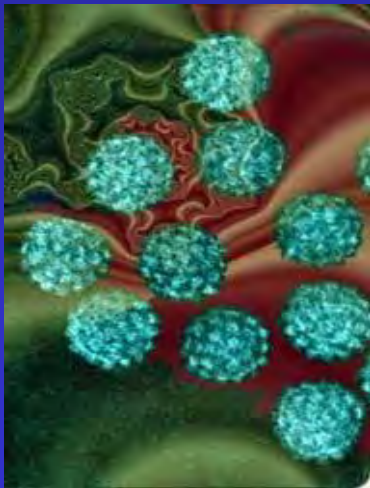


# HPV From the Bottom Up

*Evolving Strategies for the Treatment &  
Prevention of Anal Disease*



Rebecca A. Levine, MD

Assistant Professor of Surgery

Colon & Rectal Surgery

Montefiore Medical Center

Einstein College of Medicine

# Disclosures

- nothing financial



# Overview

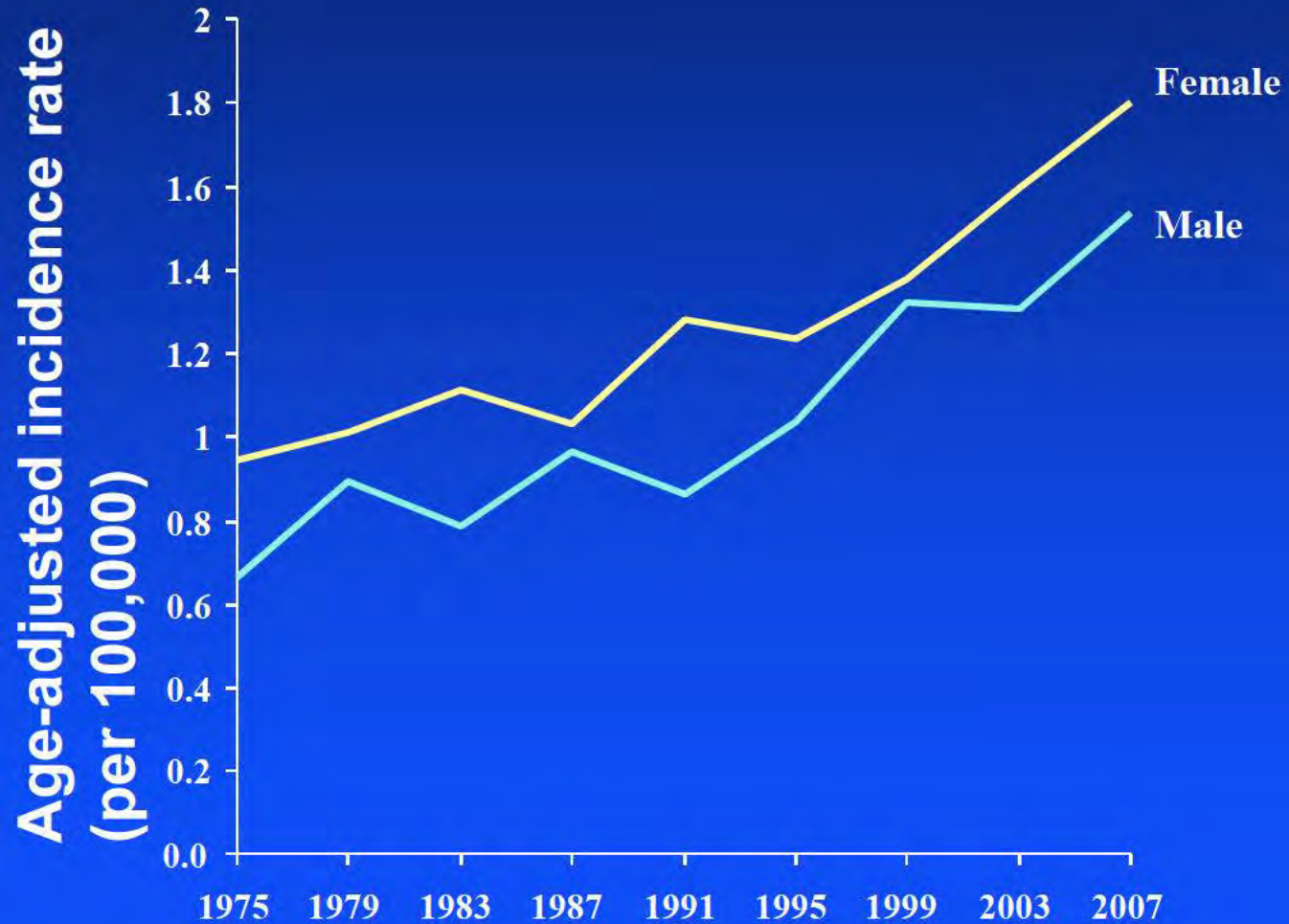
- Background...Anal Cancer
- HPV
- Anal Dysplasia
- Primary Prevention – VACCINE
- Secondary Prevention
  - screening
  - treatment
- Future Directions...



# Anal Cancer *Epidemiology*

- overall US incidence **1.8/100,000** (2008-2012)
- mostly squamous, more common in women
- median age **57** (men), **68** (women)
- **7270 new cases, 1010 deaths predicted 2015**
- most occur in **HIV NEG** population
- increased incidence over age 70
  - **3.1/100,000 in men**
  - **5.2/100,000 in women**
- *cervical cancer incidence 6.7/100,000*

# Age-adjusted incidence rate of anal cancer by gender and year of diagnosis



# Risk Factors *(pre-HIV)*

- Smoking
- Chronic irritation - *hem, fistulas, fissures*
- Inflammation ??IBD
- Exposure to HPV (**oncogenic types**)
  - genital warts, other STDs
  - multiple sex partners
  - anoreceptive intercourse NOT NECESSARY
- MSM (*up to 36.9/100,000*)
- Immunosuppression

# Anal Cancer & HIV

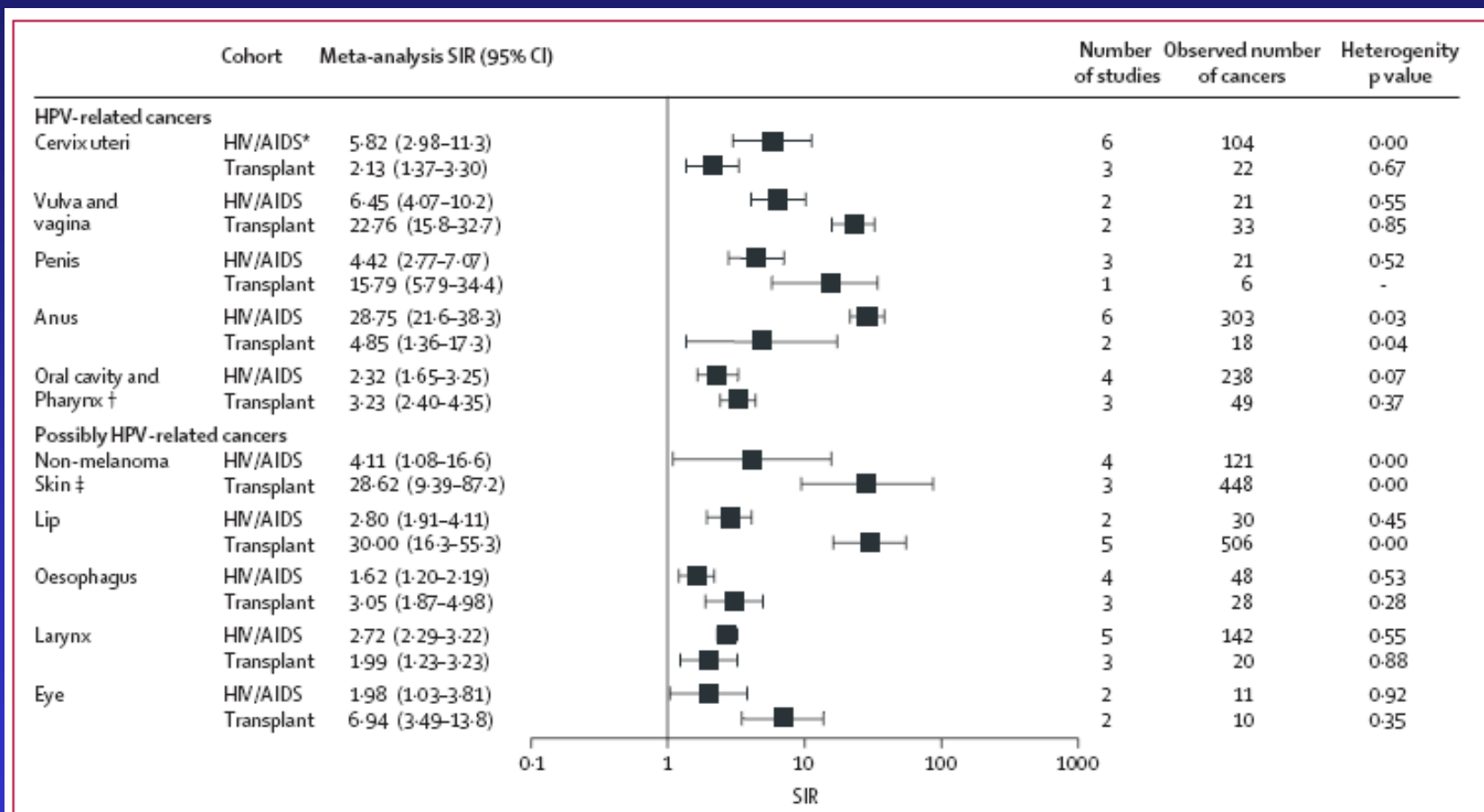
- 100 fold increased risk
- worse with lower CD4 counts
- NOT AIDS-defining malignancy
- Incidence (*per 100,000 person yrs*)
  - **111.2 HIV+ vs. 7.4 HIV neg<sup>1</sup>**
  - **131 HIV+ MSM, 46 MSW, 30 women<sup>2</sup>**
- **higher than cervical cancer incidence anywhere in the world**

1. Smola, et al. J clin Epidemiol 2001; 54: S61

2. Silverberg, et al. CID 2012.

# HPV-Related Cancers in HIV+ & in Transplant Patients

*Grulich et al, Lancet 2007; 370: 59–67*



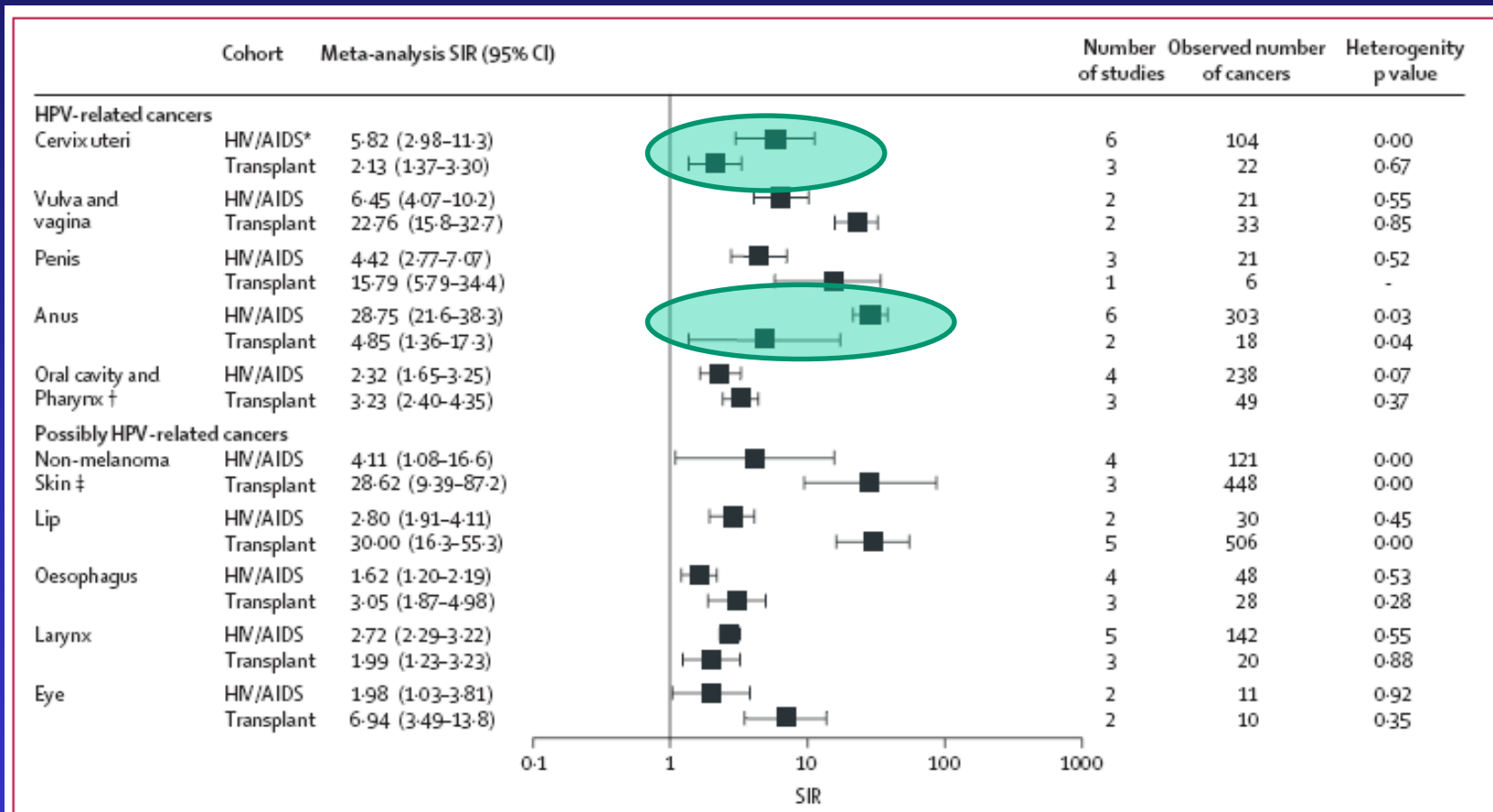
**Figure 3: Standardised incidence ratios for cancers related to, or possibly related to, human papillomavirus infection, in people with HIV/AIDS and in transplant recipients**

HPV= human papillomavirus. \*For the AIDS-defining cancer (cervical cancer), data from cohorts defined by an AIDS diagnosis included only those individuals who did not have cervical cancer at the time of AIDS. †Excluding lip and nasopharynx. ‡Any measure of non-melanoma skin.



