My Patient Wants an Anal Pap:
What Every PA Needs to Know About Anal Dysplasia

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Disclosures

I, Jonathan Baker, have no relevant financial, professional or personal relationships to disclose. I will present unbiased evidence.

- My employer receives salary support from Merck, Inovio, and Antiva

I will discuss off-label use of medications and procedures:

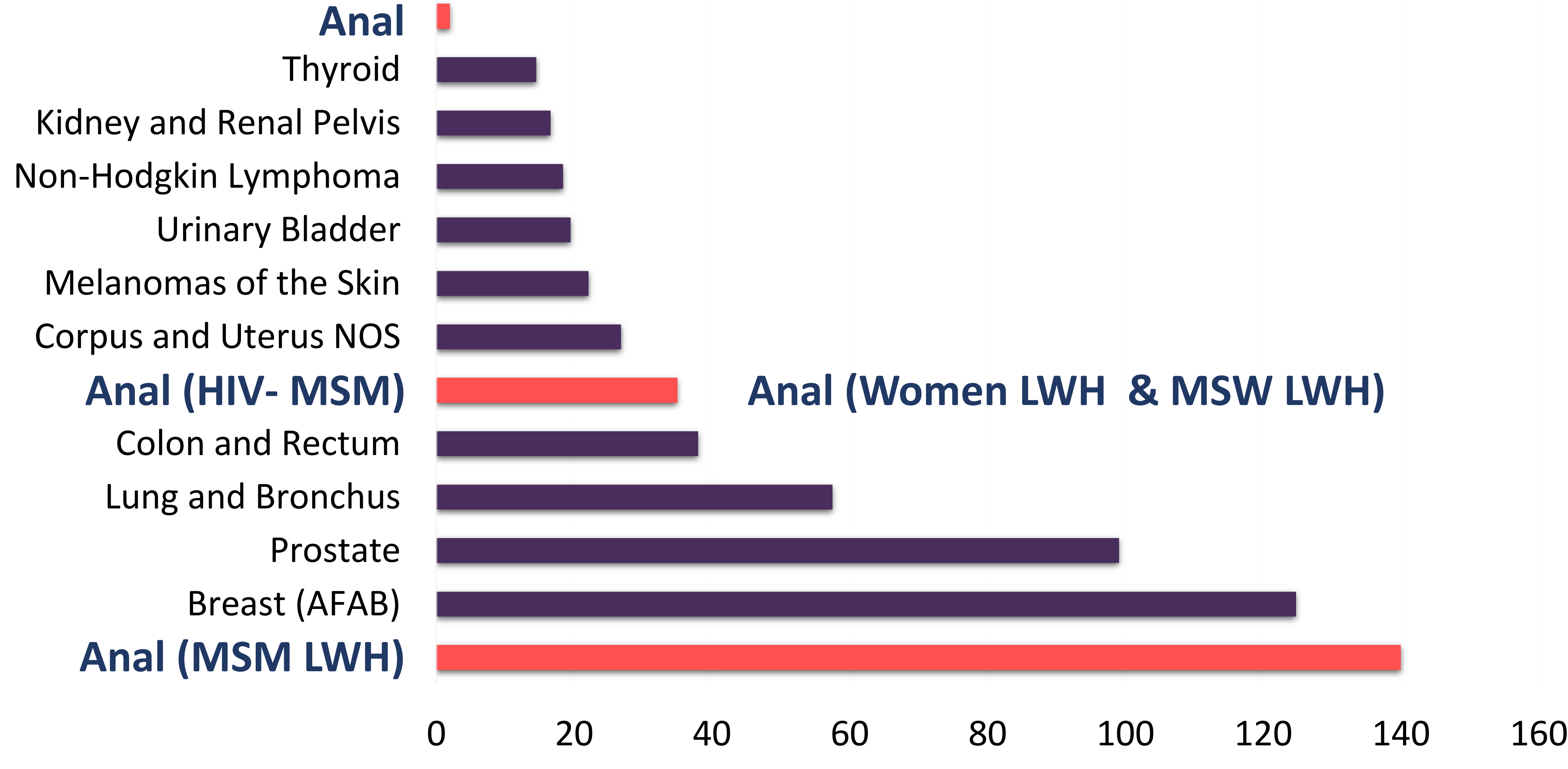
- Electrocautery
- 3.5-5% imiquimod
- 5-fluorouracil
- 80% trichloroacetic acid (TCA)
- Infrared coagulation (IRC)
- HPV vaccine
- Anal HPV testing

Learning Objectives

At the conclusion of the session participants should be able to:

