

# Anal Cancer Screening: What the OBGYN Needs to Know

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# Disclosures

- I am the site PI of a Teal Health Study. I receive no direct funding, but funds support our research staff.
- I previously was the site PI for a Pfizer vaccine study. This study has ended.
- I am currently the Secretary of the ASCCP and serve on several committees for the International Anal Neoplasia Society (IANS)

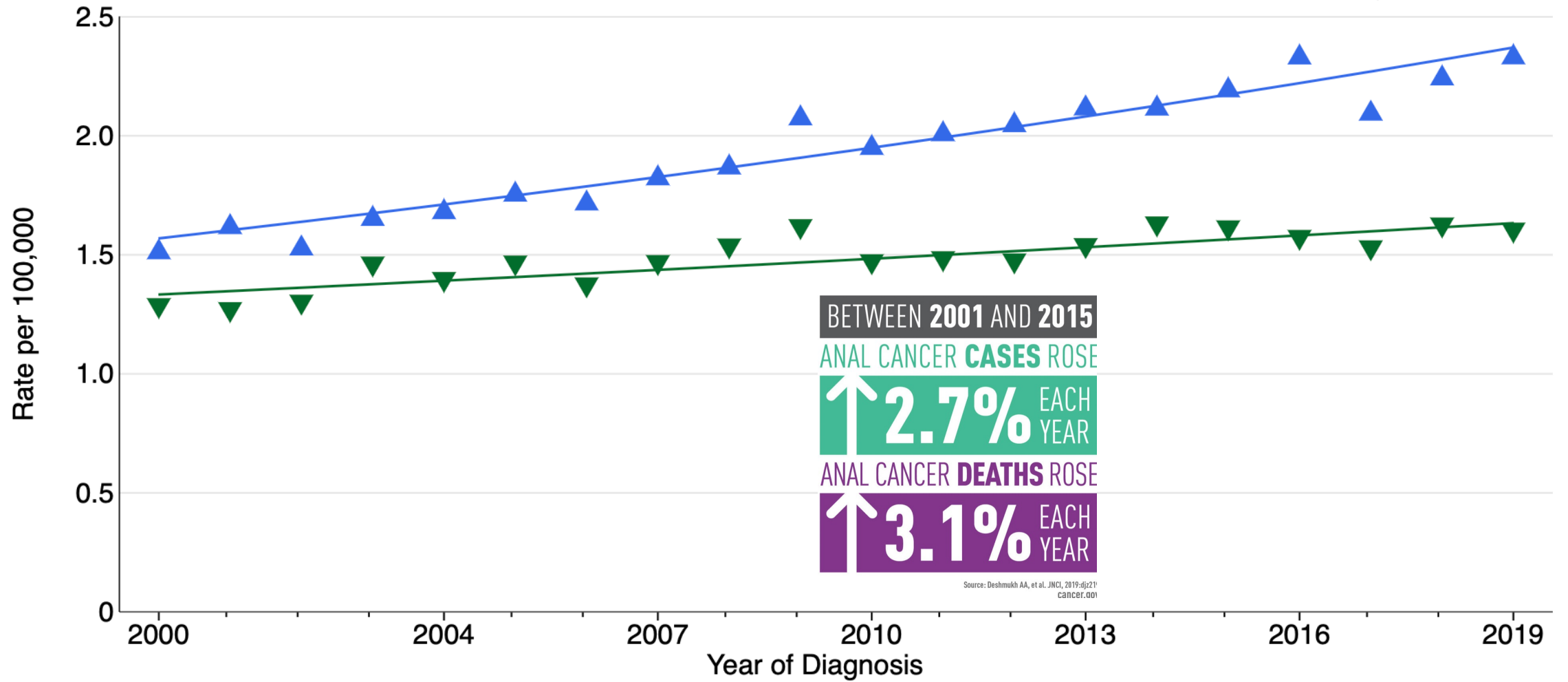
# Objectives

- Define anal cancer and describe the epidemiology
- Associate HPV and anal cancer
- Describe the role of an OBGYN in anal cancer screening
- Identify anal cancer screening strategies

# Anal Cancer Epidemiology

- 9440 new cases annually (3150 in men and **6290 in women**)
- 1670 deaths annual (**930 in women** and 740 in men)
- Most common in white women and black men
- Anal cancer rates are rising

Tap/hover on points for more details. View APC



Legend (Sex)

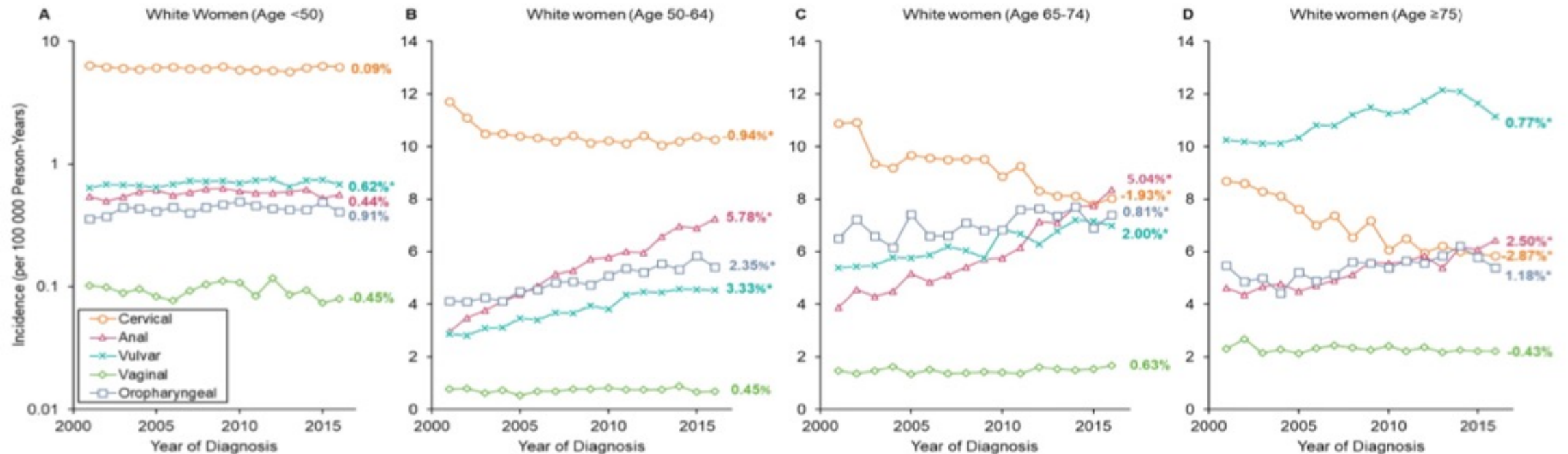
▲ Female

▼ Male

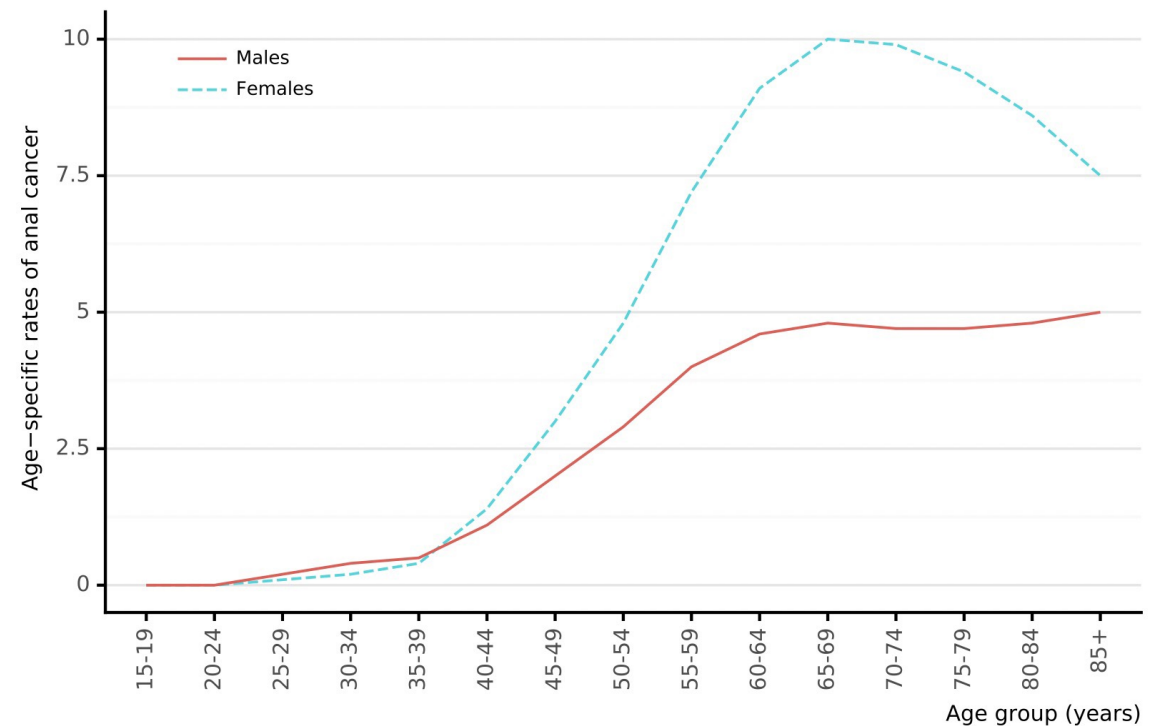
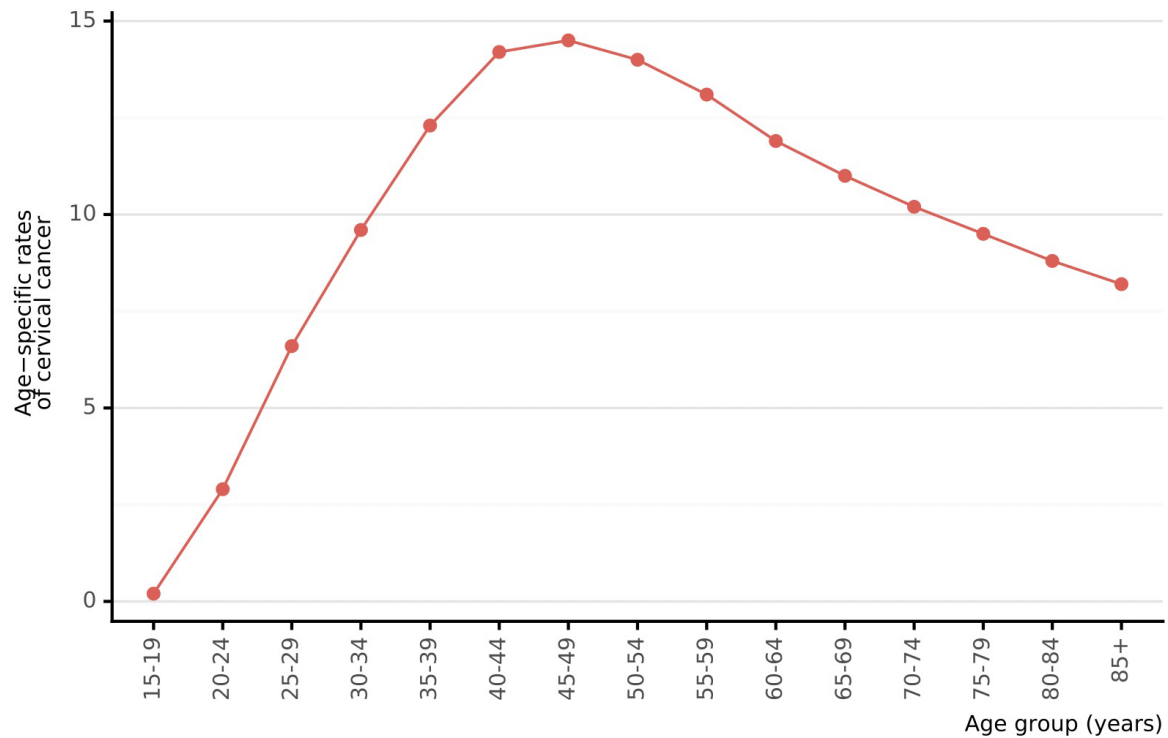
# Anal Cancer

- Most commonly in women between 55-64 years of age

SCCA among White women



# Age specific incidence rates for cervical and anal cancers in the US



# Anal Cancer

- Predominately squamous cell cancers (perianus and anus)
- Symptoms
  - Rectal bleeding (45%)
  - Feeling of a mass (30%)
  - Asymptomatic (20%)
- Treatments
  - Radiation
  - Chemotherapy
  - May need colostomy due to tumor, cancer, or complications of treatment
    - Colostomy-free 5-year survival rate 65-86%



