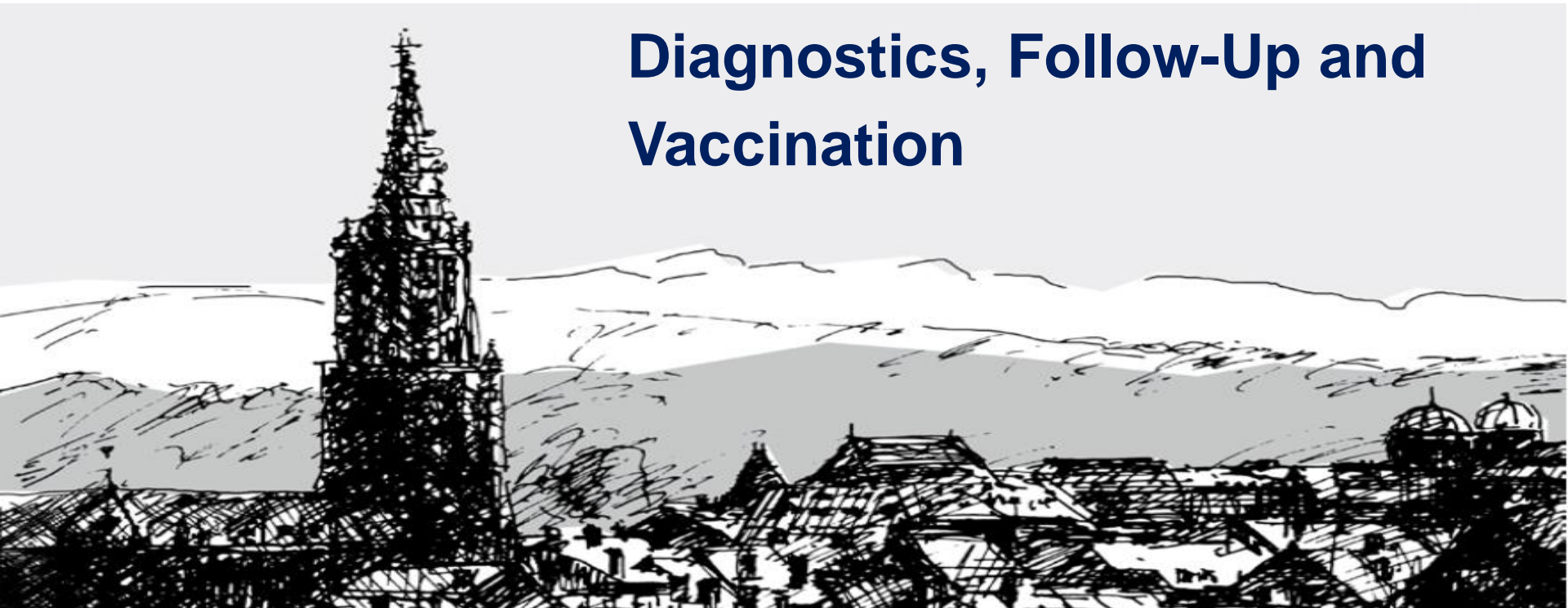


Anale intraepitheliale Neoplasien (AIN) Workshop 2018

Diagnostics, Follow-Up and Vaccination



SCHWEIZERISCHE ARBEITSGRUPPE FÜR KOLOPROKTOLOGIE
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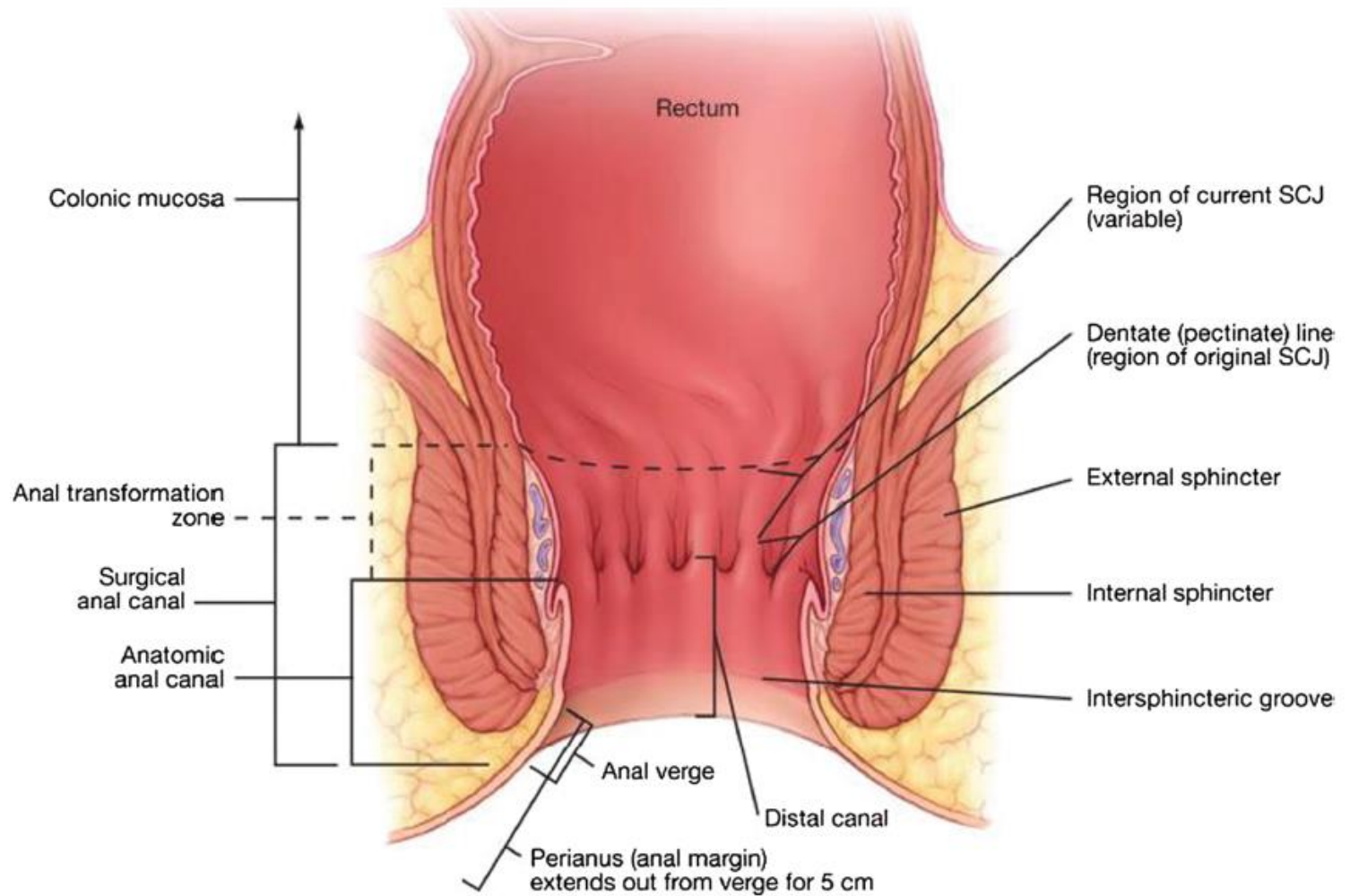
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Dr. Stephan Baumeler
Gastroenterologie Kantonsspital St. Gallen

Diagnosics



Region of Interest



The Tools



High Resolution Anoscopy (HRA)



Advantages:

- large magnification
- good image
- well-established



Disadvantages:

- small depth of field
- often not available
- no direct digital image processing



High Resolution Endoscopy (HRE)



Advantages:

- large depth of field
- direct digital image processing
- readily accessible
- extreme close-up possible



Disadvantages:

- costly maintenance
- not well-established yet, no data
- orientation difficult



Questions HRA

What is **wrong**?

1. HRA shows a good sensitifity for AIN
2. HRA identifies the lesions extend correctly
3. HRA examination has a long learnig curve



HRA Sensitivity

Problem: goldstandard for performance analysis

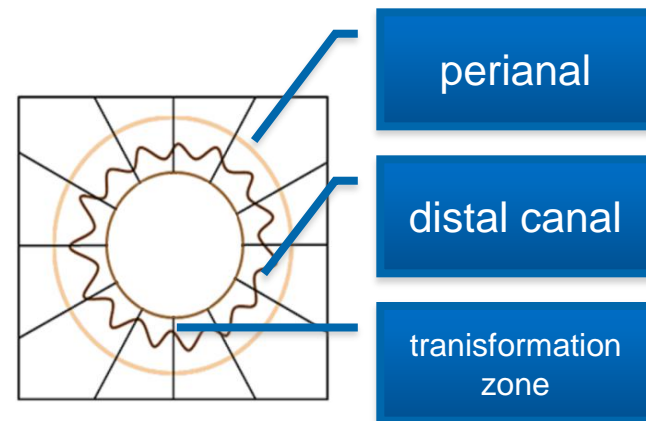
Performanceanalysis with anal mapping biopsies

Per lesion analysis:

