



ANCHORS AWEIGH! NEXT STEPS IN ANAL CANCER PREVENTION

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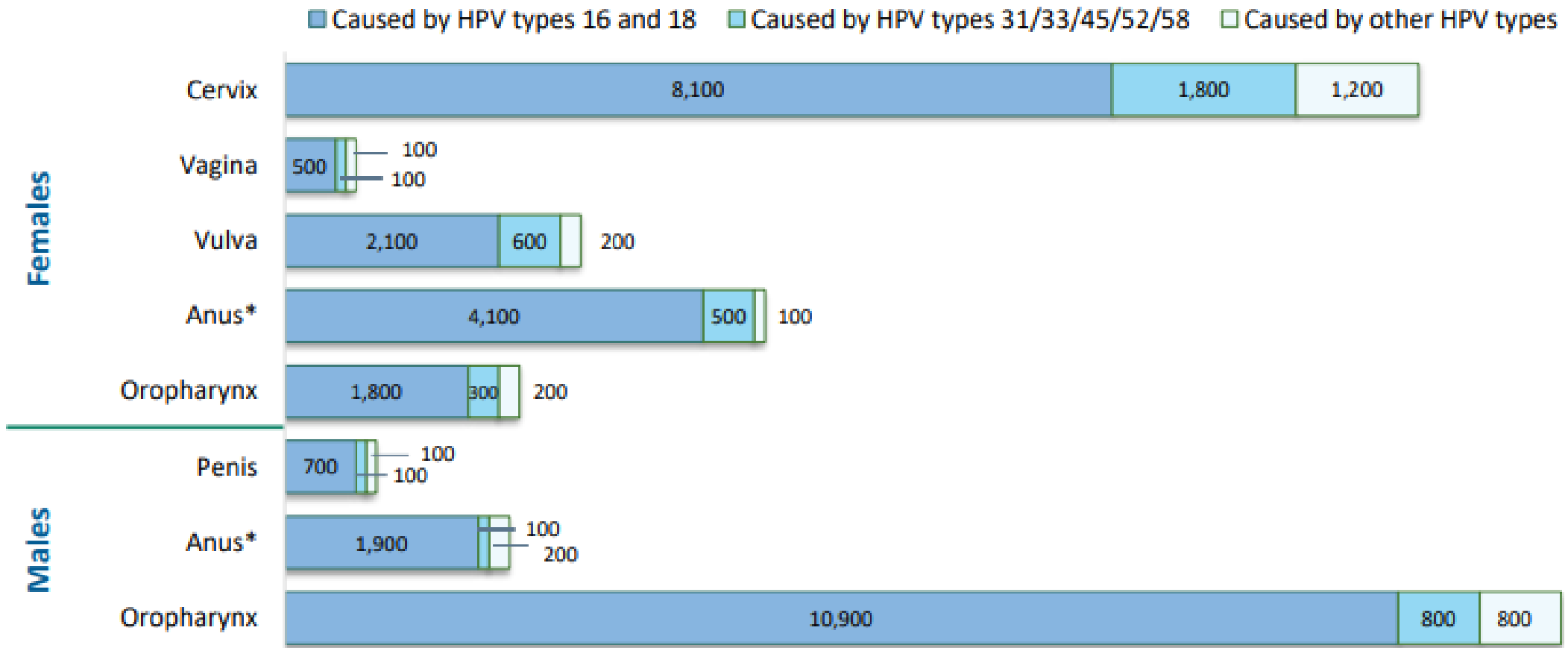
Disclosures

- *Partial Salary support through the NIH ANCHOR grant.*
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- *“Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.”*

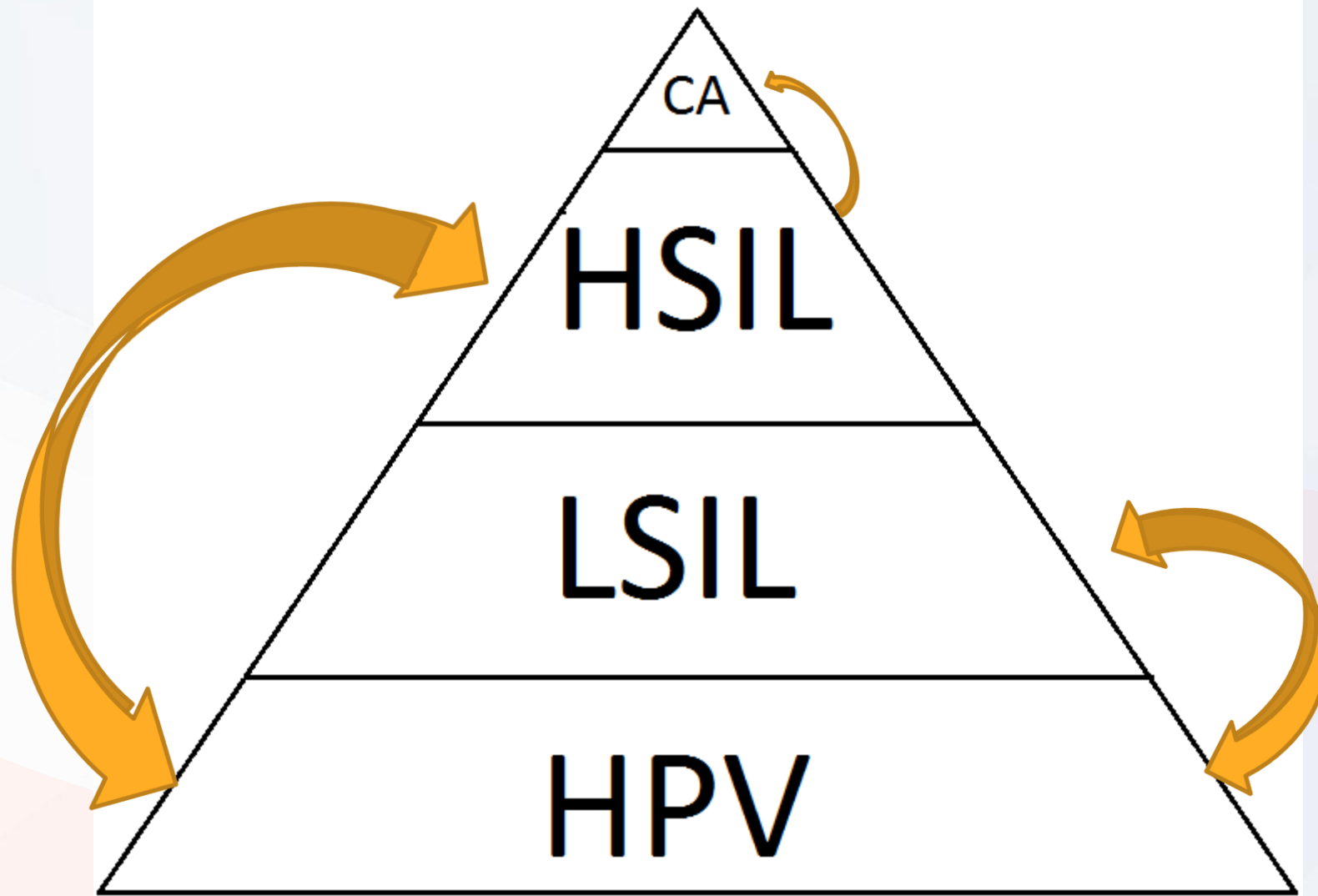
Learning Objectives

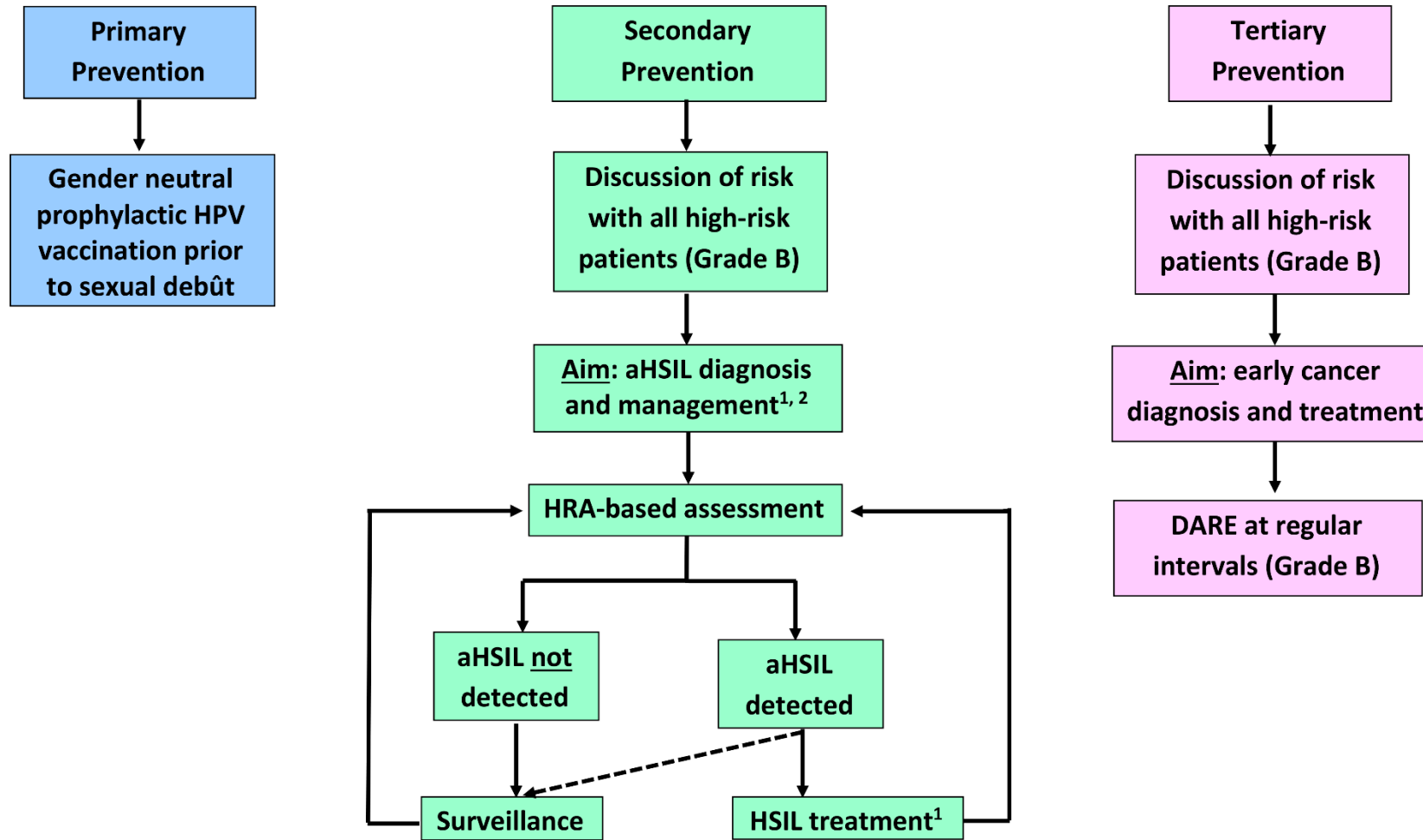
- Review anal cancer risk epidemiology
- Discuss a three pronged approach to anal cancer prevention
- Review Secondary Prevention in the context of the ANCHOR study results

Estimated Annual Number of Cancer Cases Attributable to HPV by Sex, Cancer Type, and HPV type



Centers for Disease Control and Prevention. Cancers Associated with Human Papillomavirus, United States—2015–2019. U.S. Cancer Statistics Data Brief, no. 32. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2022.





