BHIVA
British HIV Association

Management of Screening Treatment of anal precancer/cancer in PLWH

Tamzin Cuming, Consultant Colorectal Surgeon
Homerton Anogenital Neoplasia Service

BHIVA British HIV Association

Conflict of Interest

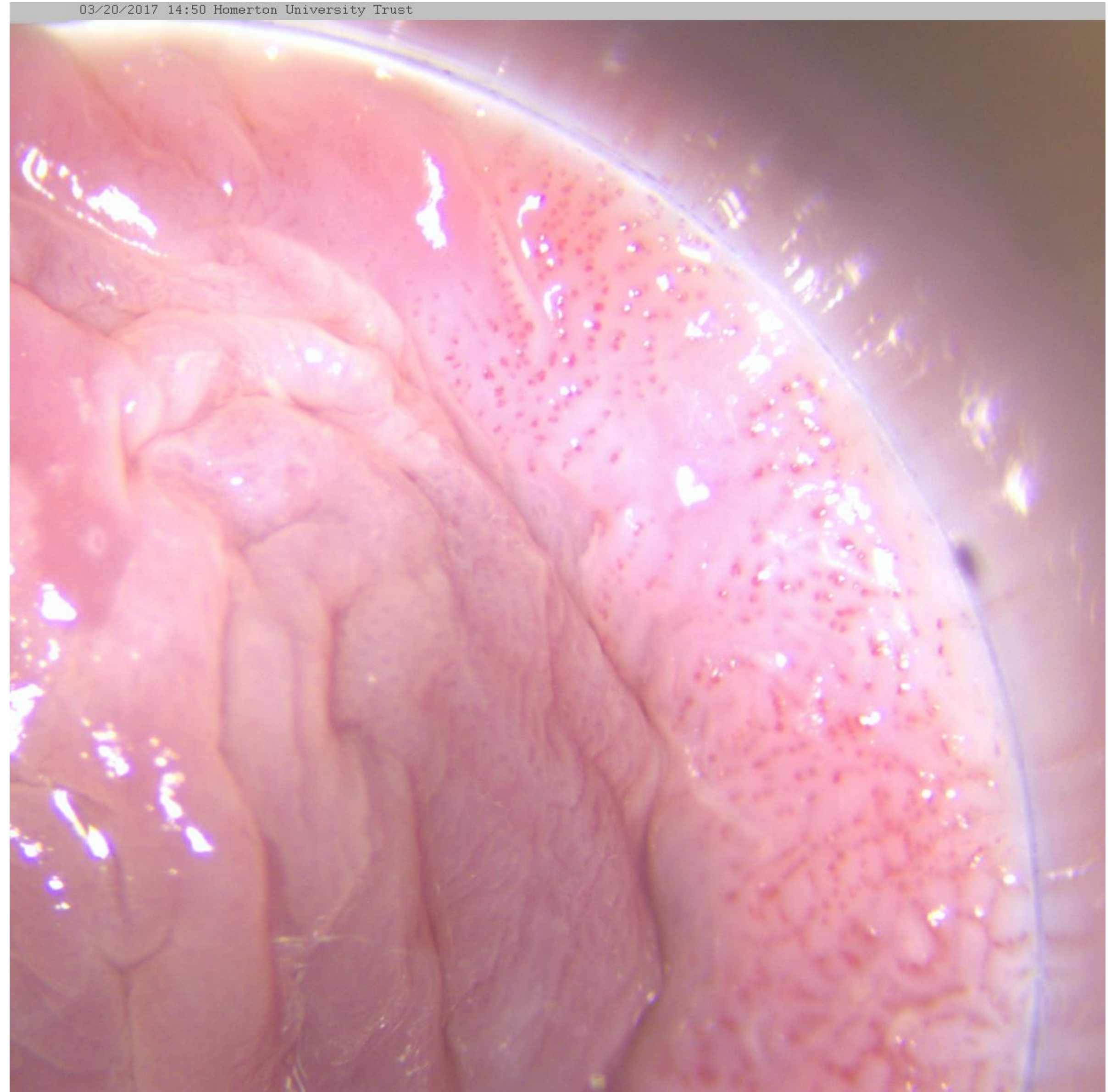
I am the Vice-President of the International Anal Neoplasia Society (unpaid role)

