



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Anal Cancer: Should Screening be Routine?

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Presentation prepared by:
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Criteria for a New Screening Intervention

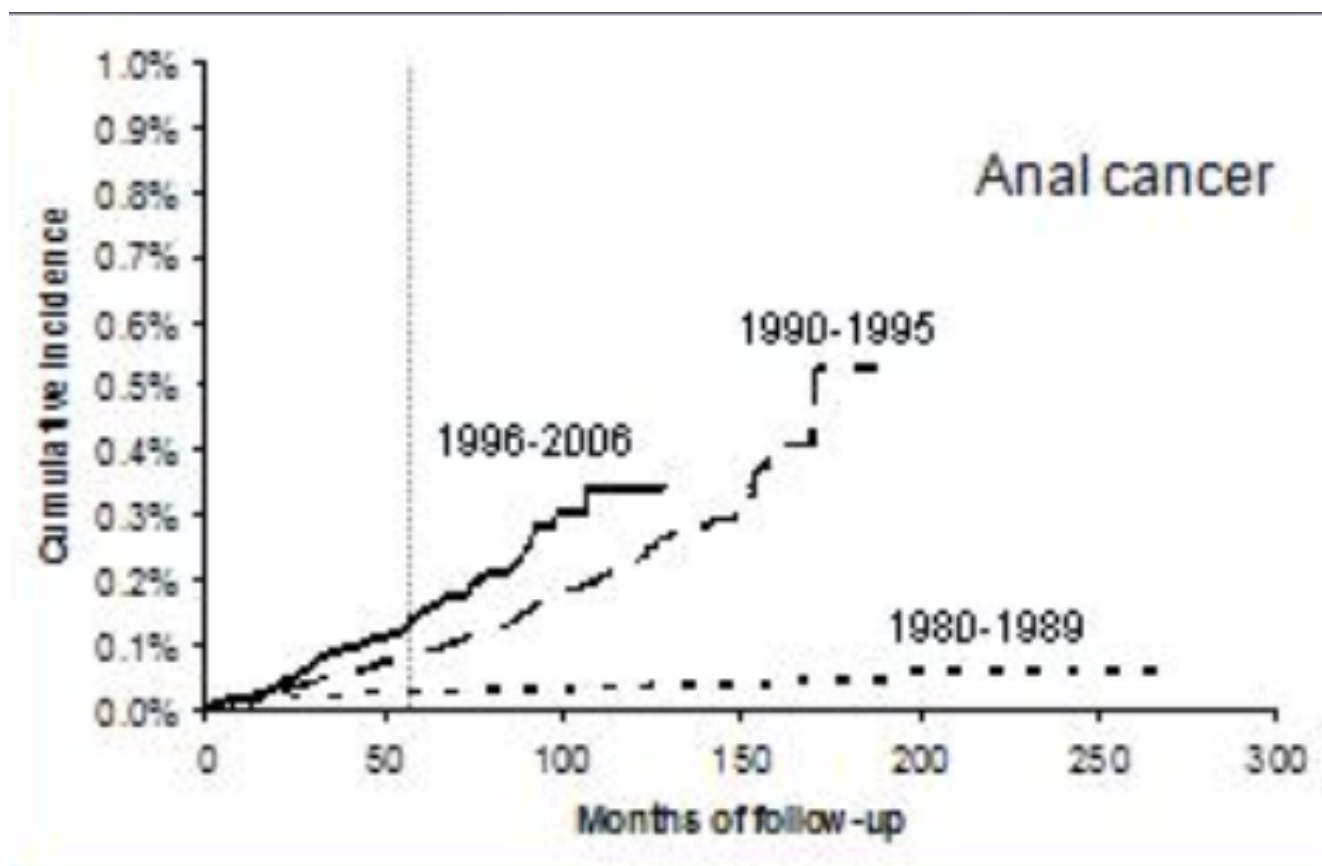
- 1) Does the burden of disease warrant action? Is this an important medical problem?
- 2) Are the components of the intervention known to be effective?
 - a) Anal paps & high-resolution anoscopy and biopsy
 - b) Treatment of abnormal lesions
- 3) Can providers manage this and will patients comply with a screening program?
- 4) Does early diagnosis and treatment change clinical outcomes?
- 5) Can we afford this?

