

**PRO:**  
**SHOULD WOMEN BE SCREENED  
FOR ANAL CANCER?**

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  - Advisory Board

# RATES OF ANAL CANCER IN THE U.S.

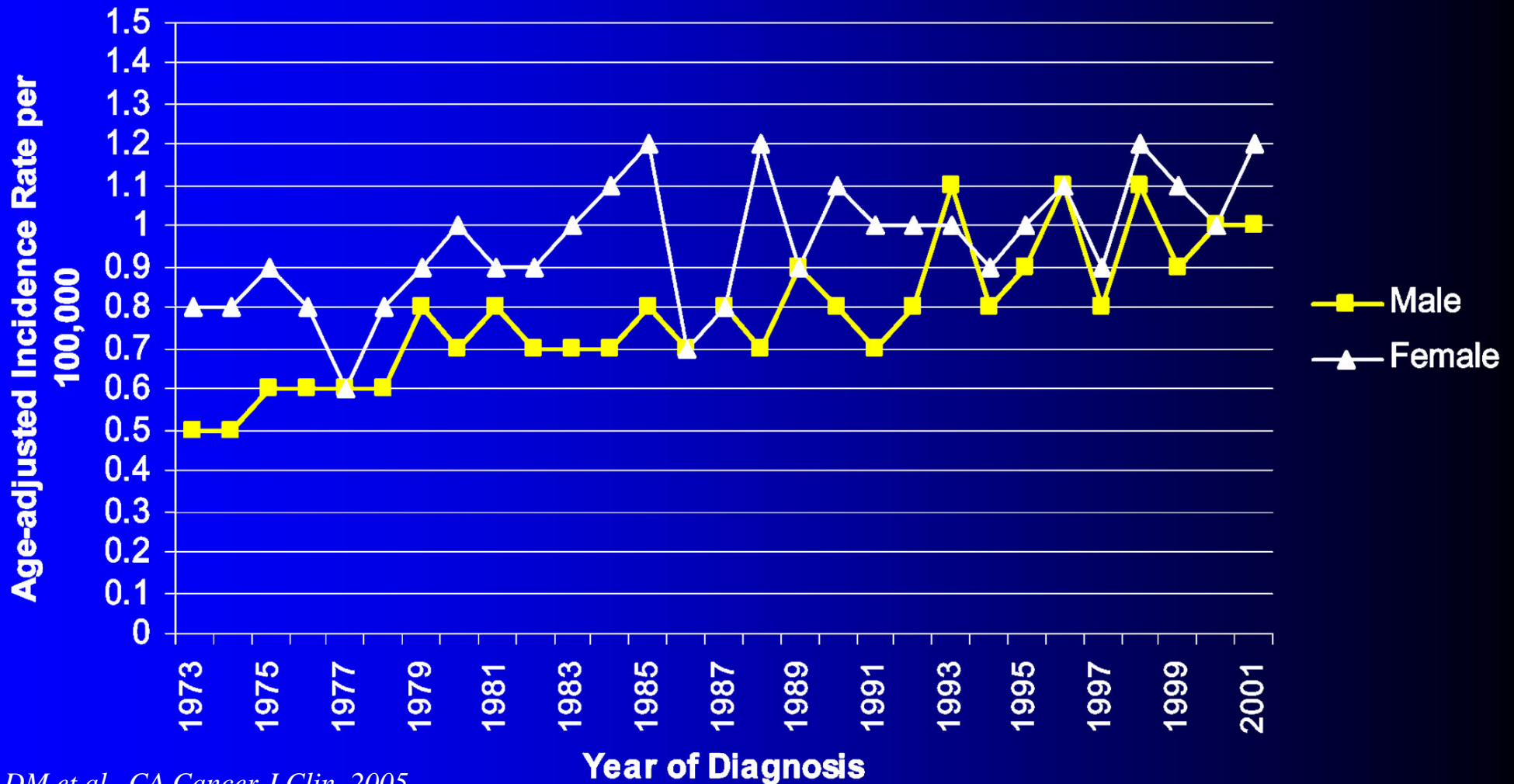
| <u>Worldwide</u> <sup>1</sup> |        | <u>U.S.</u> <sup>2</sup> |       |
|-------------------------------|--------|--------------------------|-------|
| Women                         | Men    | Women                    | Men   |
| 14,500                        | 13,500 | 3,190                    | 2,100 |