No financial disclosure

ians International Anal Neoplasia Society

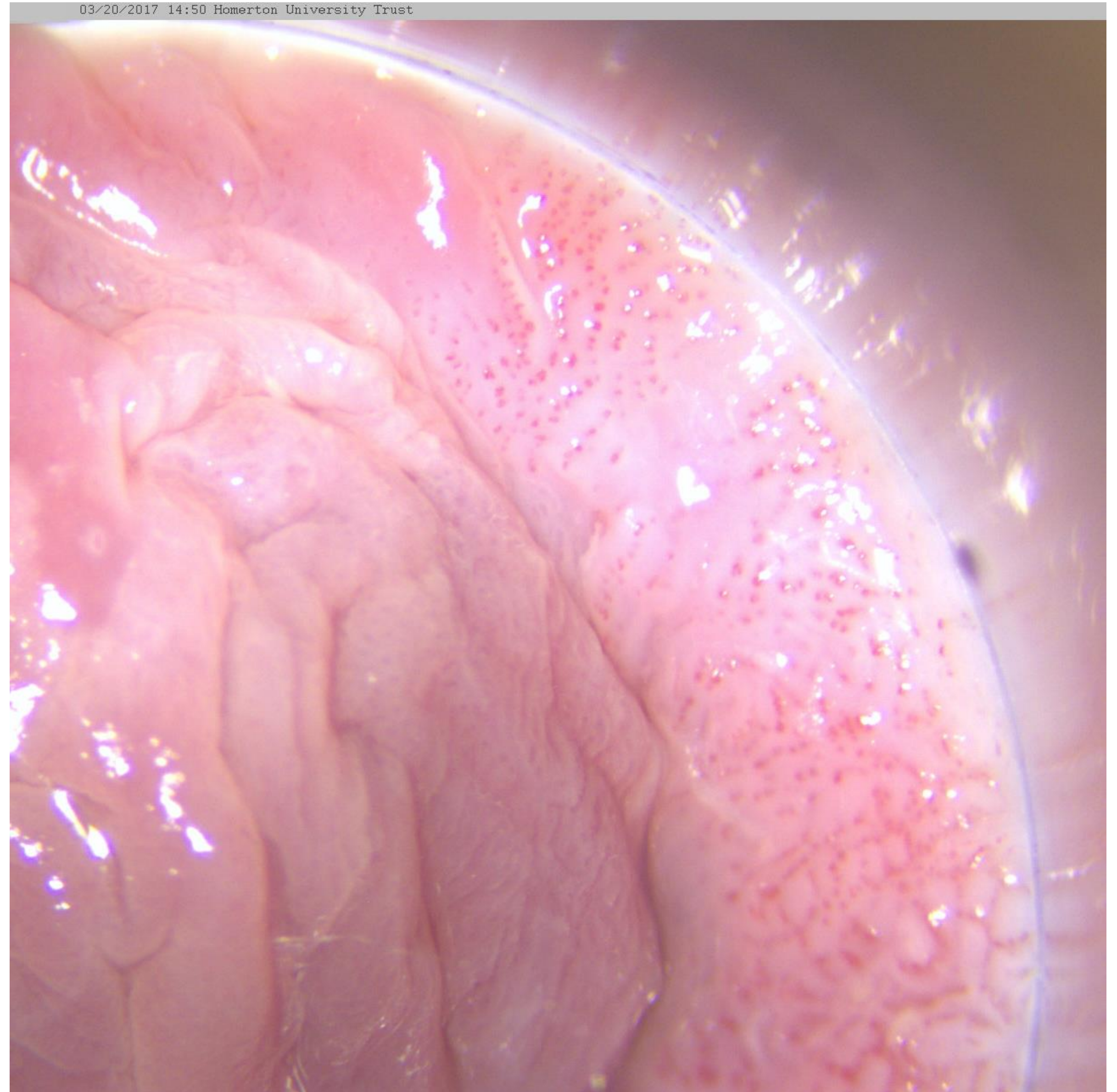
Plan of talk

1. Case for screening in PLWH
2. Screening strategies
3. Treatment anal neoplasia
4. Treatment anal cancer

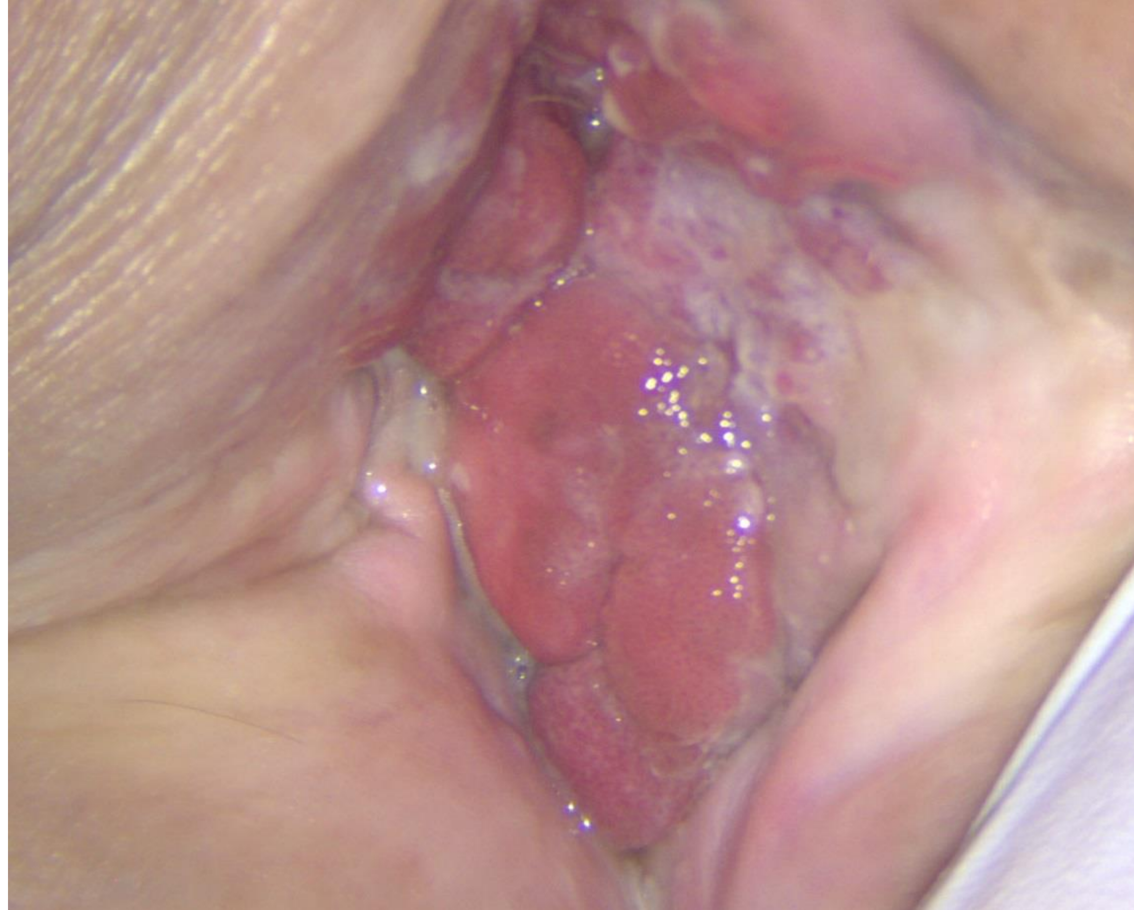


Plan of talk

1. Case for screening in PLWH
2. ~~Screening strategies~~
3. Treatment anal neoplasia
4. Treatment anal cancer



Both screening and treating anal neoplasia – aim is to avoid this



advanced anal cancer

Screening

- Risk for some high risk groups > CRC
- No national screening programme

Wilson & Junger 1968 criteria		Current situation
Should be an important health problem	++	For high risk groups, yes – anal SCC
Recognisable latent or early stage	+++	Anal HSIL/ superficially invasive SCC
Natural history should be understood	+	Studies ongoing: ANCHOR Indicators of which HSIL progress to cancer needed ?DNA methylation
There should be a suitable test	-	Cytology inadequate: SEPAC
Acceptable treatment for recognised disease	+	Wait for ANCHOR
Facilities for diagnosis/ treatment should be available	+	Colposcopes available; IANS courses (only in USA)
Agreed policy on who to treat as patients	++	MSM LWH ? Who else
Cost of case-finding should be balanced with medical care	+	Depends on screening tool. HRA alone too expensive.

Gosens et al 2017

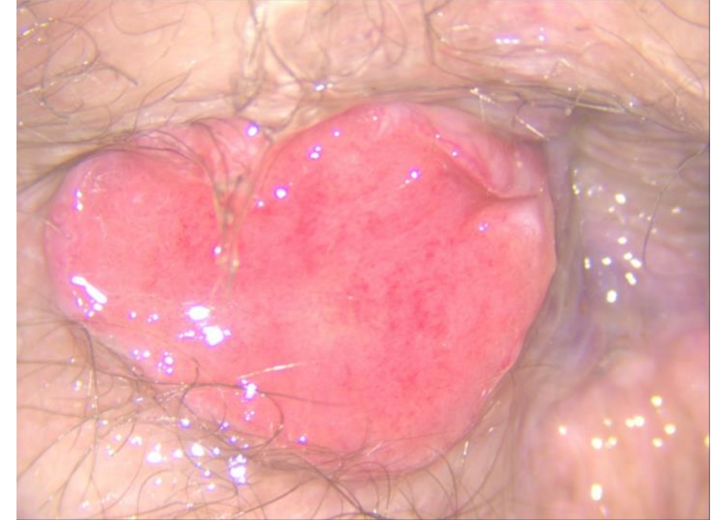
Screening is coming

- Risk for some high risk groups > CRC.
- No national screening programme - yet

Wilson & Junger 1968 criteria		Current situation
Should be an important health problem	++	For high risk groups, yes – anal SCC
Recognisable latent or early stage	+++	Anal HSIL/ superficially invasive SCC
Natural history should be understood	++	Studies ~~ongoing~~: complete: ANCHOR Indicators of which HSIL progress to cancer needed DNA methylation
There should be a suitable test	-+	Cytology inadequate ? + hrHPV SEPAC
Acceptable treatment for recognised disease	++	ANCHOR , TREPAC/SHINE
Facilities for diagnosis/ treatment should be available	++	Colposcopes available: IANS online course; ANCHOR trained 23 sites in the US
Agreed policy on who to treat as patients	++	PLWH + High risk ? > incidence 25/100,000 see Clifford
Cost of case-finding should be balanced with medical care	++	HPV/cytology screening tool. HRA alone too expensive. ?NNT needs ↓

Gosens et al 2017 with TC updates 2022

Severe prolonged immune suppression ↑ anal cancer risk in PLWH



- Depth of CD4 nadir
  - 13.4 x risk anal cancer CD4 nadir <50 vs >500
  - Median CD4 of cancer cases 137 vs 259 for non cancer cases
  - 4.9 years from CD4 nadir to cancer median
- Length of time with low CD4 nadir: proportion of time between 4.5 and 8.4 years with CD4 <200
- Inverse relationship with VL suppression – length of time undetectable – not independent predictor (of CD4 level)