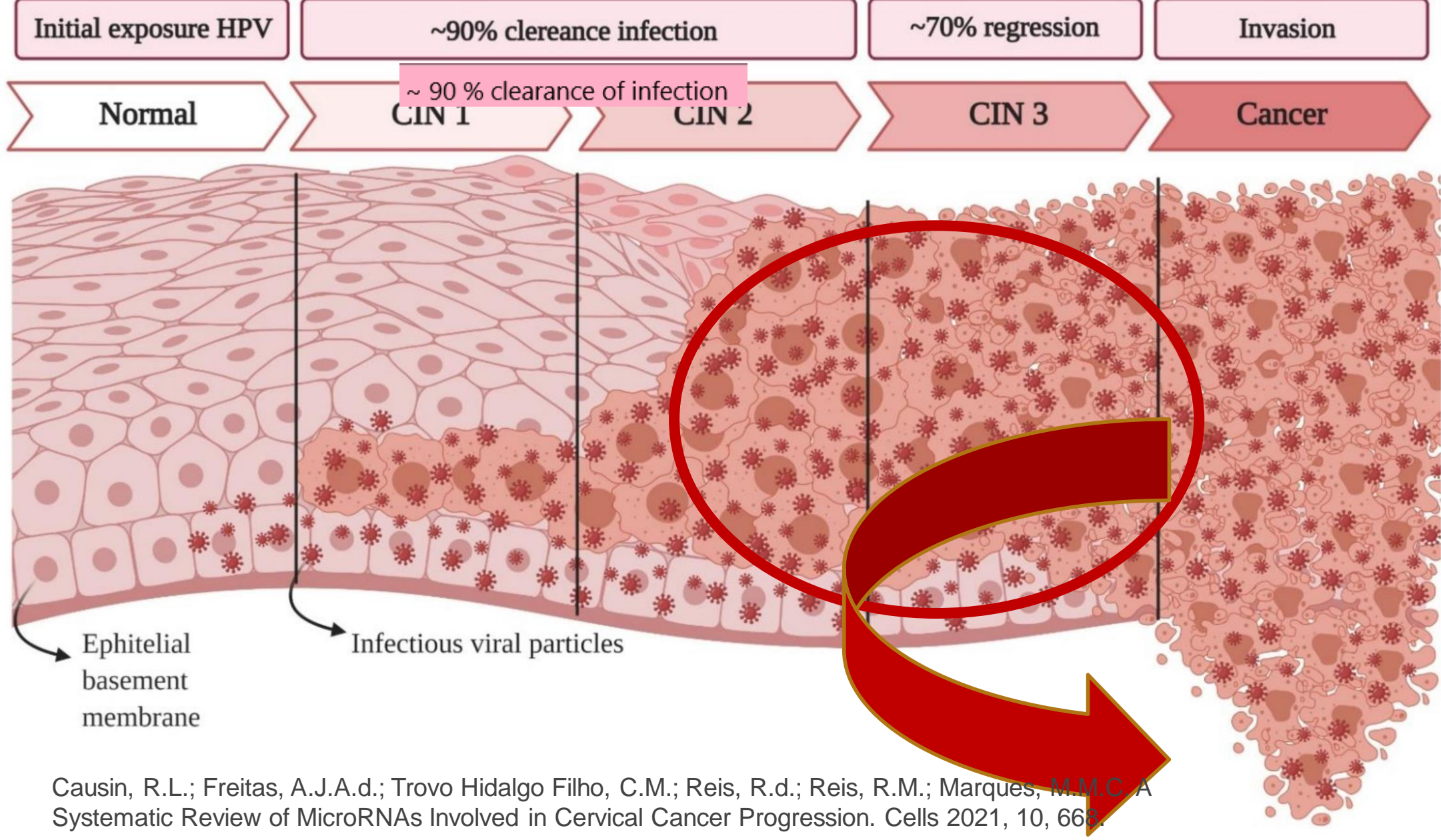
¹ Grade A for PLWH ≥ 35 yo

² Typically includes screening tests such as anal cytology +/- HPV testing

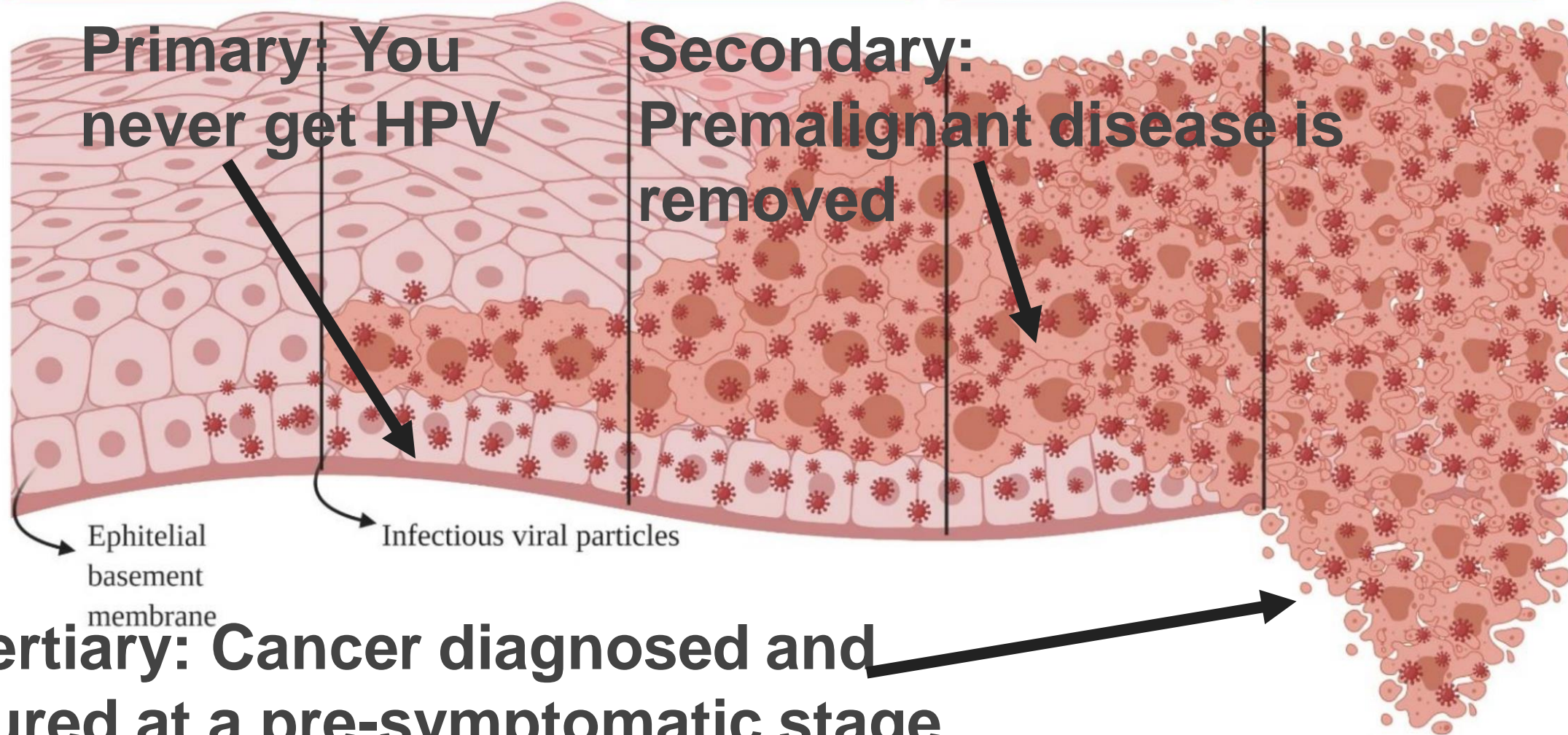
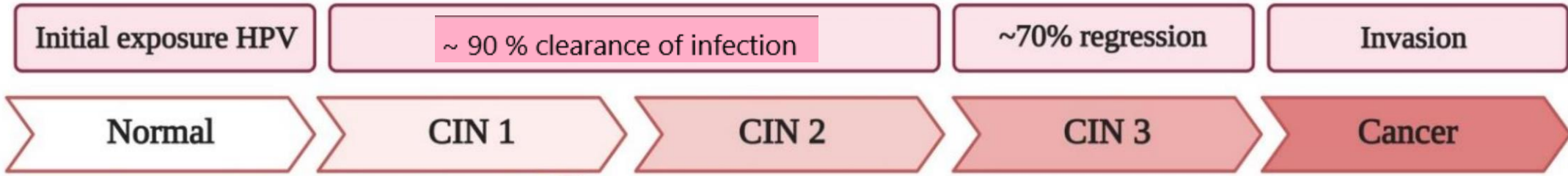
HSIL = histologic anal High grade Squamous Intraepithelial Lesion

DARE = Digital Anal Rectal Examination

Luis Barroso, Elizabeth Stier, Richard Hillman, Joel Palefsky, Anal Cancer Screening and Prevention: Summary of Evidence Reviewed for the 2021 Centers for Disease Control and Prevention of Sexually Transmitted Infection Guidelines, *Clinical Infectious Diseases*, Volume 74, Issue Supplement 2, 15 April 2022, Pages



Causin, R.L.; Freitas, A.J.A.d.; Trovo Hidalgo Filho, C.M.; Reis, R.d.; Reis, R.M.; Marques, M.M.C. A Systematic Review of MicroRNAs Involved in Cervical Cancer Progression. Cells 2021, 10, 668.



Primary: You never get HPV

Secondary: Premalignant disease is removed

Tertiary: Cancer diagnosed and cured at a pre-symptomatic stage

Who?

- “The wise man learns from the mistakes of the fool.”
- Otto von Bismark

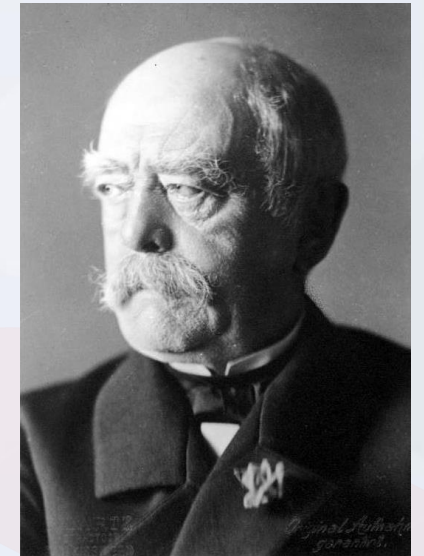
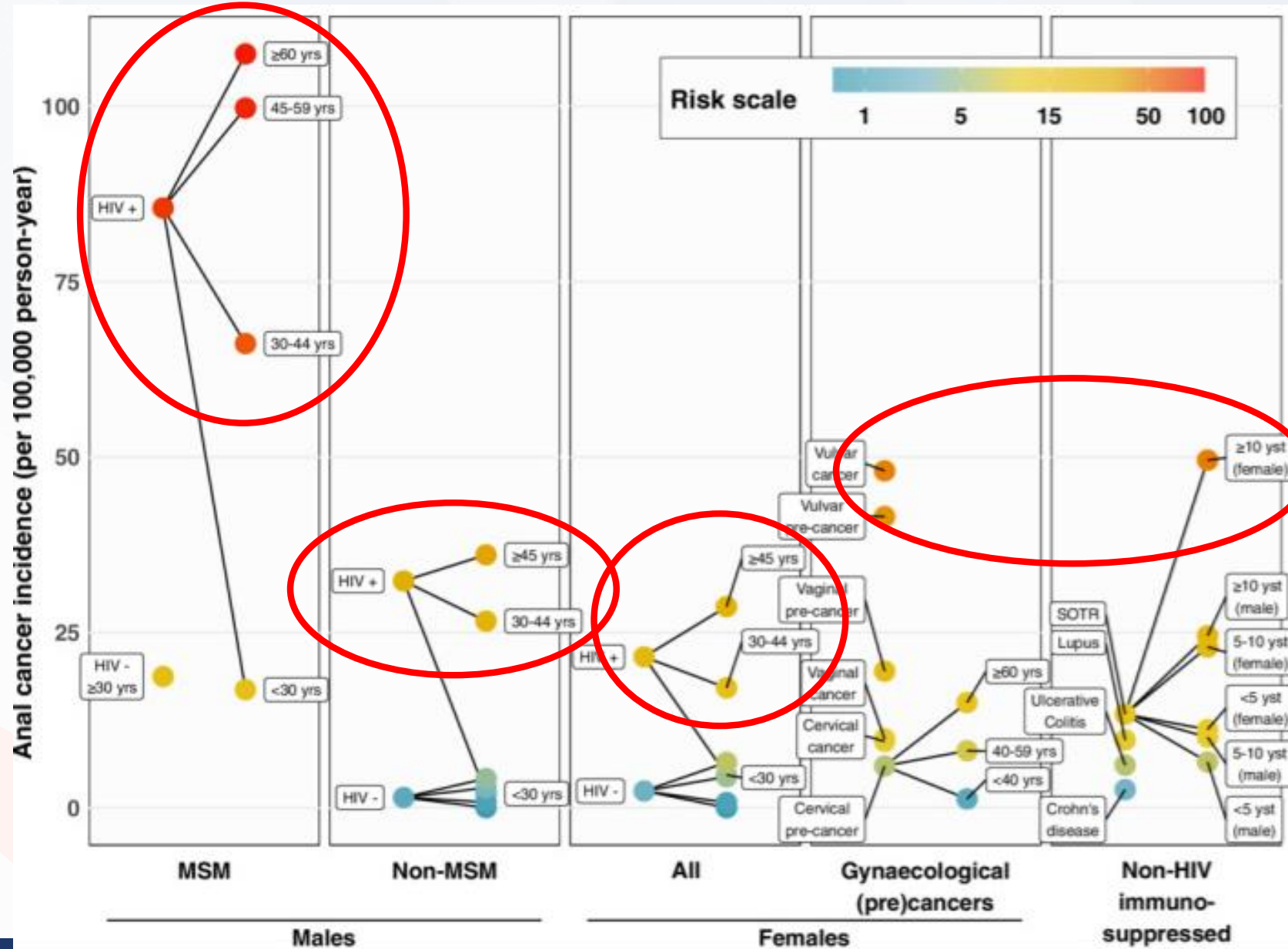
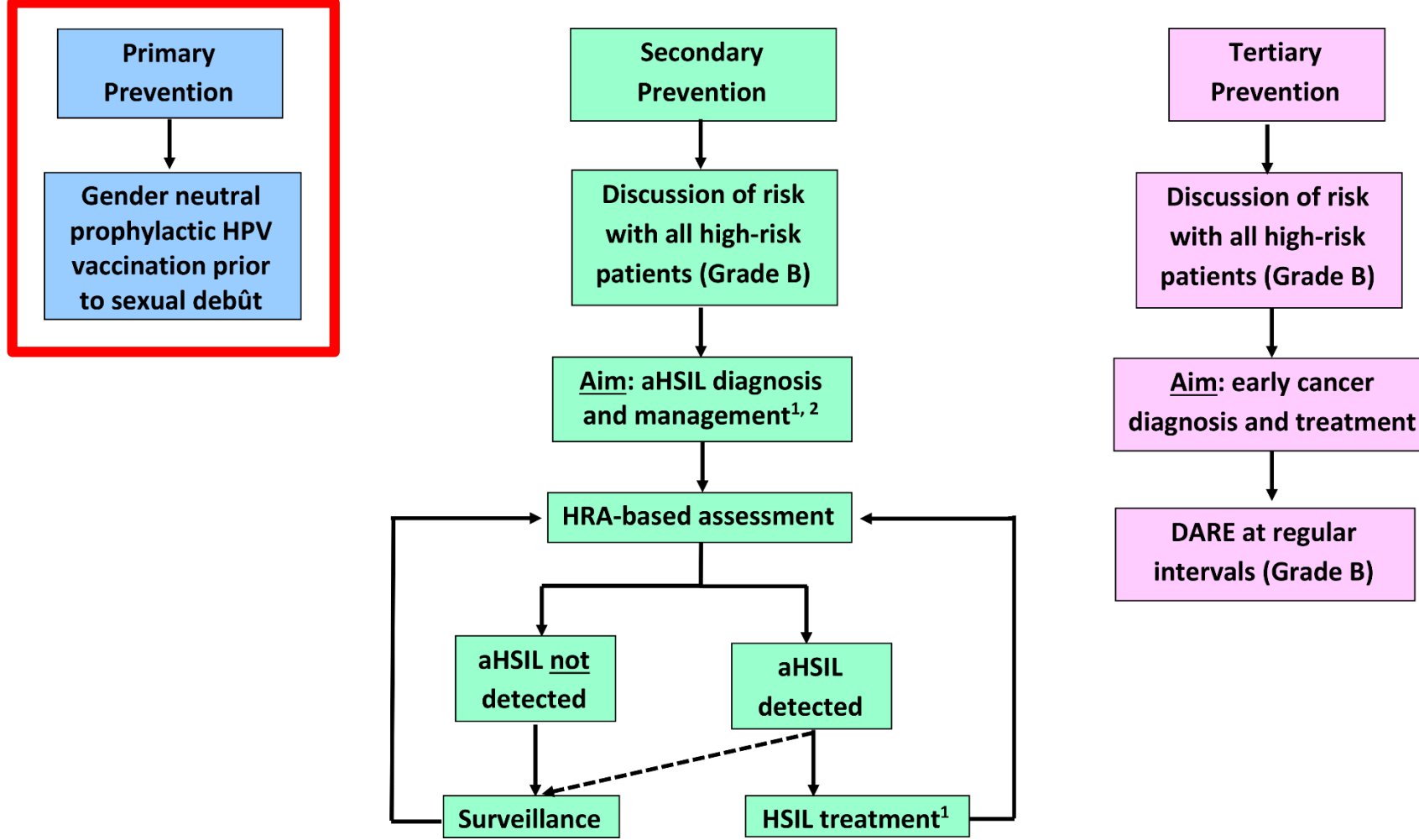