# Anal Cancer

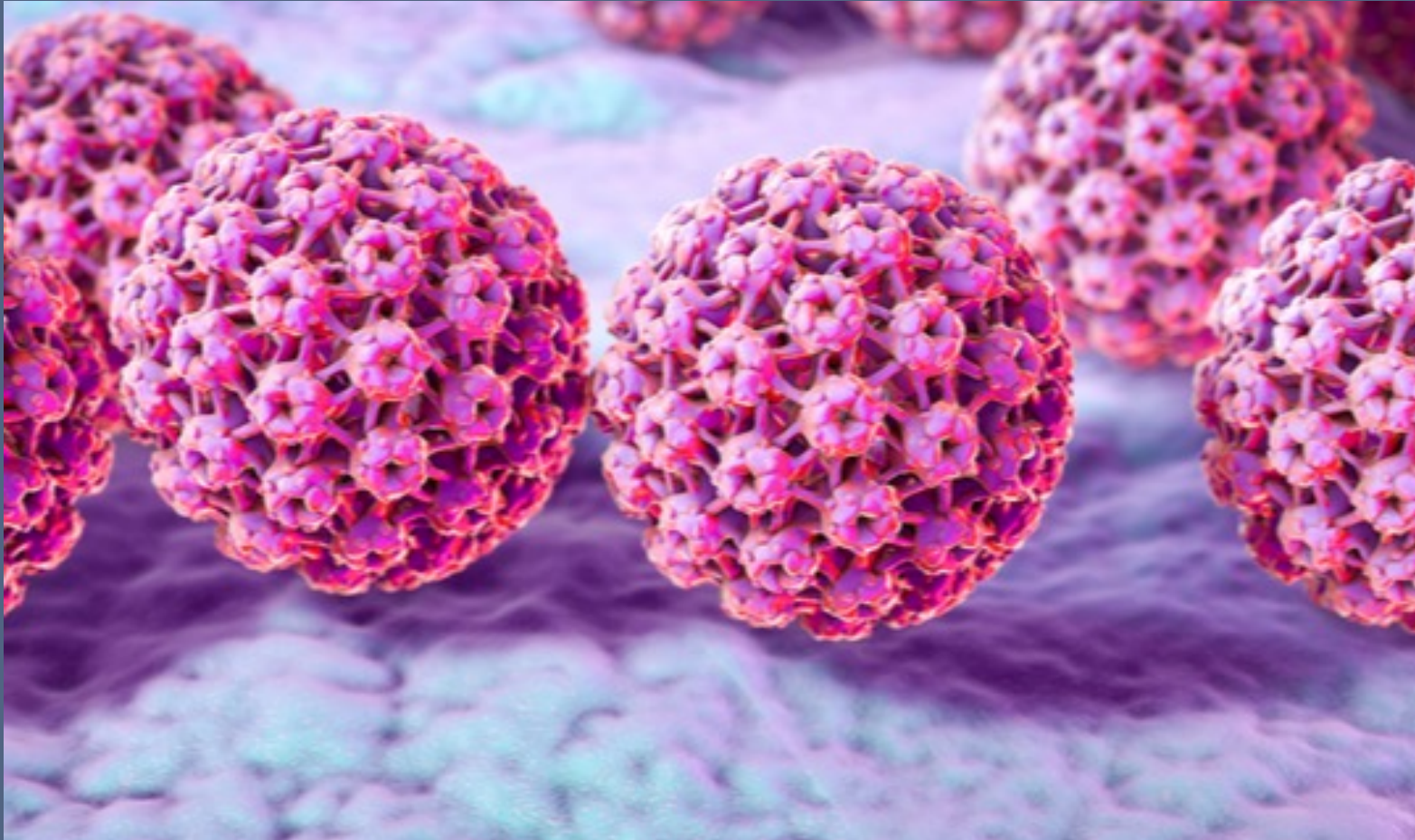
- 50% of anal cancers are diagnosed at stage II or worse
- 5-year survival (all cases) = 71.1%
- 37% positive LNs at diagnosis

Stage	5- year Survival Rate (%)
T2N0	82
T3N0	74
T4N0	57
T2N+	70
T3N+	57
T4N+	42

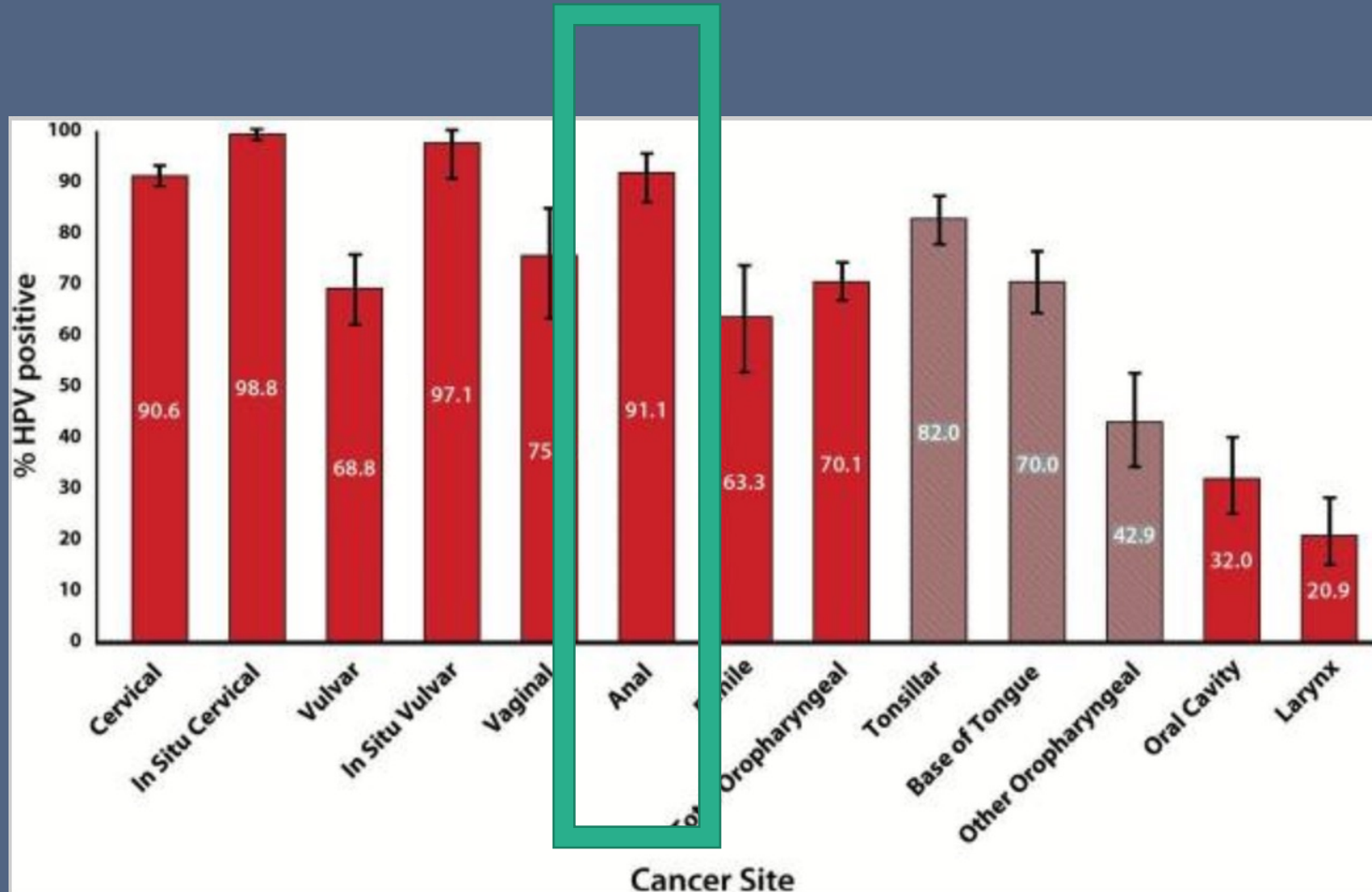
# Risk Factors for Anal Cancer

- Any factor associated with new HPV acquisition
  - Multiple sexual partners
  - Anal condylomas
  - Anal receptive intercourse
  - PWC: history of cervical, vulvar, vaginal dysplasias and cancer
- Age
- Tobacco
- Defects in cell-mediated immunity
  - HIV
  - Immunosuppression

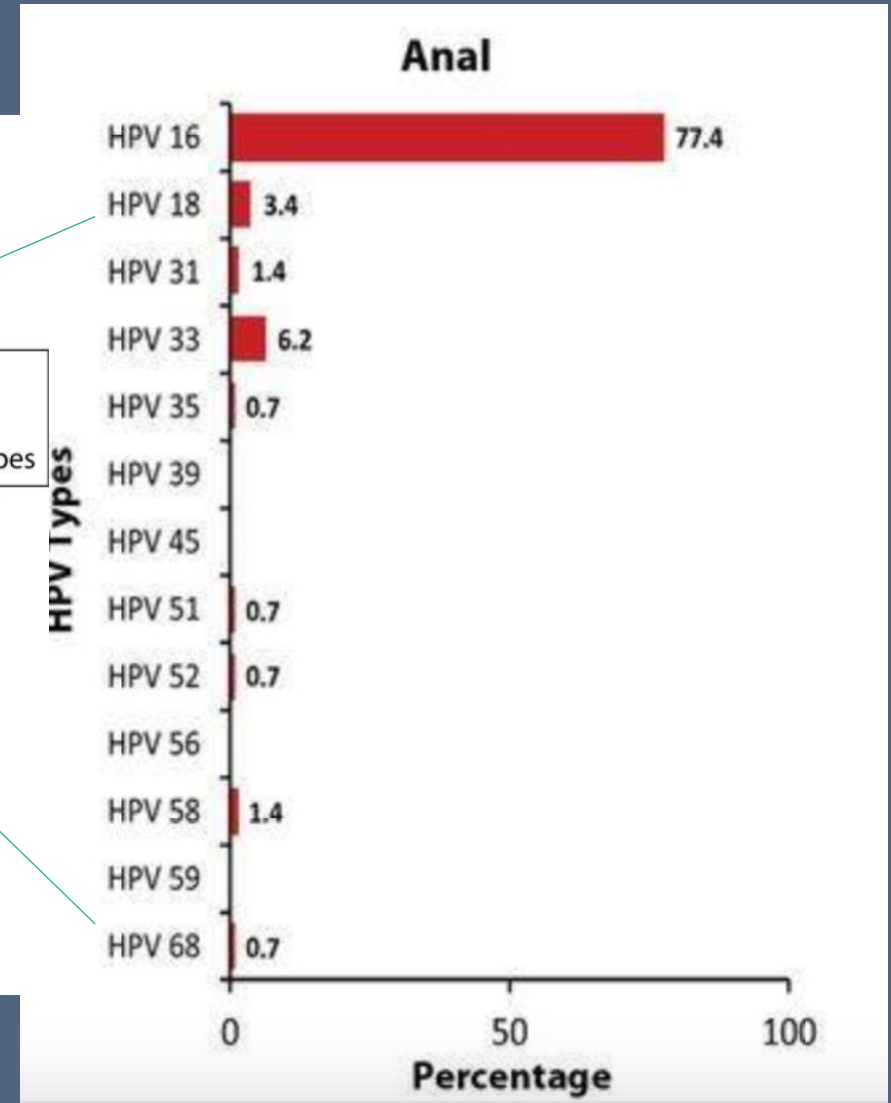
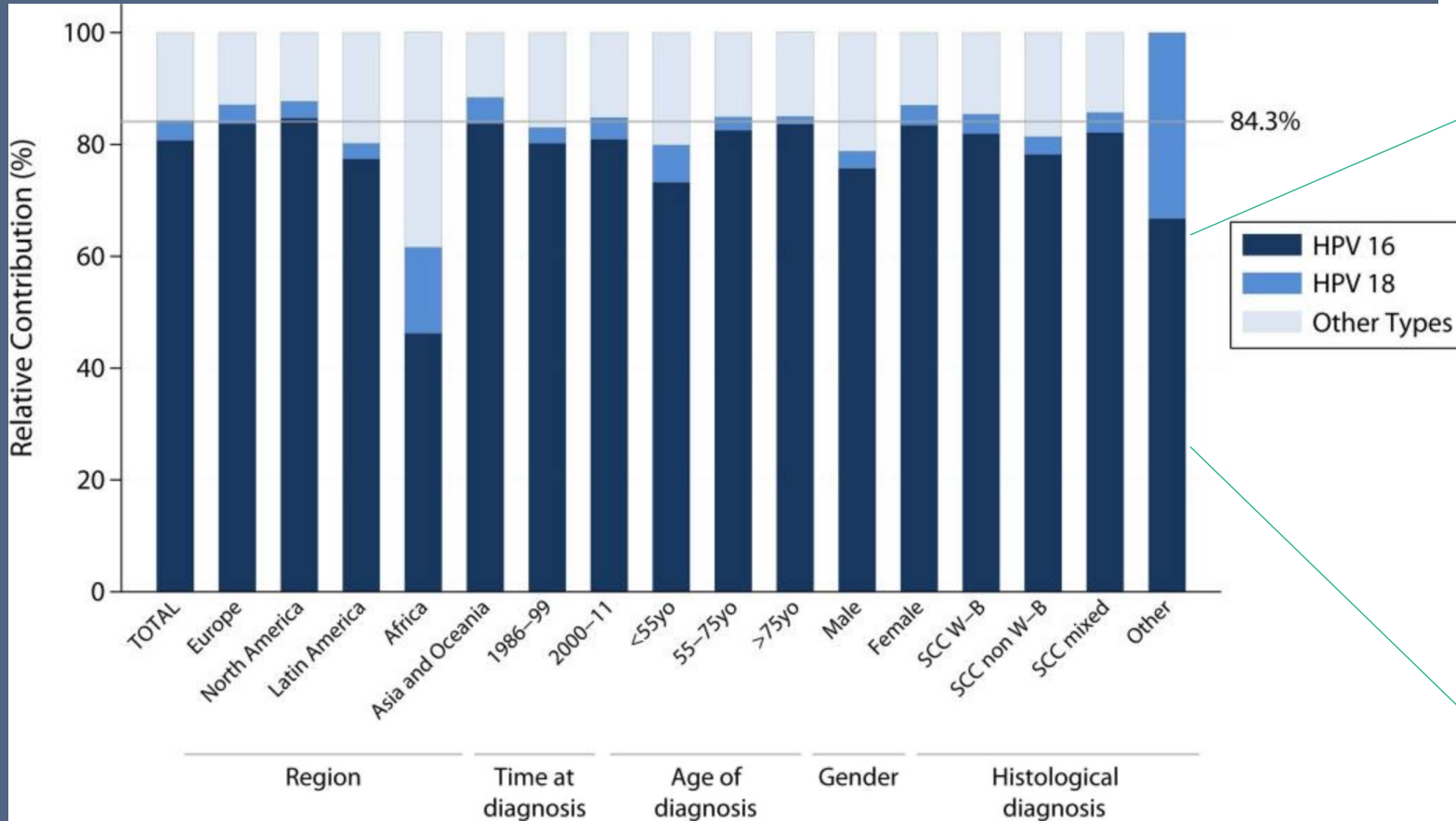
# Epidemiology of Anal HPV & Anal Neoplasias