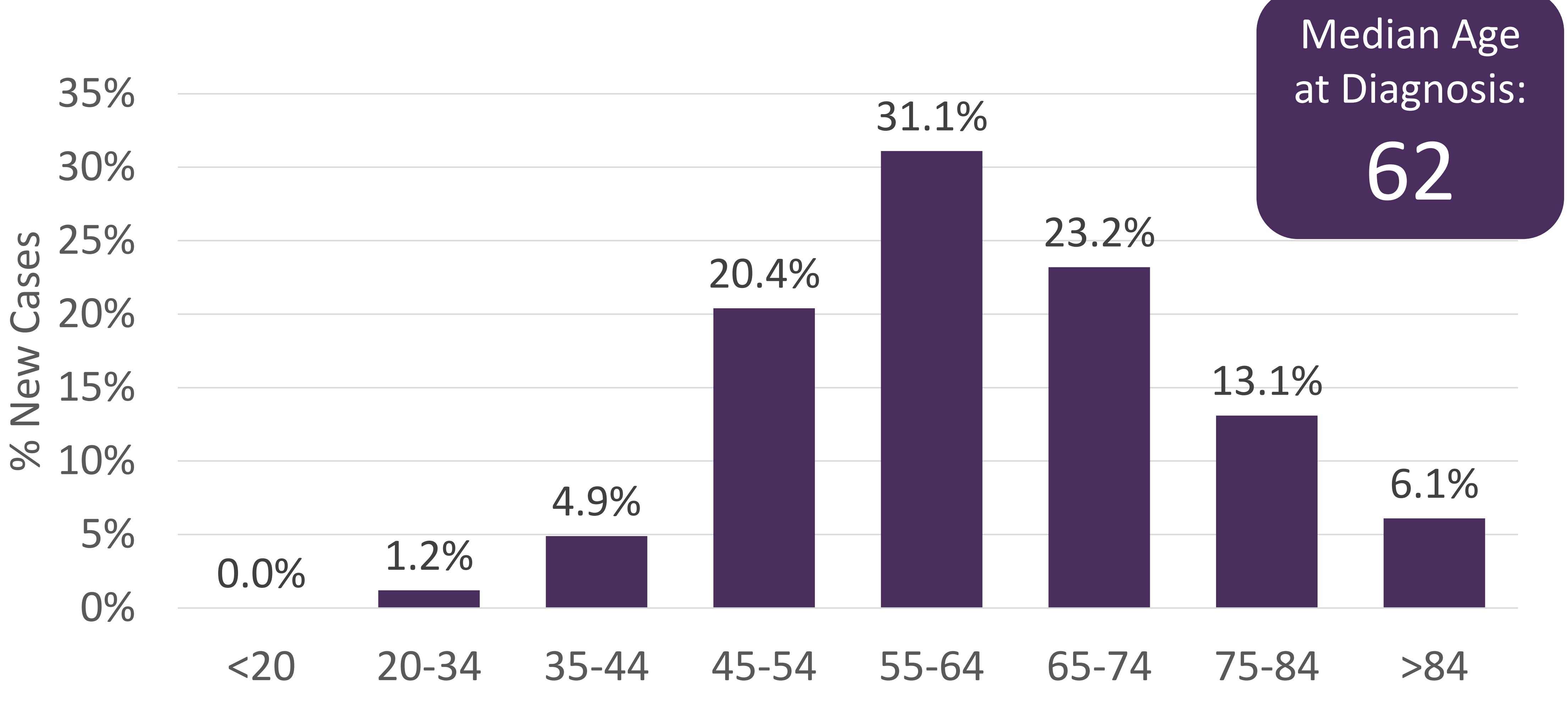
1. Understand risk factors for anal cancer and consider adjustments in screening/prevention across diverse populations.
2. Discuss the standard screening options for anal dysplasia including anal cytology (pap) and HRA
3. Understand how to perform anal cytology (pap) and identify referrals for abnormal findings

