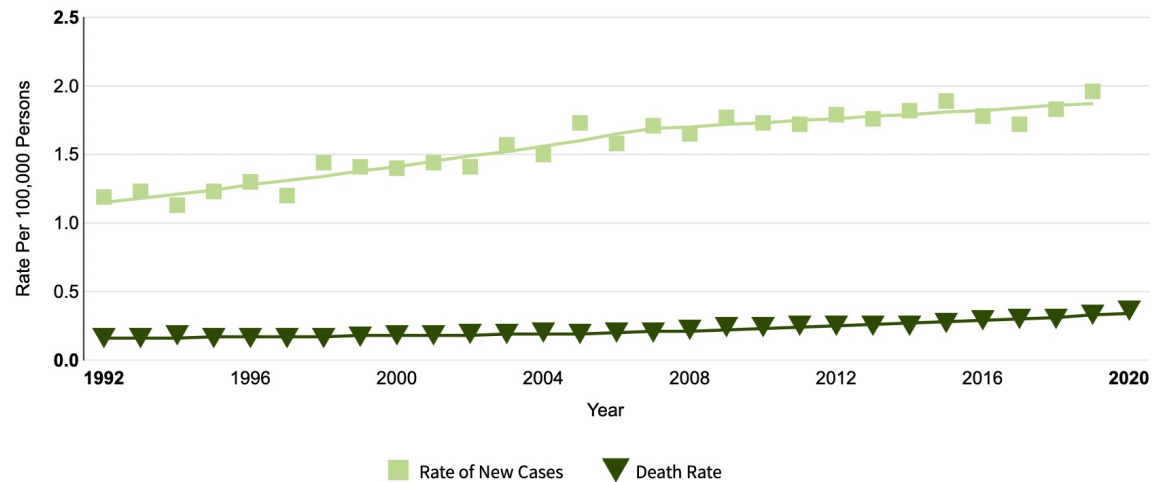
1. de Martel C et al. *Lancet Glob Health*. 2020;8:e180–e190. 2. Patel H et al. *BMC Infect Dis*. 2013;13:39. 3. Hartwig S et al. *Infect Agent Cancer*. 2017;12:19. 4. United Nations Department of Economic and Social Affairs. Growing at a slower pace, world population is expected to reach 9.7 billion in 2050 and could peak at nearly 11 billion around 2100. Accessed August 16, 2023. www.un.org/development/desa/en/news/population/world-population-prospects-2019.html 5. Eurostat. Population on 1 January 2015. Accessed August 16, 2023. ec.europa.eu/eurostat/databrowser/view/tps00001/default/table?lang=en 6. Bray F et al. *CA Cancer J Clin*. 2018;68:394–424. 7. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 14th ed. Public Health Foundation; 2021. Accessed August 16, 2023. <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hpv.pdf> 8. Centers for Disease Control and Prevention. HPV and oropharyngeal cancer. Accessed August 16, 2023. https://www.cdc.gov/cancer/hpv/basic_info/hpv_oropharyngeal.htm 9. Centers for Disease Control and Prevention. Human papillomavirus (HPV) infection. Accessed August 16, 2023. <https://www.cdc.gov/std/treatment-guidelines/hpv.htm>

The incidence of anal cancer continues to rise

At a Glance

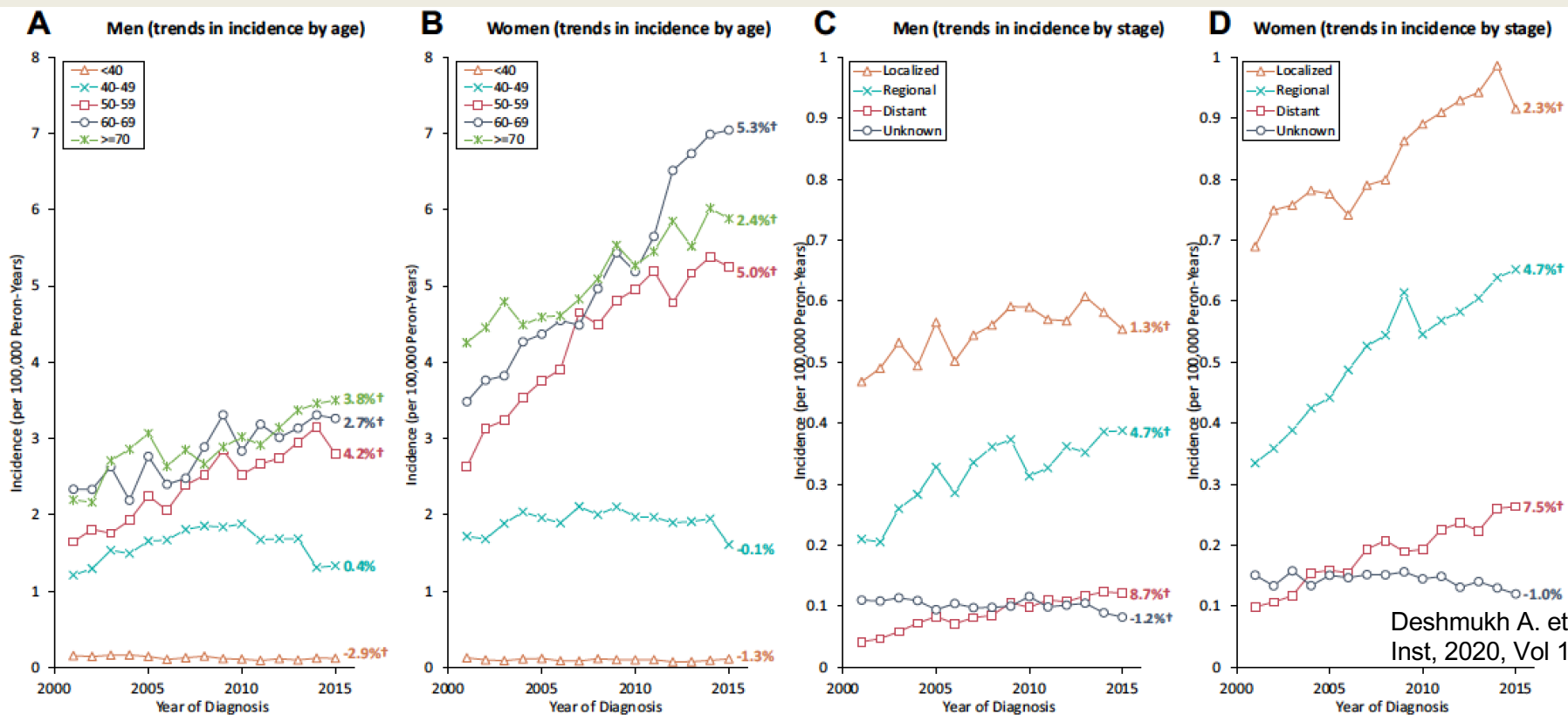
Estimated New Cases in 2022	9,440
% of All New Cancer Cases	0.5%
Estimated Deaths in 2022	1,670
% of All Cancer Deaths	0.3%

