Anal Dysplasia and Anal Cancer Prevention

Advances in Cytology and Small Biopsies
9 June, 2025

Benjamin Davis, MD
Assistant Professor of Medicine
Harvard Medical School
Infectious Disease Unit
Massachusetts General Hospital

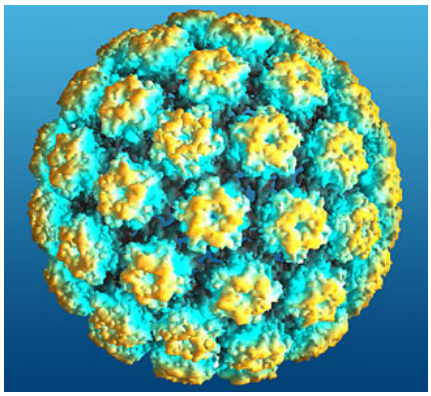
Learning Objectives

1. Understand the current state of the art for detection and treatment of anal dysplasia to prevent anal cancer.

Summary

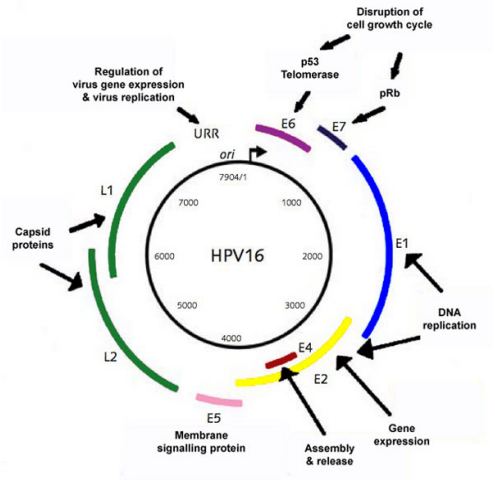
- HPV Biology
- Epidemiolgy of HPV, Dyplasia, and Cancer
- Screening
- Treatment
- Prevention

Human Papilloma Virus

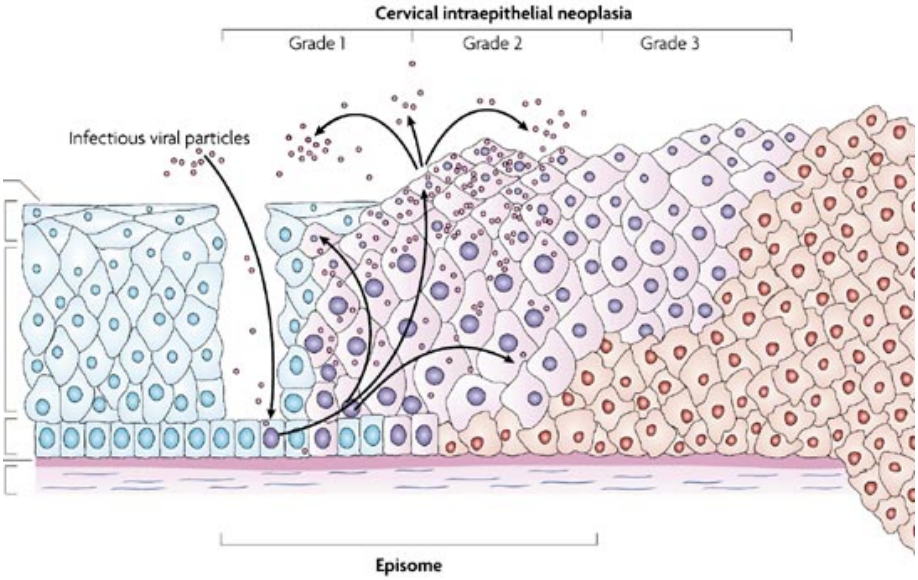


- Non-enveloped
- Double-stranded DNA
- >100 types identified
- 30-40 anogenital
- Oncogenic
  16, 18, 31, 33, 35, 39, 45, 51, 52, 58
- Non-oncogenic
  6, 11, 40, 42, 43, 44, 54

Human Papilloma Virus



- Early HPV protein
  E1,E2, E4, E5, E6, E7
- E6 and p53
  DNA integrity
- E7 and Rb
  Cell replication
- Late HPV protein
  L1, L2



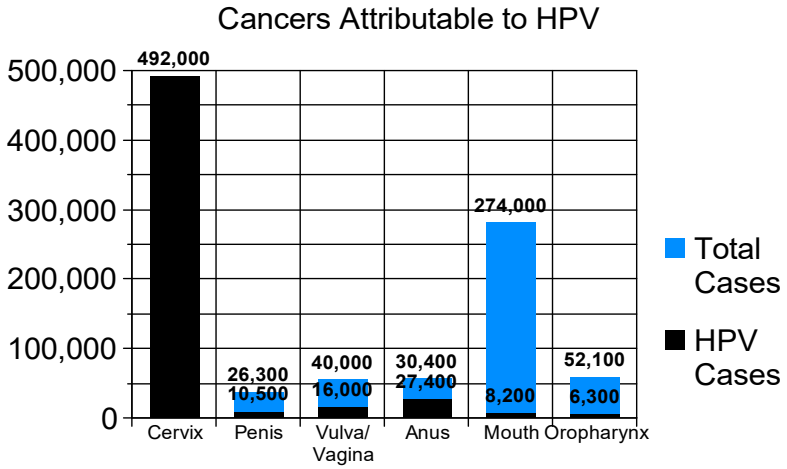
***Nature Reviews Cancer* 7, 11-22 (January 2007)**