<sup>1</sup>Chaturuedi A et al, JAHC 2010

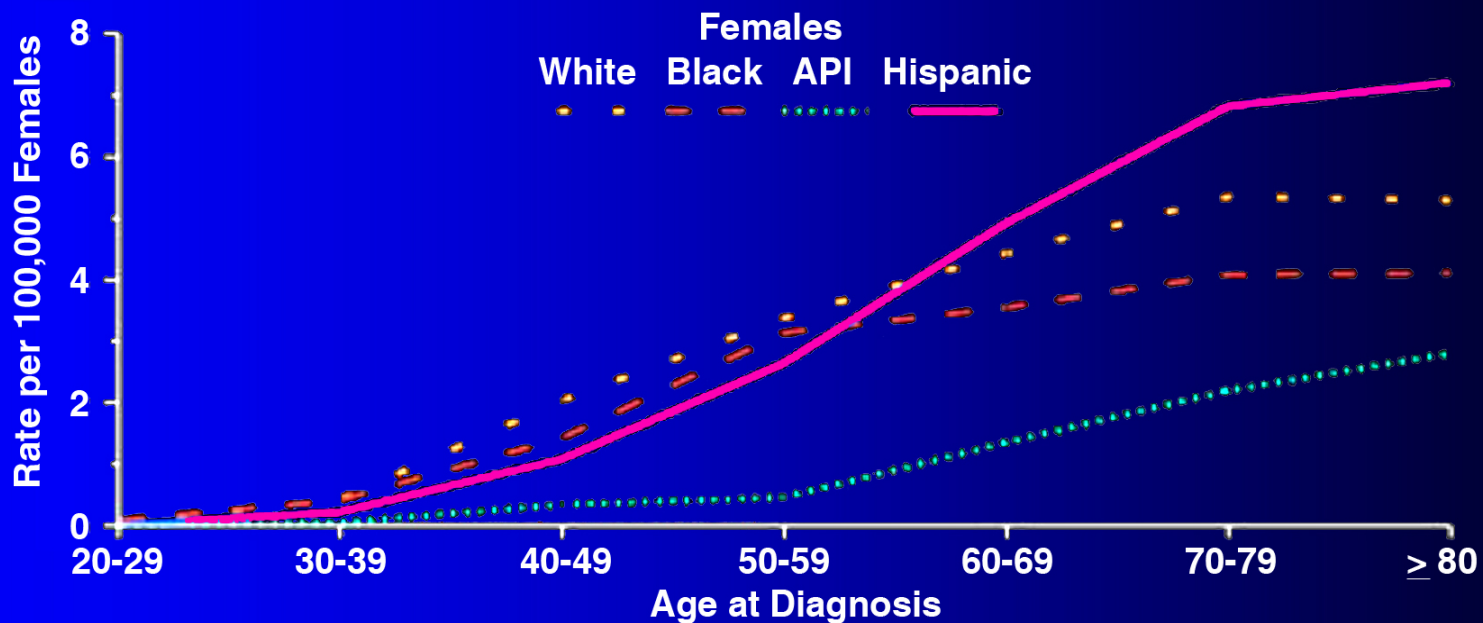
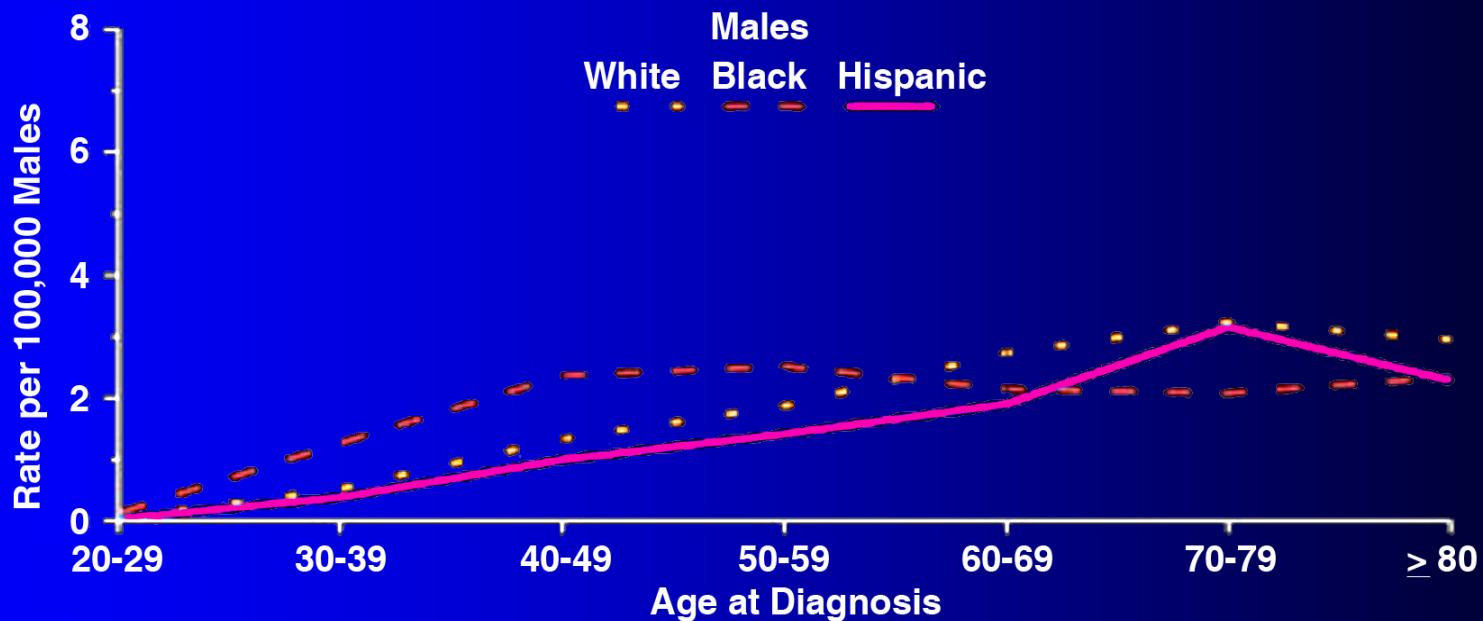
<sup>2</sup>Am Ca Soc 2009