5-Year Relative Survival
70.1%
2012-2018



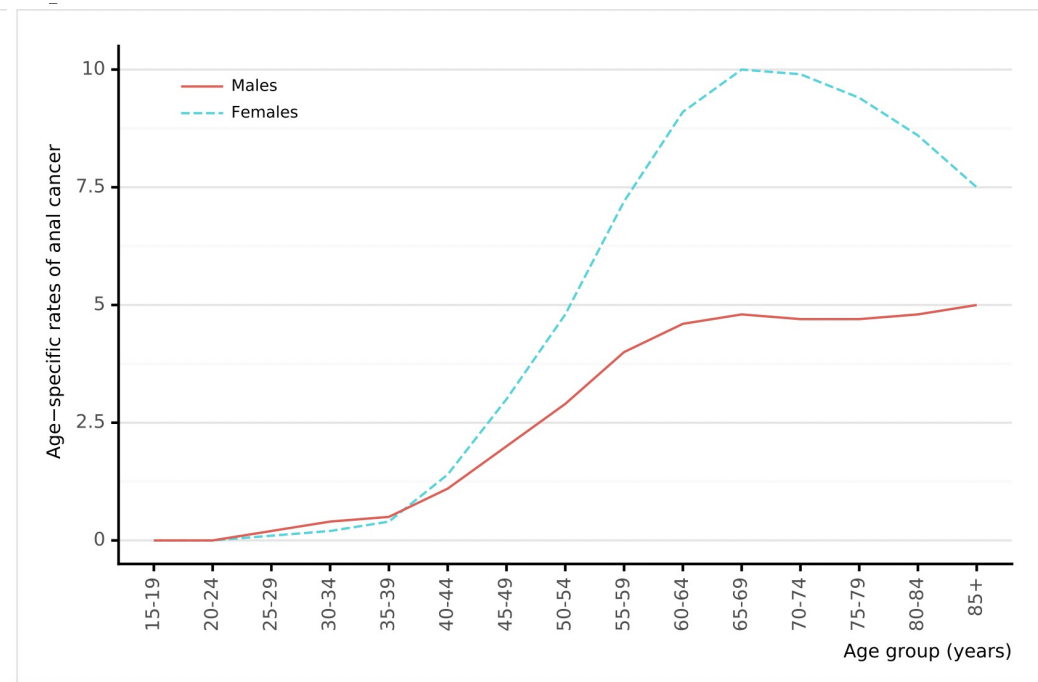
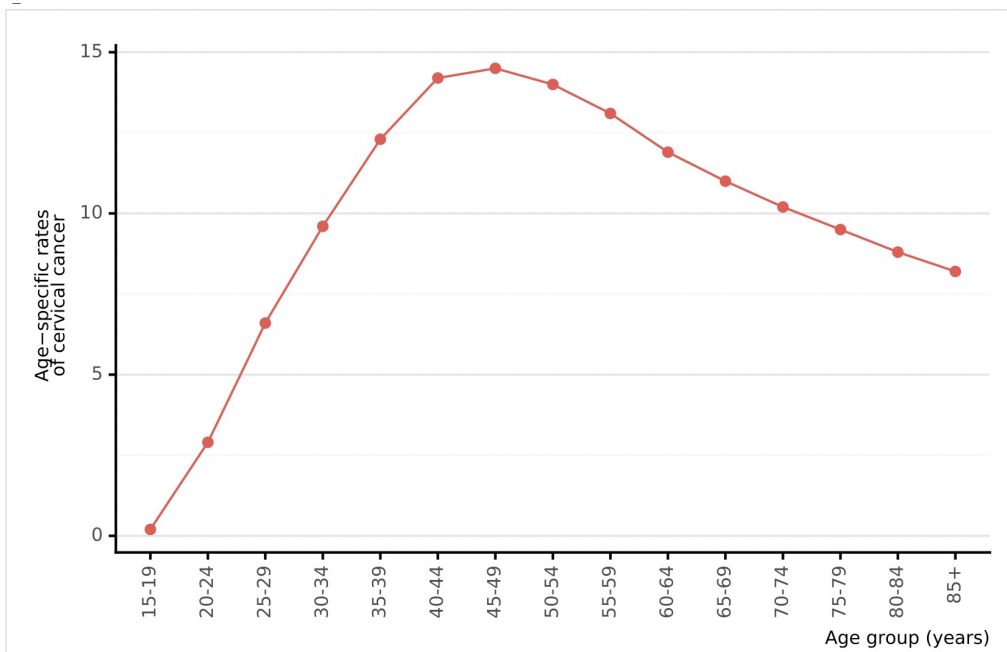
<https://seer.cancer.gov/statistics-network/explorer/application.html> accessed Jan 3, 2023

Rising HPV-Associated Anal Cancer (SCCA) Rates in Both Sexes



Deshmukh A. et al. J Natl Cancer Inst, 2020, Vol 112, No. 8:829-38.

Age-specific incidence rates for cervical and anal cancer in the U.S.