Risk Factors for HPV Persistence

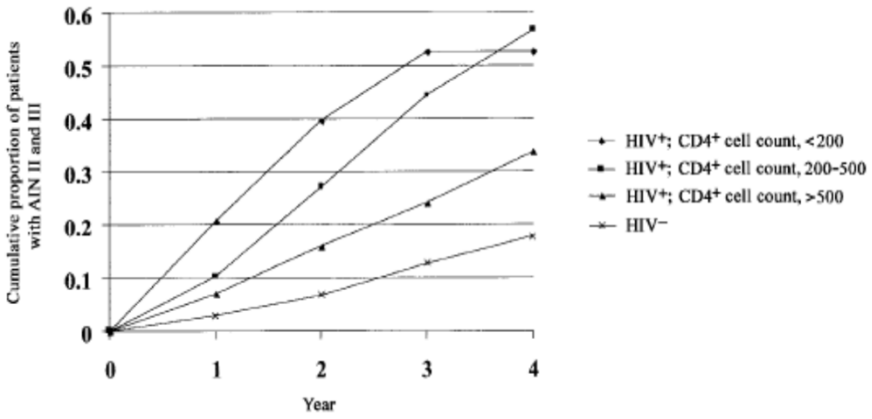
- HIV or other immunosupression
- Infection with multiple subtypes
- Infection with subtypes 16,18 (high risk)
- Age >30
- Smoking

- 80% of HPV infections are successfully cleared. Mean duration 8 months

NEJM (1998) 338:423-8.

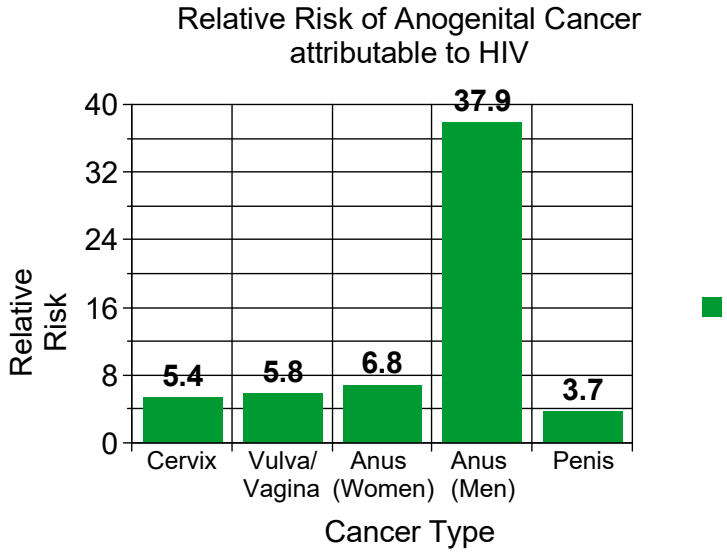


Parkin, DM. Int J Cancer:118, 3030-3044 (2006)