HPV Epidemiology

- Anal cancer is caused by human papillomavirus (HPV)
 - Over 80 types – most do not cause cancer, types 16 and 18 most common causes of cervical and anal cancer
- Most people have been infected with at least one HPV type
- HPV prevalence in HIV+ MSM ~90% - 72% have ≥ 1 oncogenic type

Anal Cancer: A Rare Cause of Death, But Rates are Rising

- Rate anal cancer among HIV+ MSM ~46/100,000 (range 13-131)
- 2003-06 San Francisco – 8 (0.6%) of 1161 deaths in persons with AIDS



Anal Cancer and CD4 Count

NA-ACCORD Rate Ratios Anal Cancer

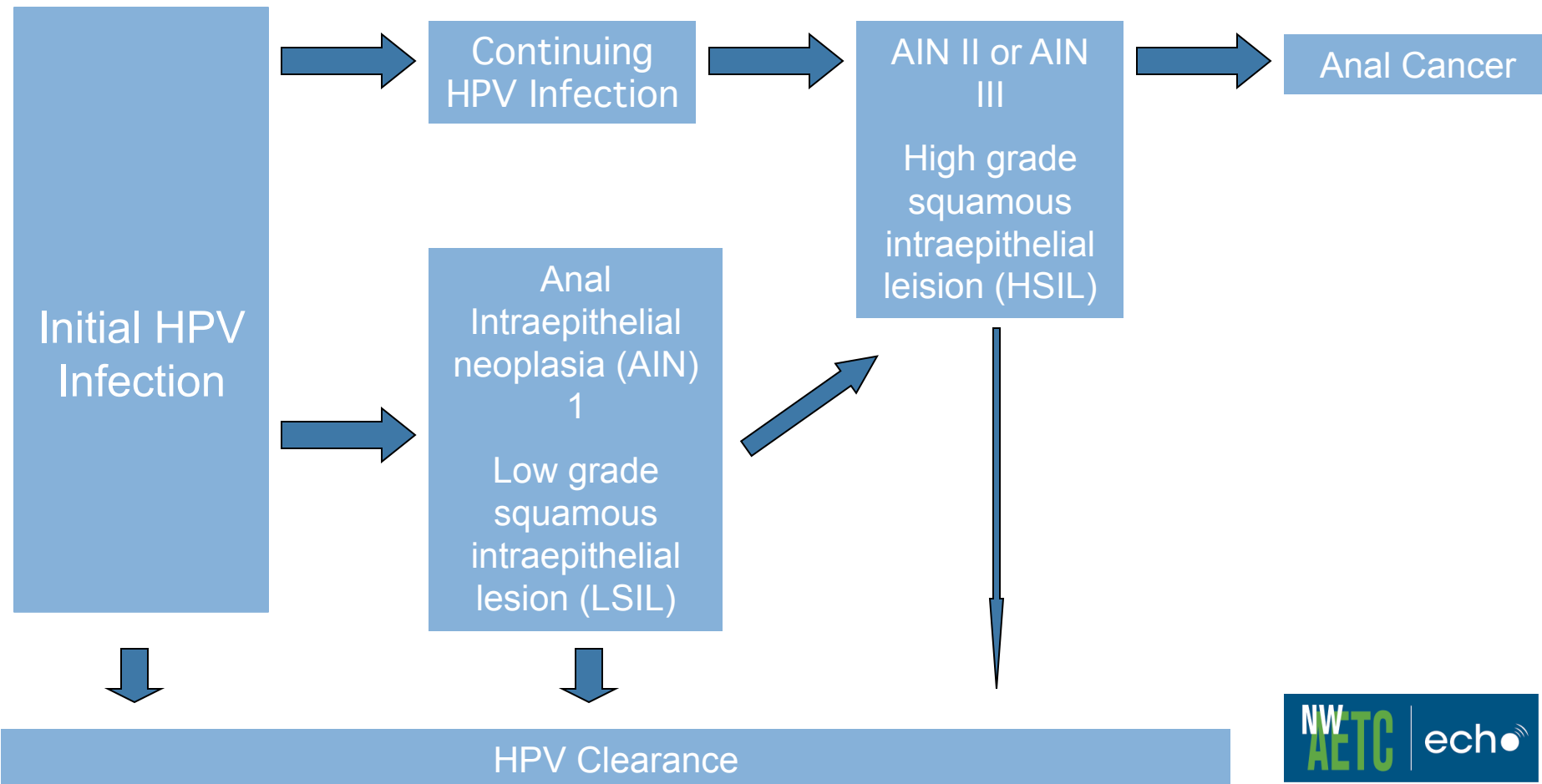
<u>CD4 Count</u>	<u>RR</u>
<200	1.0
201-349	0.5 (.3-.7)
350-499	0.5 (.3-.7)
≥500	p.2 (.1-.3)

