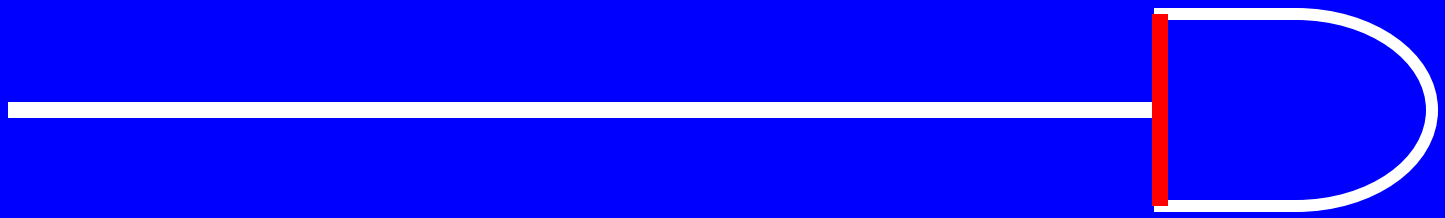
How Good a Diagnostic Tool is Colposcopy?



RCOG Senior Staff Conference 2008

Colposcopic activities

Diagnosis

Selection for biopsy

Selection for treatment

Acetowhitening

Metaplasia → CIN3

Density

Vasculature - mosaic

LG CIN → HG CIN

Coarseness

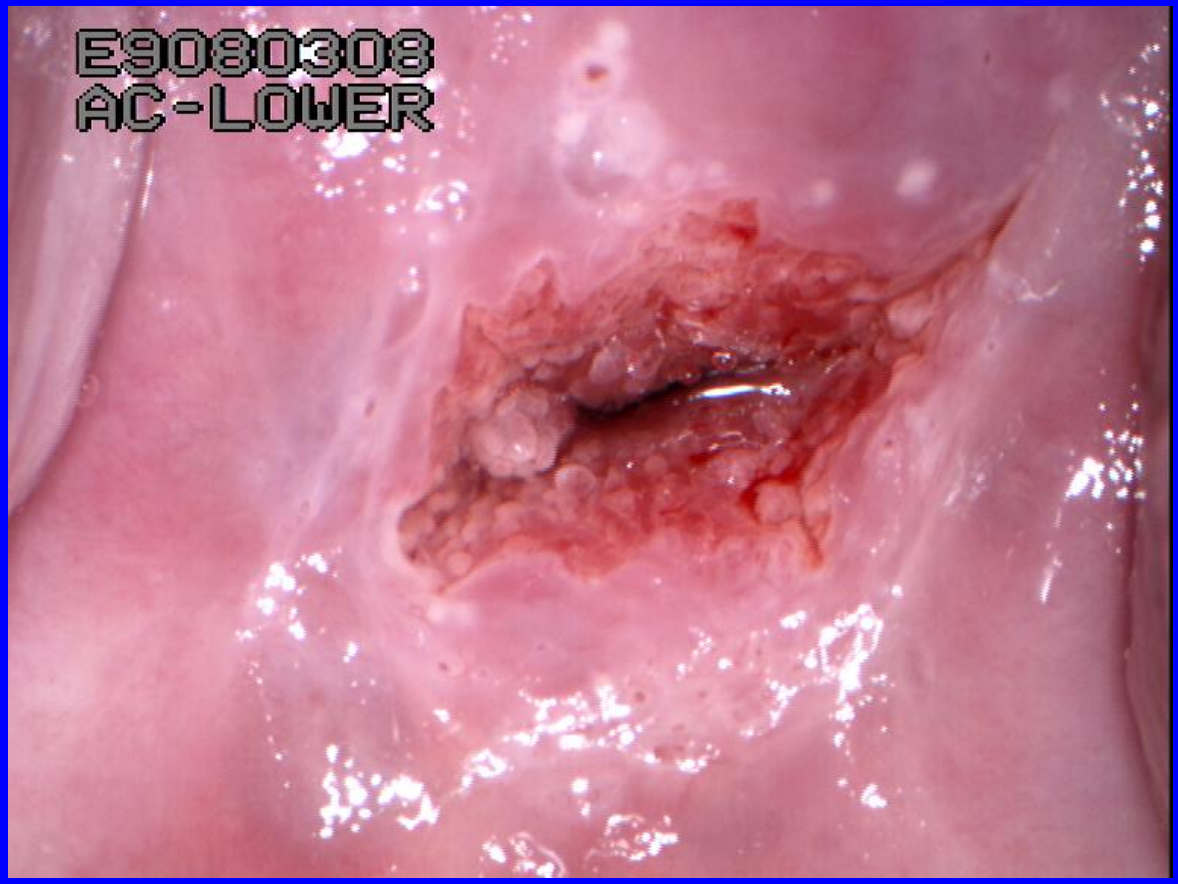
Making the diagnosis

Making a diagnosis at colposcopy

- Colposcopic imaging
- Referral cytology
- Previous history
- Age