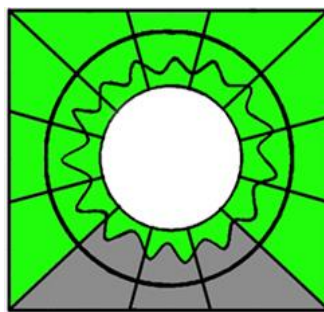
Sensitivity: 86%
Specificity: 60%

Per field analysis

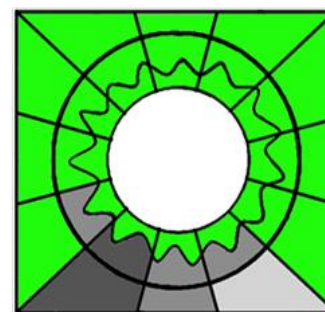
Sensitivity: 44%
Specificity: 96%



HRA



Mapping Biopsies

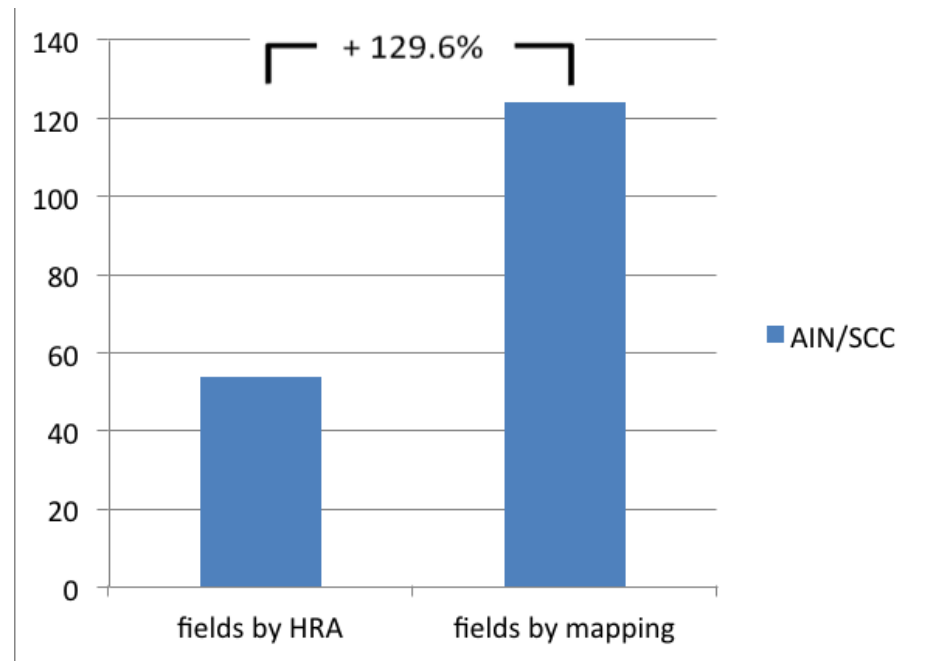
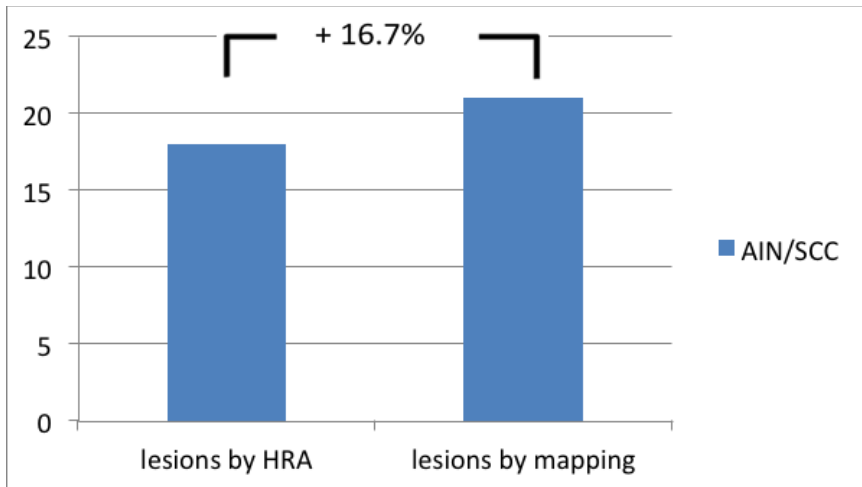


normal
 AIN I
 AIN II
 AIN III

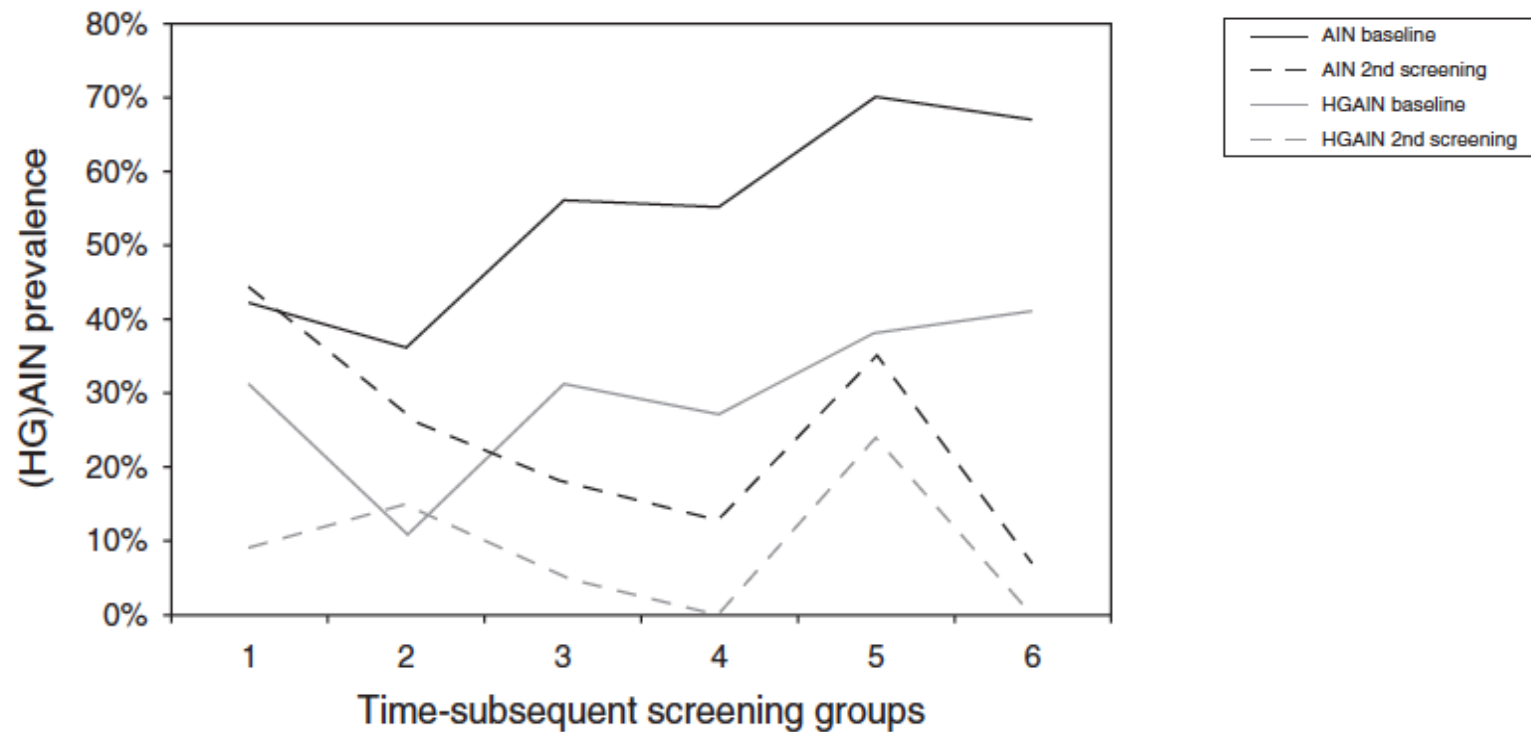


HRA – Lesions Extend

HRA underestimates lesions extent !



Long Learning Curve for AIN Diagnostics



Baseline (n):	64	64	64	64	64	63
2nd screening (n):	32	33	22	24	17	14



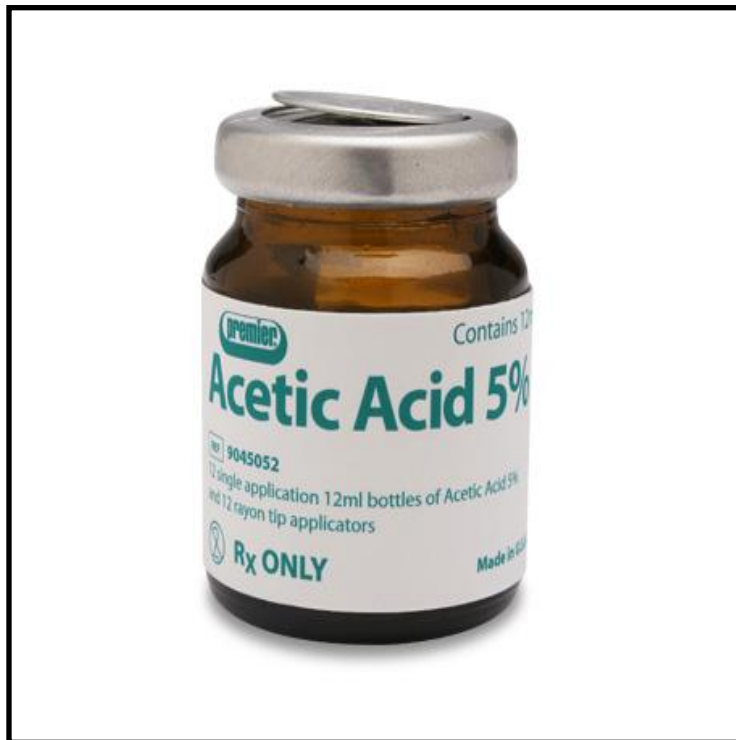
Answer HRA

What is **wrong**?