Anal Cancer Incidence per 100,000



USCSWG (CDC) 2017, Silverberg 2012

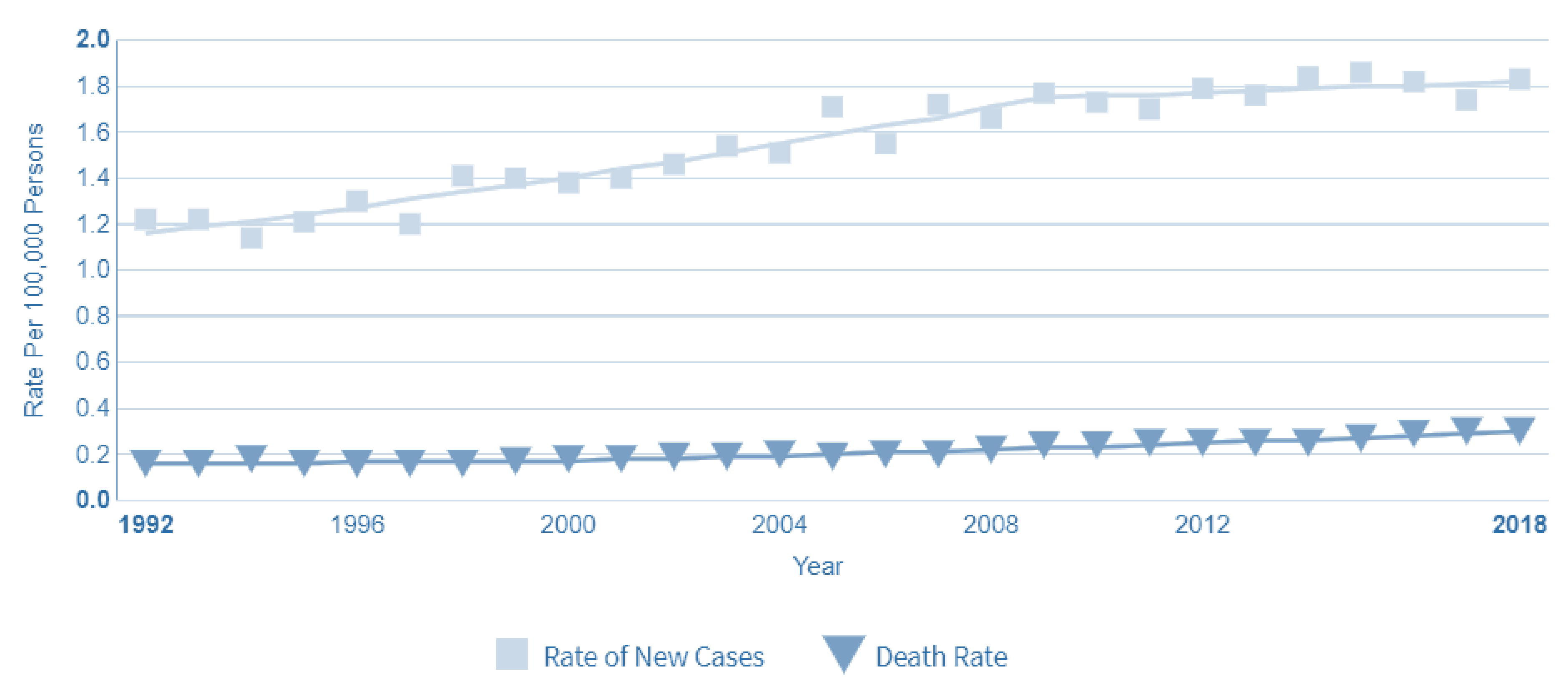
Anal Cancer Incidence by Age



Wilkin 2018, IANS 2016, Deshmukh 2017, NCI 2019

Adapted from: NCI 201; Data: Seer 2012-2016

Increasing Rates of Anal Cancer



NCI 2021

At Risk Populations

- HIV+
- MSM (men who have sex with men)
- Iatrogenic immunosuppression (ie transplant and biologicals)
- Gynecologic disease (cervical/vaginal/vulvar dysplasia)
- Inflammatory Bowel Disease

Silverberg 2012, Cranston 2017

FOR IMMEDIATE RELEASE
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Source: Elizabeth Fernandez (415) 502-6397
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Treating Anal Cancer Precursor Lesions Reduces Cancer Risk for People With HIV

Groundbreaking National Clinical Trial Halted Due to Therapy's High Success Rates