Anal CA also associated MSM,
older age, calendar yr (1996-99)

- Antiretrovirals don't lower the risk
- Trend toward more anal cancer
- Divergent trends
 - People aren't dying of other things – more time to get anal cancer
 - If fewer people have low CD4 counts, that should decrease anal cancer risk

Anal Cancer Natural History

- Like cervical cancer, anal cancer is thought to progress from a precancerous lesions, anal intraepithelial neoplasia (AIN)



Anal Cancer Screening Algorithm

Anal Pap



High resolution
anoscopy & biopsy



Treatment

Prevalence
abnormal pap

HIV+ = 41-97%

HIV- = 4%

HIV+

Sensitivity=70-90%

Specificity=30-60%

HIV-

Sensitivity=25-50%

Specificity=92-98%

PPV

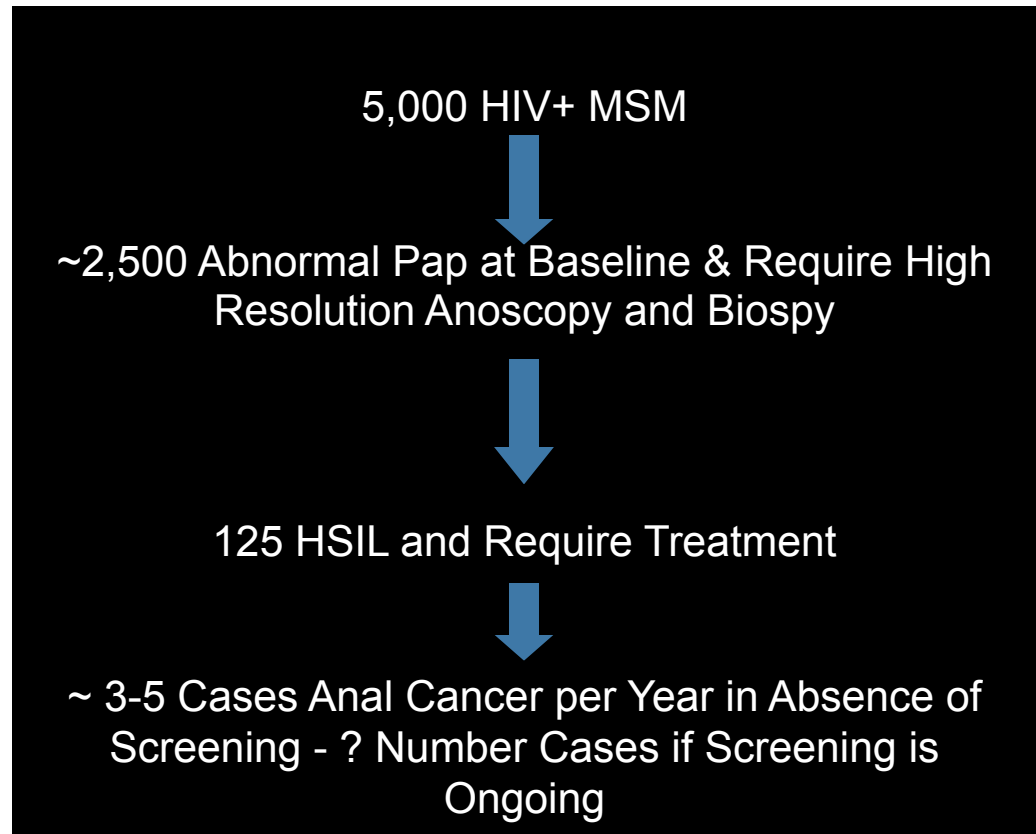
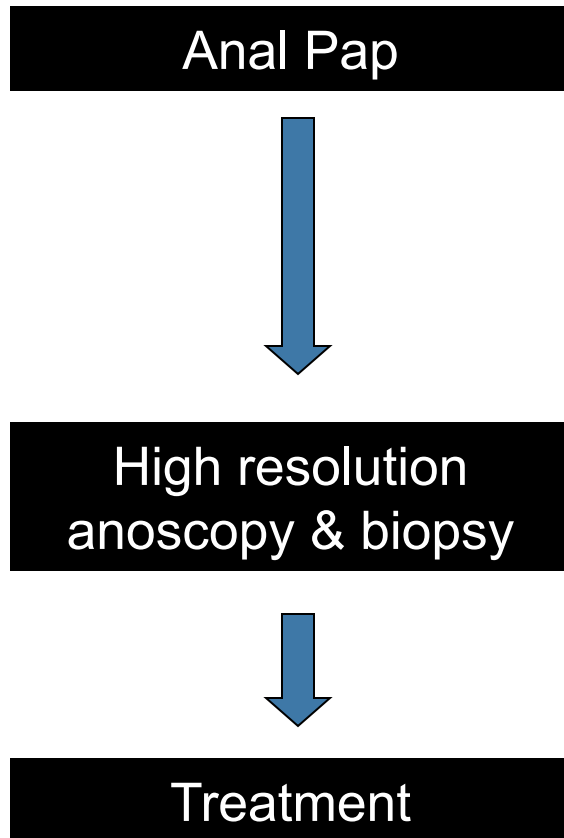
HIV+ = 38-46%