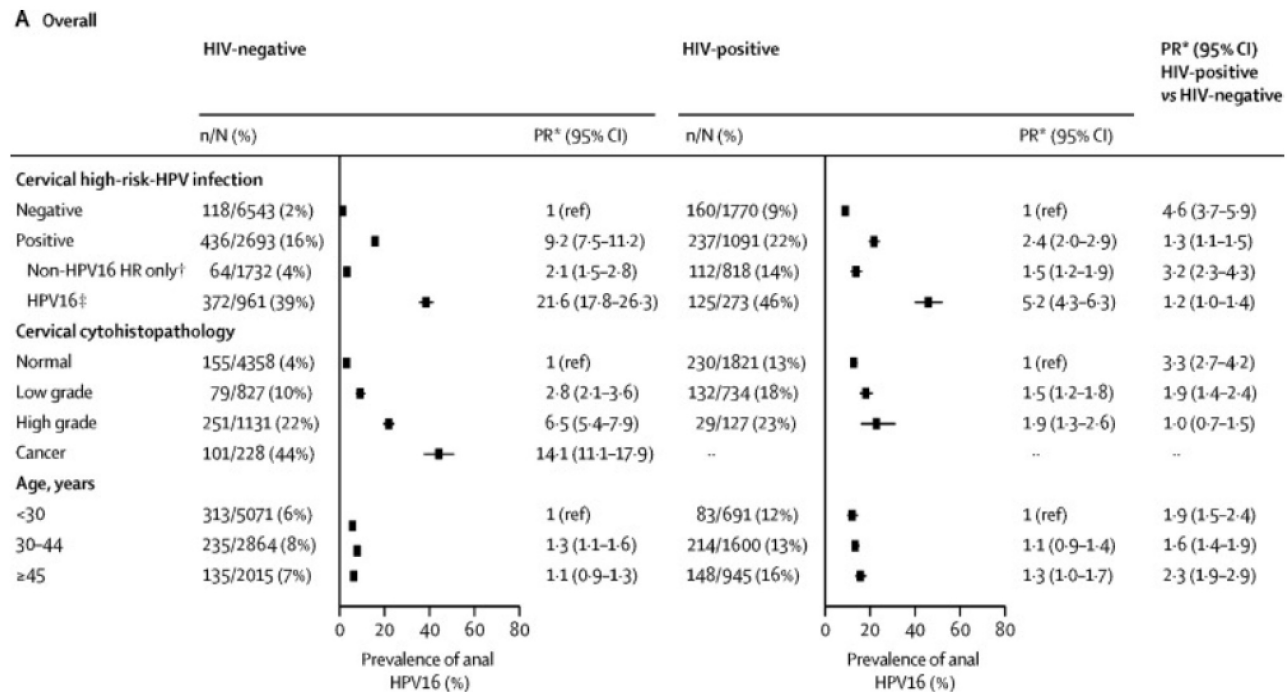
Bruni L et L. *ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in United States of America. Summary Report 22 October 2021. [Accessed 3/1/23]*

Anal cancer incidence compared to other HPV-associated cancers (US women)

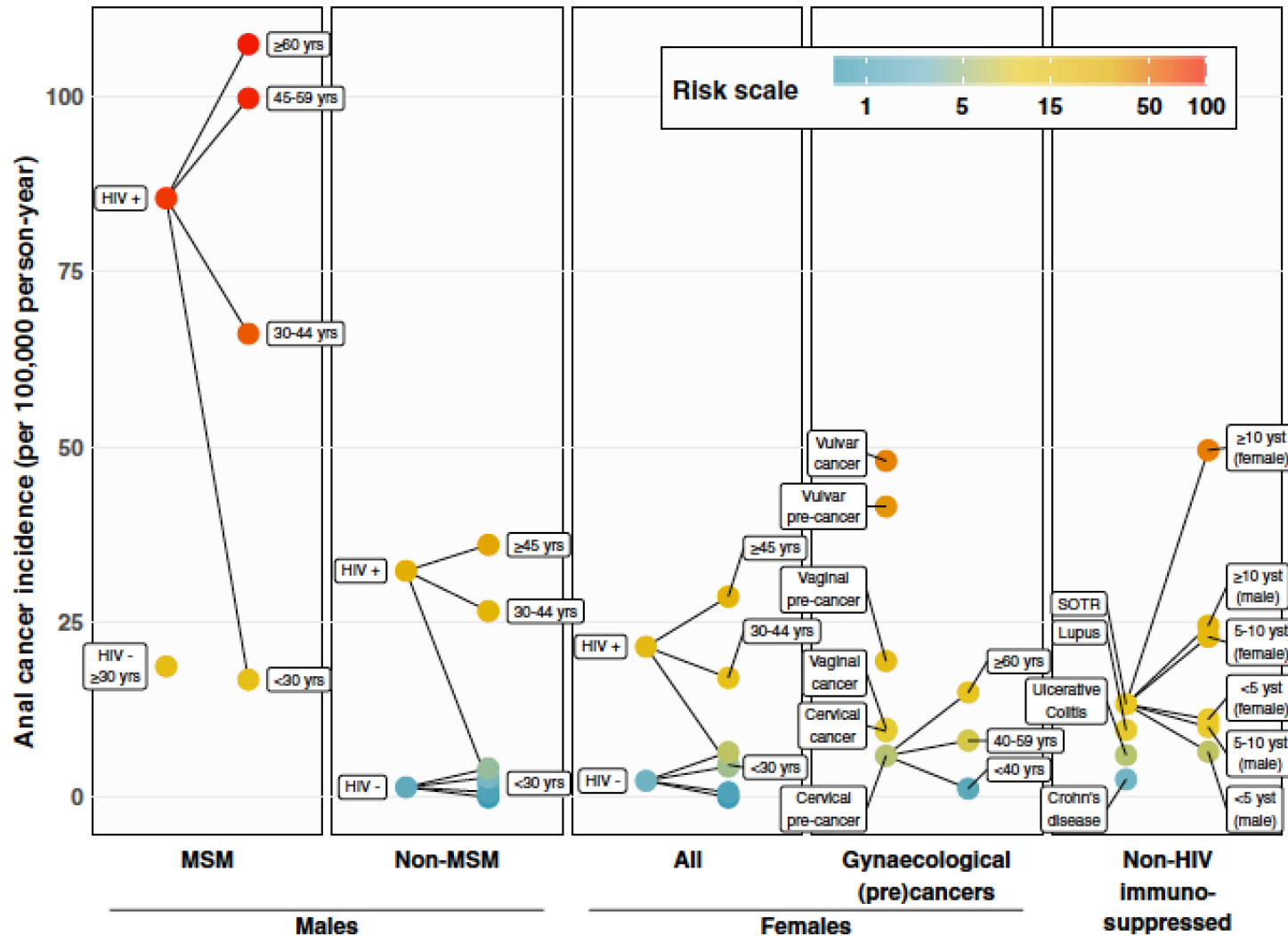


Deshmukh et al. J Natl Cancer Inst (2021) 113(6):792-6

Prevalence of anal HPV 16, by cervical high-risk HPV infection, cervical cytohistopathology, age, and HIV status