1. HRA shows a good sensitifity for AIN
2. **HRA identifies the lesions extend correctly**
3. HRA shows a long learnig curve



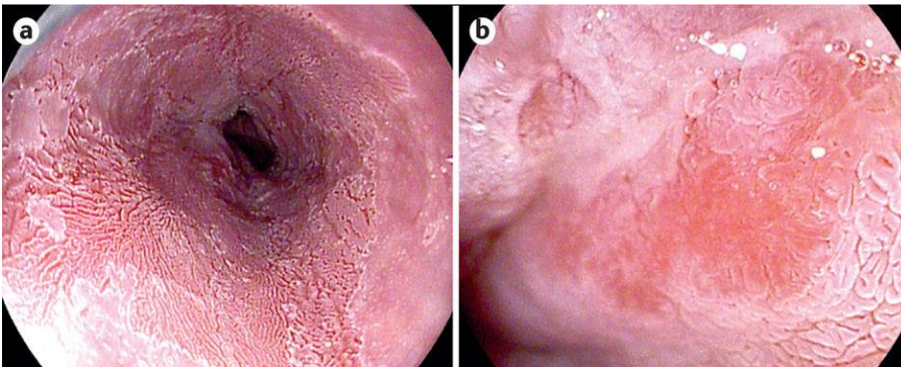
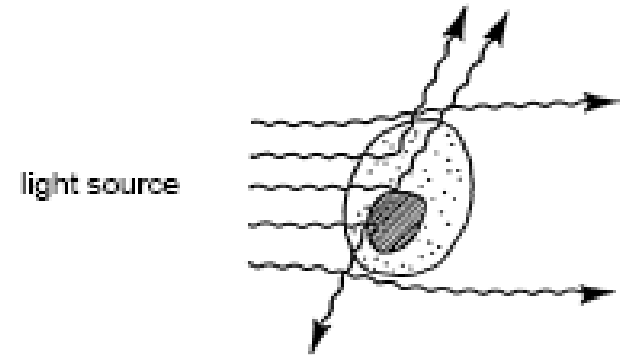
The Staining



Acetic Acid 5%

Effect

Wide angle side scattering from nucleus and cytoplasm increases when acetic acid is applied to the cell



Lugol's Solution 2% (Iodine)

Effect

Brown staining of superficial glycogen.

Application with

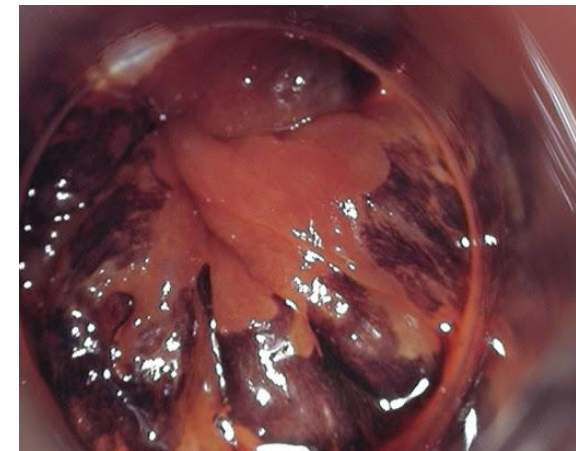
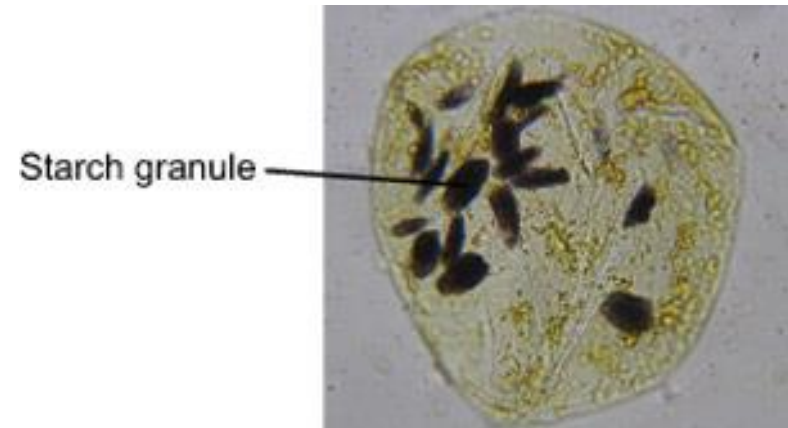
- Cotton swab
- Acetic acid soaked gauze
- spray catheter

Wait 2 minutes!!

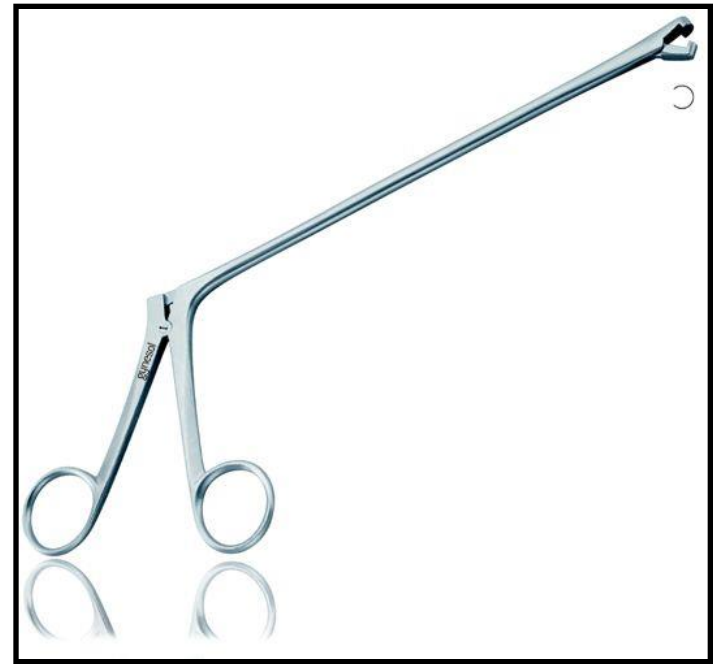
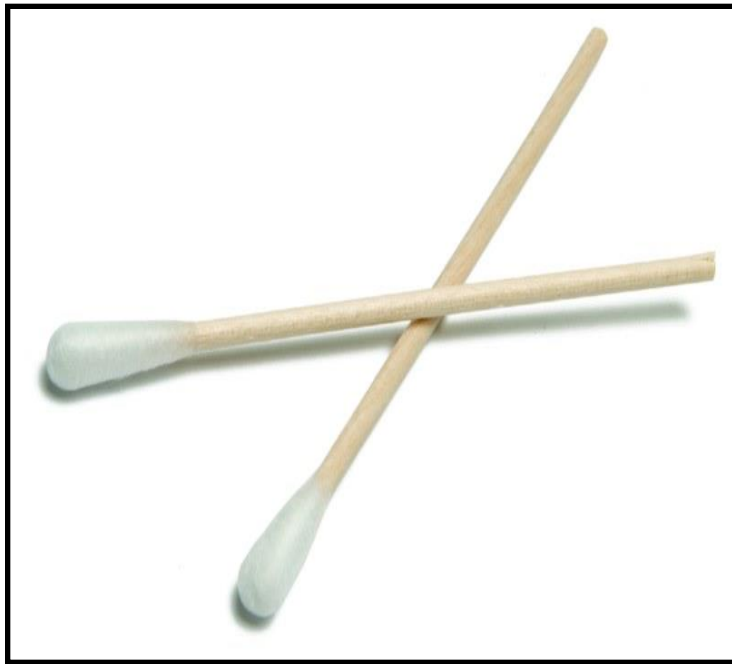
Lugo negative

Sensitivity HG-AIN: 86%

Specificity HG AIN: 43%



Cytology and Biopsy



Cytology

1. Insert moistened synthetic swab until it bypasses internal sphincter
2. Rotate swab to sample cells from all aspects of the anal canal
3. Swab should bend slightly with gentle pressure for adequate collection of cells
4. Count slowly to 10 before removing swab