# HPV association with Anal Cancer

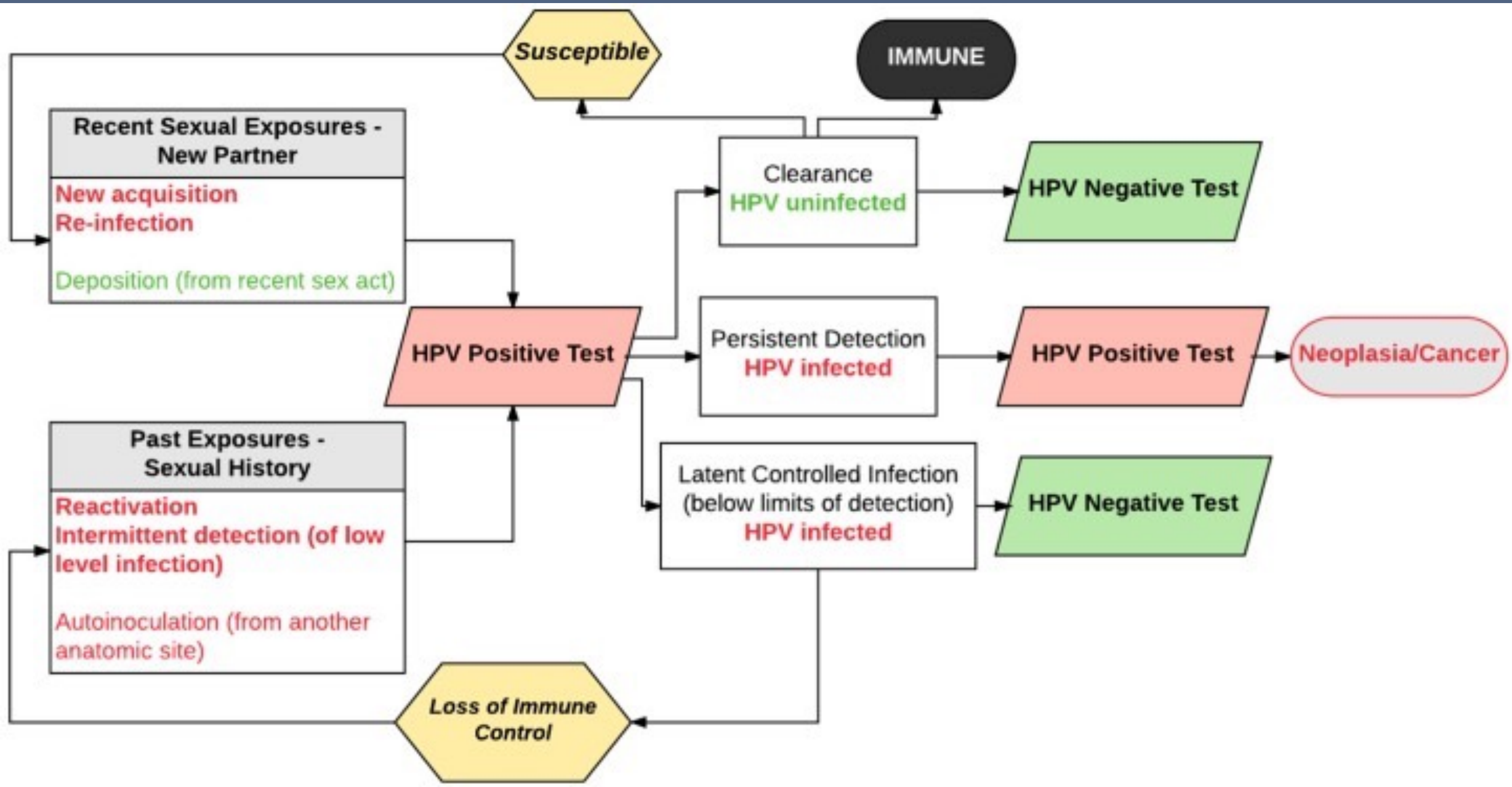


# HPV association with Anal Cancer



# Lessons from the cervix – anal assumptions

- High Grade Squamous Intraepithelial Lesions (HSIL) is the anal cancer precursor lesion
- Natural history of HPV, HSIL, and anal cancer is similar to cervical HPV, HSIL, and cervical cancer
- Hypothesized that:
  - *Screening at risk populations -> Identification of anal HSIL -> treatment of anal HSIL -> prevent progression of anal cancer*

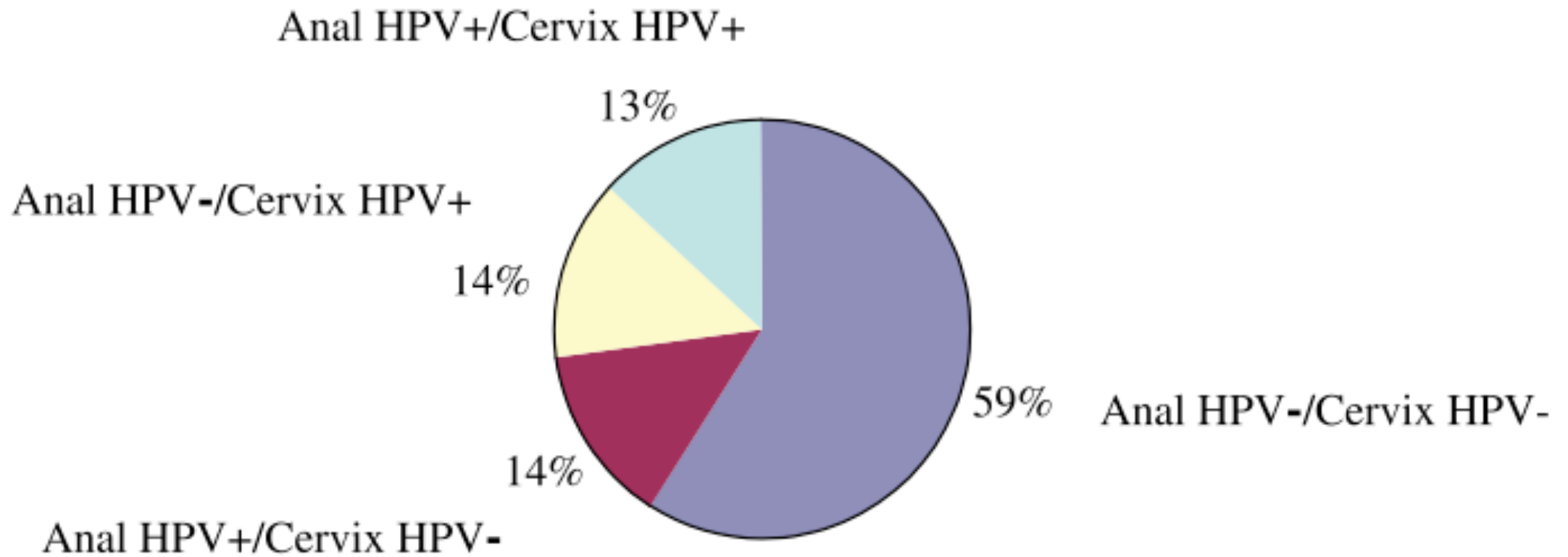


# HPV in Women in the General Population – Hawaiian Cohort Study

- 1378 ethnically diverse healthy women > 18 years of age
  - Mean age 38 years
- Underwent cervical and anal sampling for HPV
  - Baseline
    - 29% had cervical HPV
    - 27% had anal HPV
  - 3-fold increased risk of anal infection if cervix positive
- 80% shared at least one HPV type between sites



# HPV in Women in the General Population – Hawaiian Cohort Study



# HPV in Women in the General Population – Costa Rica Vaccine Trial

- Control of the HPV vaccine trial
  - 2107 women ages 22-29 years
  - Single anal swab provided at year 4
- Anal and cervical HPV prevalence was high
  - Cervical prevalence 31.6% and anal prevalence 36.5%
  - Anal HR HPV prevalence 22.0%
  - Increased risk in women with history of anal intercourse

**Table 2. Univariate and Multivariate Analyses of Determinants for Any Anal Human Papillomavirus (HPV) Infection Among 2107 Young Adult Women From Costa Rica**

Characteristic	No. of Women	Univariate		Multivariate
		HPV Positivity, No. (%) of Women	OR (95% CI)	OR <sup>a</sup> (95% CI)
<b>Lifetime no. of sex partners</b>				
1	552	96 (17.4)	1.0	1.0
2	440	127 (28.9)	<b>1.9 (1.4–2.6)</b>	<b>1.6 (1.2–2.3)</b>
3	335	109 (32.5)	<b>2.3 (1.7–3.1)</b>	<b>1.8 (1.2–2.5)</b>
≥4	780	334 (42.8)	<b>3.6 (2.7–4.6)</b>	<b>2.3 (1.7–3.1)</b>
<i>P</i> for trend			<b>&lt;.0001</b>	<b>&lt;.0001</b>
<b>Lifetime no. of anal intercourse partners</b>				
No history of anal intercourse <sup>b</sup>	1655	470 (28.4)	1.0	1.0
1 <sup>c</sup>	367	147 (40.1)	<b>1.7 (1.3–2.1)</b>	<b>1.6 (1.3–2.1)</b>
≥2	85	49 (57.6)	<b>3.4 (2.2–5.3)</b>	<b>2.8 (1.7–4.5)</b>
<i>P</i> for trend			<b>&lt;.0001</b>	<b>&lt;.0001</b>
<b>Anal fissures</b>				
No	2064	648 (31.4)	1.0	1.0
Yes	43	18 (41.9)	1.6 (.9–2.9)	1.6 (.8–3.2)
<b>Cervical HPV status at 4-year study visit</b>				
Negative	1339	250 (18.7)	1.0	1.0
Positive	768	416 (54.2)	<b>5.1 (4.2–6.3)</b>	<b>4.8 (3.9–5.9)</b>