Image sourced from
Wikipedia

WHEN?



Clifford et. al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale
 Int J Cancer. 2021 Jan 1;148(1):38-47.
 doi: 10.1002/ijc.33185.
 Epub 2020 Jul 29.

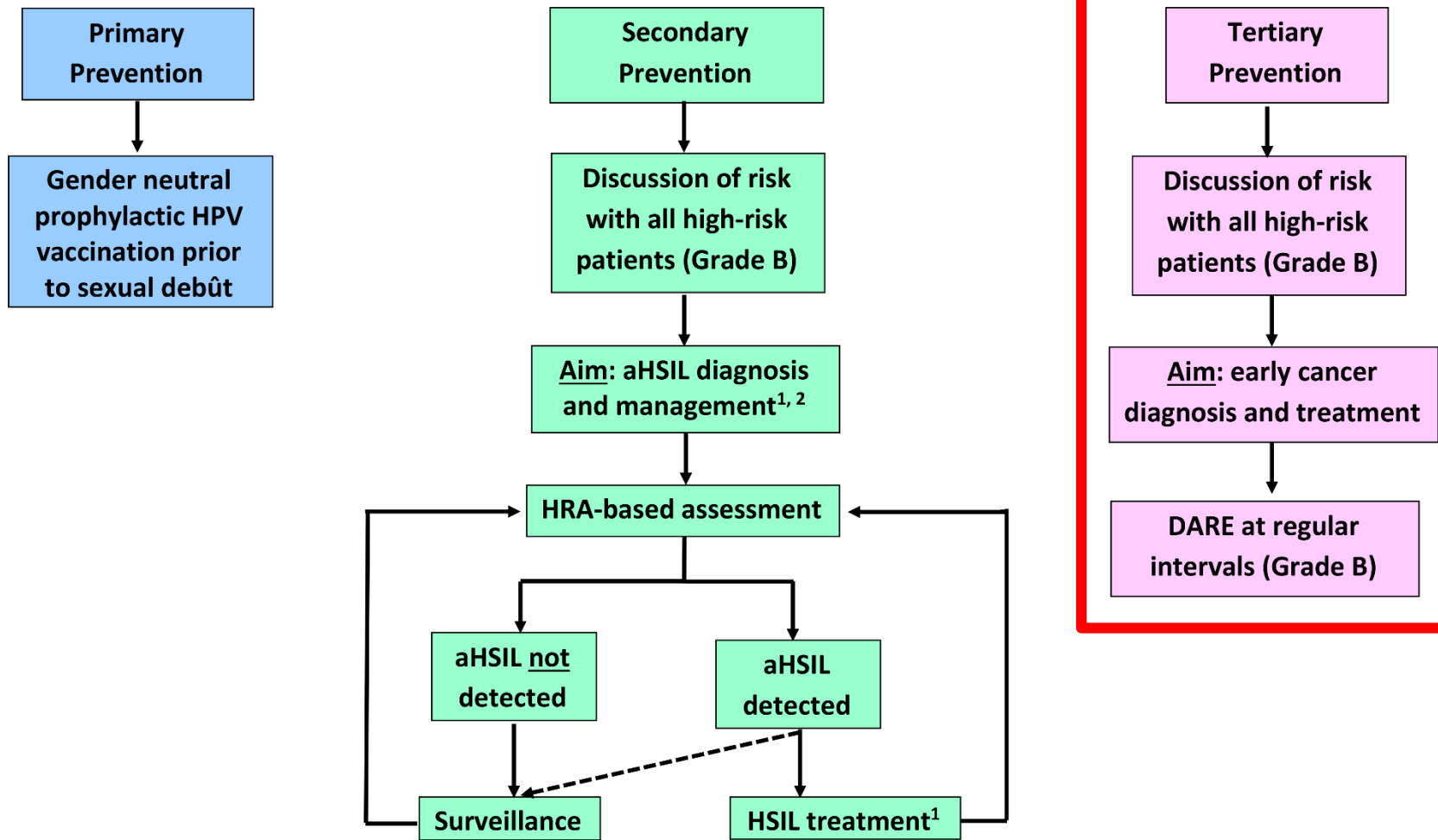


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HSIL = histologic anal High grade Squamous Intraepithelial Lesion

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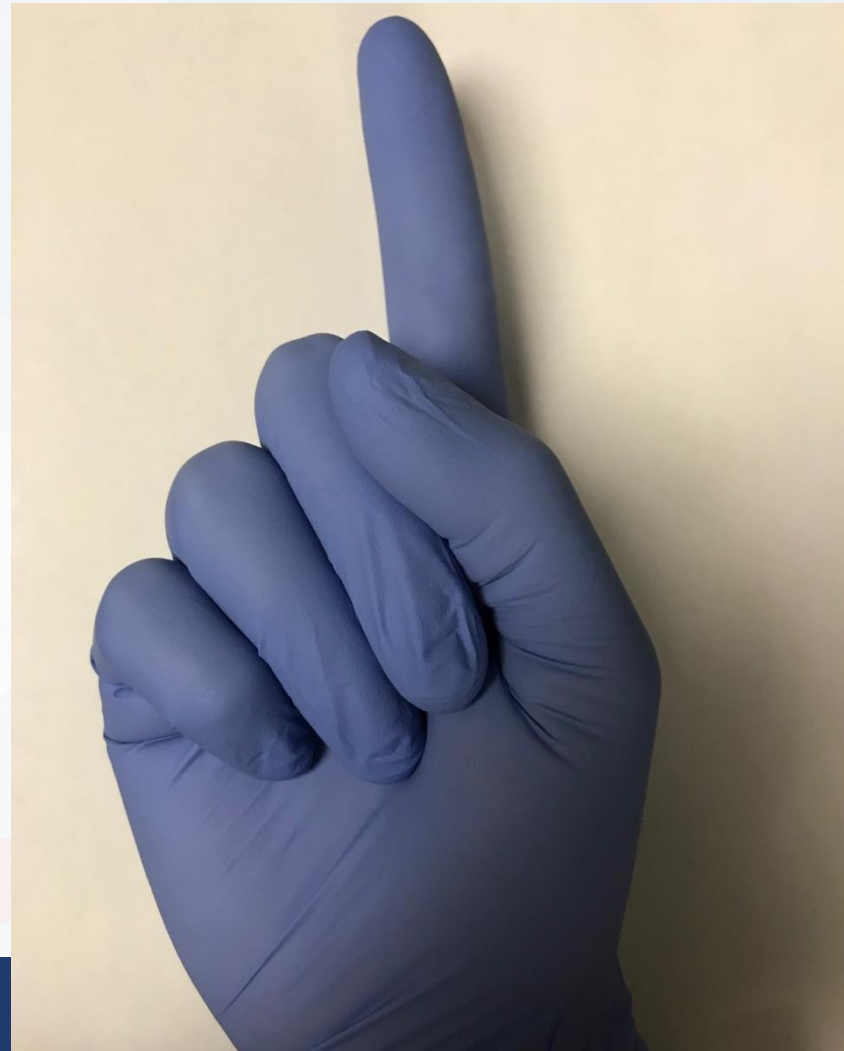
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Anal Cancer risk: What to do about it?



DARE to DARE

- **Symptomatic anal cancer is usually a late presentation**
- **The anal canal is readily accessible during the physical exam**
- **Anal cancer outcome is inversely related to size and stage**

Anal Cancer risk: What to do about it?

International Anal Neoplasia Society Guidelines for the Practice of Digital Anal Rectal Examination

Richard John Hillman, MD,¹ J. Michael Berry-Lawhorn, MD,² Jason J. Ong, PhD,³ Tamzin Cuming, MD,⁴ Mayura Nathan, MD,⁴ Stephen Goldstone, MD,⁵ Olivier Richel, MD, PhD,⁶ Luis F. Barrosso, MD,⁷ Teresa M. Darragh, MD,⁸ Carmella Law, MD,⁹ Céline Bouchard, MD,¹⁰ Elizabeth A. Stier, MD,¹¹ Joel M. Palefsky, MD,² Naomi Jay, PhD,¹² on behalf of the International Anal Neoplasia Society

Anal Cancer risk: What to do about it?

TABLE 4. Proposed DARE Adequacy Criteria

Informed consent has been obtained as per local protocols
A lubricated, gloved finger is used
The entire circumference and length of the anal canal has been palpated
The entire circumference of the perianus (anal margin) has been inspected and palpated
Adequate documentation of the whole examination has occurred
Palpation for inguinal lymphadenopathy may be included for patients with suspected lymphogranuloma venereum and cancer.
A full physical examination is indicated in those with a high suspicion of cancer.

iniques such as HIVA, or as coincidental findings when surgery has occurred for other reasons.⁴²

TABLE 6. Proposed DARE Quality Assurance Metrics

Metric	Recommendation
Entire anal canal palpated and perianus fully visualized	>90% of examinations
Detection of abnormalities requiring further examination ^a	≥5% of examinations

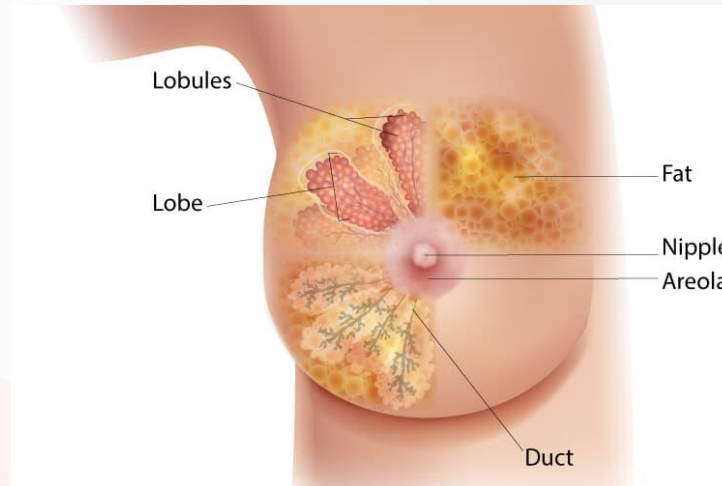
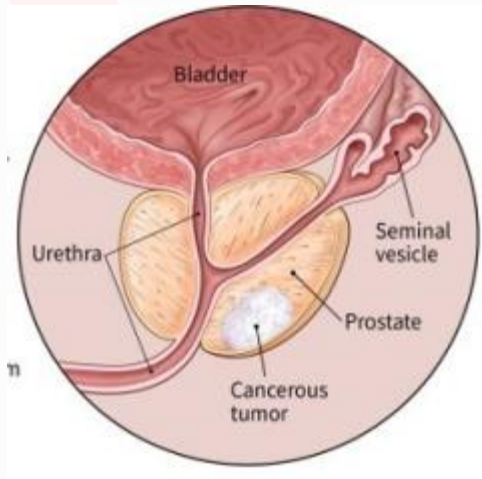
^aWill depend on mix of patients, such as referral practices, new or return, high risk, and treatment experience.

