Latest Guidelines for Screening and Treatment for Human Papillomavirus and Anal Cancer



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IAS–USA

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Wilkin reported serving as a consultant for Merck & Co, Inc, and ViiV Healthcare, and receiving research grant funding from Merck & Co, Inc. (Updated May 9, 2025)

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Learning Objectives

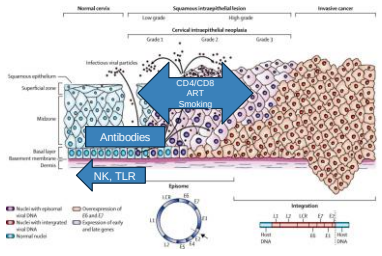
After attending this presentation, learners will be able to:

- Describe the epidemiology of anal, cervical, and oropharyngeal cancers in people with HIV
- Describe anal cancer screening strategies in people with HIV
- Explain evidence for prevention of anal and oropharyngeal cancers with human papillomavirus vaccination

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HPV Primer (Slide 2 of 3)

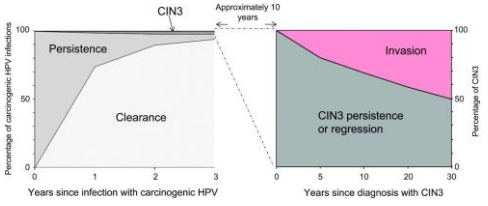


Slide 6

Cohen PA, et. al. Lancet. 2019.
Adapted from Anna-Barbara Moscicki, MD

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HPV Primer (Slide 3 of 3)



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Schiffman, et. al. J Natl Cancer Inst. 2011.

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Lifetime Risk of HPV Infection

- Heterosexual risk: 84%
  - Approximately 80% of women and men by age 45.
- MSM: Likely higher
  - Based on point prevalence of anal infection of 80-90% in some groups.
- HPV-related cancer cases (US)
  - 37,700 per year (2016)
  - Increasing at about 2.3% per year
- Cervical Cancer (Worldwide)
  - 311,000 cervical cancer deaths each year.
  - Leading cause of cancer death in women in low and middle income countries
  - 85% of cases occur in low resource settings

Chesson, HW, et. al. Sex Trans Inf. 2014.
Burgos J, et. al. AIDS 2017.
Viens LJ, et. al. MMWR 2016.
Cheng, LI, et. al. J. Clin. Onc.. 2022.
Frisch M, et.al. JNCI 2000.
Mbulaiteye SM, et. al. Int J of Cancer 2006.
Parkin DM, et. al. Int J of Cancer 2001.
Parking DM, et. al. CA 2005.

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HPV-related cancer: US Trends

Cervical cancer rates continue to decline	Anal cancer increasing
• 9.5% per year in the post-vaccination era!	• 1.8% annually among men in general population • 2.3% among women • Still relatively rare among the general population

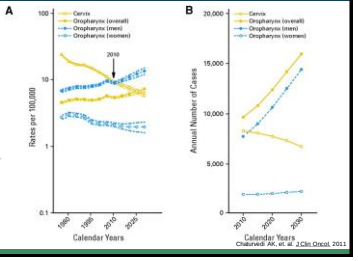
Slide 9

Cheng, Ch., et. al. JAMA Open Net. 202

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Observed and Projected Incidence Rates for OPC vs Cervical Cancer (US)

- Oral/oropharyngeal Cancer (OPC) rates are rising quickly particularly among elderly men
  - 3.1% per year
  - Related morality also increasing.
- 60-70% attributed to HPV infection



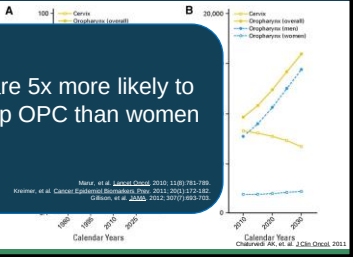
Chaturvedi AK, et. al. J Clin Oncol. 2011

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  - 3.1% per ye
  - Related mo increasing.
- 60-70% attrib infection



Men are 5x more likely to develop OPC than women

Marur, et al. Lancet Oncol. 2010; 11(8):781-789.
Kreimer, et al. Cancer Epidemiol Biomarkers Prev. 2011; 20(1):172-182.
Gillison, et al. JAMA. 2012; 307(7):693-703.