# Anal HPV infection in the CVT

- Independent risk factors for anal HPV detection among women who report anal intercourse
  - Cervical HPV (aOR 5.4 95%CI 3.4-8.2)
  - Number of sexual partners (aOR 2.2; 95% CI 1.1-4.6) for > 4 partners
  - Number of anal intercourse partners (aOR 1.9; 95% CI 1.1-3.3) for > 2
- Independent risk factors for anal HPV detection among women who reported NO anal intercourse
  - Cervical HPV (aOR 4.7; 95% CI 3.7-5.9)
  - Number of sexual partners (aOR 2.4; 95%CI 1.7-3.4)
  - Report of anal fissures (aOR 2.3; 95% CI 1.1-4.8)

# Why is anal cancer more common among women?

- Anal HPV infection is more common among women than men
- Among men, main acquisition is receptive anal intercourse
  - Relatively small proportion of the population
- Among women there are two methods:
  - Receptive anal intercourse
  - Spread of HPV from the vulva and cervicovaginal tract

# How do Women get anal HPV infections?

- Cross sectional study of women with a previous HPV-mediated gynecologic neoplasia in Tasmania, Australia
- Women presenting for follow-up GYN care had anal swab samples taken for anal cytology and HPV genotyping
- Women with abnormal anal cytology were referred for HRA

# How do Women get anal HPV infections?

- Of the 123 women tested for HR HPV DNA, 48 (39.0%) had anal HR HPV detected
- Front to back wiping was associated with significantly increased prevalence of cytological and histological abnormality and HR HPV carriage/co-carriage (prevalence 1.99-3.6)
- Dabbing post-toilet was significantly associated with decreased prevalence (PR range 0.5-0.62)



# Why Should Gynecologists Care about Anal Cancer Screening?





# Your patients will ask!



Actress Marcia Cross



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On Battling Anal Cancer and Breaking the Stigma of HPV



Published Jan 20, 2022

**Actress Marcia Cross Beat Anal Cancer & She's Made a Point to Give Her Daughters the HPV Vaccine: Here's What You Should Know about the Vaccine and HPV-Linked Cancers**

**Leading Ladies Affected by Anal Cancer Brings New Awareness to Rare Disease**

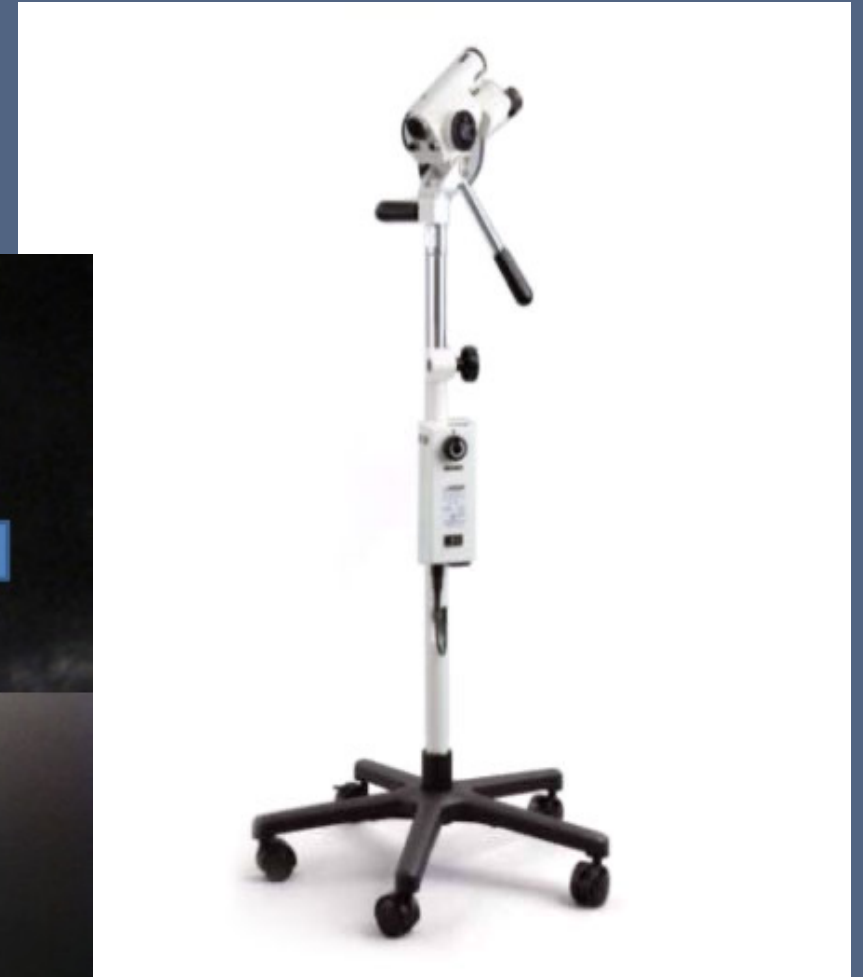
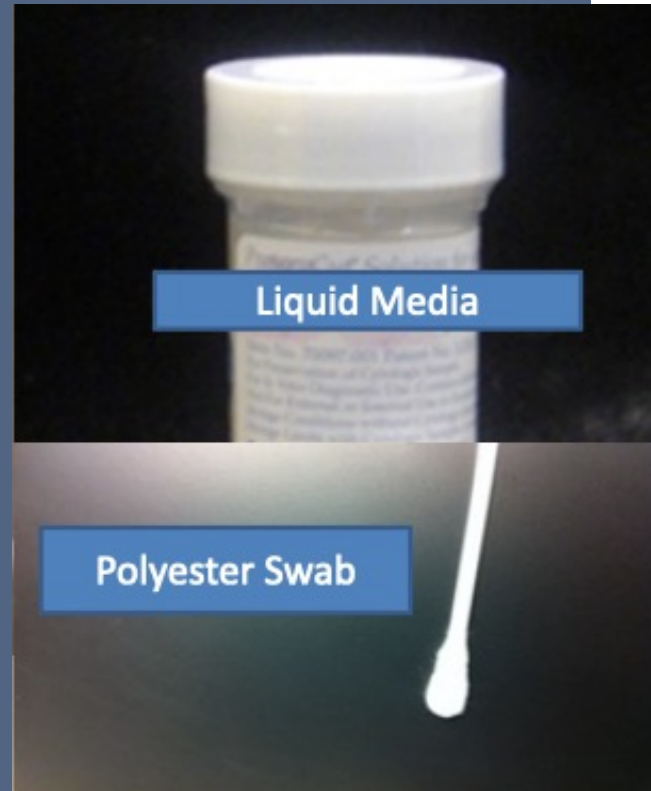


What are the symptoms of anal cancer? Farrah Fawcett put disease in spotlight



# Why Should Gynecologists Care about Anal Cancer Screening?

- You already have most of the tools!!



# Why Should Gynecologists Care about Anal Cancer Screening?

- Experts in HPV-related dysplasias and colposcopy
  - High prevalence of anal HPV in women with cervical and vulvar HPV
  - Anal cancer most commonly diagnosed in women
  - Risk of *multi-zonal disease*

# Multi-Zonal Disease

- Definition – presence of high-grade squamous intraepithelial lesions (HSIL)/carcinoma concurrently at two or more of the following sites/zones: perianus, anal canal, vulva, vagina, or cervix
- Retrospective study from London (Homerton Anogenital Neoplasia Service)
  - January 2012-March 2017
  - All patients who underwent multizonal anogenital neoplasia (MZN) assessment
  - History of any lower genital tract neoplasia (LSIL, HSIL or cancer)

# Multi-Zonal Disease

- MZN Assessment
  - Vulvar, vaginal and cervical colposcopy
  - Examination of the perianus
  - High resolution anoscopy
  - Biopsy any area suspicious for HSIL
- 253 patients underwent MZN
  - Median age 47 years
  - Median duration of followup 12 months
  - 20% history of anogenital cancer

**Table 1** Characteristics of the women with multizonal anogenital neoplasia assessment included in this study ( $n=253$ )

Parameter	Descriptive statistics <sup>a</sup>
Age at first visit (years) median (IQR)	47 (36-56)
Duration of the follow-up (months) median (IQR)	12 (21)
Previous cervical HSIL/cancer, n (%)	94/251 (37)
Previous vulval HSIL/cancer, n (%)	91 (36)
Previous vaginal HSIL/cancer, n (%)	16 (6)
Previous anal HSIL/cancer, n (%)	62 (25)
Previous perianal HSIL/cancer, n (%)	34 (13)
Previous history of anogenital tract HSIL/cancer any site, n (%)	191(75)
One site HSIL/cancer, n (%)	112 (59)
Two sites HSIL/cancer, n (%)	61 (32)
Three sites HSIL/cancer, n (%)	14 (7)
Four sites HSIL/cancer, n (%)	3 (1.5)
Five sites HSIL/cancer, n (%)	1 (0.5)
Previous anogenital cancer/per patient, n (%)	51 (20)
Cervical	9
Vulval	16
Anal	21
Perianal	8
One anogenital cancer site, n (%)	48 (94)
Two anogenital cancers sites, n (%)	3 (6)

# First Visit

## MZN At first visit (n=50)

### Disease location

Site	Number of cases HSIL/cancer
Cervical	3
Vulval	37
Vagina	14
Anal	34
Perianal	40

Number of sites HSIL/cancer	N (%)
Two sites	27 (54)
Three sites	18 (36)
Four sites	5 (10)
Five sites	0 (0)

- 20% with MZN at first visit
  - Most common sites anal canal or perianus
- Most unsuspected or new zone
- Cancer diagnosed in 9 patients

# Follow-up Visits

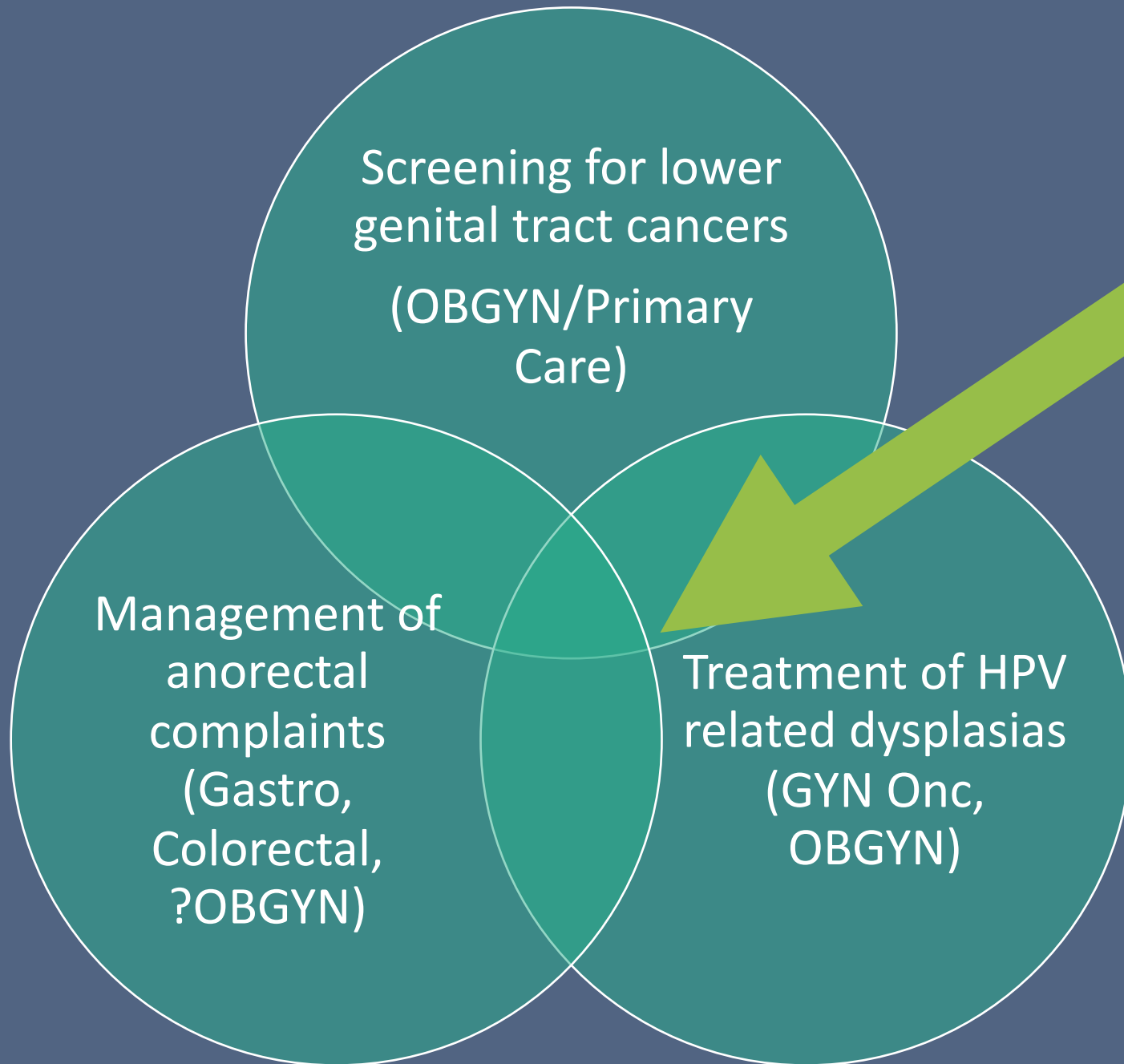
## MZN at follow-up (n=20)

