# Anal Cancer and Screening Opportunities

## Identifying patients at risk for Anal Intraepithelial Neoplasia

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# Clinical decisions

DECISION 01

Patient Population

## Which patients warrant screening and HRA?

Identifying high-risk demographics, immunocompromised groups, and establishing routine referral pathways.

DECISION 02

Lesion Stratification

## Which lesions need treatment?

Distinguishing low-grade vs. high-grade dysplasia and deciding between active surveillance and therapeutic ablation.

DECISION 03

Trial Standards & Scope

## What did ANCHOR establish, and where does extrapolation begin?

Analyzing key trial findings on cancer risk reduction and evaluating generalizability across non-ANCHOR cohorts.

Sources in speaker notes

# LSIL and HSIL describe different disease

LOW-GRADE LESION

## LSIL

AIN1 / condyloma

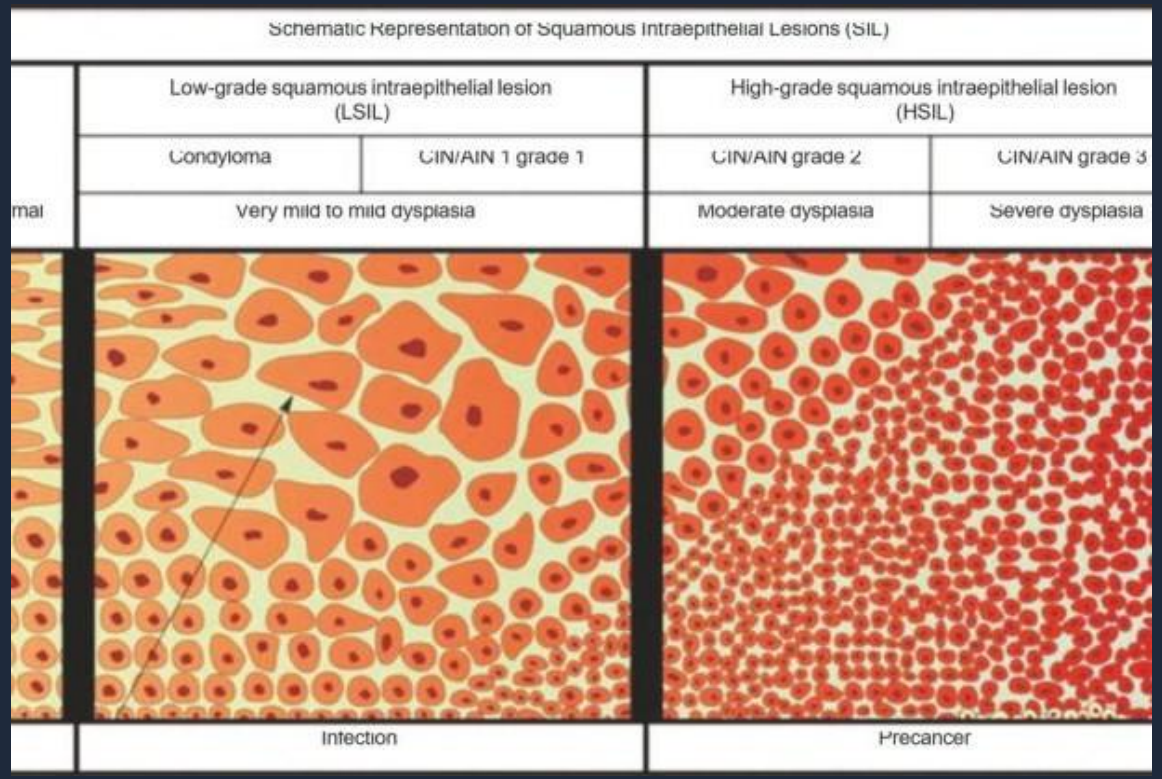
HIGH-GRADE LESION

## HSIL

AIN3 or p16-positive AIN2

CLINICAL MANAGEMENT

**Invasion requires a cancer workup**




Schematic: Brickman & Palefsky, 2015, as reproduced in the supplied chapter

Sources in speaker notes

# Persistent oncogenic HPV drives risk

VIRAL FACTOR

Squamous Dysplasia

## Promotes Squamous Dysplasia

Oncogenic HPV, especially HPV16, directly promotes squamous dysplasia development in affected tissue.

