Bridging the Gap: Comprehensive Approaches to HIV and HPV in Women's Health Care

Barcelona, 5 de junio de 2025

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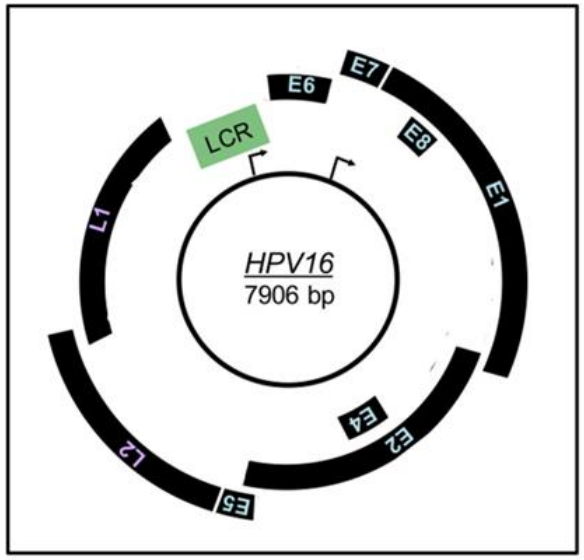
AGENDA

- ❑ Reminder of basic HPV virology.
- ❑ HPV infection and impact on a woman's sexuality after diagnosis.
- ❑ HPV infection and cancer genesis.
- ❑ Other cancers related to HPV infection beyond cervical cancer.
- ❑ Tools to prevent anal cancer beyond HPV vaccination.
- ❑ Prioritize risk groups for anal cancer screening.
- ❑ Take-home messages

HPV genotypes, tropism and associated diseases



EARLY REGION: proteins necessary for viral replication

LATE REGION: viral capsid proteins

LONG CONTROL REGION: sequences controlling viral replication & transcription

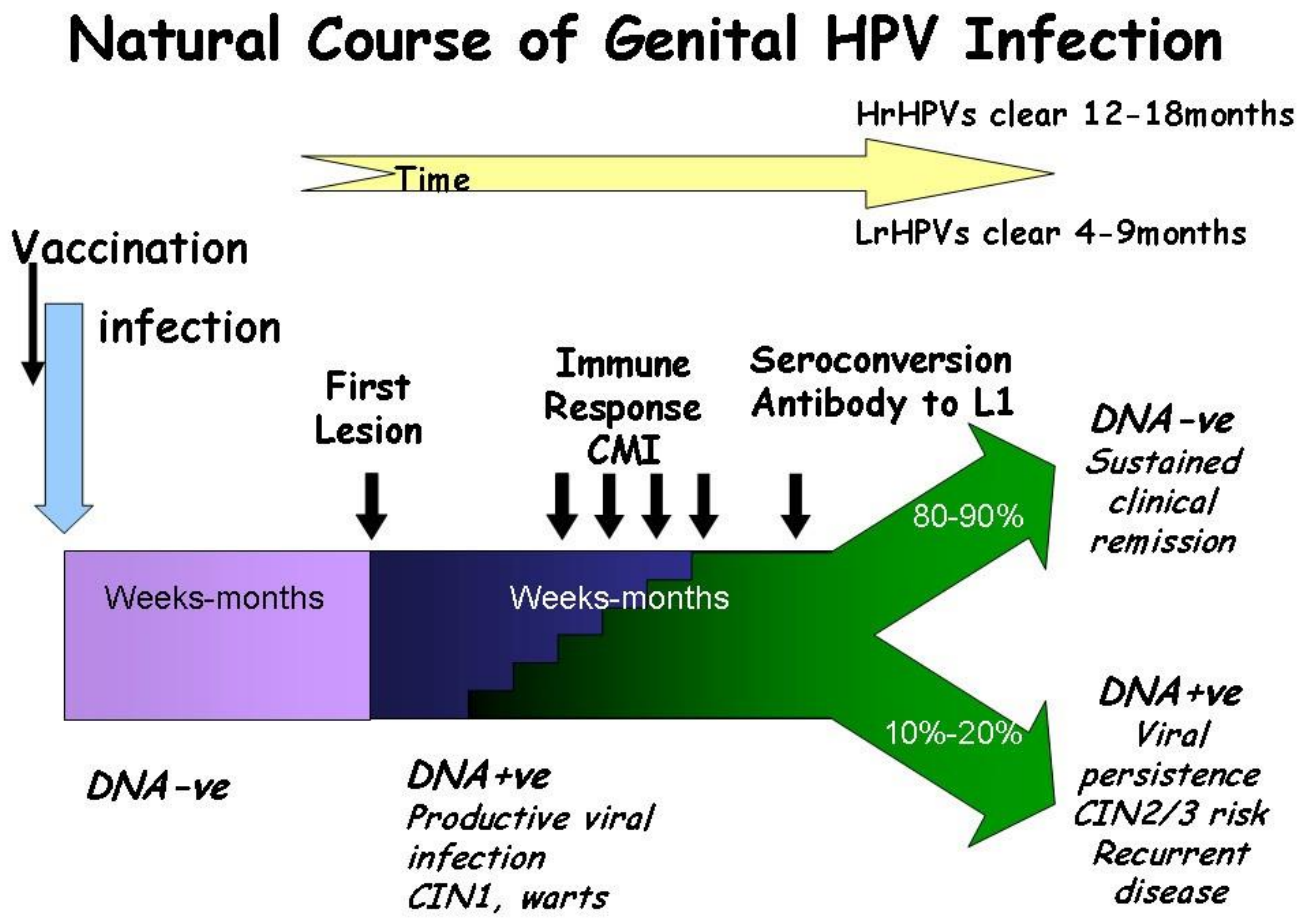
ORF	HPV16 PROTEIN FUNCTION
E1	origin binding protein, ATPase-dependent helicase involved in genome replication
E2	regulator of viral gene transcription, association with E1 (origin binding), viral genome partitioning
E4	expressed abundantly as E1^E4 fusion protein, cytokeratin network destabilization, virus release and transmission
E5	small transmembrane protein, interacts with EGF receptor activating mitogenic pathways
E6	drives cell cycle allowing genome amplification in upper epithelial layers, association with E6AP and degradation of p53, PDZ-protein binding, hTert activation
E7	drives cell cycle allowing genome amplification in upper epithelial layers, association with and degradation of pRB, mitotic mutator
E8	expressed as E8^E2 fusion protein, acts as a repressor of transcription and replication during the viral life cycle
L1	major capsid protein, assembles into pentameric capsids forming the icosahedral virion (prophylactic vaccines)
L2	minor capsid protein, involved in viral DNA encapsidation, facilitates viral entry and trafficking

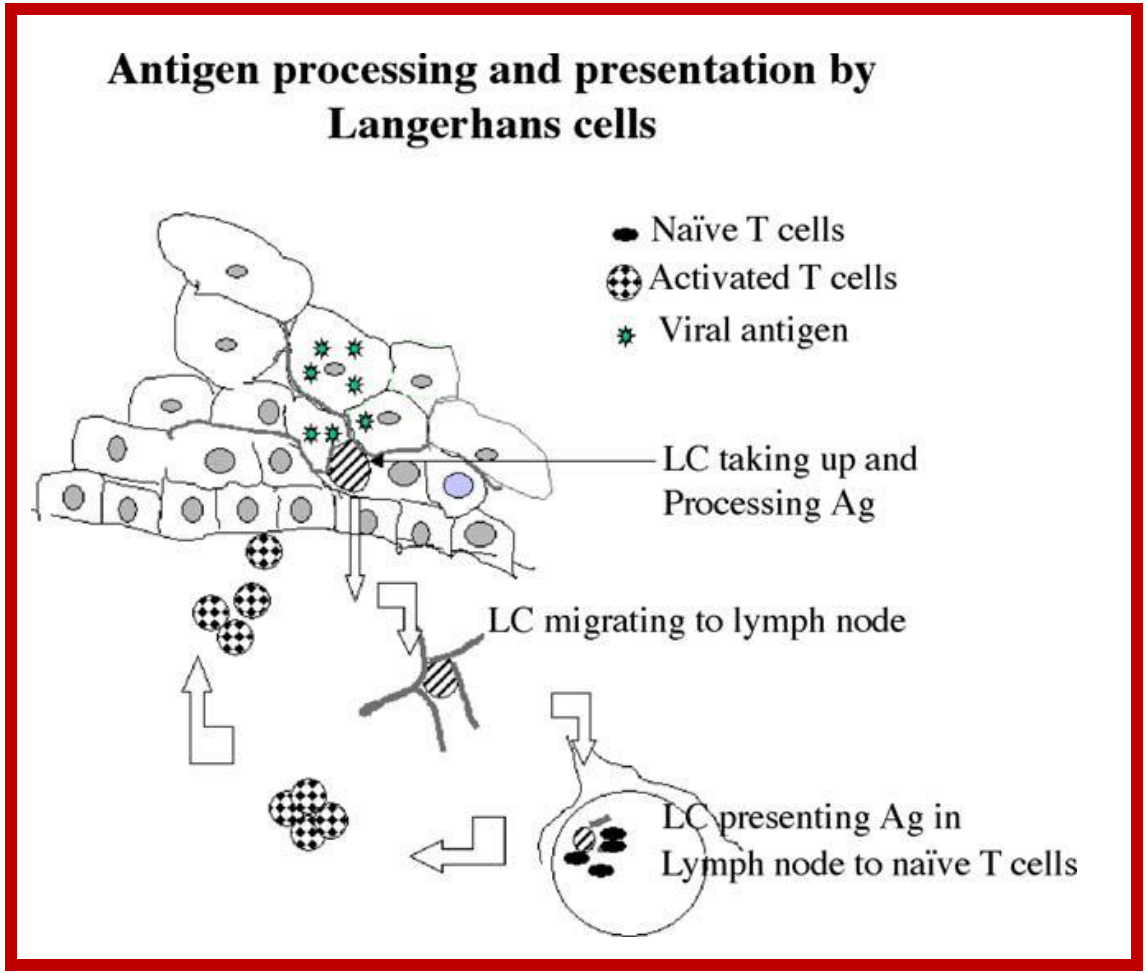
Genus	Species	Representative HPV types	Tropism	Associated Diseases
Alpha-PV	α1	32	mucosal	Heck's disease
	α2	3, 10, 28	cutaneous	flat warts
	α4	2, 27, 57	cutaneous	common warts
	α7	18, 39, 45, 59, 68	mucosal	intraepithelial neoplasia, invasive carcinoma
	α9	16, 31, 33, 35, 52, 58	mucosal	intraepithelial neoplasia, invasive carcinoma
	α10	6, 11	mucosal	condylomata acuminate
		13		Heck's disease
Beta-PV	β1c	5, 8, 12, 14, 19, 20, 21, 24, 25, 36, 47	cutaneous	Epidermodysplasia verruciformis
	β2	9, 15, 17, 22, 23, 37, 38	cutaneous	Epidermodysplasia verruciformis
	β3	49	cutaneous	Epidermodysplasia verruciformis
Gamma-PV	γ1	4, 65	cutaneous	Warts
	γ4	60	cutaneous	Warts
Mu-PV	μ1	1	cutaneous	plantar warts
	μ2	63	cutaneous	Warts
Nu-PV	ν	41	cutaneous	Warts

Harden M. E et al. Mutat. Res 2017

HPV Infection

*HPVs infections are very common and it is estimated that 50-80% of sexually active men and women will acquire a genital HPV (both high and low risk) in their lives





80 - 90% of infections will clear up after 6 months to 2 years
10 - 20% persistent infections

Peto J et al, Br J Cancer. 2004, 91: 942-953
M. Stanley / Vaccine 24S1 (2006) S1/16–S1/22

The Information Management Processes of Women Living With HPV

Immediate Emotional and Cognitive Responses

"I thought something funny was going on … So, I went to the doctor. When she came back with the test results and gave them to me, I just started crying hysterically. She said that she would leave the room and give me 5–10 minutes to calm down and then she would come back and discuss every thing with me. So, in that 5–10 minutes I did NOT calm down, and I just kept crying and crying … I was so shocked"

Immediate Behavioral Responses

"The first time I didn't ask that much about it because I didn't really understand what it was. I was just in shock. But, after the emotional parts subsided a bit, I did."

Secondary Behavioral Responses

"I was just really angry because I didn't know who gave it to me. When I confronted my last partner, he was not really receptive, and he did not want to acknowledge that he had it. Yeah, that made me even more angry."