### Disease location

Site	Number of cases HSIL/cancer
Cervical	2
Vulval	12
Vagina	8
Anal	13
Perianal	13

Number of sites HSIL/cancer	N (%)
Two sites	13 (65)
Three sites	6 (30)
Four sites	1 (5)
Five sites	0 (0)

- 11% with MZN during followup
  - New diagnosis
  - Most common sites anal canal or perianus
- 4 new cancers diagnosed during followup



## OBGYNs

- Screen recommendations
- Treat and manage HPV related dysplasia
- Provide treatments and recommendations for anorectal complaints (hemorrhoids, colorectal screening)

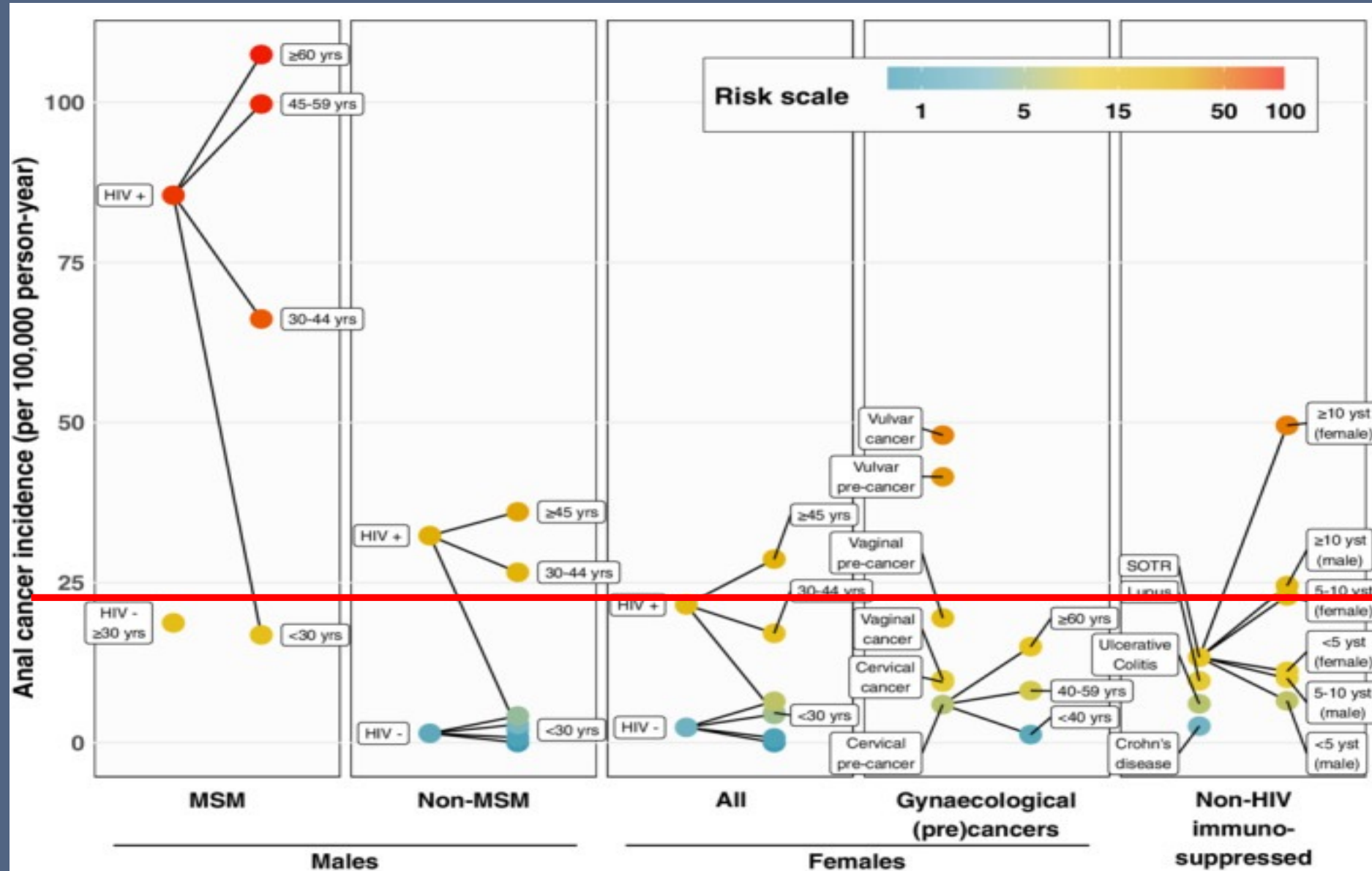
If not  
gynecologists,  
then who??

# Anal Cancer Screening – Who to screen?

- HIV positive women (SIR 18-47)
- Women with HPV-associated cancers (SIR 13.6)
- History of vulvar cancer (SIR 45.5)
- History of cervical cancer (SIR 6.3)
- History of CIN 3/HSIL (SIR 5.9-6.7)
- Condyloma (SIR 7.8-9)



# Anal Cancer Screening – Who to Screen?



# International Anal Neoplasia Society's Consensus Guidelines for ACS

**TABLE 1** Populations for screening.

Population—Risk category	When	Anal cancer incidence <sup>2,5</sup> per 100,000 person-years
Risk Category A (incidence ≥ 10-fold compared to the general population)		
MSM and TW with HIV	Age 35	>70/100,000 age 30–44 >100/100,000 age 45+
Women with HIV	Age 45	>25/100,000 age 45+
MSW with HIV	Age 45	>40/100,000 age 45+
MSM and TW not with HIV	Age 45	>18/100,000 age 45–59 >34/100,000 age 60+
History of vulvar HSIL or cancer	Within 1 year of diagnosis	>40/100,000
Solid organ transplant recipient	10 years post-transplant	>25/100,000
Risk Category B (incidence up to 10-fold higher compared to the general population)		
Cervical/vaginal cancer	Shared decision age 45 <sup>a</sup>	9/100,000
Cervical/vaginal HSIL	Shared decision age 45 <sup>a</sup>	8/100,000
Perianal warts (male or female)	Shared decision age 45 <sup>a</sup>	Unknown
Persistent cervical HPV 16 (>1 year)	Shared decision age 45 <sup>a</sup>	Unknown
Other immunosuppression (e.g., Rheumatoid arthritis, Lupus, Crohn's, Ulcerative colitis, on systemic steroid therapy)	Shared decision age 45 <sup>a</sup>	6/100,000

Incidence among the general population: 1.7 per 100,000<sup>b</sup>



# Screening Strategies for Anal Neoplasia

- Digital Anal Rectal Exam
- Cytology
- High-Risk HPV (HR HPV)
- High Resolution Anoscopy (HRA)



# Summary Recommendations for Anal Cancer Screening in Individuals with Cervices

Population at Risk	SIR Per 100,000	PE Symptoms pain/bleeding	DARE	Anal Cytology	HRA
Women with HIV (age over 45 years)	27		X	X	X
Current or hx of vulvar HSIL or vulvar cancer	45-47		X	X	X
Current or history of cervical or vaginal HSIL	10	X	X		
Organ Transplant Recipients (> 10 years ago)	51		X	X	X
Healthy individuals with cervices with none of the above risk factors	< 25	X	X		

# DARE as a Screening Tool for Anal Cancer

- DARE = Digital Anal Rectal Exam
  - Definition: Palpation of the complete anal canal and visual inspection and palpation of the anal margin (5 cm distal to the anal verge)
  - Goal = Identify palpable lesions in the anal canal
  - Sensitive to palpation of lesions as small as 3 mm
  - Found to be acceptable and low cost
  
- Necessary to perform in women with symptoms (bleeding or pain)

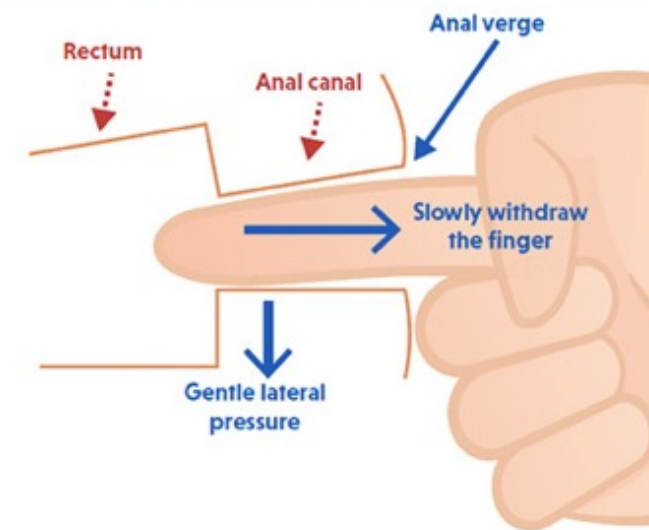
# DARE Positioning



# The DARE

- Expose the anus by separating the buttocks
- Use lubricated, gloved index finger to apply gentle pressure on the anal verge and enter the anal canal
- Pull your finger back to the sphincter feeling the circumference of the anal canal; palpate the perianal region
- Sweep the finger 360 in the rectum applying gentle pressure to the lateral walls

*Figure 1*  
How to perform a digital anal rectal examination (DARE)



# Anal Cytology as a Screening Strategy for Anal Neoplasia

Studies	Sensitivity	Specificity	PPV	NPV
Moscicki 2016	55-93%	32-81%	26-57%	82-88%
Ramos-Cartagena 2020	85.4%	38.8%	45.6%	81.6%
Chiao 2020	83%	50%	37%	
Sambursky 2018	89%	51%	24%	96%
Heard 2015	82%	76%	22%	98%
Albuquerque 2018	71%	73%	55%	84%

Sensitivity, Specificity, PPV and NPV for Anal Cytology to predict anal HSIL

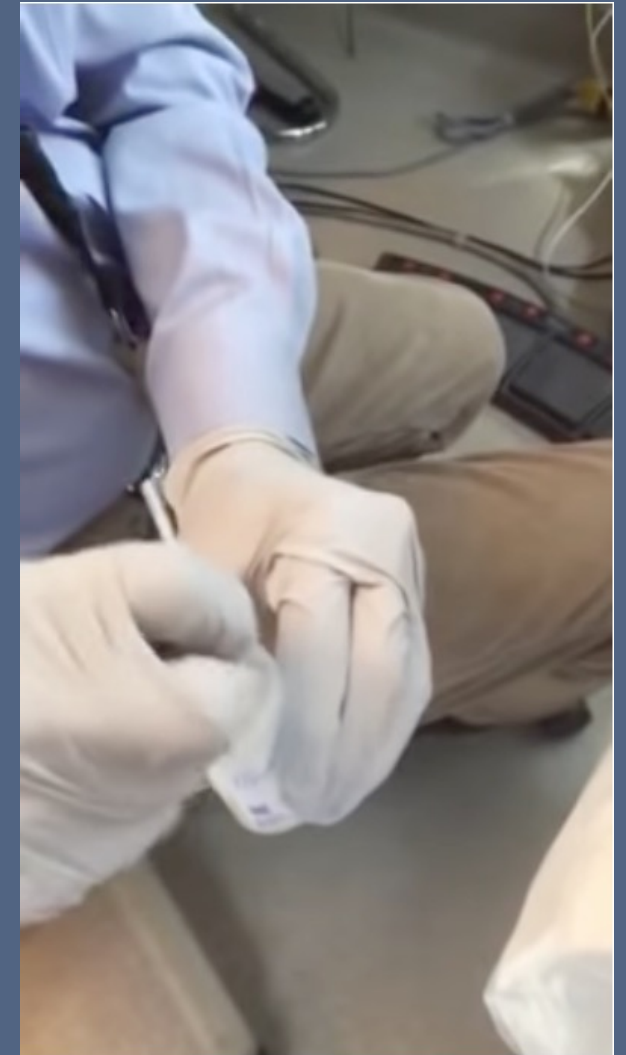
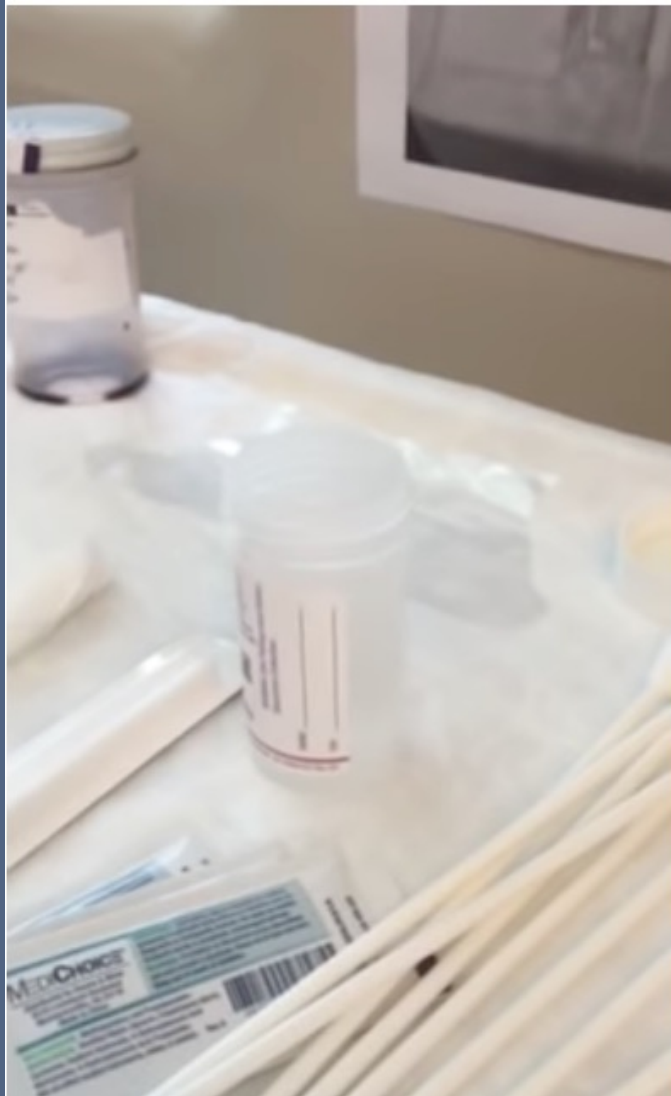


