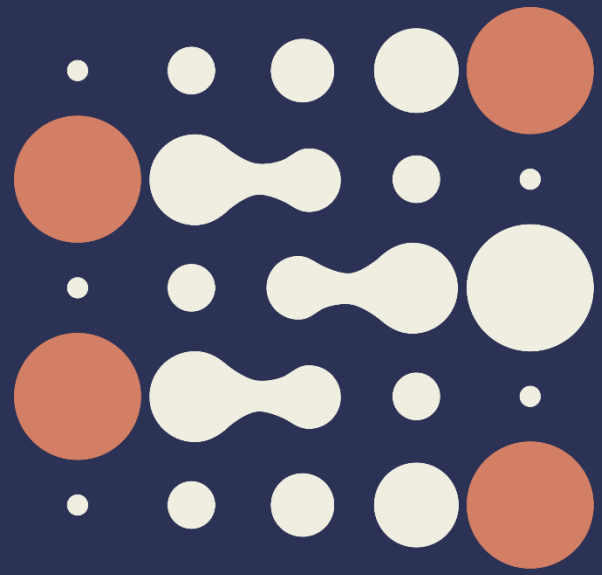
Epidemiology of HPV-related disease in the anal canal: similarities and differences with the cervix

Dr Gary Clifford

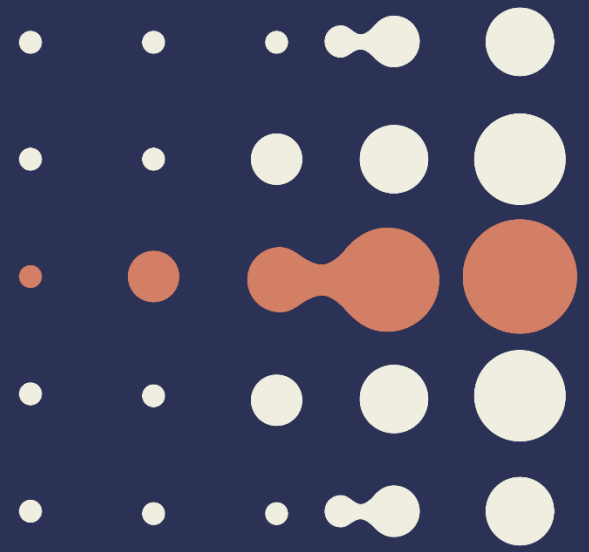
Early detection, Prevention and Infections Branch
International Agency for Research on Cancer (IARC/WHO)
Lyon, France



International Agency for Research on Cancer

World Health Organization

No disclosures



International Agency for Research on Cancer

World Health Organization

Outline

PART 1

Epidemiology of anal cancer

- Gender, Male sexuality
- Age
- HIV status

PART 2

Epidemiology of anal HPV(16)

- Gender, Male sexuality
- Age
- HIV status
- HPV vaccination

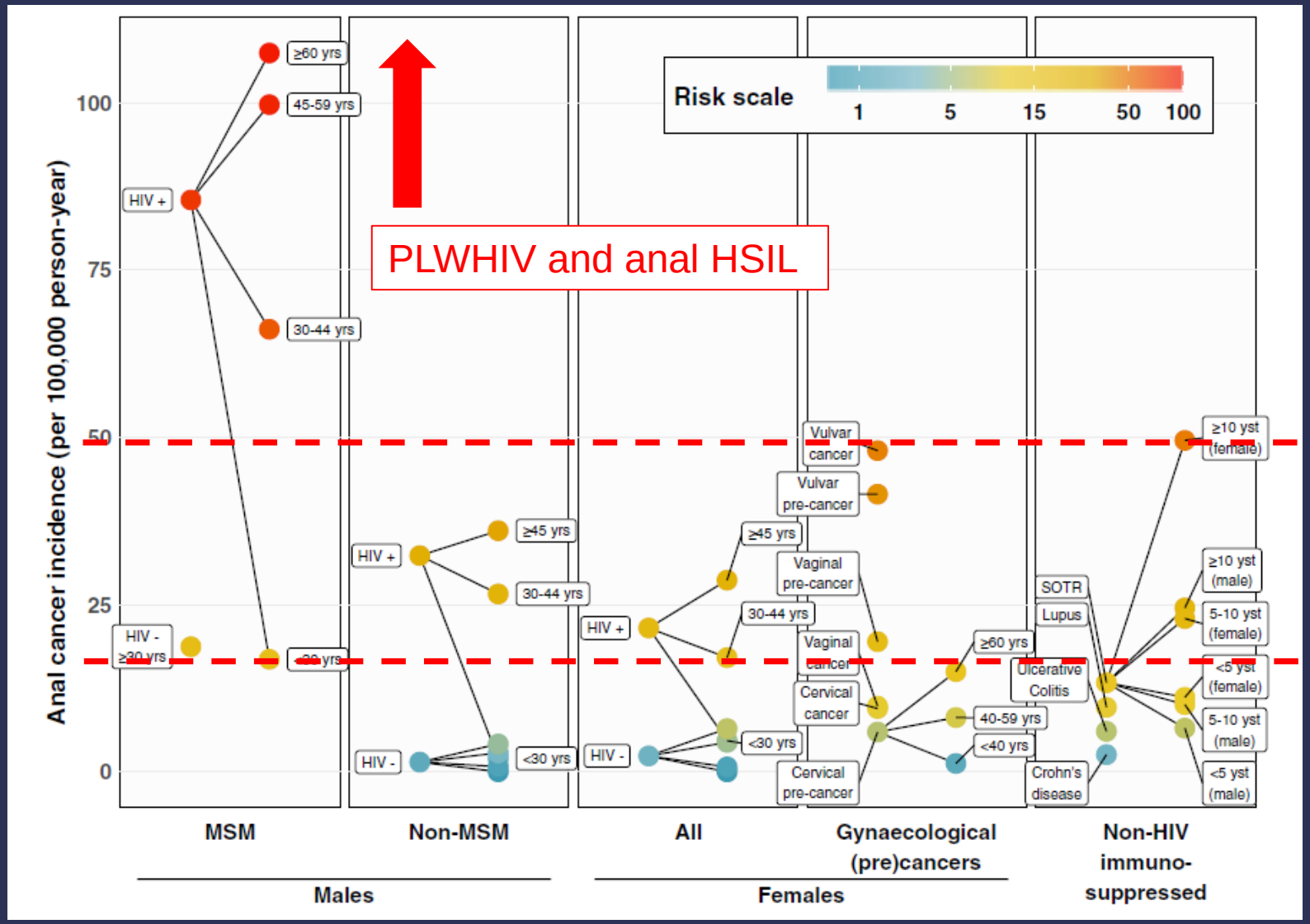
Epidemiology of anal cancer

Groups at established elevated anal cancer risk

- Persons infected with HIV, in particular, but not only, MSM
- HIV-uninfected MSM
- Women with HPV-related gynae cancer
- Women with HPV-related gynae pre-cancer
- Transplant recipients
- Patients treated for auto-immune diseases