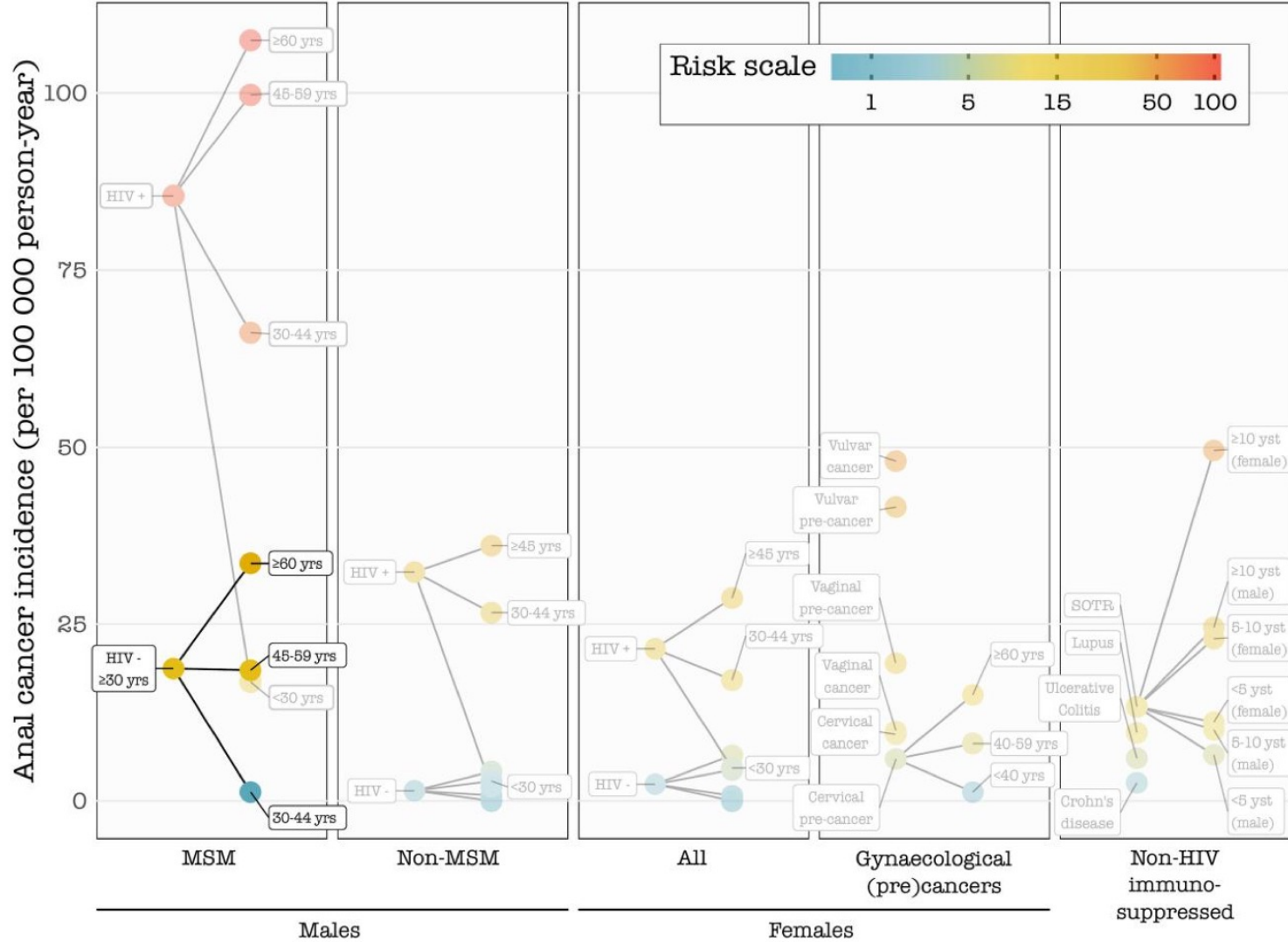


Anal cancer risk scale

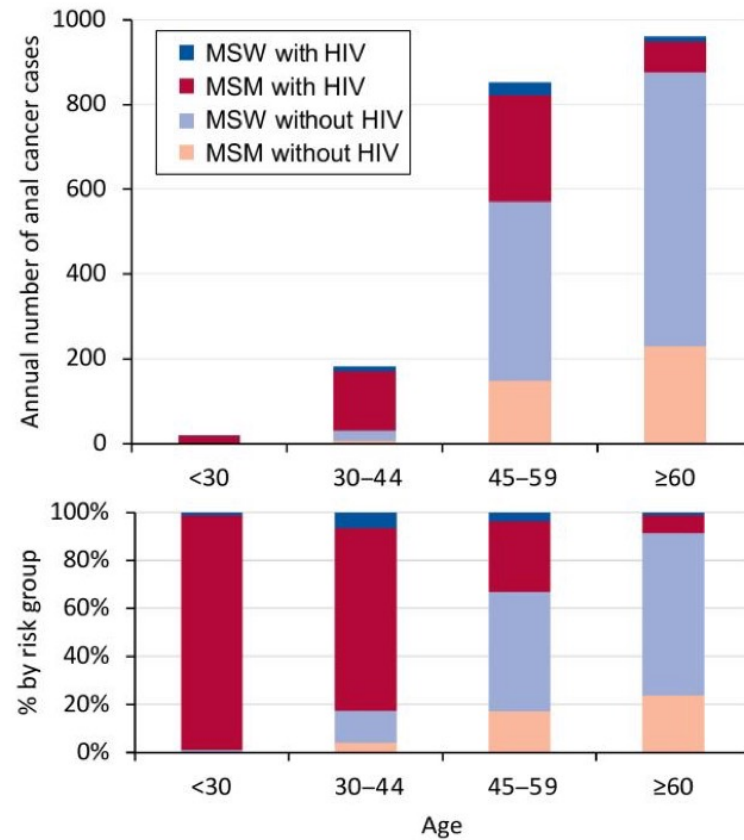


Clifford et al. Int. J. Cancer. 2020;1-11

Anal cancer risk scale



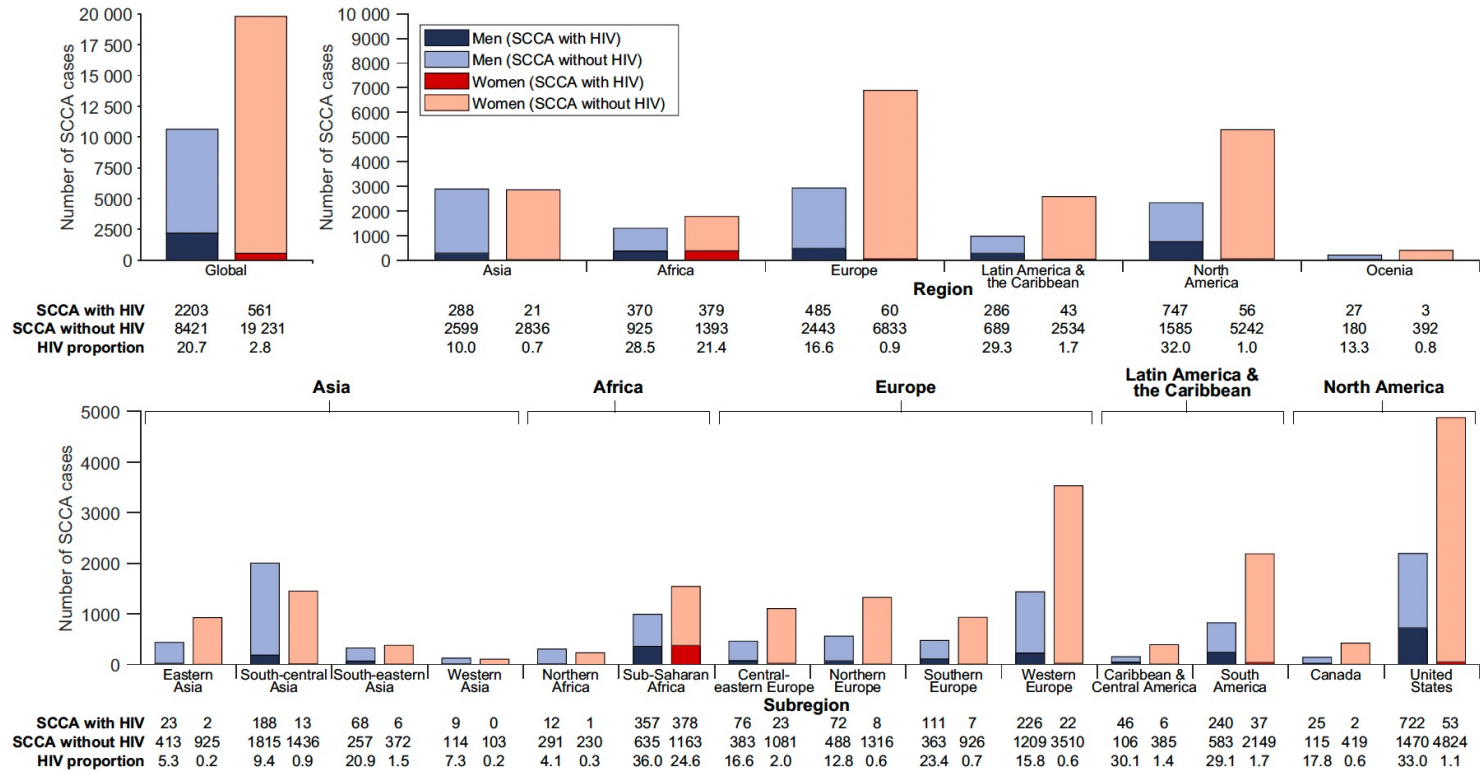
Anal cancer by age and HIV status



Footer Text

