

ANCHOR study update

The BCN HPV Course
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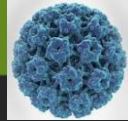
Disclosures

Research Support: Merck and Co.

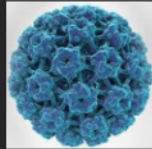
Board Member/Advisory Panel: Merck and Co, Vir,
Vaccitech, Virion Therapeutics

Speaker's honorarium: Merck and Co.

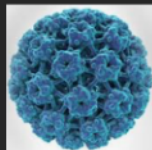
Objectives



Understand the rationale
for the ANCHOR Study

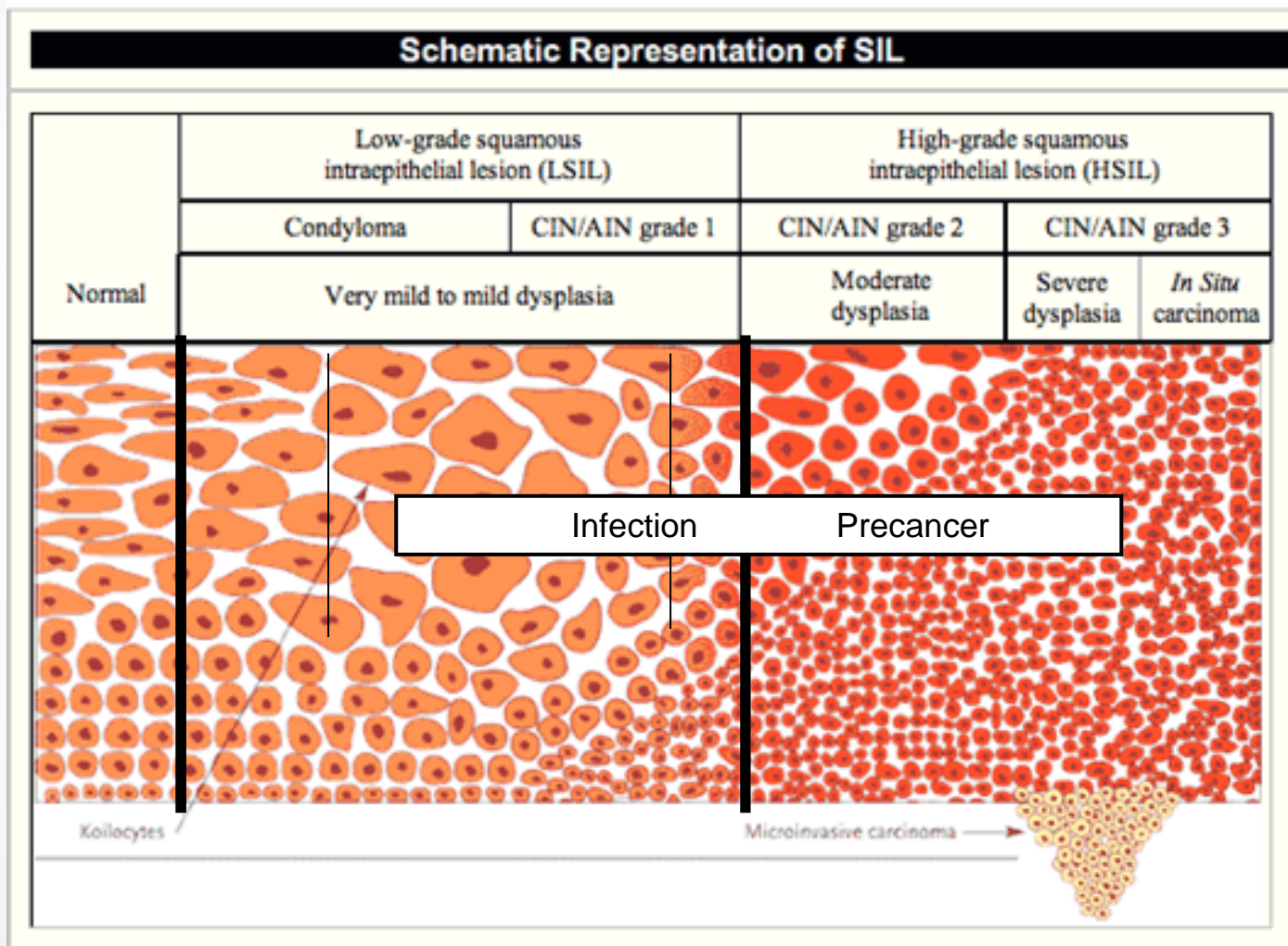


Understand the design of
the ANCHOR Study

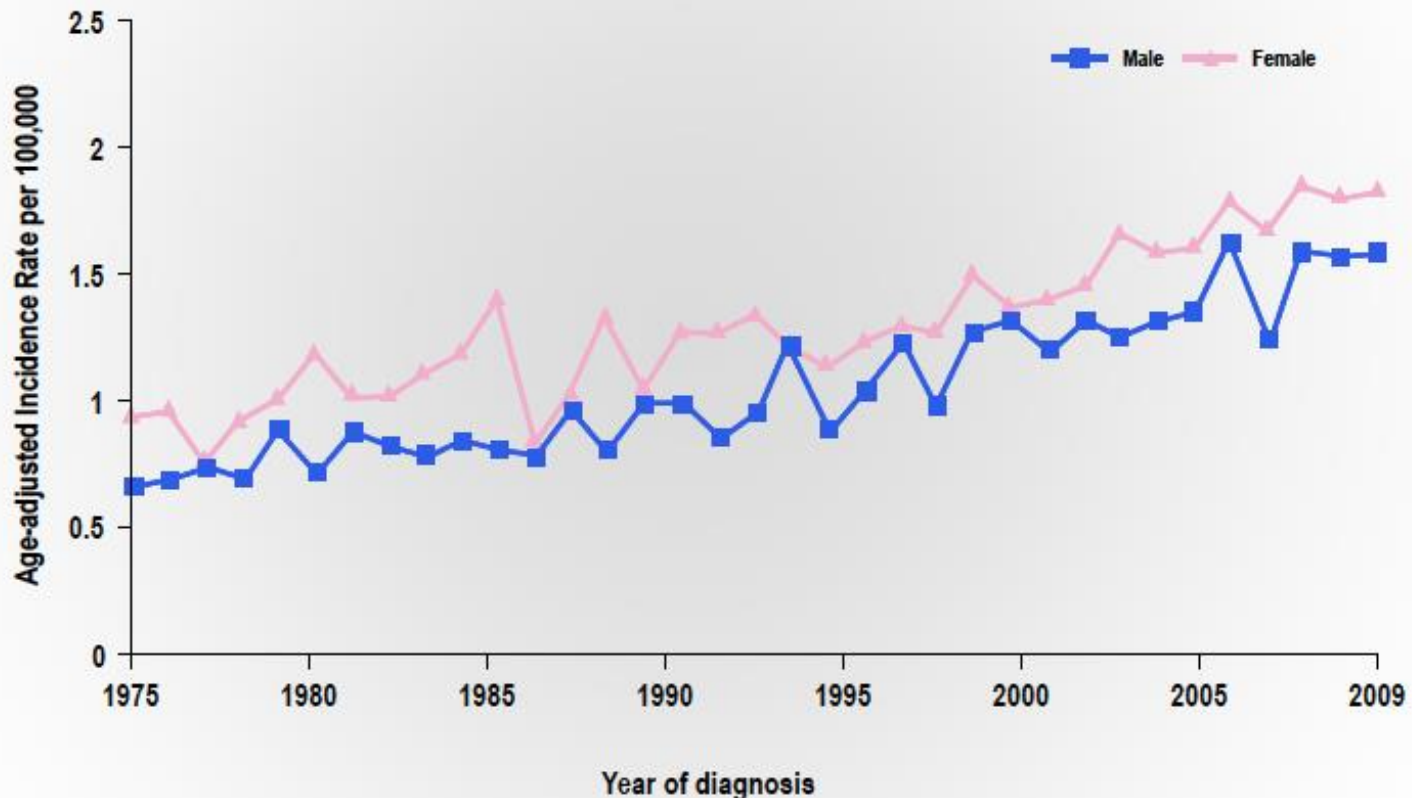


Results of the ANCHOR
Study

2-tiered system: LSIL & HSIL