Anal Cancer risk: What to do about it?

- **How often to repeat DARE?**
- **How many should you do to be proficient?**
- **Where do you refer abnormal results?**

Cancer “Screening”

EARLY DETECTION



PREVENTION

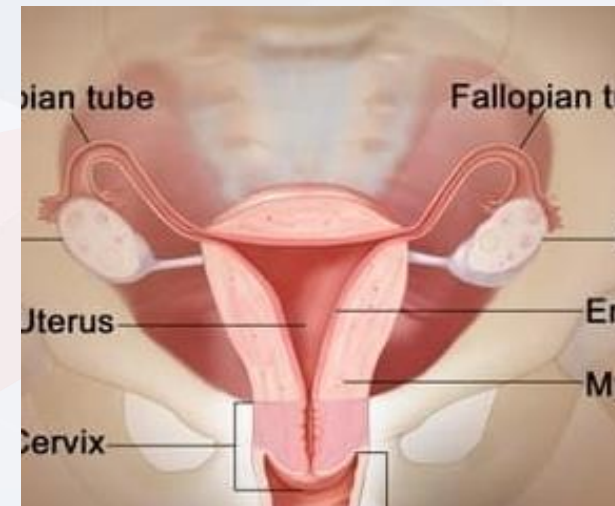
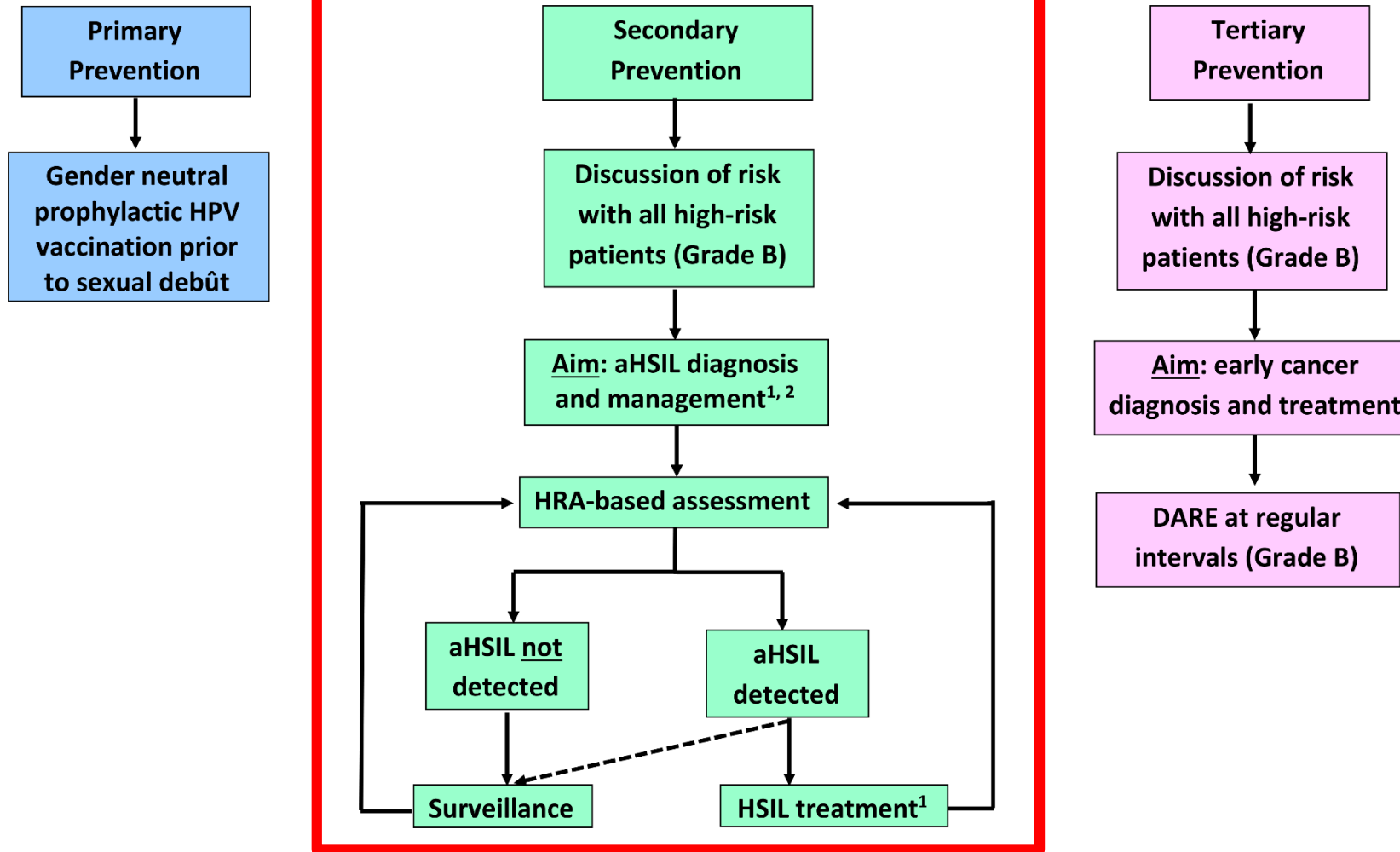


Image sourced from American Cancer Society, Center for Disease Control



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“The supreme art of war is to subdue the enemy without fighting.”

-Sun Tzu, The Art of War

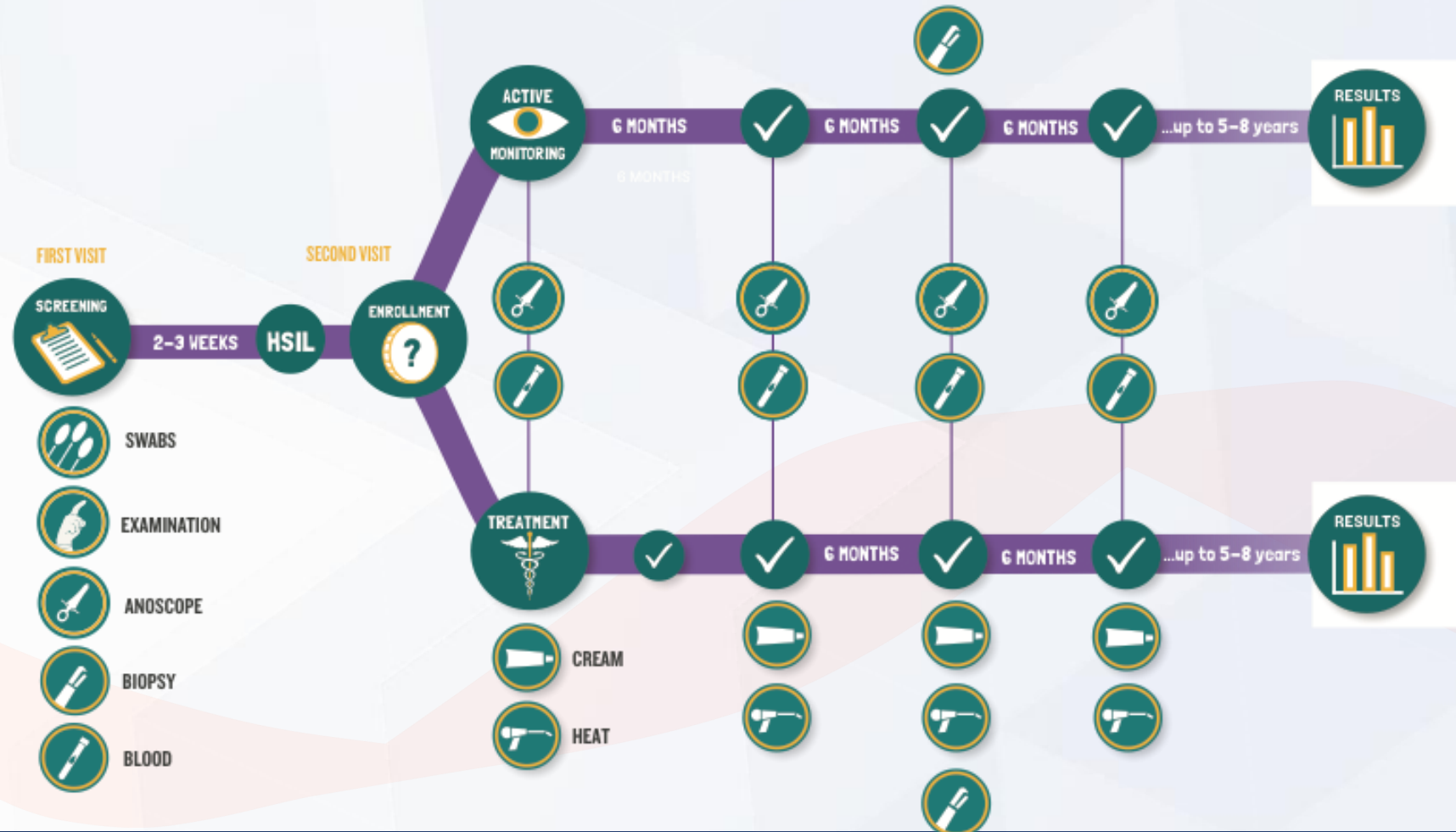
“The best way to treat anal cancer is never to get it.”