HOST IMMUNITY

Immune Response

## Influences Persistence & Recurrence

Immune status heavily dictates whether HPV infection persists or recurs over time.

PRECURSOR RISK

Disease Trajectory

## Precursor with Variable Progression

HSIL acts as a direct cancer precursor, though individual progression rates vary across patients.

Sources in speaker notes

# Anal cancer risk differs markedly by population

| Population | Cases / 100,000 person-years |
|---|---|
| General population | ~1.7 |
| MSM with HIV | 85 |
| Women with prior vulvar precancer / cancer | 42 / 48 |
| MSM without HIV | 19 |
| Solid-organ transplant recipients | 19 overall |

# Who Gets Screening

| Group | Suggested initiation |
| --- | --- |
| MSM and transgender women with HIV | Age 35 |
| Other people with HIV | Age 45 |
| MSM and transgender women without HIV | Age 45 |
| Prior vulvar HSIL or cancer | Within 1 year of diagnosis |
| Solid-organ transplant recipients | 10 years after transplant |

Age ≥45: consider screening for cervical/vaginal HSIL or cancer, persistent cervical HPV16, perianal warts, or autoimmune disease

# Screening requires access to diagnostic care

**01. Screening Modality**

Anal cytology, with or without high-risk HPV co-testing

**02. Examination Technique**

Swab first without lubricant, then digital anorectal examination

**03. Diagnostic Confirmation**

HRA and biopsy establish the diagnosis after an abnormal screen

**04. Care Continuum**

A screening program needs an HRA referral and treatment pathway

# Abnormal screens and suspected cancer

| Finding | Next step |
| --- | --- |
| ASC-H / HSIL cytology or HPV16 positivity | HRA with directed biopsy |
| ASC-US with negative high-risk HPV | Repeat screening per algorithm |
| Other abnormal combinations | Triage by test strategy and HRA capacity |
| Mass, ulcer, induration or concerning symptoms | Prompt diagnostic evaluation and biopsy |

**Screening results guide referral. Histology determines treatment.**

Sources in speaker notes

# HRA identifies lesions for biopsy and treatment

**01. Visual Inspection**

Magnified examination with acetic acid and Lugol iodine

**02. Tissue Diagnosis**

Directed biopsy confirms grade and excludes invasion

**03. Lesion Mapping**

Lesion mapping records extent and guides targeted therapy

**04. Advanced Evaluation**

Extensive or suspicious disease may require evaluation under anesthesia

# Treatment choices depend on grade and extent

| Approach | Clinical role / limitation |
| --- | --- |
| Observation | Selected LSIL with reliable surveillance |
| Electrocautery or infrared coagulation | Targeted HSIL treatment, often repeated |
| Imiquimod, 5-FU, TCA or cidofovir | Selected lesions or adjuncts, irritation and recurrence |
| Focal excision | Selected lesions or concern for invasion |
| Wide local excision of diffuse AIN | Avoid routine use due to stenosis and functional harm |

# Targeted treatment preserves anal function

**01. Preservation Focus**

Treat visible HSIL while preserving healthy tissue

**02. Tissue Protection**

Avoid deep injury and large circumferential defects

**03. Repeat Therapy**

Recurrence and new lesions often require repeat treatment

**04. Surgical Risk**

Wide excision can produce stenosis and impaired continence

# ANCHOR tested cancer prevention

**Does treating biopsy-proven anal HSIL reduce invasive anal cancer?**

01. TRIAL SCOPE

## Phase 3 Trial

- Randomized study across 25 US sites
- Over 4,400 participants enrolled

02. POPULATION

## Study Cohort

- People living with HIV
- Age 35 years and older

03. OUTCOME

## Primary Endpoint

- Time to development of invasive anal cancer

# Randomization and follow-up

| Treatment: n = 2,227 | Active monitoring: n = 2,219 |
|---|---|
| Eradication of all identified HSIL | No HSIL treatment |
| HRA at least every 6 months | HRA every 6 months |
| Biopsy suspicious HSIL, retreat recurrence | Annual biopsy of visible lesions |
| Biopsy possible cancer at any time | Biopsy possible cancer at any time |