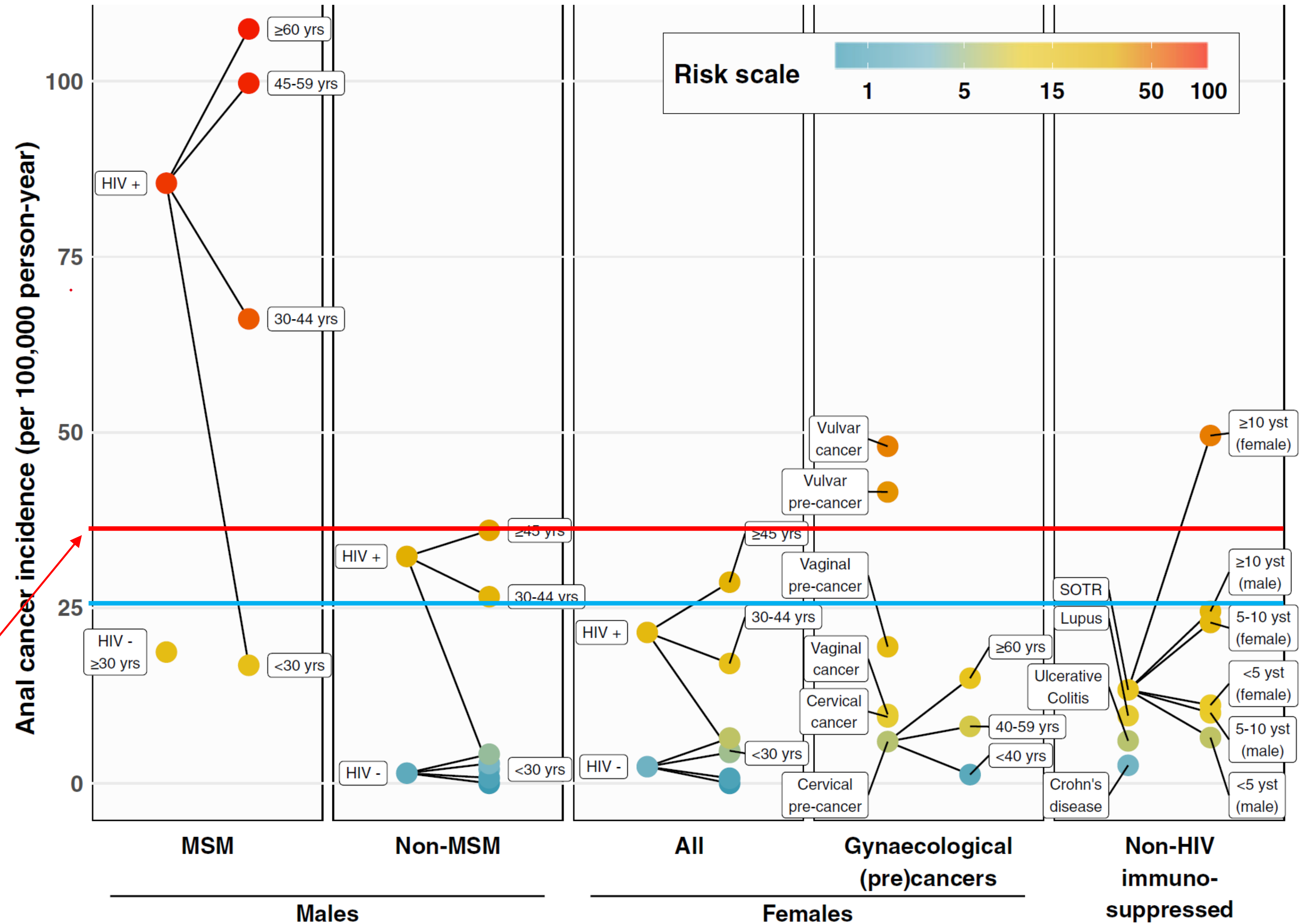
Hernandez-Ramirez CID 2020. 70:1176-85

Anal SCC risk & immune suppression….

General Population risk
1.8/100,000

Women >50 most prevalent
I: 5-8/100,000

prescreening cervical cancer risk: 34/100,000



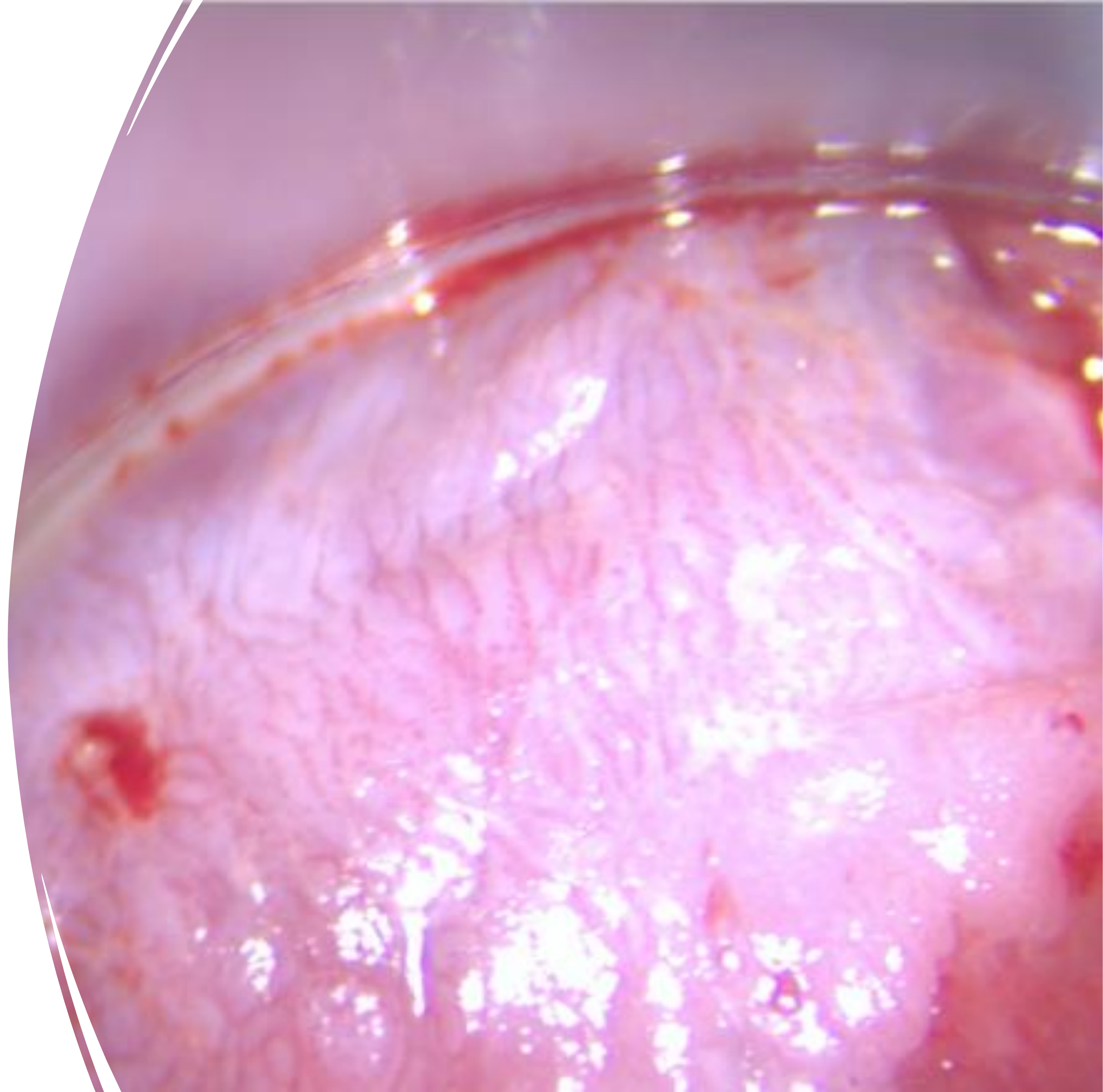
Clifford et al 2021 Int J Cancer 148(1):38-47