- Smoking

Scoring systems acknowledge the diagnostic shortcomings of colposcopy

The Normal Cervix



Colposcopic Caveat

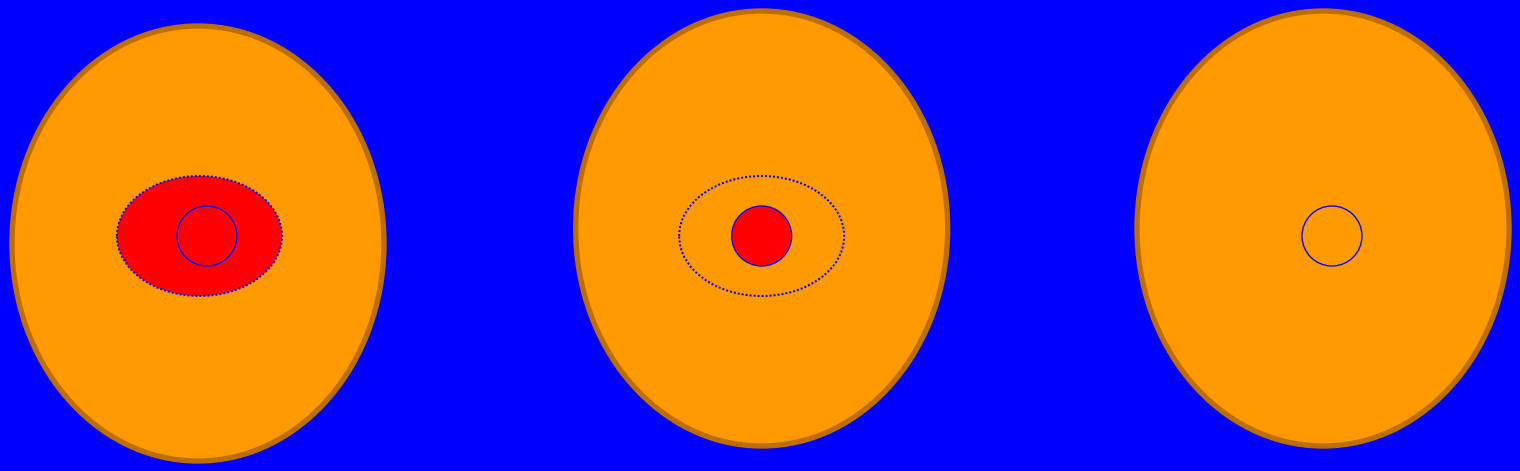
What you seen may not the whole story

What we know: the pitfalls

- SCJ not visible

TZ Classification

I II III



What we know: the pitfalls

Colposcopic process has to be contextual

Pragmatic view

Detection of invasive cancer

√

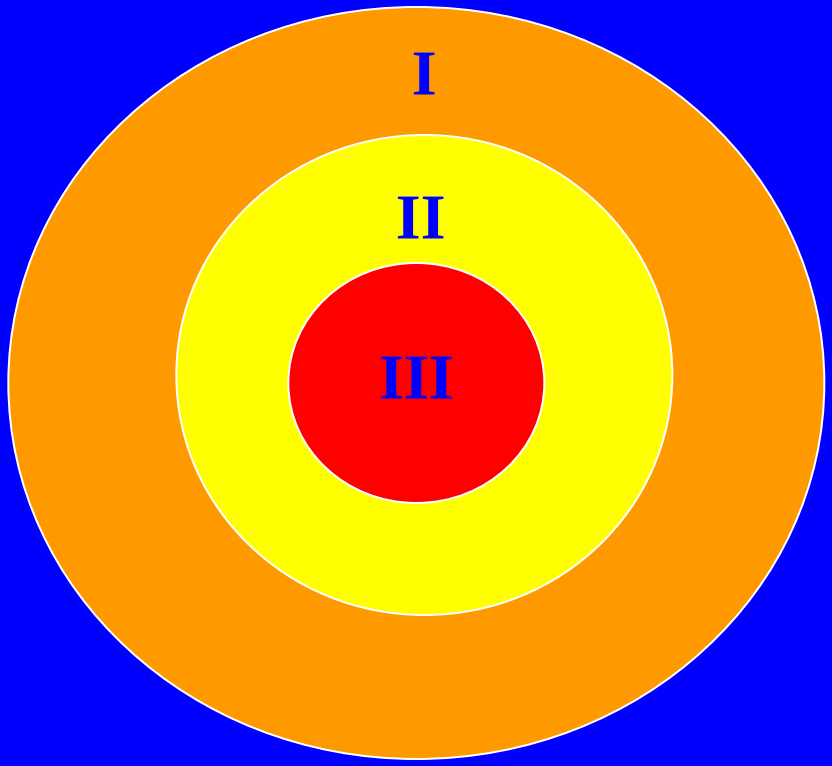
Management of suspected HG disease