Kosneko et al, Journal of Health Communication, 19:813–824, 2014

J Sex Marital Ther. 2022;48(7):748-755. doi: 10.1080/0092623X.2022.2079575.
Epub 2022 May 30.

Effects of HPV Positivity in Women on Couples Sexual Behavior

Murat Ekmez [1], Fırat Ekmez [2]

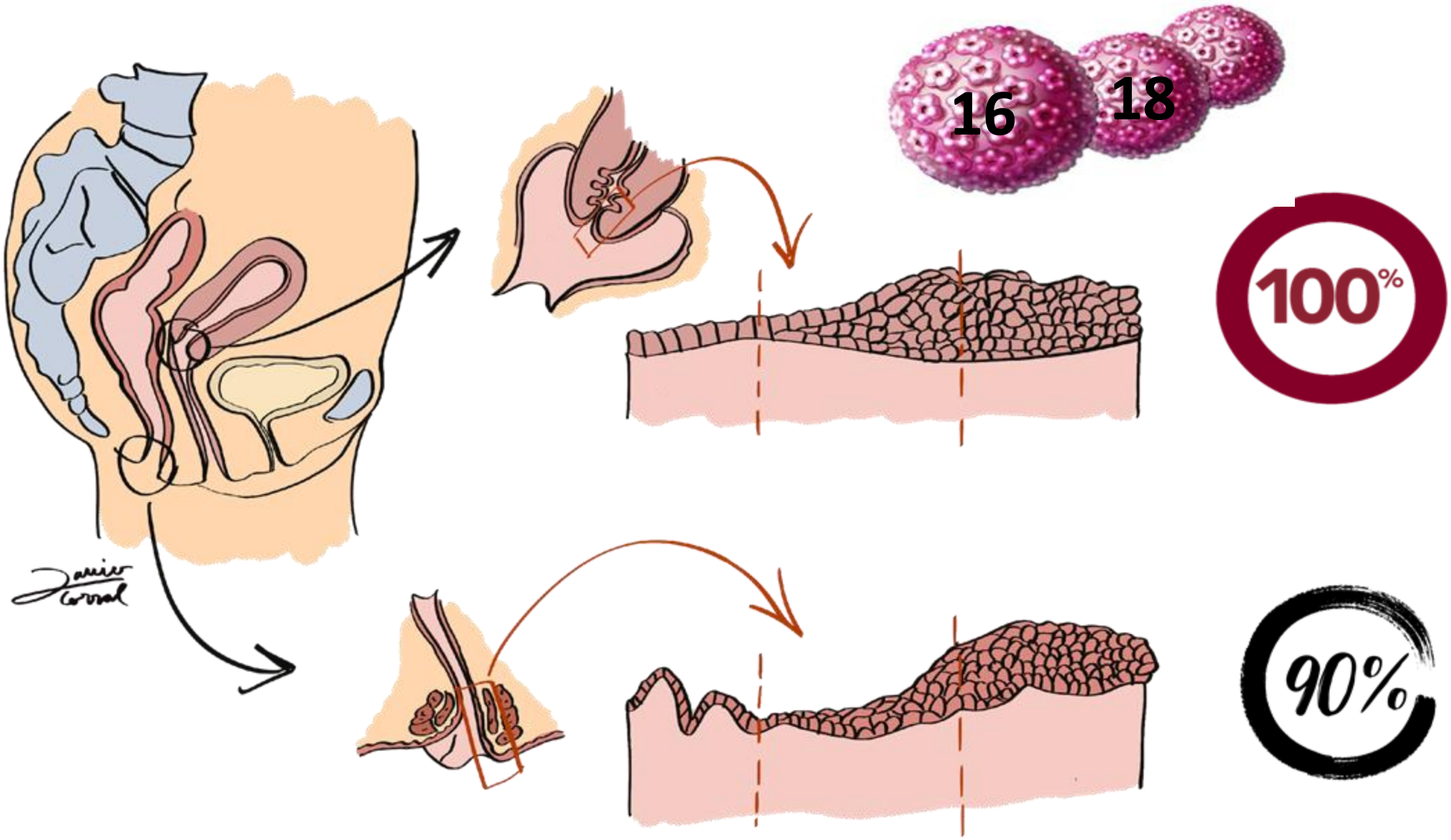
Affiliations + expand

Femenine index sexual function (FSFI)
The International Index of Erectile Function (IIEF) Score.
The Beck anxiety inventory (BAI)
The premature ejaculation diagnosis tool (PEDT) form

Significant deterioration in women's psychological and sexual health caused by HPV positivity.

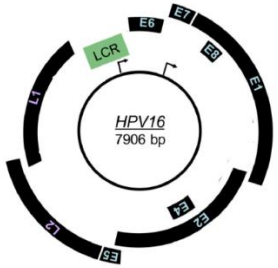
Men were significantly more likely to suffer from erectile dysfunction and premature ejaculation.

HPV genotypes, tropism and associated diseases



Harden M. E et al. Mutat. Res 2017

From anal dysplasia to cancer.



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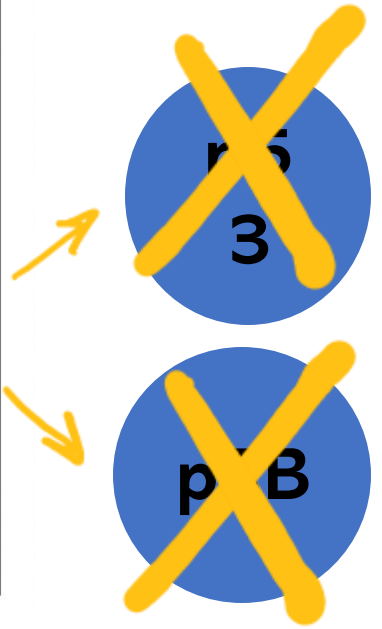
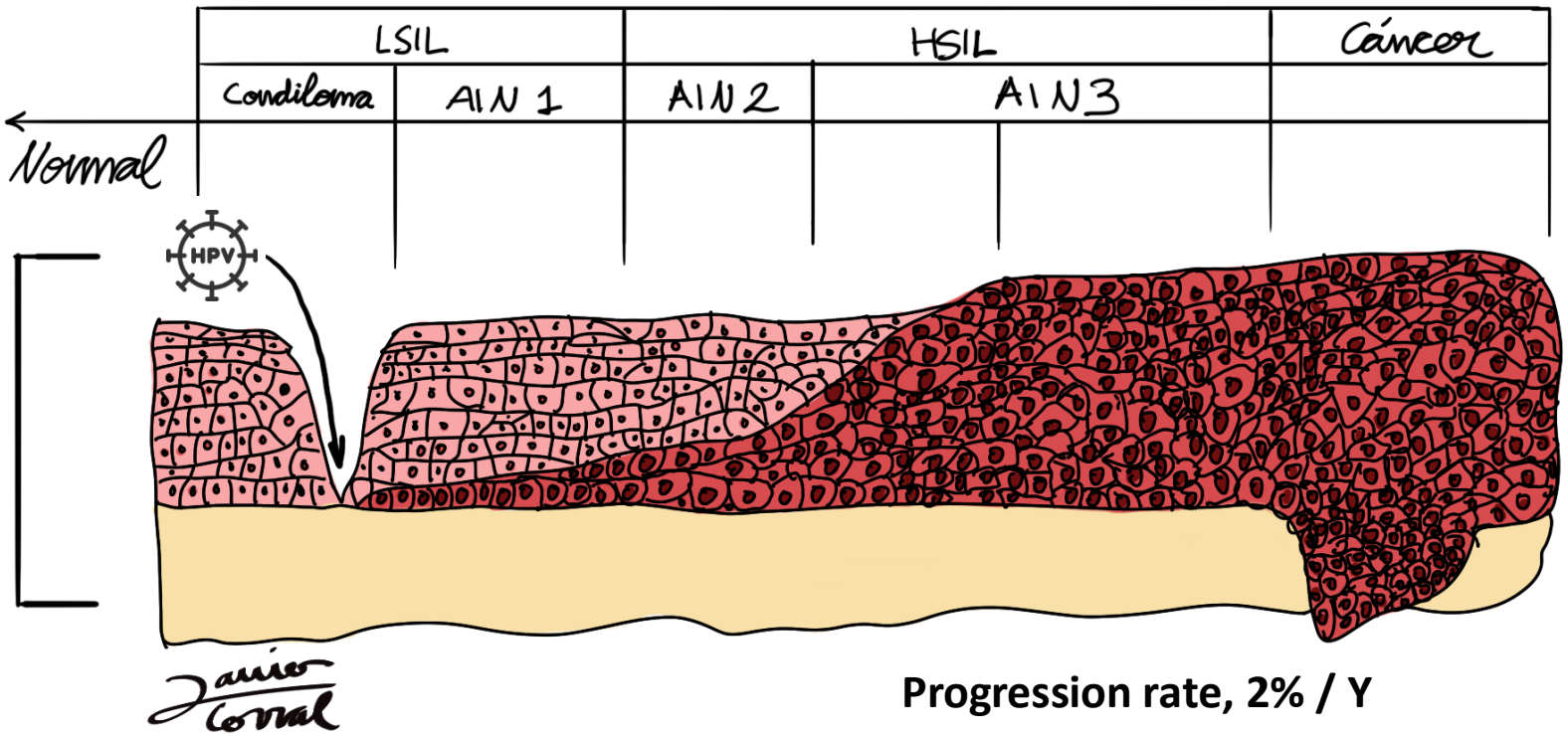
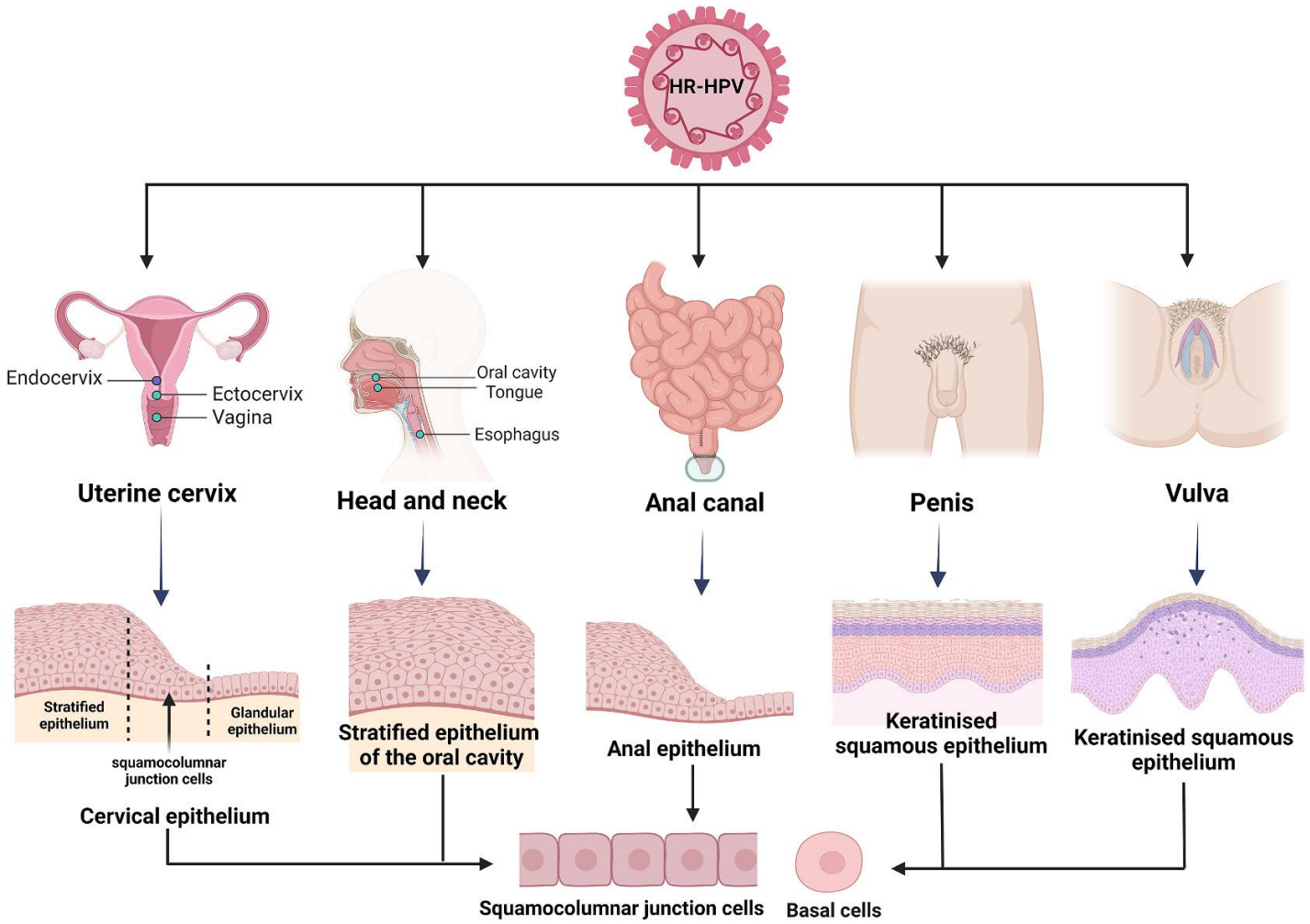