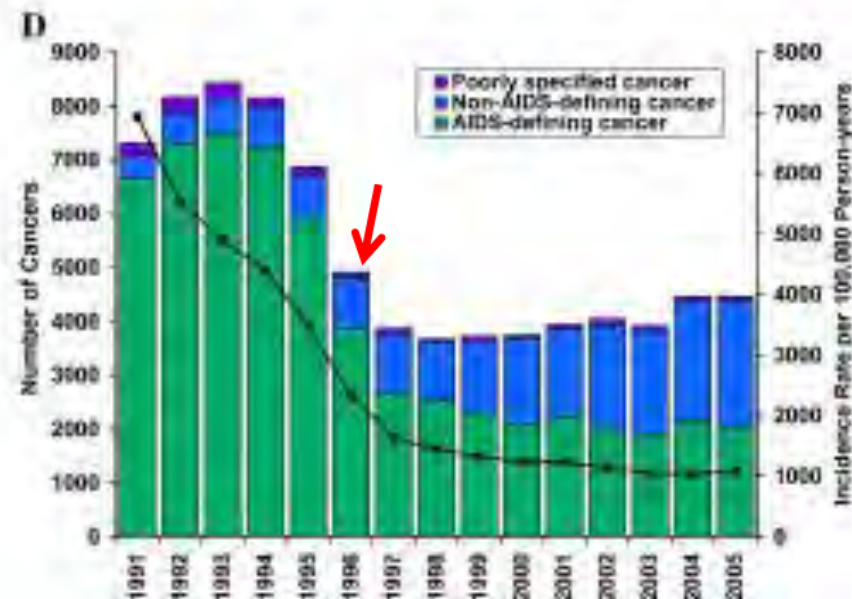
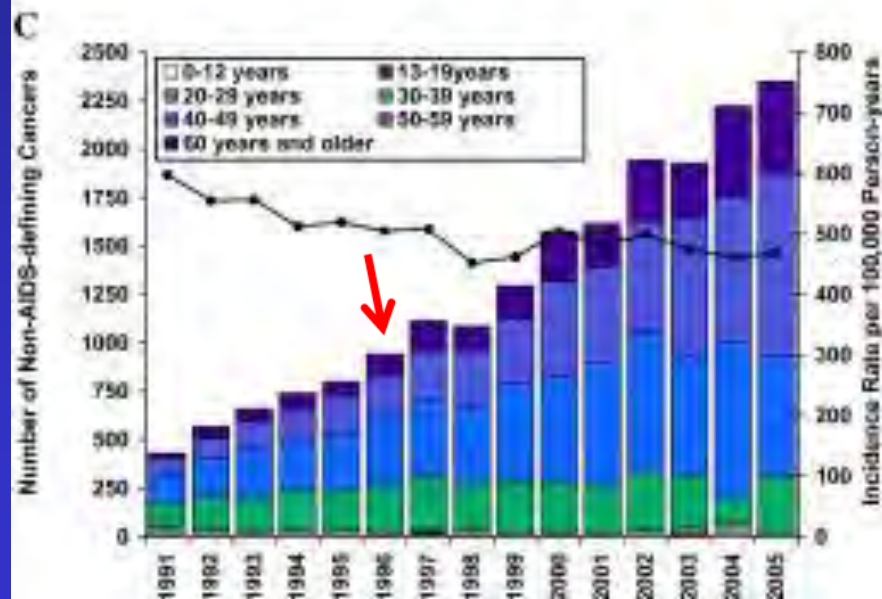
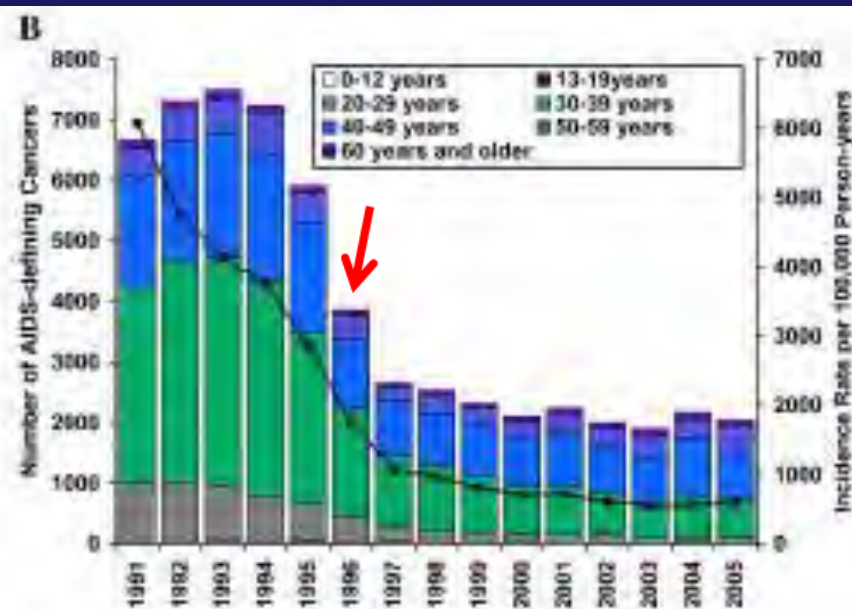
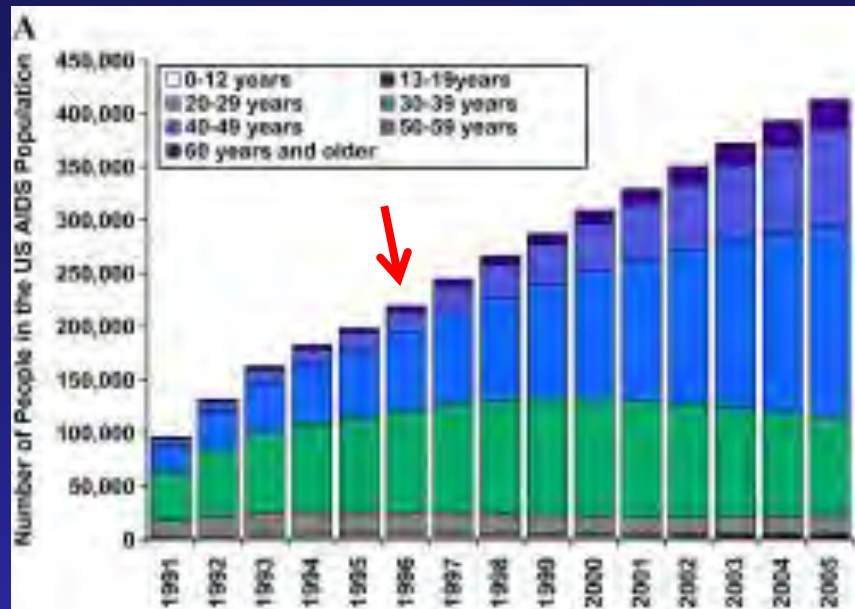
# HPV-Related Cancers in HIV+ & in Transplant Patients

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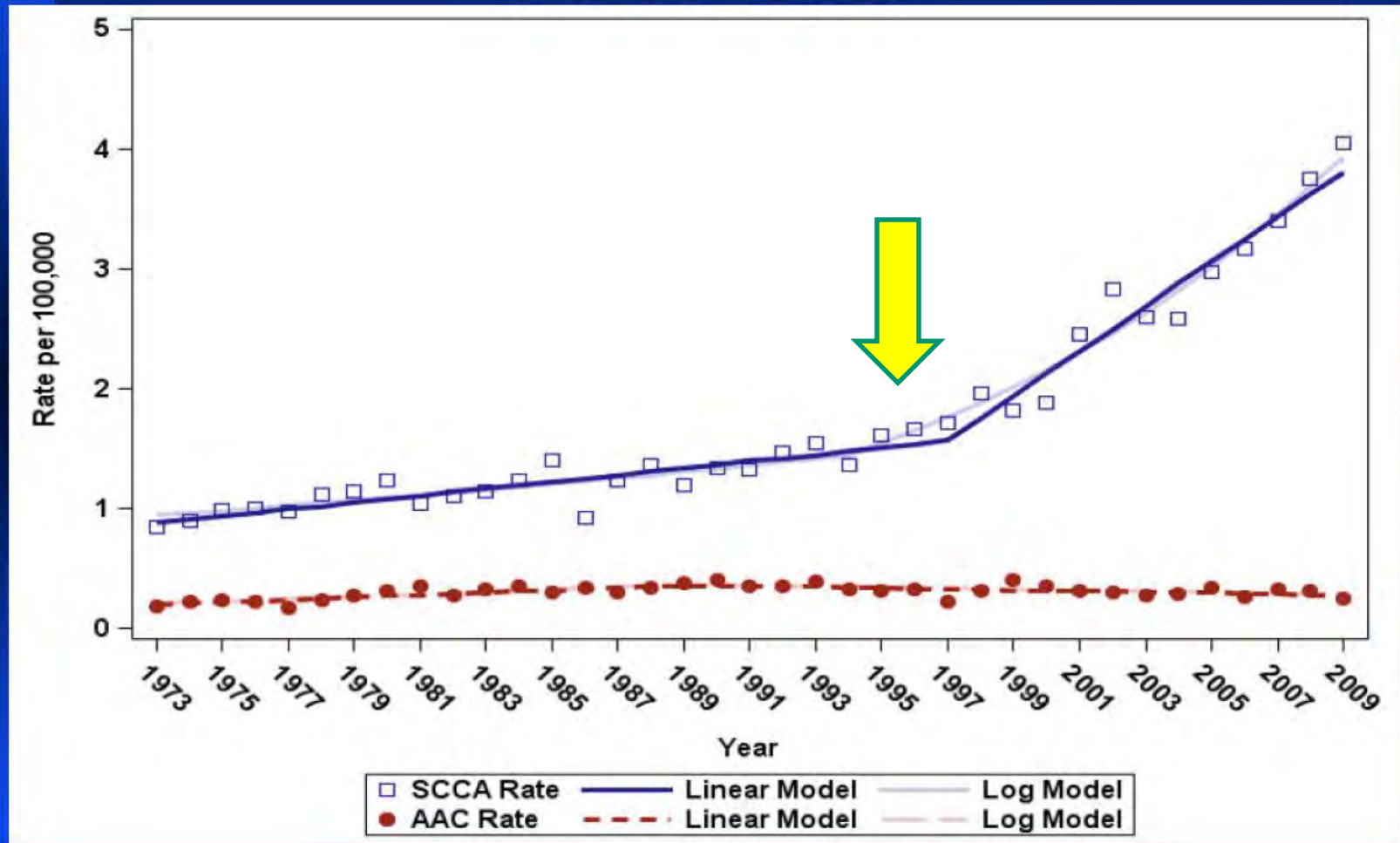


**Figure 3: Standardised incidence ratios for cancers related to, or possibly related to, human papillomavirus infection, in people with HIV/AIDS and in transplant recipients**

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# Incidence of anal cancer in the ART era



# Impact of ART therapy

- **8640 HIV+MSM in London** (*Bowers, et al. JAIDS 2004*)
  - Pre-ART 35/100,000
  - Post-ART 92/100,000
- **SEER data** (*Chiao, et al. JAIDS 2005; 40: 451*)
  - Pre-HIV (1973-1981) 0.6/100,000
  - HIV pre-ART (1982-1995) 0.8/100,000
  - HIV post-ART (1996-2001) 1.0/100,000

# Impact of ART therapy

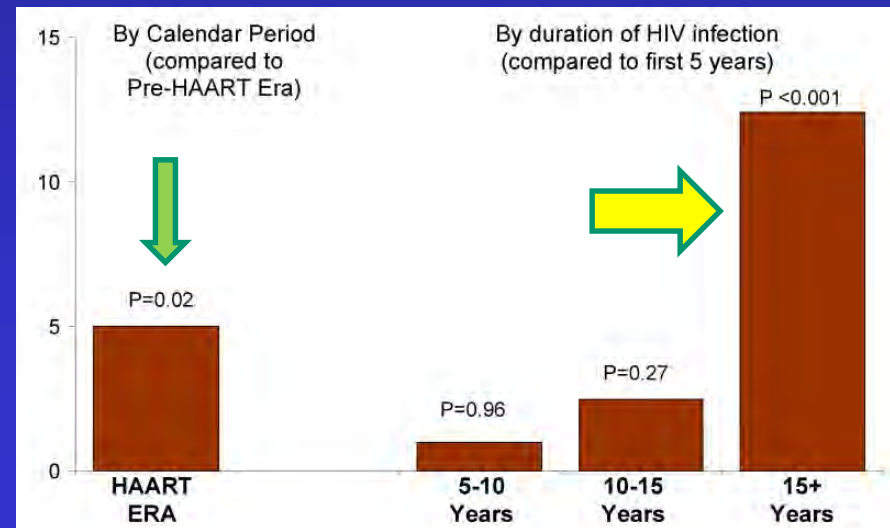
Anal cancer among HIV-infected persons Crum-Cianflone *et al.*

Table 2. Age-adjusted incidence rates of anal cancer by calendar period among men during the HIV epidemic (1985–2008).