**4,446 analyzed • Median follow-up 25.8 months**

# ANCHOR mainly used office electrocautery

PRIMARY TREATMENT MODALITY

**83.6%**

**Initial treatment with office electrocautery**

01. ALTERNATIVE MODALITIES

Other options included infrared coagulation, treatment under anesthesia and topical therapy

02. STUDY DESIGN NOTE

Treatment modality did not undergo randomization

Sources in speaker notes

# HSIL treatment reduced anal cancer

| Outcome | Treatment | Monitoring |
|---|---|---|
| Invasive cancers | 9 | 21 |
| Cases / 100,000 person-years | 173 | 402 |
| 95% CI for incidence rate | 90–332 | 262–616 |

## 57% lower cancer rate

95% CI 6–80% • P = 0.03

# Absolute benefit and remaining risk

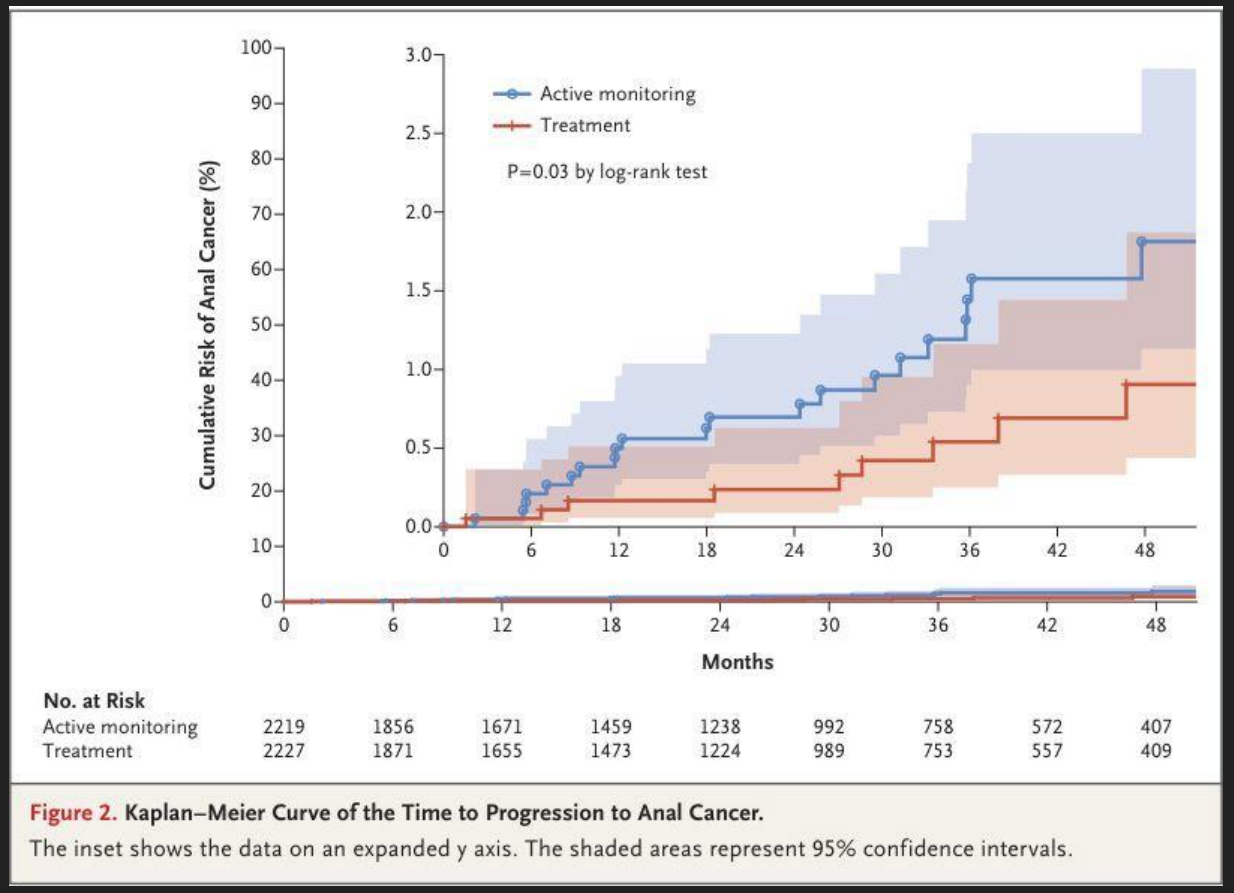



**Figure 2. Kaplan–Meier Curve of the Time to Progression to Anal Cancer.**
The inset shows the data on an expanded y axis. The shaded areas represent 95% confidence intervals.

Figure 2: Palefsky et al., NEJM 2022

**48-month estimates**
**0.9% vs 1.8%**

Absolute difference
0.9 percentage points

Approximate NNT
≈111
from rounded estimates

# Lesion burden and treatment harms

Progression Risk

## HR 5.26

95% CI: 2.54–10.87

Lesion extent >50% correlates with significantly higher progression risk

Serious Adverse Events

## 7 vs 1

Treatment group vs. Active monitoring

Higher incidence of trial-related serious adverse events in treated group

Treatment Harms

## Pain, Abscess & Ulceration

Primary reported treatment-associated localized adverse effects and complications

Overall Efficacy Limit

## Risk Reduced, Not Eliminated

While intervention significantly lowers risk, cancer risk persists post-treatment requiring ongoing surveillance

# What ANCHOR establishes

| Direct evidence | Remaining questions |
| --- | --- |