Progression rate, 2% / Y

*lee et al. 2018. DCR

HR-HPV genotypes and cancer

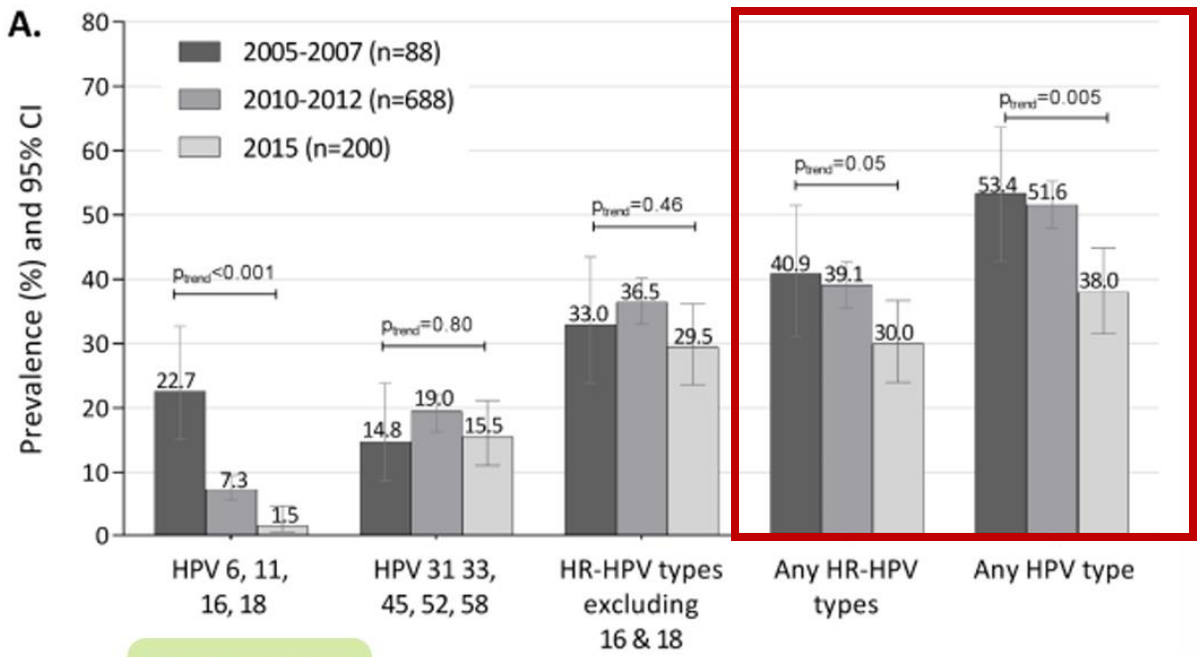


HPV is responsible for approximately 4.8% of all cancers worldwide

Catalán-Castorena O et al, Heliyon, july 2024
Loopik, D.L et al, Int. J. Cancer 2020, 147, 897–900

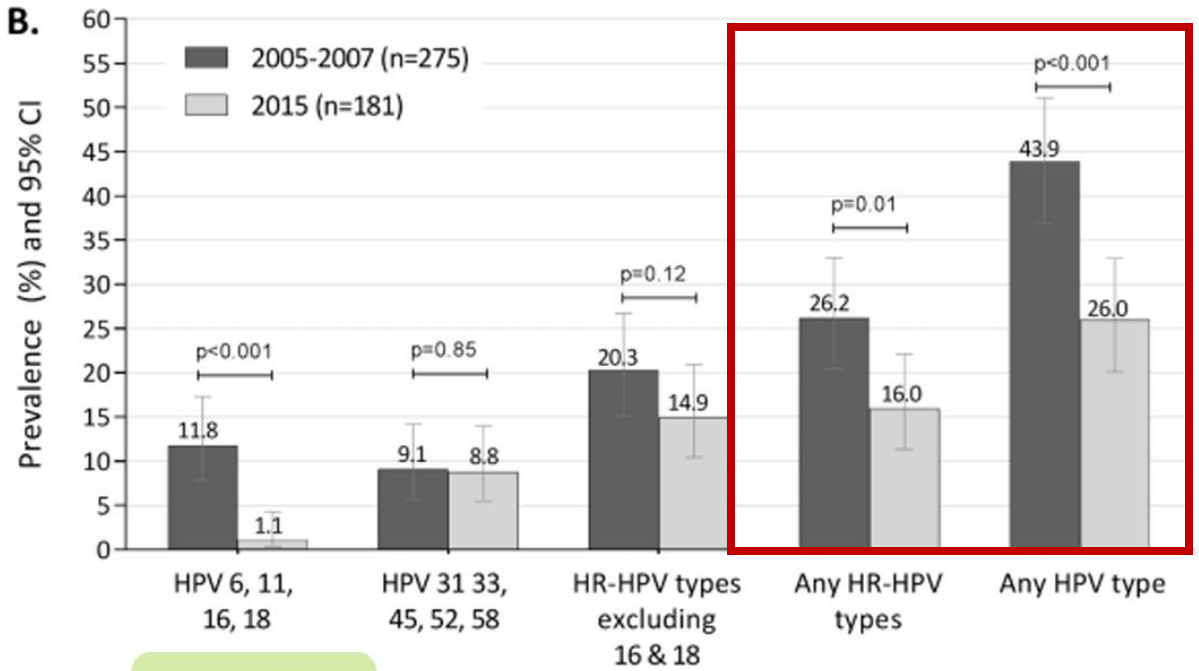
Cervical HPV infection prevalence, 9 years following implementation of vaccination

18-24 anys



93% decrease
P_{trend} <0.001

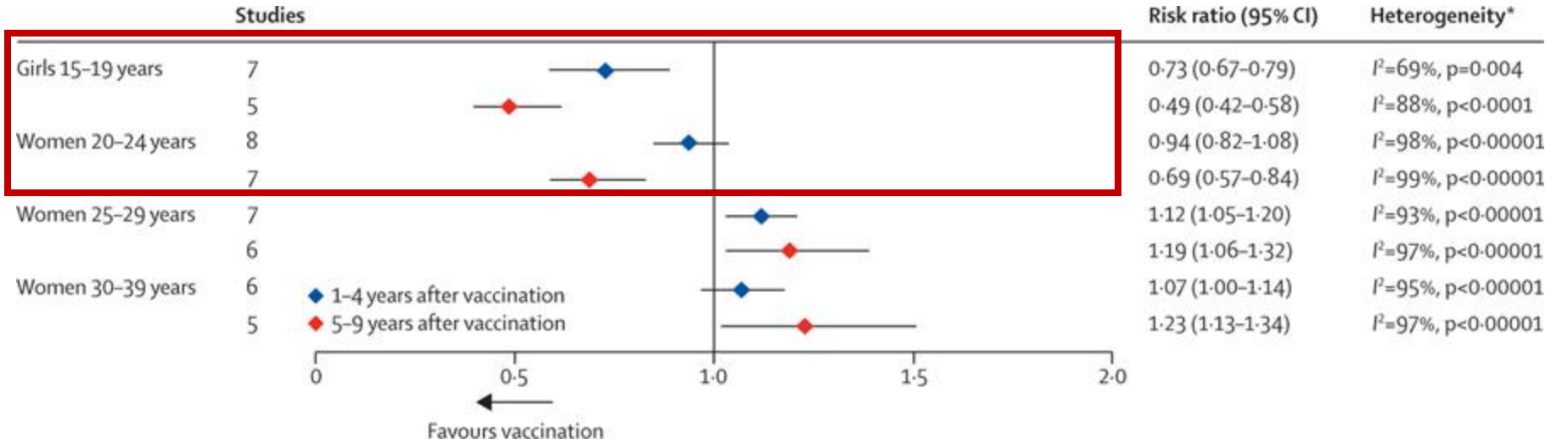
25-35 anys

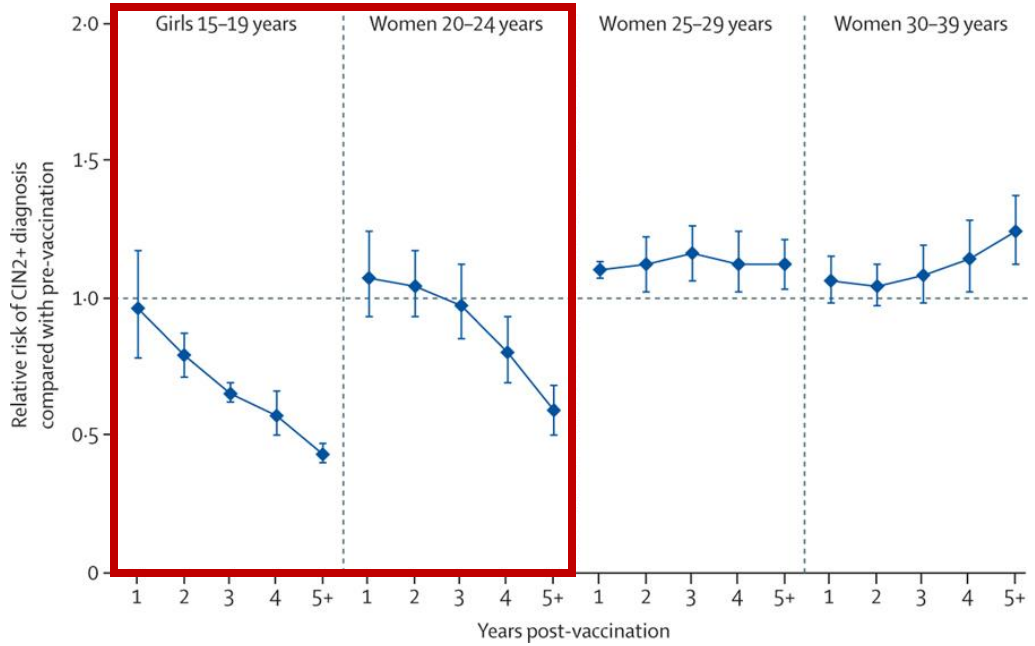


91% decrease
P_{trend} <0.001

Machalek D et al, J Infect Dis 2018

Changes in CIN2+ among screened girls and women between the pre-vaccination and post-vaccination periods.