Interval	Number of people followed	Years of follow-up	Number of events	Rate	95% CI	Rate ratio	95% CI	P
Pre-HAART (1985–1995)	3252	18 905	3	11.0	2.0–60.2	Referent		
HAART (1996–2008)	3222	18 893	16	55.0	8.9–339.1	5.0	1.4–18.4	0.02
1985–1998	2391	7956	1	7.9	1.0–61.9			
1991–1995	3004	10 944	2	11.0	1.2–99.3			
1996–2000	2547	8553	2	13.4	1.4–124.7			
2001–2005	2029	7483	7	51.1	6.2–442.9			
2006–2008	1546	2849	7	127.6	15.6–1042.2			
Overall	4506	37 806	19	61.9	7.6–502.7			

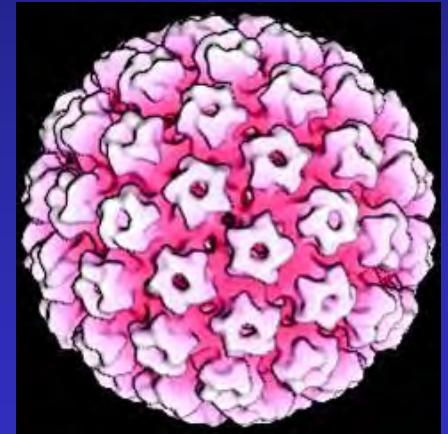
- 5x increased rates post ART
- 12x increase with HIV>15 yrs
- ART is not protective

**NEED PREVENTION**



# Human Papilloma Virus

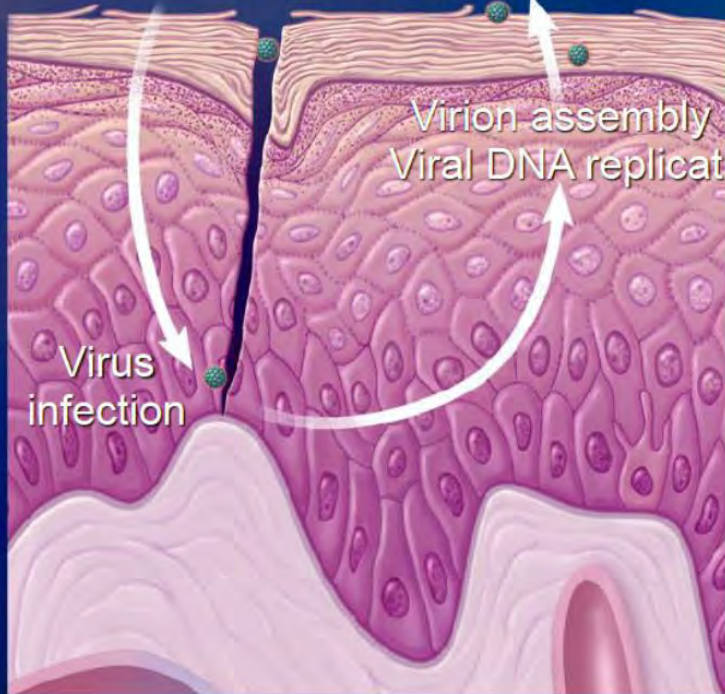
- circular, non-enveloped, double stranded DNA
- species specific & epitheliotropic
  - skin to skin contact
  - very stable
- over 100 types in humans
  - CUTANEOUS (1-4)
  - ANOGENITAL (6,11,16,18,31,33,35....)
  - over 12 oncogenic → **Types 16 & 18** in US



# HPV Infection and Productive Life Cycle

Virus introduced through microabrasion

Infectious virions shed



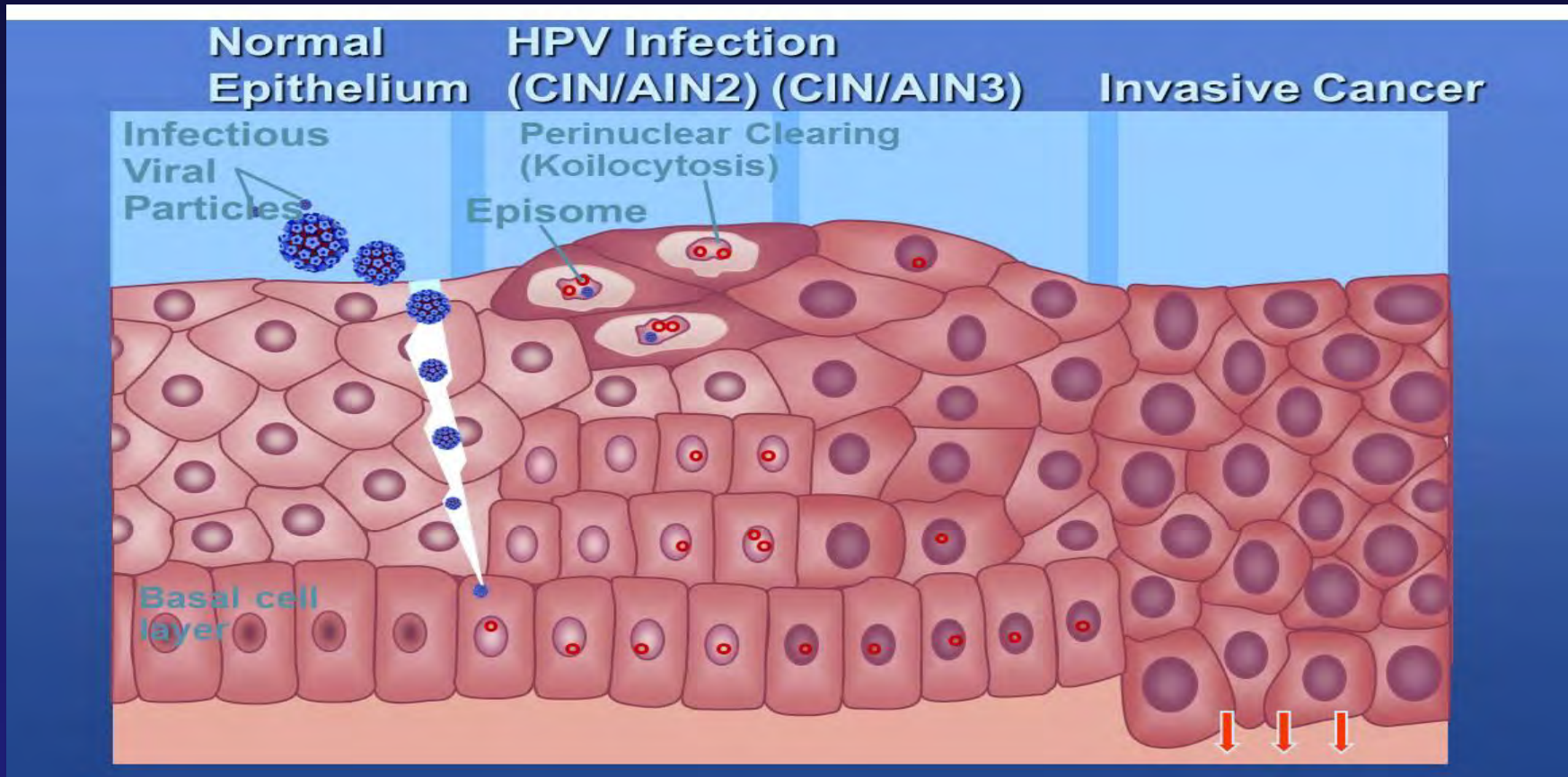
Virion assembly  
Viral DNA replication

Virus infection

Late HPV protein production  
L1 & L2

Early HPV protein production  
E1, E2, E4, E5, E6, & E7

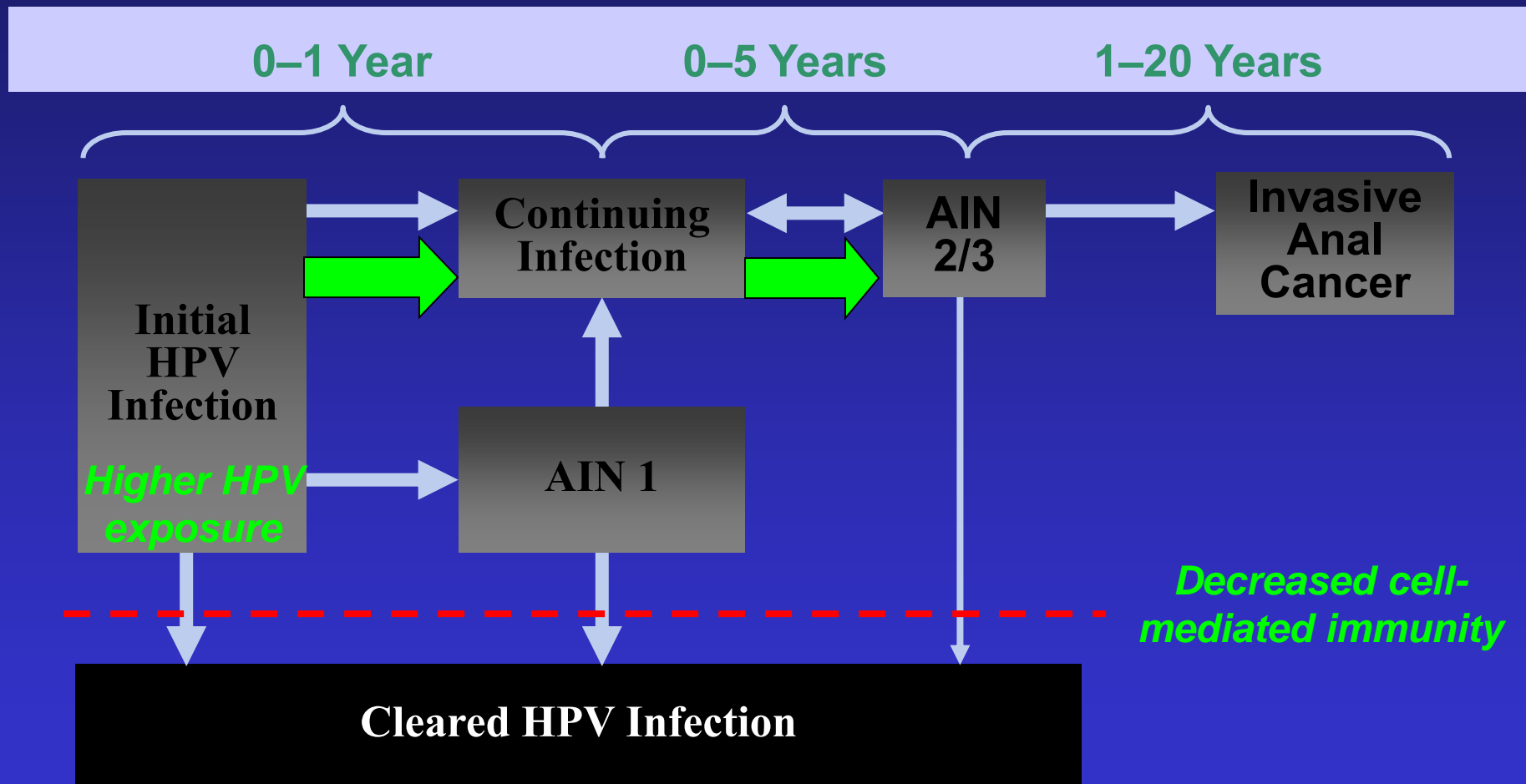
# HPV Oncogenesis



- inhibits & destroys tumor suppressor proteins (E6/E7)
- interferes with apoptosis & normal growth regulatory processes & stimulates cell division