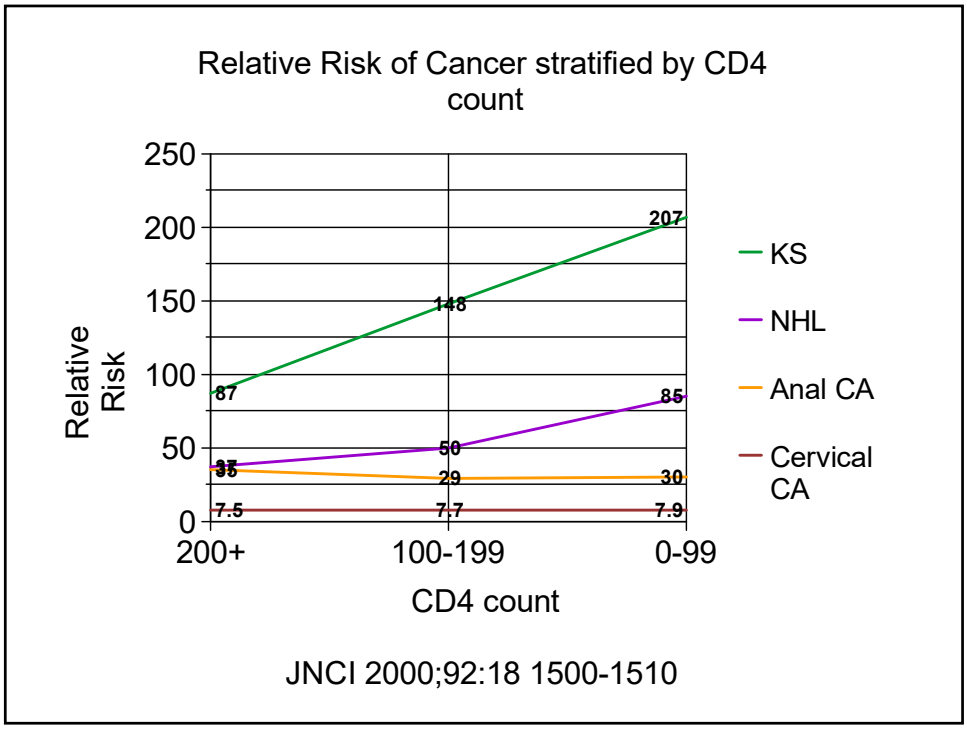


Incidence of AIN 2,3 in HIV (+) MSM

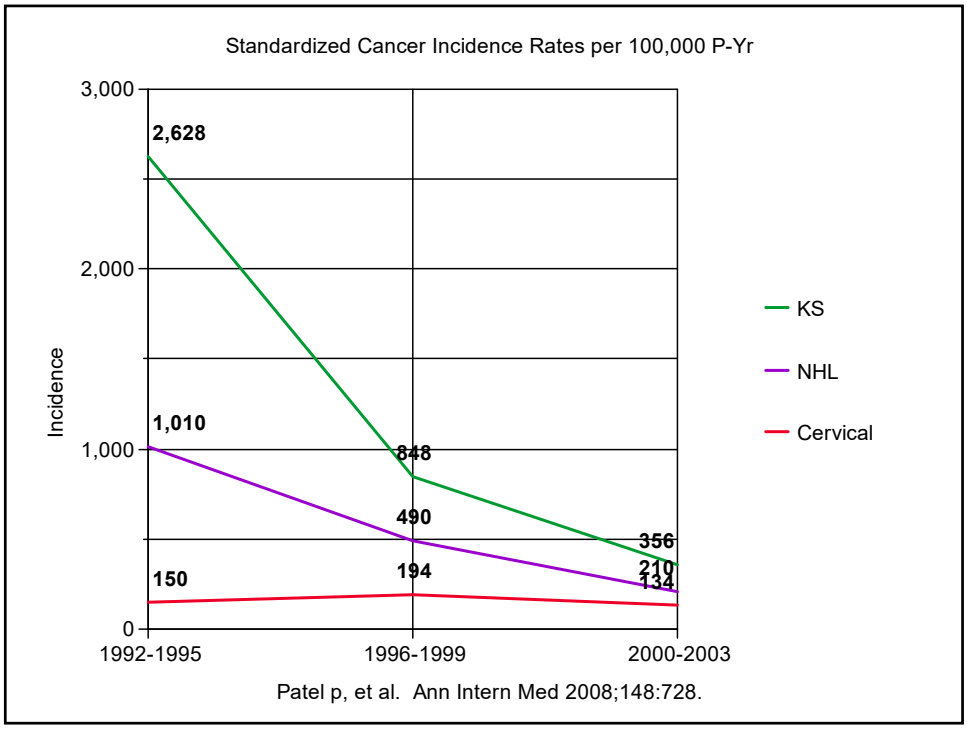
CID (2002) 35:1127-1134



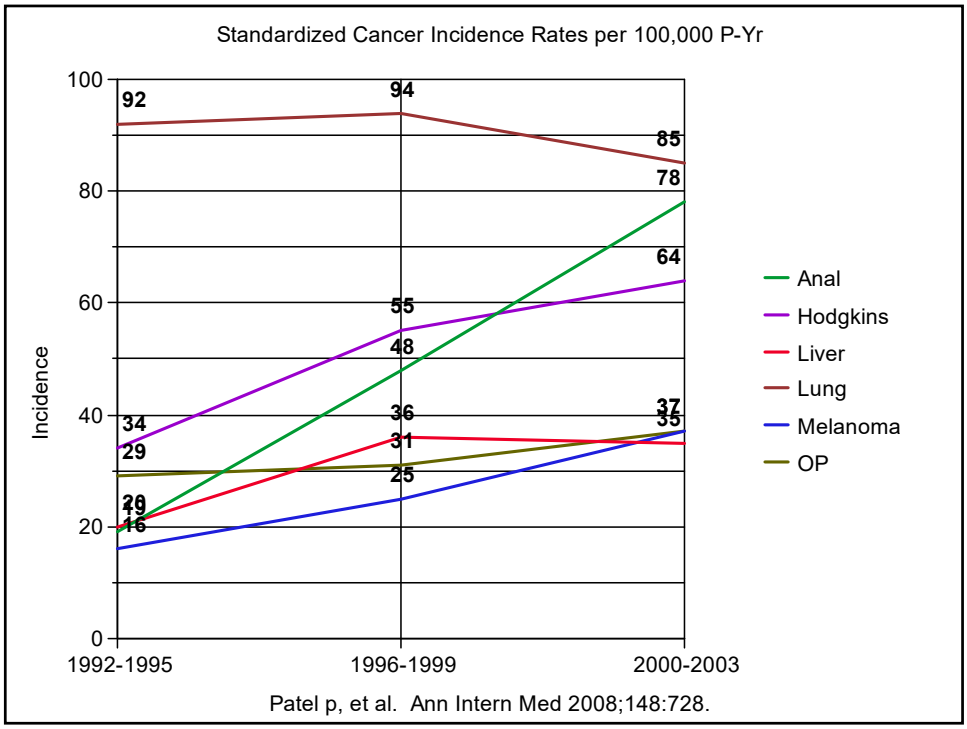
JNCI (2000);92:18, 1500-1510.