√

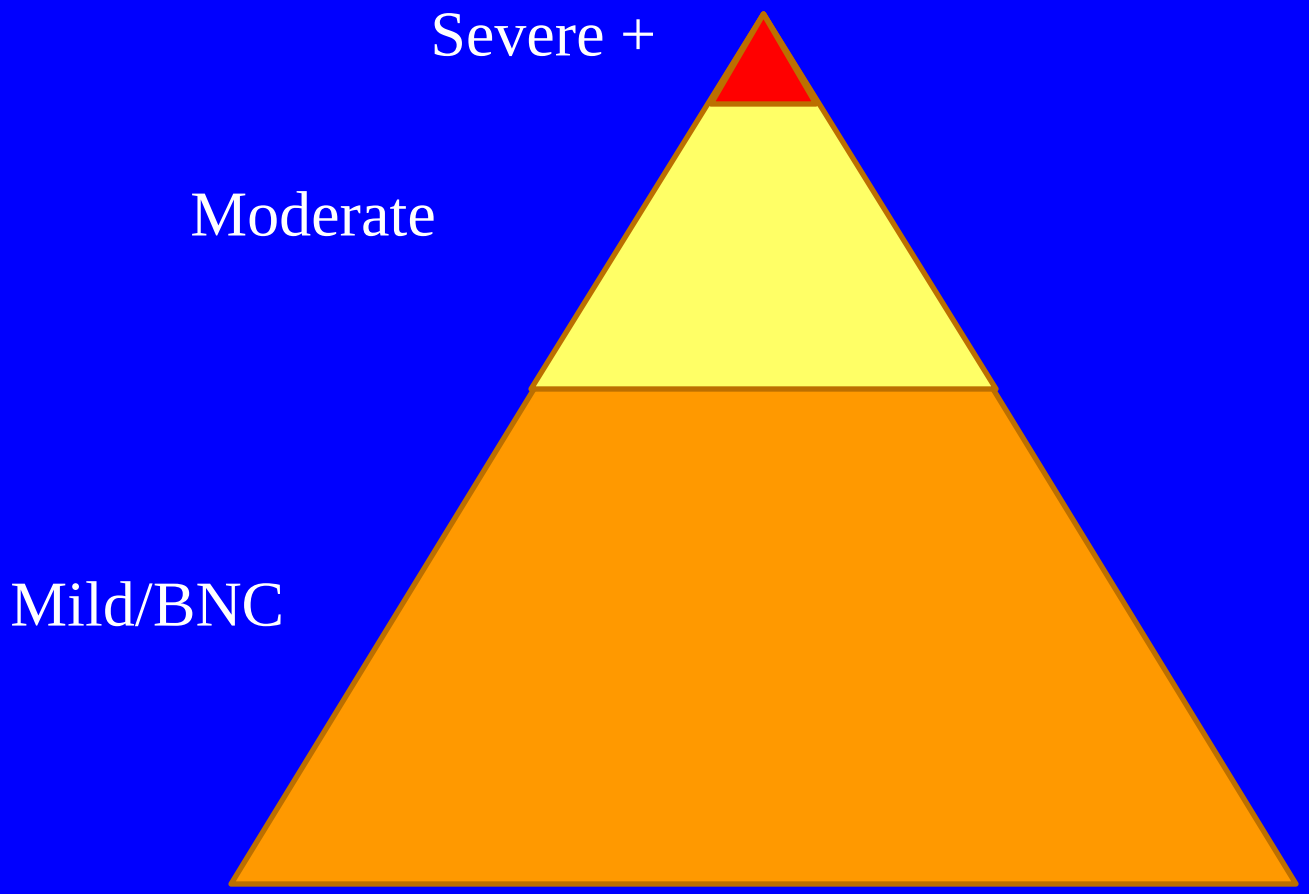
Management of suspected LG disease

?

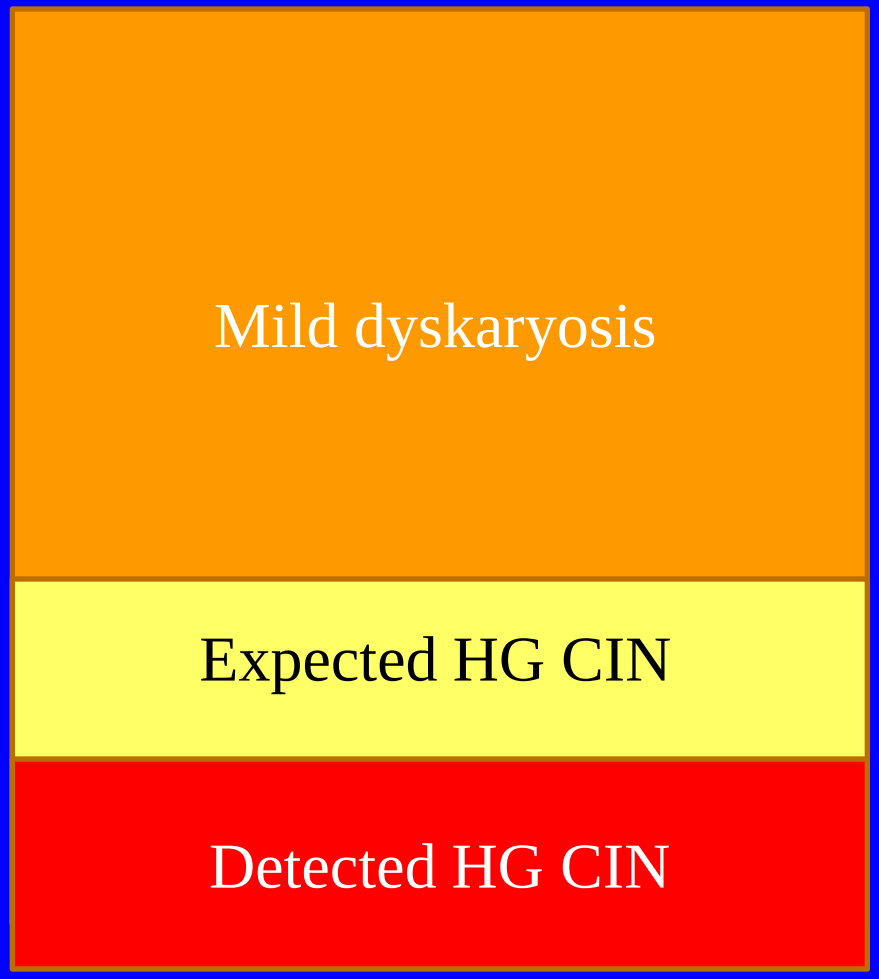
Selection:



Management of LG disease



Management of LG smears



85% certified colposcopists

All have PPV > 70%

Negative loops < 15%

What we know: performance

SCJ status √

Presence/absence of lesion √

Assessment of lesion +/-

Can miss micro-invasive lesions

Performs less well in low-risk situations

What we know or do we?