# THE INCIDENCE OF HPV-RELATED CANCERS IS INCREASING

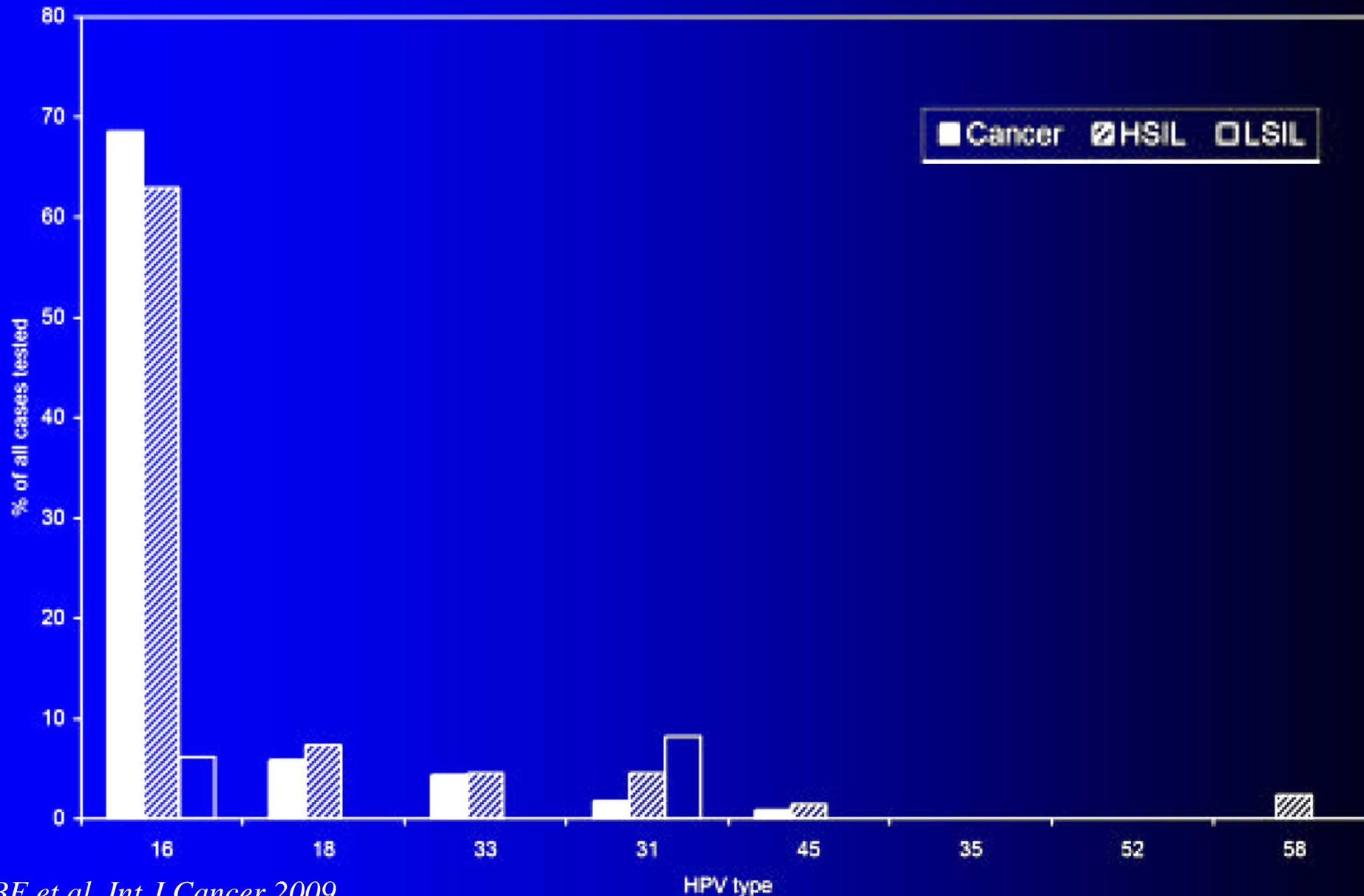
Age-adjusted Incidence Rate of Primary, malignant Anal cancer by Gender and Year of diagnosis



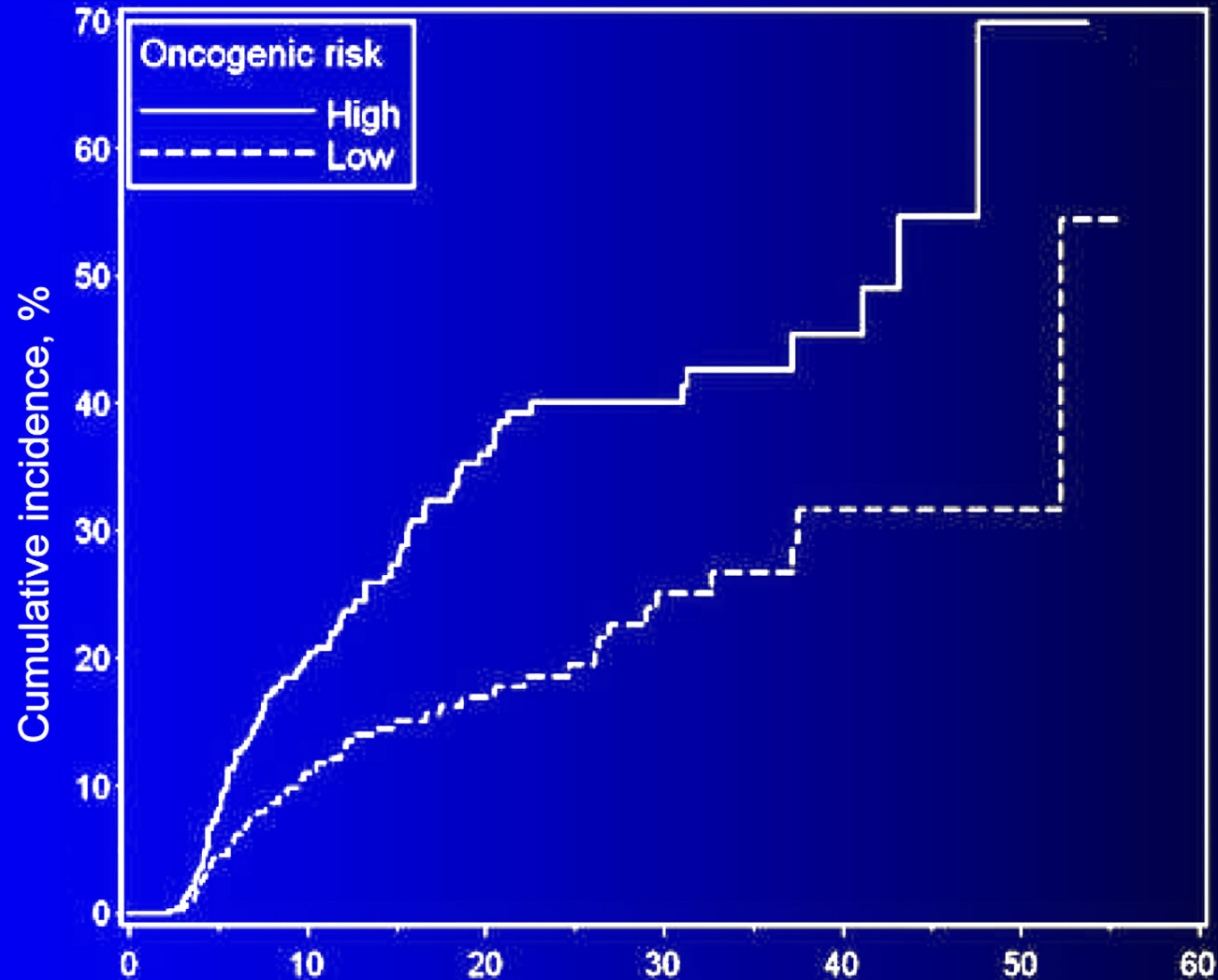
# AGE-SPECIFIC INCIDENCE OF INVASIVE SQUAMOUS CELL ANAL CANCER BY SEX AND RACE/ETHNICITY, UNITED STATES, 1998-2003