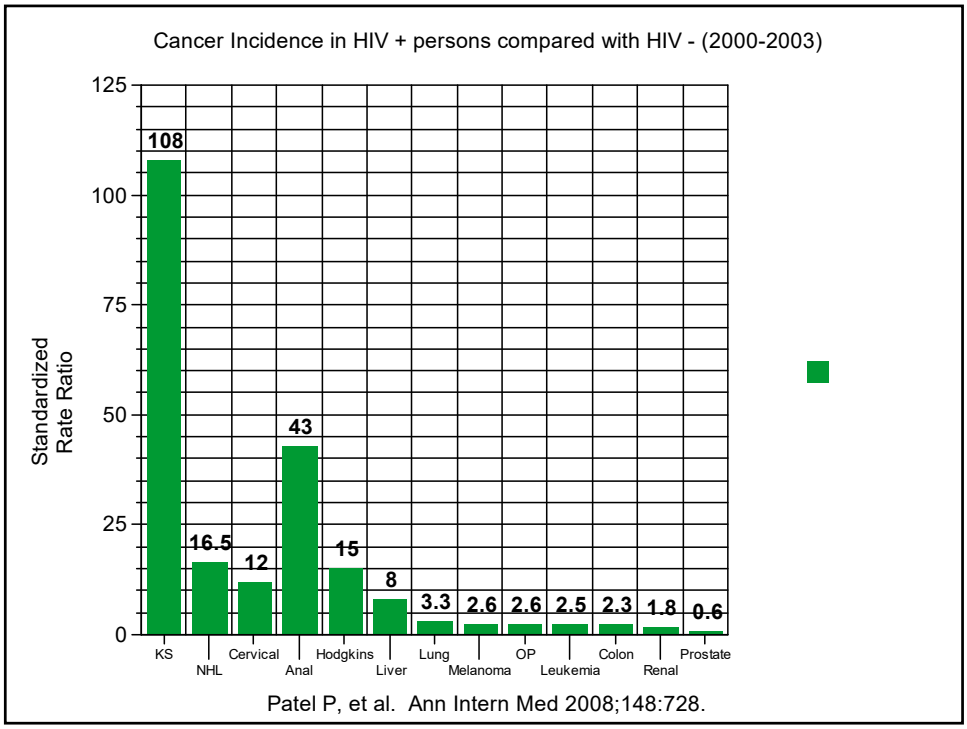


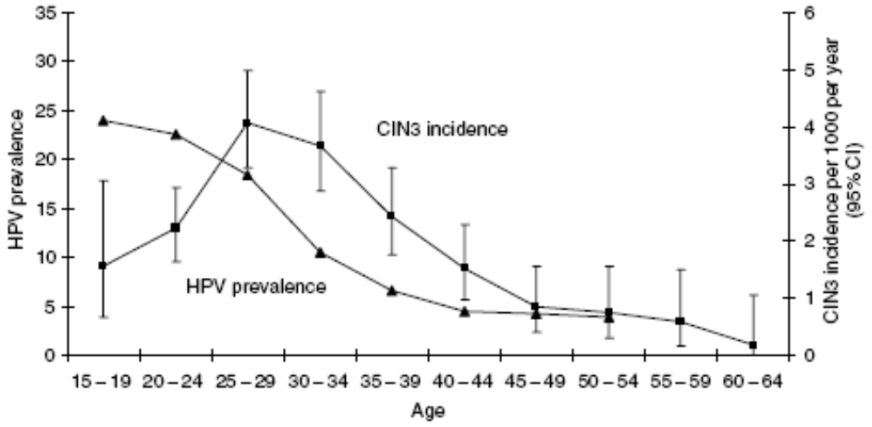
JNCI 2000;92:18 1500-1510



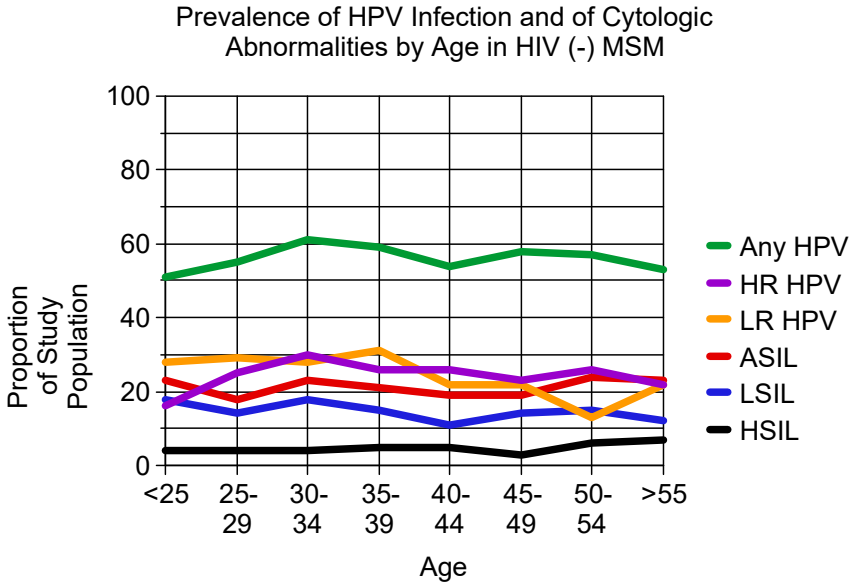
Patel p, et al. Ann Intern Med 2008;148:728.