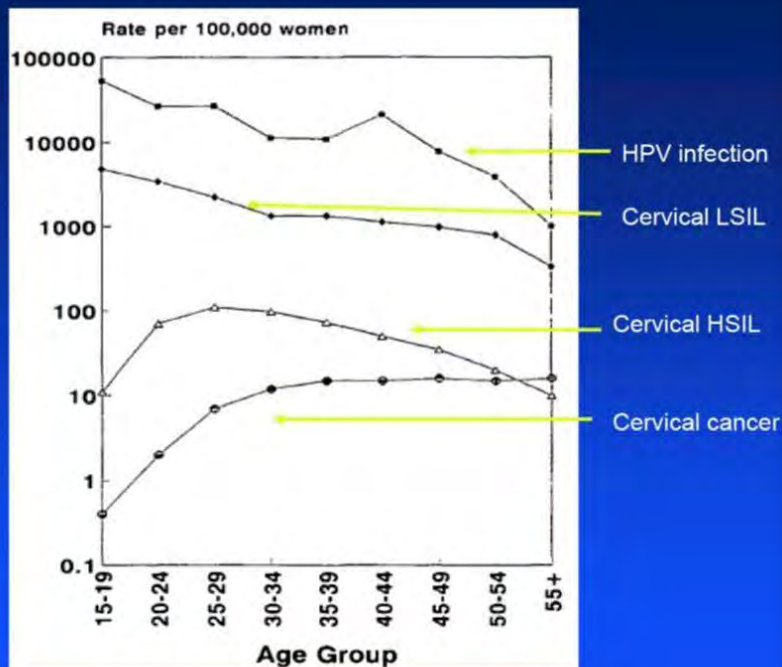


# Natural History of HPV Infection and Potential Progression to Anal Cancer

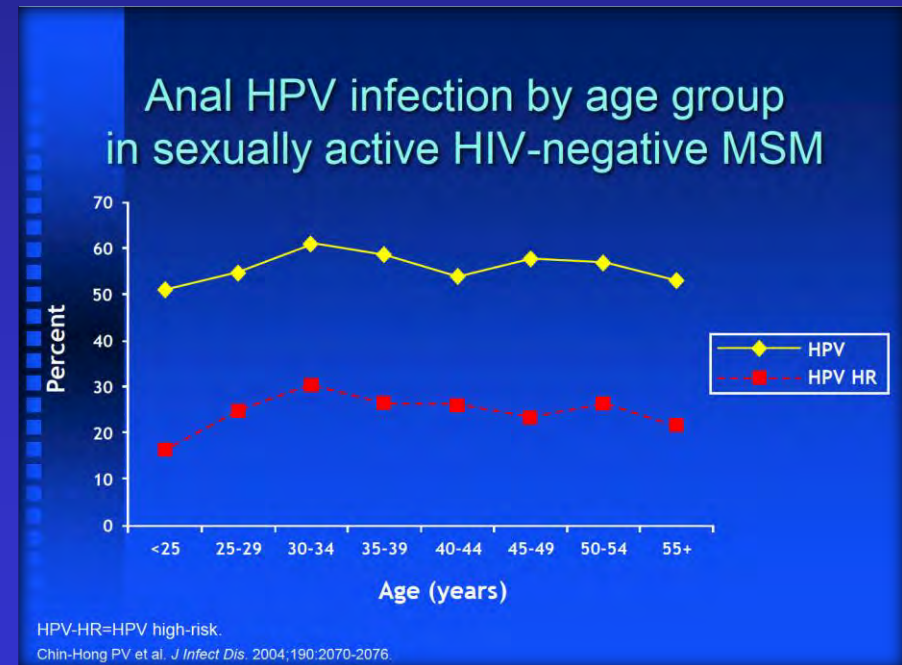


# Epidemiology of Anal HPV

- most studies performed in MSM & HIV
  - 90% have HPV (multiple types, at least one oncogenic)
  - no difference with ART, unclear relation to CD4<sup>1</sup>
- CERVIX → declines with age; ANUS → remains stable

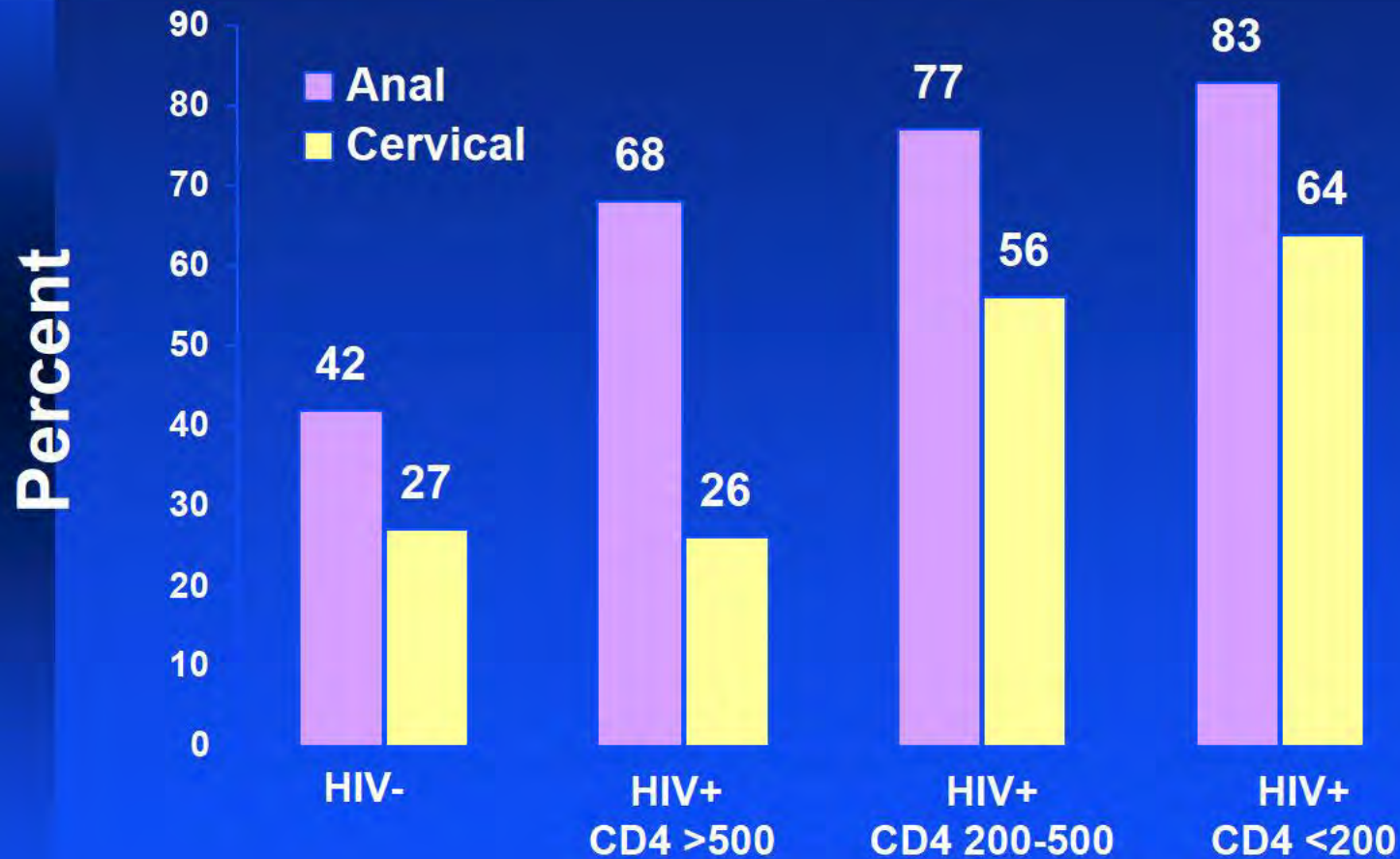


Schiffman, MH. J Natl Cancer Inst. 1992; 84:394-98



<sup>1</sup>Wilkin, et al. J Infect Dis 2004; 1685.

# Anal and cervical HPV infection in HIV-positive women and HIV-negative women at high risk of HIV infection



# Epidemiology of Anal HPV

- **MEN** *prevalence varies greatly...*
  - HIV+MSM 96%, MSW 59%<sup>1</sup>
  - HIV+MSM 100% (oncogenic 80%)<sup>2</sup>
  - HIV-MSM 60% (oncogenic 20-30%)<sup>3</sup>
  - HIV-MSW 12% (oncogenic 7%)<sup>4</sup>
  - anal intercourse is risk factor but **NOT NECESSARY**  
in MSW → number of partners & frequency of sex
- **WOMEN**
  - lower than men, sometimes higher than cervical  
(79% vs. 53% HIV, 43% vs. 24% high risk HIV neg)<sup>5</sup>
  - threefold increased in the presence of cervical HPV in healthy<sup>6</sup>
- **TRANSPLANT**
  - 21% of renal recipients<sup>7</sup>

1. Conley, L. *J Infect Dis* 2010: 1567.

2. Chin-Hong. *J Infect Dis* 2004: 2070.

3. Palefsky. *J Infect Dis* 1998: 361.

4. Nyitray, A. *J Infect Dis* 2010: 1499.

5. Palefsky. *J Infect Dis* 2001: 383.

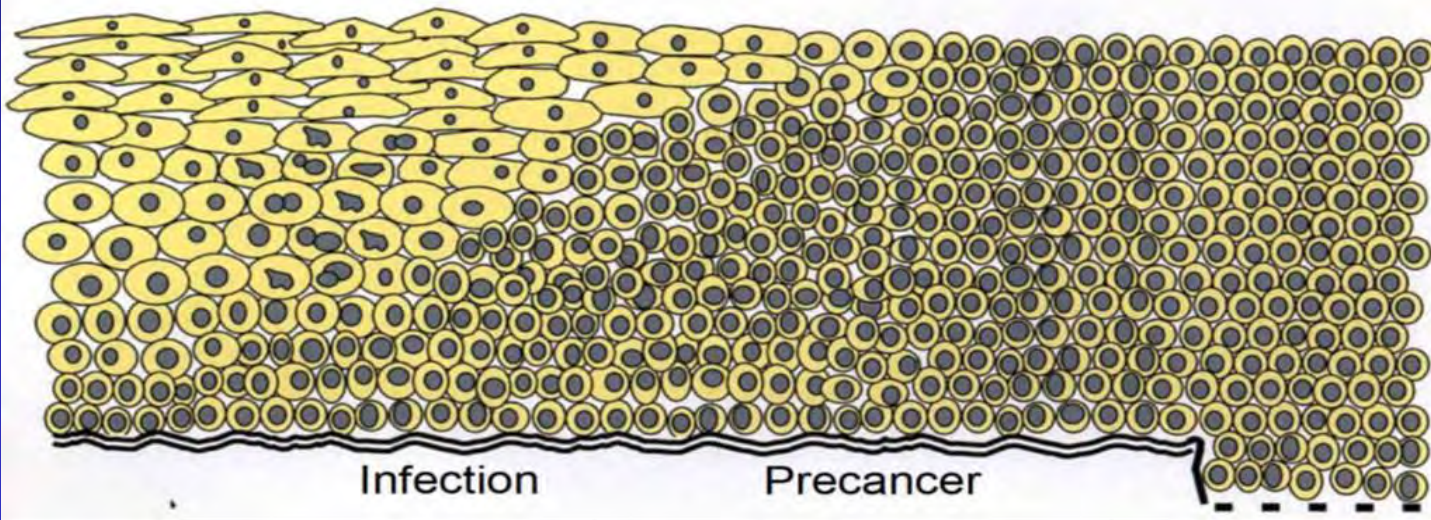
6. Hernandez. *Cancer Epidemiol Biomark Prev* 2005: 2550.

7. Patel. *Br J Surg* 2010: 1716.

# Epidemiology of AIN

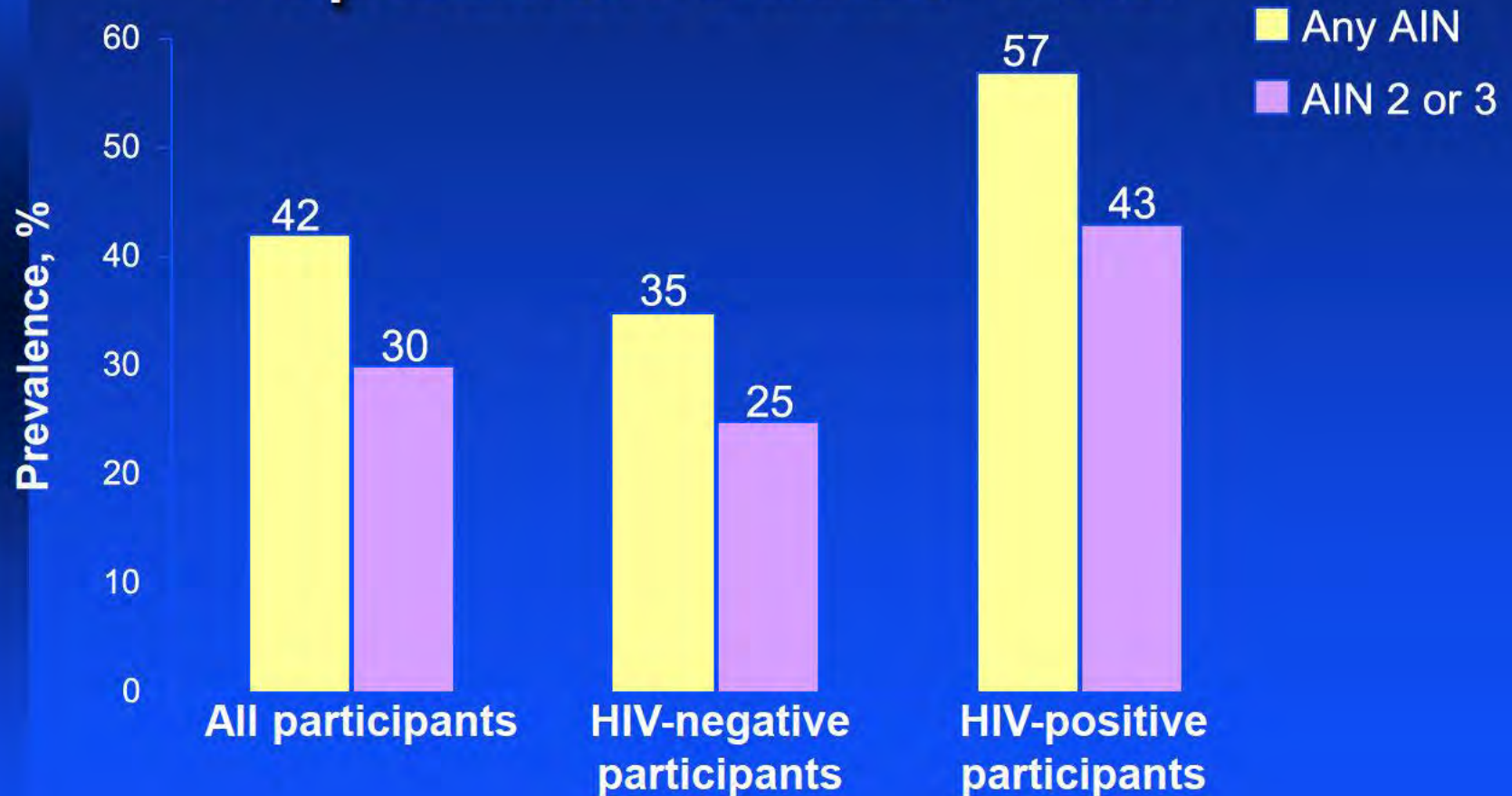
## HPV-associated Disease

NORMAL	LOW GRADE SIL		HIGH GRADE SIL			INVASIVE CANCER
	CONDY- LOMA	AIN1	AIN2	AIN3		
		MILD DYSPLASIA	MODERATE DYSPLASIA	SEVERE DYSPLASIA	IN SITU CARCINOMA	