MSW with HIV	1.2%	6.5%	3.7%	1.3%
MSM with HIV	97.6%	76.1%	29.4%	7.5%
MSW without HIV	1.1%	13.1%	49.6%	67.3%
MSM without HIV	0.1%	4.2%	17.3%	23.9%

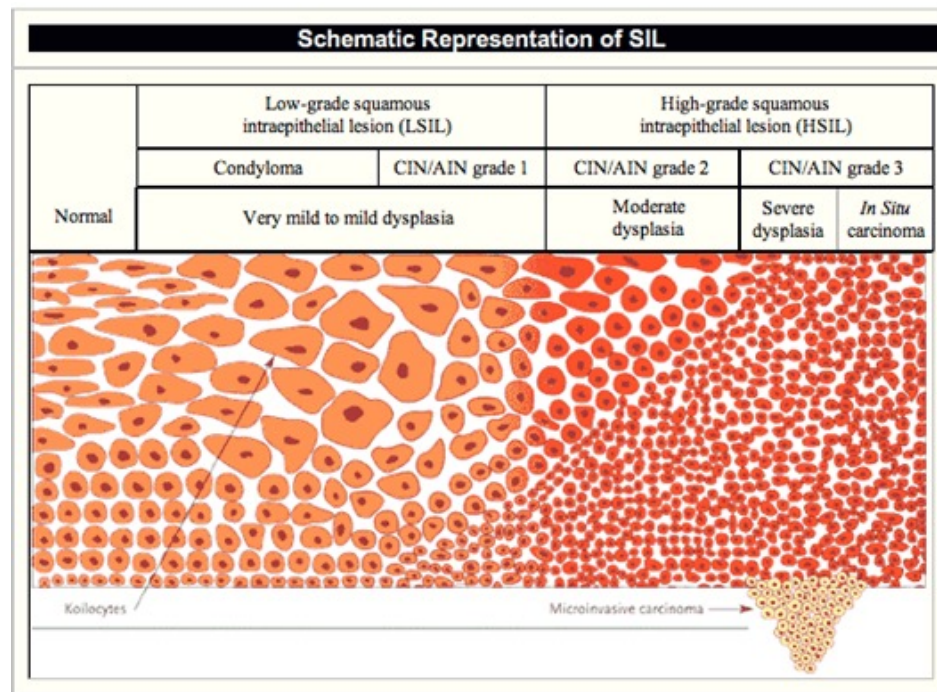
Estimated proportions of new squamous cell carcinoma of the anus in persons living with HIV in 2020