Chaturvedi AK, et. al. J Clin Oncol. 2011

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HIV Infection and HPV-related Malignancy

- HIV increases risk of HPV-related malignancy

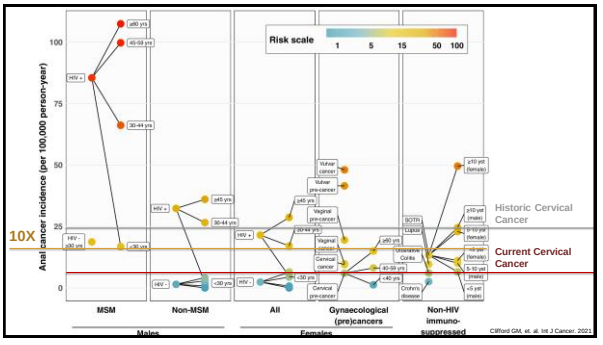
Cancer	Increased Risk vs General Population
Cervical	6x
Anal	19x (up to 39x in MSM with HIV)
OPC	2-3x

- Cervical/anal cancer risk among persons with HIV also associated with
  - # lifetime sex partners
  - Prior history of AIDS
  - History of low CD4 nadirs
  - Smoking status

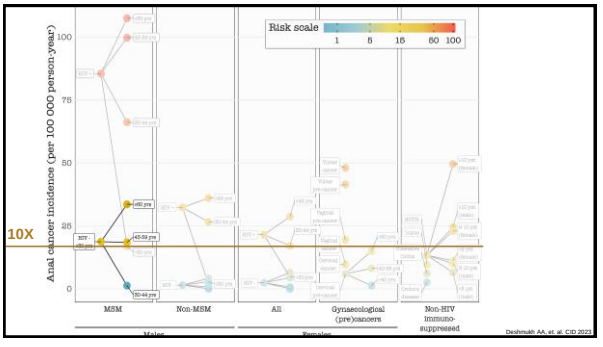
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Stelzel, et al. Lancet Global Health. 2021
Colón-Lopez, V. et al. J Clin Oncology. 2019
Beachler, Abraham et al. Oral Oncol. 2014

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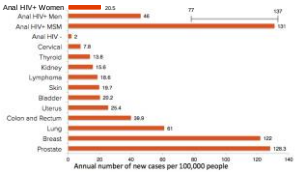


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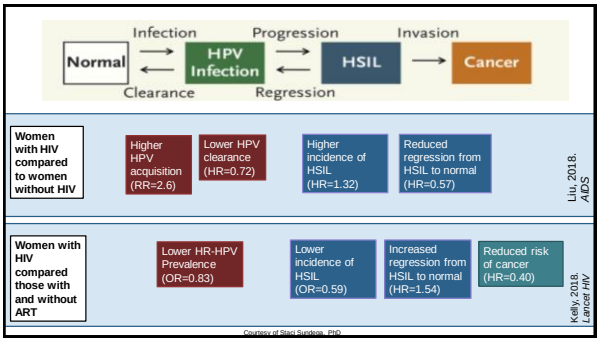
Anal Cancer Rates in Perspective



Silverberg, Lau et al. Clin Infect Dis. 2012.
Colon-Lopez, Shiels et al. J Clin Oncol. 2017.
www.anchorstudy.org

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High Resolution Anoscopy (HRA)



Virtual HRA Course is available: IANS International Anal Neoplasia Society

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High Resolution Anoscopy (HRA)



Invasive cancer



Perianal HSIL

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the ANCHOR study Results

	Treatment	Active Monitoring	Overall
Invasive Cancer Cases	9	21	30
Cancer Incidence (per 100,000 PY)	173	402	-
Months of follow-up (median, IQR)	25 (12-42)	27 (12-42)	25.8