Standardized Cancer Incidence Rates per 100,000 P-Yr
Incidence
100
80
60
40
20
0
92
94
85
78
64
55
48
34
29
36
31
37
35
25
20
19
16
1992-1995
1996-1999
2000-2003
Anal
Hodgkins
Liver
Lung
Melanoma
OP
Patel p, et al. Ann Intern Med 2008;148:728.


Cancer Incidence in HIV + persons compared with HIV - (2000-2003)
Standardized Rate Ratio
125
100
75
50
25
0
108
16.5
12
43
15
8
3.3
2.6
2.6
2.5
2.3
1.8
0.6
KS
NHL
Cervical
Anal
Hodgkins
Liver
Lung
Melanoma
OP
Leukemia
Colon
Renal
Prostate
Patel P, et al. Ann Intern Med 2008;148:728.



Br J Cancer (2004)91(5)):942-953.

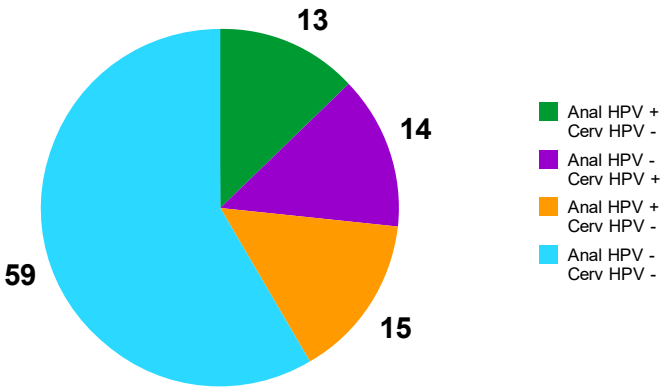


Adapted from EXPLORE study, JID (2004);190:2070-6. JNCI (2005);97:896-905.

Incidences of Anal and Cervical Cancer

- Cervical Cancer prior to PAP smears
  50/100,000
- Cervical Cancer, now
  8/100,000
- Anal Cancer in the general population
  0.8/100,000
- Anal Cancer among HIV (-) MSM
  5-35/100,000
- Anal Cancer among HIV (+) Women
  30/100,000
- Anal Cancer among HIV (+) MSM (HAART era)
  131/100,000

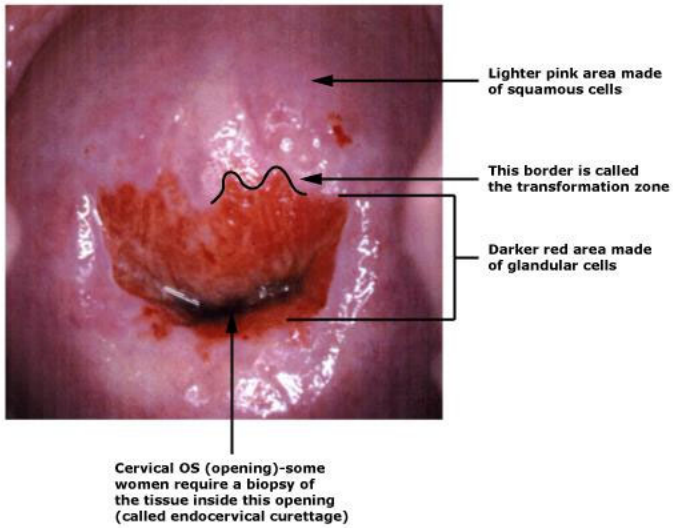
HPV Infection in Anal and Cervical Specimen Pairs