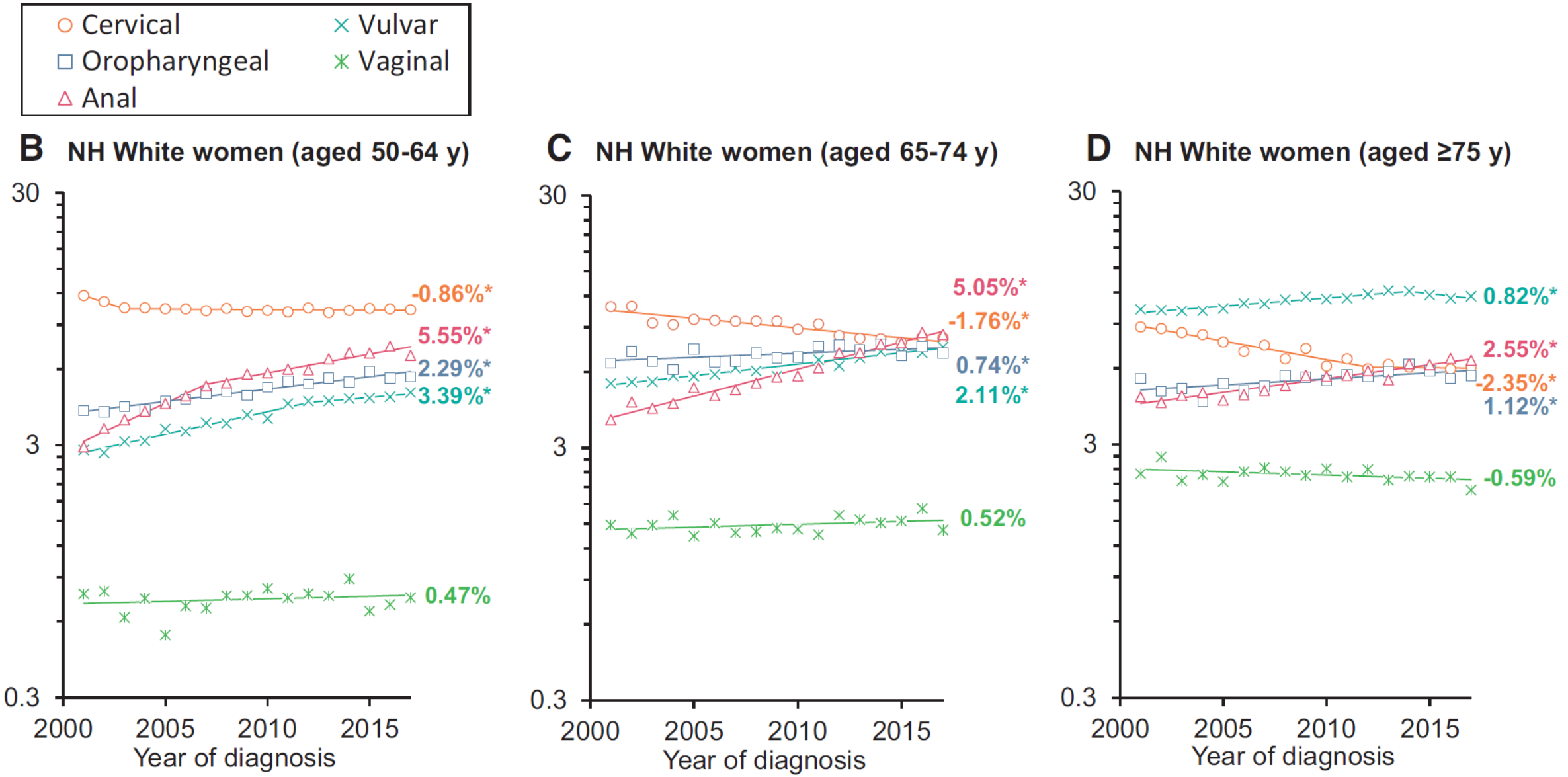




Changes in CIN2+ among screened girls and women during the first 7 years after the introduction of girls-only human papillomavirus vaccination, in countries with multi-cohort vaccination and high vaccination coverage.

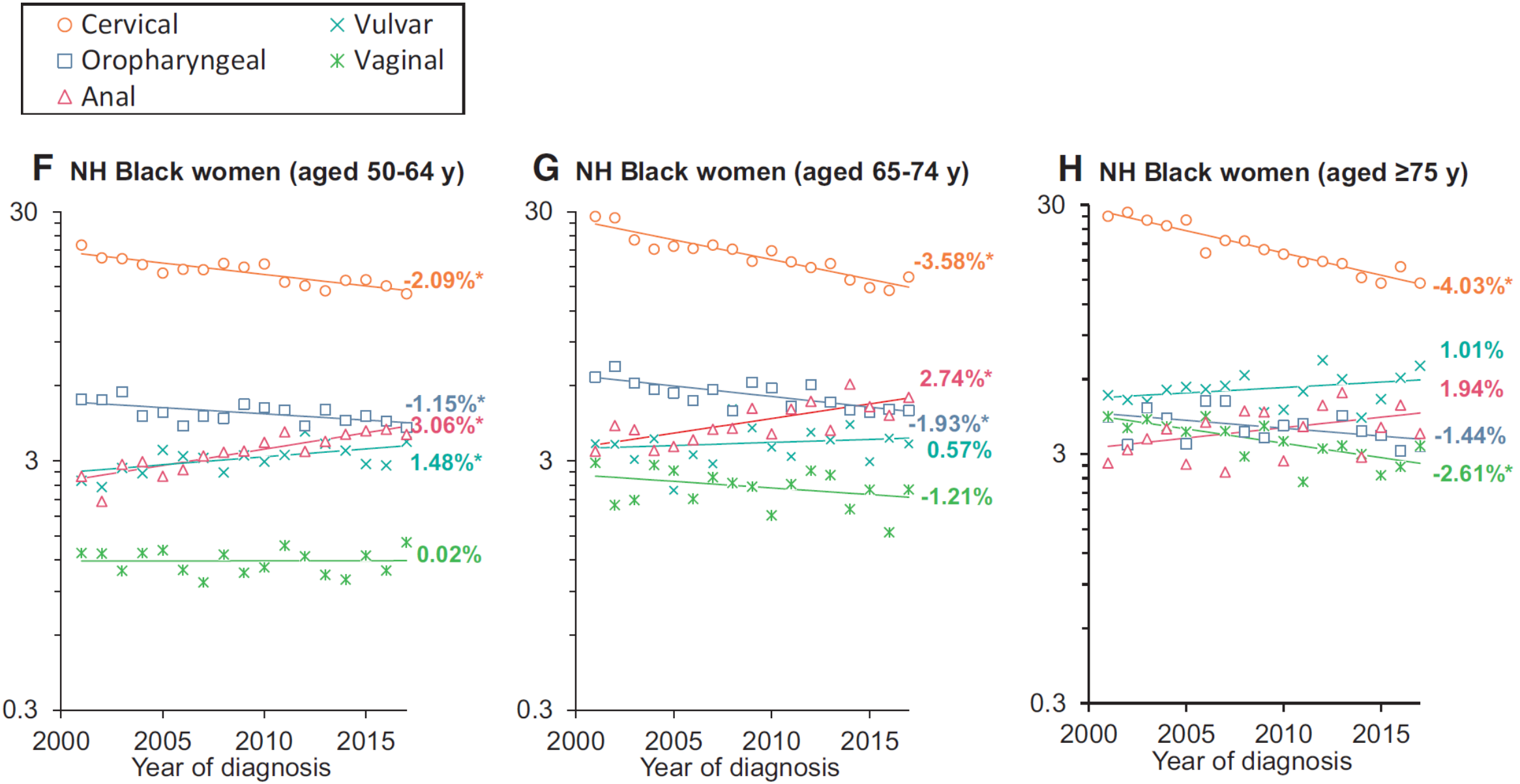
Drolet M et al, Lancet 2019.

HPV- Associated Cancers Among Women in the United States, 2001-2017



JDeshmukh et al, J Natl Cancer Inst 2021

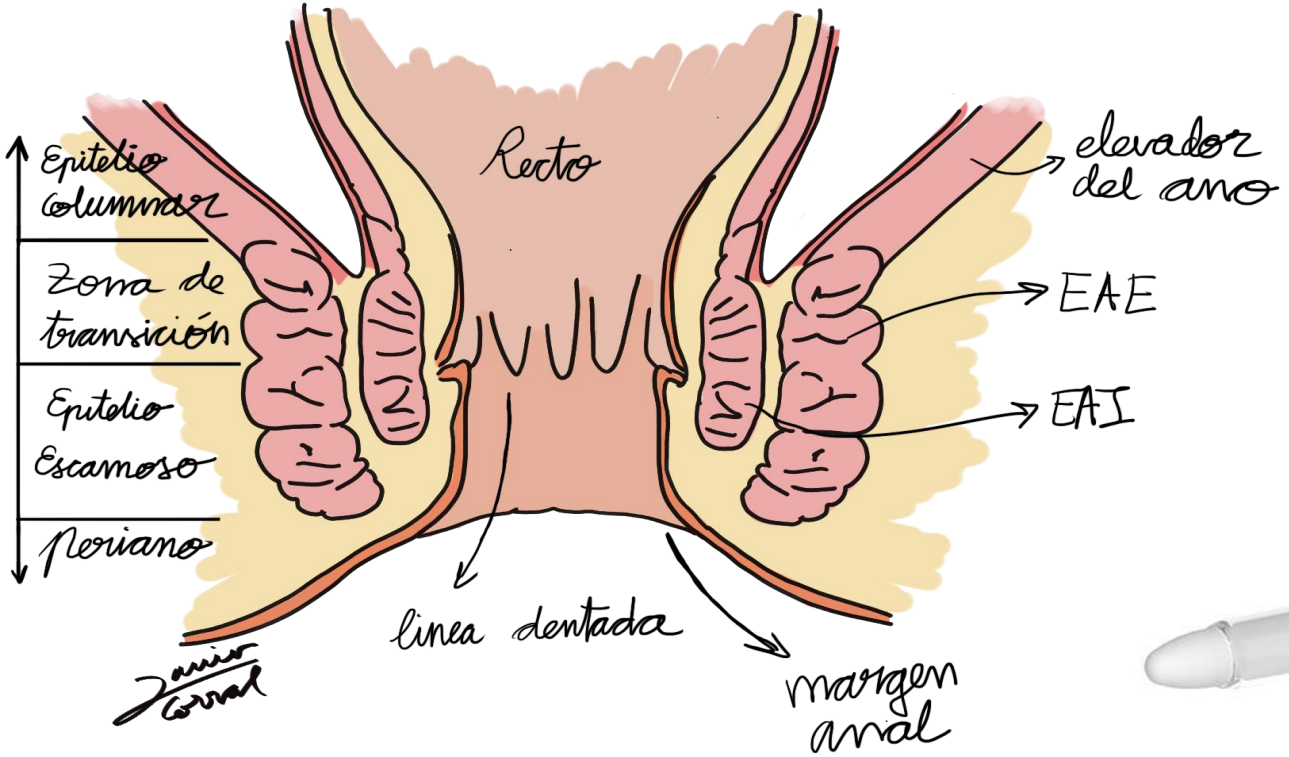
HPV- Associated Cancers Among Women in the United States, 2001-2017



JDeshmukh et al, J Natl Cancer Inst 2021

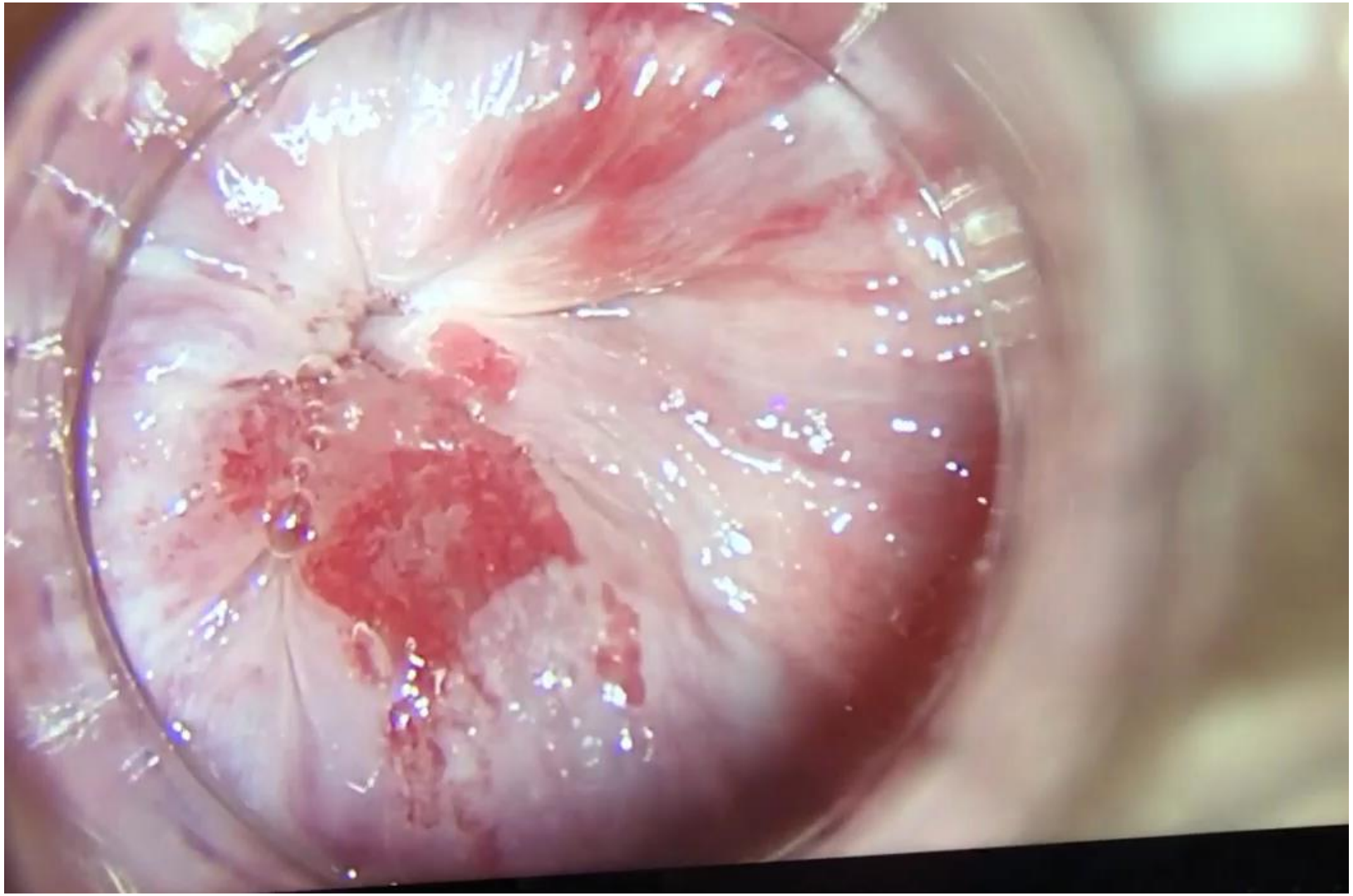
High-resolution anoscopy (HRA)