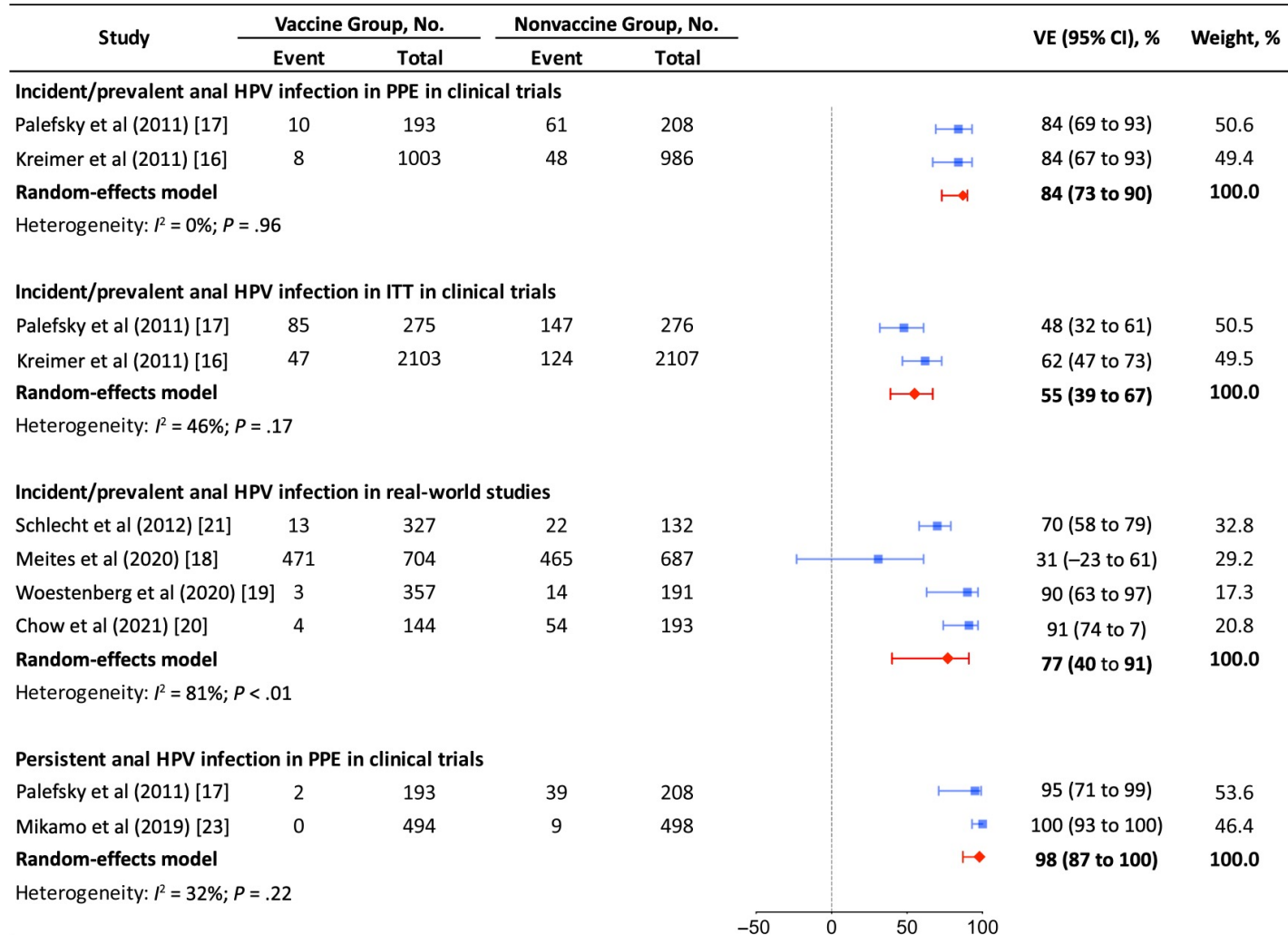
The cervical model

Cervical and anal cancer are very similar diseases
Cervical and anal cancer are caused by HPV
Cervical cancer and anal cancer are preceded by HSIL

Primary prevention of cervical HPV/HSIL/cancer works
Can primary prevention of anal HPV/HSIL/cancer work?

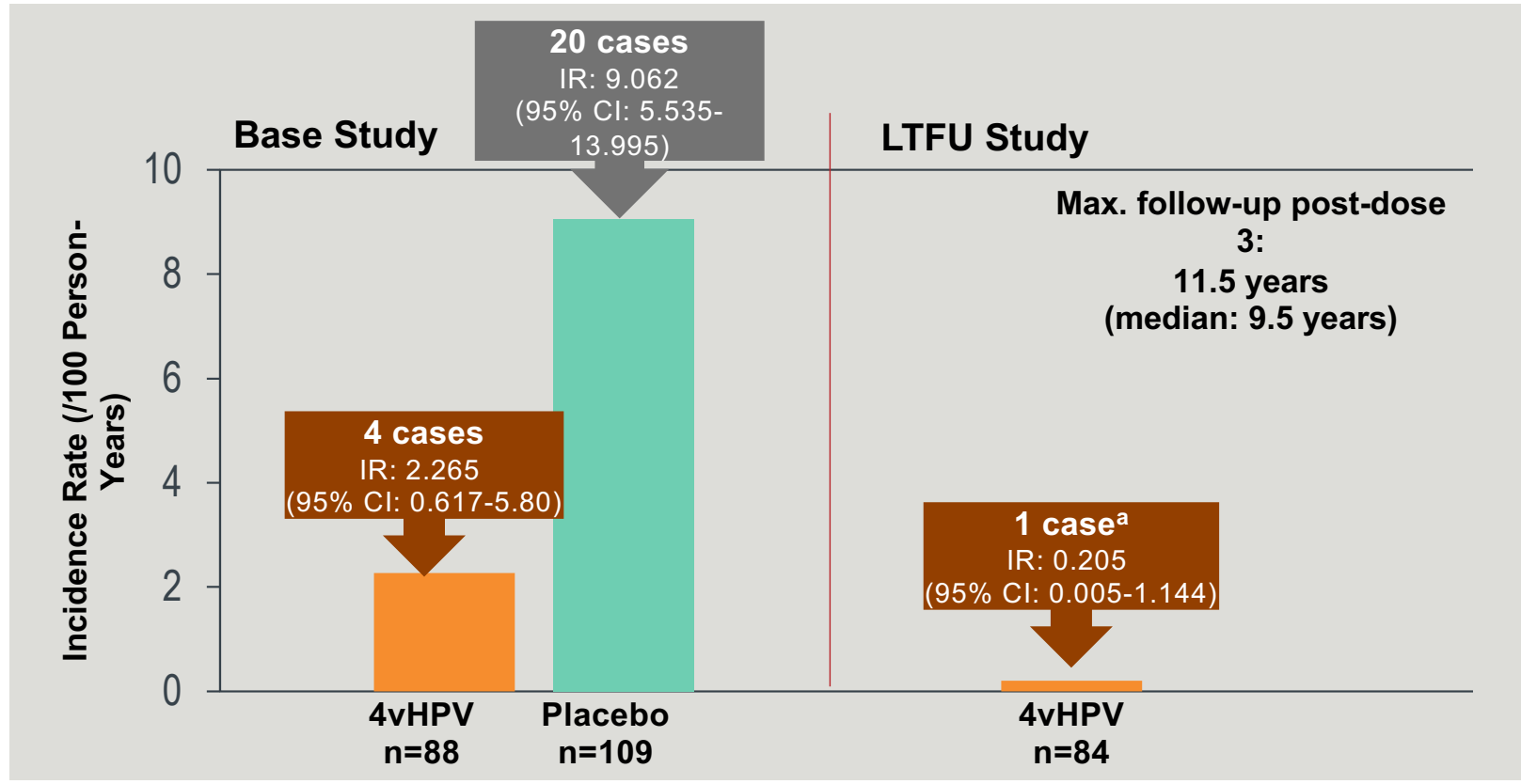


HPV vaccine to prevent anal HPV infection/disease



Foot:

Low Rates of HPV6/11/16/18-Related AIN and Anal Cancer in MSM 4vHPV Vaccine LTFU Study



Per-protocol population (LTFU participants)
^aHPV6-related AIN1 (HPV58 co-detected)

Goldstone S, et al.
Lancet Infect Dis.
2022; 22:413-425

Vaccine efficacy in MSMLWH over 26 ACTG 5298

- Study stopped for futility
- Vaccine efficacy was 22% for prevention of persistent anal infection or single detection at the final visit
- 0% for improving HSIL outcomes