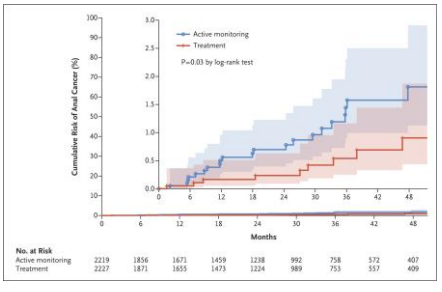
Treatment resulted in a 57% reduction in anal cancer (95% CI, 6% to 80%, P=.029)

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Palefsky, et. al. N Engl J Med. 2022

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Palefsky, et. al. N Engl J Med. 2022.
Graphic: anchorstudy.org

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Persisting Controversies - Anal Cancer Screening

There is a need to improve anal HSIL treatment efficacy

- Improve clinical skills
- Novel or adjunctive therapies

There is not widespread access to quality HRA

- Need for large scale training programs
- Improved screening tools (biomarkers) and algorithms
- No proven biomarkers for HSIL regression/progression

Can ANCHOR results be extrapolated to other at-risk groups?

- Probably?

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IANS Guideline

Screening test
CYTOLOGY, HPV OR BOTH

Triage test
HPV, CYTOLOGY, OR NONE

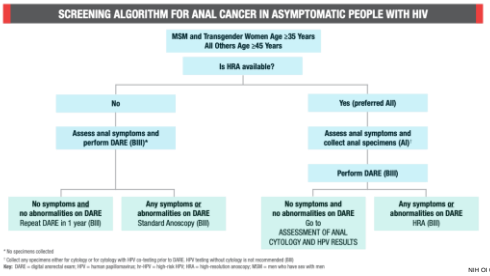
Management
HRA, REPEAT SCREEN OR ROUTINE SCREEN

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

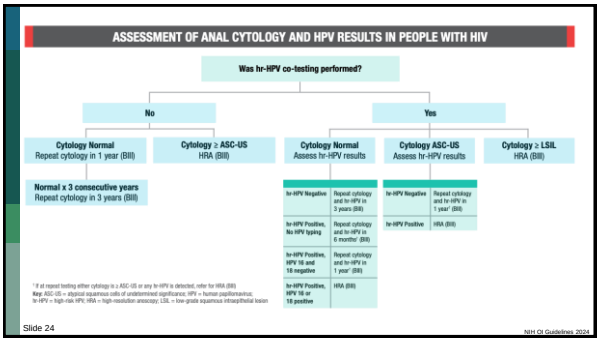
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NIH/CDC/IDSA/HIVMA OI Guidelines

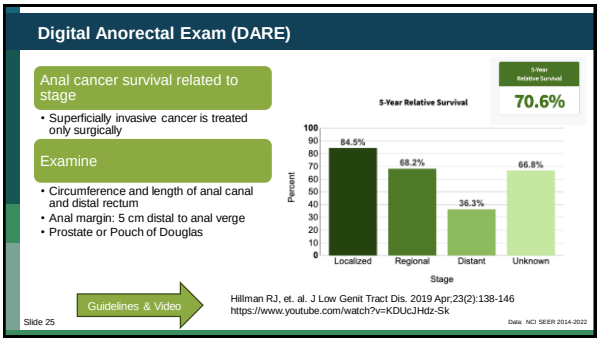


Slide 23 NIH OI Guidelines 2024

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ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV
Was hr-HPV co-testing performed?
No
Yes
Cytology Normal
Repeat cytology in 1 year (BIII)
Cytology ≥ ASC-US
HRA (BIII)
Normal x 3 consecutive years
Repeat cytology in 3 years (BIII)
Cytology Normal
Assess hr-HPV results
Cytology ASC-US
Assess hr-HPV results
Cytology ≥ LSIL
HRA (BIII)
hr-HPV Negative
Repeat cytology and hr-HPV in 5 years (BIII)
hr-HPV Positive, No HPV typing
Repeat cytology and hr-HPV in 6 months* (BIII)
hr-HPV Positive, HPV 16 and 18 negative
Repeat cytology and hr-HPV in 1 year* (BIII)
hr-HPV Positive, HPV 16 or 18 positive
HRA (BIII)
hr-HPV Negative
Repeat cytology and hr-HPV in 1 year* (BIII)
hr-HPV Positive
HRA (BIII)
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NIH OI Guidelines 2024