Examination of the anus, anal canal and perianus using a colposcope with 5 or 3% acetic acid and Lugol's solution

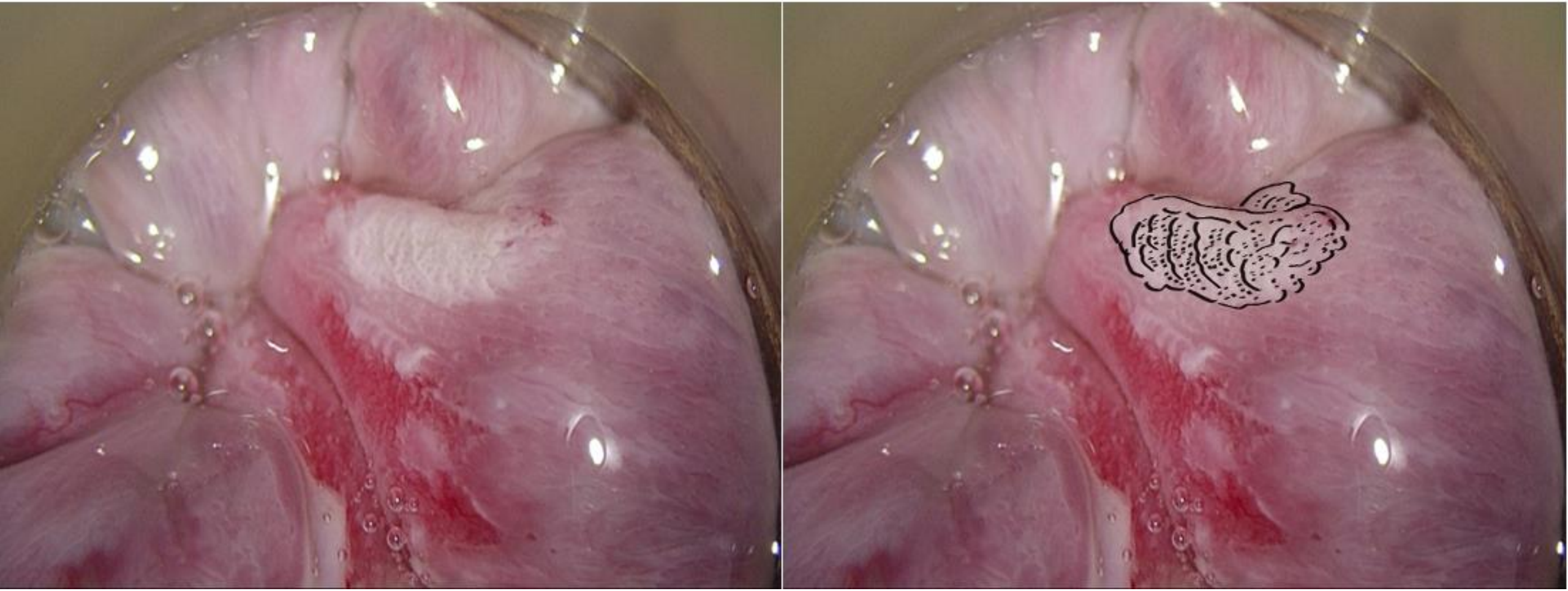


HRA

- ❑ Operate a colposcope.
- ❑ Repeatedly apply 5 or 3% acetic acid and Lugol iodine.
- ❑ Examine the SCJ at the border of the distal rectum, the anal transformation zone, the distal canal, through to the anal verge and perianus.
- ❑ Identify, anatomically locate, and describe any abnormalities.
- ❑ Perform adequate anal canal and perianal biopsies.
- ❑ Achieve hemostasis

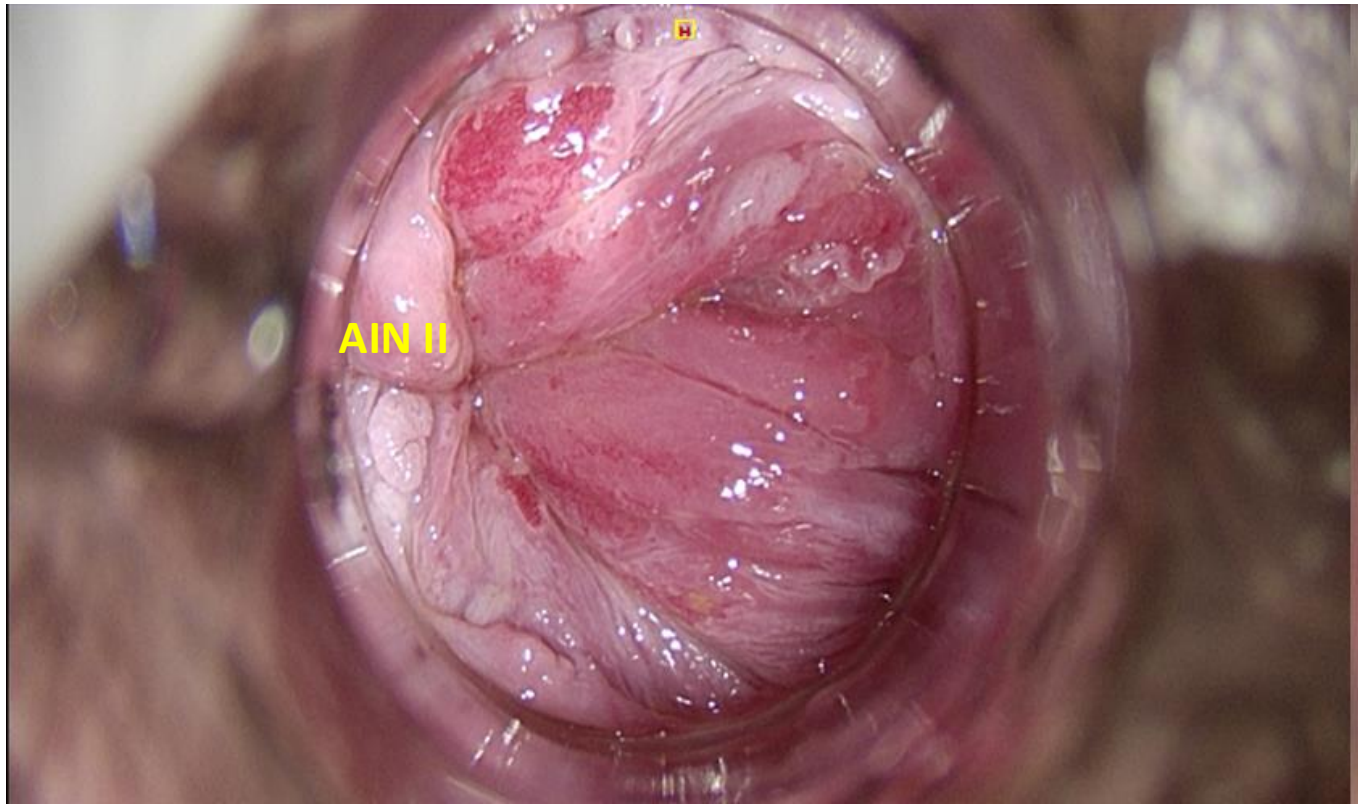


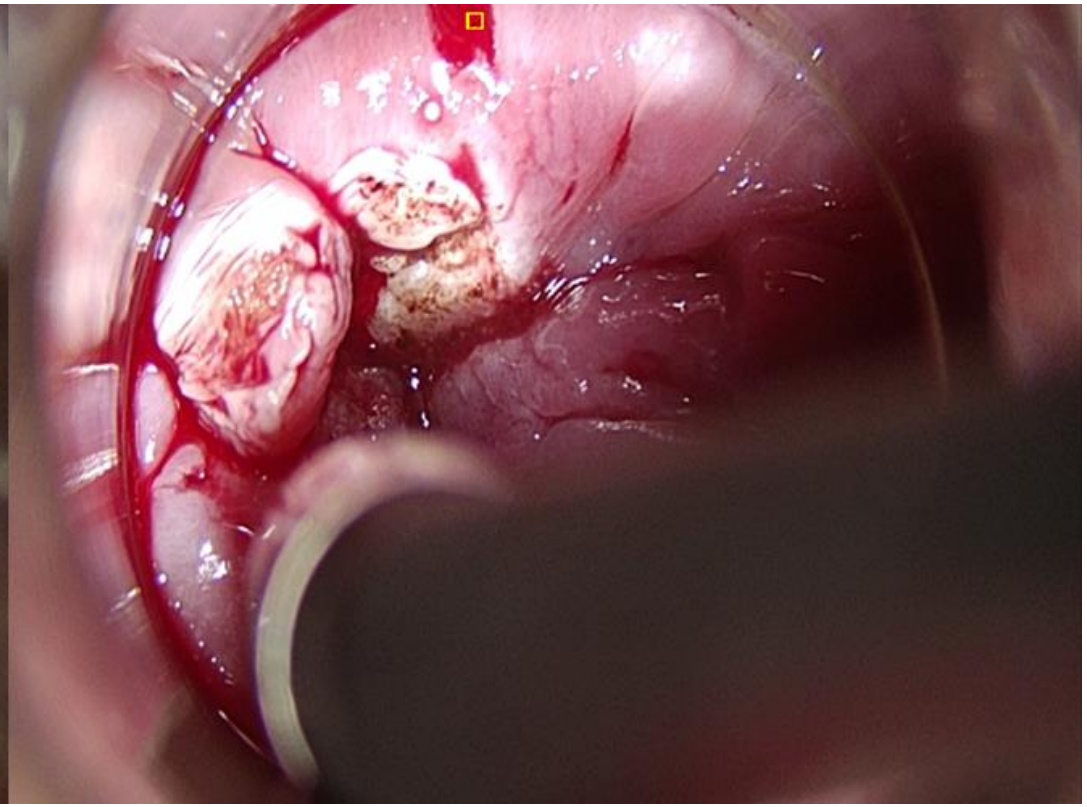
- Hillman R et al. Journal of Lower Genital Tract Disease20(4):283-291, October 2016
- Imagen Dr.Boris Revollo