Future post-ANCHOR: screening and AIN treatment

Anal precancer = high grade AIN = anal HSIL

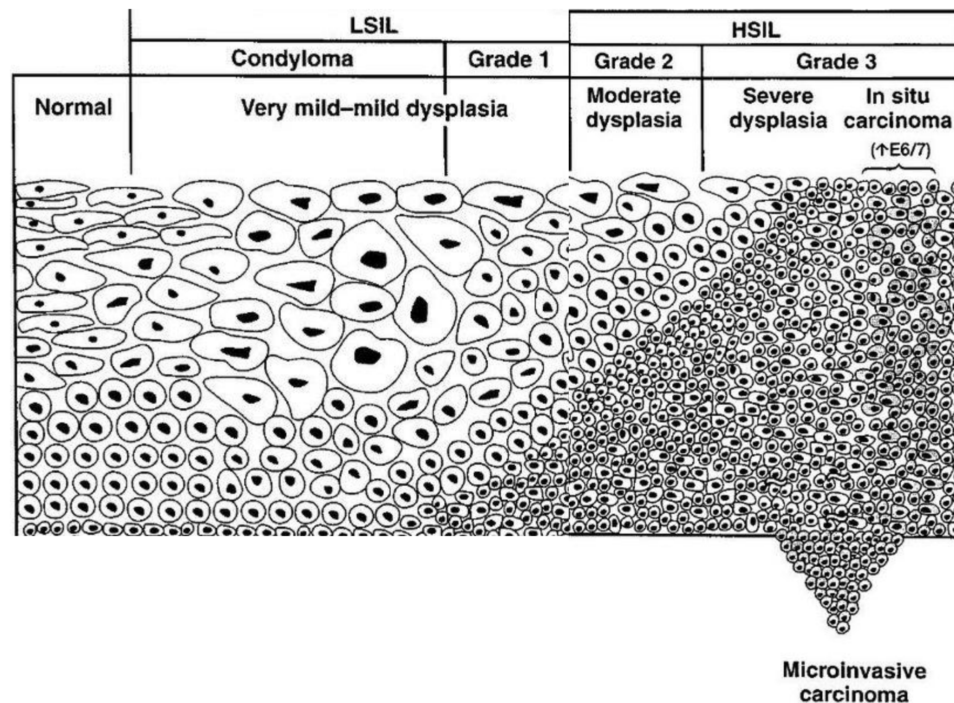
- Treatment

- QUESTION 1: What is it?
- QUESTION 2: Does it all need treating?



AIN = anal intraepithelial neoplasia

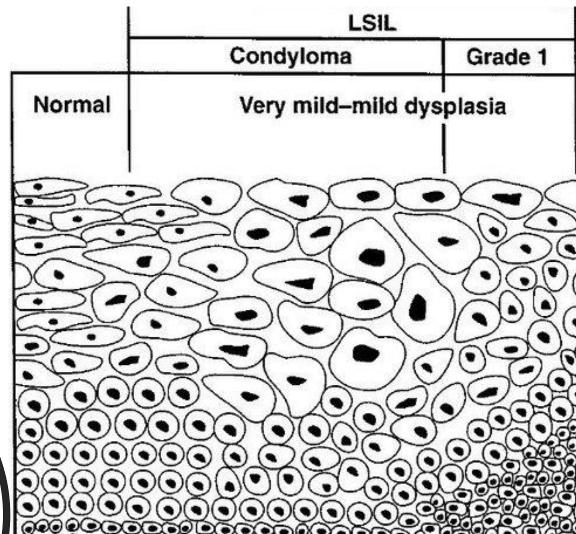
= SQUAMOUS INTRAEPITHELIAL LESIONS (SILs)



AIN = anal intraepithelial neoplasia

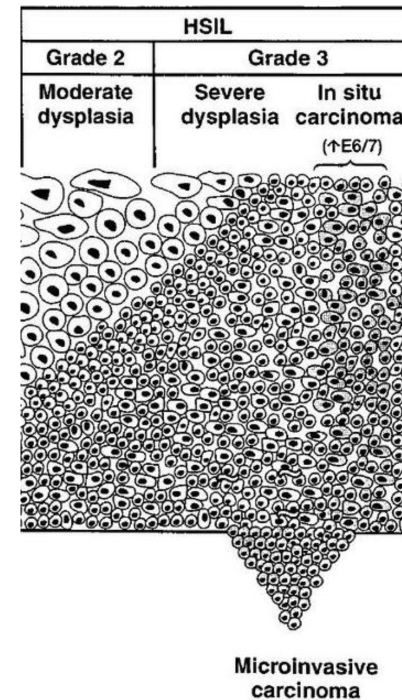
= SQUAMOUS INTRAEPITHELIAL LESIONS (SILs)