- similar to HPV statistics
- highest in HIV+ MSM, then HIV- MSM, **no diff with ART tx**

# Prevalence of AIN among MSM Population-based data



# Progression to Cancer

## *Indirect Evidence*

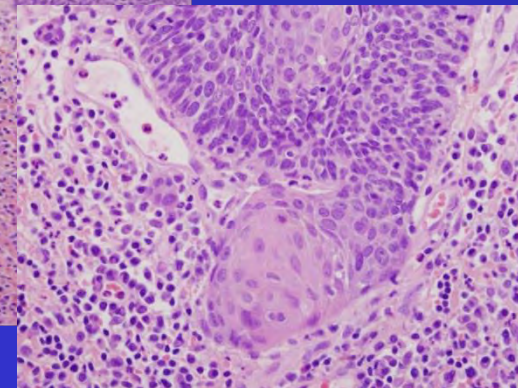
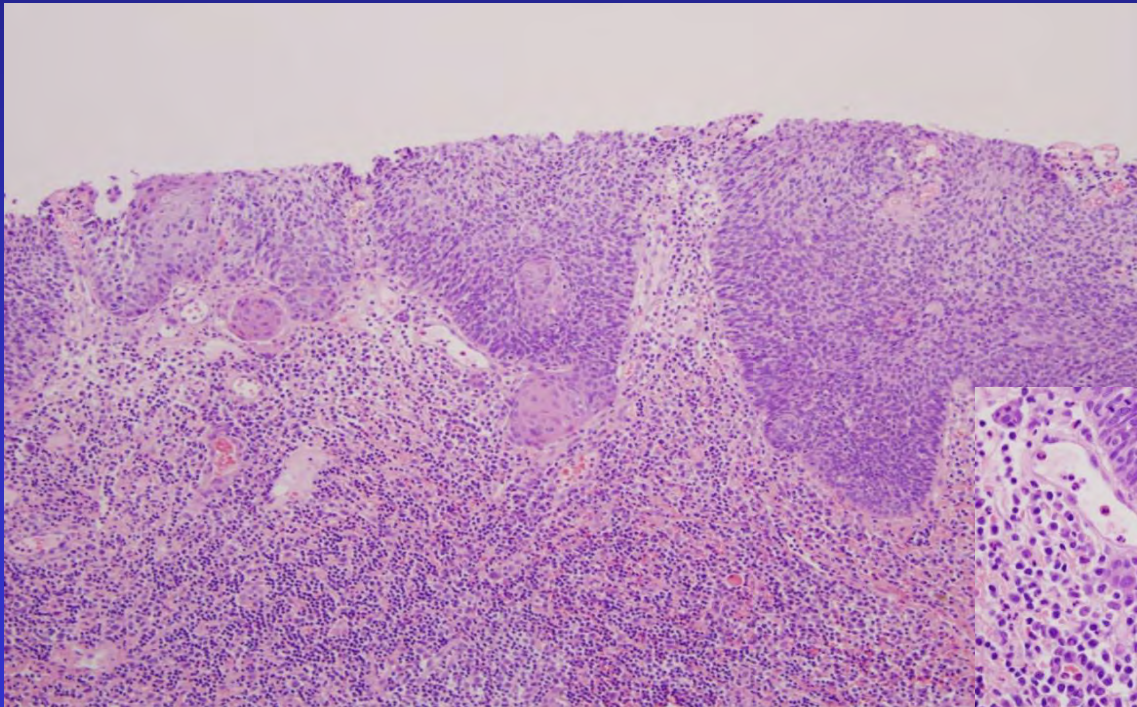
- SAN FRANCISCO<sup>1</sup> → 246 pts surgically treated for HSIL
  - **3 developed cancer**
  - 1.2% compared to 7.5% of pts observed
- TEXAS<sup>2</sup> → 124 pts with HSIL
  - 22 delayed or refused tx
  - **2 cancers** at 9 & 28 months
- GERMANY<sup>3</sup> → 156 HIV+MSM with HSIL
  - 5 refused treatment
  - **cancer in 3.2%** untreated (median of 8.6 mos.)
  - compared to 0% treated
- NEW ZEALAND<sup>4</sup> → 55 women & men treated for HSIL
  - **8 developed cancer** (median of 42 mos.)

1. Pineda. *Dis Colon Rectum* 2008: 829.
2. Weis. *Dis Colon Rectum* 2012: 1236.
3. Kreuter. *Br J Dermatol* 2010: 1269.
4. Watson. *ANZ J Surg* 2006: 715.

# Progression to Cancer

*Direct Evidence??*

- most patients with cancer have co-existent HSIL adjoining or overlying the malignant lesion



- superficially invasive cancer always develops from HSIL lesions



# Progression to Cancer

- Meta-analysis estimates (Machalek, et al. 2012)
  - 1/377 HIV+MSM with HSIL will progress to cancer
  - approximately 10% lifetime risk
  - *lower than CIN3 to cervical cancer (1/80)*
- most WILL NOT PROGRESS
- **BUT cannot predict which lesions will...**

# Anal Cancer

- Early detection makes a difference!

Stage at Diagnosis	Stage Distribution	5-year Survival
Localized (confined to primary site)	50%	80%
Regional (spread to regional lymph nodes)	29%	60%
Distant (cancer has metastasized)	12%	30%
<i>Unknown (unstaged)</i>	9%	56%

# Strategies for Prevention

- PRIMARY

- HPV Vaccine
- for both anal & cervical infection
- *best efficacy if administered PRE-EXPOSURE*

- SECONDARY

- Screening & treatment of dysplasia
- adapted from cervical protocols

# qHPV Vaccine

- In 2009, FDA approved qHPV for boys, age 9-26, to prevent warts
  - routine in all boys (age 9-21)
  - routine in MSM or immunosuppressed (age 22-26)
  - permissive in men (age 22-26)
- In 2010, FDA approved for women & men to prevent AIN & anal cancer

# HPV Vaccine

## *Other Indications & Concerns*

- **prevention of HSIL recurrence??**
  - 202 HIV-neg men treated, 88 vaccinated afterwards
  - decreased risk of recurrence, 13.6% vs. 30.7% (**HR 0.5, CI 0.26-0.98, p=0.04**)<sup>1</sup>
- **Efficacy in HIV patients**
  - will vaccine prevent anal HPV infection?
  - can pts mount immune response & maintain titers?
  - is there sufficient lack of exposure to HPV?
  - SAFETY

# Secondary Prevention

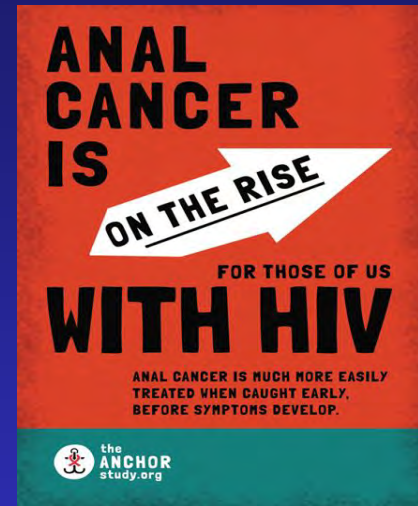
- Center for Disease Control & NIH & IDSA<sup>1</sup>
  - “anal cytology screening of HIV-seropositive MSM and of women might be useful preventive strategies. However, studies of screening and treatment programs for AIN 2 or 3 should be implemented before definitive recommendations for anal cytology screening can be made. **No national recommendations exist for routine screening for anal cancer**”
  - acknowledges that some specialists recommend cytology/HRA
- American College of Surgeons
  - “**anal cytology...may be useful** in early diagnosis of anal cancer and precancer...some doctors already recommend this test for people at high risk”

# Secondary Prevention

- American Society of Colon & Rectal Surgeons
  - 2012 Practice Parameters
  - **anal cytology may be useful** in the detection and follow-up of LGAIN/HGAIN
  - strong recommendation based on *low quality* evidence
- New York State Dept of Public Health
  - **“screening for cellular dysplasia is prudent and recommended, particularly in persons at high risk for infection with papilloma viruses”**
  - annual cytology for HIV+MSM, anyone with anogenital condylomas, women with CIN/VIN

# Secondary Prevention

- no formal screening guidelines
- no randomized data to support the efficacy of screening
- no standard of care
- extrapolation from cervical outcomes
  - prior to screening: incidence of cervical cancer 40-50/100,000
  - now 8-10/100,000
  - *rates of anal cancer in high risk populations over twice what cervical cancer was pre-screening, and increasing despite ART tx*