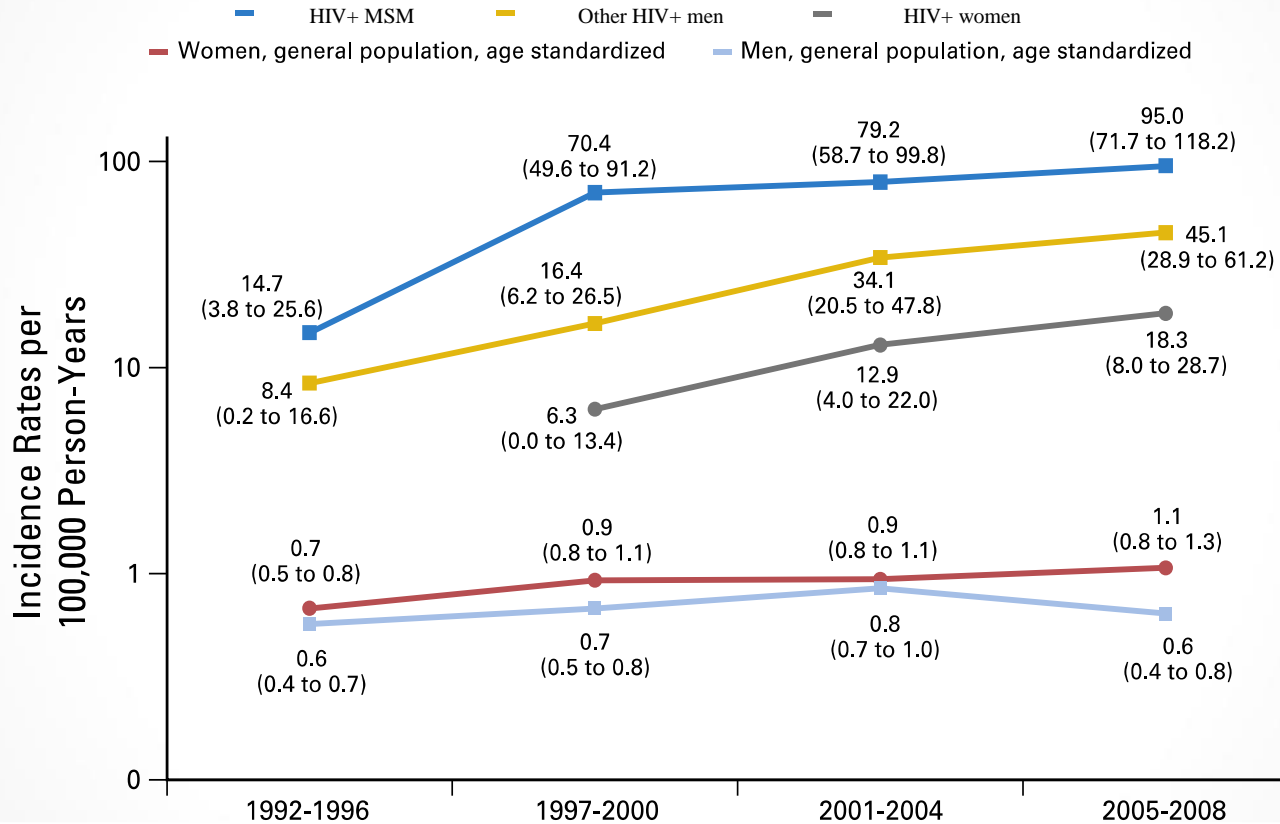


Age-Adjusted Incidence of Invasive Anal Cancer by Gender and Year of Diagnosis: United States



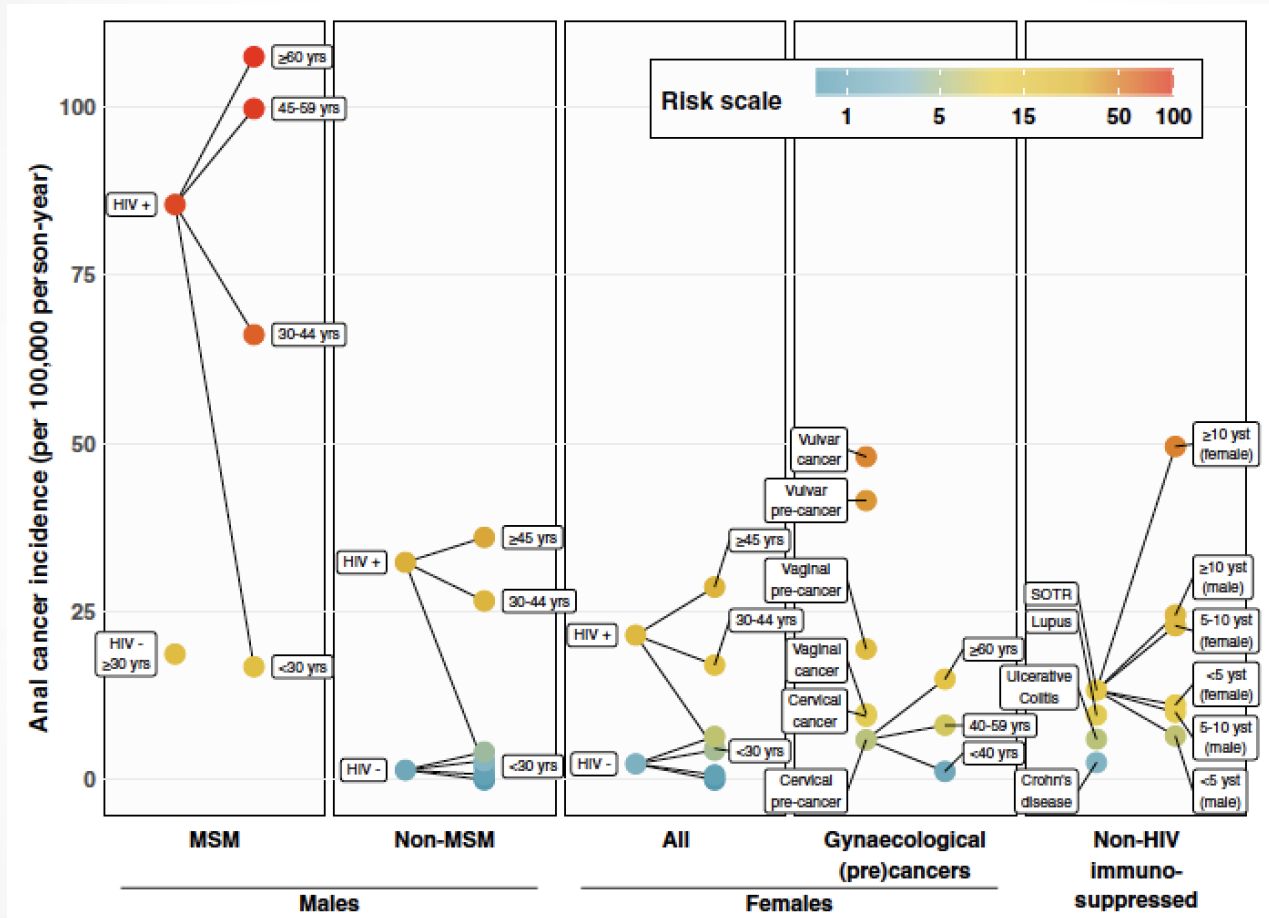
Howlander N et al. (eds). SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). http://seer.cancer.gov/csr/1975_2009_pops09/. Accessed June 21, 2012.