LOW GRADE vs HIGH GRADE



AIN2

p16
+ve
-ve



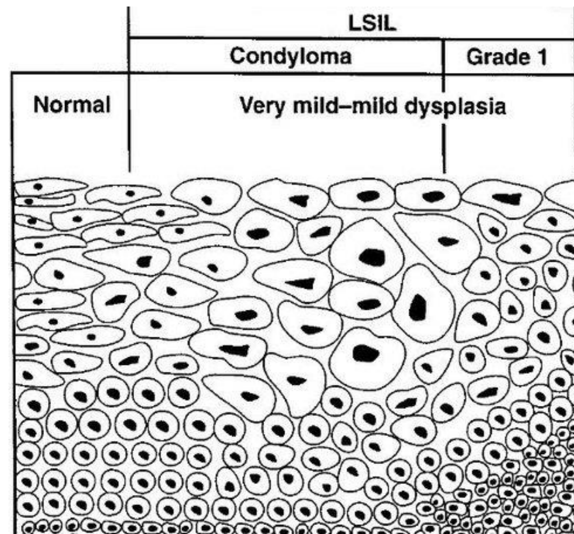
Proliferation
HPV 6, 11
LSIL

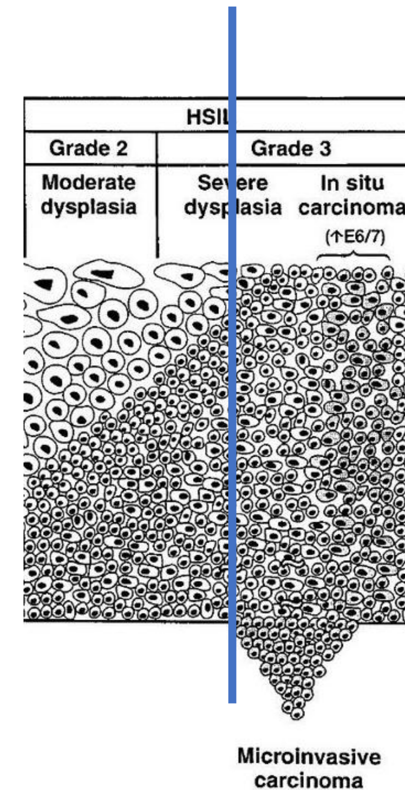
Transformation
hrHPV
HSIL

However there is a regression rate

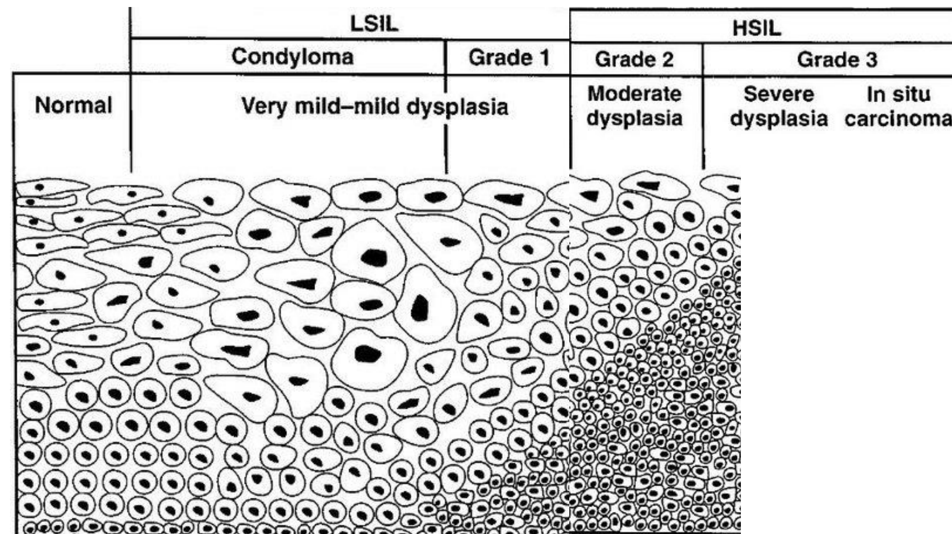
LOW GRADE

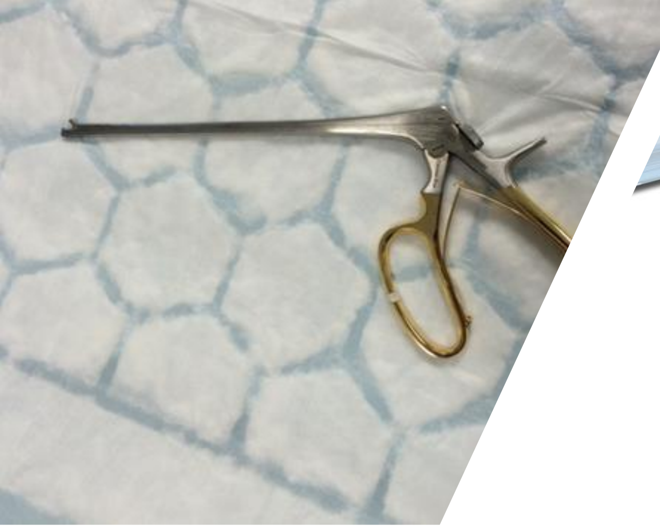
HIGH GRADE





HSIL → LSIL or negative ≈ 30%





To Treat you have to be able TO SEE: High resolution anoscopy (HRA)

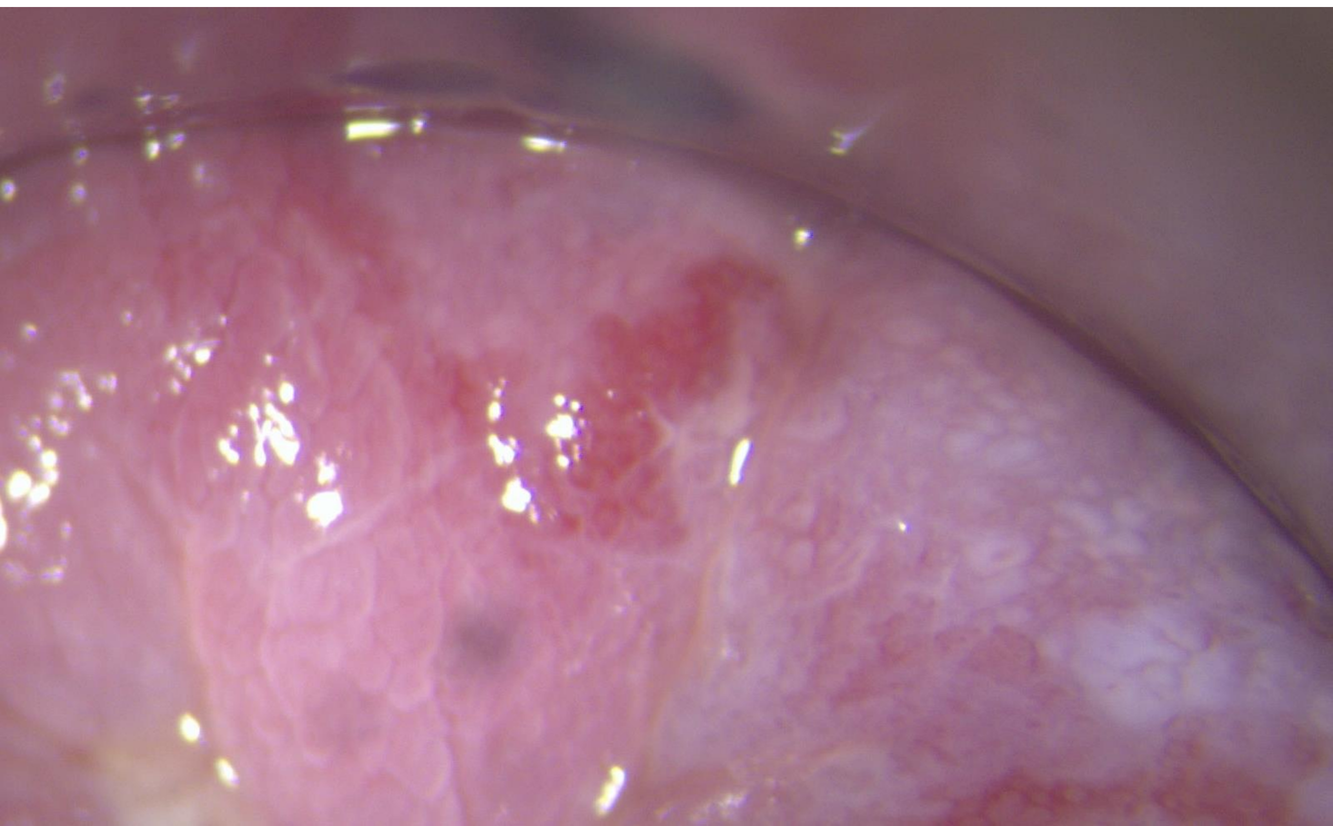
- Examination x 30
- 5% acetic acid

High resolution anoscopy (HRA)

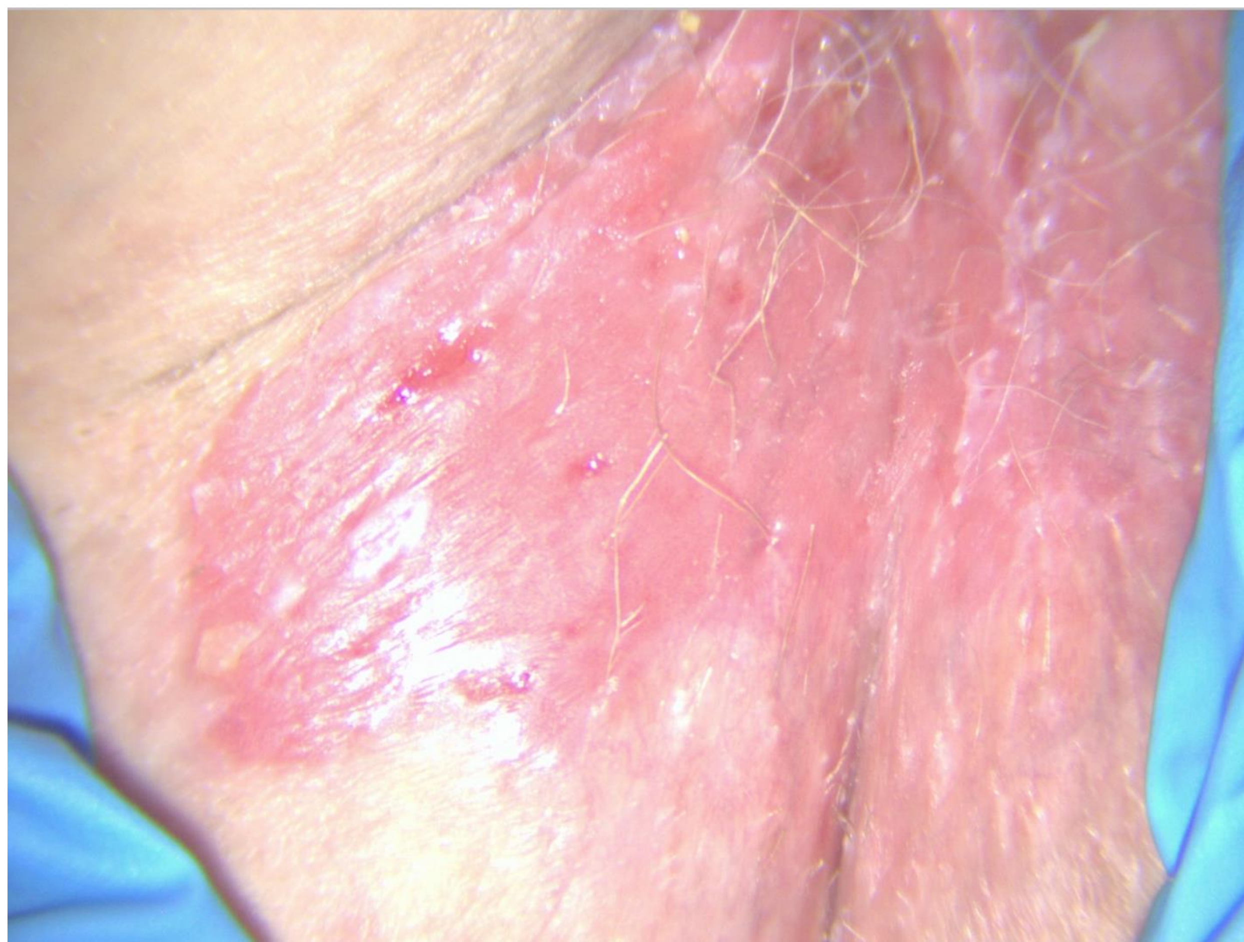
- Gold standard for diagnosis: HRA-targeted