Facts Cytology

HIV negative MSM

Sensitivity for HG-AIN: 55%

Specificity for HG-AIN: 76%

HIV positive MSM

Sensitivity for HG-AIN: 84%

Specificity for HG-AIN: 47%

In combination with HPV: Sensitivity > 90%

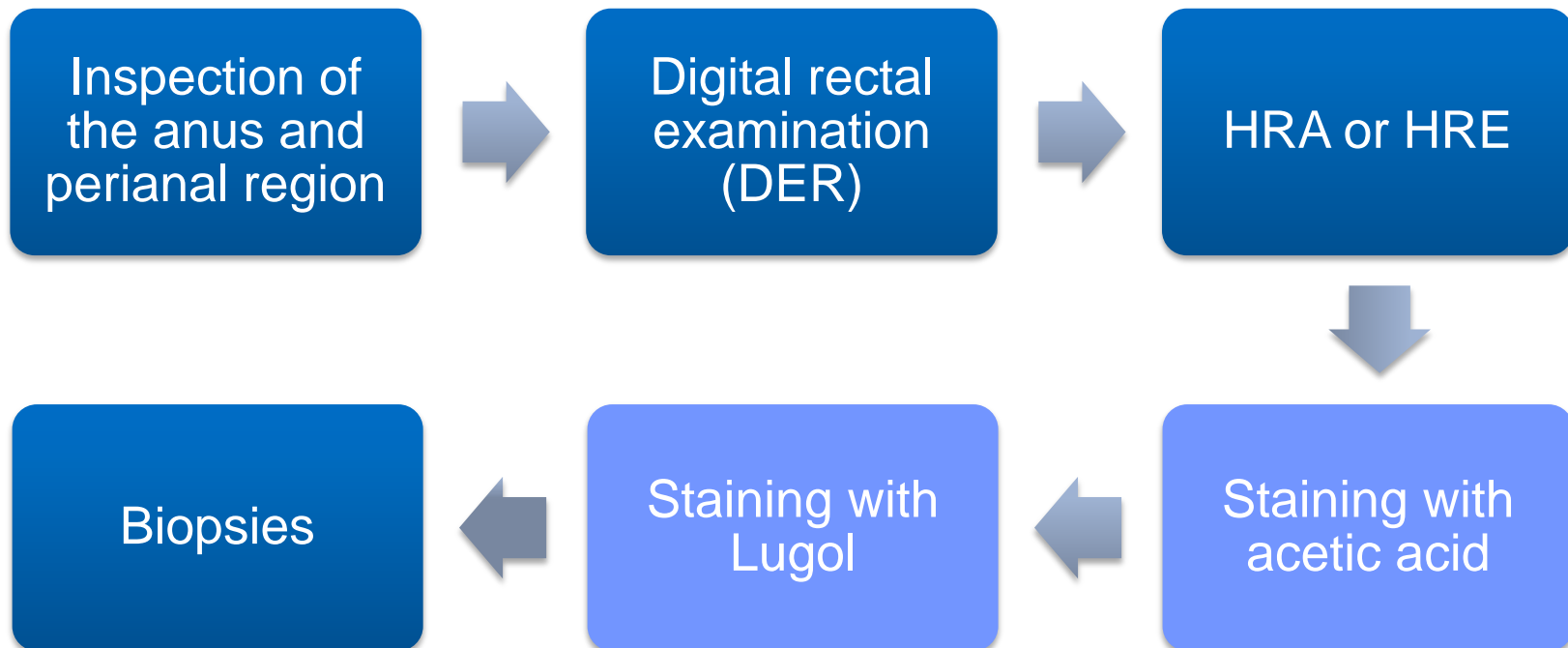
NPV AIN vs negative: 84%

PPV AIN vs negative: 54%

Specificity improves with increasing age



The Screening Procedure

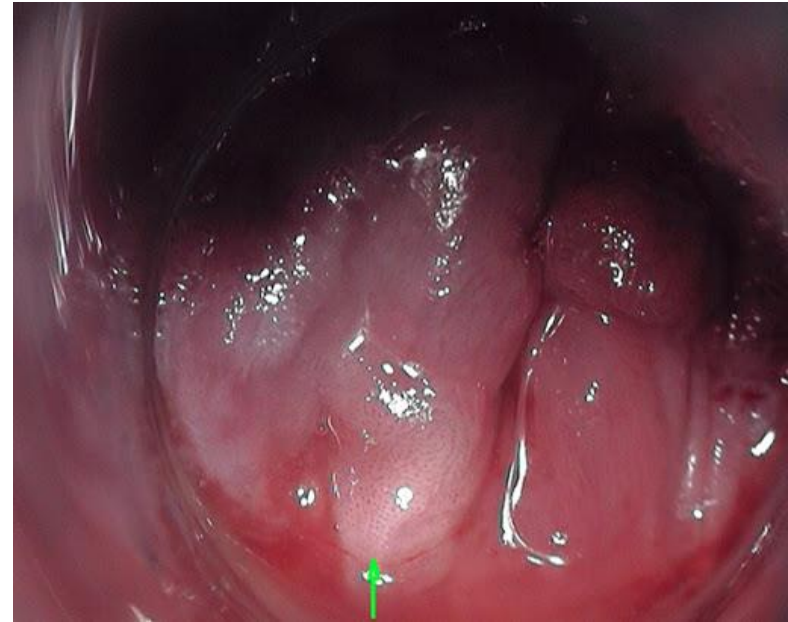


Which Lesions Should be Biopsied?

Punctuation:

Dotted appearance of capillaries

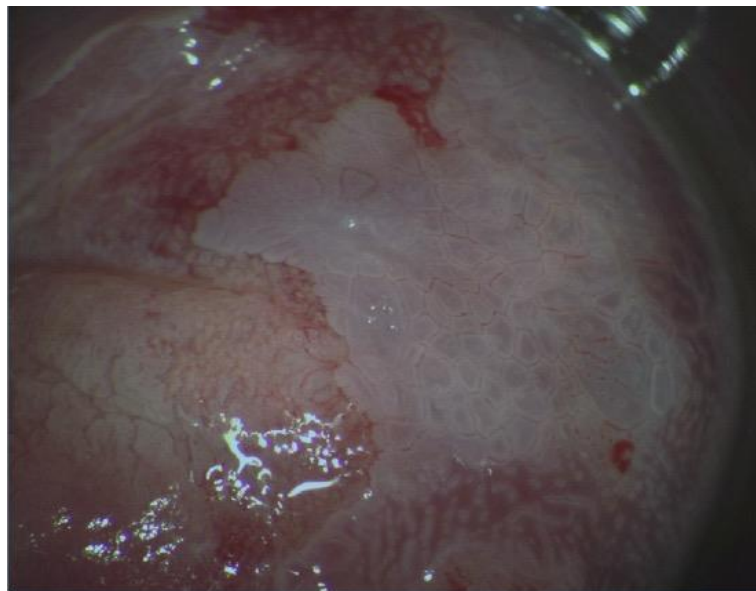
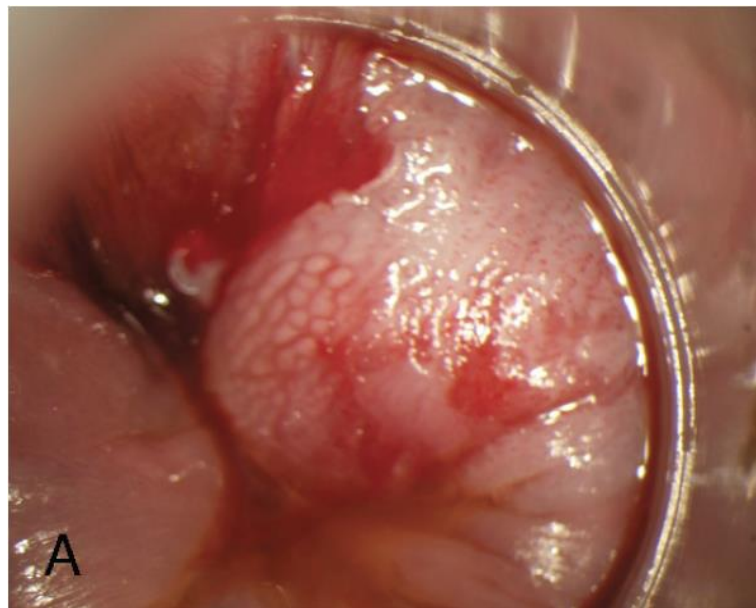
Often within acetowhite areas appearing as fine to coarse red dots.



Which Lesions Should be Biopsied?

Mosaicism:

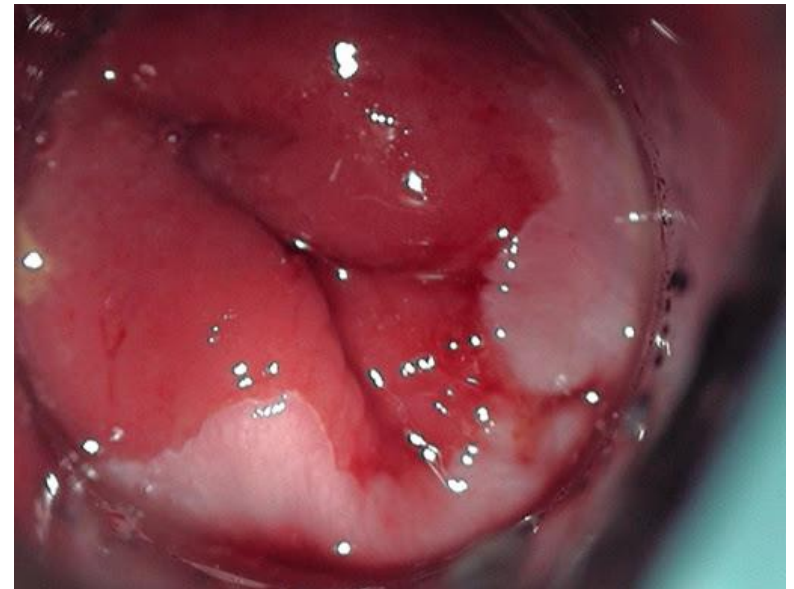
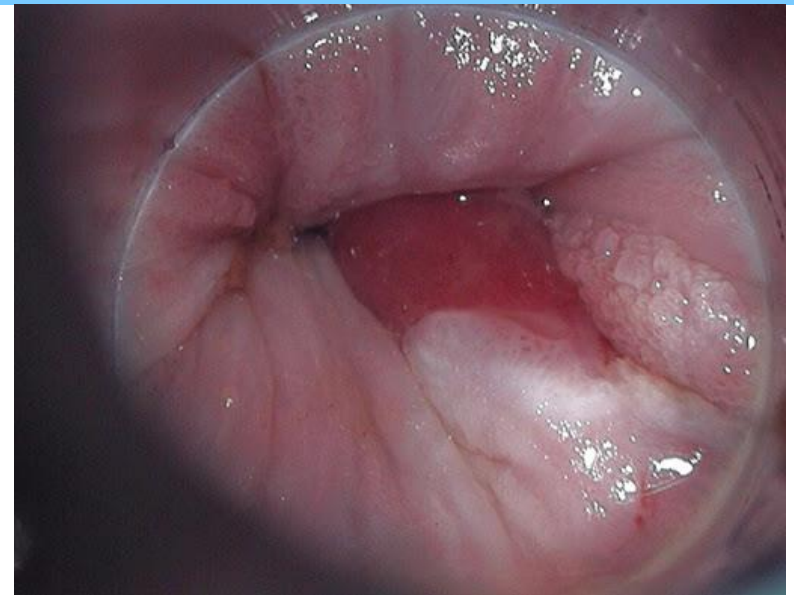
Abnormal small blood vessels suggesting a "tiled floor" or "wire fence" appearance.