**PREVALENCE OF THE MOST COMMON HPV TYPE (TYPE-SPECIFIC PREVALENCE ESTIMATES ARE RESTRICTED TO STUDIES THAT OBTAINED HPV DNA FROM BIOPSIES AND TYPED FOR AT LEAST HPV 16 AND 18) IN BIOPSY SPECIMENS OF INVASIVE ANAL CANCER (N 5 810), HSIL (N 5 178), AND LSIL (LOW-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS, LSIL ESTIMATES INCLUDE ONLY 2 BIOPSIED CASES FROM WOMEN.) (N 5 49)**



# CUMULATIVE INCIDENCE OF ANAL HPV INFECTIONS IN WOMEN



# RISK FOR ANAL CANCERS

- HIV infection
- Cervical cancer/CIN 3
- Vulvar/vaginal cancer
- Practice regular anal intercourse



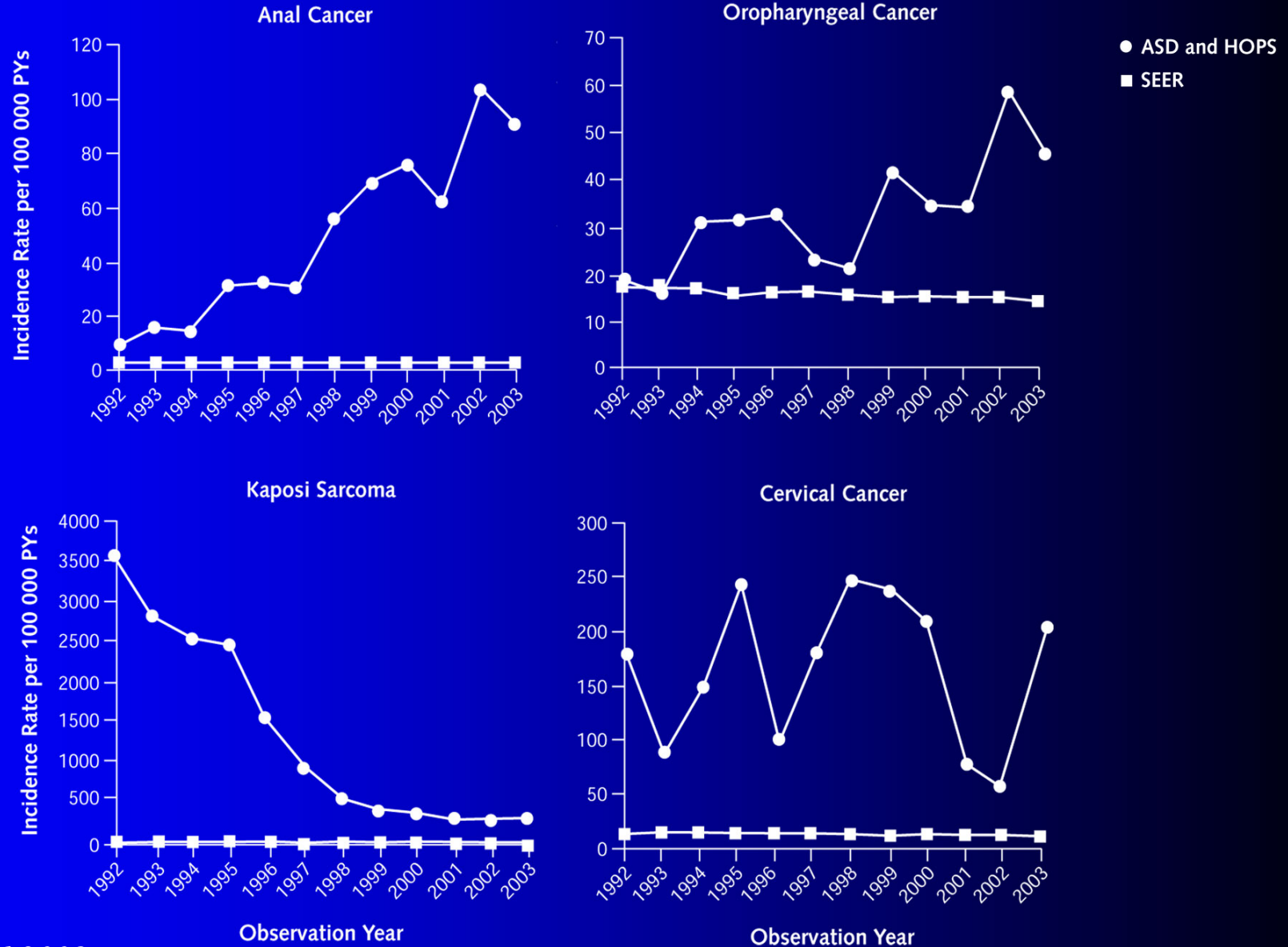
# RELATIVE RISKS (BY AGE OF AIDS ONSET) OF HPV-ASSOCIATED ANOGENITAL CANCERS AMONG 309,365 PATIENTS WITH AIDS