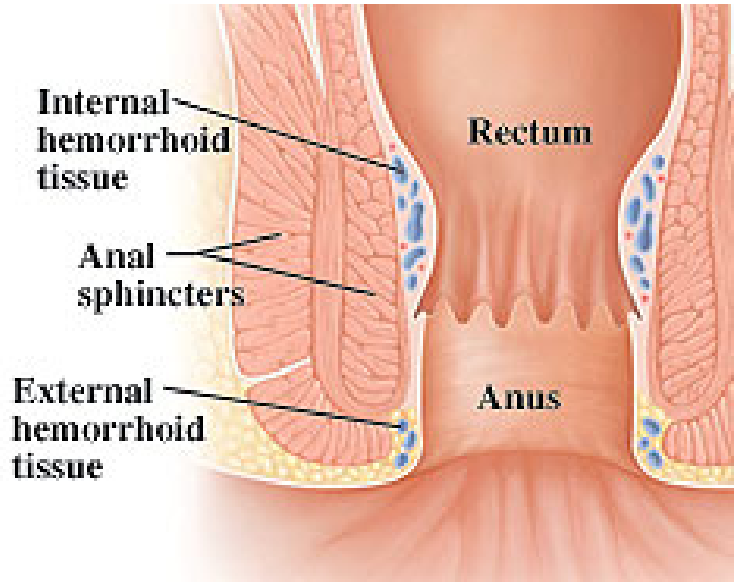


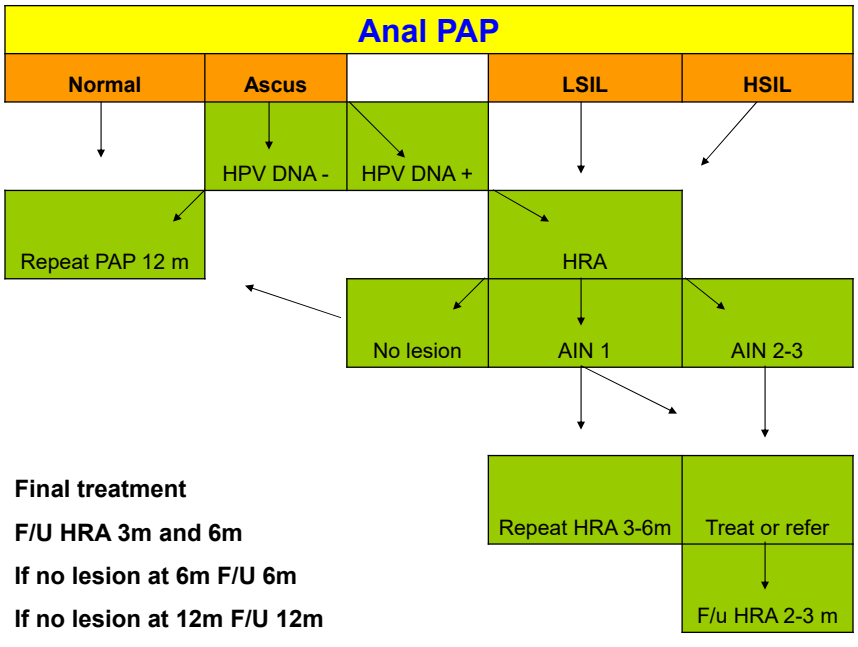
Cancer Epidemiology Biomarkers Prev. 2005;14(11). Nov 2005

Cervical PAP screening

- Baseline GYN exam with PAP smear for all HIV positive women.
- Repeat PAP in 6 months, and every 12 months thereafter if normal.
- If PAP is abnormal, repeat every 6 months until two sequential PAP smears are normal.
- PAP every six months if CD4 <200.
- Refer ASCUS and all higher grade cytology to GYN for colposcopy.
- After colposcopy:
  - CIN1: PAP every 4-6 months
  - CIN2-3: Refer to GYN for Ablation (LEEP, conization) Then PAP q3-4m for 1yr.







Final treatment

F/U HRA 3m and 6m

If no lesion at 6m F/U 6m

If no lesion at 12m F/U 12m

HIVMA Primary Care Guidelines

Aberg, JA, et al. *Clin Infect Dis*, 2014:**58** e1-53.

Anal cytology for:

- HIV infected MSM.
- HIV-infected women with a history of receptive anal sex or abnormal cervical PAP smear.
- HIV-infected persons with ano-genital warts.
- Abnormal results should prompt HRA.

Weak recommendation, Moderate quality evidence.

ANCHOR Study Top Line Results

- Randomized trial to establish efficacy of destruction of HGAIN to prevent anal cancer
- 4446 patients enrolled in >10 sites in US and Puerto Rico. HIV pos men and women with biopsy-proven HGAIN. Broad gender and ethnic/racial diversity
- Randomized to treatment (93% had HYF although other treatments were permitted) vs observation
- Treatment associated with 57% reduced risk of anal cancer. P 0.029

Notable details

- 52% of patients had HGAIN at screening visit. This is high.
- Protocol initially did not permit prior treatment for HGAIN, but this was modified to increase enrollment.
- Thus, the study population was not only HIV pos and HGAIN, but also enriched for patients who had failed prior treatment for HGAIN.
- Cancer rates were much higher than historical controls:
  - Treatment 173/100,000 vs Observation 442/100,000
  - Compare this with cancer incident rate of 120/100,000 in HIV pos MSM 4x excess cancer risk.
- Treatment effect was 57% risk reduction. Compare this with 10-fold risk reduction for cervical cancer in average risk women .