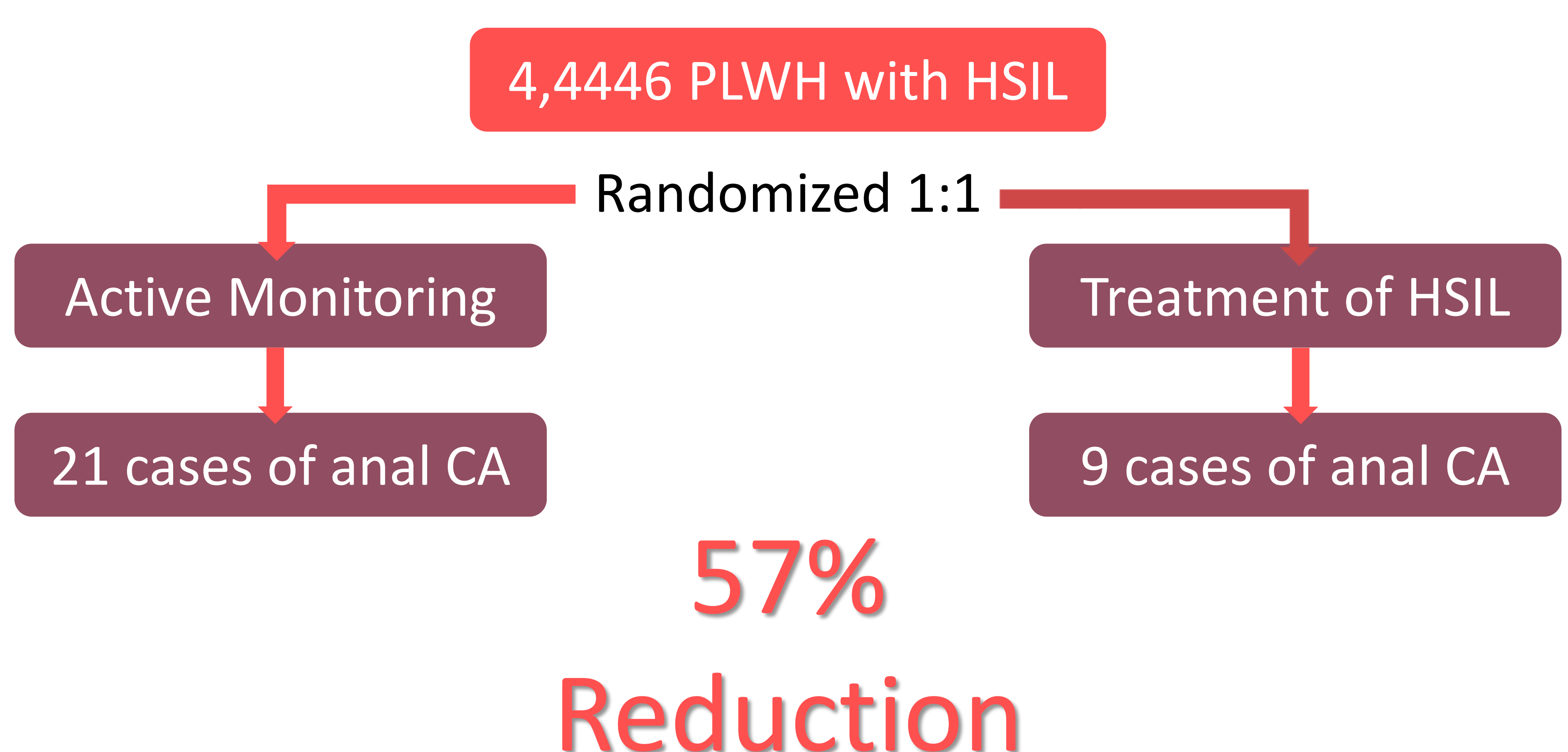
Treating precursor anal cancer lesions can significantly reduce the risk of progression to full blown anal cancer among people living with HIV, according to results of a large, phase 3 study led by researchers at UC San Francisco.

In a randomized clinical trial with 4,446 participants, known as the Anal Cancer/HSIL Outcomes Research (ANCHOR) study, researchers found that by removing high-grade squamous intraepithelial lesions (HSIL), chances of progression to anal cancer were significantly reduced.

The trial is the first to show such findings and was performed at 21 clinical sites around the United States. Results are being prepared for peer-reviewed publication and are being shared now because of the public health importance of the findings.

The study caps decades of research into the history, prevention and treatment of anal cancer and its precursors. It also provides important information for developing standard of care guidelines for people at