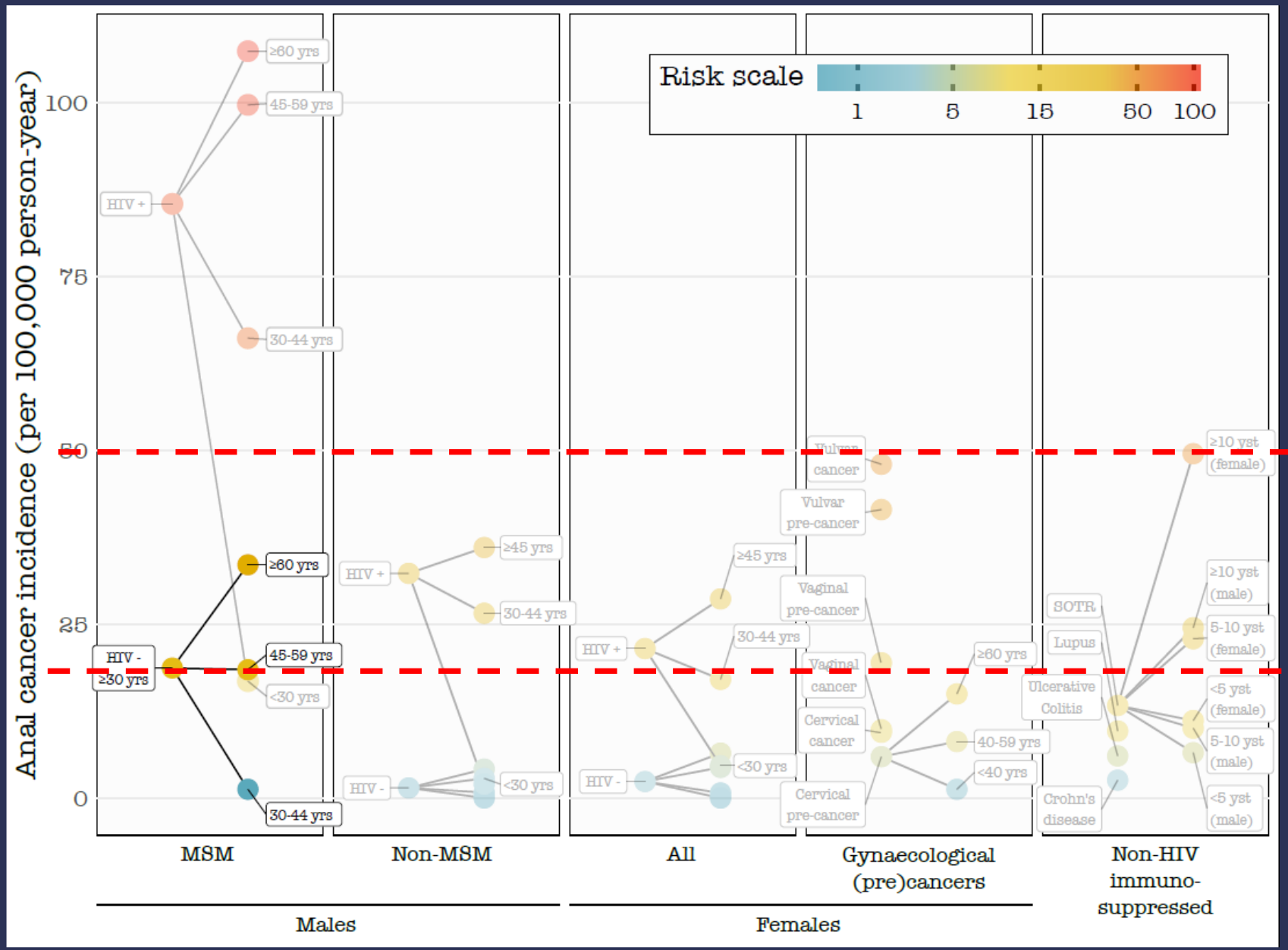
- (Persons with anal high-grade lesions - ANCHOR)

Anal cancer risk scale : a meta-analysis of anal cancer incidence



IPVC 2021

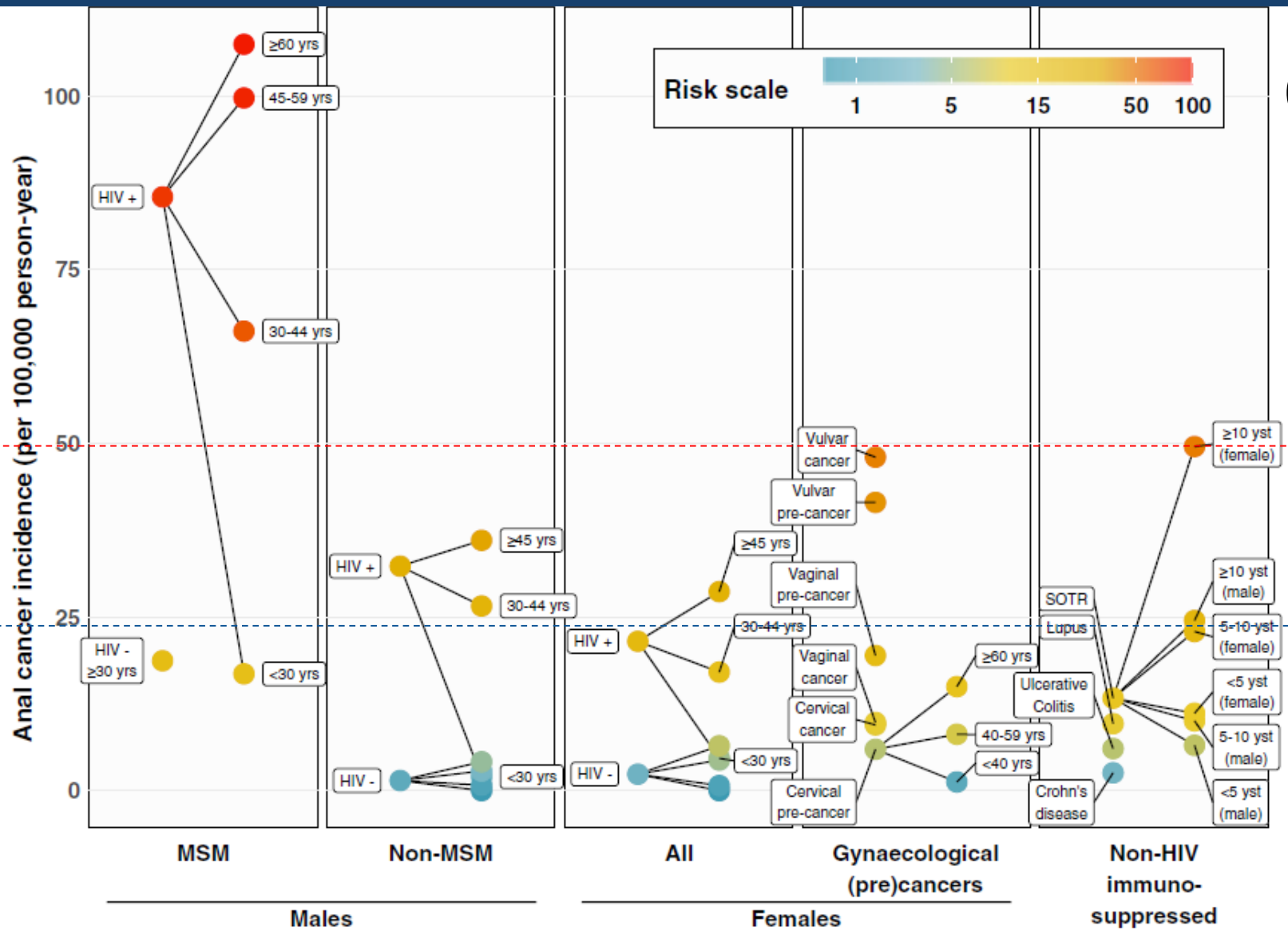
[Clifford et al, IJC, 2020]