# High-Risk HPV as a Screening Strategy for Anal Neoplasia

Studies	Sensitivity	Specificity	PPV	NPV
Moscicki 2016	55-93%	32.81%	26-57%	82-88%
Ramos-Cartagena 2020	95.8%	31.3%	45.5%	92.6%
Chiao 2020	77%	67%	45%	
Sambursky	96%	48%	24%	99%
Heard 2015	91%	44%	12%	98%

Sensitivity, Specificity, PPV and NPV for HR HPV to predict anal HSIL

# Obtaining Anal Cytology/HPV



<https://www.youtube.com/watch?v=YyzmLYFc7Yc> (Jeff Logan – How to Perform anal Cytology)

**SO GLAD YOU ASKED**

But... should we  
screen??



# Lessons from the cervix – anal assumptions

- High Grade Squamous Intraepithelial Lesions (HSIL) is the anal cancer precursor lesion
- Natural history of HPV, HSIL, and anal cancer is similar to cervical HPV, HSIL, and cervical cancer
- Hypothesized that:
  - *Screening at risk populations -> Identification of anal HSIL -> treatment of anal HSIL -> prevent progression of anal cancer*

# High Resolution Anoscopy (*Identification*)

- Office-based procedure for examination of the anus, anal canal and perianus using a colposcope with 5% acetic acid and Lugol's solution
- Adapted from cervical colposcopy
- Tools, terminology, lesion descriptions and patterns validated for anal canal
- Differences from cervical colposcopy? Yes
  - Long learning curve

## HRA

- Synthetic polyester swab
- Anoscopes – flat end 15mm
- Forceps  $\leq$  3mm

Flat-end baby Tischler

- Colposcope

Focal length 250-300mm

Direct view

Magnification ( $>$ )

Angled eyepieces

Side-arm or overhead

## Cervical Colposcopy

- Cytobrush & spatula
- Specula
- Forceps – large & small

Variety of sizes and cups

- Colposcope

Focal length 300-350mm

Direct or videoscope

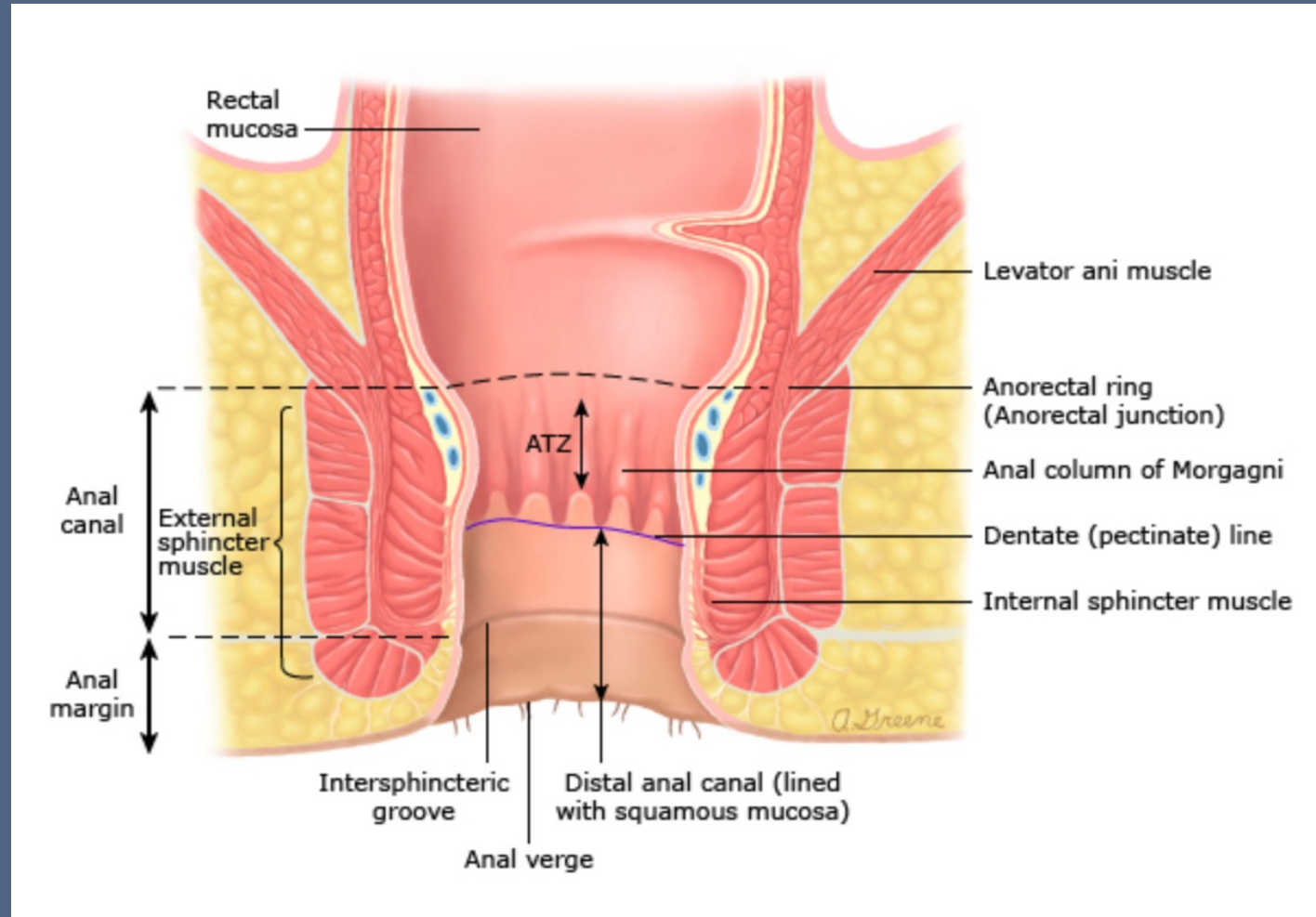
Magnification (low field ok)

Straight-on eyepieces

Center, side-arm, overhead

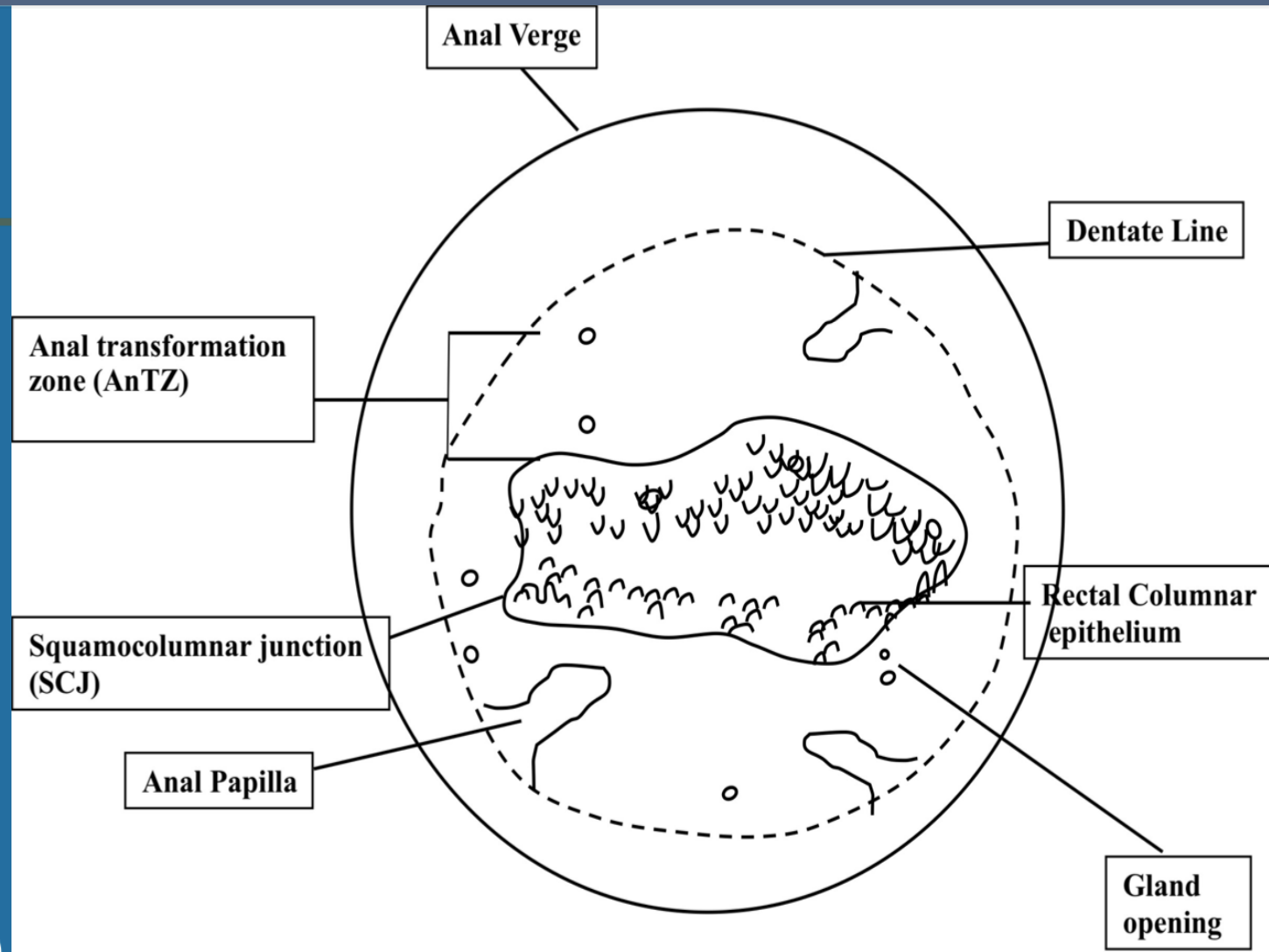
# Anal Cancer – Transformation Zone

- Morphologically analogous to the cervical transformation zone
- Region of squamous metaplasia
- “Immature” squamous metaplasia
  - Leading edge at SCJ
  - Most susceptible to HPV