We CAN Prevent Anal Cancer



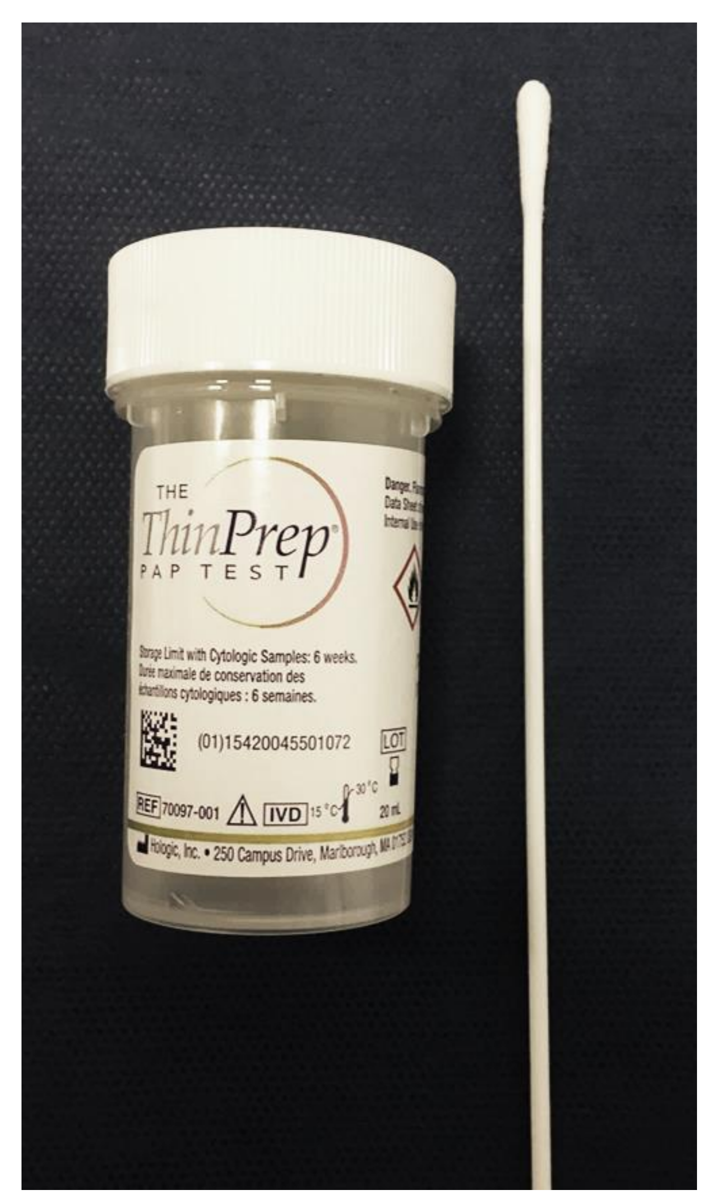
Palefsky 2022

Anal Cytology

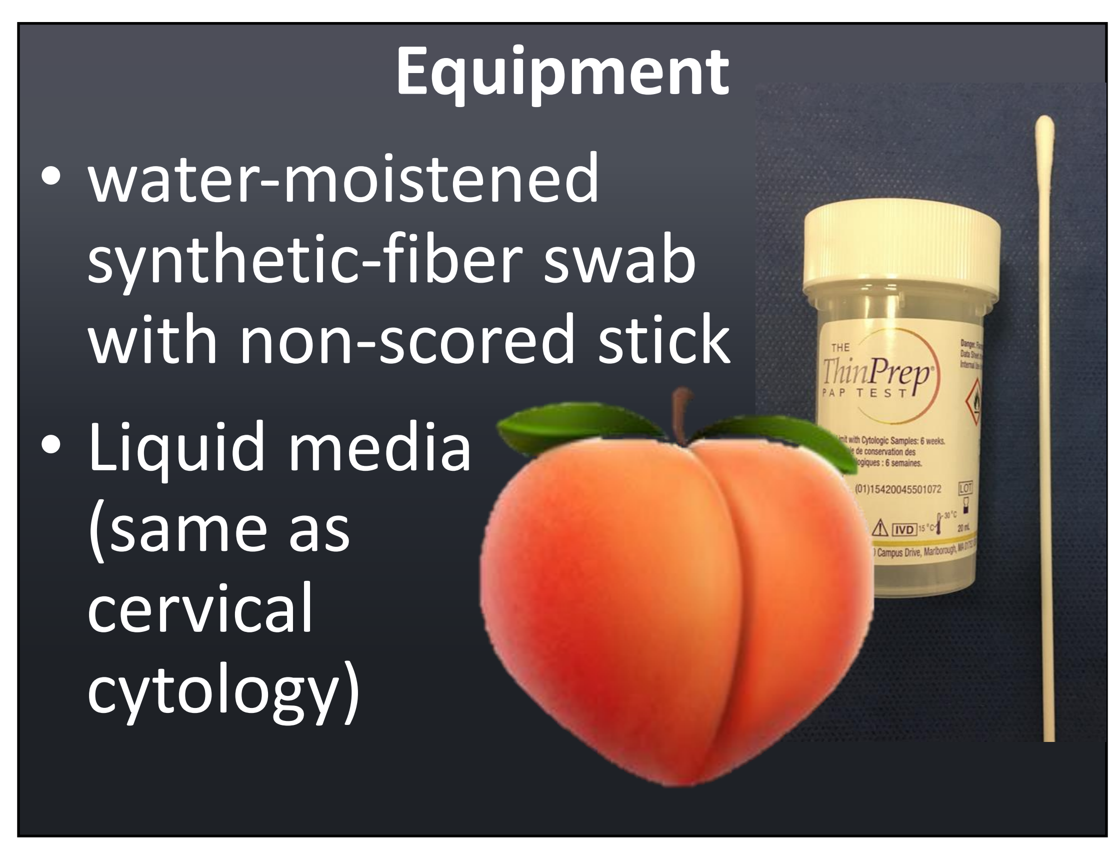
- ↑ Sensitivity ↓Specificity
- Various methods
- 3-10% unsatisfactory