ANAL CANCER RISK SCALE : IMPUTATION FOR MSM UNINFECTED BY HIV

[Deshmukh, Clin Infect Dis, 2023]

Thresholds versus other cancer screening programs ?



0.5

0.25

Breast cancer 45y+ in U.S. = 0.89%

colorectal cancer 50y+ in U.S.

Cervical cancer 30y+ pre-screening

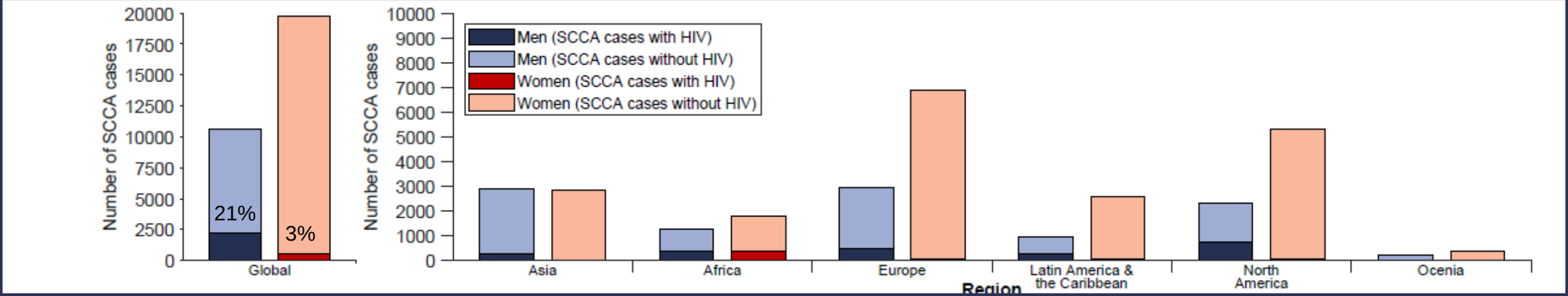
5 year cancer risk

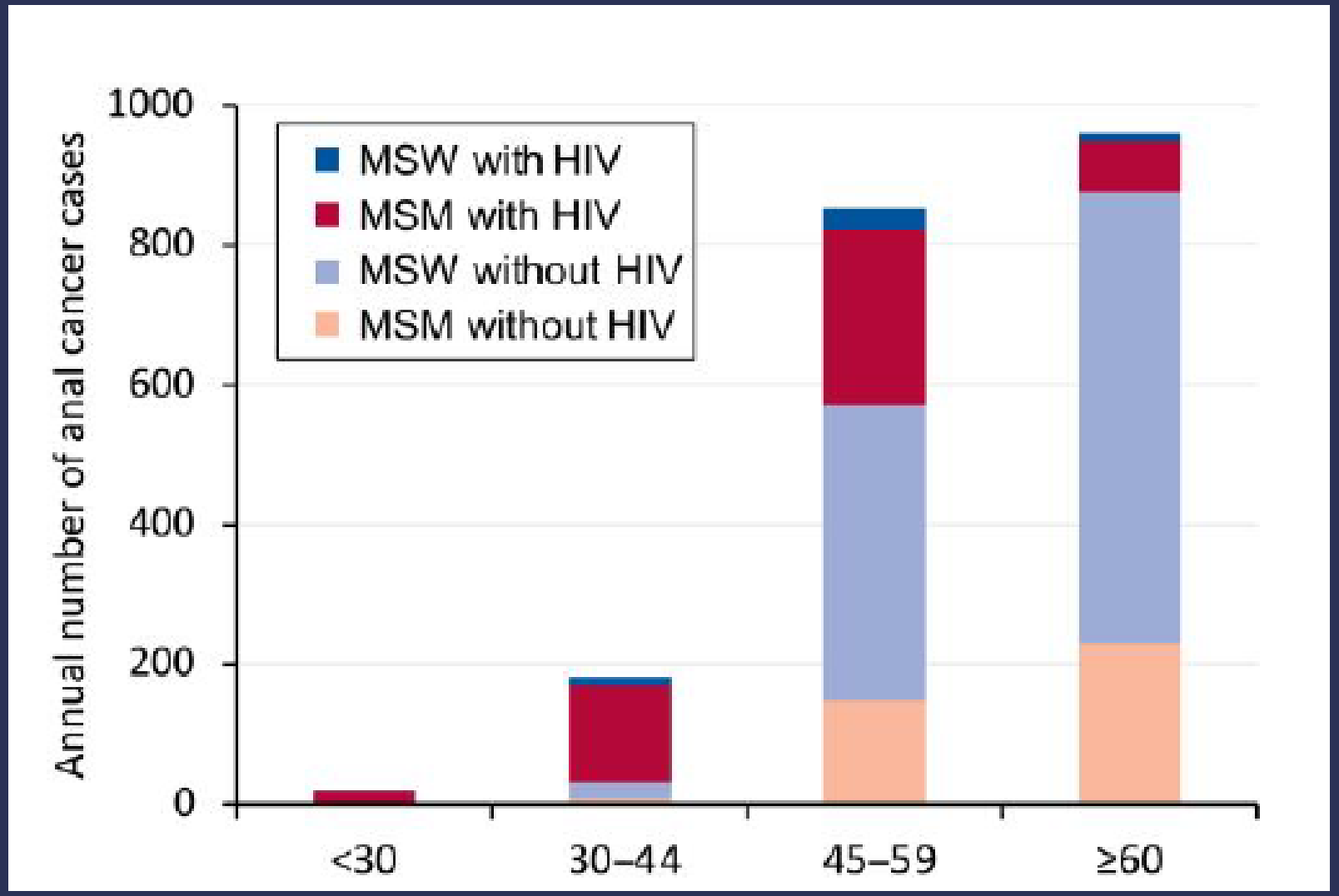
Ab

Most of the global burden of anal cancer falls on populations at the bottom of the anal cancer risk scale:

anal SCC burden, by region, gender and HIV status

(Deshmukh A et al, Int J Cancer, 2022)