Image sourced from Historia Universal Amino Wiki

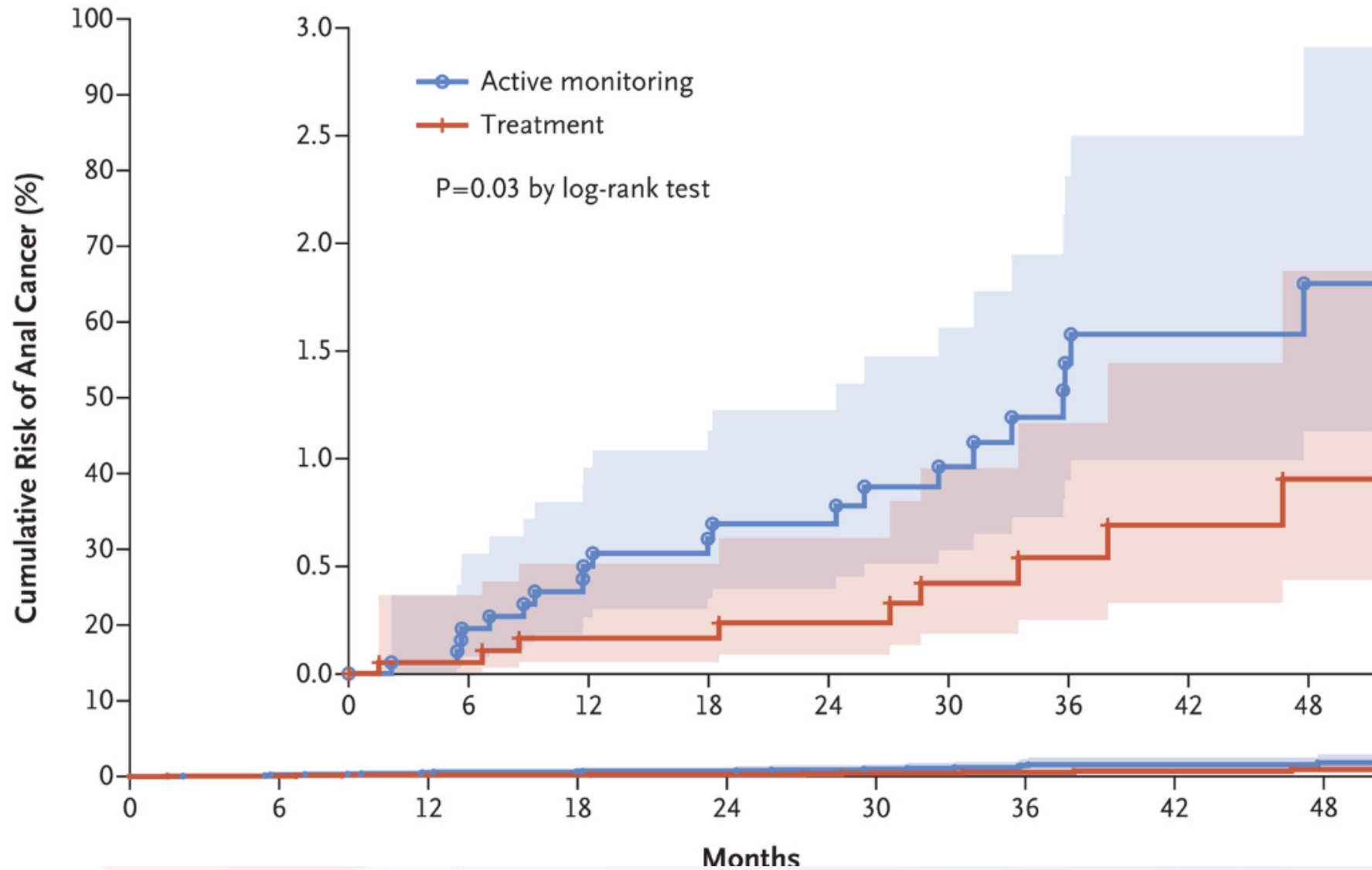
ANCHOR Study Timeline

Here's what you can expect as a volunteer

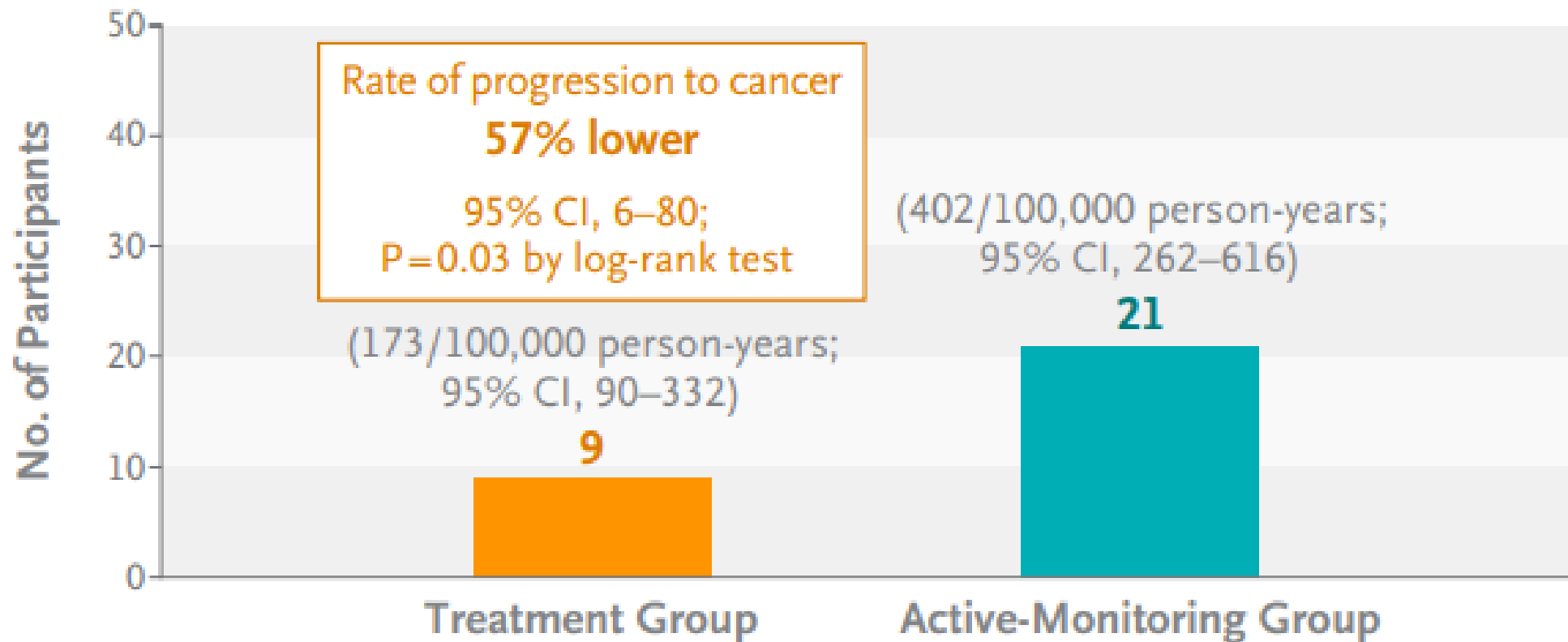


What did ANCHOR Show?

- **Anal cancer risk is high in PLWH \geq 35 yo**
- **HSIL is a risk factor for cancer, not all HSIL turns into cancer**
- **Cancer incidence was lower in the treatment arm**



Invasive Anal Cancer (Median Follow-up, 25.8 Mo)



What didn't ANCHOR Show?

- **Topical (imiquimod, 5-FU) and ablation (electrocautery, IRC, surgical) therapies were all allowed and the study will not be able to compare them**
 - **The overwhelming majority of patients were treated with office-based electrocautery**

What didn't ANCHOR Show?

- **All ANCHOR patients had HRA q6 months per protocol**
 - **The best and most practical ways to screen all PLWH ≥ 35 were not assessed**

Cervical Paps

- **Speculum**
- **Cytobrush**
- **Colposcopy**
- **LEEP**

Anal Paps

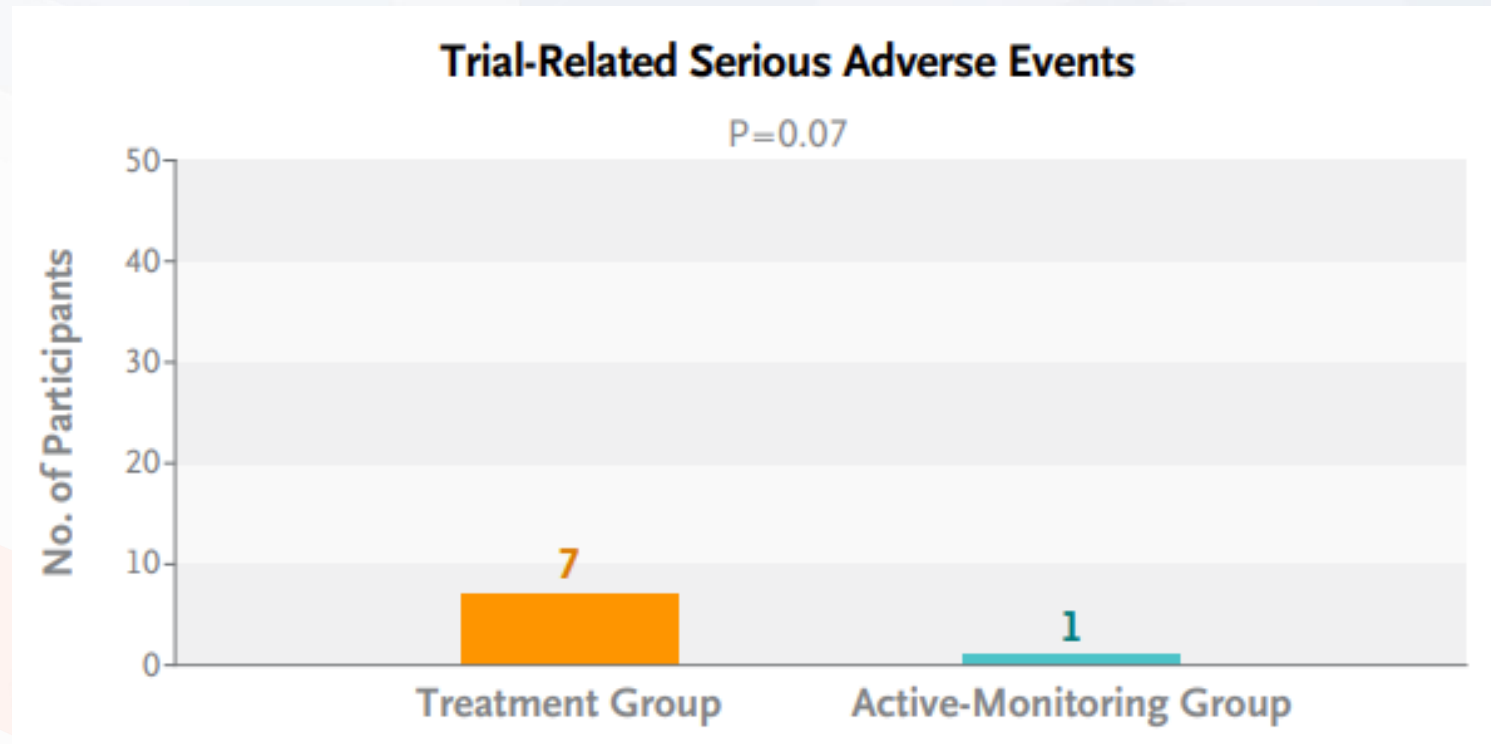
- **Anoscope**
- **Dacron Swab**
- **High Resolution Anoscopy (HRA)**
- **HRA guided targeted electro-cautery**

High Resolution Anoscopy

- **Colposcopy of the anal canal**
- **5% acetic acid and iodine used to stain mucosa (just like cervix)**
- **Biopsies taken from abnormal areas (just like cervix)**

High Resolution Anoscopy: Side Effects

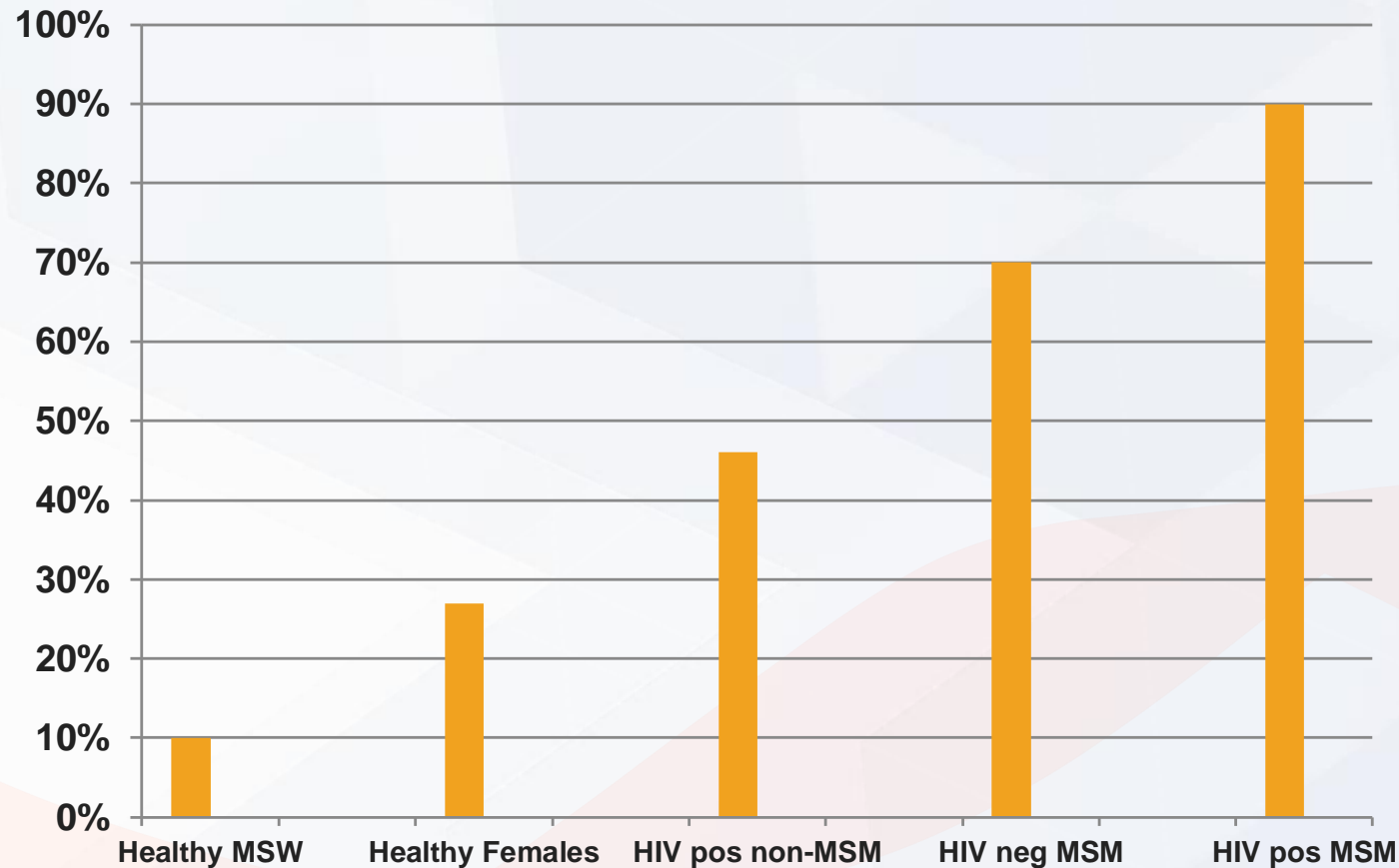
- There is an ongoing QoL study to look into long term side effects