- Diagnosis is multifactorial
- Acetowhitening important
- Size matters
- Vasculature contributary

Methodological problems

- Bias: cytology

Influence of referral cytology

- HG CIN missed when smear LG or less
- Diagnostic accuracy (and management improves) with cytology

Pretorius et al: J Reprod Med 2001

Etherington et al: Br J Obstet Gynaecol 1997

Methodological problems

- Bias: cytology
- Verification bias

Methodological problems

- Bias: cytology
- Verification bias
- Quality assurance: colposcopist/pathologist

Colposcopic Experience

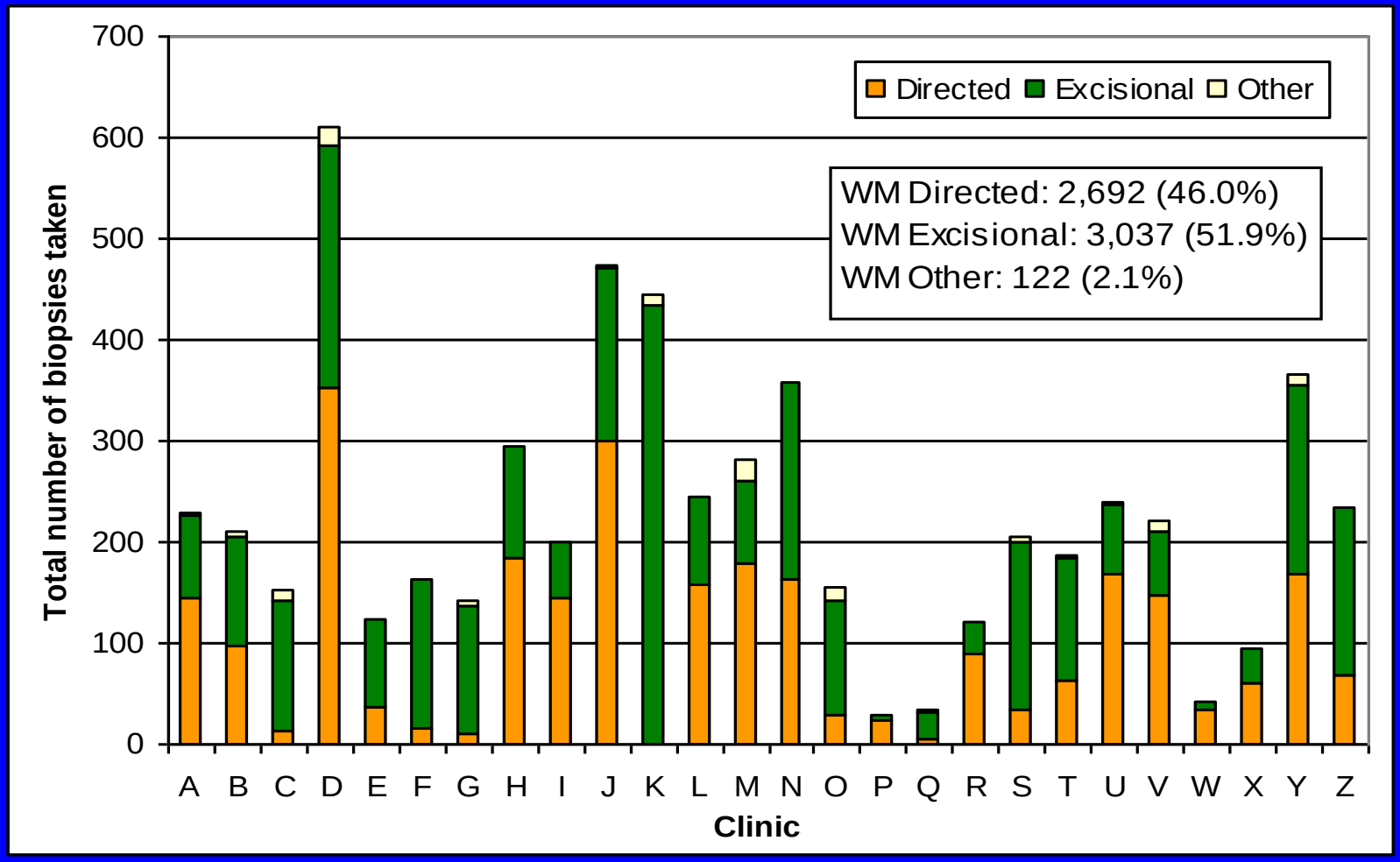
Number of biopsies and sensitivity of colposcopy
Gage et al (ALTS Group): Obstet Gynecol 2006