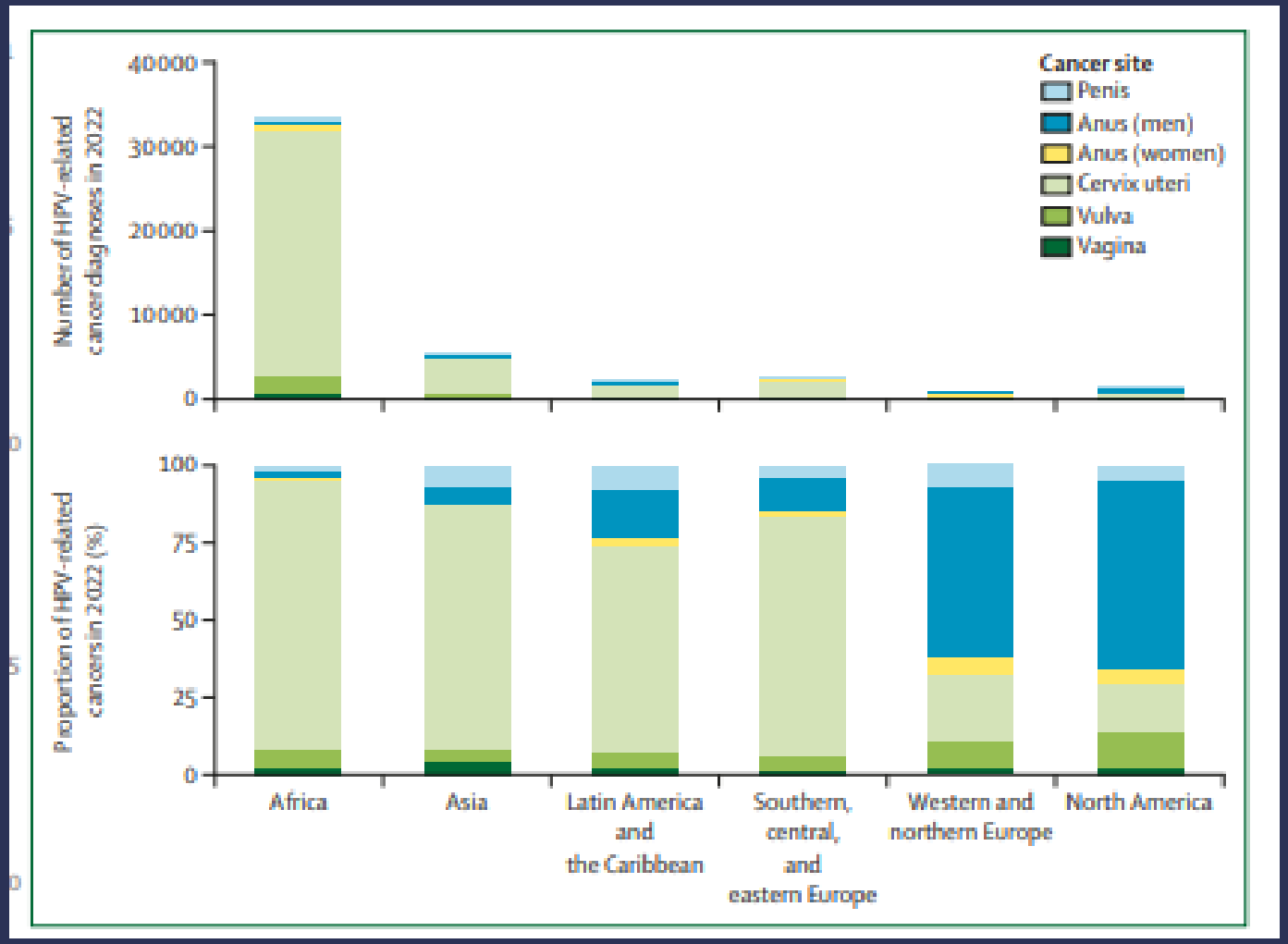
Population-level burden of male anal cancer

Age, HIV and sexual orientation

[Deshmukh, Clin Infect Dis, 2023]

Absolute, and relative, burden of HPV-related cancers among persons living with HIV varies around the world