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Digital Anorectal Exam (DARE)
Anal cancer survival related to stage
• Superficially invasive cancer is treated only surgically
Examine
• Circumference and length of anal canal and distal rectum
• Anal margin: 5 cm distal to anal verge
• Prostate or Pouch of Douglas
5-Year Relative Survival
70.6%
5-Year Relative Survival
Percent
100
90
80
70
60
50
40
30
20
10
0
84.5%
68.2%
36.3%
66.8%
Localized
Regional
Distant
Unknown
Stage
Guidelines & Video
Hillman RJ, et. al. J Low Genit Tract Dis. 2019 Apr;23(2):138-146
https://www.youtube.com/watch?v=KDUcJHdz-Sk
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Data: NCI SEER 2014-2022

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HPV VACCINATION
An Update
IAS–USA

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Basis for US FDA Indications of 9vHPV for Adults up to Age 45

- V501-019: 3819 Colombian women ages 24 to 45 with *no history* of cervical disease or genital warts in the last 5 years.
- Efficacy to prevent combined endpoint of prevention of genital warts, CIN, or persistent infection due to qHPV types (6, 11, 16, 18)

Baseline Status	Efficacy, %	95% CI
Seronegative/DNA negative (Per-protocol efficacy)	88.7	78.1, 91.3
Seropositive/DNA negative	66.9	4.3, 90.6

- Approval of the 9vHPV vaccine based on combination of efficacy/safety/non-inferior immunogenicity in other populations

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Castellsagué X, et. al. Br J Cancer.
US FDA Drug Label. https://www.fda.gov/media/90064/download

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Current ACIP Recommendations

Ages	Recommendation	Series
9-10	Early vaccination okay	
11-12	**RECOMMENDED**	9vHPV, 2 doses
13-15	Catch up vaccination	
16-26		9vHPV, 3 doses
27 and older	Not routinely recommended	



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Meites E, et. al. MMWR. 2019

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Current ACIP Recommendations

Ages
9-10
11-12
13-15
16-26
27 and older

Mass HPV Vaccination of Adults (ages 30-45):

> $300,000 per QALY gained

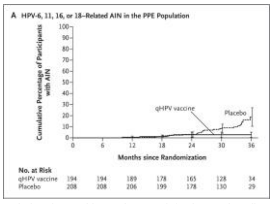


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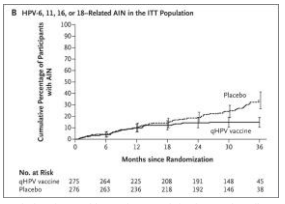
Meites E, et. al. MMWR. 2019

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HPV Vaccination: Anal Cancer Prevention



Excludes those with vaccine type infections at baseline



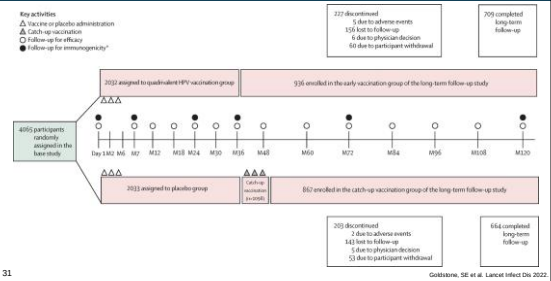
Includes those with vaccine type infections at baseline

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Palefsky JM et al. N Engl J Med 2011
Goldstone SE et. al. Lancet Infect Dis. 2022