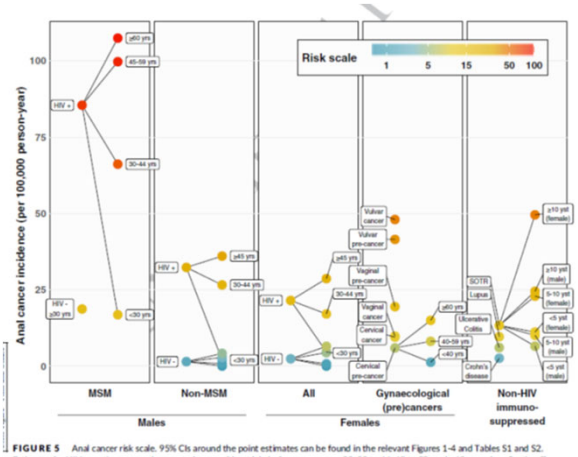


FIGURE 5 Anal cancer risk scale. 95% CIs around the point estimates can be found in the relevant Figures 1-4 and Tables S1 and S2. Estimates for HIV-negative men and men are shown, without labels, for age-groups <30, 30 to 44, 45 to 59, and ≥60 years (see Section 3). CI, confidence interval; MSM, men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

Who should be screened with Anal Cytology?

- All HIV (+) MSM, annually.
- All HIV (+) patients with anogenital condylomata.
- All HIV (+) women with abnormal cervical or vulvar cytology.

? All HIV (+) women

? All HIV (-) MSM, if neg repeat every 2-3 years.

? All men and women with transplant associated immunosupression

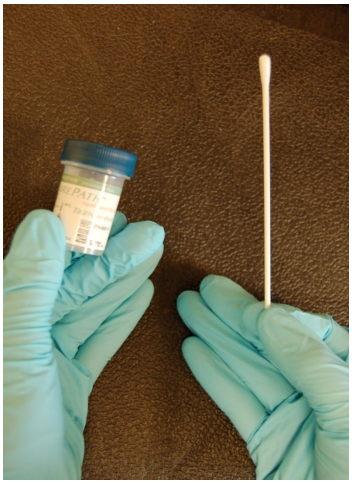
Cervical HPV and HSIL predicts anal HPV in HIV neg and HIV pos women

• Anal HPV-16 prevalence	41%	Cervical HPV-16 +
HIV NEG	2%	Cervical HPV-16 -
• Anal HPV-16 prevalence	46%	Cervical HPV-16 +
HIV POS	11%	Cervical HPV-16 –
• Anal HSIL	24%	Cervical HPV-16 +
HIV NEG	2%	Cervical HPV-16 –
• Anal HSIL	17%	Cervical HPV-16 +
HIV POS	8%	Cervical HPV-16 -
• Anal HPV-16 prevalence	44%	Cervical CA
HIV NEG		