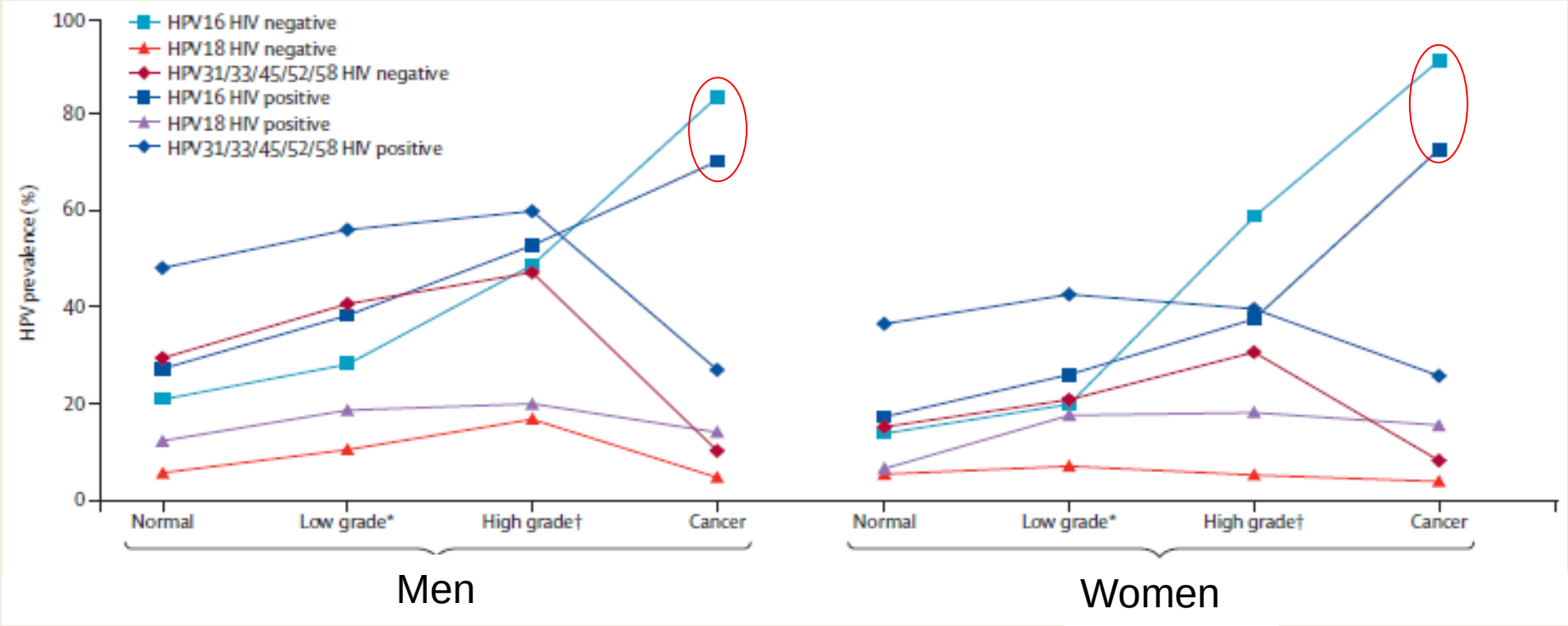
Uuskala et al, Lancet HIV, 2024



Epidemiology of anal HPV(16)

Anal HPV16

- **HPV16 is by far the most carcinogenic HPV type at the anus, representing the large majority of anal cancers, even in HIV-positive persons**



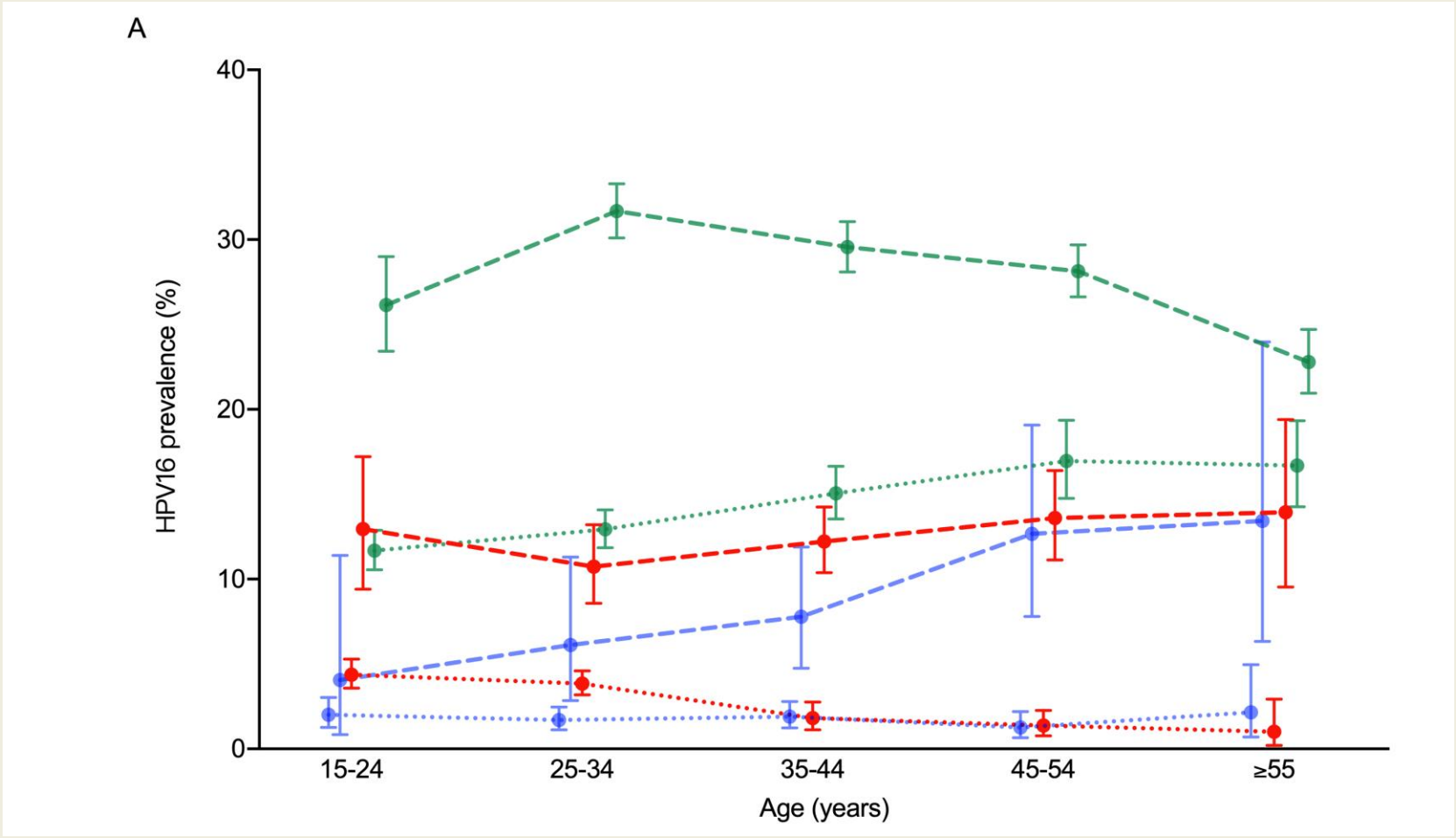
- Thus, HPV16 prevalence can also be a useful indicator to classify sub-populations at different anal cancer risk

[Lin et al, Lancet Infect Dis, 2018]

Anal HPV16 prevalence, by gender, HIV status, male sexuality, and age: collaborative pooled analyses