Special Equipment

Special Training



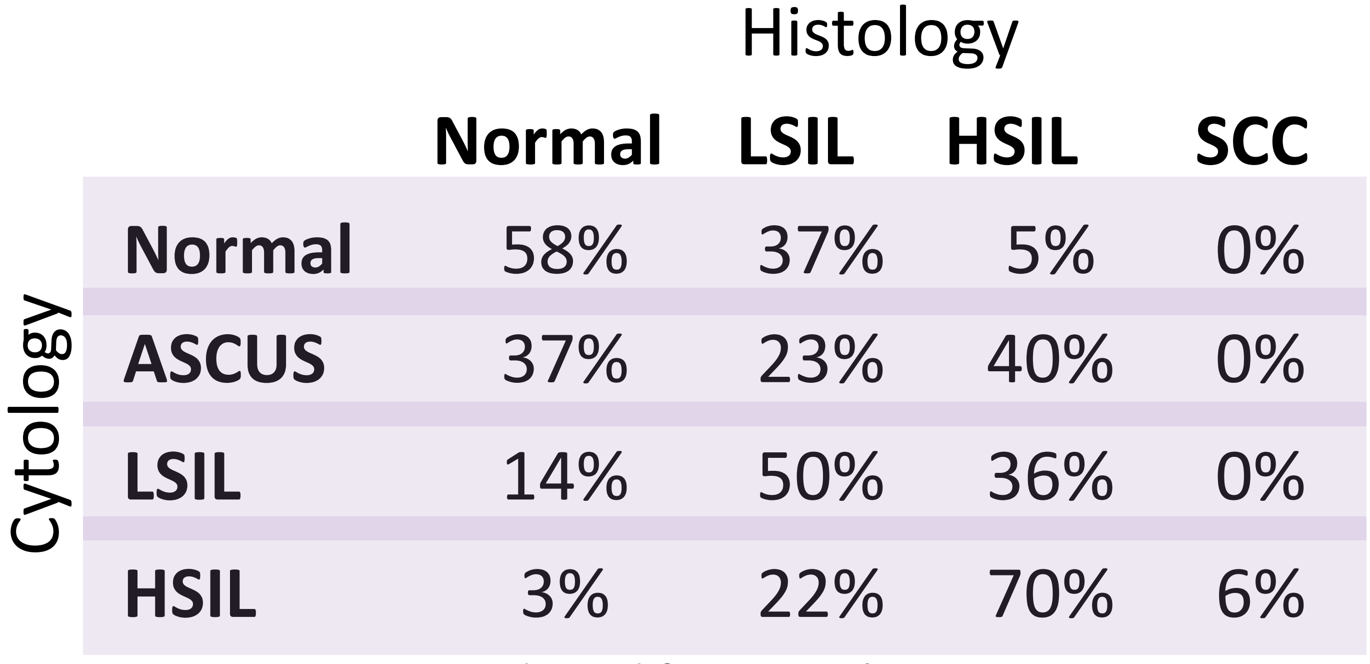
Cranston 2004, Darragh 2011



1. Evert anal verge.
2. Blindly insert one half of swab through the anal verge.
3. Apply lateral pressure in a circular motion while withdrawing the swab (10+ seconds)
4. Stir into liquid preparation (15+ seconds)

https://www.youtube.com/watch?v=YyzmLYFc7Yc

Histologic Grades & Paired Cytology



Cytology \ Histology	Normal	LSIL	HSIL	SCC
Normal	58%	37%	5%	0%
ASCUS	37%	23%	40%	0%
LSIL	14%	50%	36%	0%
HSIL	3%	22%	70%	6%

Adapted from: Panther 2004

Panther 2004, Swedish 2011, Nahas 2009, Salit 2010, Bean 2010

Management of Anal HSIL

- Observation only
- Topical therapy
- Ablative therapy
- Surgical therapy

*****ALL TREATMENTS OF ANAL HSIL ARE OFF-LABEL**

Anal HSIL Natural Regression & Progression

Regression (HSIL→benign/LSIL)

Around **25%** of HSIL spontaneously regress /year[1-5]

- SPANC: 24% regression of HSIL mostly to LSIL[1]
  - 19% HIV+ and 37% HIV-
- Regression ↓ with age[1,2,5]

Progression (HSIL→Cancer)

Takes several years (~5 yrs?) [4,5]

- Rate of progression: 1 in 377 HSIL to CA(HIV+ MSM)[2]
- SPANC: 2 HSIL progressed; 1.2% per year (95% CI 0.31–4.95)[1]
- Progression risk ↑ with age[1,2,5]

[1]Tong 2013, [2]Machalek 2011, [3]Goldstone 2018, [4]Berry, [5]Expert Opinion

Anal HSIL Treatment

156 HIV+ MSM w/ HSIL

	Topical imiquimod	Topical 5FU	Electo-cautery
Complete Clinical Response	**24%**	**17%**	**39%**
Recurrence – Wk 24		22%	
Recurrence – Wk 48		46%	
Recurrence – Wk 72		67%	
Recurrence – Wk 98	71%	58%	68%
S/E (Grade 3+) (Pain, bleeding, and itching)	43%	27%	18%

Richel 2013, Goldstone 2014

***ALL TREATMENTS OF ANAL HSIL ARE OFF-LABEL

Anal Cancer Morbidity

- Most incident anal cancer is extensive enough to require CT/RT +/- surgery
- Early identified cancers can be excised
- Long term physical, sexual sequalae