Colposcopy with biopsy detected 2/3 HG CIN

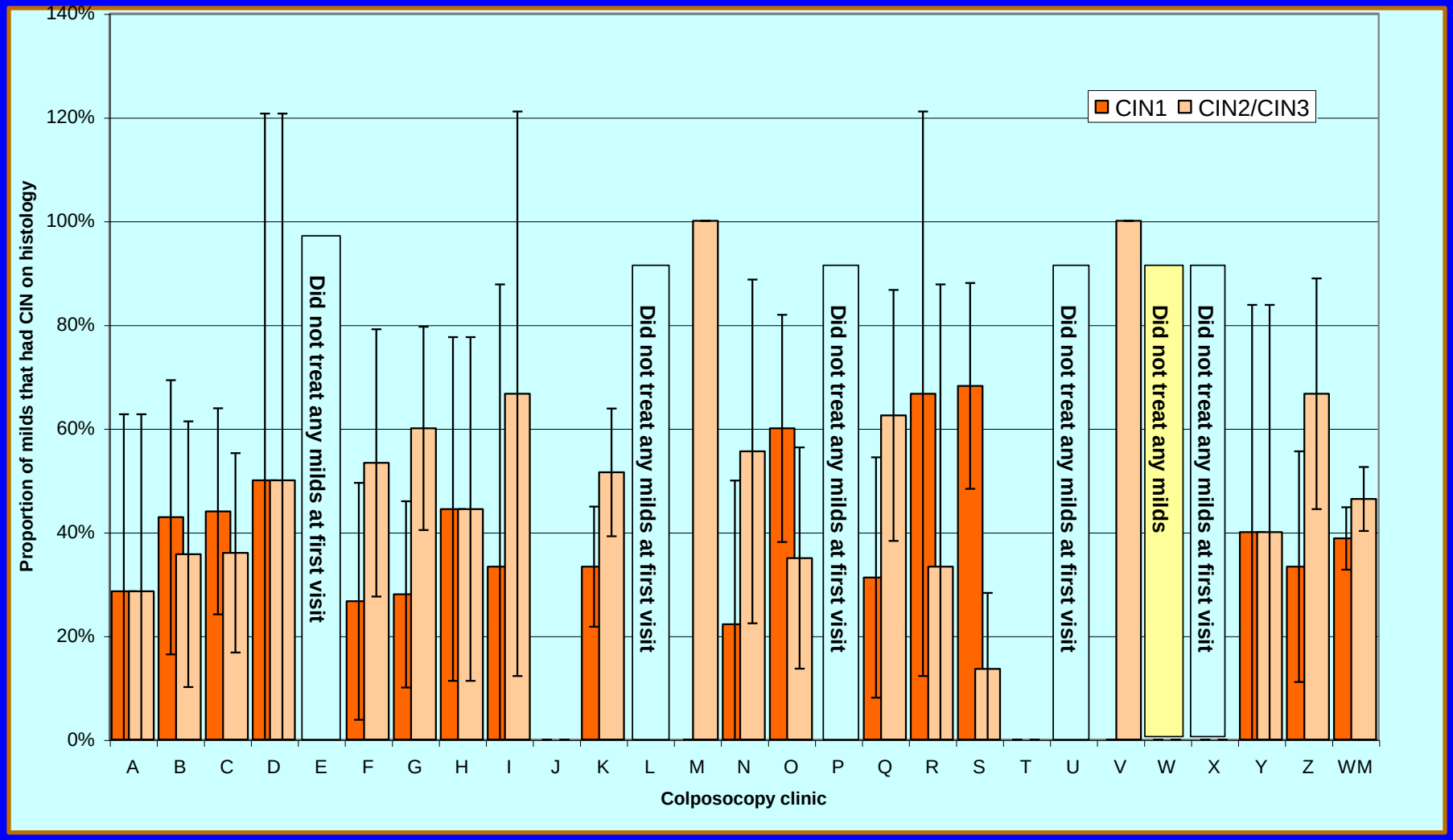
Sensitivity was not influenced by type of practitioner

No of biopsies the most important factor

Number of biopsies (directed and excisional)



Mild dyskaryosis: loop excision at first visit



Should we being doing (more) punch biopsies?