64 studies of 29,000 men
Wei et al, Lancet HIV, 2021

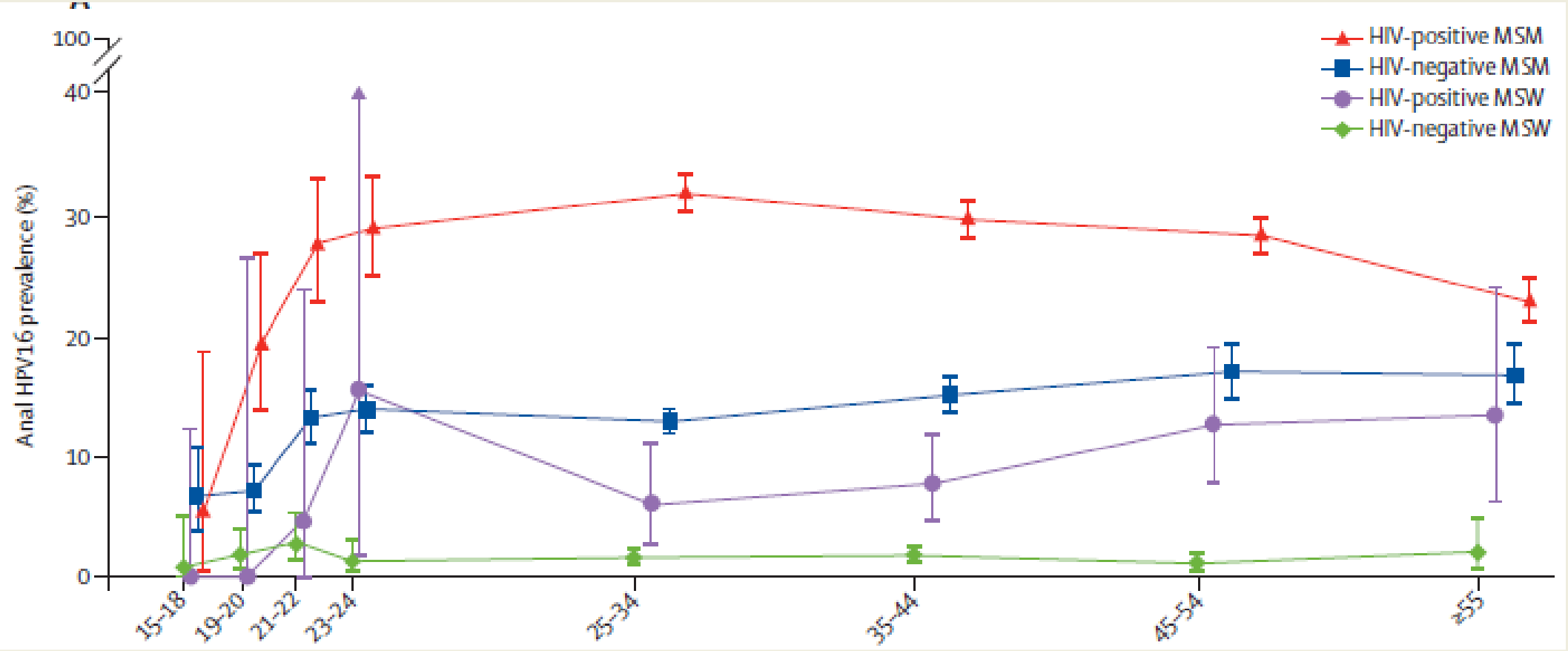
26 studies of 11,000 women
Wei et al, J Infect Dis, 2022