Anal Cancer in PLWH



Piketty C 2012 et al. *JCO* 2012; 30(35); 4360-4366.

Anal cancer risk scale



Clifford et al. Int. J. Cancer. 2020;1–11. <https://doi.org/10.1002/ijc.33185>

Effect of Antiretroviral Therapy

- Unclear
- Likely some but incomplete protection against HPV infection and HSIL

Brickman C & Palefsky J (2017). Prevention of Complications from Human Papillomavirus in the HIV-infected Host. In Bachman L (ed), *Sexually Transmitted Infections in HIV-infected Adults and Special Populations* (pp 141-163): Springer.

Recent trends in anal cancer incidence

AIDS and cancer registry match study

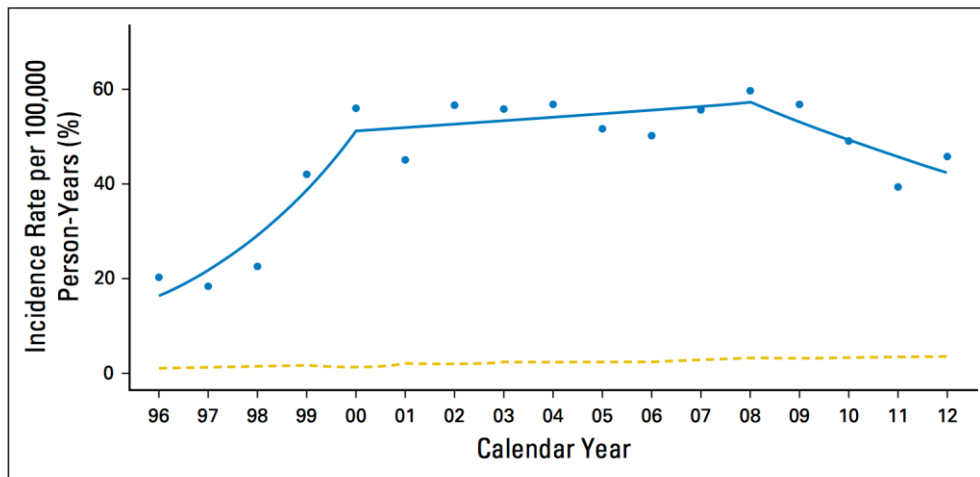


Fig 1. Trend in anal cancer incidence among people with HIV infection and the general population in the United States, 1996 to 2012. Dots indicate the observed incidence of anal cancer among people with HIV in the study population as a function of calendar year. The solid line is the model fitted by Joinpoint, with changes in slope for the incidence trend indicated in 2000 and 2008. The dashed line is the expected incidence in the general population standardized to reflect the demographic characteristics of the HIV population.

Colon-Lopez V. et al J Clin Oncol 2018; 36:68-75

Progression to anal cancer

- Indirect calculation
 - 1 in 377 MSMLWH with HSIL per year
=265/100,000
 - 1 in 4196 HIV-negative MSM per year

Machalek DA et al. *Lancet Oncology*. 2012;13(5): 487-500.

What should we do about this?

- **The cervical model: anal and anal cancer are very similar diseases**
- **Cervical cancer and anal cancer are preceded by high grade squamous intraepithelial lesions (HSIL)**
- **Treatment of cervical HSIL is proven to reduce the incidence of cervical cancer**
- **Treating anal HSIL might reduce the incidence of anal cancer and so we should be screening for anal HSIL**

What is the problem with no screening and treatment guidelines?

- Insurance carriers don't pay
- Clinicians interested in getting trained to do HRA face barriers
- HRA and treatment services are hard to find
- There are no quality assurance programs
- Net result: too few people getting screened

Key questions

- **Will treatment of anal HSIL reduce the risk of anal cancer?**
- **Will the effects of treatment on quality of life be acceptable?**
- **Overall benefit of a screening and treatment program should outweigh its potential harms**

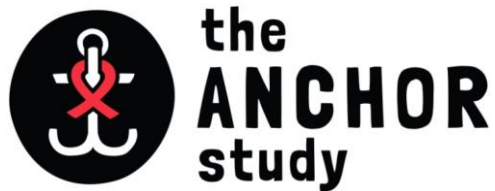
Why anal screening and treatment might not work

- In many at-risk people lesions are large and multifocal
- Clinicians may miss lesions
- Clinicians may inadequately treat lesions
- New lesions often arise- anal whack-a-mole!