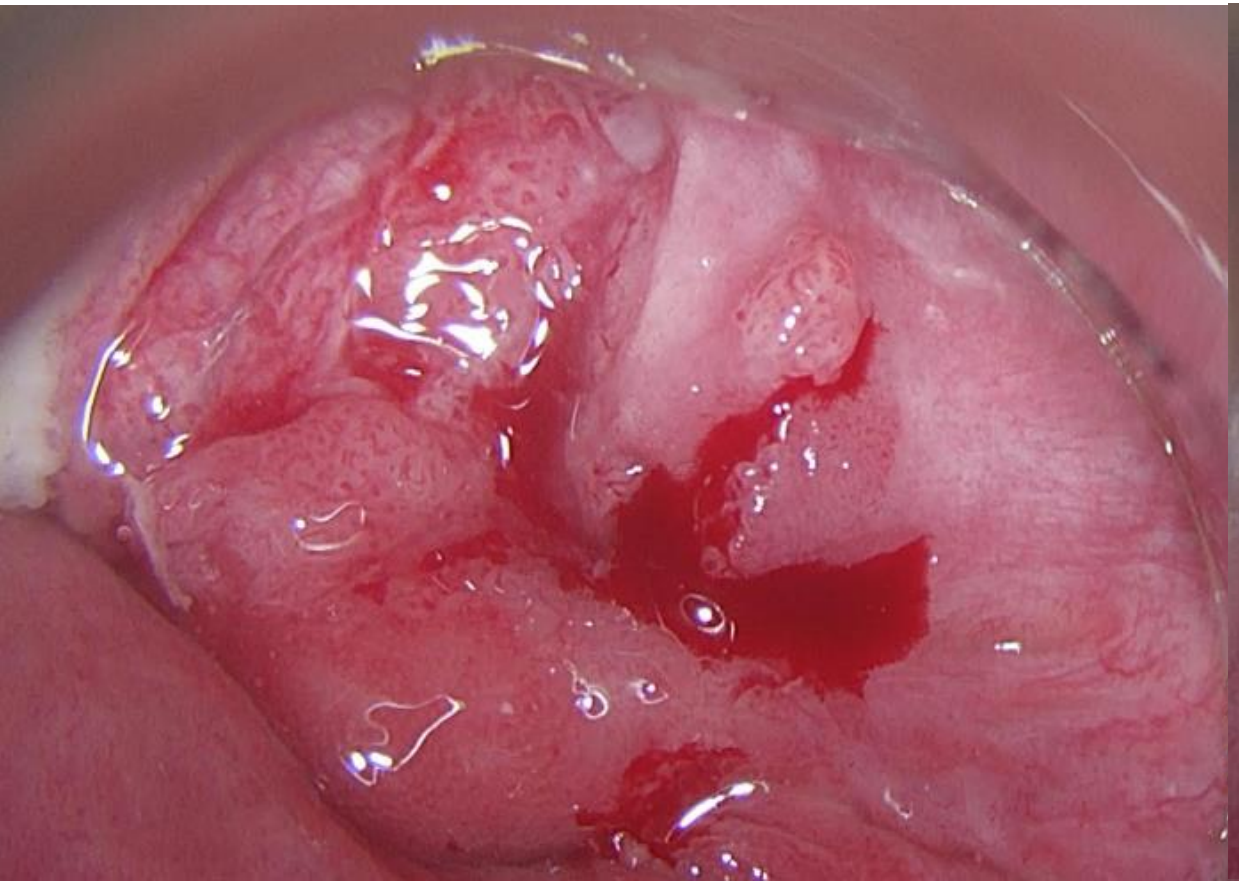


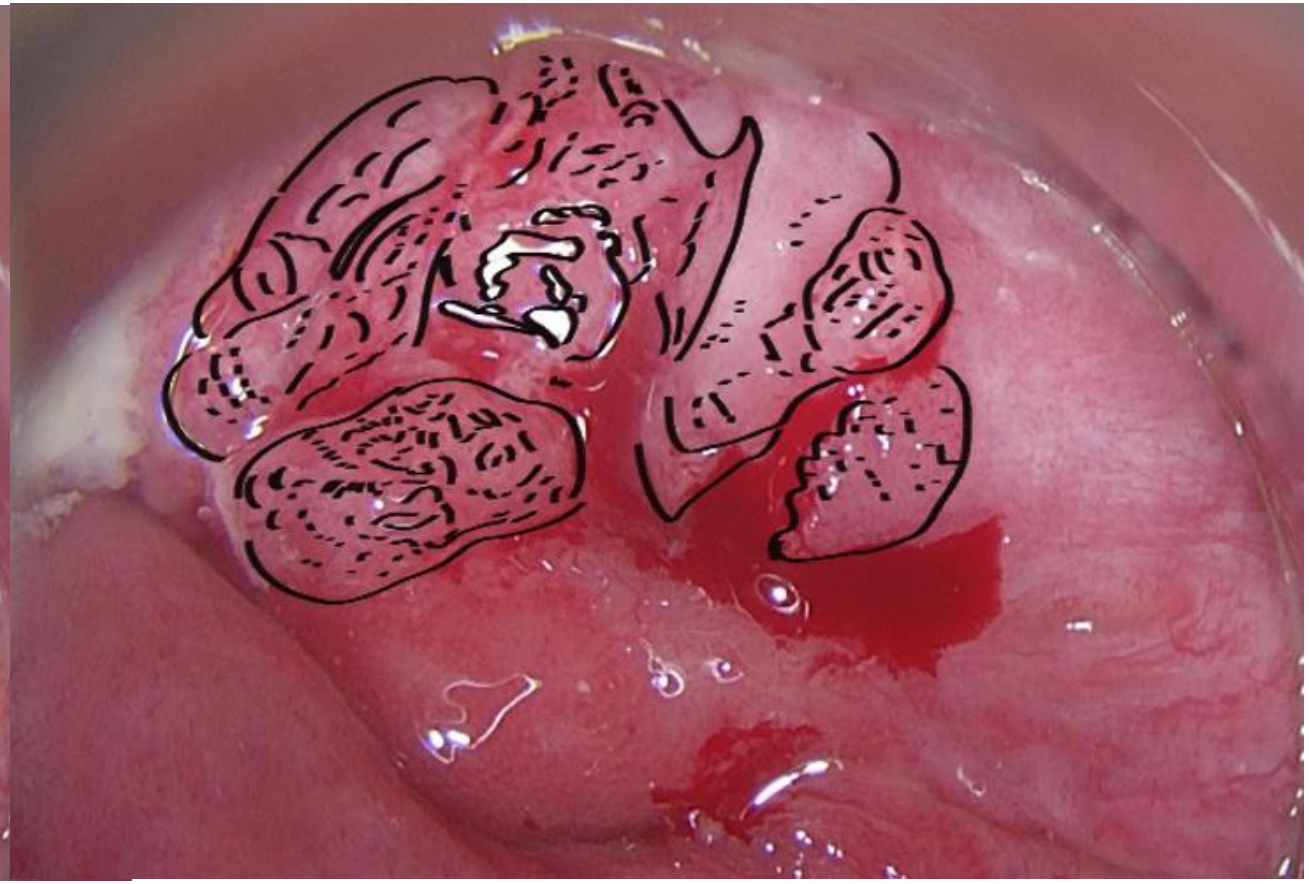
Cortesía Dr. Corral

Infrared coagulation – HRA









Cortesía Dr. Corral

Risk of Invasive Anal Cancer in HIV-infected subjects With High-Grade Anal Dysplasia

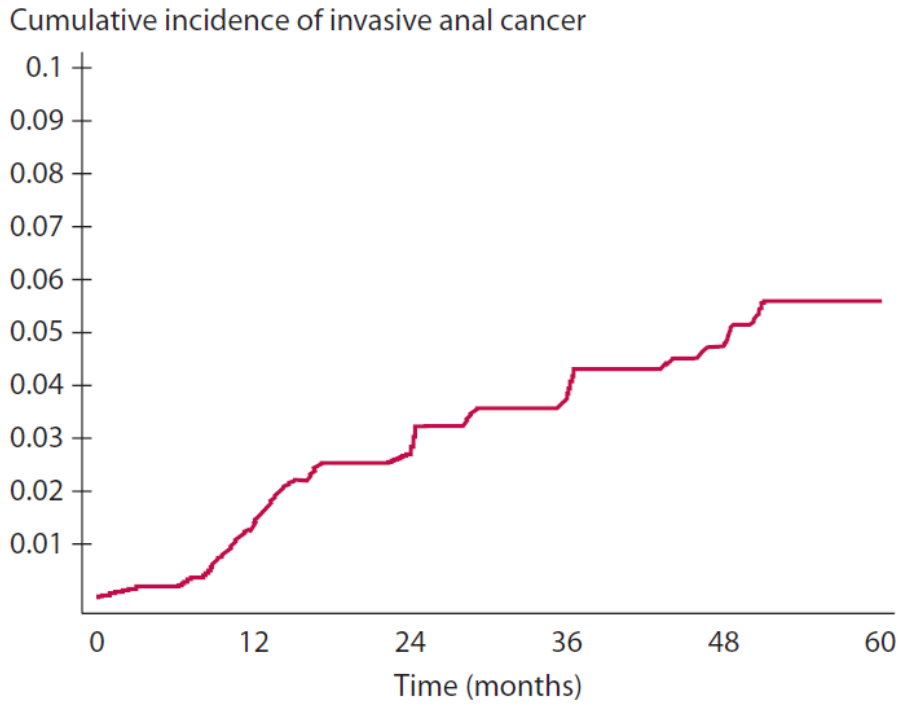


FIGURE 1. Cumulative incidence curve for invasive anal cancer among HIV-infected subjects with anal intraepithelial neoplasia grade III.

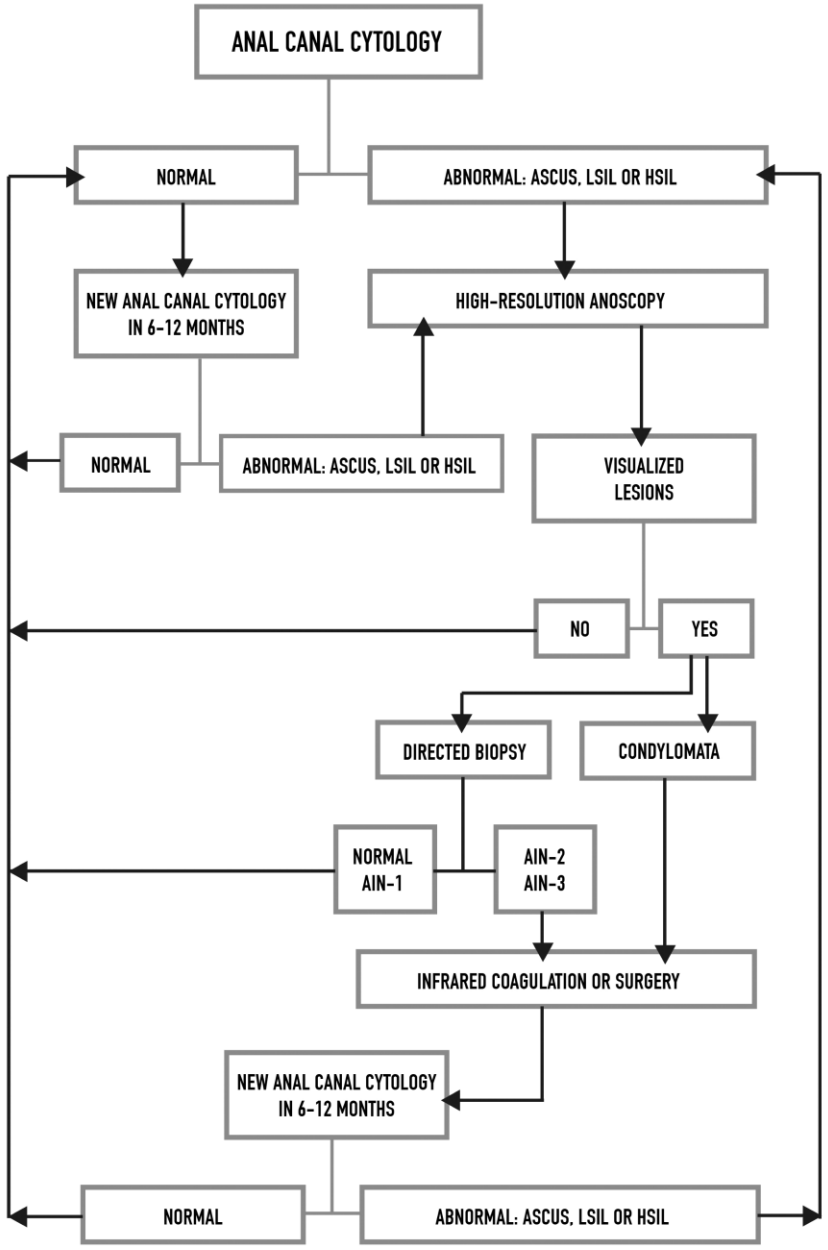
TABLE 2. Cumulative incidence of SCCA among those with baseline AIN III diagnosis, unadjusted