HIV- = 35-56%

Among HIV+ men receiving serial PAPs, most will need high resolution anoscopy and biopsy.

Only HSIL are treated. Approximately 5-9% of those with an abnormal anal Pap have HSIL

Anal Cancer Screening Algorithm



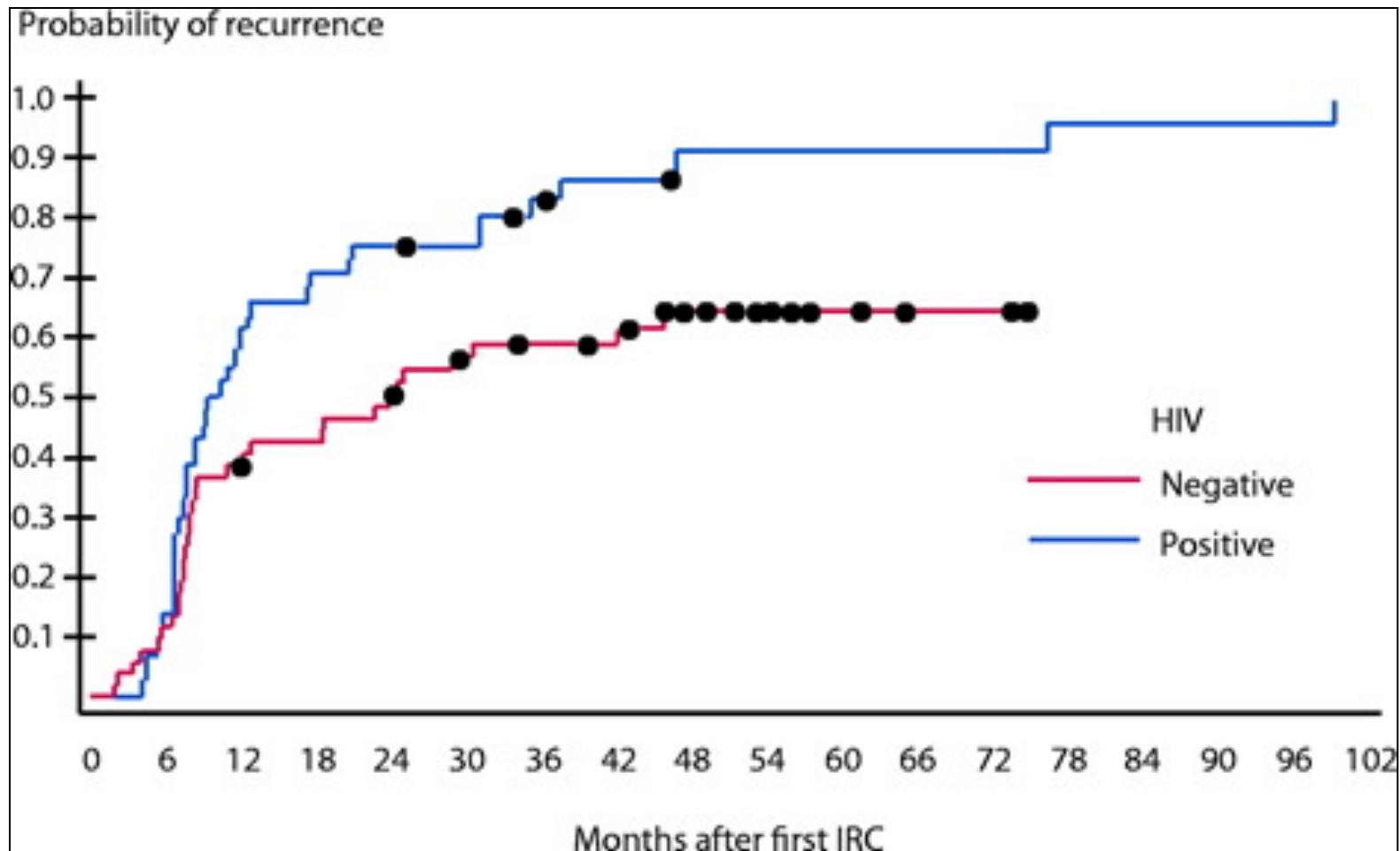
Randomized Trial for AIN: Imiquimod, Topical 5-FU, Electrocautery