Rapid increases in HPV16 prevalence in MSM aged 15 to 25 years

64 studies of 29,000 men

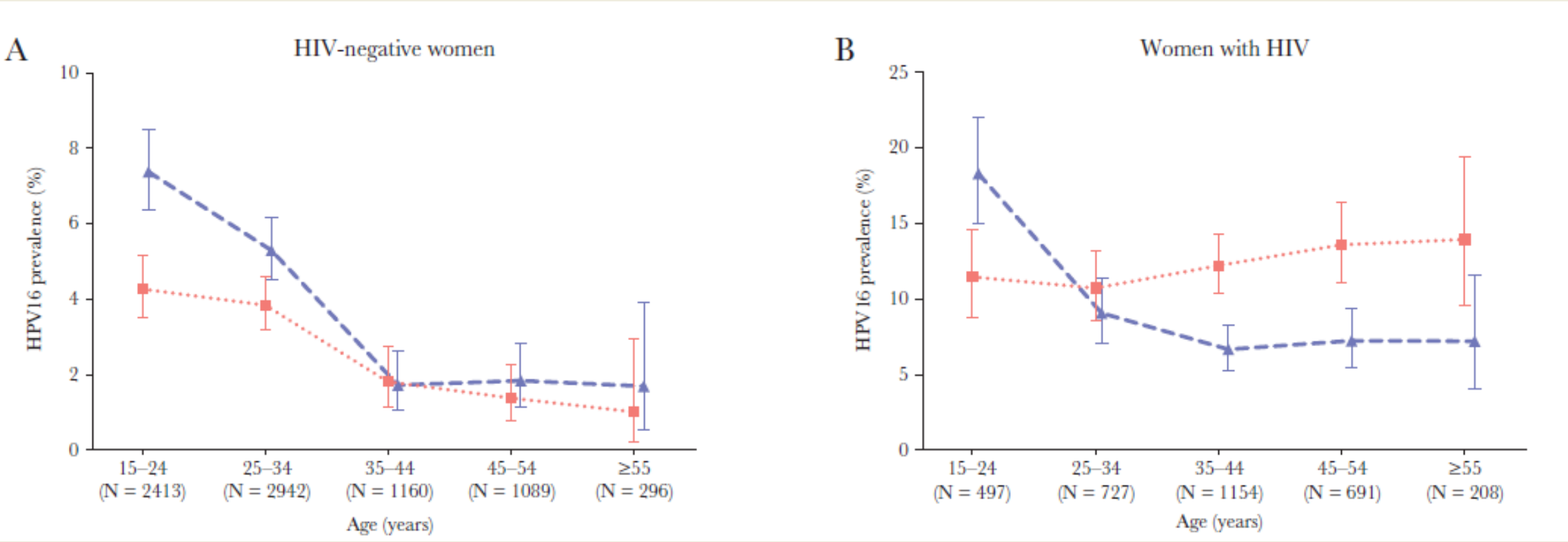
Wei et al, Lancet HIV, 2021



Anal and cervical HPV16 prevalence by HIV status and age

26 studies of 11,000 women

Wei et al, J Infect Dis, 2022



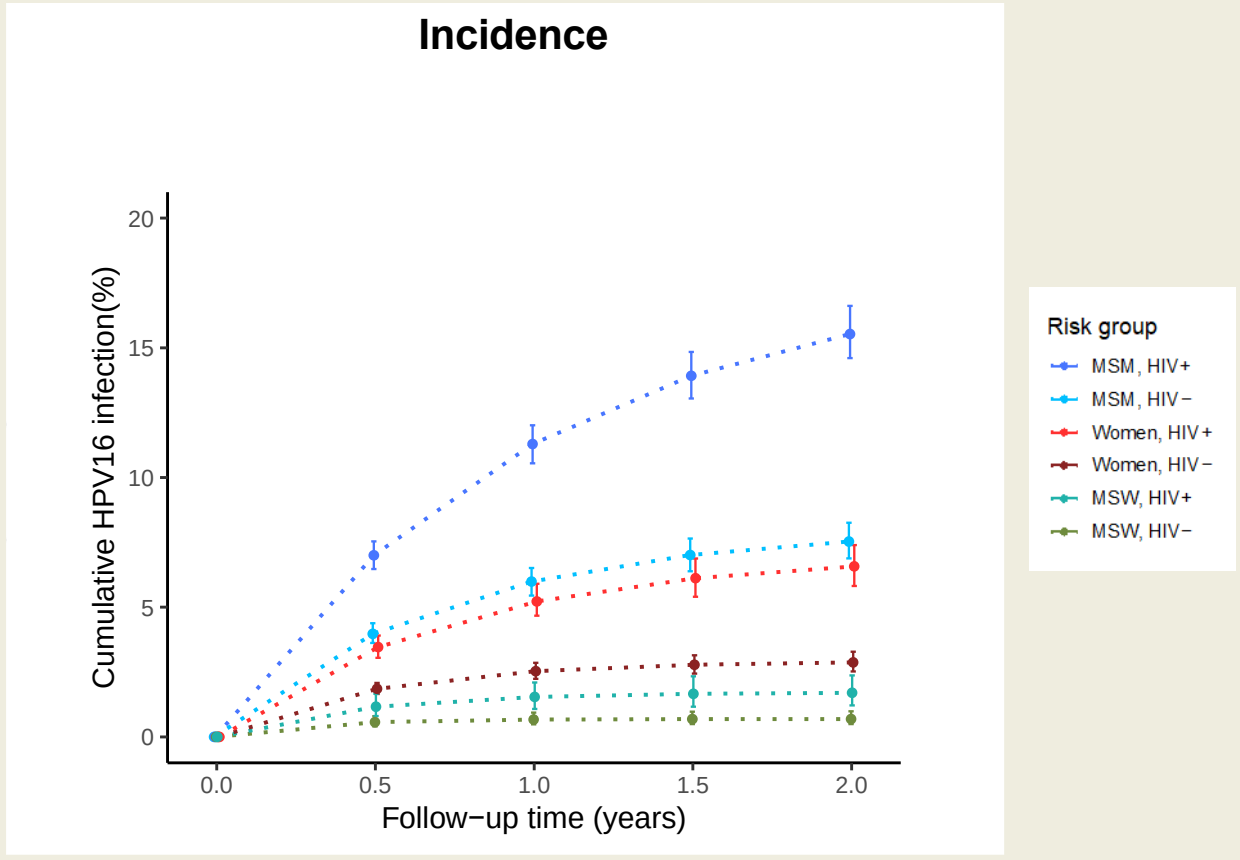
Shifts in HPV from cervix to anus with increasing age

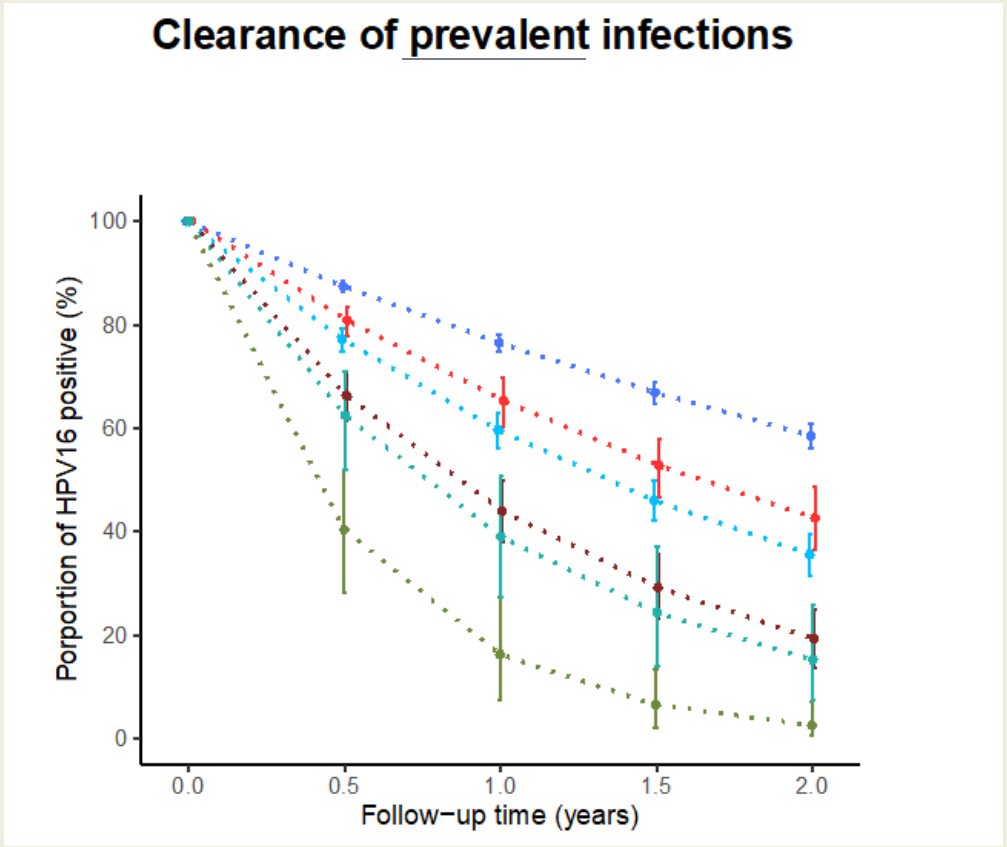
HPV16 incidence and clearance by risk group