Wilkin T et al Clin Infect Dis. 2018 Oct 15;67(9):1339-1346

Previous HPV exposure in young MSMLWH (16-26 years old)

HPV 6 78%

HPV 11 52%

HPV 16 47%

HPV 18 34%

34% had HSIL

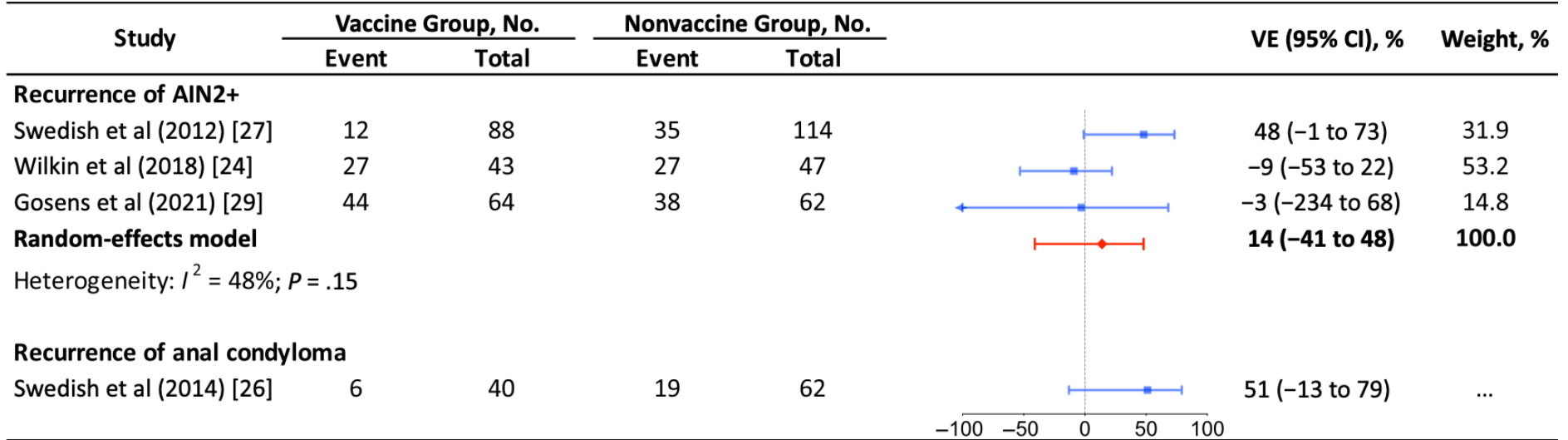
Efficacy of vaccination in AMC-072: prevention of HSIL

- 0/100 person-years in AMC-072 naïve vaccinated group
- 14.6/100 person-years in AMC-072 previously-exposed vaccinated group
- 3.1/100 person-years in Merck 020 placebo group

Palefsky JM et al. Clin Infect Dis 2021; 73: 1388–1396

Palefsky JM et al. N Engl J Med 2011;365:1576-85

HPV vaccine to prevent recurrent anal disease



Footer Text

ACIP HPV vaccine dosing recommendations

- All females and males up to 26 years of age
- 2 doses if initiating vaccination younger than 15 years
- 3 doses if 15 or older
- Target age: 9-12 years
- 27- 45 years of age on individual basis after one-on-one discussion with health care provider

ACIP recommendations for HPV vaccine in PLWH

- Same age recommendations as for HIV-negative
- Vaccine is safe
- 3 doses for all ages
- Duration of protection not known
- Definitely vaccinate up to age 26 years, ideally before onset of sexual activity
- 27-45?
- Over 45?

New dosing recommendations for the HPV vaccine

- WHO now recommends:
- A one or two-dose schedule for girls aged 9-14 years
- A one or two-dose schedule for girls and women aged 15-20 years
- Two doses with a 6-month interval for women older than 21 years

https://www.iarc.who.int/wp-content/uploads/2023/04/IARC_Evidence_Summary_Brief_4.pdf

Accessed 1/21/24

New dosing recommendations for the HPV vaccine

- British NHS recommendations:
- people under 25 usually only need 1 dose
- people aged 25 to 45 usually need 2 doses (given between 6 months and 2 years apart)
- people with a weakened immune system (including HIV!) need 3 doses (ideally given within a 12-month period)