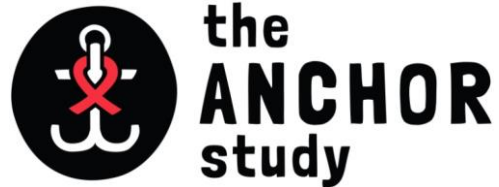


"I just want to apologize beforehand if you miss."

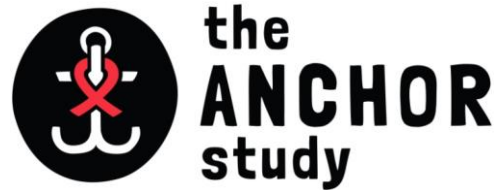


NCI UM1CA121947

- **Aim 1:** To determine whether treating anal high-grade squamous intraepithelial lesions (HSIL) is effective in reducing the incidence of anal cancer in HIV-infected men and women



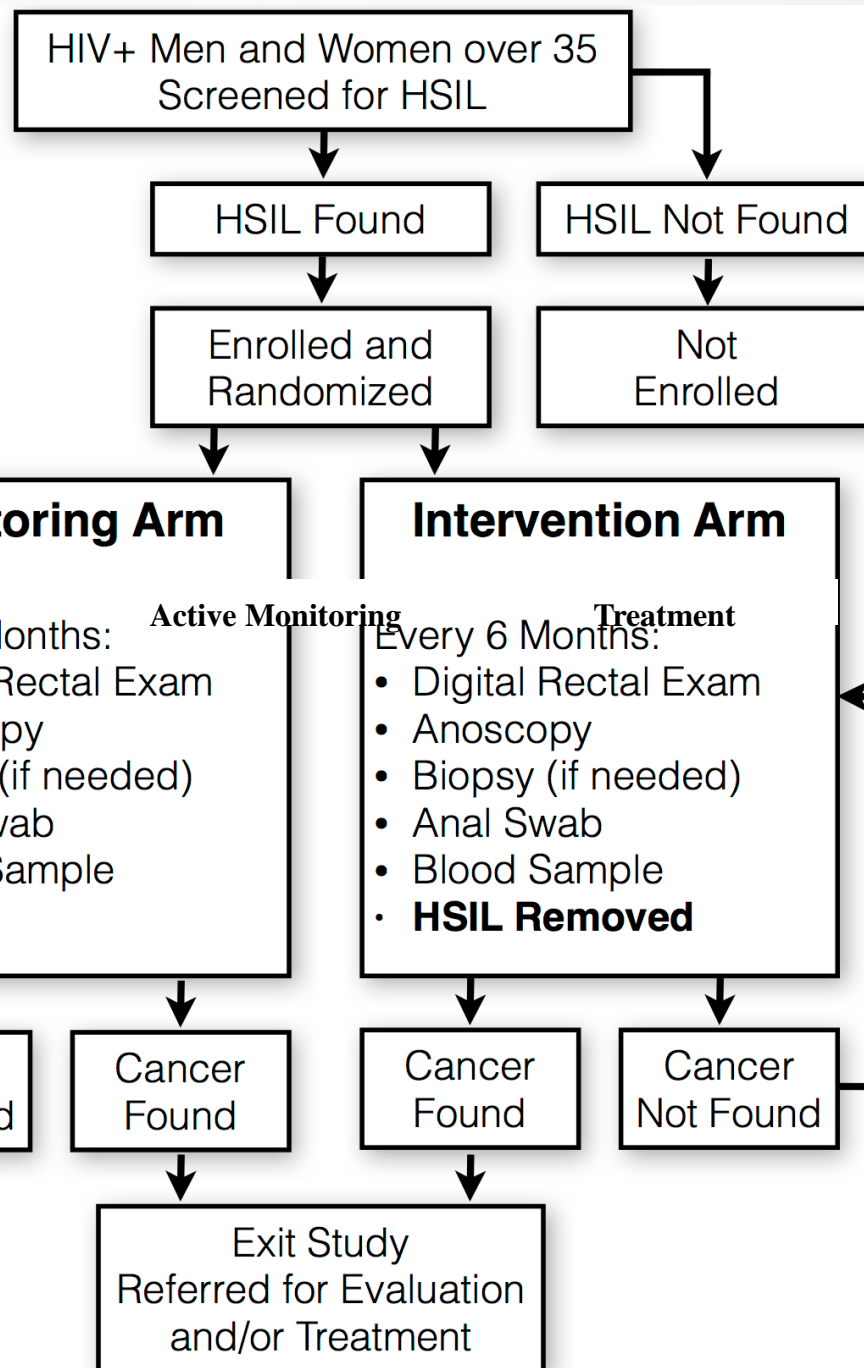
- **Aim 2:** To determine the safety of infrared coagulation (IRC), electrocautery, imiquimod, laser and 5- fluorouracil treatments for anal HSIL
- **Aim 3:** To develop and implement an instrument to measure the impact of ANCHOR procedures on QoL (ANCHOR Health-Related Symptom Index (A-HRSI))