## INVASIVE CANCERS

Relative risk (95% C.I.)

| Age at AIDS onset, y | Anus (men)                   | Anus (women)                |
|----------------------|------------------------------|-----------------------------|
| < 30                 | <b>162.7 (103.1 – 244.0)</b> | <b>134.3 (16.3 – 484.8)</b> |
| 30 – 39              | 40.1 (31.2 – 50.8)           | 12.2 (2.5 – 35.7)           |
| 40 – 49              | 39.3 (31.3 – 48.7)           | 2.8 (0.1 – 15.6)            |
| ≥ 50                 | 23.4 (16.6 – 32.0)           | 2.4 (0.1 – 13.5)            |
| All                  | 37.9 (33.0 – 43.4)           | 6.8 (2.7 – 14.0)            |

# ANNUAL INCIDENCE RATES OF 3 AIDS-DEFINING (TOP ROW) AND 9 NON-AIDS-DEFINING TYPES OF CANCER AMONG HIV-INFECTED PERSONS AND THE GENERAL POPULATION



# RISK OF DEVELOPING SUBSEQUENT CANCER AFTER CANCER OF CERVIX (SEER 1973-2000)

- Cumulative incidence of developing a second cancer among 30,563 who survived 2 or more months was 13.2% at 25 years (adjusted for competing causes of death).
- Higher in younger women at dx
- Higher in those who received radiotherapy
- Higher in blacks

# SIGNIFICANT INCREASES INCLUDED

- Tobacco-related (e.g., lung, bronchitis, buccal cavity, bladder)
- HPV-related (anus, vagina, vulva, tonsils, pharynx)
- Radiotherapy (bladder, ovary, vagina, vulva, bone, rectum)

# RISK OF SUBSEQUENT PRIMARY ANAL CANCERS AFTER PRIMARY CANCER OF THE CERVIX, VAGINA, AND VULVA

|         | Primary |      |        |      |        |      |
|---------|---------|------|--------|------|--------|------|
|         | Cervix  | EAR  | Vagina | EAR  | Vulva  | EAR  |
|         | O/E     |      | O/E    |      | O/E    |      |
| Anus    | 3.24*   | 0.53 | (3.18) | 0.79 | 8.04*  | 2.89 |
| Cx      | --      |      | (2.52) |      | (1.52) |      |
| Vagina  | 16.87*  |      | --     |      | 6.12*  |      |
| Vulva   | 5.12*   |      | 8.06*  |      | --     |      |
| Tonsils | 3.92*   |      | (0)    |      | (1.59) |      |

\* $p < 0.05$ ; ( ) = NS

O/E = observed/expected

EAR = excess absolute risk per 10,000 person-years

# RISK (O/E) OF ANAL CANCER AFTER CANCER OF THE CERVIX (SEER 1973-2000)

Years after 1<sup>st</sup> primary cervical cancer

|     |        |       |       |
|-----|--------|-------|-------|
| < 1 | 1-4    | 5-9   | 10-14 |
| (0) | (2.61) | 3.32* | 5.21* |

Age (yrs) of cervical cancer diagnosed

|       |       |      |
|-------|-------|------|
| < 50  | > 50  | > 70 |
| 4.13* | 3.41* | NS   |

*O/E = observed/expected*

*New malignancies among cancer survivors: SEER 1973 - 2000*

# RISK (O/E) OF ANAL CANCER AFTER CANCER OF THE VULVA (SEER 1973-2000)

Years after 1<sup>st</sup> primary cervical cancer

| < 1    | 1-4    | 5-9    | >10  |
|--------|--------|--------|------|
| 12.44* | 7.40** | (2.39) | 13.4 |

Age of vulvar cancer diagnosed

| < 55   | > 55  |
|--------|-------|
| 22.02* | 5.53* |

*O/E = observed/expected*

*New malignancies among cancer survivors: SEER 1973 - 2000*

**RISK OF ANAL, VAGINAL, AND VULVAR CANCER IN  
WOMEN WITH CIN 3: PROSPECTIVE  
POPULATION-BASED STUDY IN SWEDEN (1968 – 2004)**

|         | <b>Adjusted IRR*</b> |
|---------|----------------------|
| Anal    | 4.68 (3.9 – 5.6)     |
| Vaginal | 6.74 (5.2 – 8.6)     |
| Vulvar  | 2.22 (1.8 – 2.7)     |