Which Lesions Should be Biopsied?

Leukoplakia:

Elevated, white plaque seen
prior to acetic acid application.



Which Lesions Should be Biopsied?

Atypical vessels:

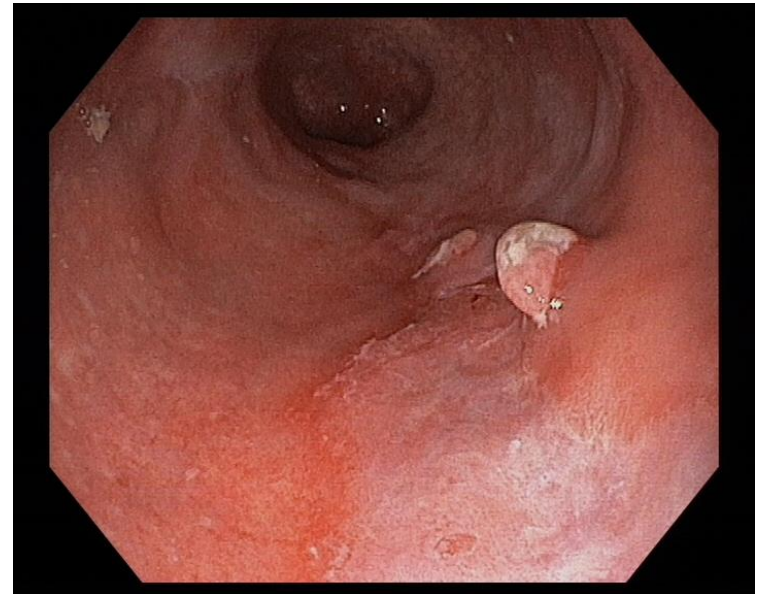
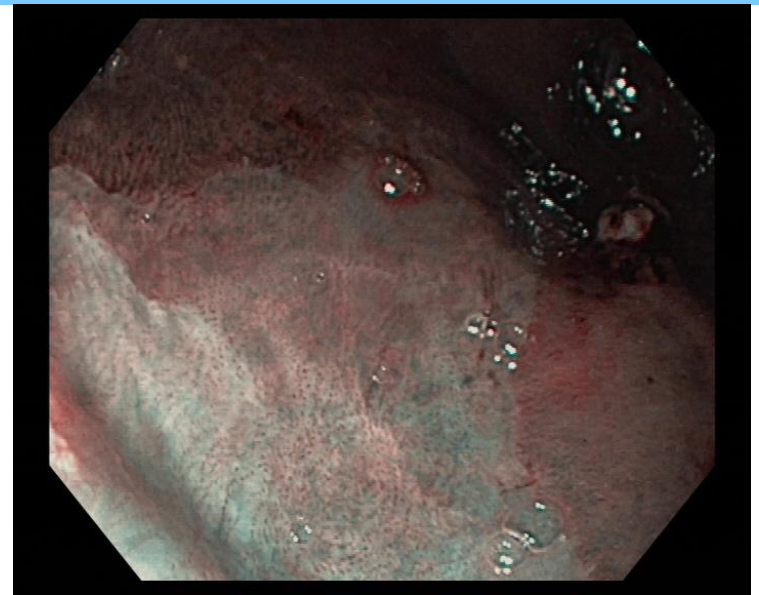
Irregular vessels with abrupt ending

No definite pattern is recognised, as with punctuation or mosaicism.



Which Lesions Should be Biopsied?

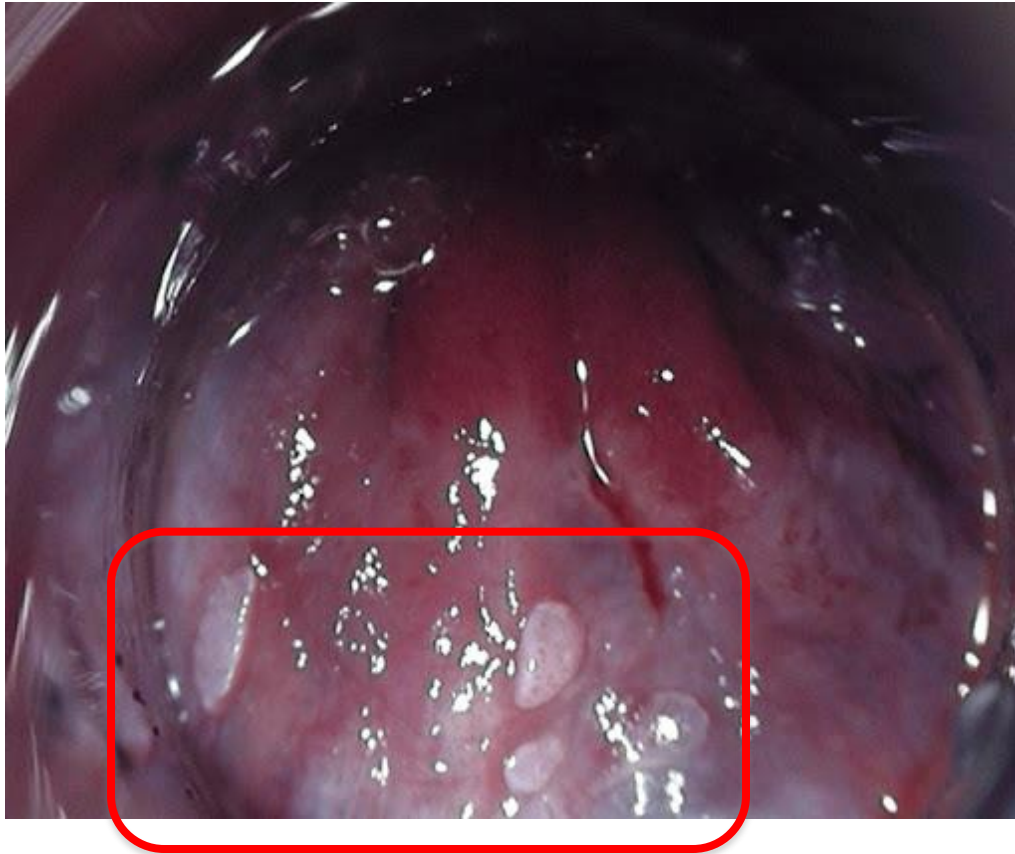
Irregularities near the transformation zone



Large AIN 3



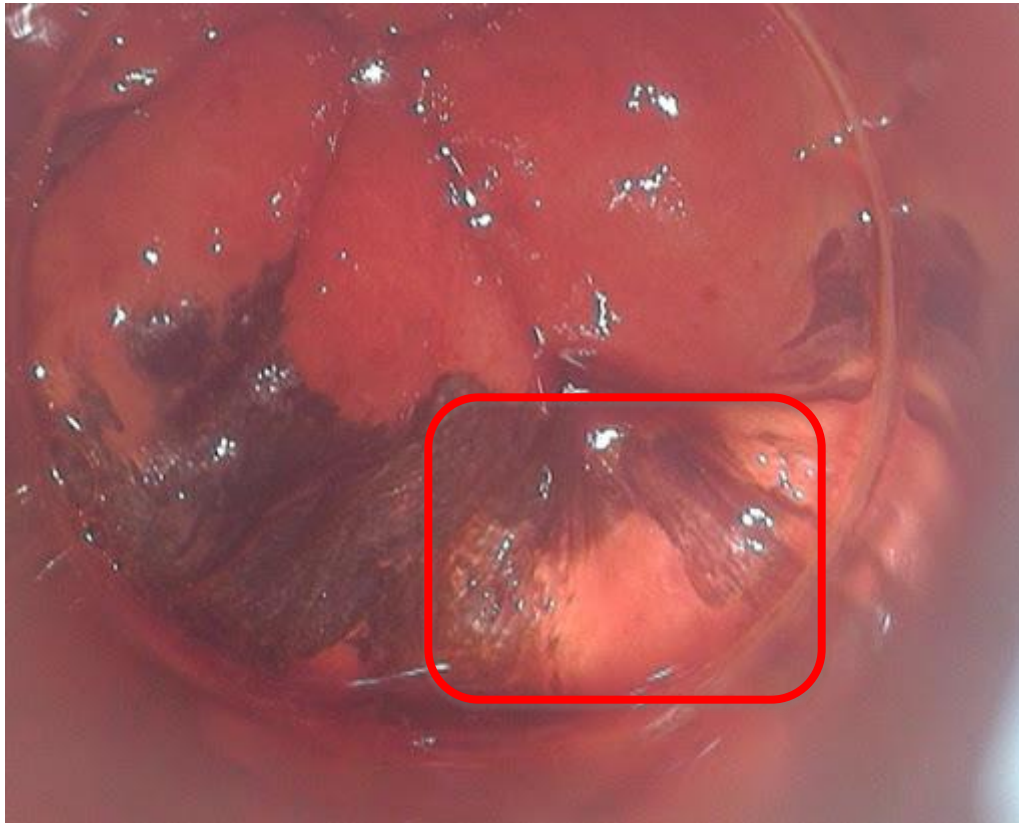
Do You See the Lesion?



Condyloma



Do You See the Lesion?