- **Aim 4:** Collect clinical specimens and data to create a bank of well-annotated specimens that will enable correlative science:
 - Identify host and viral factors in HSIL progression to cancer;
 - Identify host and viral biomarkers of progression from HSIL to cancer;
 - Identify medical history and behavioral risk factors for HSIL progression to cancer

Enroll 5,058

Screened
>100



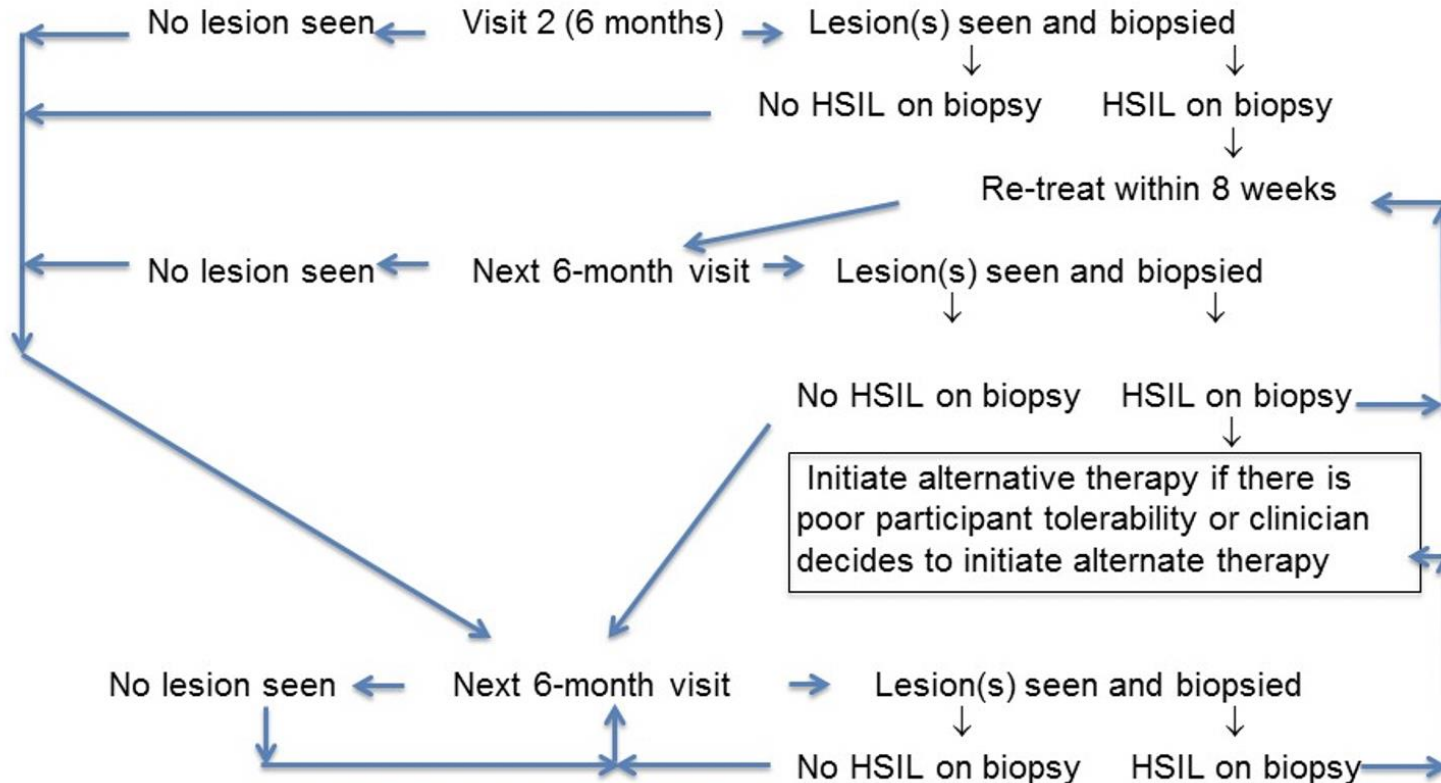
Retain for 5 or more years

Follow-up in each arm

- Screening LWH, 35 years or older, cytology, HRA, biopsy
- Randomization at least one week later if biopsy + for HSIL
- Randomized to monitoring arm, seen every 6 months, every 3 months if concern, biopsied annually to confirm HSIL and no cancer
- Randomized to treatment arm, treated immediately, and then seen according to treatment algorithm, then seen every 6 months, every 3 months if concern, biopsied at each visit if suspicion for HSIL

Hyfrecation

Figure 4-B: IRC, hyfrecation, or electrocautery performed at visit 1 (randomization visit)