ANCHOR FAQ

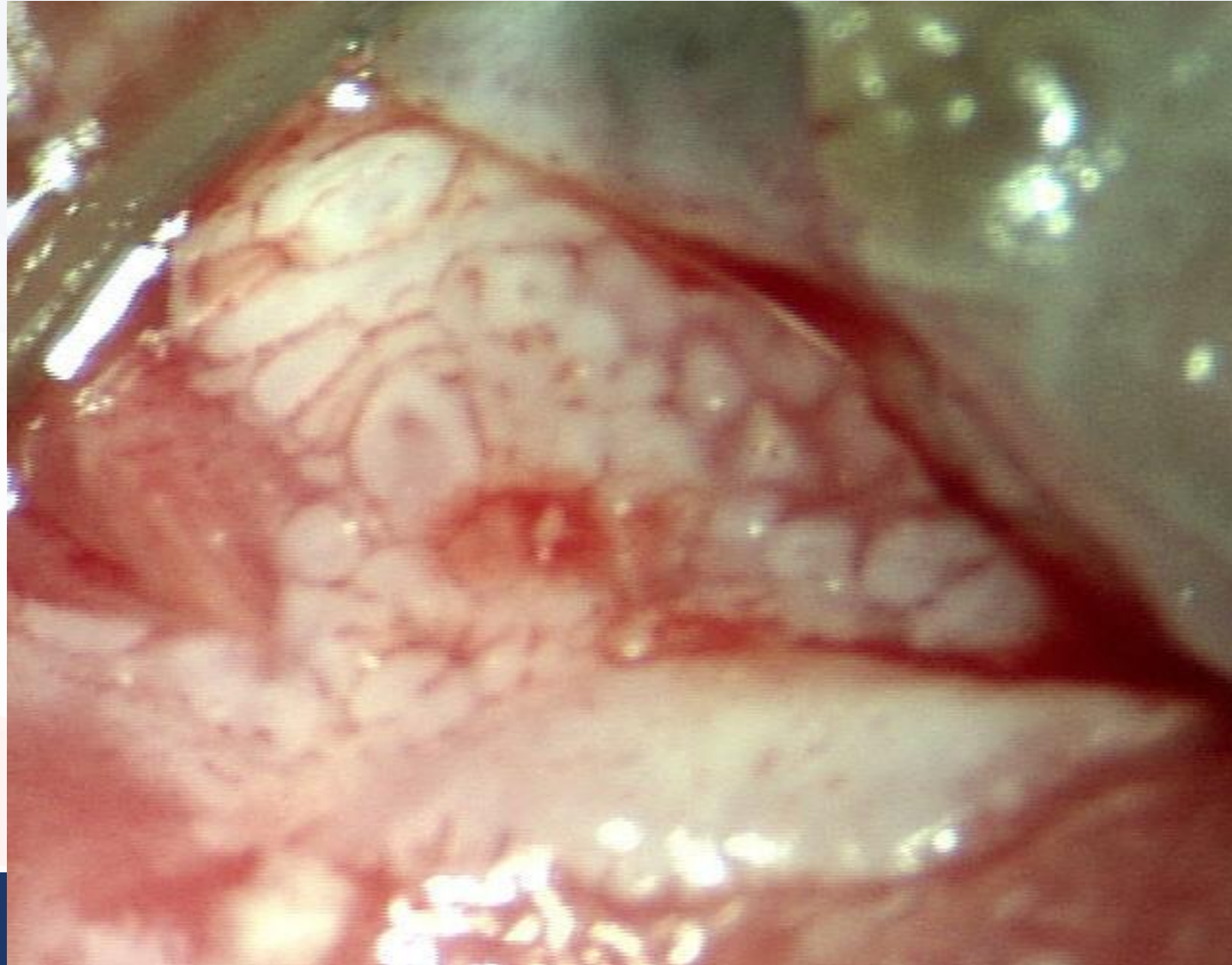
- **But I've never had anal sex, so I don't have to worry about it.**
 - **Actually, yes. Yes you do.**
 - **There is plenty of anal dysplasia and anal HPV in men and women who have NEVER had anal sex.**

Anal HPV Infection is Common



Chin-Hong, *et. al.* , The Journal of infectious diseases, 2004 Nielson, C.M., *et.al.* Cancer epidemiology, biomarkers & prevention, 2009 Ostor, A.G. International journal of gynecological pathology ,1993 Hernandez, B.Y. *et. al.*, Cancer epidemiology, biomarkers & prevention, 2005