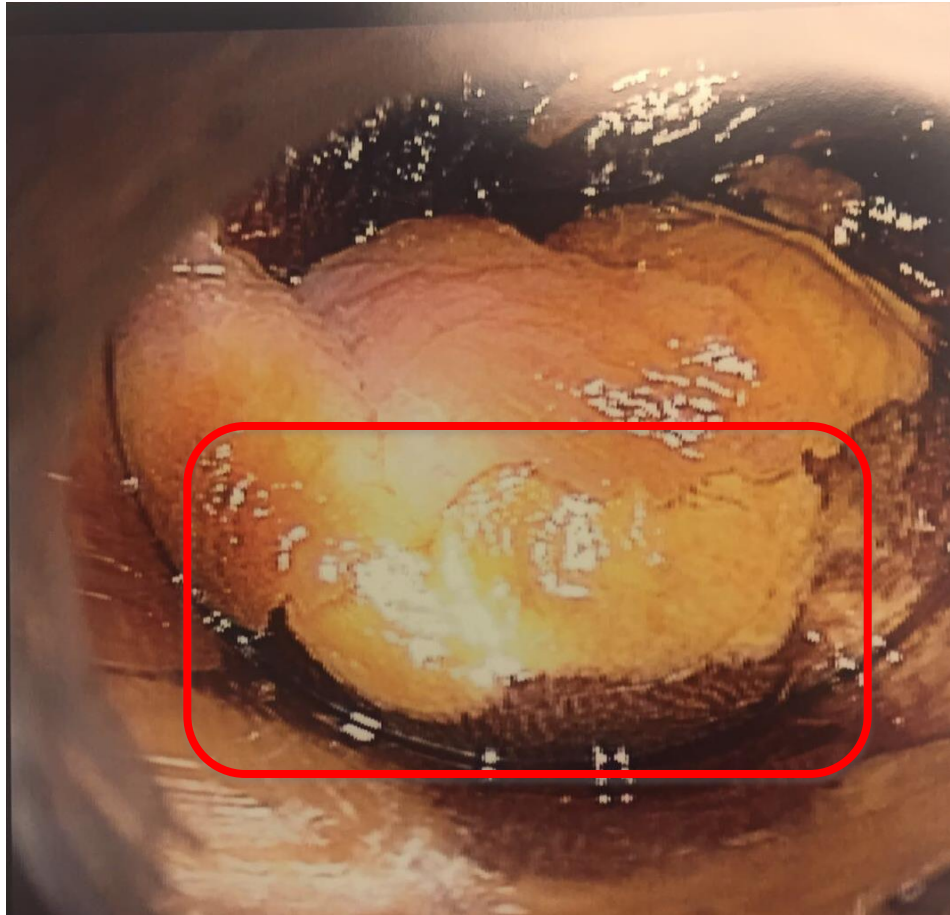


AIN 3

Lugol unstained lesion



Do You See the Lesion?



AIN 3

Lugol unstained lesion



Follow-up after AIN Therapy



Risk new AIN?

Risk Recurrence?



Question - Recurrence

Risk recurrence HG-AIN after 2 years in HIV pos MSM?

1. 20%
2. 30%
3. 40%
4. 50%



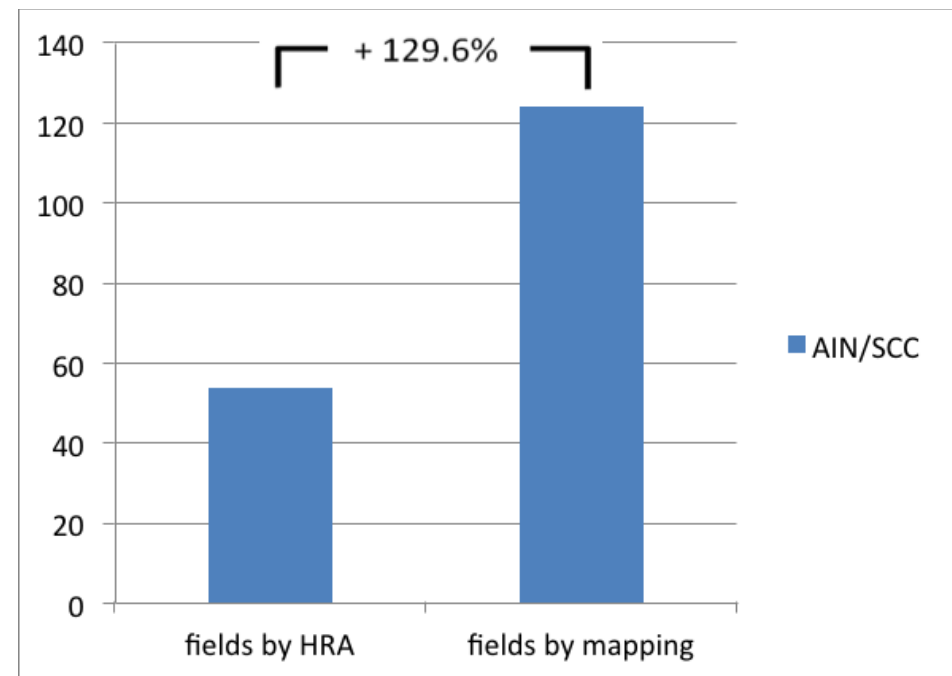
Risk AIN Recurrence (HG-AIN)

Do we underestimate the lesions?

per-field analysis

Sensitivity: 44%

Specificity: 96%



Answer - Recurrence

Risk recurrence HG-AIN after 2 years in HIV pos MSM?

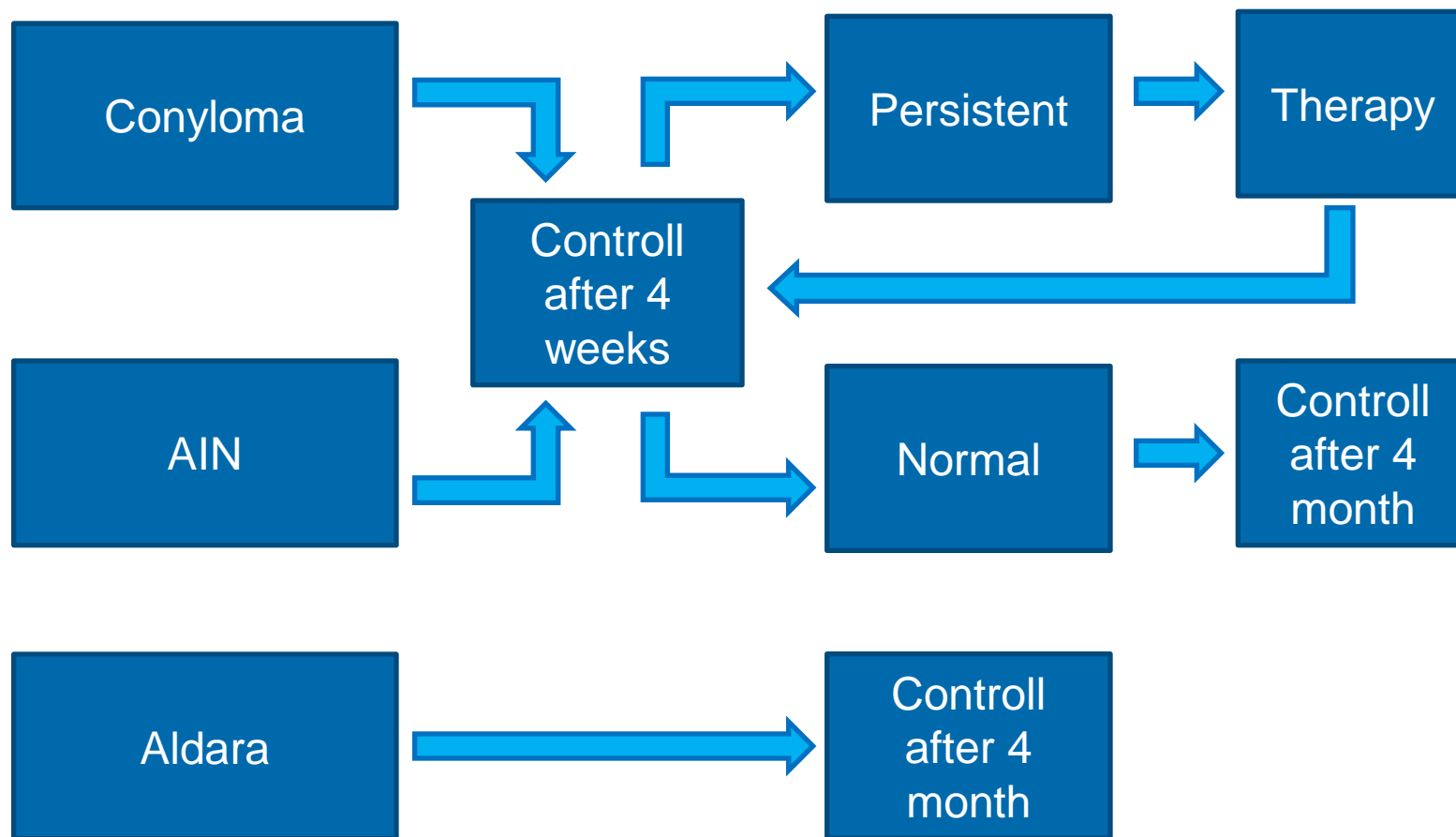
1. 20%
2. 30%
3. 40%
4. **50%**

Very High Recurrence Rate!