- 148 HIV+ MSM (60% HGAIN)
- 16 wks Rx – Imiquimond 3x/wk, 5-FU 2x/wk, electrocautery monthly
- Follow-up at 6 months

	4 Week Response ITT (95% CI)		Recurrence 6 Months	Severe Pain
	Complete	Partial		
Imiquimond	26% (13-39)	13% (6-25)	21%	43%
5-FU	17% (8-30)	13% (5-25)	38%	27%
Electrocautery	41% (28-56)	7 (2-18)	17%	13%

P=.04

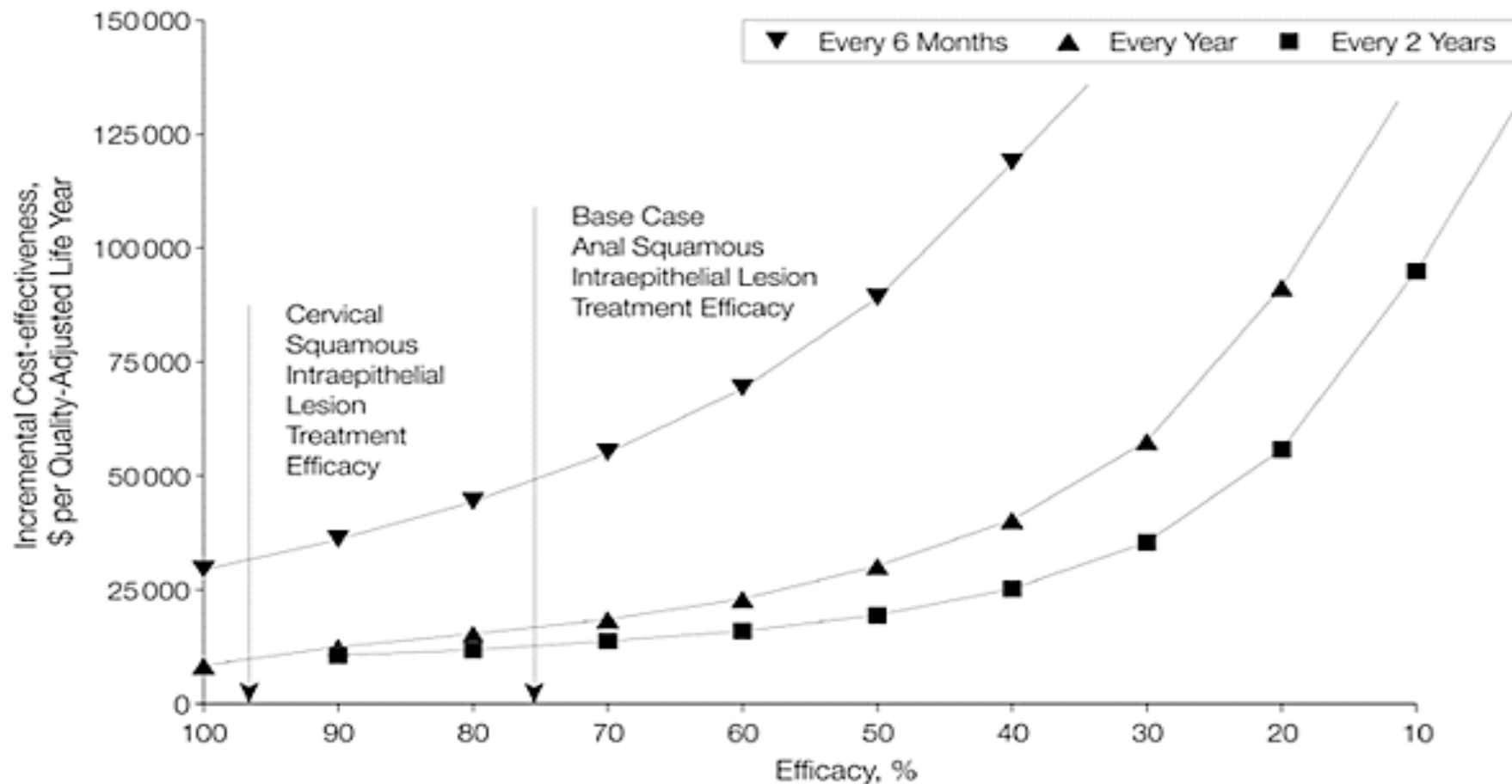
Recurrent of High-Grade Intraepithelial Squamous Lesions Among 96 MSM Following Infrared Coagulator Ablation