*Edgren and Sparen, Lancet Onc 2007*

*Adjusted for age, time period, SES, and parity*

*\*IRR = incident risk ratio*



**RISK OF CANCER OF THE ANUS OF WOMEN WITH A HISTORY OF GRADE 3 CIN COMPARED WITH THOSE WITHOUT SUCH HISTORY, STRATIFIED BY ATTAINED AGE**

|                    | <b>Anal cancer</b>  |
|--------------------|---------------------|
|                    | <b>IRR (95% CI)</b> |
| <b>18–29 years</b> |                     |
| CIN 3 history      | 31.09 (3.74–258.44) |
| <b>30-39 years</b> |                     |
| CIN 3 history      | 7.59 (3.35–17.20)   |
| <b>40-49 years</b> |                     |
| CIN 3 history      | 5.82 (3.87–8.75)    |
| <b>50-59 years</b> |                     |
| CIN 3 history      | 4.70 (3.40–6.50)    |
| <b>≥ 60 years</b>  |                     |
| CIN 3 history      | 3.97 (2.96–5.32)    |

*IRR = incident rate ratios*

# RISK OF CANCER OF THE ANUS OF WOMEN WITH A HISTORY OF GRADE 3 CIN COMPARED WITH THOSE WITHOUT SUCH HISTORY, STRATIFIED BY TIME SINCE FIRST DIAGNOSIS

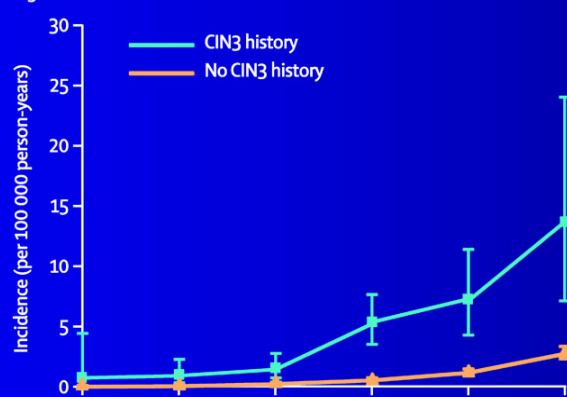
|                  | Anal cancer |                   |
|------------------|-------------|-------------------|
|                  | Events (n)  | IRR (95% CI)      |
| <1 year          | 0           | 0.00 (0.00–2.06)* |
| 1–4 years        | 4           | 1.67 (0.41–4.36)  |
| 5–9 years        | 12          | 3.90 (2.08–6.60)  |
| ≥10 years        | 115         | 4.98 (4.07–6.04)  |
| No CIN 3 history | 857         | 1.00              |

*\*For reasons of model convergence, these point estimates could not be estimated in the multivariate model and are therefore taken from the univariate model. Adjusted for attained age, calendar period, socioeconomic status, and parity. The number of person-years may not add up because of rounding. Reference category is no CIN3 history.*

*IRR = incident rate ratios*

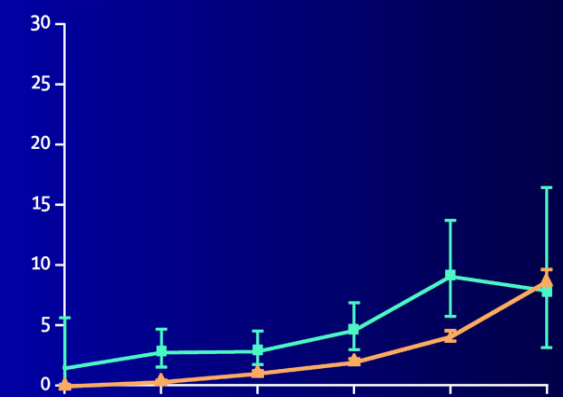
# AGE-SPECIFIC INCIDENCES OF VAGINAL, VULVAR, ANAL, AND RECTAL CANCER IN WOMEN WITH AND WITHOUT A HISTORY OF GRADE 3 CIN

Vaginal cancer



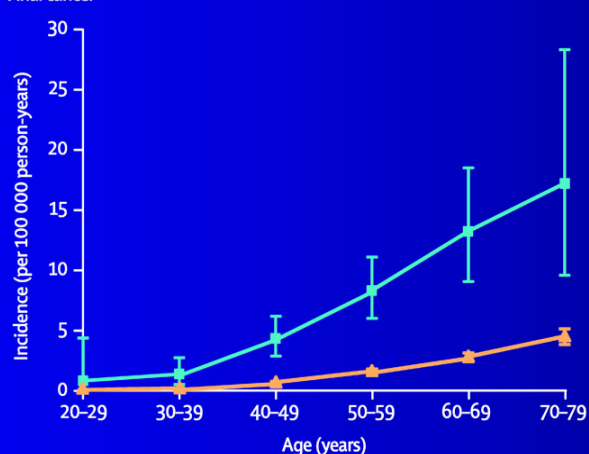
|                 |      |      |      |      |      |       |
|-----------------|------|------|------|------|------|-------|
| CIN3 history    | 0.79 | 0.96 | 1.49 | 5.28 | 7.21 | 13.76 |
| No CIN3 history | 0.03 | 0.09 | 0.26 | 0.57 | 1.20 | 2.78  |
| Risk difference | 0.76 | 0.87 | 1.23 | 4.71 | 6.01 | 10.98 |