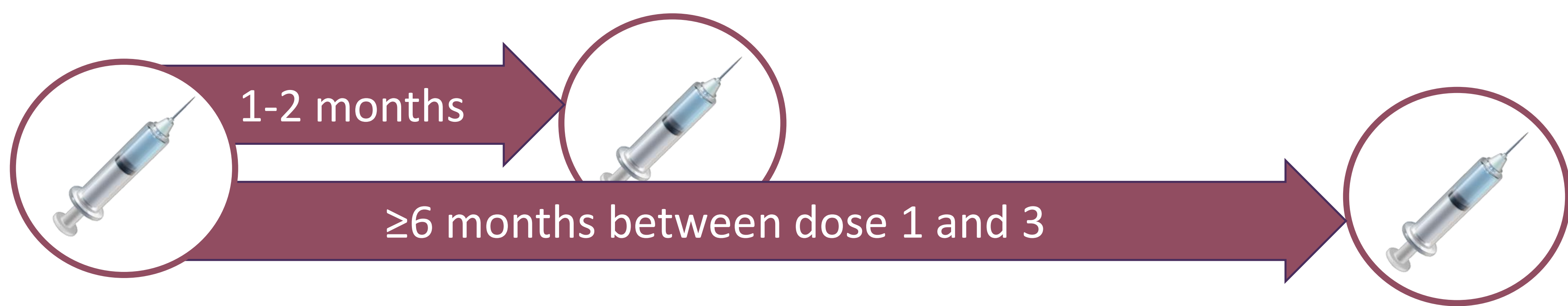
Addressing Psychological Burden

- HPV might be the patient’s first STI
  - May be anxiety or concern surrounding sexual practices
- Sexual practices post diagnosis -- “Am I contagious?”
  - “Do I have to tell my partner?”
- Destigmatize HPV infection
- Patients often don’t understand “atypical cells” or “precancer”
- Stress the importance of periodic screening
- Consider partner screening
- Trauma informed care

Slide adapted from Goldstone 2017

HPV Prophylactic Vaccine

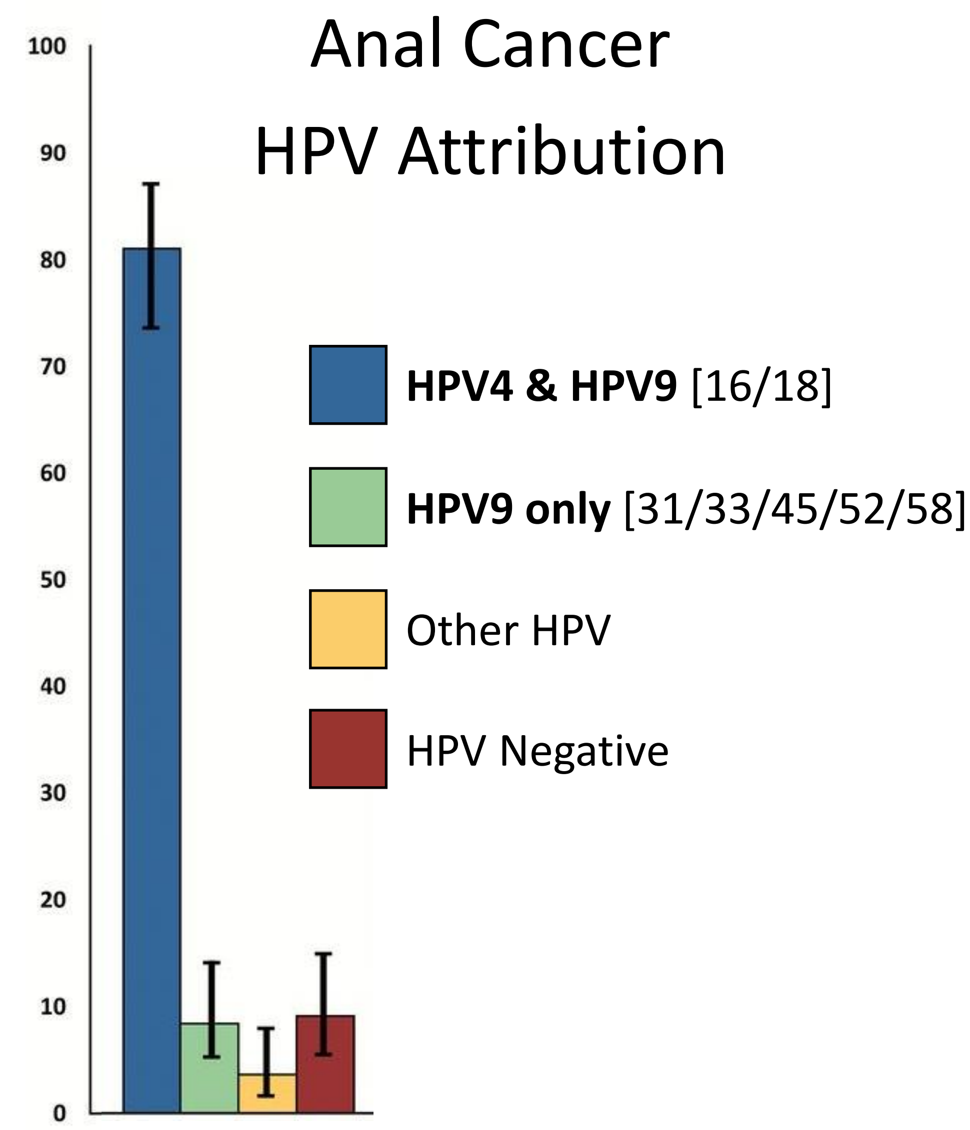
11-12 yo	**ACIP (CDC) recommended for boys and girls**
9-14 yo	2 doses
15-26 yo	3 doses (catchup vaccination)
27-45 yo	Discuss R/A/B with provider



CDC 2019

HPV9 after HPV4?