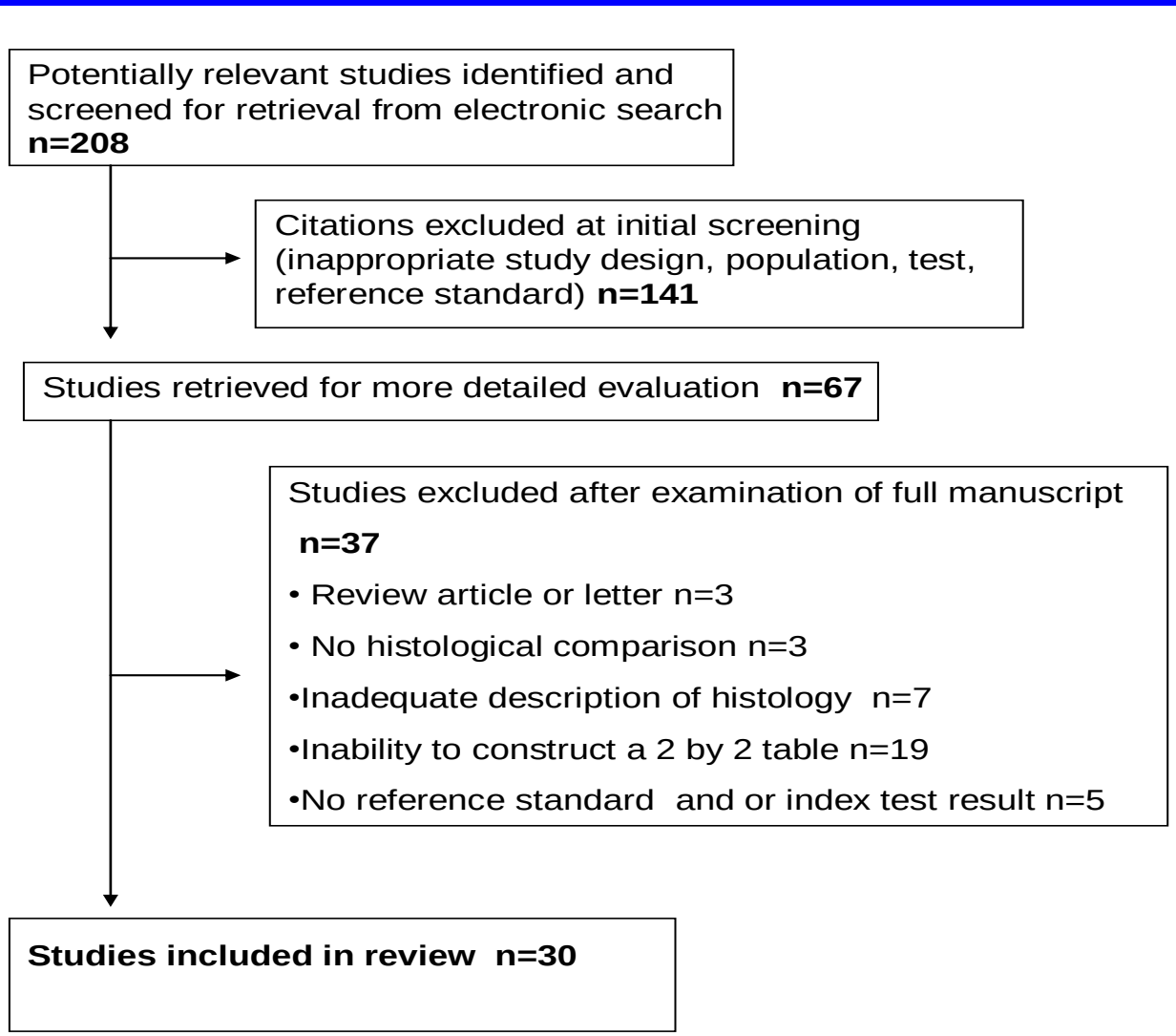
Colposcopy directed punch biopsy

- Widespread use
- Overtreatment vs underdiagnosis
- ? Improves detection rates of CIN
- ? Reliable
- ? Improves accuracy of the colposcopic process

Framing the Question

Population:	Women undergoing colposcopy
Index test:	Punch biopsy
Reference test -	LLETZ, cone or hysterectomy