  visualisation + biopsy

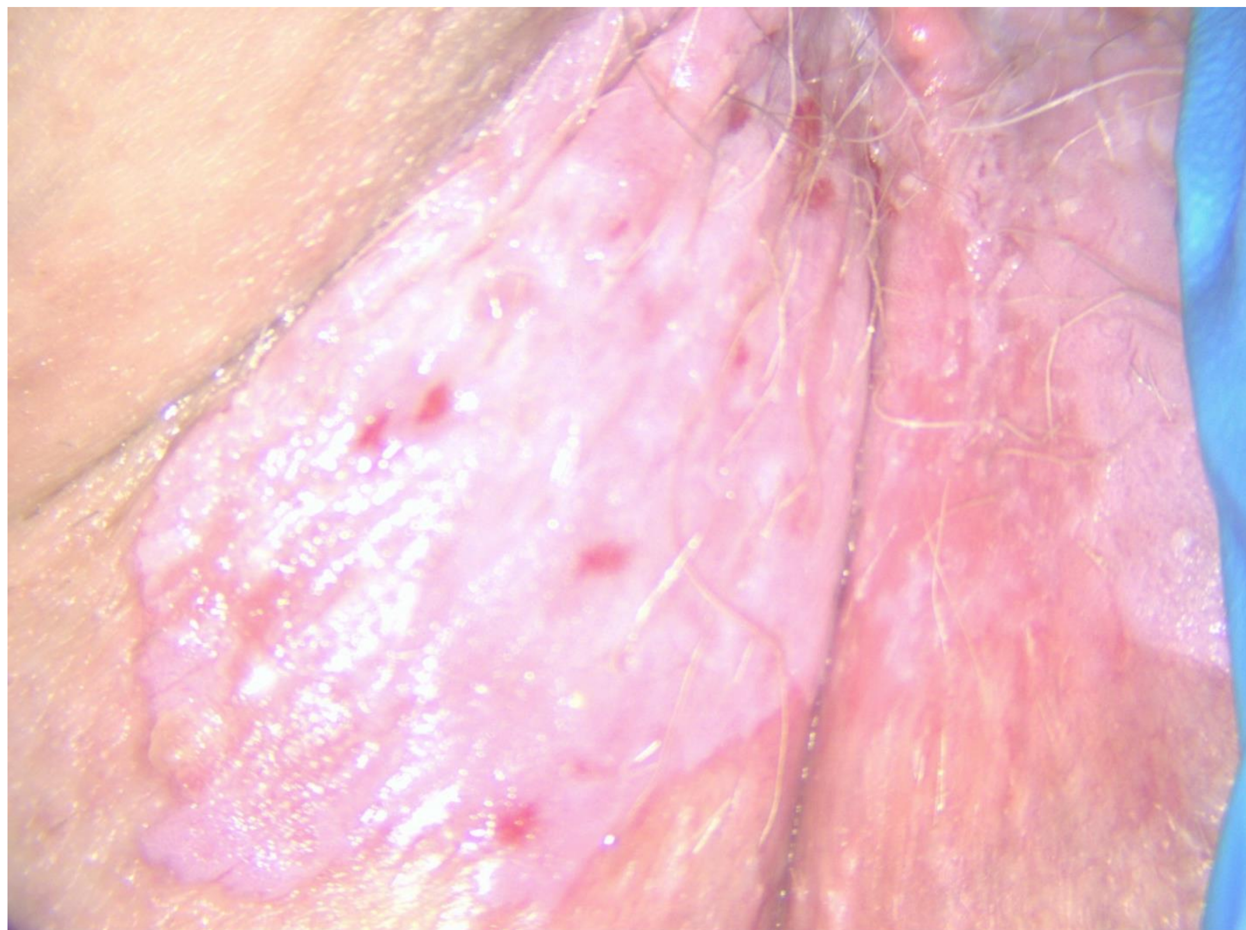
  ablative therapy



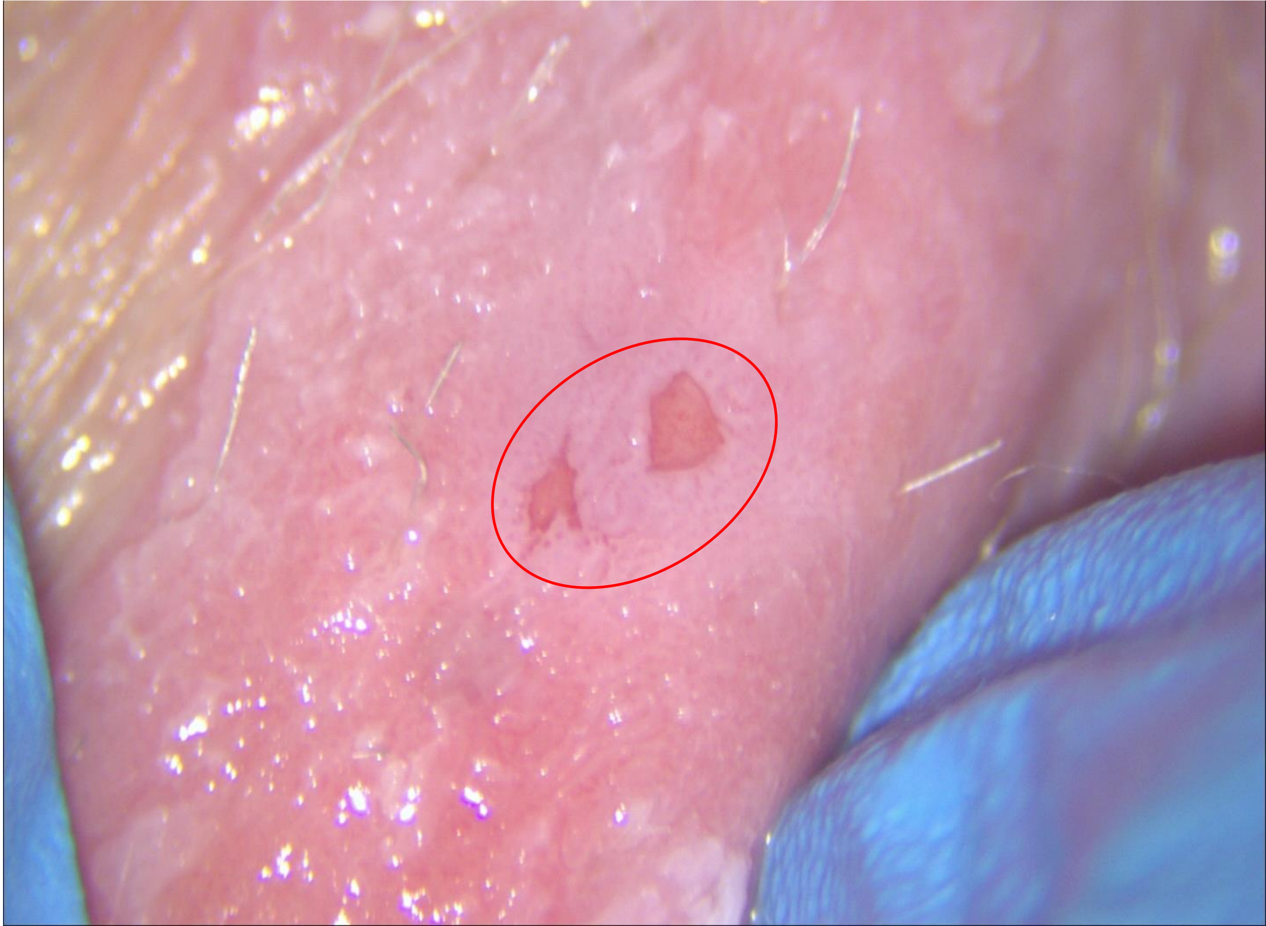
Perianus – HSIL without acetic acid



With acetic acid



with 5% acetic acid and magnification



Treatment of AIN

Excision?

- Of AIN: risks to the sphincter: 5/34 cases stoma for FI/stenosis (>1cm)[1]
- For early cancer: <2cm (T1) only; perianal only; get 1mm margin; leave open!

Topicals (imiquimod/Catephen/5FU)

- External – 3 months, pain and soreness
  - Equivalent outcome to electrocautery[2]
- Anal canal – success rate 9-17%[2]