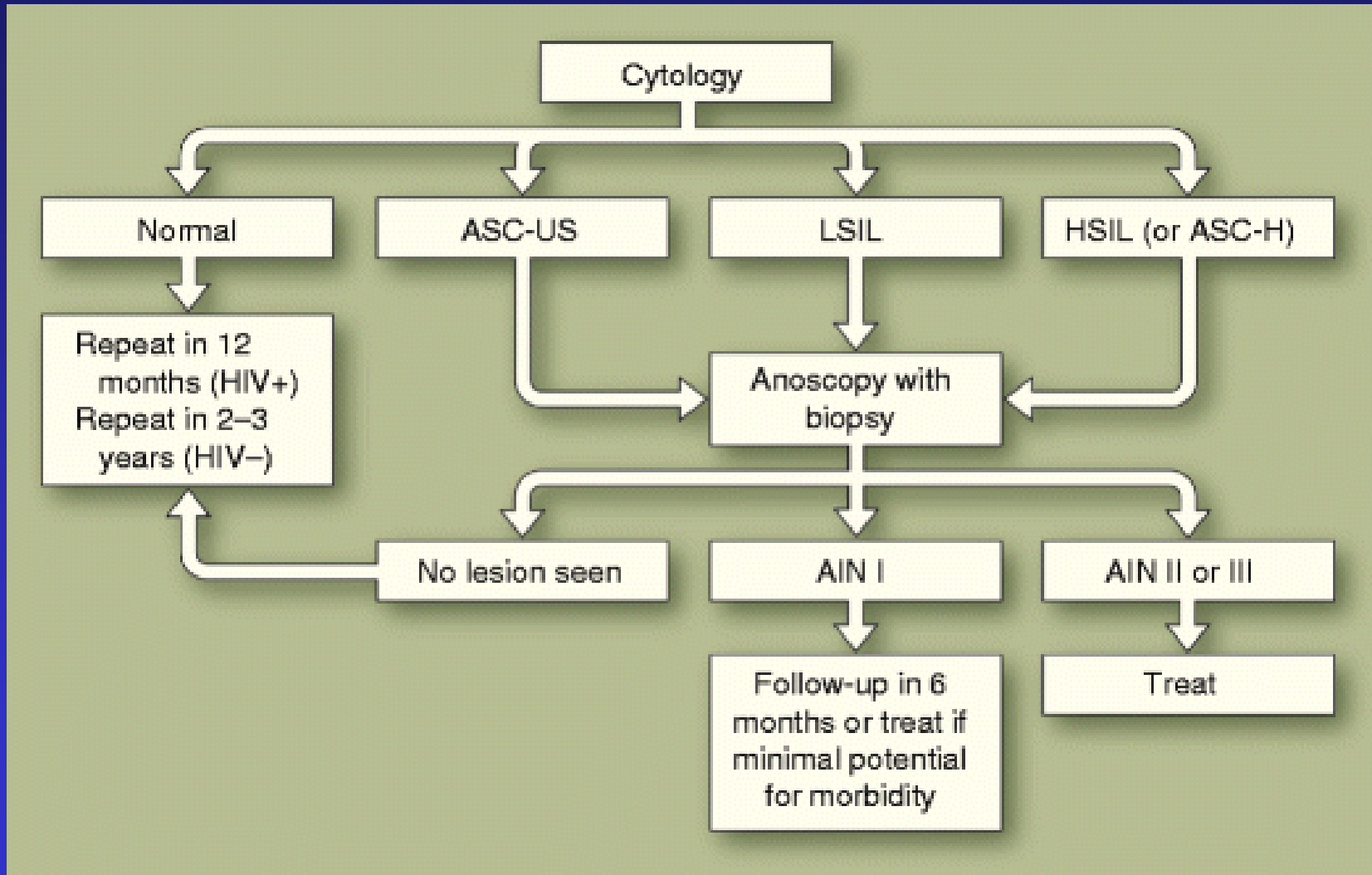


# Who should be screened?

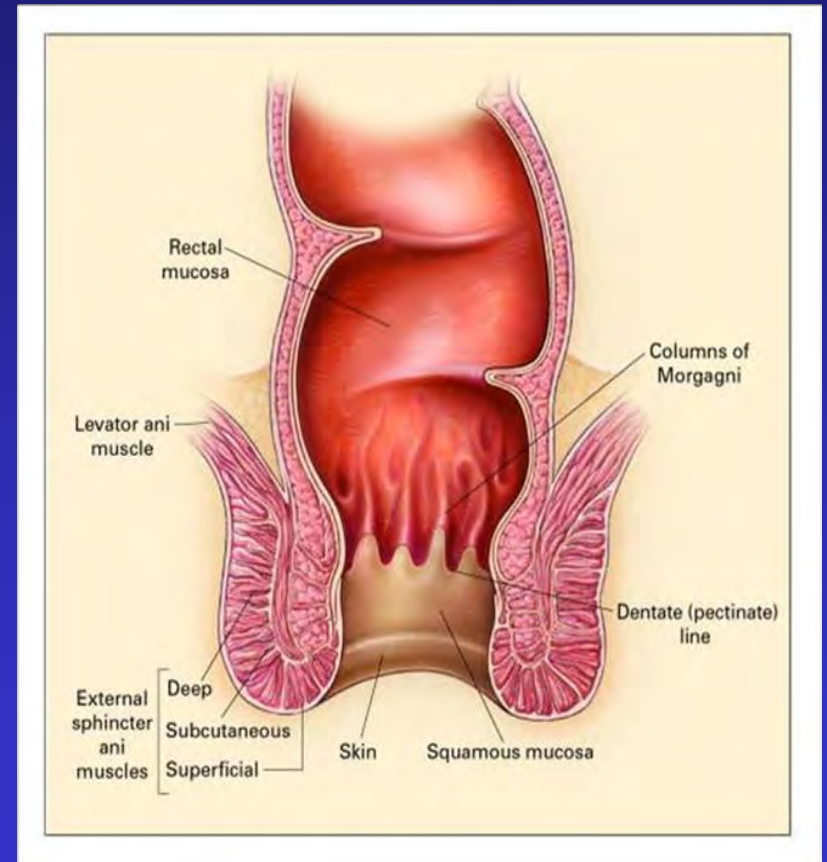
- all HIV positive men (MSM/MSW)
- all HIV positive women
- all MSM (HIV neg/pos)
- women with CIN/VIN
- solid organ transplant recipients
- pts with any form of immunosuppression??
- pts with perianal condylomas??
  - *over 30 if immunosuppressed*
  - *over 40 if immunocompetent*



# How should we screen?



# Anal Cytology



# Cytology performance

## Abnormal cytology and HSIL biopsy

	# Subjects	Sensitivity	Specificity	NPV	PPV
Panther et al	153 HIV+ & -	47%	90%	65%	81%
Salit et al	401 HIV+	84%	39%	88%	31%
Nahas et al	222 HIV+	16%	97%		
Bean et al	42 HIV+	92%	8%	33%	67%

## Benign cytology and AIN biopsy

	HSIL Cytology/non HSIL biopsy	Benign Cytology/ASIL biopsy	Benign Cytology/HSIL biopsy
Salit et al	26/47 (55%)	43/133 (32%)	16/133 (12%)
Nahas et al	8/13 (62%)	56/101 (55%)	7/101 (7%)
Panther et al	8/32 (25%)	8/19 (42%)	1/19 (5%)

Panther et al. Clinical Infectious Diseases 2004; 38:1490–2

Nahas et al Dis Colon Rectum 2009; 52: 1854–1863

Salit et al AIDS 2010, 24:1307–1313

Bean et al Journal of Lower Genital Tract Disease 2010; 14: 90-96

# 2010 screening results

1510 cytology results recorded and 848 had HRA

- mean age 43 (20-79) years
- Cytology results

non diagnostic	53 (4%)	ASCUS	553 (38%)
benign	582 (40%)	ASC-H	14 (1%)
		LSIL	286 (20%)
		HSIL	22 (2%)

	HISTOLOGY DIAGNOSIS				
CYTOLOGY	BENIGN	LSIL	HSIL	SCC	TOTAL
<b>BENIGN</b>	88 (52%)	48 (28%)	34 (20%)	0 (0%)	170 (20%)
<b>ASCUS</b>	166 (42%)	107 (27%)	126 (32%)	0 (0%)	399 (47%)
<b>ASC?H</b>	1 (8%)	3 (23%)	9 (69%)	0 (0%)	13 (2%)
<b>LSIL</b>	21 (9%)	96 (39%)	127 (52%)	2 (1%)	246 (29%)
<b>HSIL</b>	0 (0%)	1 (5%)	18 (90%)	1 (5%)	20 (2%)
<b>TOTAL</b>	276 (33%)	255 (30%)	314 (37%)	3 (0.4%)	848 (100%)

# Montefiore Experience

*(HIV+ women, 2008-2010)*

Preceding Cytology	Normal	Warts	AIN 1	High Grade AIN	Total
Atypical	2 (33.33%)	1 (16.7%)	3 (50.0%)		6 (7.4%)
ASCUS	6 (40.0%)	3 (20.0%)	2 (13.3%)	4 (26.7%)	15 (18.5%)
LGSIL	16 (41.0%)		13 (33.3%)	10 (25.6%)	39 (48.2%)
HGSIL	2 (33.3%)			4 (66.7%)	6 (7.4%)
None*	7 (46.7%)	1 (6.7%)	2 (13.3%)	5 (33.3%)	15 (18.5%)
Total	33 (40.7%)	5 (6.2%)	17 (21.0%)	26 (32.1%)	81

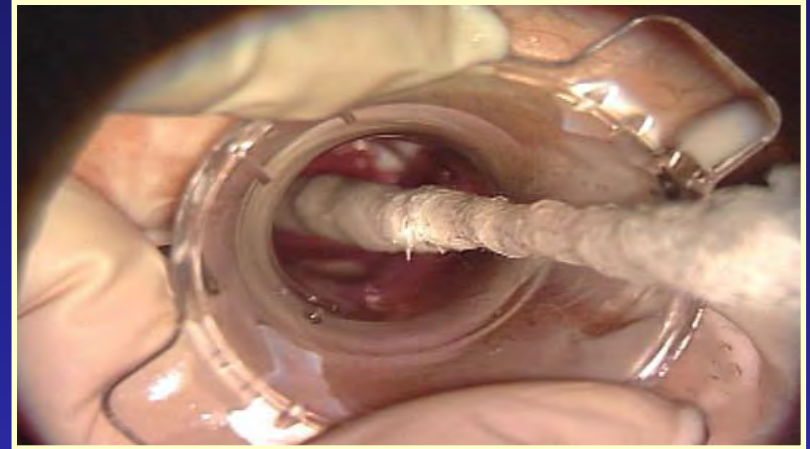
*\*715 unique women with abnormal anal Pap  
(abnormal rate over 11%)*

- can HPV testing improve accuracy?

# High Resolution Anoscopy



# High Resolution Anoscopy

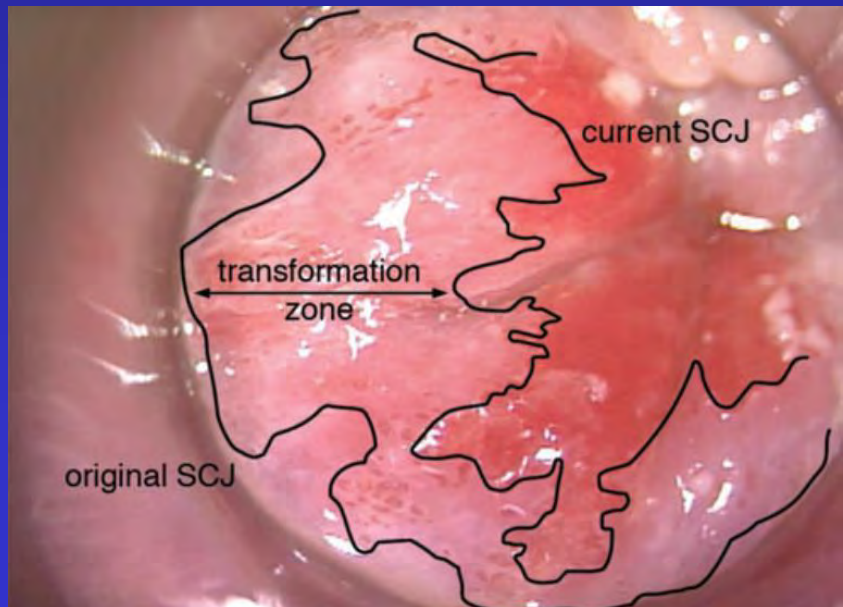
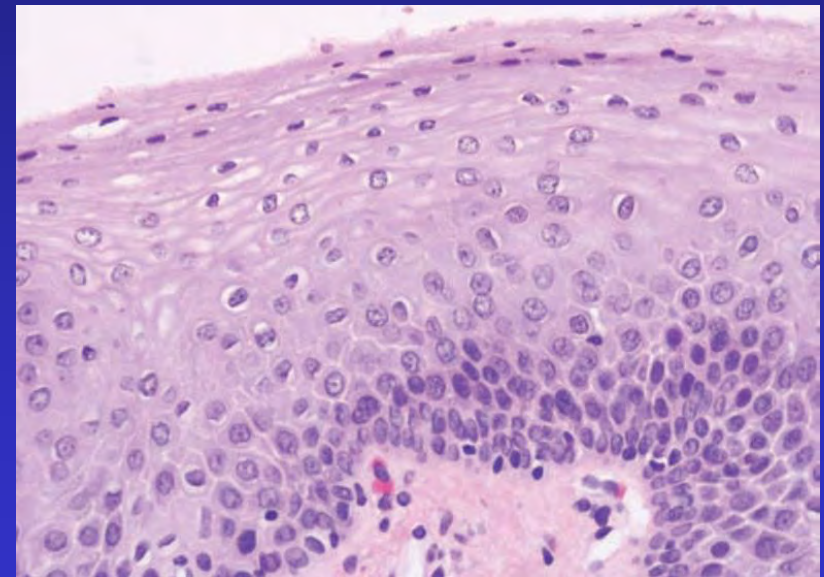
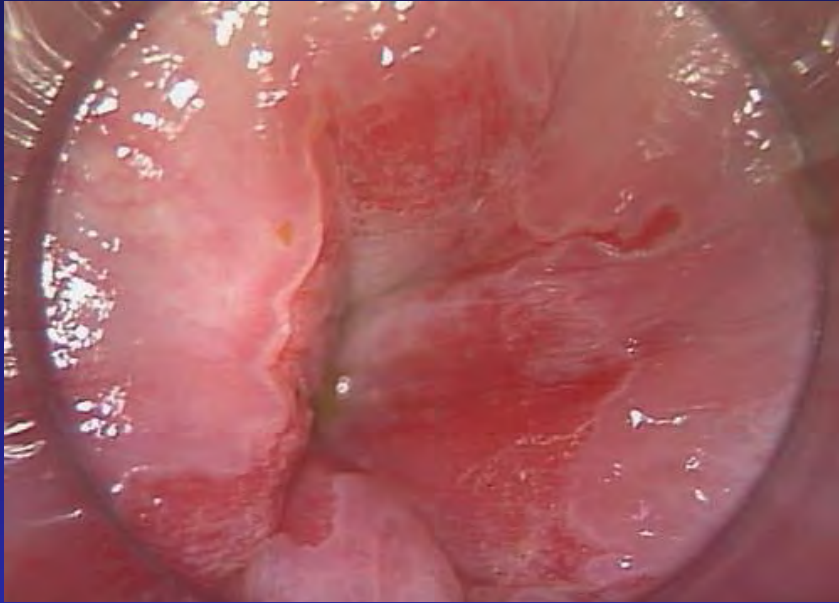


- examine perianus, verge, proximal & distal canal
- 5% Acetic Acid, Lugol's





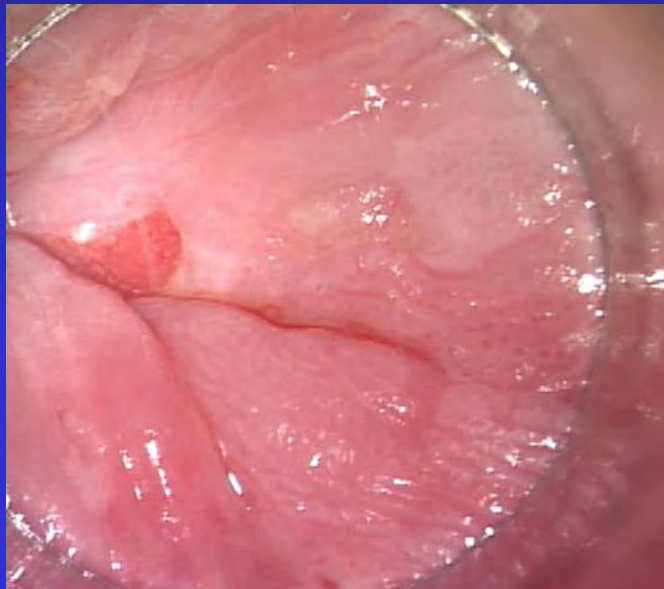
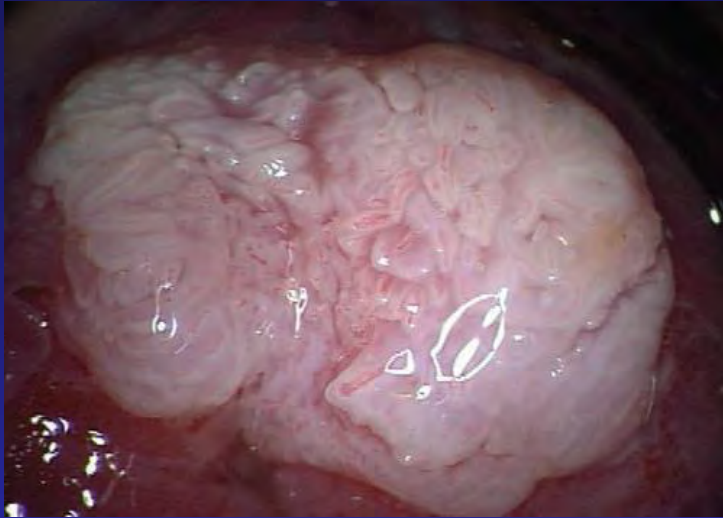
# Anal Transition Zone *(normal)*