a collaborative pooled analysis

34 longitudinal studies of 16,000 men and women

Wei et al, Clin Infect Dis, 2022



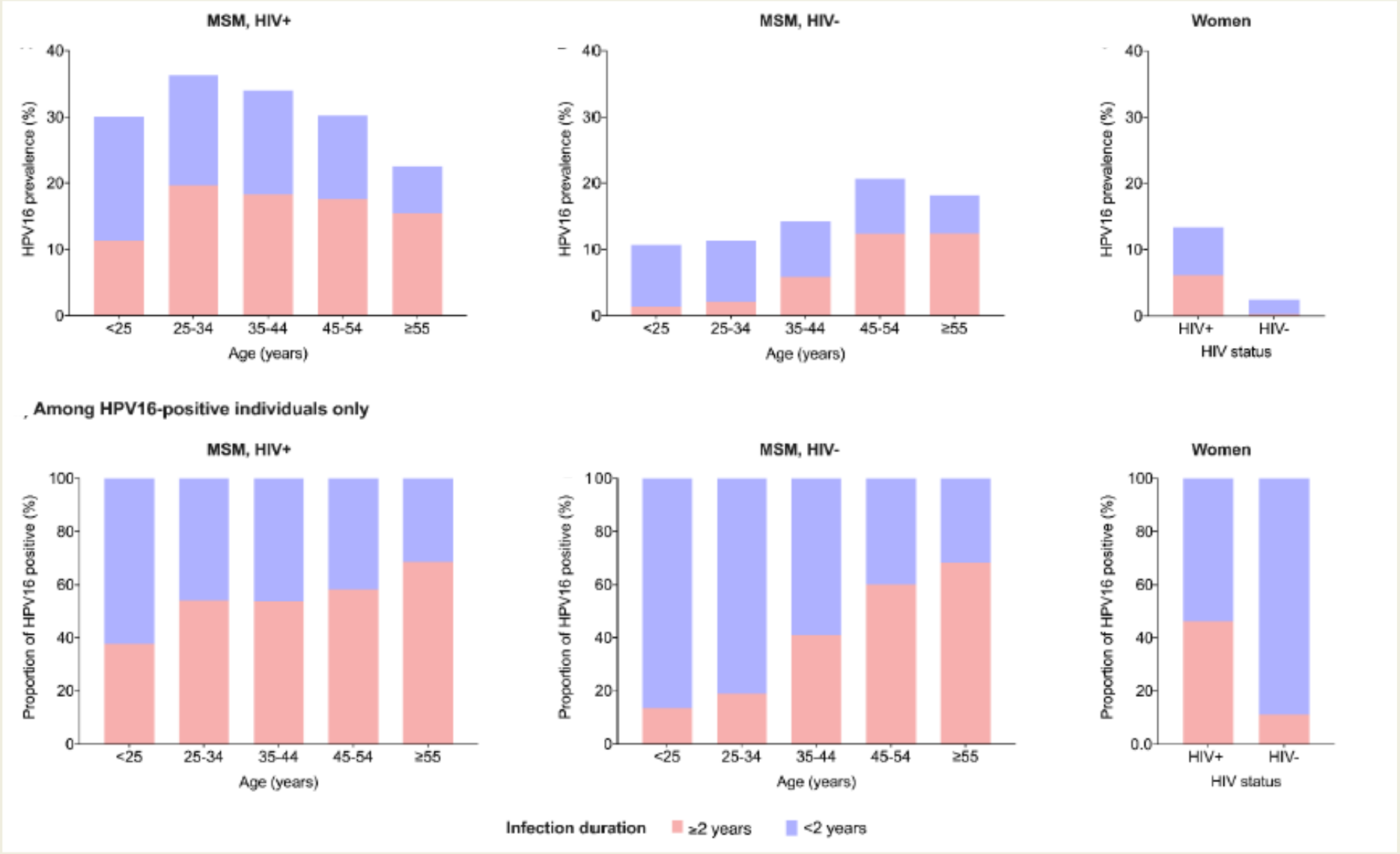


Risk factors for anal HPV16 incidence

Wei et al, Clin Infect Dis

	Incidence		
	MSM (aHR, 95%CI)	Women (aHR, 95%CI)	MSW (aHR, 95%CI)
HIV status			
Negative	Ref.	Ref.	Ref.
Positive	**1·42 (1·22–1·64)**	**1·90 (1·47–2·46)**	**3·33 (1·46–7·64)**
Lifetime number of sexual partners*			
Low	Ref.	Ref.	Ref.
High	**1·22 (1·01–1·47)**	**2·58 (1·86–3·57)**	**4·79 (1·38–16·7)**
Recent number of sexual partners†			
Low	Ref.	Ref.	Ref.
High	**1·76 (1·38–2·23)**	**1·67 (1·12–2·47)**	1·90 (0·52–6·91)
Ever having receptive anal sex			
No	Ref.	Ref.	..
Yes	**1·43 (1·11–1·85)**	0·79 (0·60–1·04)	..
Lifetime number of anal sexual partners‡			
Low	Ref.	Ref.	..
High	**1·58 (1·18–2·13)**	0·79 (0·60–1·04)	..
Recent number of anal sexual partners§			
Low	Ref.	Ref.	..
High	**1·45 (1·17–1·8)**	0·80 (0·48–1·34)	..

Age-specific HPV16 prevalence at 2 years after baseline, according to prior duration of infection



Wei et al,
Clin Infect Dis, 2022

Vaccination is efficacious at the anus, but effectiveness varies enormously by surrogates of naivety to anal HPV exposure, e.g. age

Wei et al, J Infect Dis, 2003

Outcome	Population in clinical trial		Population in real-world study
	PPE	ITT	
Infection			
12-26 years*	**83% (72% - 89%)**[1,2]	**51% (35% - 63%)**[1,2]	**73% (37% - 88%)**[3-6]
≥26 years*	…	-6% (-123% - 49%)[7]	…
Persistent infection			
16-26 years*	**95% (81% - 98%)**[1]	**59% (43% - 62%)**[1]	…
≥26 years*	31% (-82% - 74%)[8]	35% (-5% - 60%)[8]	…
AIN1/2/3			
16-26 years*	**80% (51% - 92%)**[8,9]	**50% (30% - 65%)**[8,9]	…
≥26 years#	…	17% (-6% - 35%)[8]	…
AIN2/3			
16-26 years*	**70% (7% - 90%)**[1,9]	**54% (21% - 73%)**[1,9]	…
≥26 years#	…	-9% (-165% - 55%)[7]	…

PPE=per-protocol. ITT=intention-to-treat. Significant vaccine efficacy and effectiveness was shown in bold.

References:
1. Palefsky JM, et al. *N Engl J Med* 2011. 2. Kreimer AR, et al. *Lancet Oncol* 2011. 3. Schlecht NF, et al. *PLoS One* 2012. 4. Meites E, et al. *J Infect Dis* 2020. 5. Woestenberg PJ, et al. *J Infect Dis* 2020. 6. Chow EPF, et al. *Lancet Infect Dis* 2021. 7. Hidalgo-Tenorio C, et al. *Viruses* 2021. 8. Wilkin TJ, et al. *Clin Infect Dis* 2018. 9. Palefsky JM, et al. *Clin Infect Dis* 2021.

Vaccination can be efficacious even at 27-45 years, but huge variations by surrogate markers of naivety to anal HPV exposure

DeSisto CL et al, J Infect Dis, 2025

Ages 18–26 y[d]	
HPV vaccination	
No	Ref
Yes	**0.80 (.68–.95)**
Age at first vaccination, y	
Unvaccinated	Ref
< 18	**0.13 (.08–.22)**
18–26	**1.31 (1.11–1.54)**
Time since first vaccination, y	
Unvaccinated	Ref
≥ 2	**0.52 (.42–.64)**
< 2	**1.50 (1.25–1.80)**
Time since first vaccination (y) among those vaccinated at age 18–26 y	
Unvaccinated	Ref
≥ 2	1.10 (.88–1.36)
< 2	**1.57 (1.30–1.89)**

Ages 27–45 y[e]	
HPV vaccination	
No	Ref
Yes	**0.79 (.70–.89)**
Age at first vaccination, years[f]	
Unvaccinated	Ref
18–26	**0.68 (.57–.82)**
>26	0.88 (.77–1.01)
Time since first vaccination, y	
Unvaccinated	Ref
≥ 2	**0.66 (.57–.77)**
< 2	0.98 (.85–1.13)
Time since first vaccination (y) among those vaccinated at age 18–26 y	
Unvaccinated	Ref
≥ 2	**0.67 (.55–.82)**
< 2	0.88 (.56–1.39)
Time since first vaccination (y) among those vaccinated at age >26 y	
Unvaccinated	Ref
≥ 2	**0.71 (.56–.89)**
< 2	1.02 (.88–1.18)