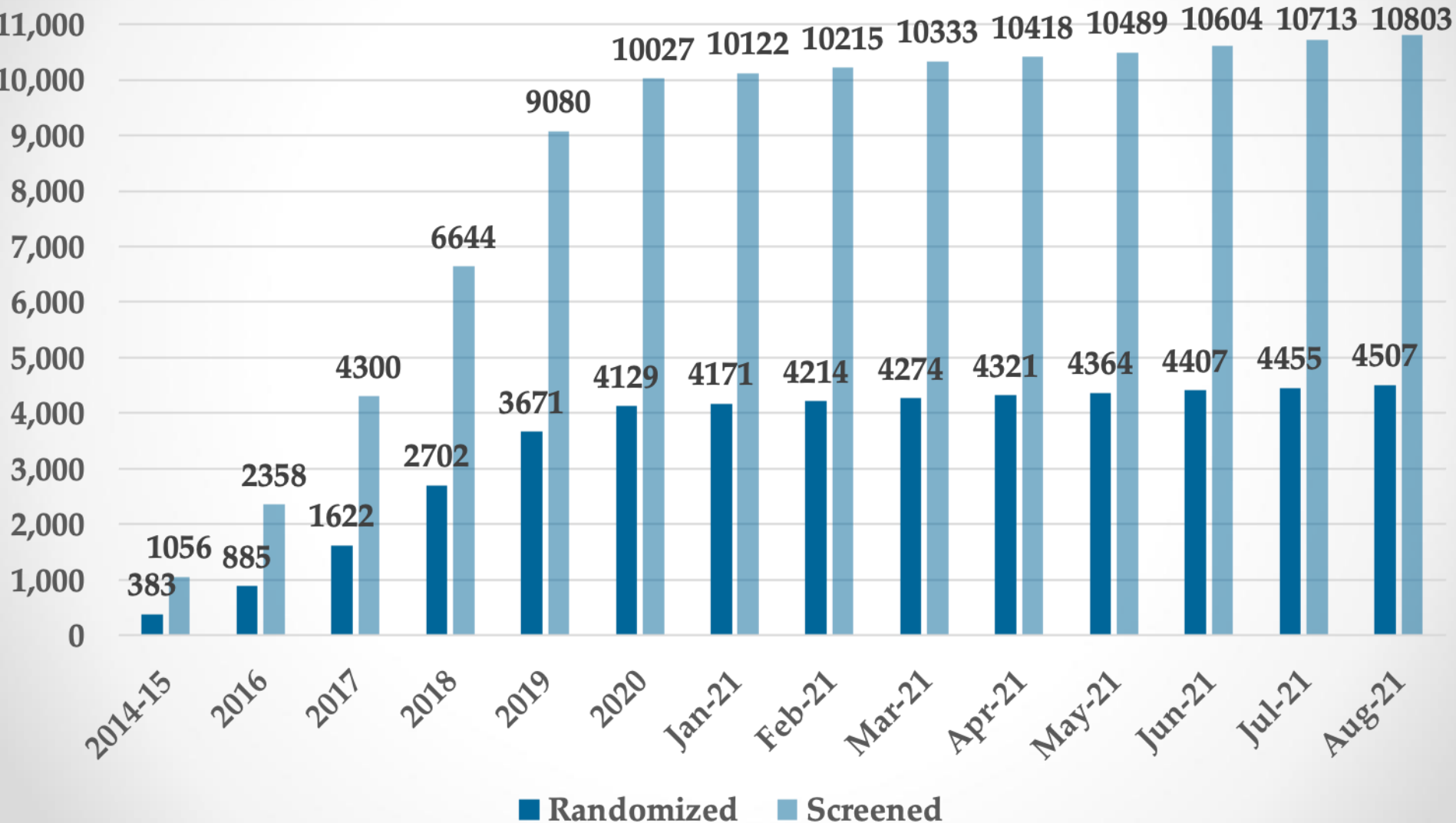


If no lesions are seen, participant will return for HRA at the next 6 month visit. If HSIL is found, alternative treatment is initiated per guidelines