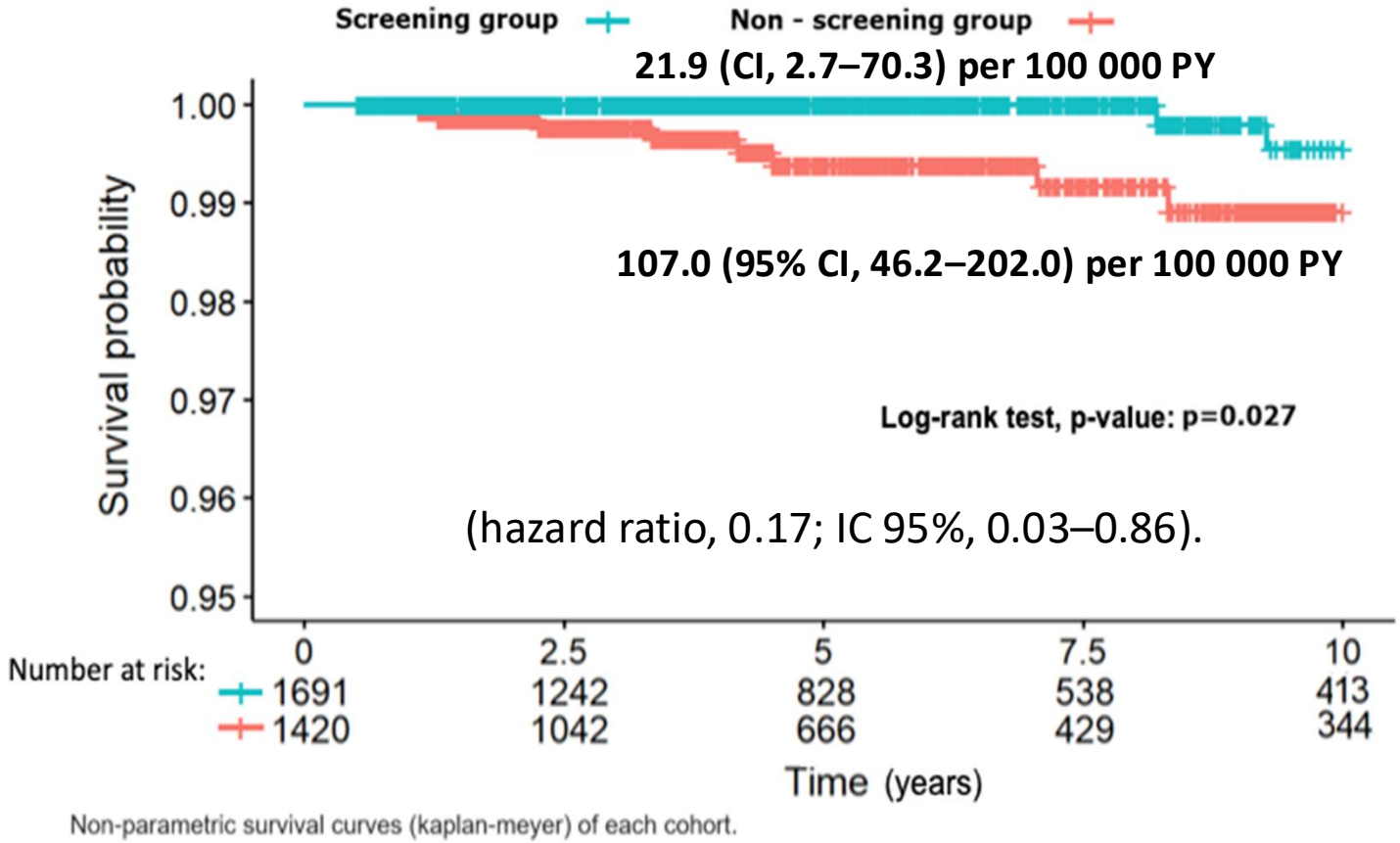
Time	*Incidence, %*	*95% CI, %*
12 months	1.2	0.7–2.5
24 months	2.6	1.6–4.3
36 months	3.7	2.4–5.6
60 months	5.7	4.0–8.1

AIN III = anal intraepithelial neoplasia, grade III; SCCA = squamous cell carcinoma of the anus.

Arens Y, et al. Dis Colon Rectum 2019

The Can Ruti Cohort



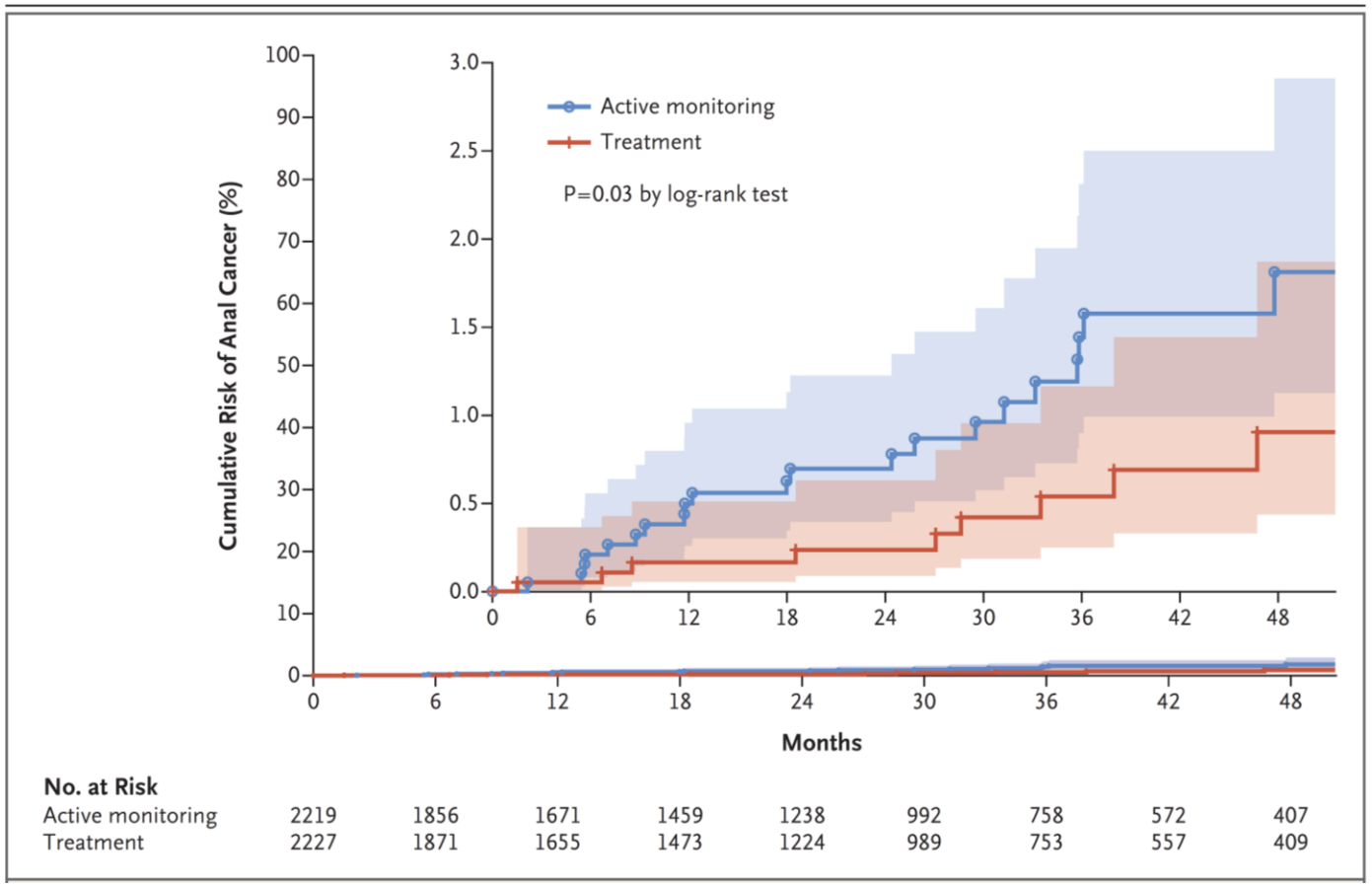


(hazard ratio, 0.17; IC 95%, 0.03–0.86).

Non-parametric survival curves (kaplan-meyer) of each cohort.

Revollo et al, CID 2019

The ANCHOR study – Outcomes



Rate of progression to cancer:

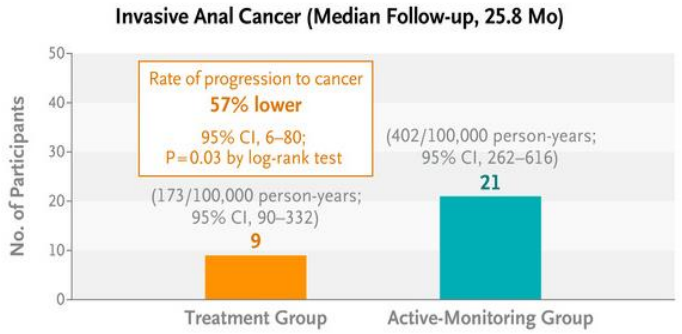
402 per 100,000 PY (95% CI, 262 to 616)

173 per 100,000 PY (95% CI, 90 to 332)

Cumulative incidence of progression to anal cancer at 48 months

1.8%

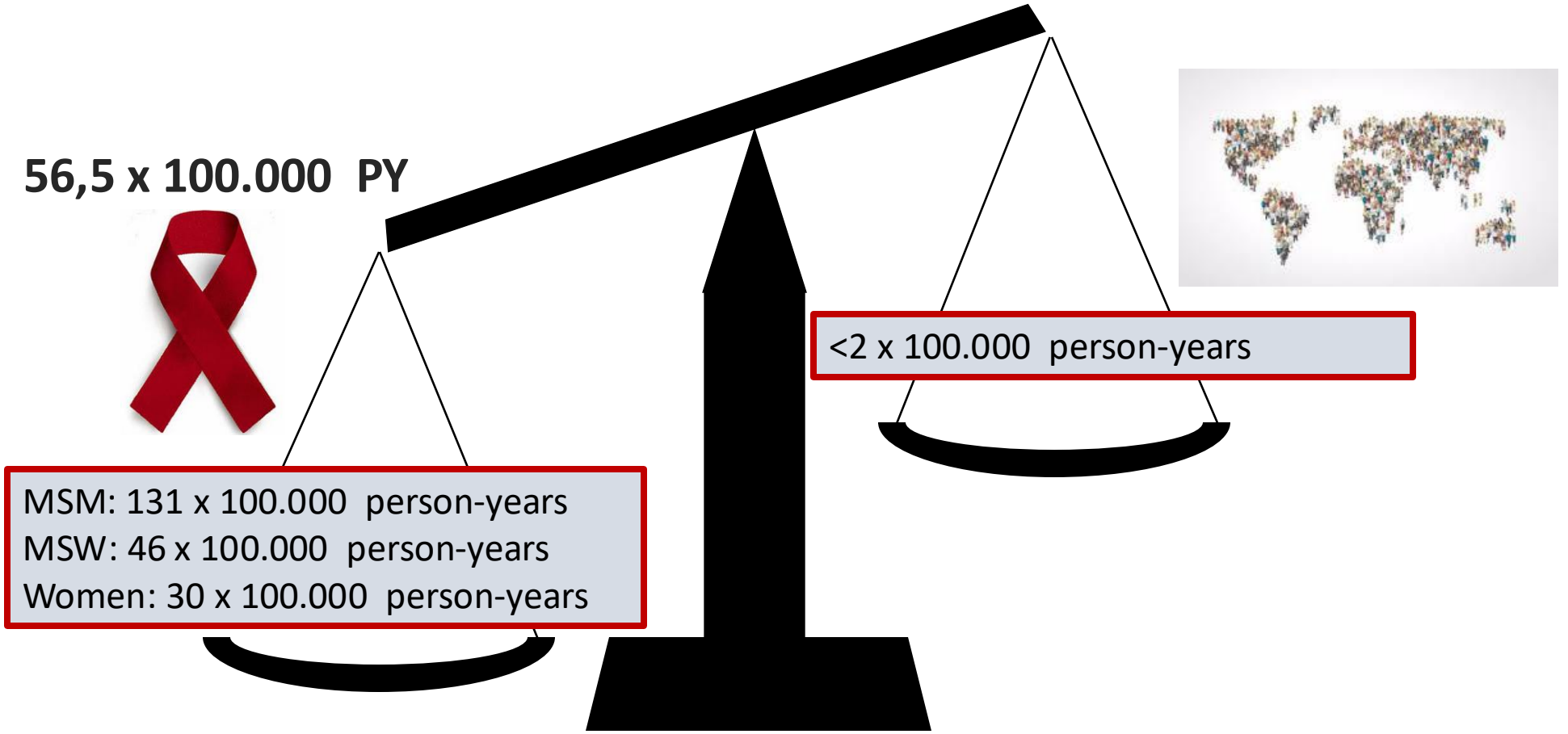
0.9%



- **Electrocautery ablation 83.6%**
- Infrared coagulation in 4.8%
- Ablation or excision under anesthesia 2.3%
- Topical fluorouracil /imiquimod 4.5% /0,5%