Vulvar cancer



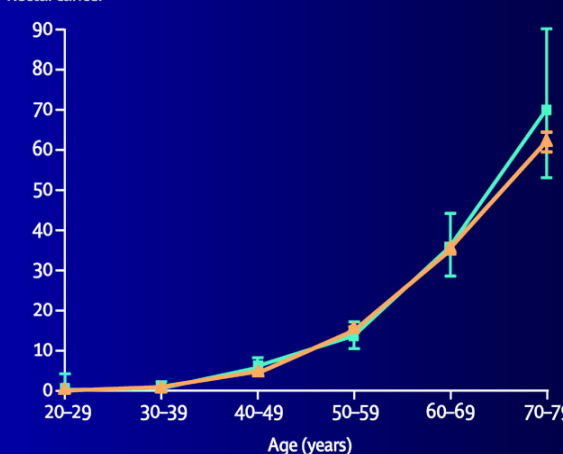
|                 |      |      |      |      |      |       |
|-----------------|------|------|------|------|------|-------|
| CIN3 history    | 1.58 | 2.89 | 2.98 | 4.72 | 9.21 | 8.03  |
| No CIN3 history | 0.07 | 0.43 | 1.13 | 2.06 | 4.18 | 8.77  |
| Risk difference | 1.51 | 2.46 | 1.85 | 2.66 | 5.03 | -0.74 |

Anal cancer



|                 |      |      |      |      |       |       |
|-----------------|------|------|------|------|-------|-------|
| CIN3 history    | 0.79 | 1.35 | 4.32 | 8.30 | 13.21 | 17.20 |
| No CIN3 history | 0.03 | 0.17 | 0.66 | 1.58 | 2.79  | 4.48  |
| Risk difference | 0.76 | 1.18 | 3.66 | 6.72 | 10.42 | 12.72 |

Rectal cancer



|                 |      |      |      |       |       |       |
|-----------------|------|------|------|-------|-------|-------|
| CIN3 history    | 0.79 | 1.16 | 6.11 | 13.39 | 34.83 | 67.66 |
| No CIN3 history | 0.22 | 1.11 | 4.82 | 15.04 | 34.43 | 60.08 |
| Risk difference | 0.57 | 0.04 | 1.30 | -1.65 | 0.39  | 7.59  |

## STANDARDIZED INCIDENCE RATIO OF ANAL CANCER IN PATIENTS WITH IN SITU AND INVASIVE GYNECOLOGIC NEOPLASM (SEER 1973 – 2007)

| Primary Gynecologic Neoplasm | Race  | Observed | Expected* | Standardized Incidence Ratio | 95 % CI†    |
|------------------------------|-------|----------|-----------|------------------------------|-------------|
| <b>Cervical</b>              |       |          |           |                              |             |
| In situ                      | Total | 137      | 8.4       | 16.4                         | 13.7 – 19.2 |
| Invasive                     | Total | 28       | 4.5       | 6.2                          | 4.1 – 8.7   |
| <b>Vulvar</b>                |       |          |           |                              |             |
| In situ                      | Total | 55       | 2.5       | 22.2                         | 16.7 – 28.4 |
| Invasive                     | Total | 28       | 1.6       | 17.4                         | 11.5 – 24.4 |
| <b>Vaginal</b>               |       |          |           |                              |             |
| In situ                      | Total | 5        | 0.7       | 7.6                          | 2.4 – 15.6  |
| Invasive                     | Total | <5‡      | <5‡       | 1.8                          | 0.2–5.3     |

*CI, confidence interval.*

*\* The expected cases were calculated from Surveillance, Epidemiology and End Results 9, stratified by age, race, and calendar-year group.*

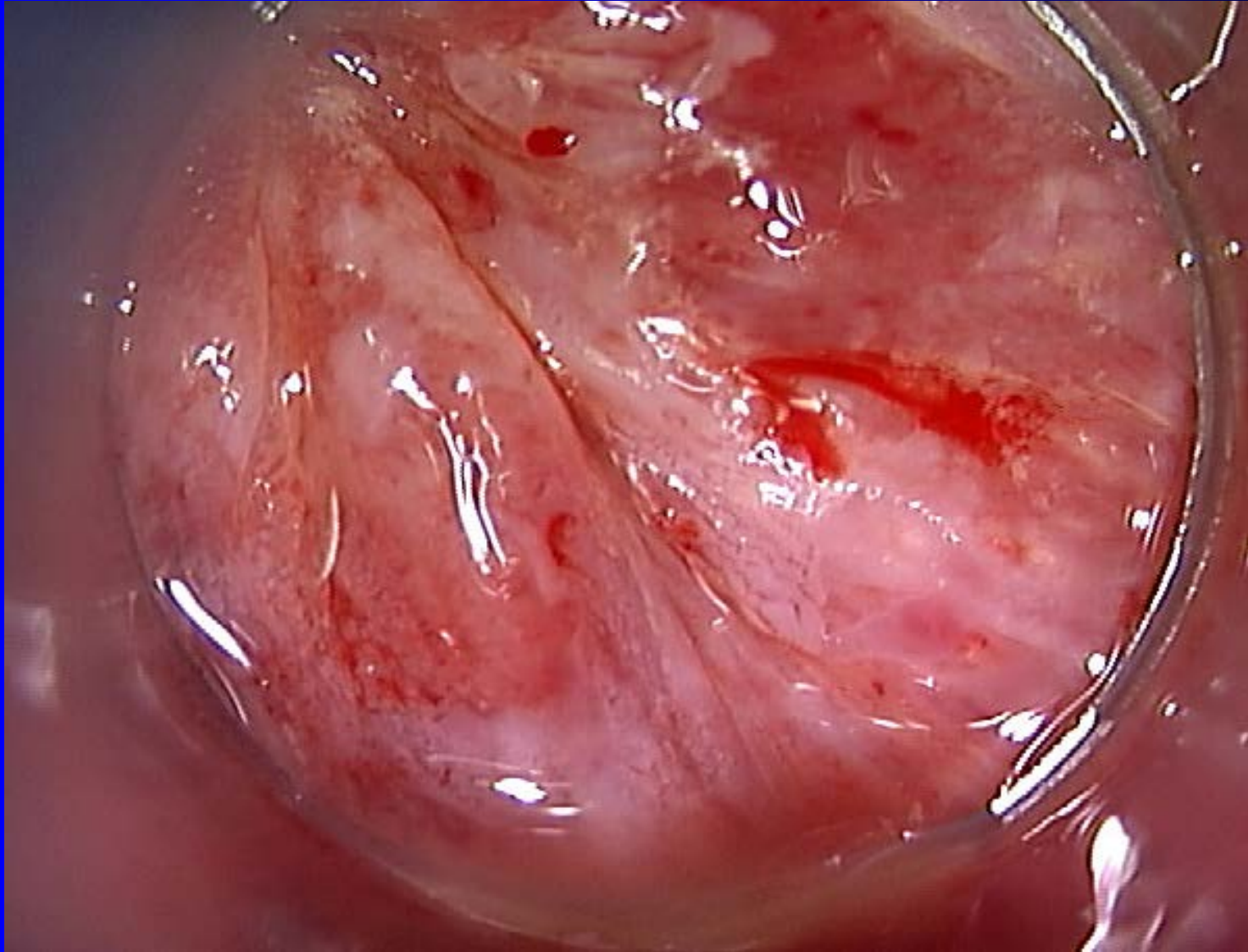
*† The CI was calculated using the Vandenbroucke method.*