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HPV vaccine: long term anal outcomes

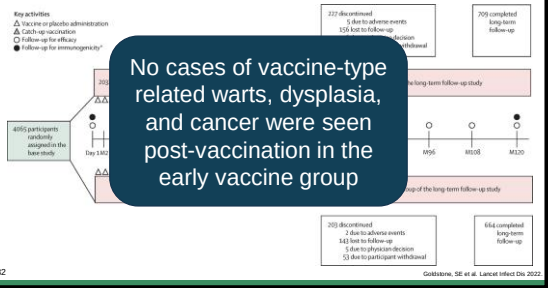


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Goldstone, SE et al. Lancet Infect Dis 2022

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HPV vaccine: long term anal outcomes



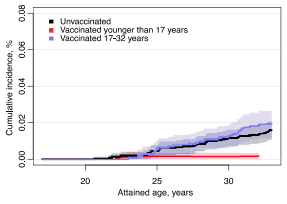
No cases of vaccine-type related warts, dysplasia, and cancer were seen post-vaccination in the early vaccine group

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Goldstone, SE et al. Lancet Infect Dis 2022

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Back to Denmark: Vaccine and Anal Cancer Incidence



Anal cancer incidence has decreased among vaccine eligible age groups since the introduction of HPV vaccination in the US (while increasing among unvaccinated adults)

Baandrup, L. et al. J Natl Cancer Inst. 2024;
Berenson, AB. et al. JAMA Oncol. 2022.

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Prevention of Persistent Oropharyngeal HPV Infection

	4vHPV (n)	Placebo (n)	HR (95% CI)
ACTG 5298 Persistent Oral Infection[1]	1	8	0.12 (0.02, 0.98)

	2vHPV (n)	HAV (n)	VE % (95% CI)
Costa Rica Vaccine Trial: Oral Prevalence of HPV 16/18 at 4 years (study exit) n = 6,352[2]	1	15	93.3 (63, 100)

[1]Wilkin TJ, et. al. Clin Infect Dis. 2018
[2]Herrero R, et. al. PLoS One. 2013

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Studies of 9vHPV to Prevent Oropharyngeal Infection

RCT of 9vHPV to prevent persistent oral infection in men (without HIV)

- V503-49 (NCT 04199689)

Study of 9vHPV to prevent oral HPV infection in Men with HIV

- Men living with HIV 20 to 50 years-old in Brazil, Mexico, and Puerto Rico (NCT 04255849)

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Next in HPV Vaccination

- Validation of and move to 2 and single dose series in persons with HIV
  - WHO guidelines support a single dose series in those without HIV (based on observational data)
  - Single dose RCTs ongoing (KEN SHE and IARC India HPV Trial)
- Expanded genotype vaccine underway
- HPV-specific vaccine targets and other vaccine platforms

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Conclusions

- HPV infection is very common
- Persons with HIV have higher rates of cervical, anal, and oropharyngeal cancer compared to the general population.
- OPC rates are rising in an aging population
- Anal and cervical cancer ARE preventable; screening guidelines exist
  - Access to HRA remains a challenge
- OPC screening modalities/recommendations lacking (but progress is being made)
- Current HPV vaccines are very effective but only when given prior to sexual debut

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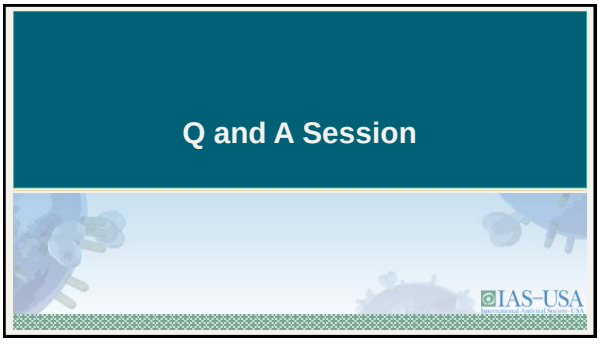
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IAS-USA Team

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