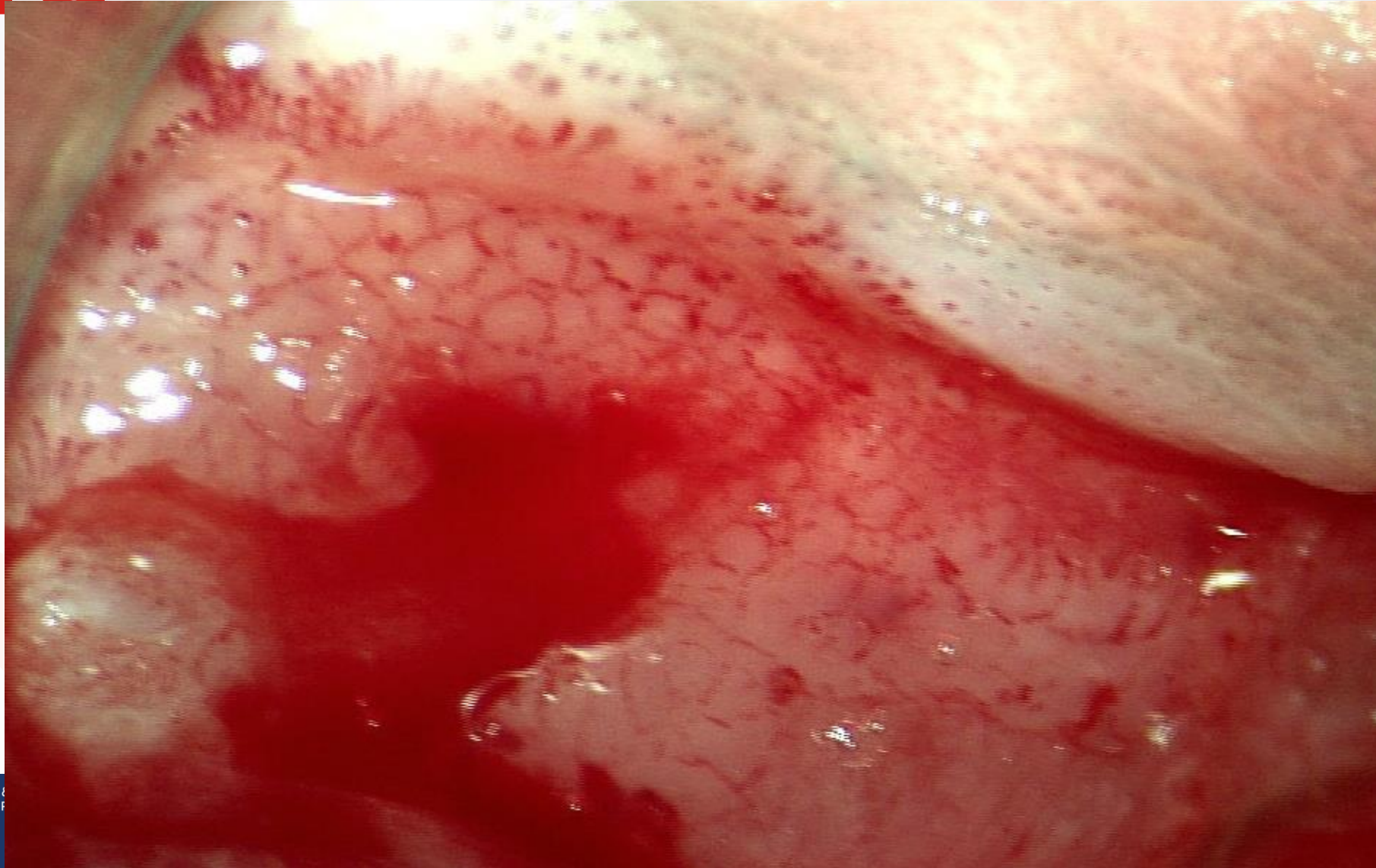
2014



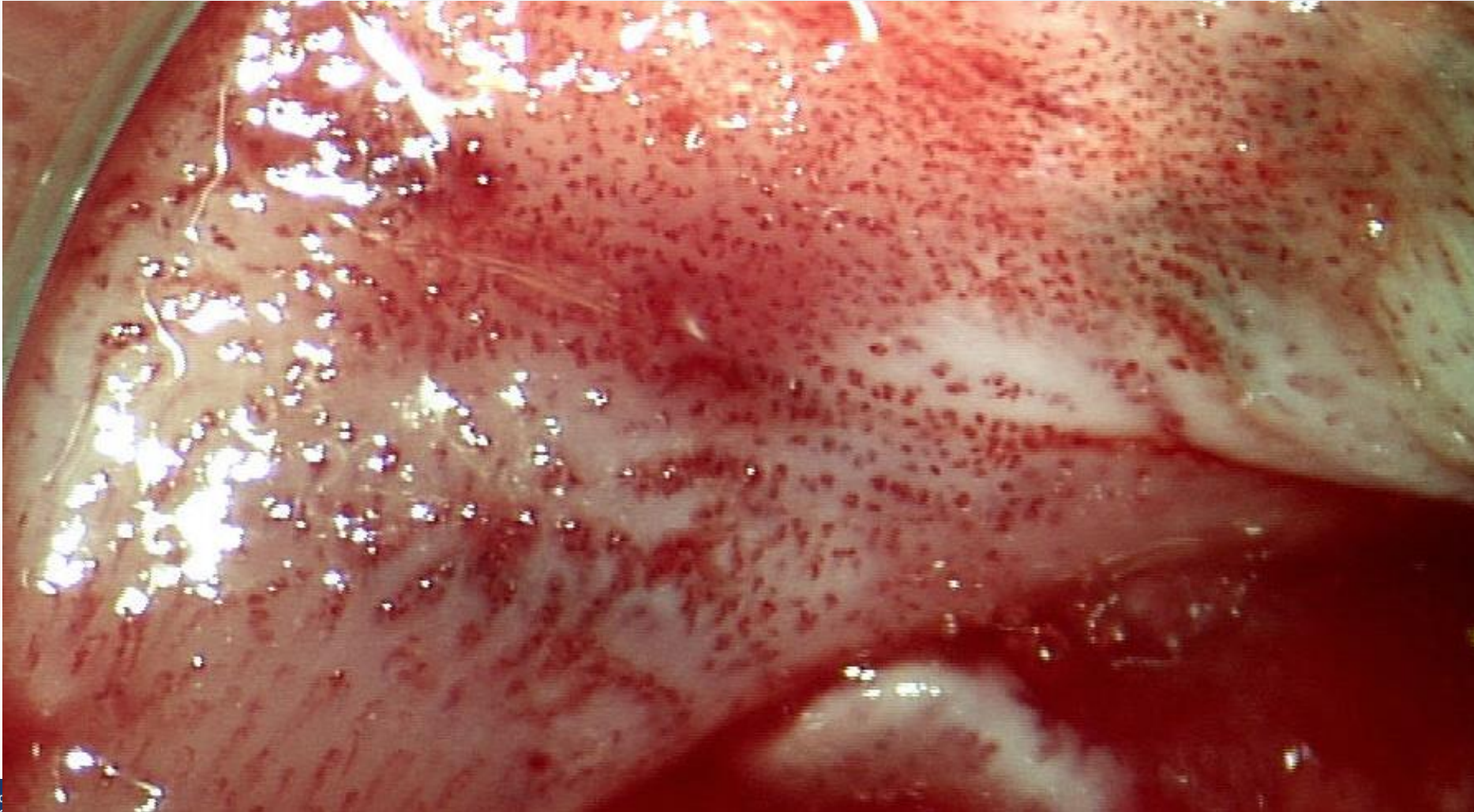
2014



2015



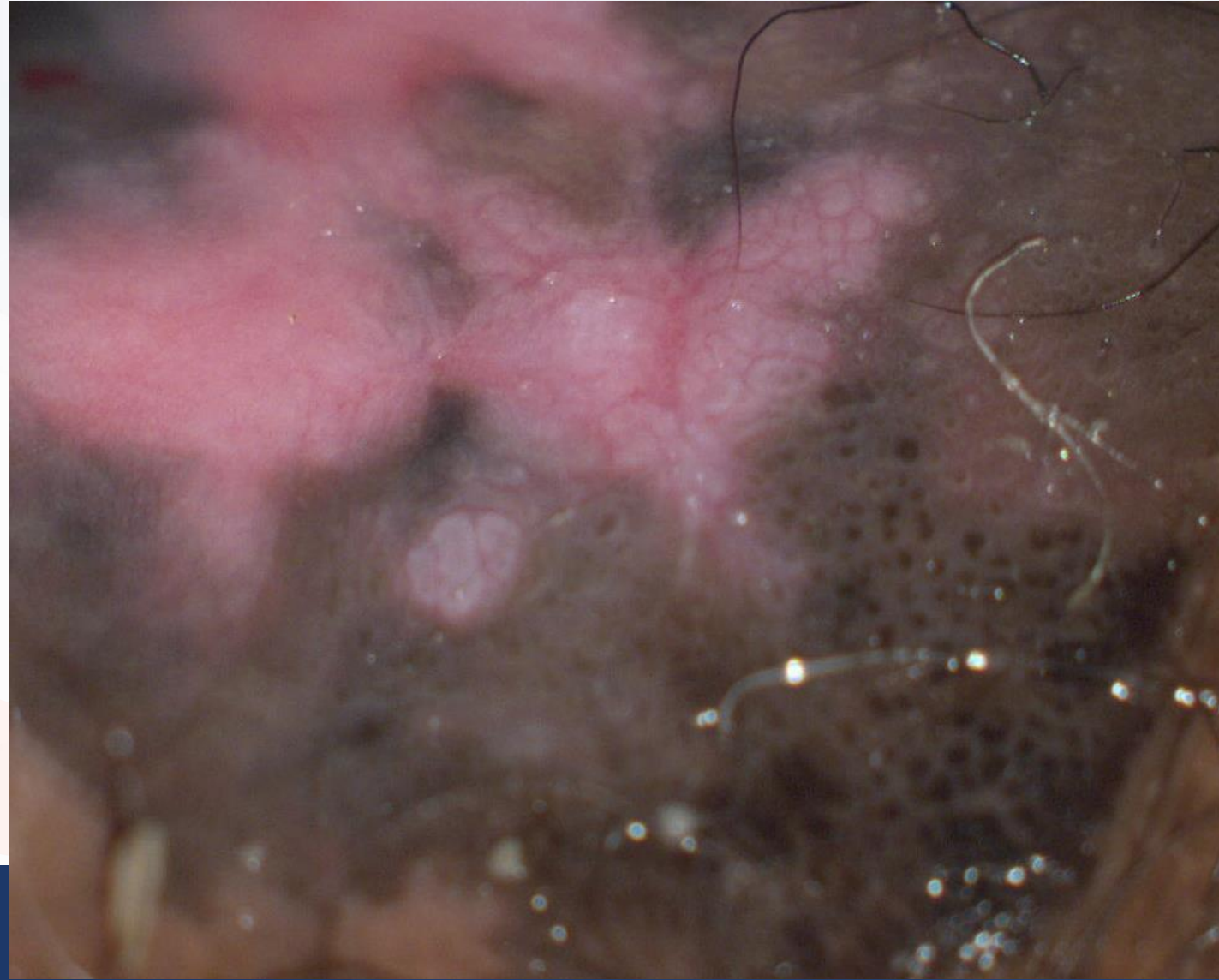
2015



2017



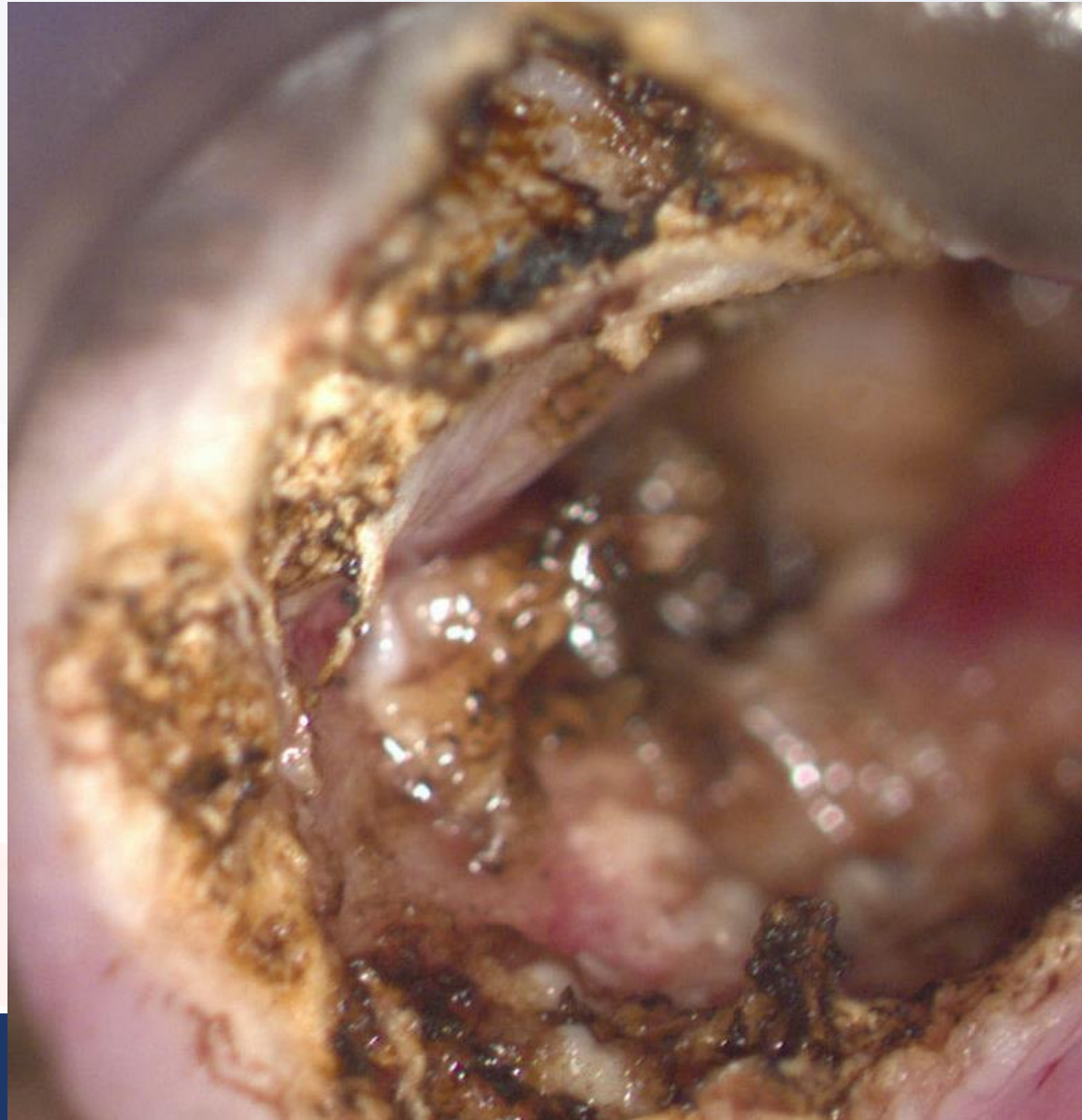
2020



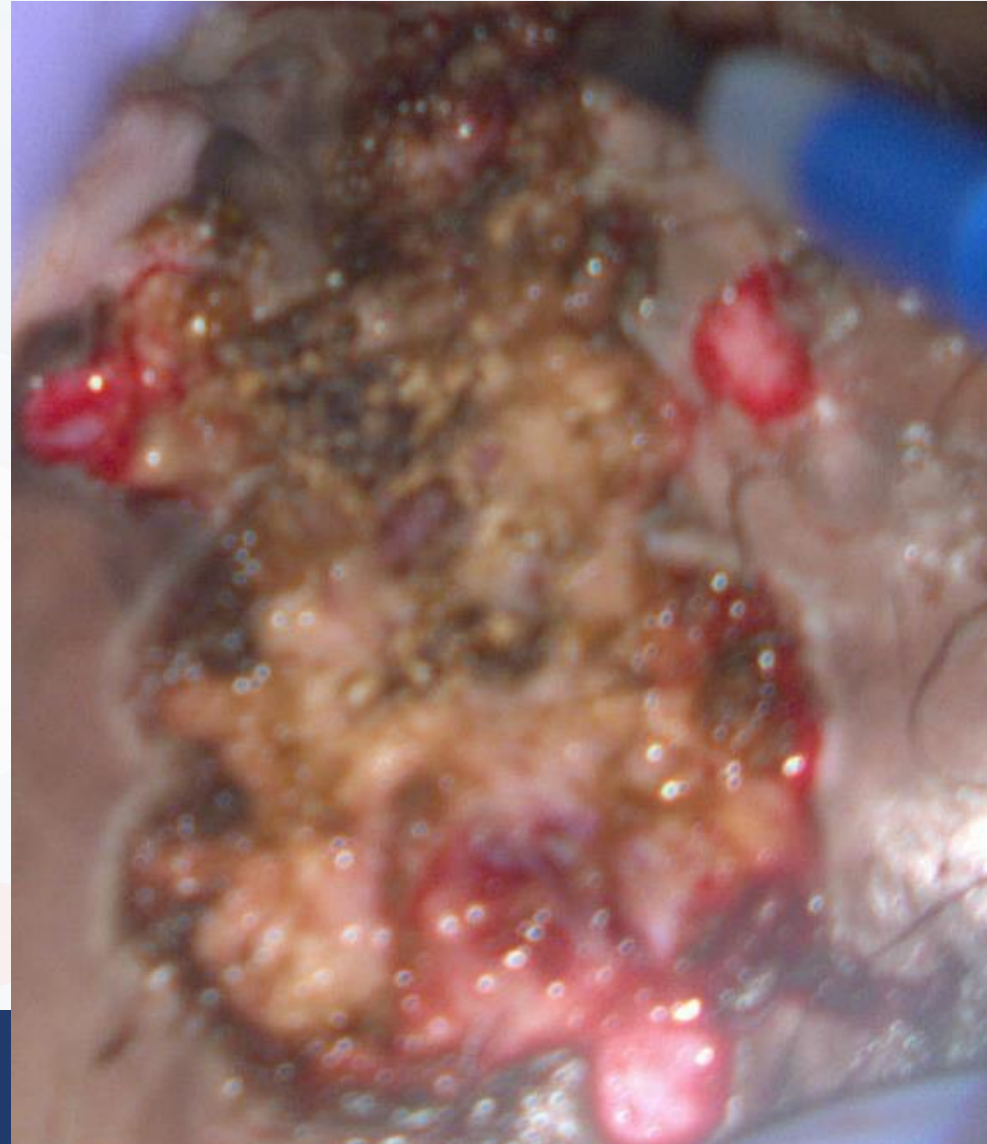
2021



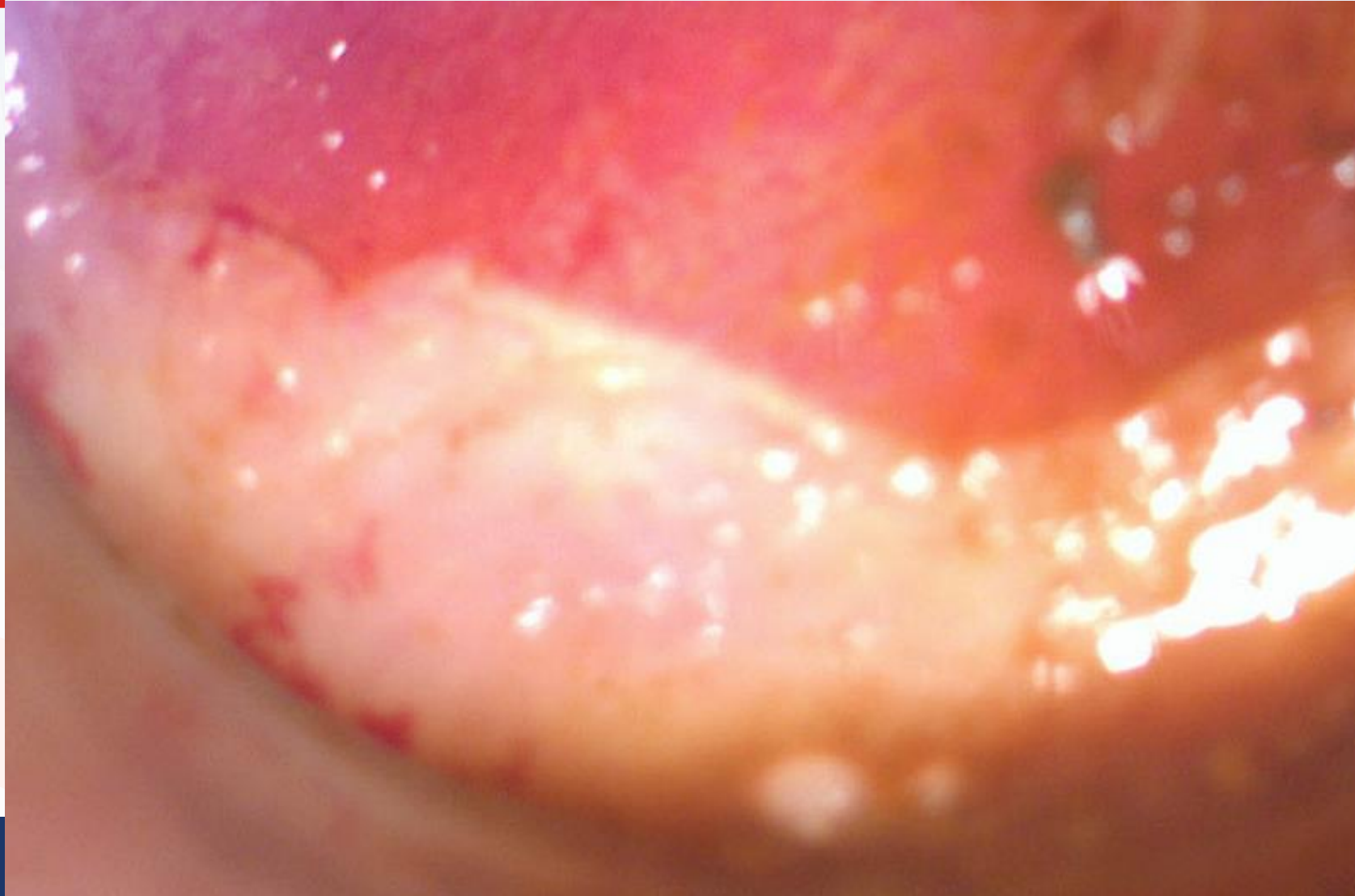
2021



2021



2022



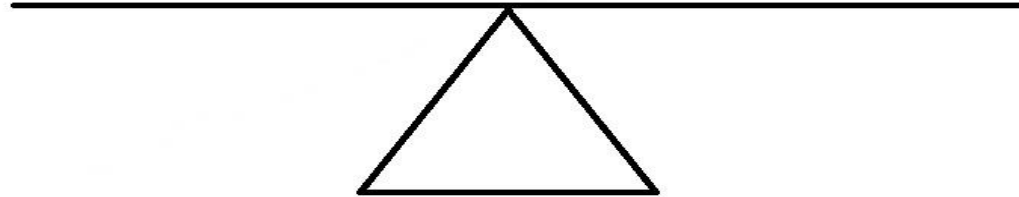
2022



2022

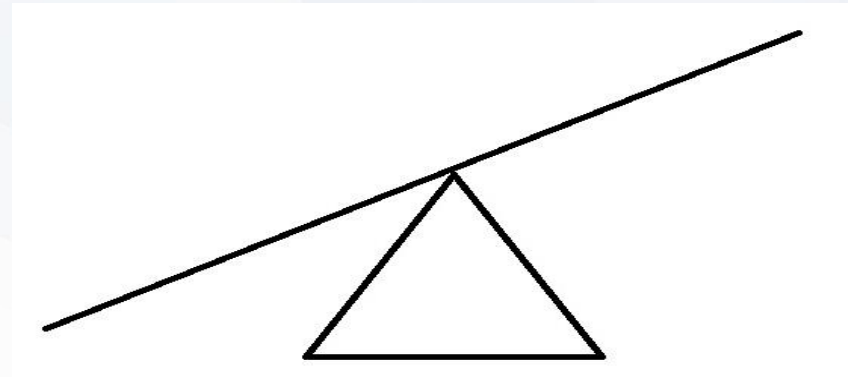


EQUIPOISE



Treat

Monitor



Treat

Monitor



- **Screening for and treating anal HSIL significantly reduces the risk of anal cancer in PLWH**

Next Steps ...