<https://www.nhs.uk/conditions/vaccinations/hpv-human-papillomavirus-vaccine/>

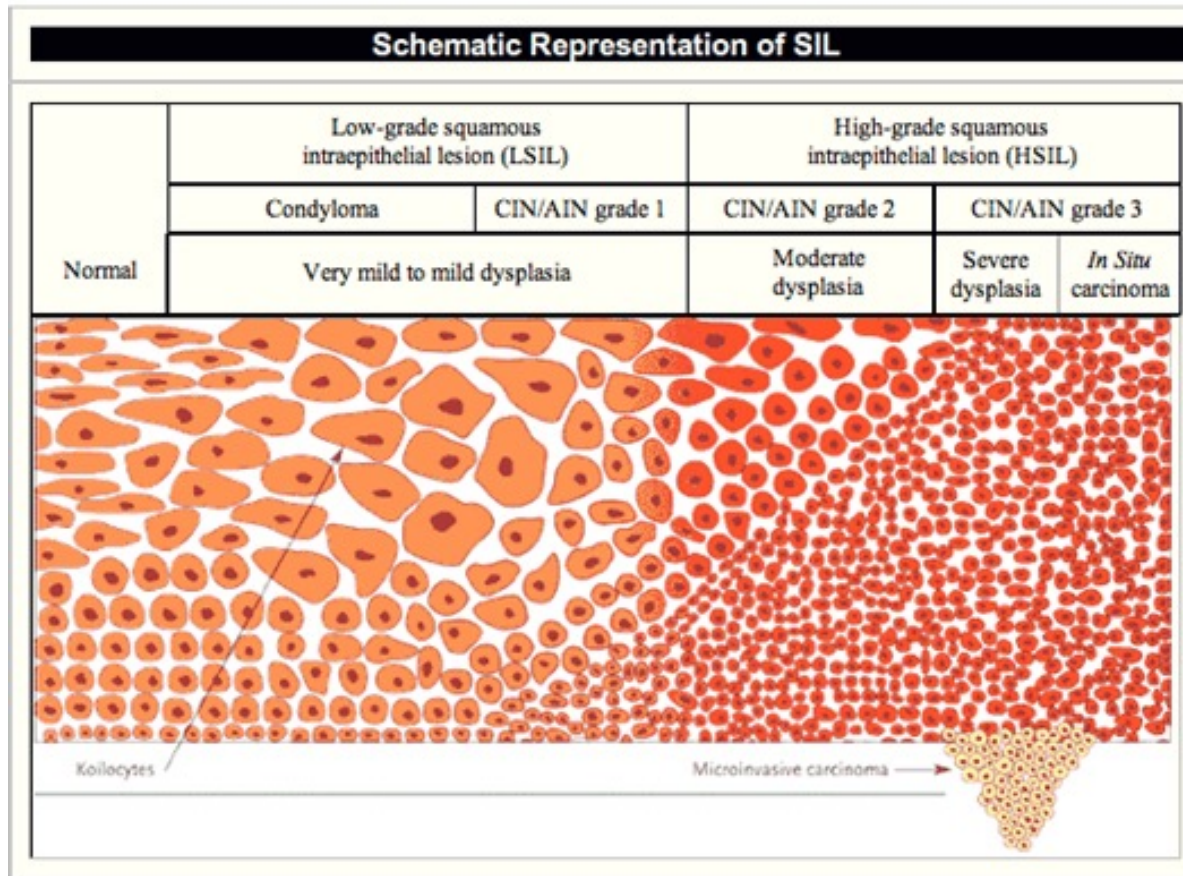
Accessed 1/21/24

Summary

- Highly effective vaccine
- Safe in both PLWH and HIV- men and women
- Long-term efficacy is established for at least 10 years
- One dose HIV-negative
- Three doses for PLWH
- No evidence in meta-analysis for prevention of recurrence of anal HSIL
- The vaccine DOES prevent cancer!!

The cervical model

Secondary prevention of cervical cancer works
Can secondary prevention of anal cancer work?





the
ANCHOR
study

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

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*

Anal HSIL and cancer at screening

10,723 PLWH underwent screening

53.3% of men

47.2% of women

67.1% of transgender individuals

17 individuals (0.16%, 160/100,000) were diagnosed with anal cancer

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

Treatments used in the ANCHOR Study

Over the course of the study: most participants had only one treatment modality (86%)= electrocautery (office-based hyfrecation)

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

Take home points from the ANCHOR Study

Treating anal HSIL can prevent invasive anal cancer

IANS guidelines are now out for screening for anal HSIL as standard of care in PLWH and other high risk groups

What does screening look like for PLWH?

- Digital anorectal exam and screening for MSMLWH and transgender PLWH over 35 years and all other PLWH over 45 years
- Combination of anal cytology and HPV co-testing

Anal cancer screening in PLWH

Table 3. Five- and 10-Year Cumulative Incidence of Anal Cancer Among People With an AIDS Diagnosis or HIV Only

Sex/Risk Group Stratified by Age*	Cumulative Incidence, % (95% CI)			
	AIDS, 5 Years	AIDS, 10 Years	HIV Only, 5 Years	HIV Only, 10 Years
MSM				
< 30	0.12 (0.05 to 0.19)	0.67 (0.51 to 0.83)	0.02 (0.00 to 0.05)	0.24 (0.12 to 0.35)
30-44 ←	0.29 (0.23 to 0.36)	0.82 (0.72 to 0.91)	0.12 (0.08 to 0.16)	0.34 (0.26 to 0.42)
45-59	0.65 (0.49 to 0.81)	1.14 (0.94 to 1.35)	0.33 (0.22 to 0.44)	0.71 (0.50 to 0.91)
≥ 60	0.52 (0.01 to 1.02)	1.08 (0.42 to 1.73)	0.32 (0.00 to 0.64)	0.95 (0.25 to 1.65)
Other males				
< 30	0.06 (0.00 to 0.12)	0.21 (0.10 to 0.33)	0.01 (0.00 to 0.03)	0.05 (0.00 to 0.11)
30-44	0.16 (0.10 to 0.21)	0.35 (0.28 to 0.42)	0.07 (0.04 to 0.11)	0.16 (0.10 to 0.22)
45-59 ←	0.10 (0.05 to 0.14)	0.21 (0.15 to 0.28)	0.04 (0.01 to 0.07)	0.15 (0.08 to 0.23)
≥ 60	0.09 (0.00 to 0.19)	0.20 (0.04 to 0.37)	0.06 (0.00 to 0.17)	0.15 (0.00 to 0.36)
Females				
< 30	0.12 (0.02 to 0.22)	0.20 (0.08 to 0.31)	0.02 (0.00 to 0.05)	0.09 (0.03 to 0.15)
30-44	0.06 (0.03 to 0.09)	0.21 (0.15 to 0.26)	0.04 (0.02 to 0.06)	0.13 (0.08 to 0.19)
45-59 ←	0.20 (0.11 to 0.29)	0.32 (0.20 to 0.43)	0.08 (0.03 to 0.13)	0.13 (0.05 to 0.21)
≥ 60	0.11 (0.00 to 0.26)	0.18 (0.00 to 0.39)	0.08 (0.00 to 0.23)	0.08 (0.00 to 0.23)

International Anal Neoplasia Society screening guidelines

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

International Anal Neoplasia Society screening guidelines

Primary screening test	Triage test	Test results	Management	Modification for low HRA capacity ^a
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

International Anal Neoplasia Society screening guidelines

Primary screening test	Triage test	Test results	Management	Modification for low HRA capacity ^a
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

CDC guidelines

- Coming soon!
- Screening PLWH= AII
- Treatment of anal HSIL in PLWH= AI
- First-line therapy is targeted ablation (hyfrecation)
- Specific screening approaches= BIII

PENDING CDC:
ANAL CANCER SCREENING & FOLLOW-UP GUIDELINES

SLIDE EMBARGOED

Guidelines for high-risk groups other than PLWH

Unlikely to replicate ANCHOR


Treatment results likely to be even better than ANCHOR

Summary

- HPV vaccination will help in the intermediate future
- ANCHOR tells us that we can reduce the risk of anal cancer now among those with HSIL
- Guidelines are now out (IANS) or coming soon (CDC) making screening for and treating anal HSIL standard of care for PLWH
- Need to determine how to extend guidelines to HIV-negative groups at high risk of anal cancer

Gaps in knowledge

- Optimal screening algorithms for different demographics
- Markers of prevalent anal cancer during screening
- Optimal follow-after treatment
- Biomarkers of risk of HSIL progression or regression
 - Methylation/gene expression
- How to train more people in HRA more quickly
- Better treatment methods
 - HPV-targeted therapies
 - Systemic therapies

A vibrant, colorful illustration of a microscopic world. The scene is filled with various biological structures, including large yellow and blue spheres, smaller green and brown particles, and intricate cellular components. The background is a mix of red, purple, and blue, creating a rich, textured environment. The overall style is highly detailed and artistic, resembling a biological or medical illustration.

Thank You for Your Attendance!

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