HG-CIN: 16% after 5 years

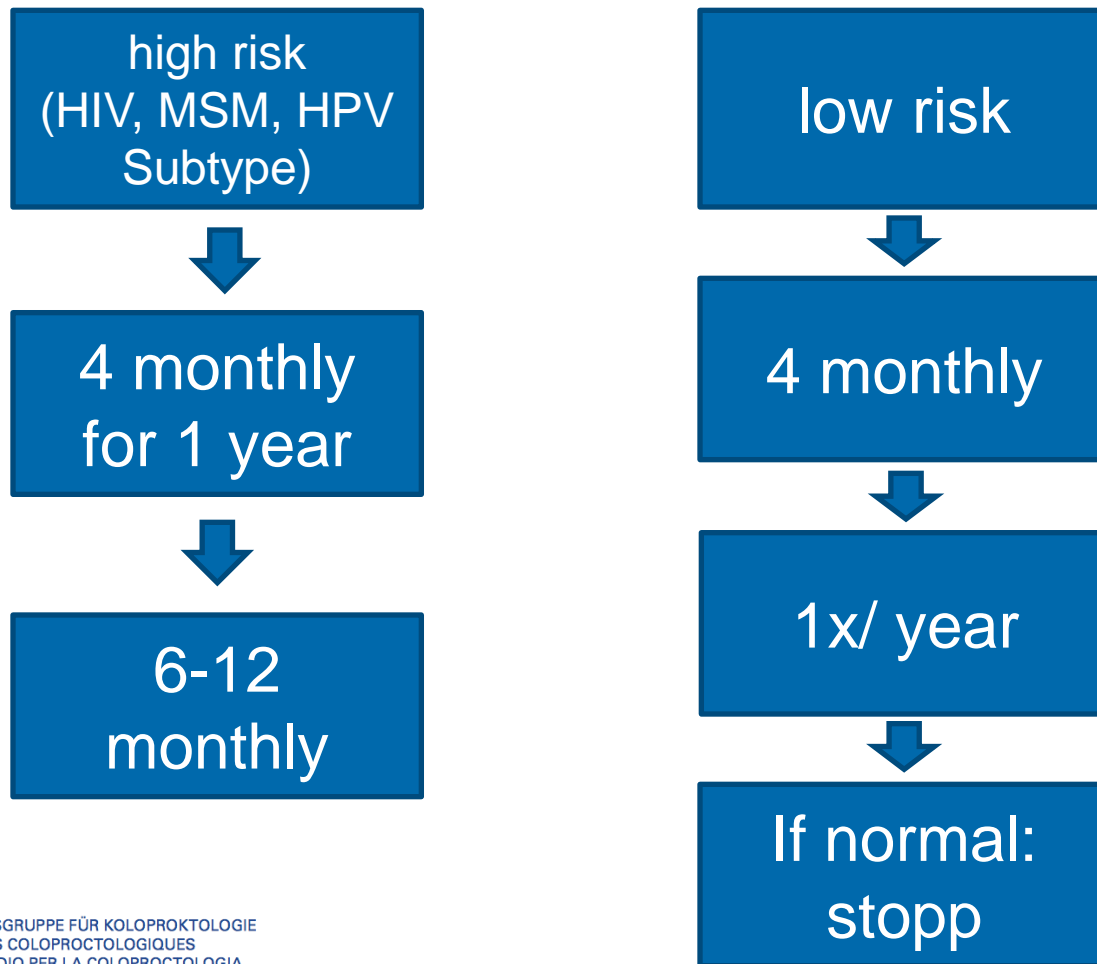


Follow-up – System St. Gallen



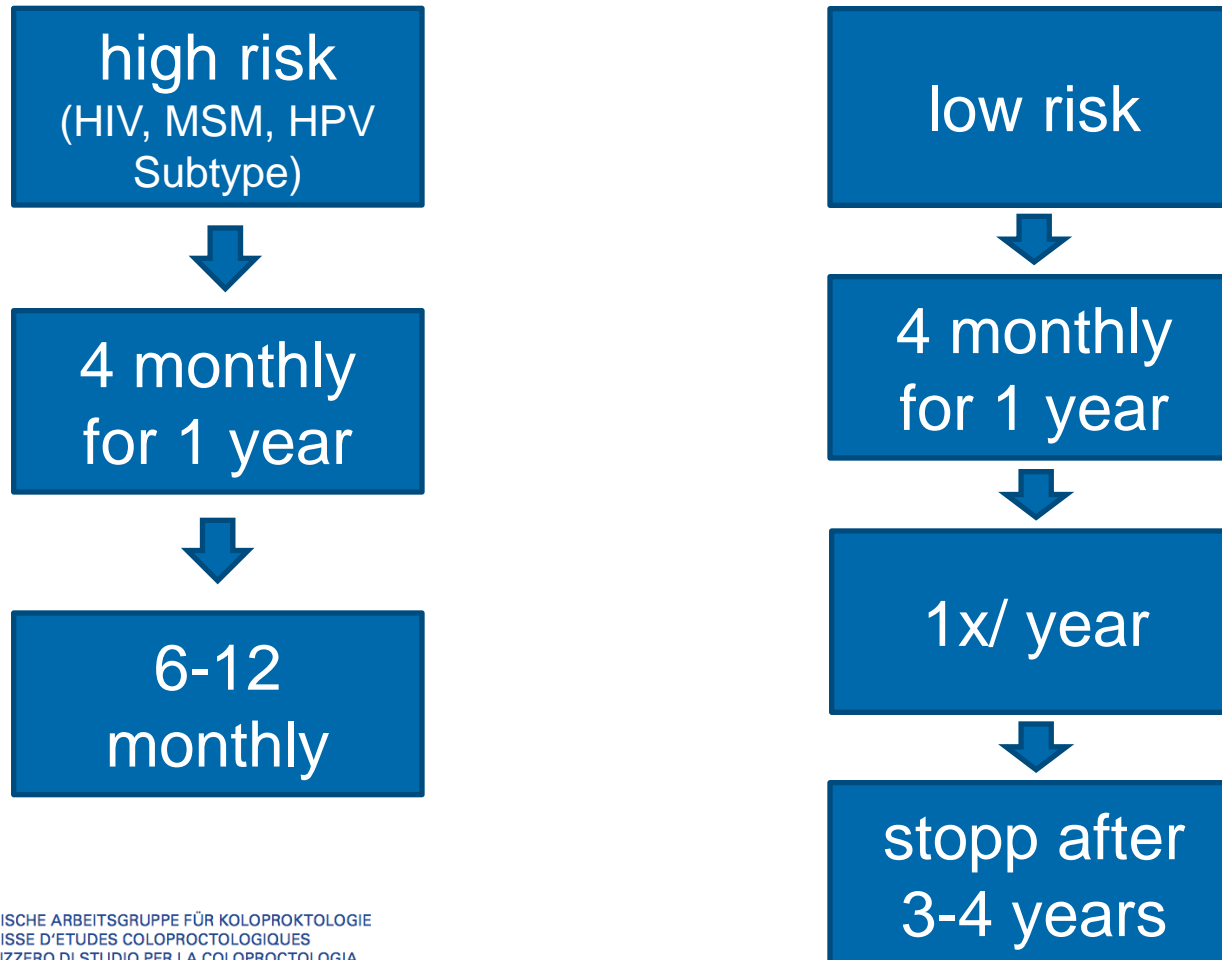
Follow-up – System St. Gallen

Condyloma



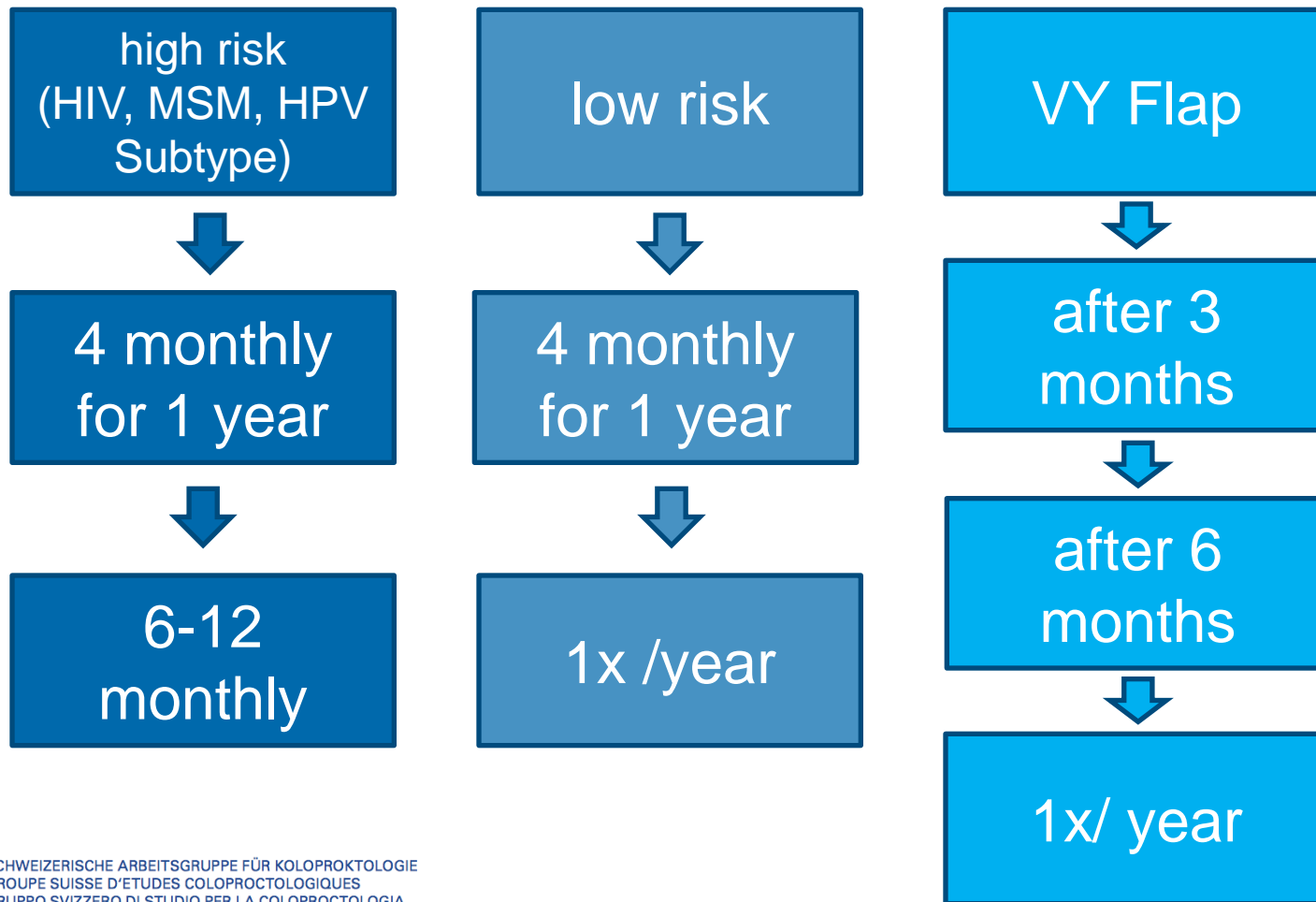
Follow-up – System St. Gallen

AIN low grade



Follow-up - St. Gallen

AIN high grade



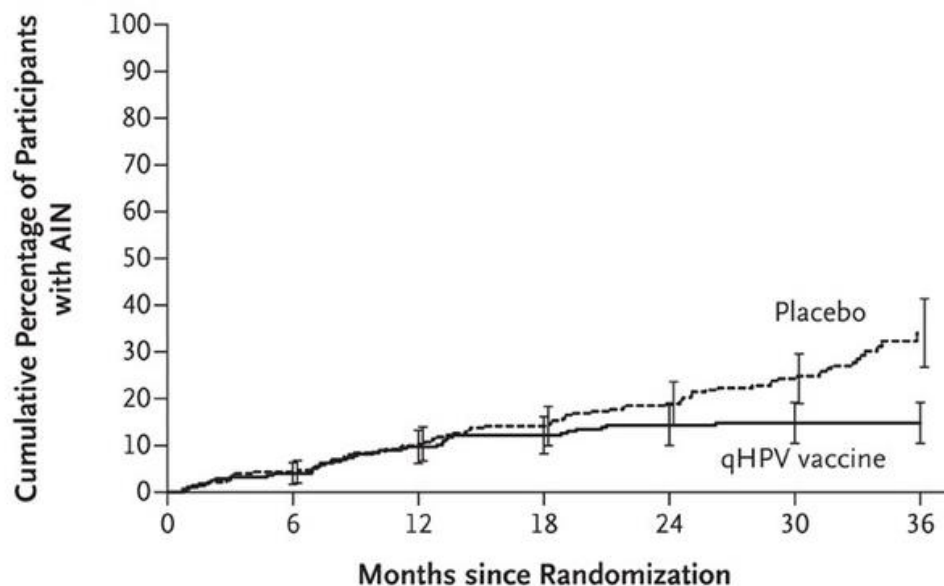
Question - Vaccination

What is **right**?

1. HPV Vaccination prevents HPV transmission but not AIN/SCC
2. HPV Vaccination does **not** affect an existing infection
3. HPV Vaccination reduces risk of AIN recurrence after treatment
4. HPV Vaccination in Switzerland is payed by health insurance for girls aged 11 to 14 years only.



Effect HPV Vaccination (qHPV 6,11,16,18) on AIN



55% less 36 month after vaccination in HIV neg MSM

End Point	qHPV Vaccine (N=299)				Placebo (N=299)			Observed Efficacy (95% CI) [†]	
	No. Included in Analysis	No. of Affected Participants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	No. Included in Analysis	No. of Affected Participants	Person-Yr at Risk		Events per 100 Person-Yr at Risk
AIN due to any HPV type [‡]	129	12	299.4	4.0	126	28	315.2	8.9	54.9 (8.4 to 79.1)

percent



Preventing Persistent HPV Infection

Table 4. Efficacy against HPV-6, 11, 16, or 18–Related Persistent Anal Infection and HPV DNA Detection at Any Time in the Per-Protocol Efficacy Population.*

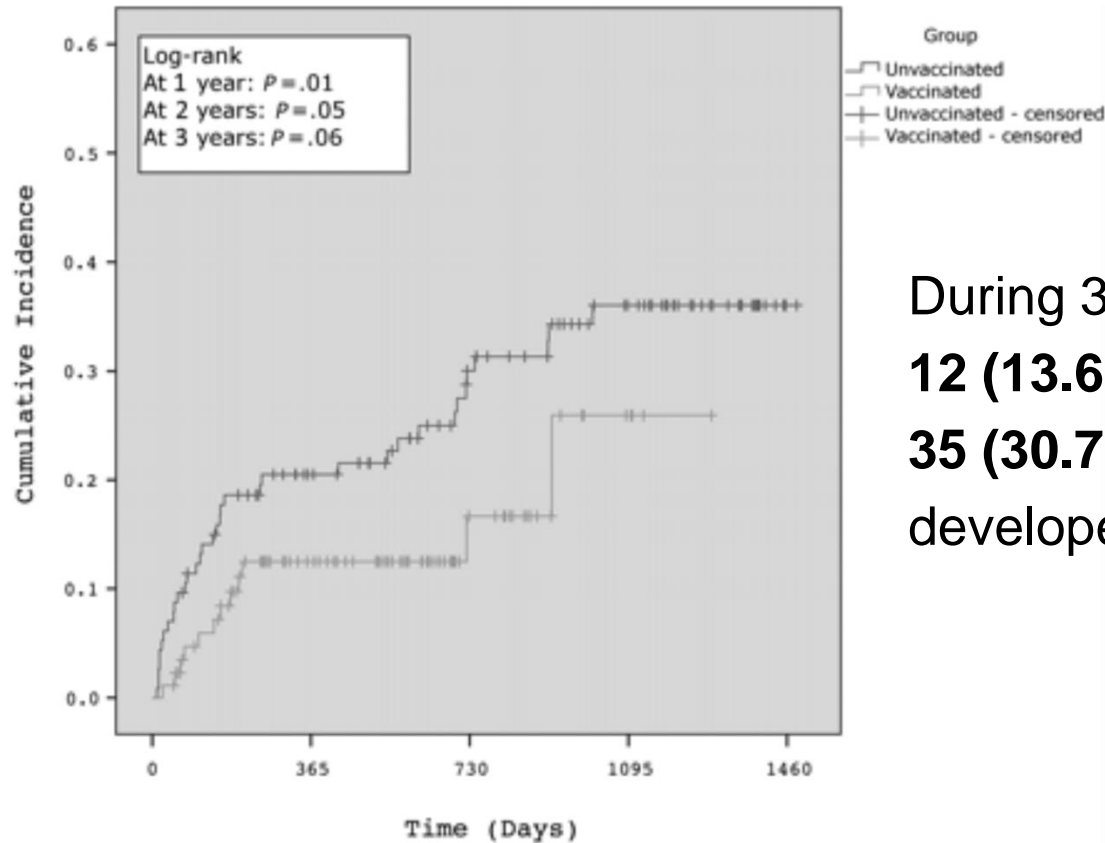
End Point	qHPV Vaccine (N = 299)				Placebo (N = 299)				Observed Efficacy (95% CI) percent
	No. Included in Analysis	No. of Affected Participants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	No. Included in Analysis	No. of Affected Participants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	