# Terminology

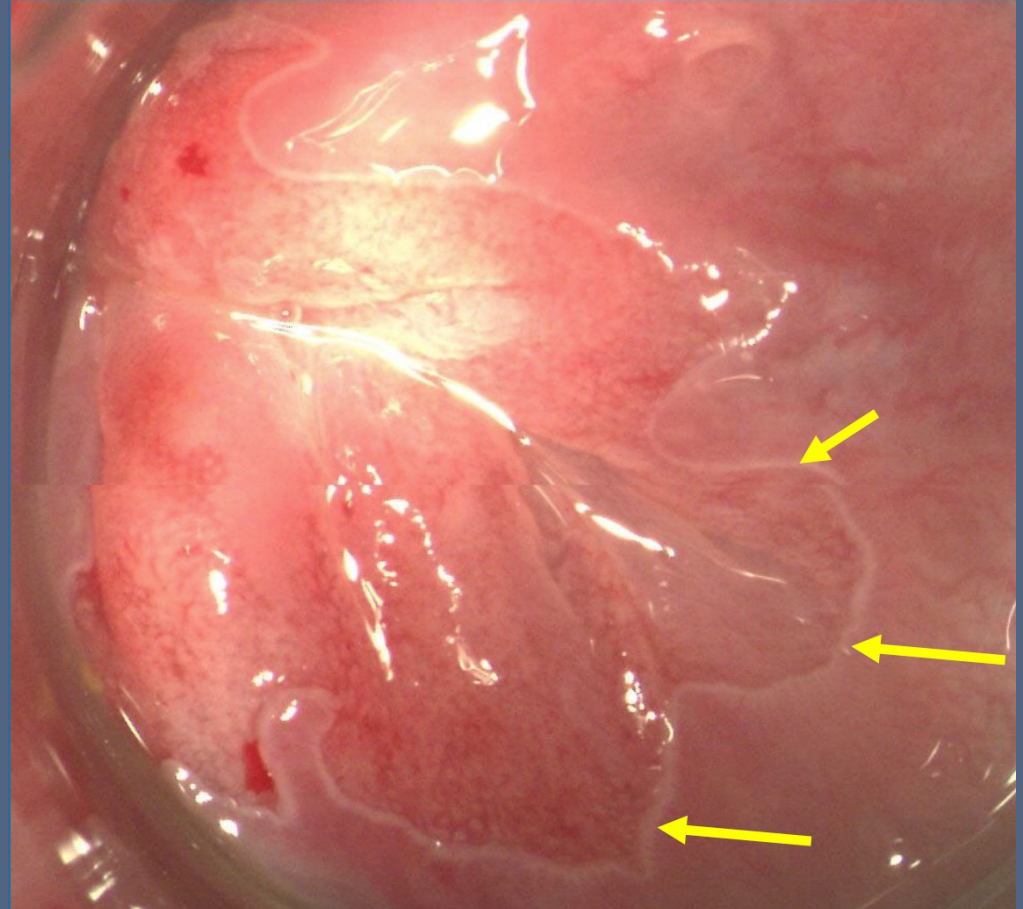
- Rectal/columnar (larger view)
- SCJ (harder to find)
- AnTZ (less features)
- Dentate Line
- Verge
- Perianus = anal margin  
5 cm (anterior midway to introitus)





# HRA View of the SCJ

- Anal squamous epithelium abuts the rectal columnar epithelium
- Thin white line of metaplasia
- Only seen with acetic acid and metaplasia
- Need manipulation to see in its entirety
- There is always an SCJ
- Close to the verge in women



# HRA Exam Steps

1) Position – lateral or prone.



2) Insert Q-tip wrapped in gauze soaked in 5% acetic acid through anoscope.

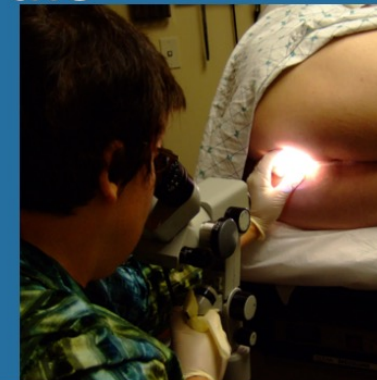


3) Remove anoscope leaving swab & gauze inside. Soak for 1-2 minutes.



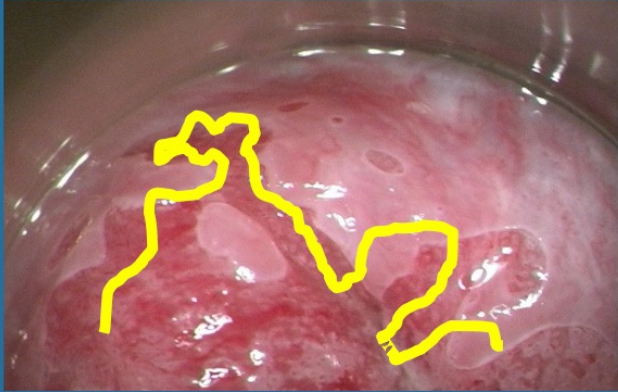
3a) inspect perianus

4) Remove gauze and re-insert anoscope.  
5) Observe through colposcope slowly withdrawing the anoscope until the SCJ is seen.

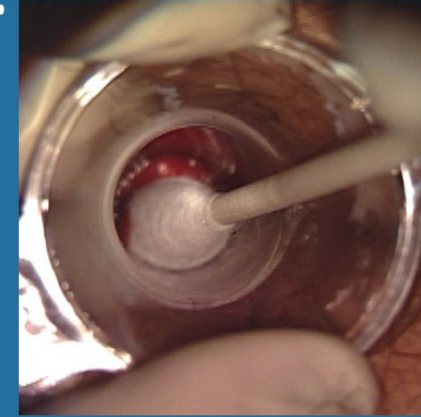


# HRA Exam (con't)

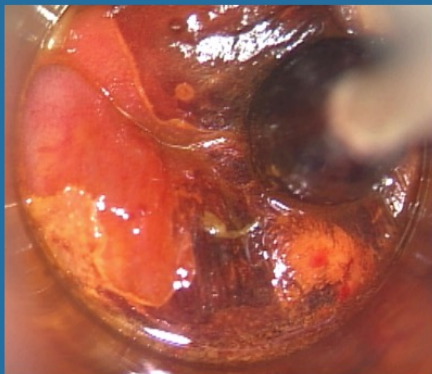
5) Examine entire SCJ



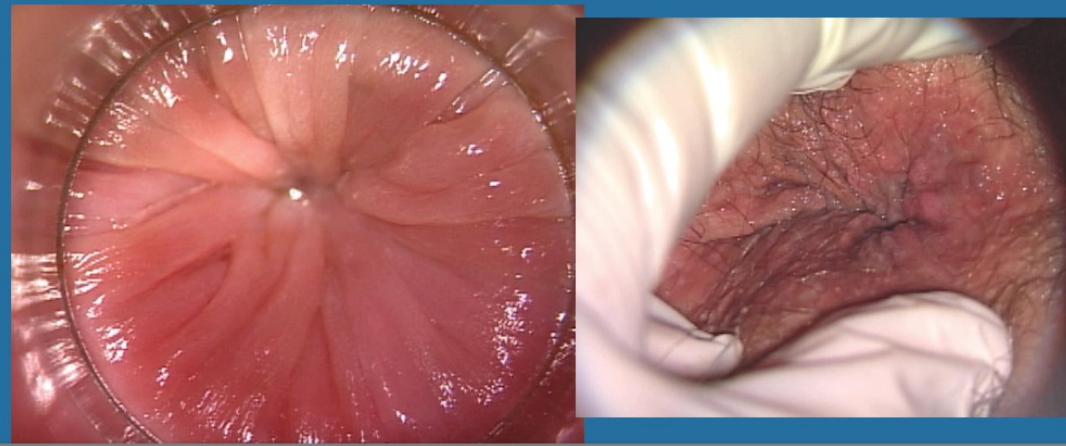
6) Reapply acetic acid liberally throughout exam.



7) Apply Lugol's solution after acetic acid w/cotton swabs



8) Observe distal canal & verge as anoscope is withdrawn, then perianus.

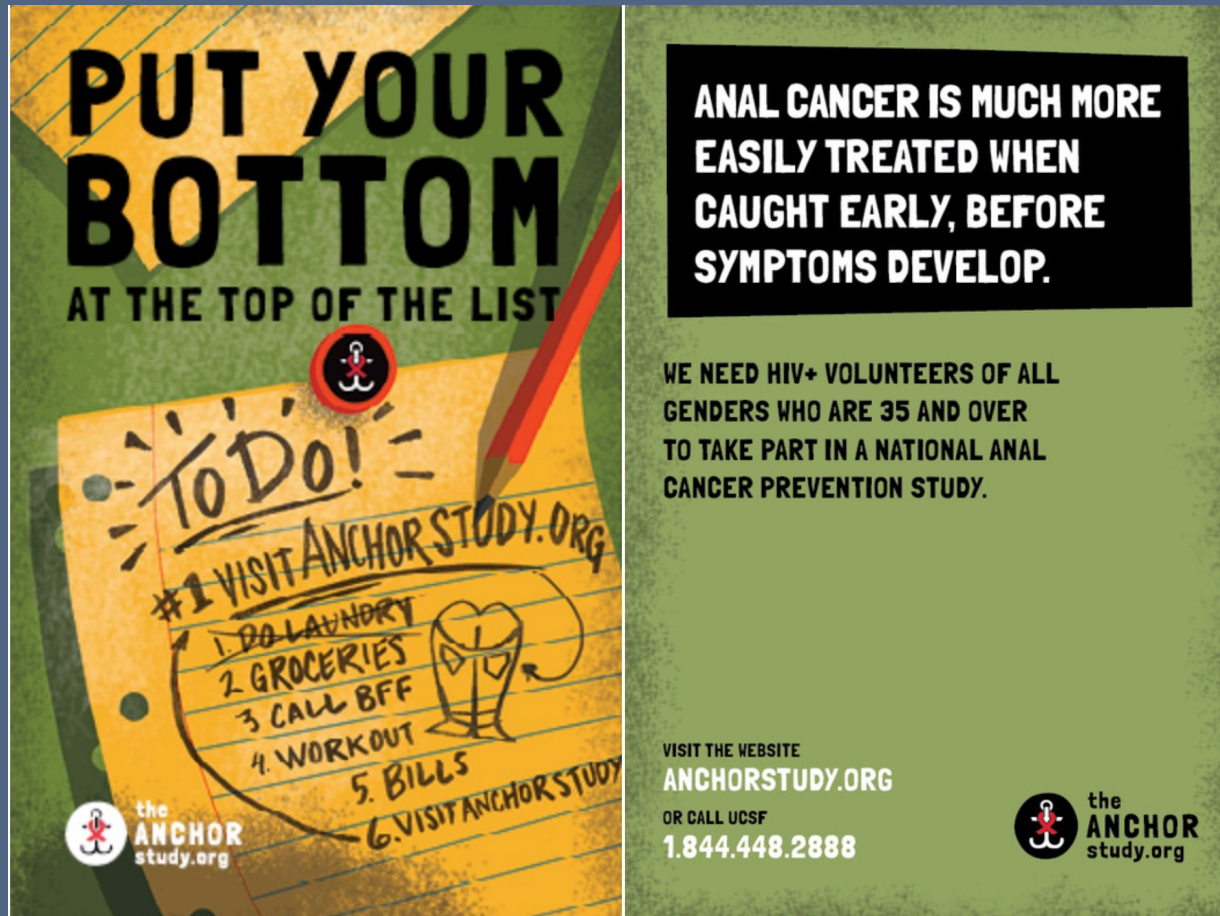


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- Natural history of HPV, HSIL, and anal cancer is similar to HPV, HSIL, and cancer
- Hypothesized that:
  - *Screening at risk individuals -> Identification of anal HSIL -> **treatment of anal HSIL -> prevent progression of anal cancer***

Does treatment work to prevent cancer??

# The ANCHOR Study



**PUT YOUR BOTTOM AT THE TOP OF THE LIST**

**ANCHOR STUDY**

**TO DO!**

1. DO LAUNDRY
2. GROCERIES
3. CALL BFF
4. WORKOUT
5. BILLS
6. VISIT ANCHOR STUDY

**ANCHOR STUDY**

the ANCHOR study.org

**ANCHOR STUDY**

the ANCHOR study.org

**ANAL CANCER IS MUCH MORE EASILY TREATED WHEN CAUGHT EARLY, BEFORE SYMPTOMS DEVELOP.**

WE NEED HIV+ VOLUNTEERS OF ALL GENDERS WHO ARE 35 AND OVER TO TAKE PART IN A NATIONAL ANAL CANCER PREVENTION STUDY.