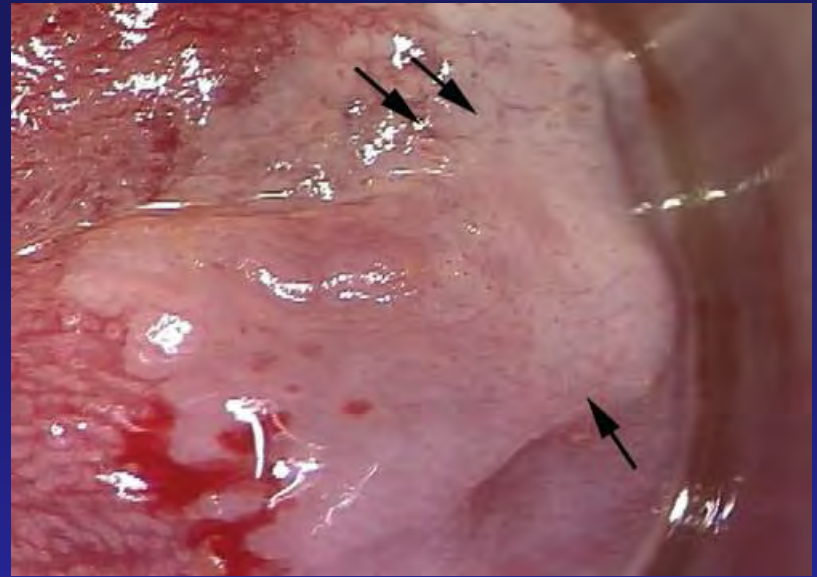
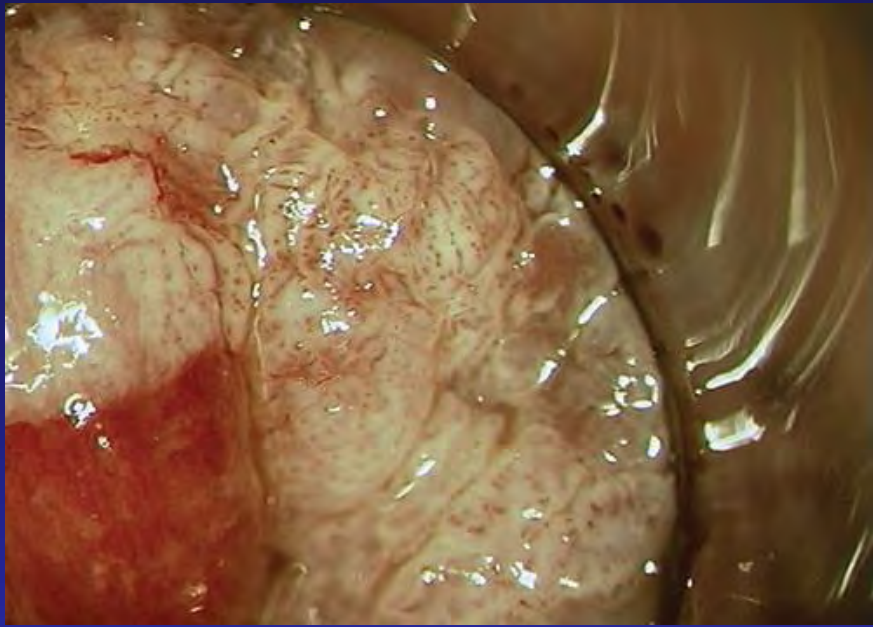


# Condyloma

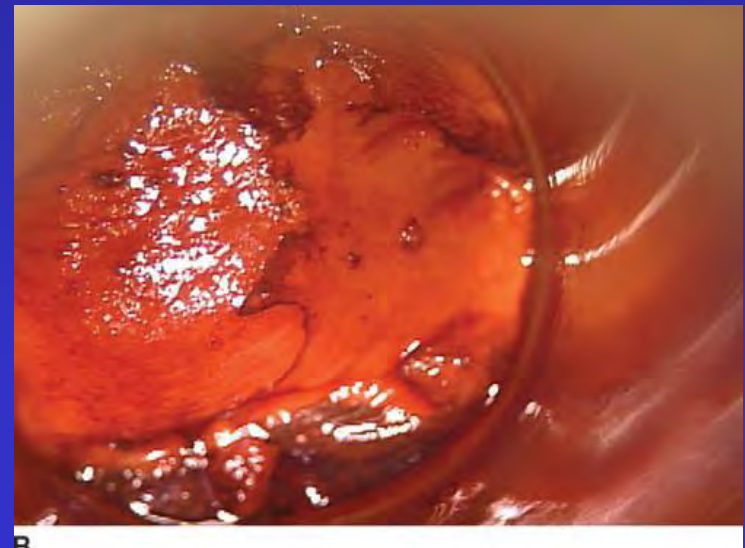
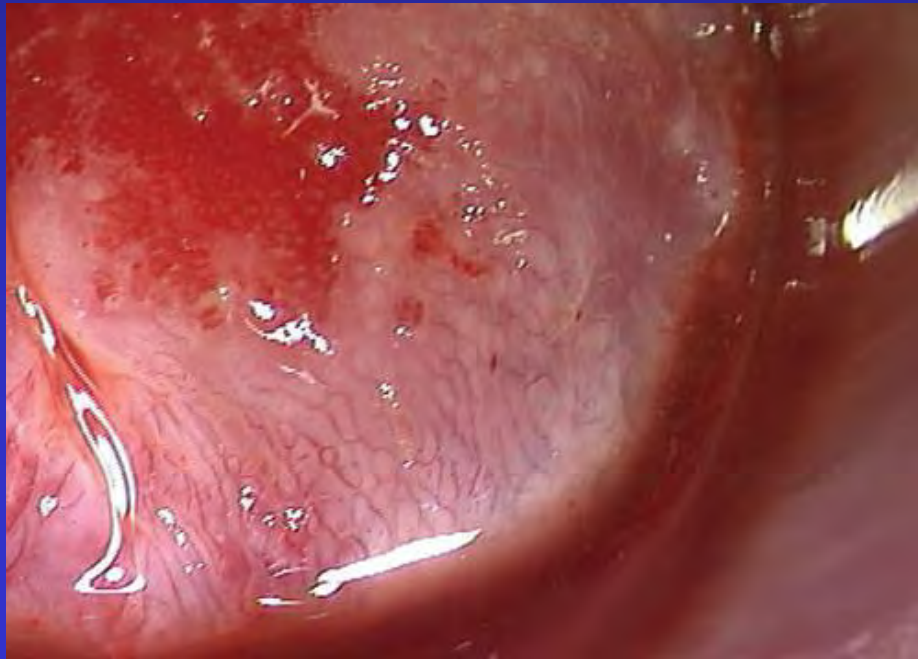


# Low Grade (LSIL)

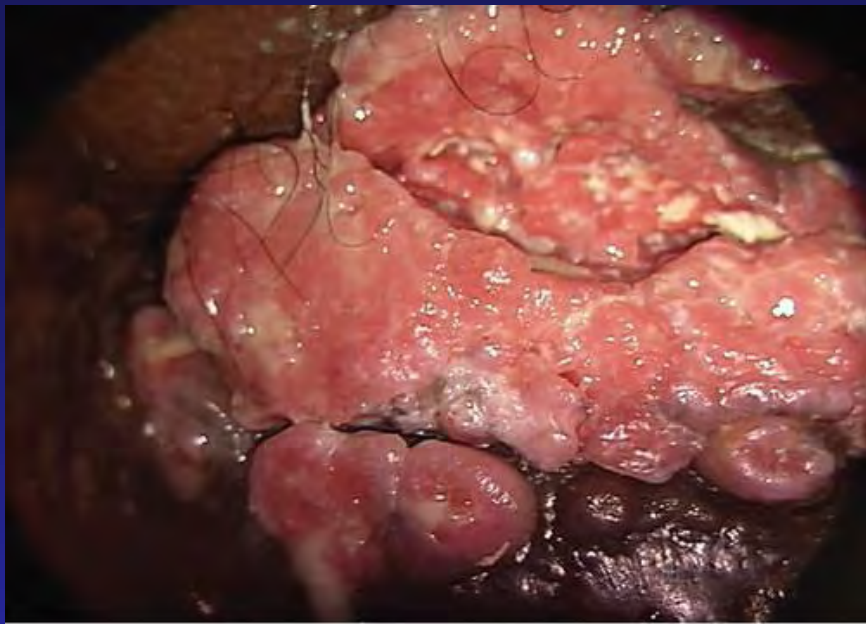




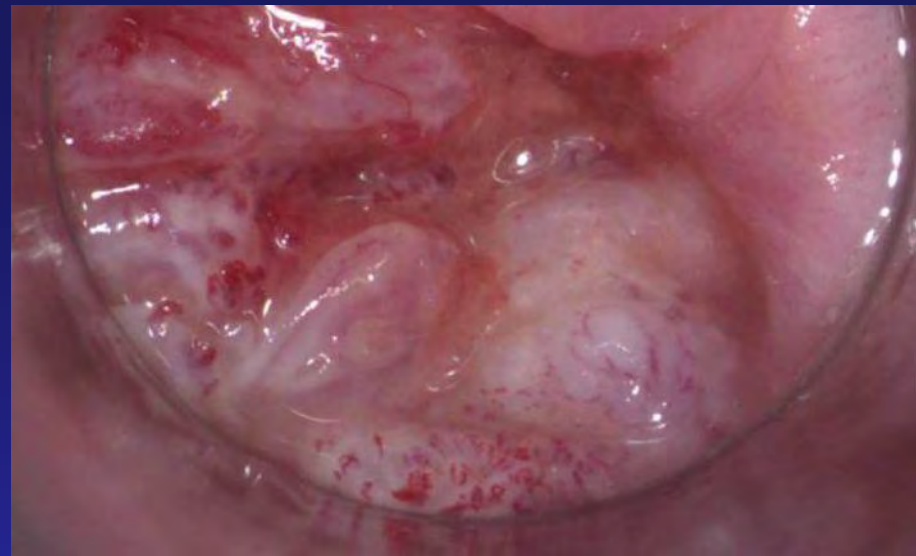
# HSIL



B



A



# SCCA



A



D

# Options for Treatment

<b>TREATMENT</b>	<b>Perianal condyloma</b>	<b>Perianal HSIL</b>	<b>Intra-anal condyloma</b>	<b>Intra-anal HSIL</b>
<b>0.5% podofilox gel</b>	Yes	No	No	No
<b>5% imiquimod</b>	Yes	Possibly	Possibly	Possibly
<b>5% fluorouracil</b>	Possibly	Possibly	Possibly	Possibly
<b>15% Sinecatechins</b>	Yes	No	No	No
<b>Cryotherapy</b>	Yes	Yes	No	No
<b>85% TCA</b>	Yes	Yes	Yes	Yes
<b>Ablation</b>	Yes	Yes	Yes	Yes
<b>Excision</b>	Yes	Yes	Yes	Yes

# Guidelines for Treatment

- choice of treatment depends on many things
  - *location, size, & volume of disease*
  - *type of lesion (LSIL, HSIL, wart)*
  - *overall health & immune status*
  - *patient preference & tolerance*
- no FDA-approved treatment for intra-anal HSIL
- multiple treatments often needed, combination of modalities
- must rule out cancer prior to treating a lesion
- **persistence, recurrence, & metachronous lesions are common no matter what...CLOSE FOLLOW-UP**

# Podofilox

- *chemically synthesized or prepared from plant*
- anti-mitotic
- EXTERNAL WARTS only



- **Advantages**

- Easy application
- Inexpensive
- No anesthesia required

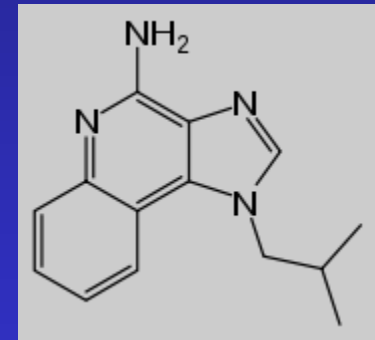
- **Disadvantages**

- Cannot use in anal canal
- Multiple visits needed
- transient erythema, burning, shallow erosions x1 wk



# Imiquimod

- acts as immunomodulator, stimulates local production of interferon
- EXTERNAL WARTS, ???perianal HSIL
- IMMUNOCOMPETENT PTS



- *prob less effective in immunosuppressed CD<200*

# 5% Flououracil (FUDex)

- not FDA approved but used to treat anal HSIL & debulk disease
- EFFICACY...limited data
  - clearance in 7/8 pts at 1 yr follow-up<sup>1</sup>
  - open label study in 46 HIV pts, 74% HSIL
    - 12 complete response, 8 downgraded
    - mild sx's 48% (*erosion, swelling, pain, irritation, ulcer*)<sup>2</sup>

1. Graham. *Dis Colon Rectum* 2005: 444.

2. Richel. *Br J Dermatol* 2010: 1301.

# Sinecatechins

- *extract of green tea*
- EXTERNAL WARTS only
- EFFICACY → pooled results of 2 RCTs<sup>1</sup>
  - *complete wart clearance 54.9 vs. 35.4% placebo*
  - *minimal side effects*
- **cannot be used in canal, for HSIL or in immunocompromised pts**