Persistent infection									
HPV-6, 11, 16, or 18	193	2	385.6	0.5	208	39	381.2	10.2	94.9 (80.4 to 99.4)

Table 4 shows vaccine efficacy against persistent infection with HPV and detection of HPV DNA at any time in the per-protocol efficacy population. The reduction in persistent anal HPV-6, 11, 16, or 18 infection was 94.9% (95% CI, 80.4 to 99.4). Ef-

qHPV: persisting HPV infection minus 94.9%



Effect qHPV on AIN Recurrence



During 340.4 person-years follow-up, **12 (13.6%) vaccinated** patients and **35 (30.7%) unvaccinated** patients developed recurrent HGAIN.



Situation Switzerland



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Bundesamt für Gesundheit BAG

Im Rahmen der kantonalen Impfprogramme ist die Impfung für **11- bis 14-jährige Mädchen** gemäss diesen Empfehlungen kostenlos. Seit 1. Juli 2016 gilt das auch für Jungen und junge **Männer** zwischen **11 und 26 Jahren**. Für **15- bis 26-jährige Mädchen und Frauen** gilt die Kostenübernahme bis 30. Juni 2018 und wird danach neu beurteilt.



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www.bag.admin.ch

Answer - Vaccination

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2. HPV Vaccination does not affect an existing infection
- 3. HPV Vaccination reduces risk of AIN recurrence after treatment**
4. HPV Vaccination in Switzerland is free of charge for girls aged 11 to 14 only.



IS YOUR BUTT GETTING ENOUGH ATTENTION?



50% OF HIV+ MEN HAVE PRECANCEROUS ANAL CELLS AND ARE SYMPTOM- FREE.

WE NEED HIV+ VOLUNTEERS OF ALL GENDERS WHO ARE 35+ TO TAKE PART IN A NATIONAL ANAL CANCER PREVENTION STUDY.

VISIT THE WEBSITE ANCHORSTUDY.ORG
OR CALL 1-800-555-5555



the **ANCHOR** study.org