So… ablation

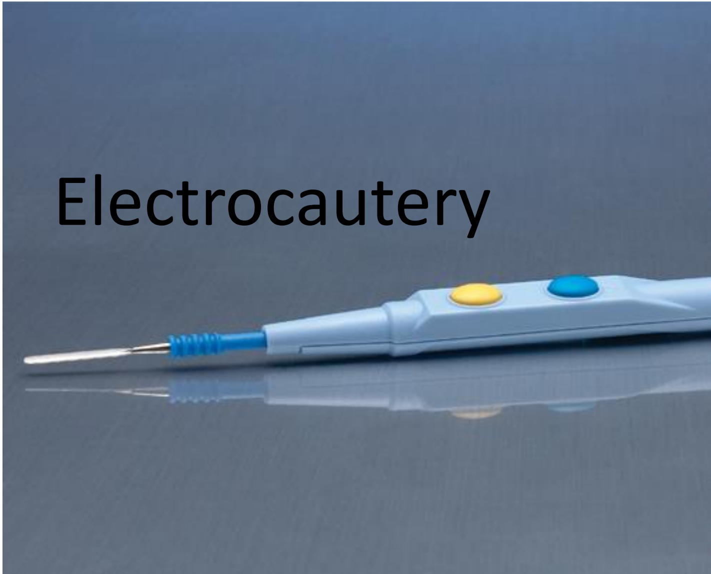
Laser/Electrocautery etc

1. Brown S et al. BJS 1999:86; 1063-6. 2. Richel et al Lancet oncology 2013

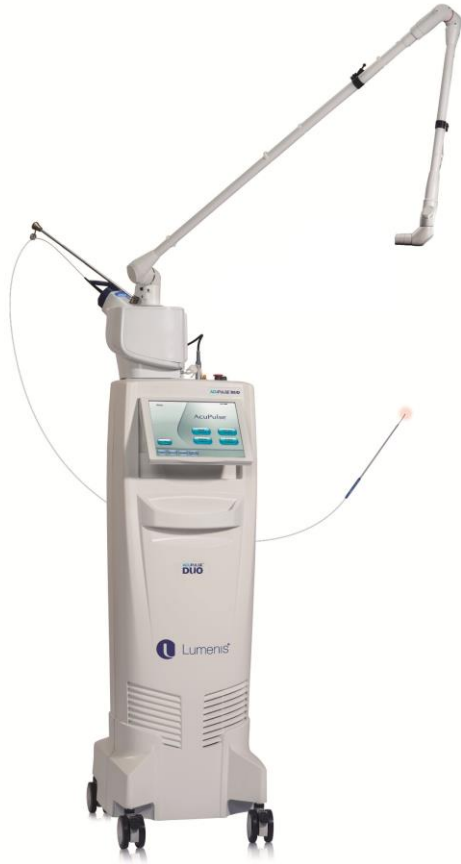
Ablative therapies

Argon beam plasma coagulation

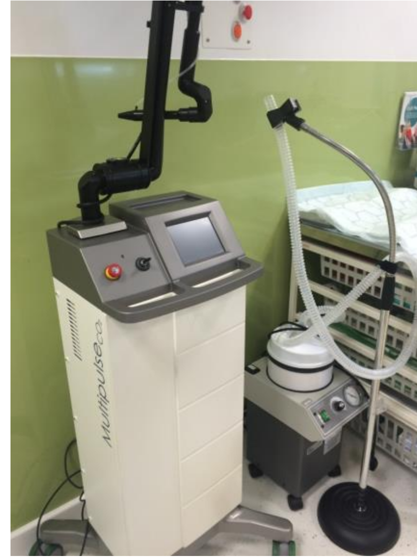
Radio-frequency ablation



Laser types internal/ external

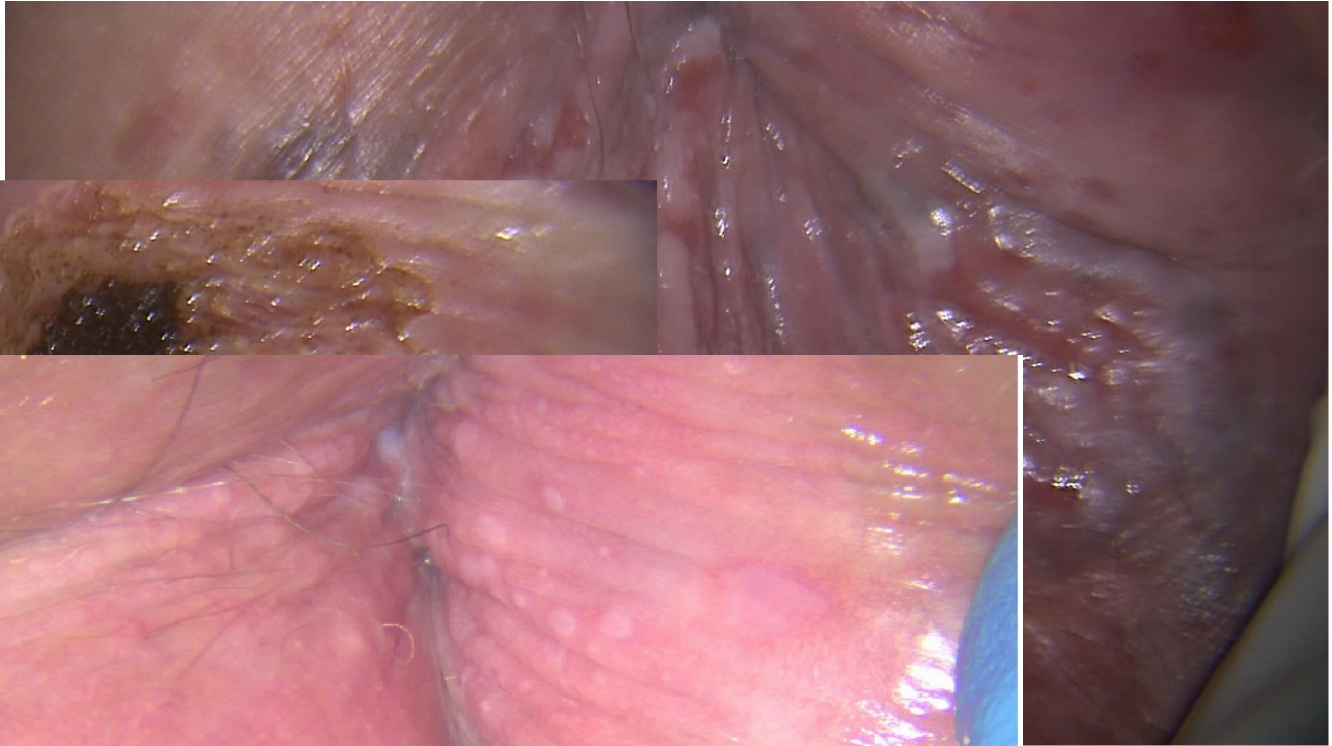
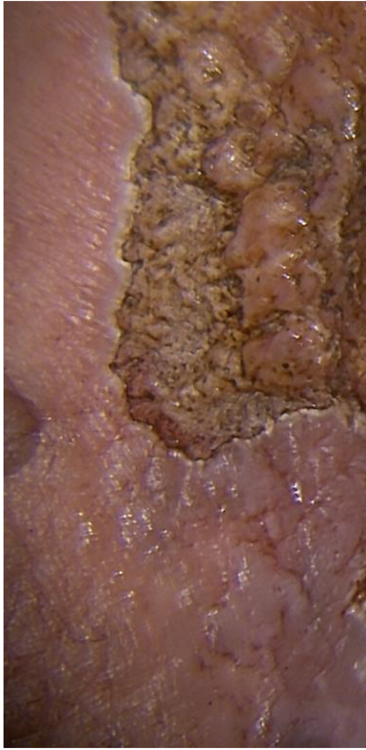
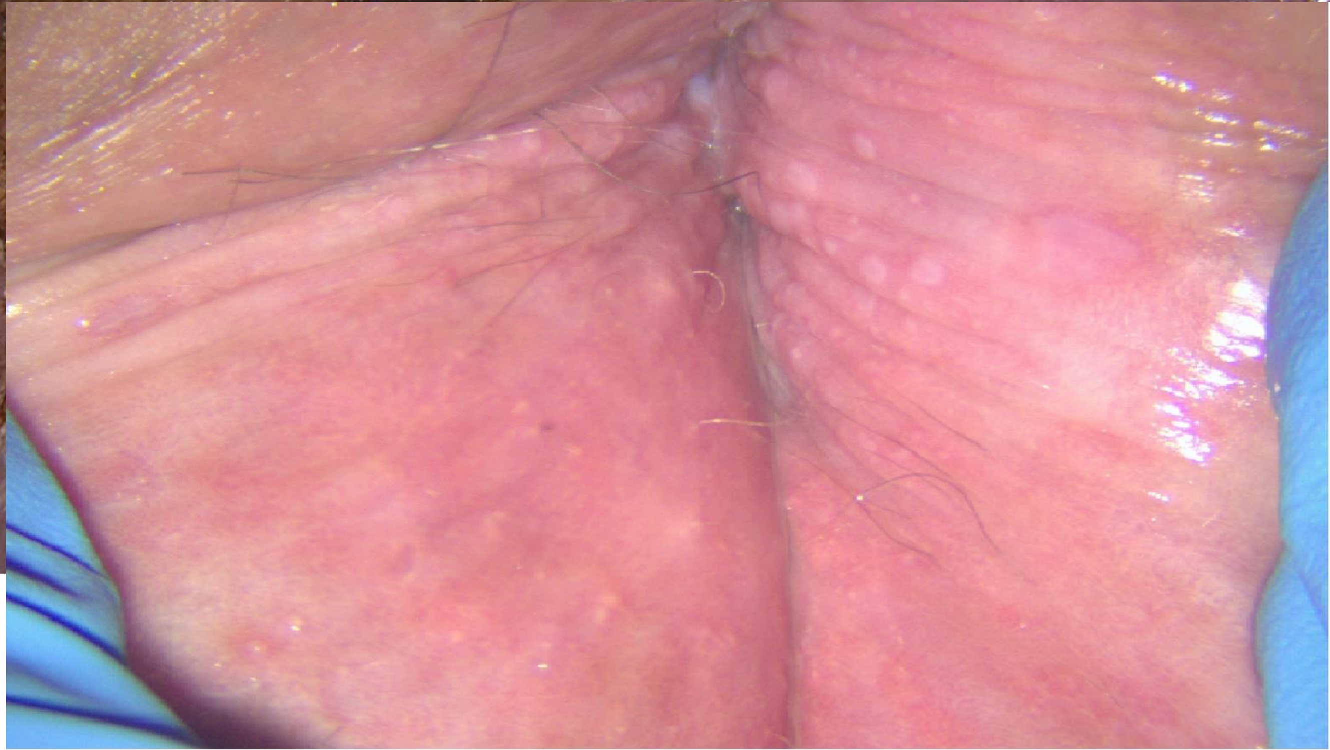


CO2 laser



DIODE/KTP

Laser does take some preparation

Success of treatment AIN

- Until recently, controversial
- High recurrence rate – 80% at 2 years
  - Different site
  - Field effect
  - Same site however – 45% at 2 years[1]
- Uncertainty about impact natural history
  - Appeared to reduce cancer rate
  - Eg 5/727 in Goldstone series[2]
    - Vs expected 5% = 36

1. Gaisa M et al 2020. Cancer, 126(7), 1470–1479   2. Goldstone SE Dis Colon Rectum 2014; 57: 316–323

FIRST VISIT:
URGENT 2 ww
STANDARD 6- 8ww
DARE+ HRA cytol+biopsy
Unable to tolerate
both negative
LSIL
HSIL
cancer
mismatching results
GA assessment
FU according to risk factors
FU according to risk factors
AIN3/AIN2 p16 +
cancer ptw
CYTO: HSIL
topical treatment
surgical treatment
RECALL <6 weeks
excision