Lancet ID 2019; 19:880-91

13,427 women with paired anal and cervical HPV DNA and cytology

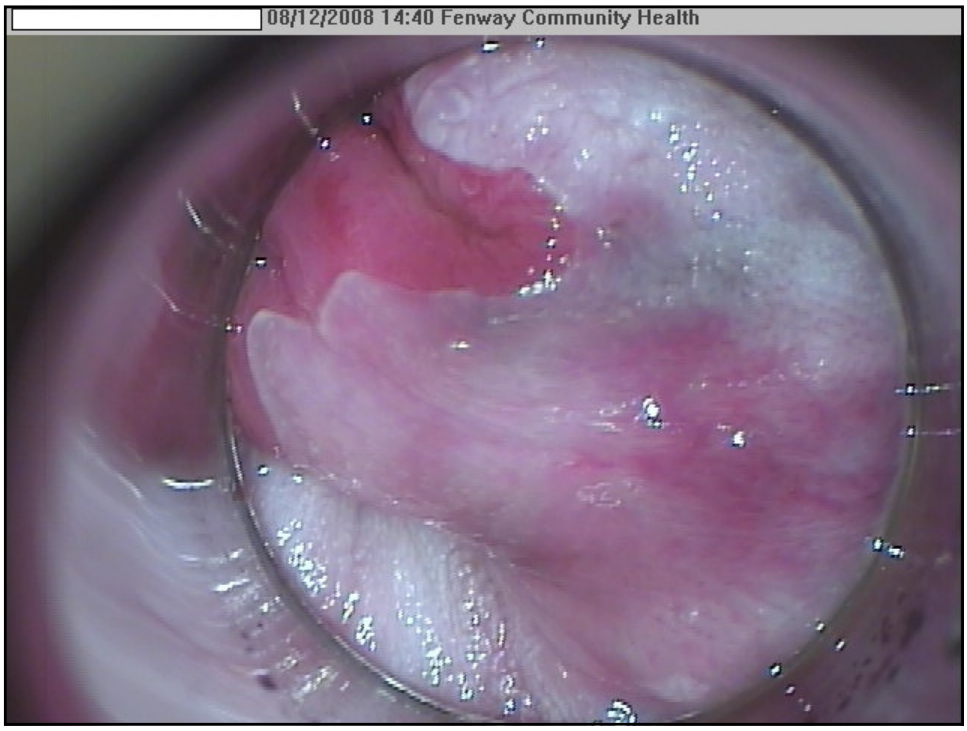
Anal Cytology

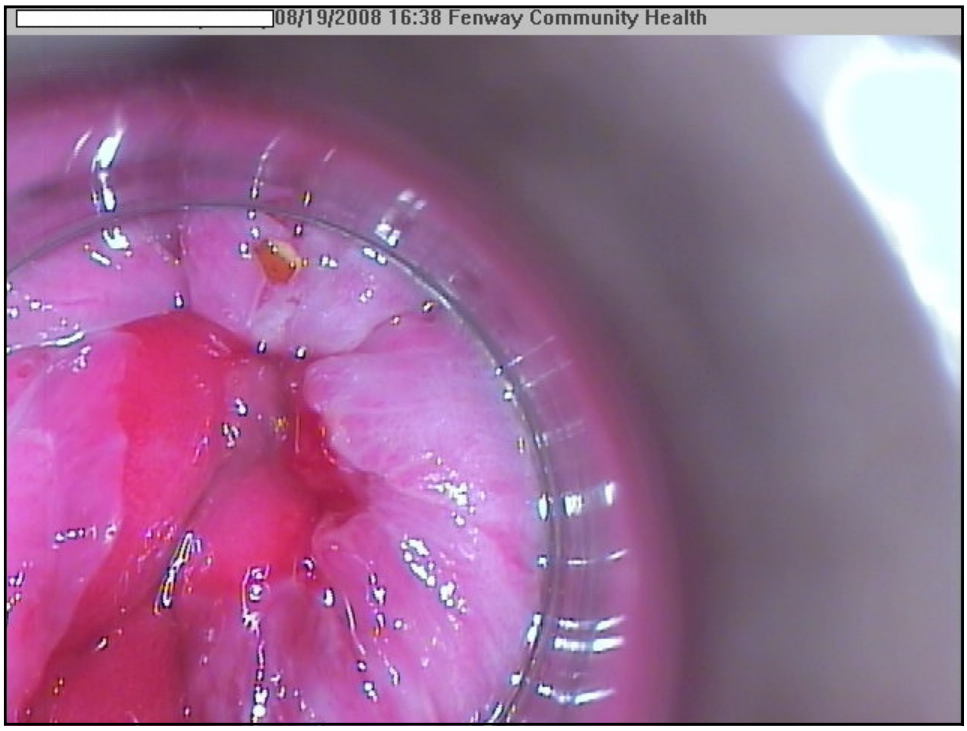


- Dacron swab moistened with tap water.
- Insert into anal canal until resistance is not met (2 cm).
- Rotate and apply pressure to walls of anal canal while slowly withdrawing.
- Liquid-based cytology or direct smear.

High Resolution Anoscopy

- Analagous to cervical colposcopy
- Application of 5% acetic acid turns dysplastic mucosa white
- Biopsy establishes degree of dysplasia
- Low-grade lesions (AIN1) may be ablated or followed.
- High-grade lesions (AIN2-3) may be ablated or referred for surgical excision.


08/12/2008 14:40 Fenway Community Health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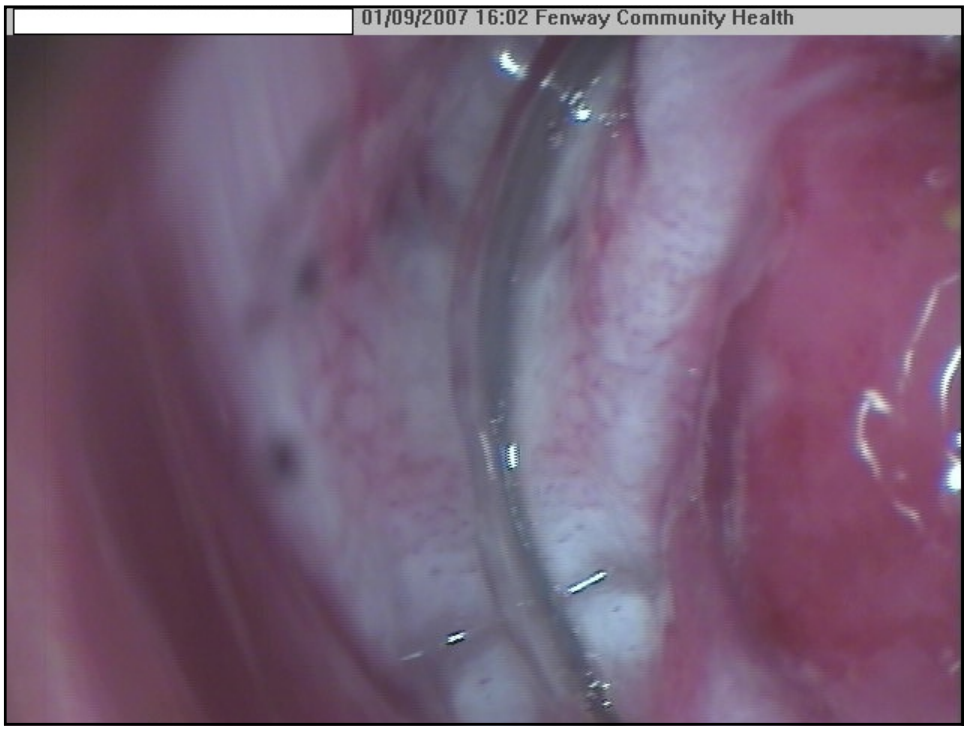
01/09/2007 16:02 Fenway Community Health