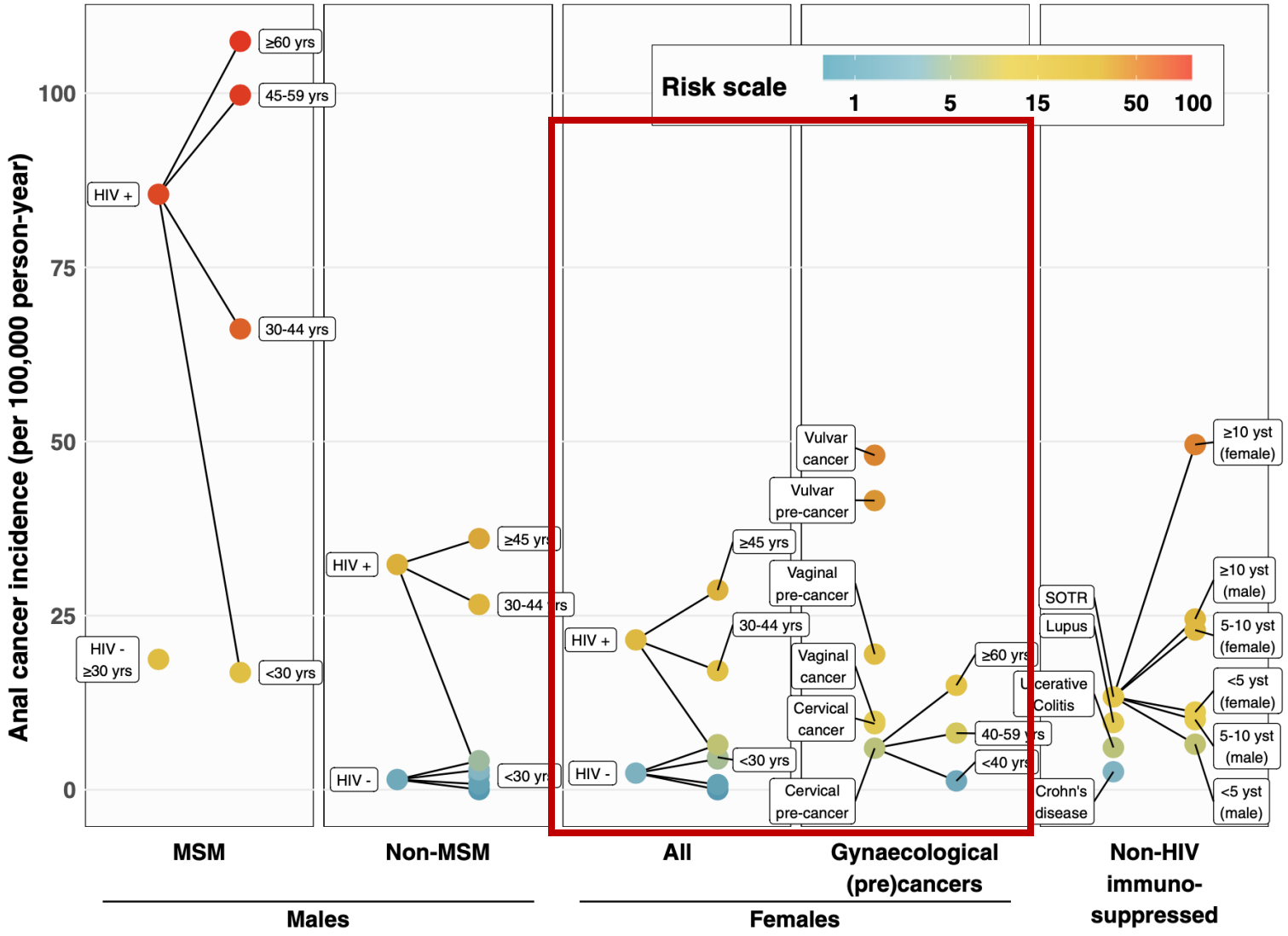
Palefsky et al, N Engl J Med 2022;386:2273-82

Anal Cancer PLWH vs general population.



Koroukian et al, Cancer 2022;128(10):1987-1995
Mahale P, et al CID 2018; 67:50-57
Silvelberg MJ, et al. CID 2012; 7:1026-1034

Anal Cancer PLWH vs general population.



Clifford et al, Int J Cancer. 2021;148:38-47

IANS consensus guidelines for anal cancer 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]		

Stier E et al, Int J Cancer 2024

Anal Cancer and Women

Two thirds of all anal cancer diagnoses are in women

Women are presenting with advanced anal disease:

43.2% presented with stage 3 disease.

14.4% presenting with stage 1 disease.

Article

Anogenital HPV-Related Cancers in Women: Investigating Trends and Sociodemographic Risk Factors

Micol Lupi [1,2,*], Sofia Tsokani [3,4], Ann-Marie Howell [2], Mosab Ahmed [5], Danielle Brogden [1], Paris Tekkis [1,2,6], Christos Kontovounisios [1,2,6,7] and Sarah Mills [1,2]

The Can Ruti Cohort

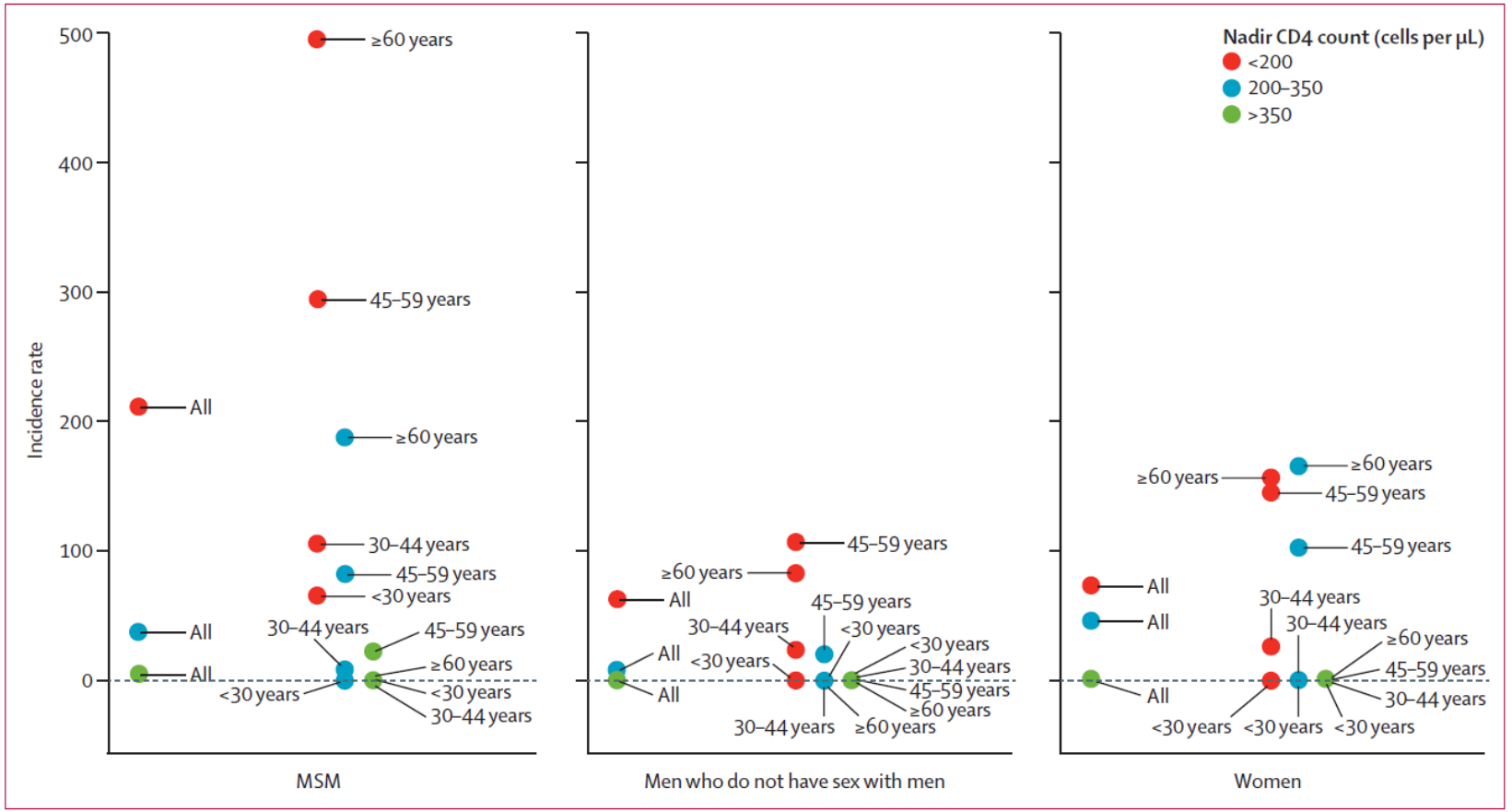
Table 3. Characteristics of Persons With Human Immunodeficiency Virus-1 Participating in the Study Diagnosed With Invasive Anal Squamous-cell Carcinoma

	Enrolled in the Screening Program (n = 2)		Not Enrolled in the Screening Program (n = 8)							
Age at IASCC, years	48	50	41	43	46	51	58	46	41	50
Symptoms at IASCC diagnosis	Hemorrhoids, anal pain	Anorectal mass	Anal Pain	No data	Anal pain	Anal pain, rectal bleeding	Rectal bleeding	Anal pain, rectal bleeding	No data	Anal pain
Length of follow-up in the cohort at cancer diagnosis, years	8.1	4.5	1.4	3.4	4.2	4.5	2.1	7.0	2.3	8.4
TNM stage	T1-2NxM0	T2N1M0	T2NxM0	T2NxM0	T2N2M0	T4N2M0	T2NxM0	T3N0M0	T2-3NxM0	T2N0M0
Sexual practice	MSM	MSM	Woman, HTSX	Woman, HTSX	MSW	MSW	MSM	MSM	MSM	MSM
Time with HIV, years	24	27	16	20	15	17	7	25	14	29
CD4 nadir, cells/μL	17	137	21	11	44	6	No data	115	41	109
CD4 at IASCC, cells/μL	317	806	107	No data	44	10	1418	366	349	555
HIV-RNA at IASCC, copies/mL	84	<40	<40	No data	1400	<40	<40	<40	140	<40
Basal anal cytology (year)	Normal	Normal	Not done	Not done	Not done	HSIL	Not done	Not done	Not done	Not done
Anal cytologies performed,[a] n	9	4	0	0	0	0	0	0	0	0
Worst cytological diagnosis and HRA result	LSIL, normal	ASCUS, normal	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
HPV genotypes at cytology sample	16, 33, 39	16, 59	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
At biopsy sample	Not done	Not done	39	Not done	Not done	Not done	16, 18, 56	Not done	Not done	Not done
Life status, final	Alive	Alive	Dead	Alive	Dead	Dead	Dead	Alive	Alive	Dead

Revollo et al, CID 2019

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**



Lancet HIV, August 2, 2024.

Take home….

- There are high rates of HPV infections in the sexually active population.
- The majority of the infected population will clear the papillomavirus spontaneously (cellular immunity).
- High psychosocial and sexual health impact of individuals diagnosed with HPV infection.
- Beyond cervical cancer, screening for other HPV-associated cancers in women is important.
- Nadir CD4 counts of less than 200 cells per µL were associated with the highest risk of developing anal cancer.

Thanks

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Hospital Universitario Ramón y Cajal.

Dr. Javier Corral
Hospital Universitario Germans Trias I Pujol