Identifying the literature



Assessing data quality

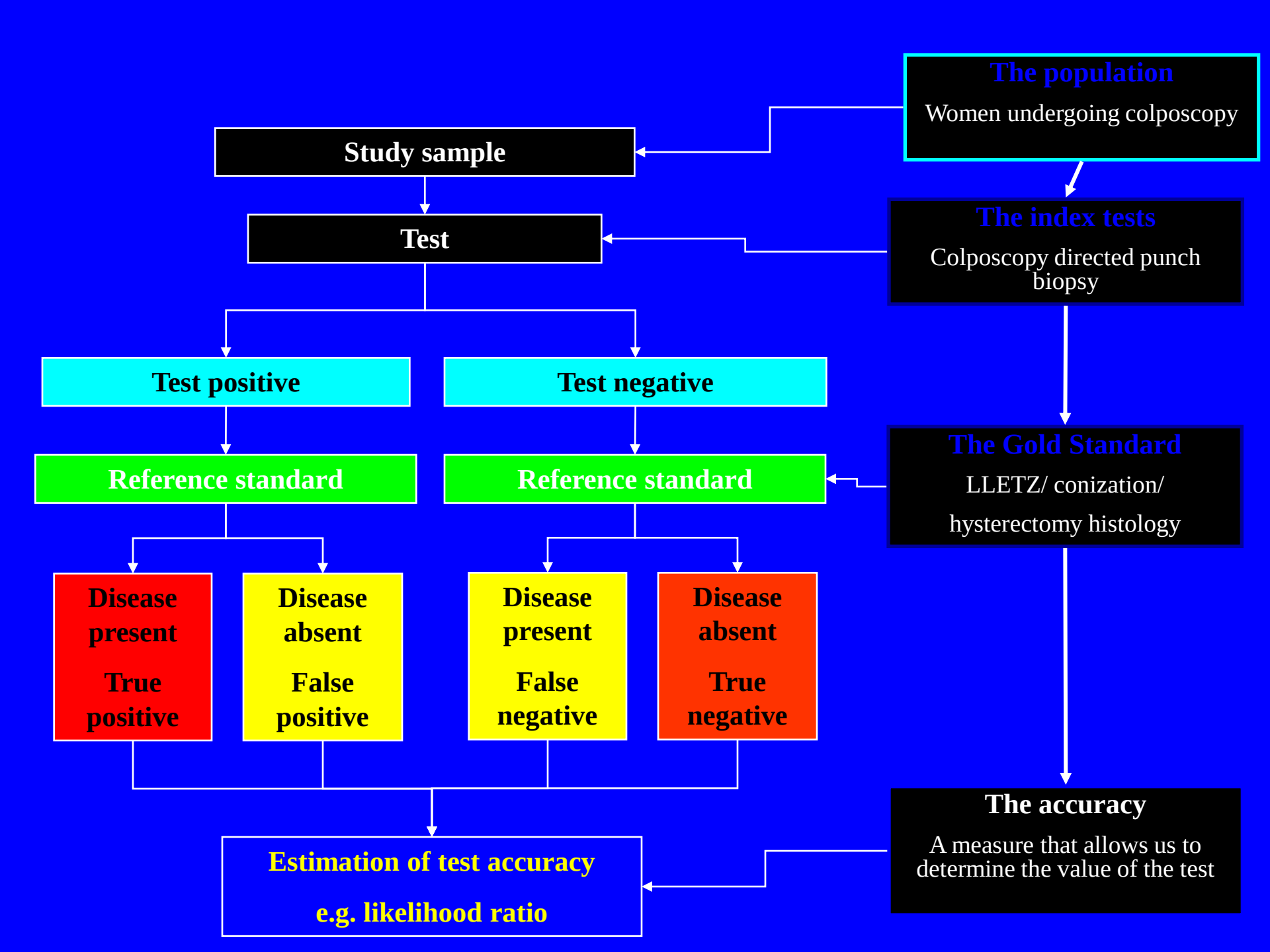
QUADAS and STARD quality assessment

Poor quality studies

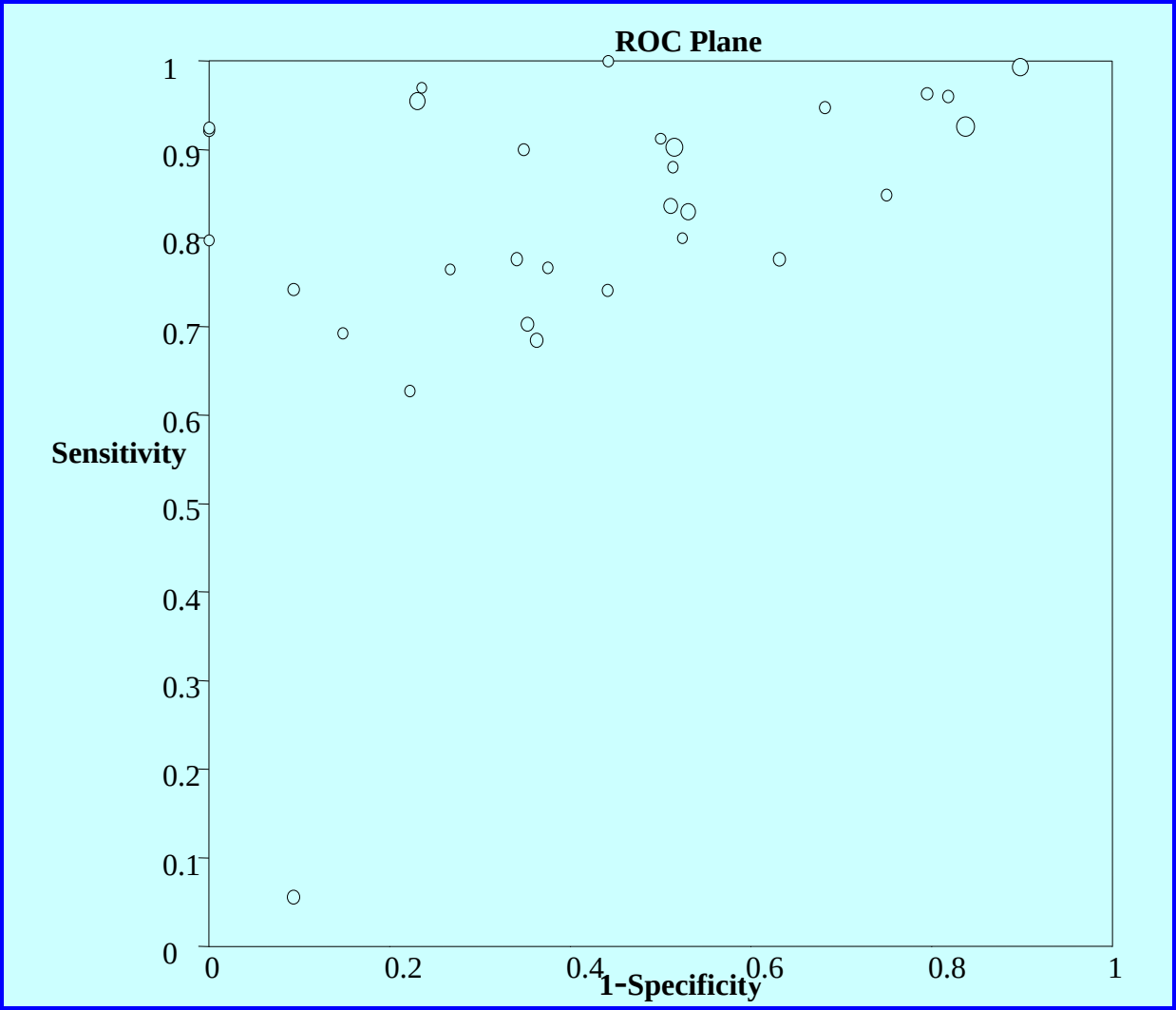
Verification bias (n=20)