Patient Adherence

- In a prospective study, ~80% of 608 participants completed at least one follow-up visit. (Palefsky J. JAIDS 1997)
- 642/1864 (34%) of MSM screened in San Diego completed at least one follow-up screening visit within 3 years (Matthews J. JAIDS 2004)

Efficacy of Treatment of High-Grade Anal Squamous Intraepithelial Lesions



Argument for Anal Cancer Screening

- Anal cancer is an important and increasing cause of morbidity and mortality in MSM, particularly HIV+ MSM
- Anal Paps can identify abnormalities that are probably precursors to anal cancer
- Some evidence suggests that treating these abnormalities decreases their progression to anal cancer
- Some evidence to suggest that screening can be cost-effective
- Although there is no direct evidence that screening decreases anal cancer morbidity & mortality, Pap smears are thought to prevent cervical cancer, the rationale for screening for anal cancer is similar, and definitive trial are not likely to occur

Argument Against Anal Cancer Screening

- Anal cancer is an important problem
- Anal pap results are very nonspecific, particularly in HIV+ men, meaning that most people will need biopsies
- Treatment is not known to be effective, existing evidence is very limited and rates of recurrence appear to be high
- Analogy to treatment for cervical cancer may be false
 - Loop excision for cervical cancer removes a much larger area of affected tissue
- It is uncertain whether providers and patients will comply with recommendations
- Experience with other cancer (e.g. prostate) screening should be a cautionary tale

Criteria for a New Screening Intervention

- | | |
|---|-----------|
| 1) Does the burden of disease warrant action? Is this an important problem | Yes |
| 2) Are the components of the intervention known to be effective? | Uncertain |
| a) Anal paps & high-resolution anoscopy and biopsy | |
| b) Treatment of abnormal lesions | |
| 3) Can providers manage this and will patients comply with recommendations? | Uncertain |
| 4) Does early diagnosis and treatment change clinical outcomes? | Uncertain |
| 5) Can we afford this? | Uncertain |