laser ablation*

Gold standard for anal squamous cell cancer: Chemoradiation

- Nigro protocol chemoradiation[1] on a regime as set out in ACT II[2]
- About to be updated with a series of studies under the **PLATO** umbrella
  - Multicentre UK study: David Sebag-Montefiore (Leeds), Andrew Renehan (Christie) et al

  - **ACT 3** – non-randomised, adjuvant CRT vs watch and wait for fully excised T1 SCC
  - **ACT 4** – RCT less radiation (41.4Gy/23) for smaller lower risk tumours T1/T2 N0 (<2cm or 2-5cm) vs standard (50.4Gy/28)
  - **ACT 5** – RCT higher radiation dose for node positive and larger tumours T3 (5cm+) or T4 (58.8 and 61.6 Gy vs standard 53.2/28)

1. Lancet. 1996 Oct 19;348:1049-54 2. Lancet Oncol. 2013 May;14(6):516-24

CRT

- PLWH = PNLWH
- Reduction in CD4 in all but more profound in PLWH
- Higher morbidity: overall survival OR 1.76, and increased toxicity[1]

1. Camandaroba J Gastrointest Oncol. 2019 Feb;10(1):48-60

Conclusion

TRAINING IS NEEDED!

Online HRA course – already available via

iansociety.org

- Advanced online - 2023
- Hands-on – 2022

- Accreditation for HRA is coming via IANS
  - OSCE type exit exam like BSCCP
  - Video-submission of HRA
  - Trainer sign off
    - 25 observing
    - 50 direct supervision

Thank you, questions?