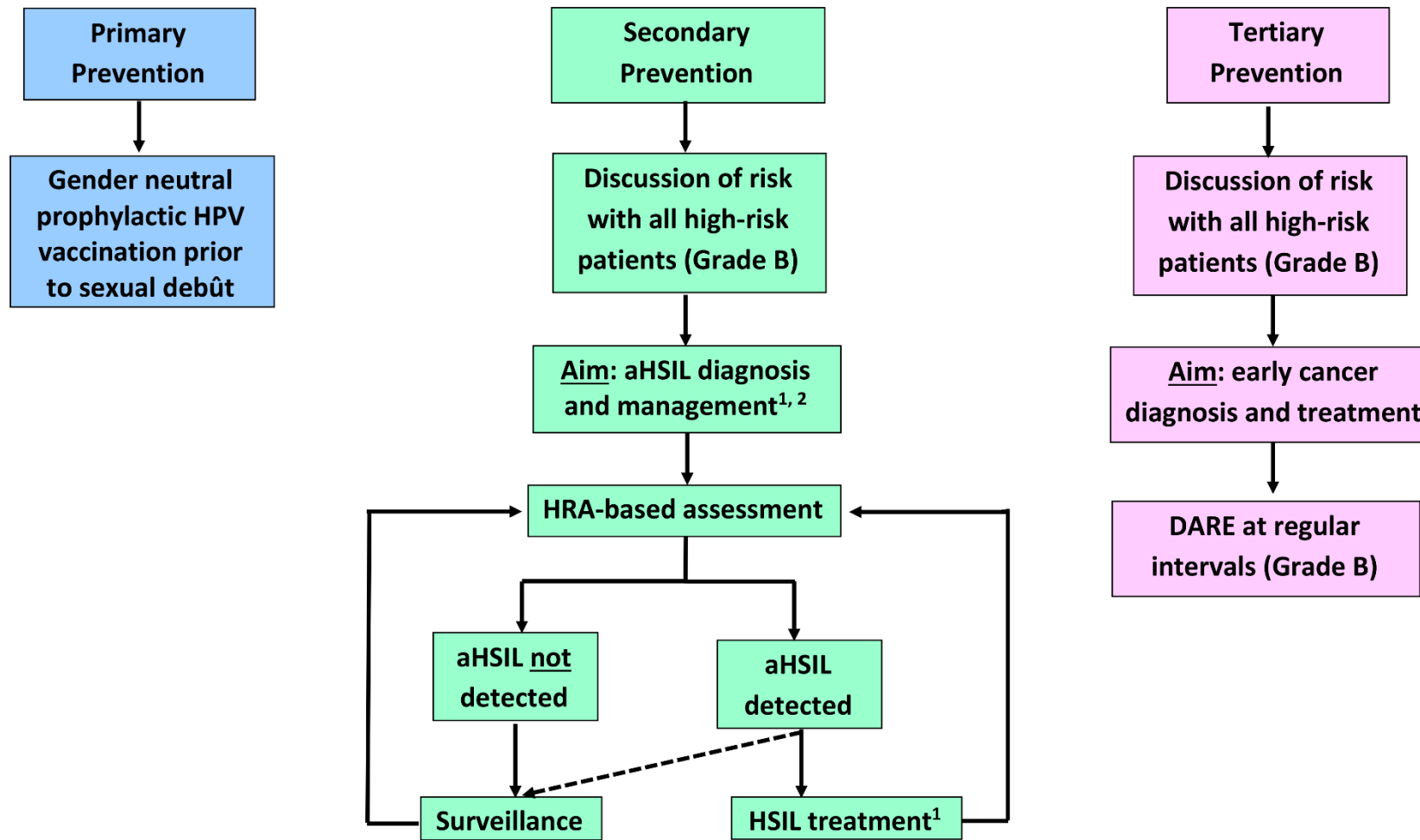
- Implementation
- Algorithms
- Triage: Can't HRA everybody

Cervical Trends

- Increasing age of screening initiation
- Shift to HPV based screening
- Risk based assessment (ASCCCP)
 - Prior history and 3-5 year risk taken into account

Translation Issues ...

- Less specificity of anal cytology
 - ASCUS, LSIL often = HSIL histology!
- HPV helpful NPV, but very high prevalence
 - 16/18 likely more predictive (but less sensitive)
- Less robust data for 3-5 year risk of anal cancer based on cytology/HPV



¹ Grade A for PLWH ≥ 35 yo

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How

- Cy
- HF
- I
- HF
- DA
- Ri
- A



Guideline are coming ...

- Stay tuned
- Just a few months (I swear)

**NOT
^**

How to Prevent Anal Cancer

- **DO NOTHING**

Anal Cancer risk: What to do about it?

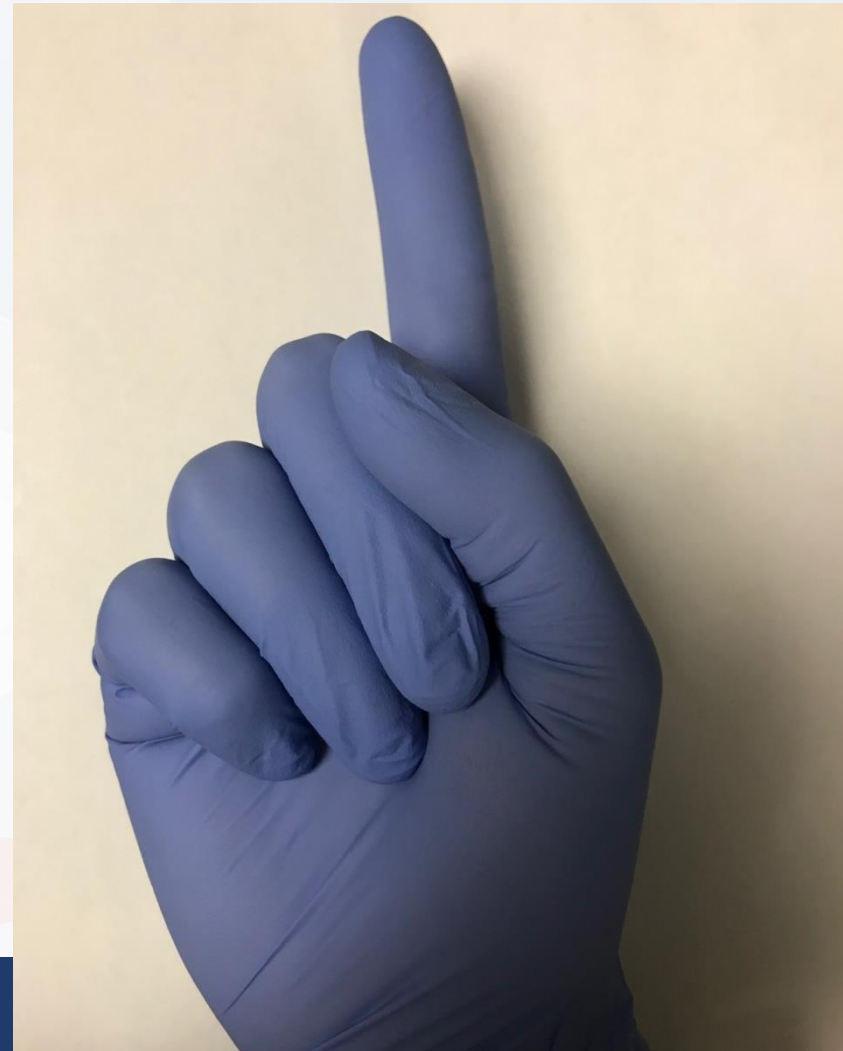


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YOU can do better!



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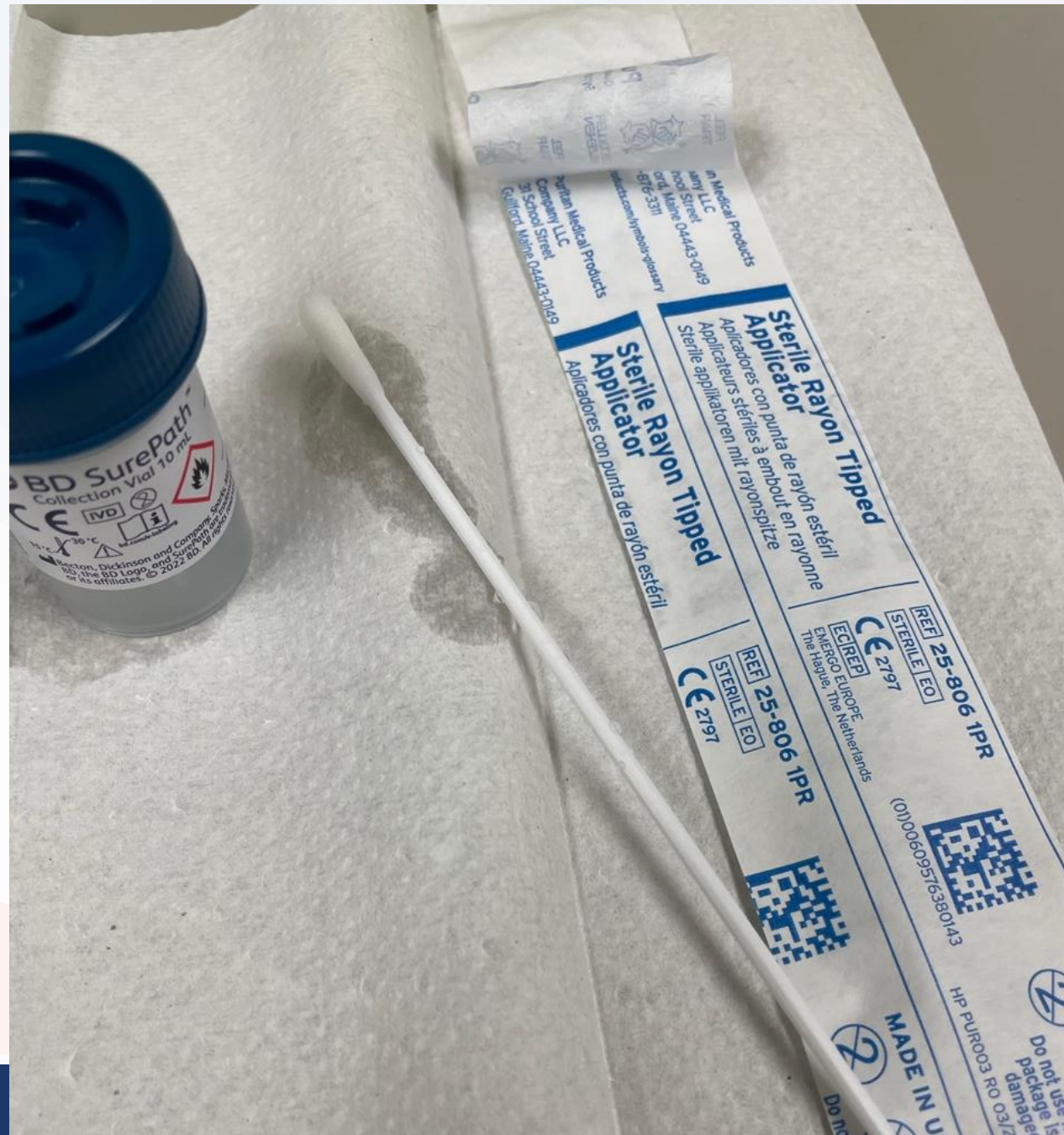


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How to pap

- **Take one moist Dacron swab**
- **With a gloved finger insert the swab 4-6 cm (until resistance from rectum)**
- **Rotate with lateral pressure for at least 10 seconds while withdrawing**
- **Transfer to medium and agitate thoroughly**

Time for a Video ...

[Anal Cytology Video](#)

SUMMARY YOU can do them all!

- **Anal cancer risk clusters in specific groups**
 - Demographics, Immune status, and age
- **A three pronged approach can help to prevent anal cancer incidence and morbidity/mortality**
 - Vaccination before sexual debut
 - Screening and treatment of premalignant disease
 - Early diagnosis of pre-symptomatic disease

Questions?