Where we are



Cumulative accrual



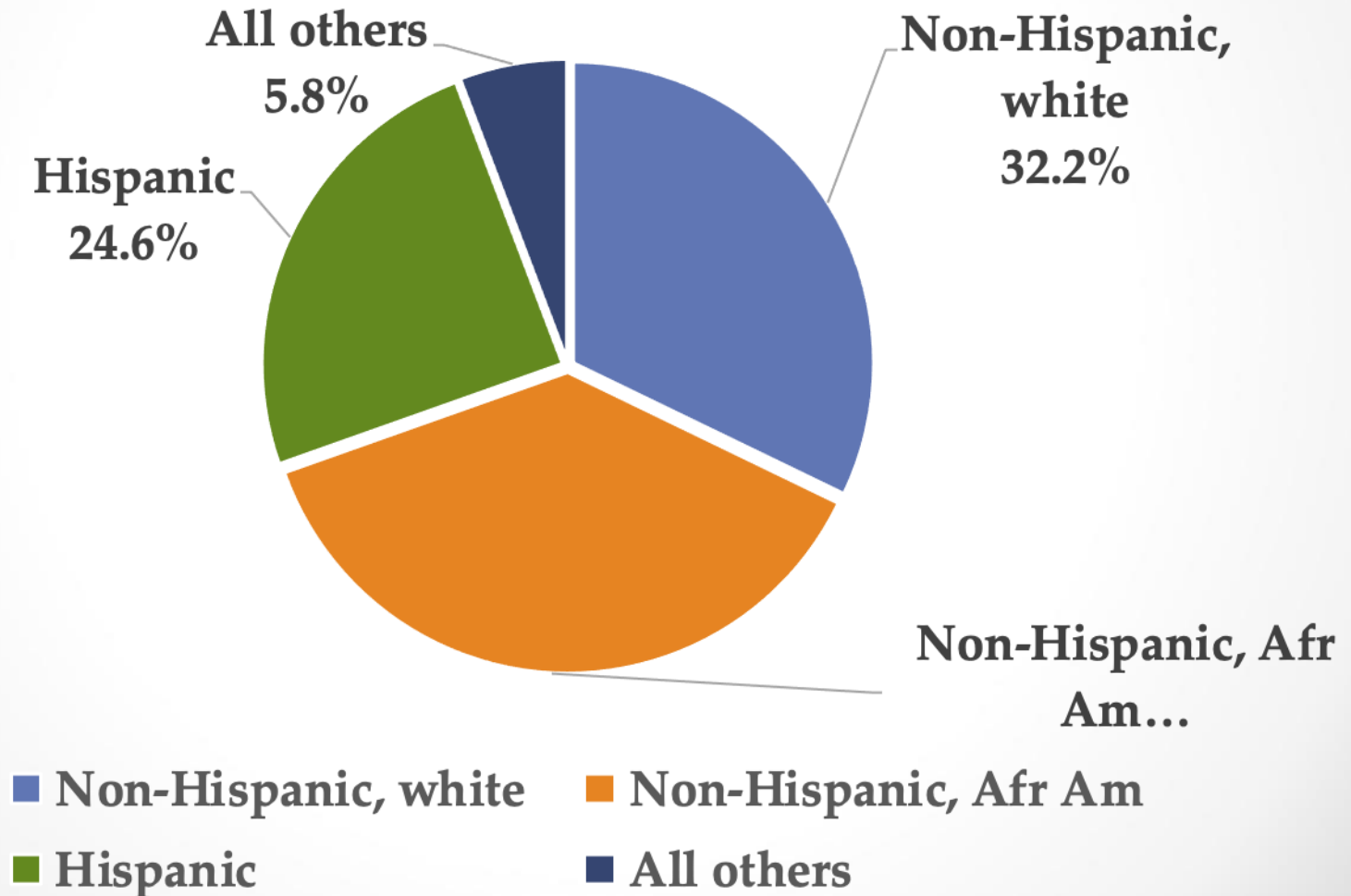
Factors associated with successful recruitment and retention

- Lengthy informed consent process, quiz at end
- Minimum one week time required to think about enrollment
- Eliminated out of pocket costs
 - Insured- covered co-pays and deductibles
 - Uninsured- covered all costs from study funds
- Reimbursed people for their time at each visit
- Used cashless payment system
- Provided gifts at different milestones, SWAG

Quality assurance

- Rigorous training of HRA clinicians with extensive certification process for diagnosis and treatment
- Ongoing quality assurance data collected
- Feedback to clinicians if metrics were not met

Participant demographics

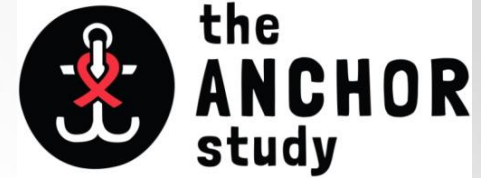


Drop in/out rates



- Low drop-in and drop-out rates reported

Adverse events



- No grade 5 AEs (death) related to the study
- Very low number of severe (grade 3) and related to study procedures

Cancer cases



- Cancer found at screening- not enrolled
- After randomization cancer found in both arms
- Event-driven analysis with interim assessments at different milestones

The result

- Prevalence of cancer at screening was higher than expected
- Prevalence of HSIL at screening was higher than expected
- The incidence of cancer in the monitoring arm was higher than expected

The result

- The incidence of anal cancer was significantly reduced in the treatment arm compared with the active monitoring arm
- DSMB halted the study and asked us to inform participants in the monitoring arm that we would now recommend treatment

The result

- There is room for improvement in treatment of anal HSIL
- Hopefully will become standard of care for high-risk groups

What's next

- Offer treatment and followup to monitoring arm participants
- Continue to offer treatment and follow-up to treatment arm participants
- Work to include screening of at- risk individuals into standard of care guidelines, PLWH and others: HIV-MSM, women with vulvar disease, men and women transplant, etc
- Once standard of care: big increase in training programs, education of medical community and the public

Gracias!