| Treating HSIL reduces cancer in people with HIV ≥35 | Magnitude of benefit in people without HIV |
| Benefit despite intensive surveillance in both arms | Optimal population screening strategy |
| Most treatment used electrocautery | Comparative effectiveness of modalities |
| Cancer remained possible after treatment | Long-term benefit, mortality and ideal surveillance |

# Surveillance remains part of treatment

6-MONTH TIMELINE

## Post-Treatment HRA

Repeat HRA around 6 months after HSIL treatment in people with HIV

INDIVIDUALIZED CARE

## Tailored Follow-Up

Subsequent follow-up follows biopsy findings and disease burden

URGENT EVALUATION

## Symptom Monitoring

New symptoms or a palpable lesion need prompt assessment

RISK REDUCTION

## Primary Prevention

Prevention includes HPV vaccination and smoking cessation

# Clinical Application

Patient Case Presentation & Clinical Management Workflow

## Patient Profile

**48-year-old man**

**Living with HIV**

INITIAL FINDINGS

- ASC-US cytology
- HPV16 positive
- Normal DRE

## HRA Biopsy

HISTOPATHOLOGY

**p16-positive AIN2**

CLINICAL SIGNIFICANCE

High-resolution anoscopy biopsy provides definitive tissue diagnosis for HSIL identification.

## Intervention

**Targeted HSIL Treatment**

SURVEILLANCE PLAN

- Planned follow-up HRA
- Continued routine monitoring

# Take-home points

01. DIAGNOSIS

## Screening & Detection

Risk-based screening leads to HRA and tissue diagnosis

02. EVIDENCE

## ANCHOR Support

ANCHOR supports treatment of biopsy-proven HSIL in people with HIV (and can likely be applied to other immunocompromised patients)

03. THERAPY

## Prevention Goals

Targeted therapy aims to prevent cancer and preserve function

# Selected references


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