*‡ These data hidden as per our data-use agreement with the Surveillance, Epidemiology, and End Results program.*

**SO?**

**CAN WE PICK UP  
PRECURSORS  
OF ANAL CANCER?**

# FOCAL HGAIN IN TEEN STUDY PT



# PREVALENCE OF AIN IN SPECIFIC POPULATIONS

|                     |                         |
|---------------------|-------------------------|
| Healthy women       | 4 – 6% <sup>1,2</sup>   |
| CIN 3               | 7% <sup>3</sup>         |
| CIN + VIN/Vulvar Ca | 21% <sup>3</sup>        |
| HIV                 | 21 – 24% <sup>2,5</sup> |
| Renal transplants   | 6% <sup>4</sup>         |

<sup>1</sup> Moscicki AB et al, *Ca Epi Biomarker Prev* 1999; <sup>2</sup> Moscicki AB et al, *AIDS* 2003

<sup>3</sup> Park et al, *Gynecol Oncol* 2009; <sup>4</sup> Patel et al, *Br J Surg* 2010

<sup>5</sup> Hessol NA et al, *AIDS* 2009

# RISK FACTORS FOR ABNORMAL ANAL CYTOLOGY

## Healthy Women

Anal intercourse<sup>1, 11</sup>

Smoking<sup>10</sup>

Genital warts<sup>1</sup>

Abnormal cervical cytology<sup>1, 2</sup>

No. lifetime partners<sup>2</sup>

## Immunocompromised

Anal intercourse<sup>4, 6, 7</sup>

Smoking<sup>9</sup>

Genital warts<sup>7</sup>

Abnormal cervical cytology<sup>5</sup>

↓CD4 (<200)<sup>4, 5, 9</sup>

<sup>1</sup> Moscicki et al, *Ca Epi Biomarker Prev* 1999; <sup>2</sup> Moscicki AB et al, *AIDS* 2003

<sup>4</sup> Conley et al, *JID* 2010; <sup>5</sup> Tandon et al, *Am J Obstet Gyn* 2010; <sup>6</sup> Hessel et al, *AIDS* 2009

<sup>7</sup> Patel et al, *Br J Surg* 2010; <sup>8</sup> Park et al, *Gynecol Oncol* 2009; <sup>9</sup> Durante et al, *CEBP* 2003

<sup>10</sup> Etienney I et al, *Dis Colon Rectum* 2008; <sup>11</sup> Jacyntho CM et al, *Am J Obstet Gynecol* 2011



# ANAL CANCER SCREENING COULD BE LIFE-SAVING

- HIV
- Cervical cancer/CIN 3
- Vulvar cancer
- ?? Practice regular anal intercourse??

# QUALITY-ADJUSTED LIFE YEARS AND INCREMENTAL COST-EFFECTIVENESS RATIOS FOR ANAL CANCER SCREENING STRATEGIES IN WOMEN WITH HIV

|             | No screening | Annual      | Biennial    |
|-------------|--------------|-------------|-------------|
| Total cost* | \$2,832,937  | \$3,314,789 | \$2,986,947 |
| QALYs       | 352.9        | 357.3       | 357.3       |
| ICER**      |              | \$108,763   | \$34,763    |
| Discounted  |              | \$112,026   | \$35,806    |

*\*Cost of screening strategy for 100 women during a 5-year cycle*

*\*\*Incremental cost-effectiveness ratio determined by (total cost of screening strategy – total cost of no screening) / QALYs no screening).*

# PRO:

- HIV-infected women  $> 25$  years
- CD4  $< 200$
- Women who engage in anal intercourse regularly – highest risk

# CERVICAL CANCER / CIN 3

- All women starting at 5 years after Dx
- Younger age at dx: higher the risk
- Women who engage in anal intercourse regularly

# VULVAR CANCERS

- All women starting at time of Dx
- Younger age at dx: higher risk