- No indication to revaccinate patients with HP9
  after completing HPV4 vaccination

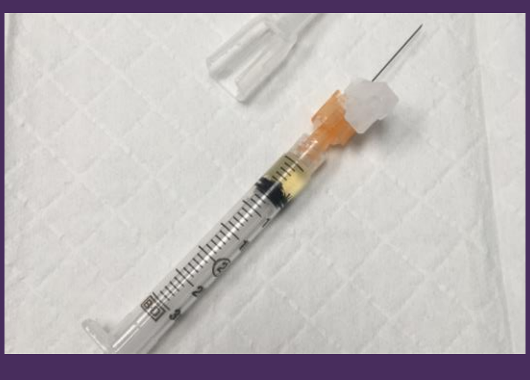


Adapted from Saraiya *et al.* (2015)

Saraiya 2015

Vaccination >26 Years

- HPV4 safe and immunogenic
- No significant difference in HPV acquisition, development of HSIL
- Trend towards protection of oral lesions



ACTG 5298 Population

- N=575 PWLH
- median age 47 yo (IQR 41-53)
- 82%♂
- 98% on ART; 83% UVL
- Median Nadir 255
- 2 year median FU
- Stopped due to futility

…emerging data

Wilkin 2016, Cranston 2018

Adjuvant HPV Vaccination

- Goal: Reduce risk of recurrence and risk of progression to CA
- N=202; 44% vaccinated, Non-concurrent observational cohort

qHPV associated with ↓risk of recurrent HGAIN

- **Year 1:** HR 0.42 (95% CI, .22–.82; *p*=.01)
- **Year 2:** HR 0.50 (95% CI, .26–.98; *p*=.05)
- **Year 3:** HR 0.52 (95% CI, .27–1.02; ***p*=.06**)

- If effect only lasts 2 years, it is probably still cost effective

Swedish 2012, Deshmukh 2017

Anal HPV Screening Guidelines

IDSA: Certain HIV+ Populations should undergo anal cytology

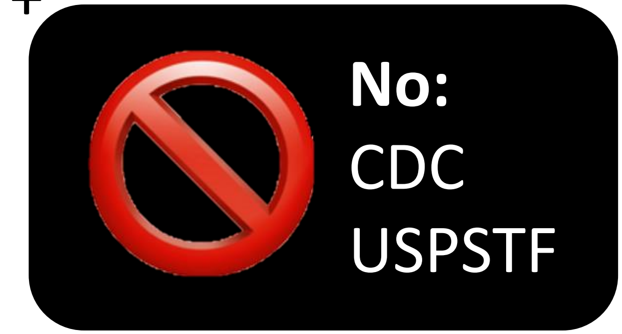
- MSM
- women with a history of RAI or abnl cervical Pap
- Persons with genital warts

NYC DOH: Anal cytology at baseline and annually in HIV+

- MSM
- H/O anogenital condylomas
- Abnormal cervical and/or vulvar histology

NYC DOH: Refer for examination, HRA, +/- biopsy

- Abnormal anal cytology
- Cervical HSIL
- Abnormal anal physical findings



Aberg 2013, NYS DOH 2007

Recommendation

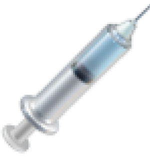
I recommend anal pap screening if your patient:

- ☑ Has a significant risk of developing anal cancer
  - (Prioritize patients with multiple risk factors: Age ≥35, PLWH, MSM, pelvic Dz, immunosuppression, etc.)
- ☑ Has available provider who is well trained in HRA & management

👉 …otherwise, quality digital anorectal examination at least annually & take anorectal complaints seriously

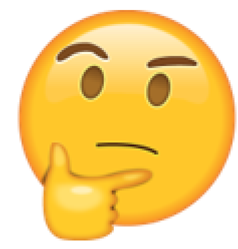
Further Recommendations

It is not always hemorrhoids



Vaccinate, vaccinate, vaccinate

Watch for national guidelines
based on ANCHOR Trial Results



Start thinking about what implementation
of an anal cancer screening program
will look like for you

HRA Provider List

Print PDF

This is a list of providers around the United States that perform HRA. Want to be added to this list? Email arezou.sadighiakha@ucsf.edu

Arizona
California
Connecticut
Colorado
Florida
Georgia
Illinois
Louisiana
Maryland
Massachusetts
Michigan
Minnesota
Missouri
New Mexico
New York
North Carolina
Oregon
Pennsylvania
Tennessee
Texas
Utah
Washington state
Washington D.C.
Wisconsin

ucsf.edu/hra-provider-list

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