Recommendations

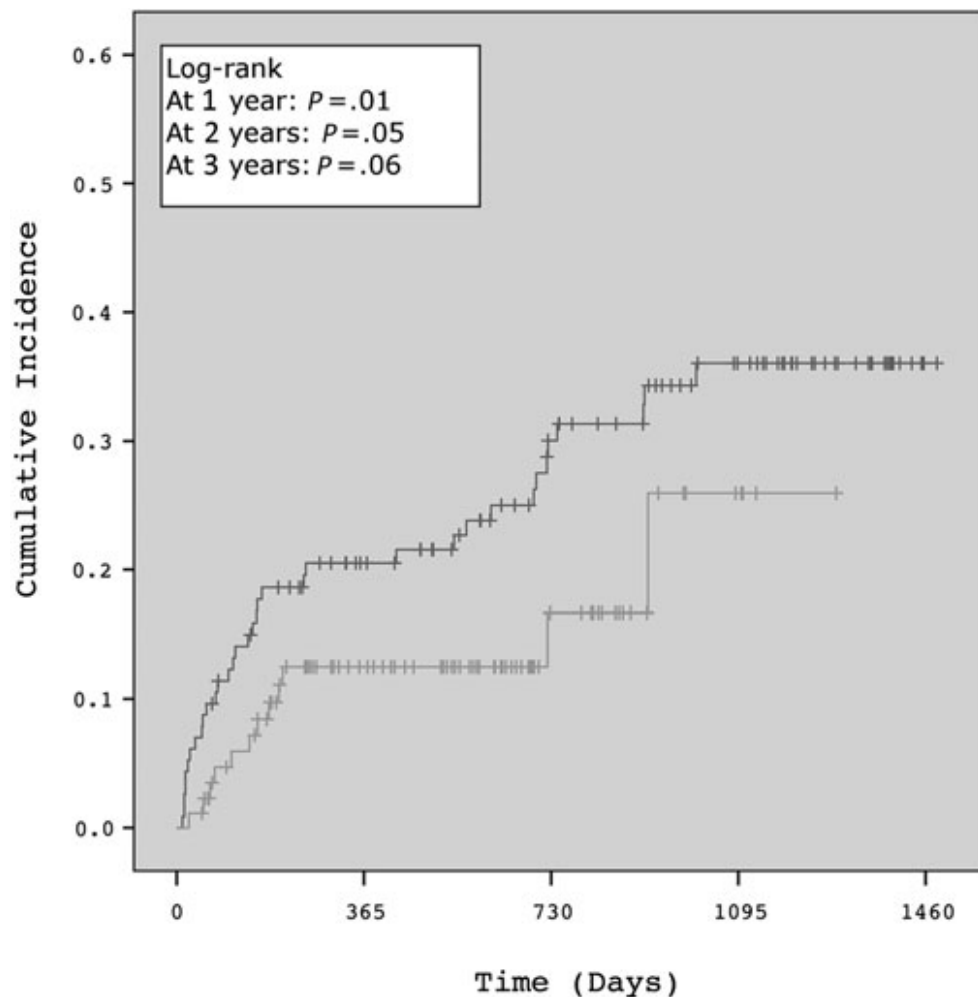
- New York State Department of Health recommends anal paps for persons with HIV
- CDC, the U.S. Preventive Services Task Force, the American Cancer Society, and the Infectious Diseases Society of America, **do not** recommend routine anal cytology screening
- If anal pap is done:
 - Baseline anal pap
 - HIV+ - twice in first year, then annually
 - HIV- men – baseline and then every 2-3 years
 - Referral for high-resolution anoscopy if cytology shows atypical squamous cells of uncertain significance or worse

Can We Know if Screening Works?

- I'm not sure
- It's not clear that we can do a large enough study to answer the question
- What outcome would be enough to convince one that the screening was helping the population?
- Cancer death, the outcome used in the prostate cancer studies, would probably require tens of thousands of people followed over many years
- If anal cancer (not death) is the outcome, one would probably need many thousands of people followed over many years to answer the question. Screening might increase detection.
- Fewer people would be needed for an AIN outcome, but would that be convincing?

HPV Vaccine and Anal Cancer

- In a RCT, quadrivalent HPV vaccine 76% effective in preventing HPV 16,18, 6 and 11 associated AIN among MSM without prior HPV infection (NEJM 2011, 365:1576)
- Observational data in MSM
Among MSM treated for high-grade AIN (HGAIN), recurrent HGAIN was less common men who also received qHPV vaccine (CID 2012)



My Conclusions

- Anal cancer is an important and probably growing problem among HIV+ persons - Relatively rare cause of death
- The rationale for anal pap testing is strong, and screening is probably safe when provided by experienced persons
- The effectiveness and cost-effectiveness of screening is unknown, and it is not certain it is knowable
- Optimally, MSM should know about anal PAPs & have them available
- Existing data are not strong enough to make a firm recommendation that MSM should be screened
- Treating PLWHA while their immune systems are strong, which is justified for other reasons, should help prevent anal cancer.
- All young men (age ≤ 26) should be vaccinated for HPV. Role in older MSM uncertain.