# Cryotherapy

- small external warts, anal LSIL/HSIL
- *apply with cotton swab until freezes & turns white (~20s), can apply TCA afterwards; 2-3 wk intervals, x3-4 cycles*
- erythema & blistering; minimal scarring
- well tolerated but requires analgesia for larger lesions

# 85% Trichloroacetic acid

- small warts, LSIL/HSIL; external & internal
- Advantages
  - Easy application
  - No anesthesia required
  - Inexpensive
  - Can be used in anal canal
- Disadvantages
  - Skin burns, multiple visits
- EFFICACY? *limited data...*
  - 35 HIV+ and 19 HIV- men with AIN<sup>1</sup>
  - complete clearance in 32% with AIN 2-3, 72% recurrence



# Infrared Coagulation (IRC)

- *coagulative necrosis through infrared light beam*
- FDA approved for—
  - hemorrhoids
  - condyloma
  - tattoo removal
- Anesthesia?? usually just local...
- staged approach for larger lesions
- recurrences managed with successive tx
- minimal scarring or bleeding
- *apply directly 1.5s pulse (corresponds to 1.5mm depth of burn), debride to submucosal vessels*



# Infrared Coagulation

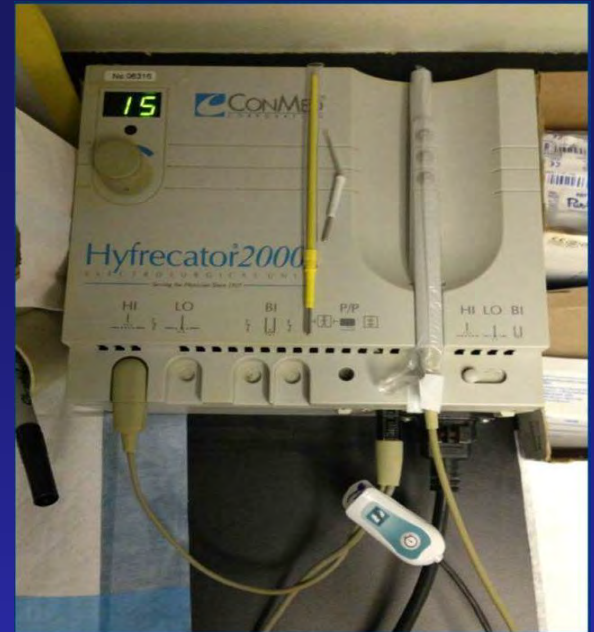
## *Efficacy Data*

- **mostly retrospective...** (*Goldstone DCR 2011: 10*)
  - HIV-MSM: 32/52 (62%) recurred (avge 14 mos.)
  - HIV+MSM: 40/44 (91%) recurred (avge 17 mos.)  
cure rate of 67%; metachronous lesions in 82%
- **one prospective pilot study** (*Stier, et al. J AIDS 2008: 56.*)
  - complete response in 10/16 pts at 1 yr
  - 37.5% persistent or recurrent lesions
- *efficacy related to volume of disease*
- *need to follow carefully due to high rates of recurrence, persistence, metachronous lesions*

# Electrocautery

- Advantages

- single session treatment
- effective for large lesions & in anal canal



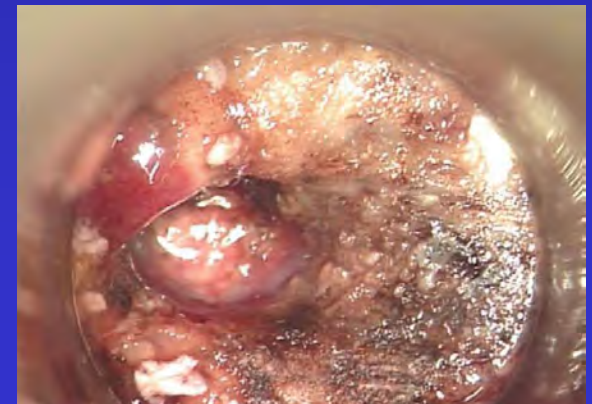
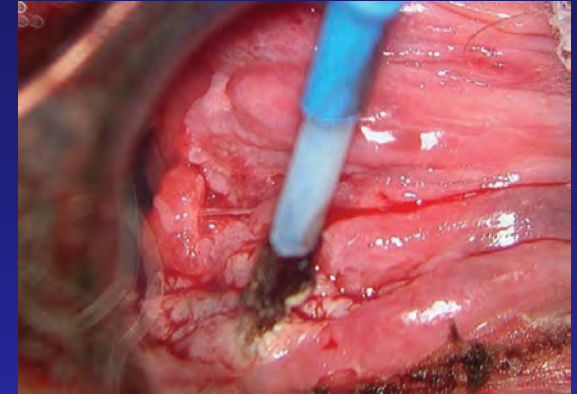
- Disadvantages

- anesthesia required
- postoperative pain
- fumes



# Electrocautery

- *Marks, et al. J AIDS 2012: 259.*
- retrospective study 2006-2010
- 100 HIV-MSM & 132 HIV+MSM
  - *53% HIV- pts recurred at median of 7 mos.*
  - *61% HIV+ pts recurred at median of 6.8 mos.*
- 1 pt progressed to cancer
- no other serious adverse events



# Surgical Excision

- **Advantages**

- most precise removal
- tissue for pathology
- suspicion for malignancy

- **Disadvantages**

- anesthesia, postop pain



- **Efficacy Data** (*UCSF 10 yr Experience - Pineda DCR 2008: 829*)

- 207 men & 39 women with HSIL
- 114 pts developed recurrent HSIL → *avge 19 mos., retreated*
- recurrence or persistence in 22%, complete clearance in 78%
- 3 pts progressed to cancer

# Ablation of HSIL

(Goldstone, et al. DCR 2014: 316)

## ORIGINAL CONTRIBUTION

### Long-term Outcome of Ablation of Anal High-grade Squamous Intraepithelial Lesions: Recurrence and Incidence of Cancer

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- treated with IRC, EC, laser, or combo
- follow-up until incident cancer
- 1998-2012

	HIV+ 456 pts	HIV- 271 pts	
Age (median) yrs	44 (17-71)	39 (21-75)	<0.0001
Follow-up (mean) yrs	3 (0.2 – 13)	3 (0.2-13)	0.6
Mean # treatments/pt	2.2 (1-8)	1.8 (1-5)	

# Recurrence Risk

	Univariate Results			Multivariable Results		
	HR	95% CI	P-value	HR	95% CI	P-value
<b>HIV Status</b>						
HIV-	1.00			1.00		
HIV+	1.43	1.22-1.67	<0.0001	1.31	1.12-1.55	0.0011
<b>Type of Surgery</b>						
CO2	1.00			1.00		
EC	0.81	0.62-1.05	0.1040	0.91	0.69-1.20	0.5022
IRC	0.83	0.63-1.09	0.1816	1.06	0.79-1.43	0.6884
<b>Age at Baseline</b>						
Per 1 Year Increase	1.01	1.001-1.02	0.0187	1.01	0.99-1.01	0.1064
<b>Previous LSIL</b>						
No Previous LSIL	1.00			1.00		
At Least 1 Previous LSIL	0.87	0.73-1.03	0.1113	0.84	0.70-0.99	0.0443
<b># of Lesions treated at Baseline</b>						
Per 1 Lesion Increase	1.17	1.12-1.22	<0.0001	1.16	1.10-1.22	<0.0001
<b>Previous External HSIL</b>						
No Previous External HSIL	1.00			1.00		
At least 1 Previous External HSIL	1.29	1.05-1.58	0.0162	1.02	0.81-1.28	0.8860

# Ablation of HSIL

*(Goldstone, et al. DCR 2014: 316)*

- **Progression to cancer**
  - 5 patients (all HIV+), only one pt actively treated
  - **overall rate of progression 0.1%**

# Randomized Data

*(Richel, et al. Lancet Oncol 2013: 346)*

- open-label study from Netherlands
- 156 HIV+MSM pts with AIN randomized→
  - imiquimod, 5-FU, electrocautery x 16 wks
  - HRA at 24, 48, and 72 months
- **ELECTROCAUTERY a/w superior results**
  - higher complete response rate (39% vs. 24% imiquimod vs. 17% 5FU)
  - fewer grade 3-4 toxicities (18% vs. 43% vs. 27%)
  - shorter duration of side effects (few days vs. 5 wks vs. 7 wks)
- *substantial recurrence after all treatments*  
*(71% imiquimod, 58% fluorouracil, 28% electrocautery)*

# Summary

- Anal cancer is increasing in the general population & high risk groups
- ART is not protective & primary prevention is not practical in most high risk groups
- biologically similar to cervical cancer
- but no direct evidence of the efficacy of secondary prevention protocols

# Summary

- Numerous drawbacks to screening & treatment of anal dysplasia
  - expensive, time-consuming, challenging
  - morbidity
  - psychological toll
  - regression???
- Are we preventing anal cancer?
- Or... are we causing more harm than benefit?

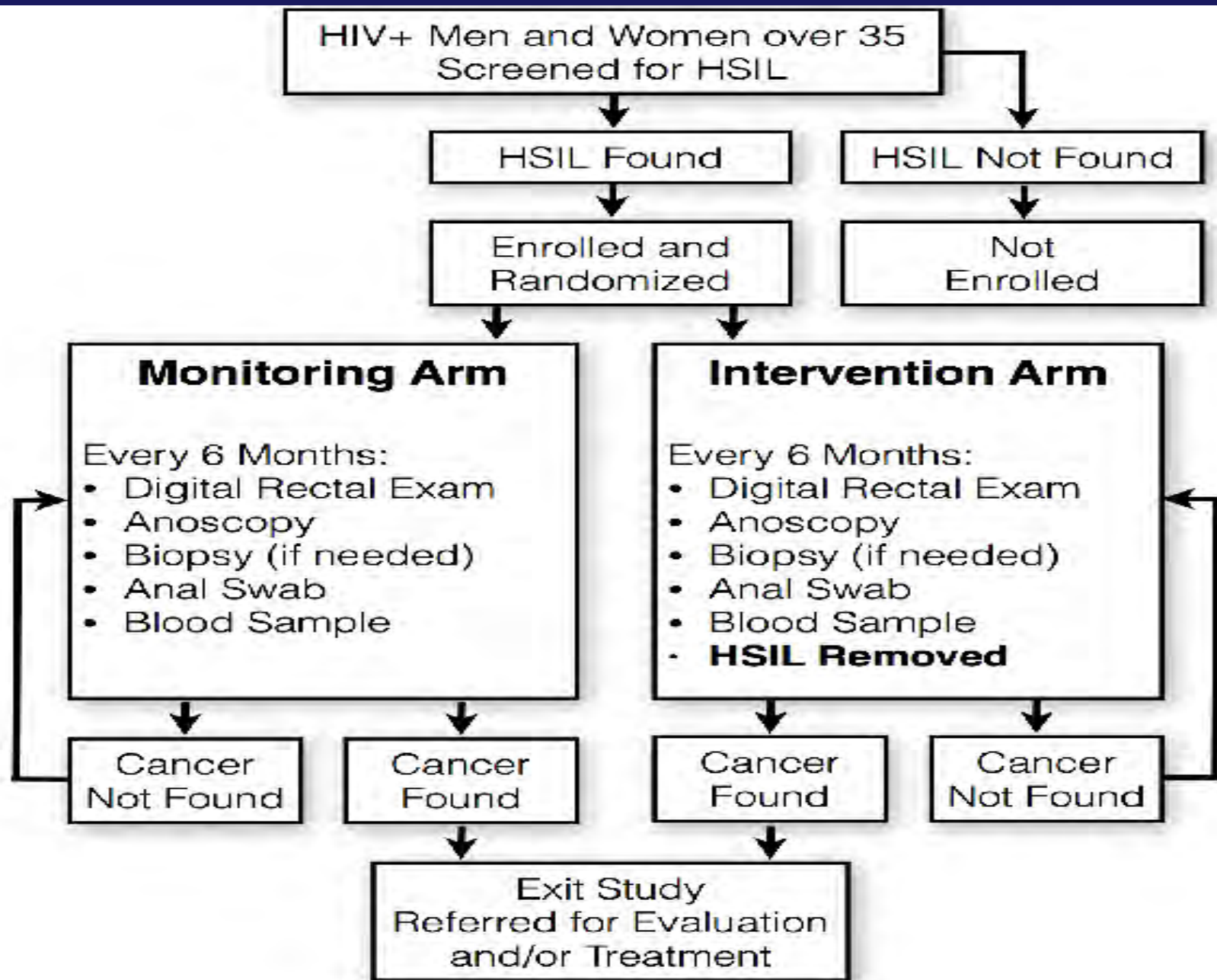


# Anal Cancer Prevention Study (ANCHOR)

- 5058 pts, 15 sites
- Randomized to...
  - TREATMENT
  - ACTIVE MONITORING
- 5 year follow-up
- Incidence of anal cancer



[www.anchordmc.com](http://www.anchordmc.com)



# Secondary Objectives & Correlative Studies

- Evaluate safety of treatment modalities
- Identify risk factors, viral/host factors & biomarkers for malignant progression
- 12,000 screened pts will not be eligible for enrollment



# Participating Sites *so far...*





the  
**ANCHOR**  
study



# Acknowledgements

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- *Naomi Jay, Steve Goldstone,  
Michael Berry, Joel Palefsky,  
Terry Darragh*



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**Giving someone the  
finger doesn't have to  
be a bad thing.**  
American School of Proctology



**Thank You...Questions?**