VISIT THE WEBSITE  
**ANCHORSTUDY.ORG**  
OR CALL UCSF  
**1.844.448.2888**



- Anal Cancer HSIL Outcomes Research
- Enrolled patients over 35 years of age with HIV and confirmed anal HSIL
- Randomized to treatment versus expectant management

# The ANCHOR Study - Results

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

## Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

J.M. Palefsky, J.Y. Lee, N. Jay, S.E. Goldstone, T.M. Darragh, H.A. Dunlevy, I. Rosa-Cunha, A. Arons, J.C. Pugliese, D. Vena, J.A. Sparano, T.J. Wilkin, G. Bucher, E.A. Stier, M. Tirado Gomez, L. Flowers, L.F. Barroso, R.T. Mitsuyasu, S.Y. Lensing, J. Logan, D.M. Aboulafia, J.T. Schouten, J. de la Ossa, R. Levine, J.D. Korman, M. Hagensee, T.M. Atkinson, M.H. Einstein, B.M. Cracchiolo, D. Wiley, G.B. Ellsworth, C. Brickman, and J.M. Berry-Lawhorn, for the ANCHOR Investigators Group\*

# The ANCHOR Study - Results

- Patients enrolled September 24, 2014 through August 5, 2021
  - Screened 10,723 total patients
  - HSIL confirmed
    - 4257/7729 men (55.1%)
    - 860/1822 women (47.2%)
    - 188/280 transgender persons (67.1%)
    - 17 patients received an anal cancer diagnosis at baseline
- 4459 enrolled patients
  - Median followup of 25.8 months

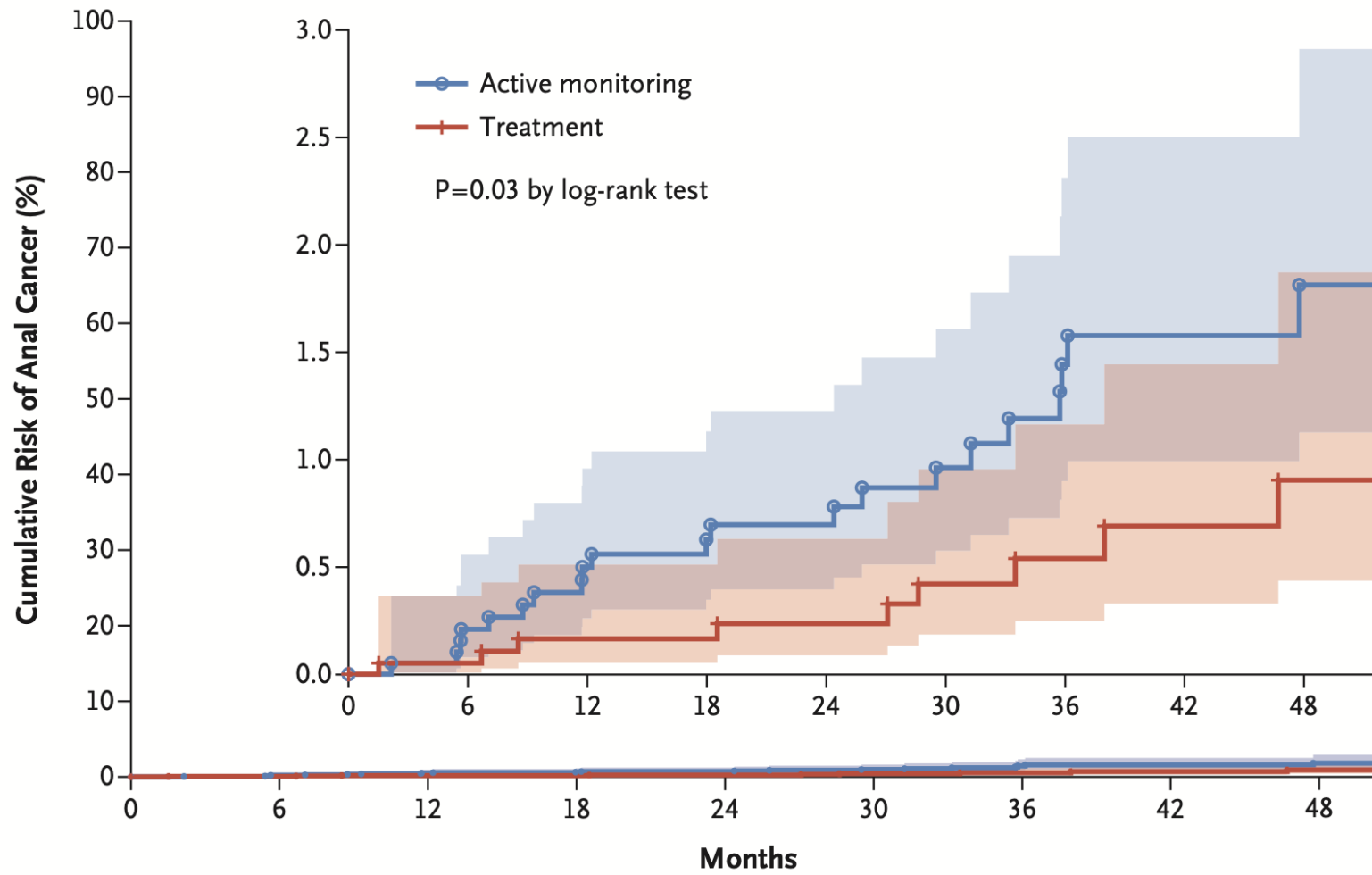
# Types of Treatment

- No specific treatment for HPV
  - Patient-applied topical: imiquimod and 5% fluorouracil cream
  - Clinician-applied topical: 85% trichloroacetic acid, cryotherapy
  - Clinician-applied ablation: infrared coagulation (4.8%), electrocautery (86.2%), laser
  - Surgical excision



# Progression to Cancer

- Cumulative progression to cancer at 48 months was 0.9% in the treatment arm and 1.8% in the monitoring arm
  - 57% reduction in anal cancer (95% CI 6% to 80%, p=0.029)
- Cancer incidence in the treatment arm was 173/100,000 PY of follow-up compared to 402/100,000 PY in the AM monitoring arm
  - 185/100,000 PY (95% CI: 115-298) for lesions less than or equal to 50% size
  - 1047/100,000 PY (95% CI: 608-1803) >50 size
  - Hazard ratio 5.26, 95% CI: 2.54-10.87



**No. at Risk**

Active monitoring	2219	1856	1671	1459	1238	992	758	572	407
Treatment	2227	1871	1655	1473	1224	989	753	557	409

- 9 cancers diagnosed in treatment group
- 22 cancers diagnosed in active monitoring
- Overall reduction in rate of cancer 57%

**Figure 2. Kaplan–Meier Curve of the Time to Progression to Anal Cancer.**

The inset shows the data on an expanded y axis. The shaded areas represent 95% confidence intervals.

# Take home points from the ANCHOR study

- Treating anal HSIL can prevent invasive anal cancer
- Almost all participants had office-based electrocautery, primarily hyfrecation
- Operating room for extensive biopsying, disease too bulky to treat in office
- Treatment for HSIL is improving but even better treatments are needed
- Careful follow-up critical as patients tend to recur despite method of treatment

# Should we screen?

- High risk patient populations
- Able to identify precancerous lesions
- Effective treatment
- Reduction of anal cancer...

OBGYNs – YES YOU SHOULD!



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**BREAKING NEWS**



**NEW GUIDELINES**



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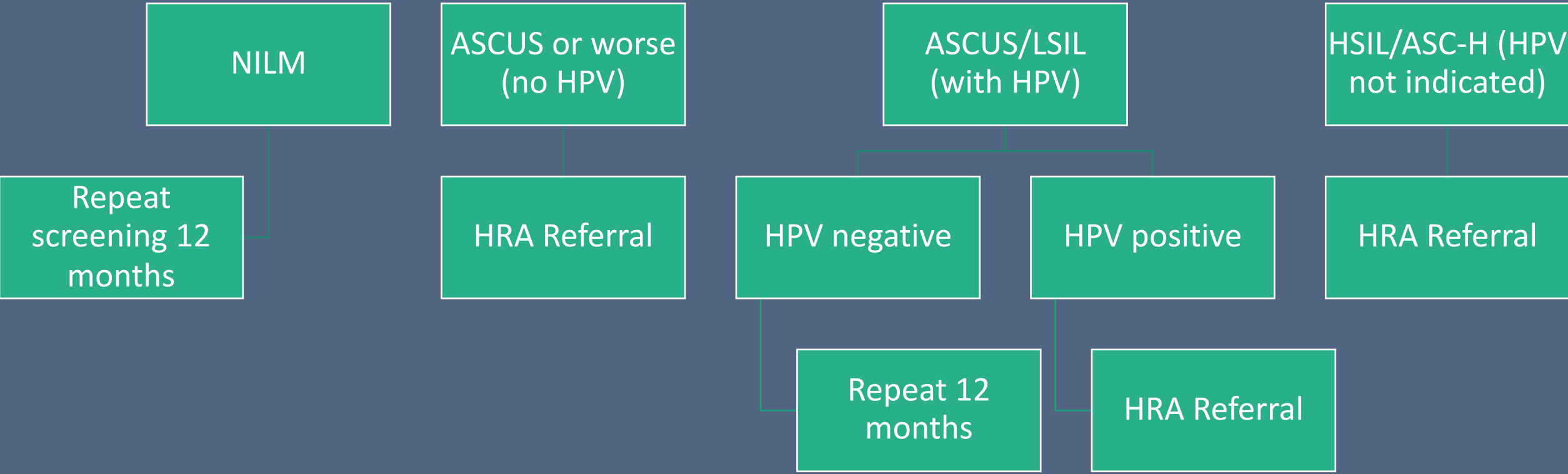
## **International Anal Neoplasia Society's consensus guidelines for anal cancer screening**

Elizabeth A. Stier , Megan A. Clarke, Ashish A. Deshmukh, Nicolas Wentzensen, Yuxin Liu, I. Mary Poynten, Eugenio Nelson Cavallari, Valeria Fink, Luis F. Barroso ... [See all authors](#)

First published: 31 January 2024 | <https://doi.org/10.1002/ijc.34850>

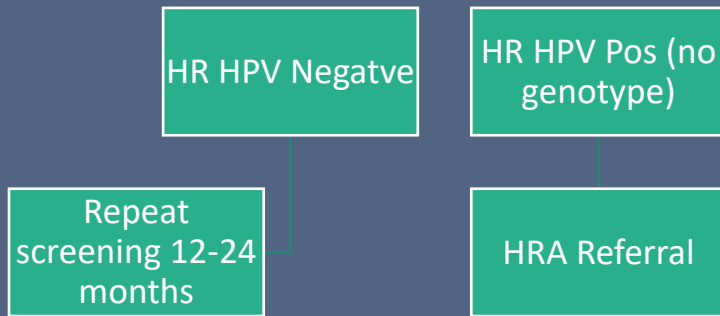
**FROM THE DESK OF RON BURGUNDY**

# Management of Results – Cytology (+/- HPV)

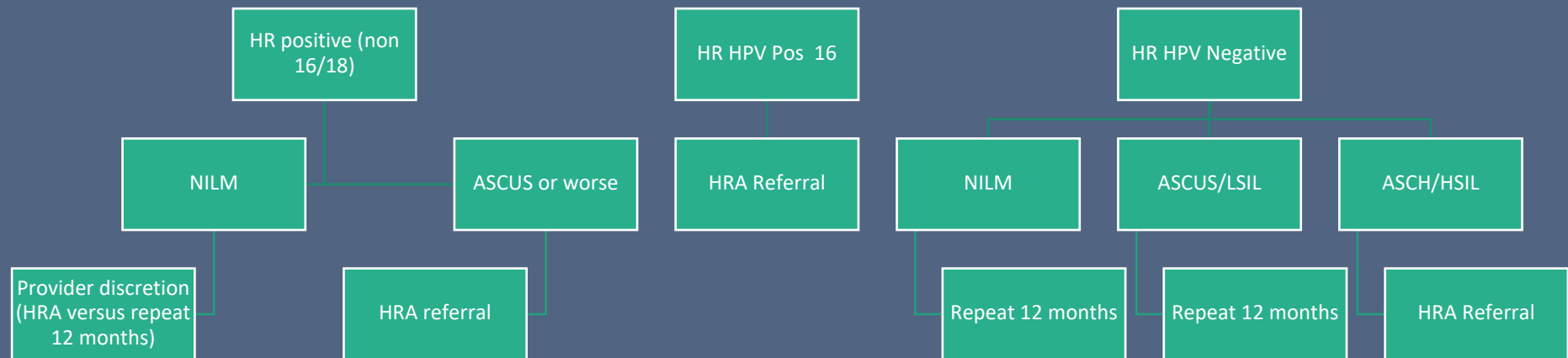


# Management of Results – HR HPV Testing

## Primary HPV – No Cytology



## Primary HPV – Reflex Cytology



# Objectives

- Define anal cancer and describe the epidemiology
- Associate HPV and anal cancer
- Describe the role of an OBGYN in anal cancer screening
- Identify anal cancer screening strategies





DARE to CARE..  
BACK THERE!

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