Other sources of bias

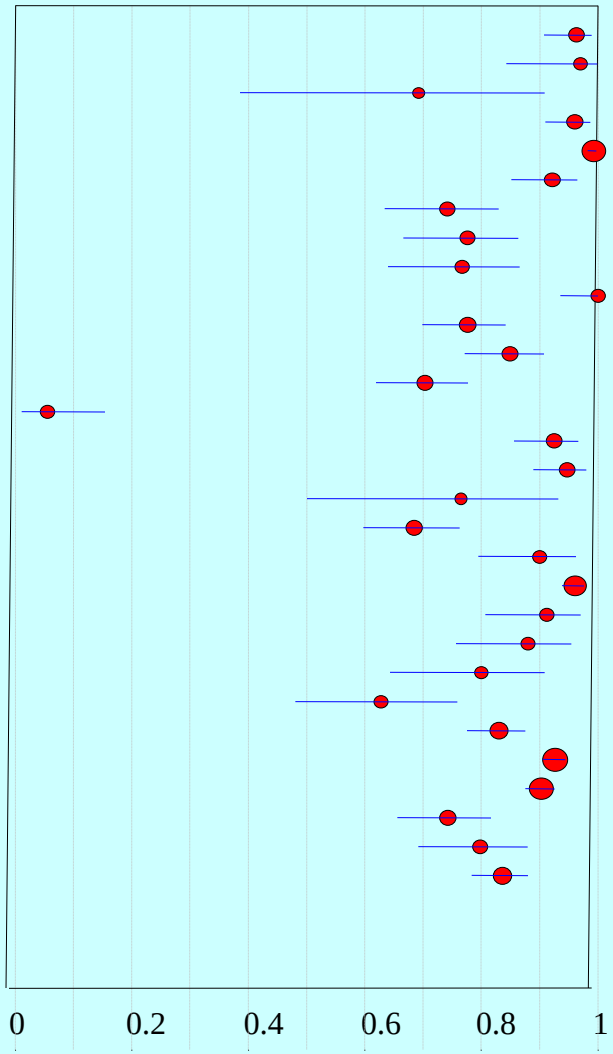
Study design


The population
Women undergoing colposcopy
Study sample
Test
The index tests
Colposcopy directed punch biopsy
Test positive
Test negative
Reference standard
Reference standard
The Gold Standard
LLETZ/ conization/
hysterectomy histology
Disease present
True positive
Disease absent
False positive
Disease present
False negative
Disease absent
True negative
The accuracy
A measure that allows us to determine the value of the test
Estimation of test accuracy
e.g. likelihood ratio

Receiver Operating Characteristic (ROC) Curve



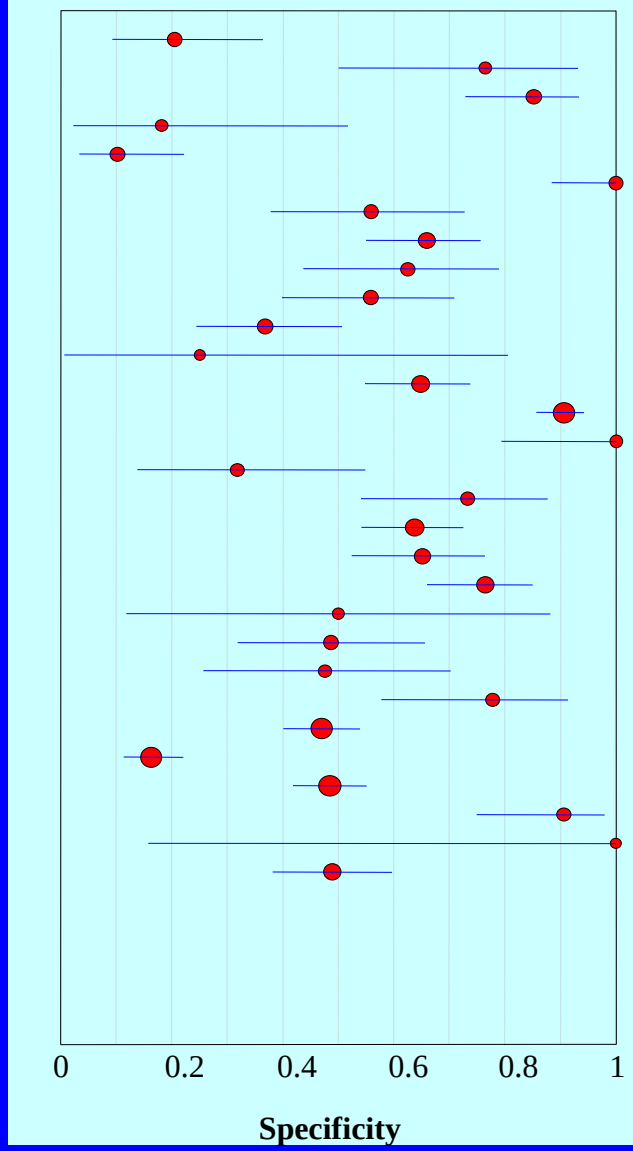
Sensitivity



	Sensitivity (95% CI)	
Ortiz	0.96	(0.91 - 0.99)
Savage	0.97	(0.84 - 1.00)
Hovadhanakul	0.69	(0.39 - 0.91)
Kirkup	0.96	(0.91 - 0.99)
Veridiano	0.99	(0.98 - 1.00)
Helmerhorst	0.92	(0.85 - 0.97)
McIndoe	0.74	(0.63 - 0.83)
Cinel	0.78	(0.67 - 0.86)
Skehan	0.77	(0.64 - 0.87)
Chappatte	1.00	(0.94 - 1.00)
Howe	0.78	(0.70 - 0.84)
Vergote	0.85	(0.77 - 0.91)
Buxton	0.70	(0.62 - 0.78)
Bonardi	0.06	(0.01 - 0.15)
Burger	0.92	(0.86 - 0.97)
Srisomboon	0.95	(0.89 - 0.98)
Massad	0.76	(0.50 - 0.93)
Ang	0.68	(0.60 - 0.76)
Powell	0.90	(0.79 - 0.96)
Baldauf	0.96	(0.94 - 0.98)
Heatley	0.91	(0.81 - 0.97)
Fung	0.88	(0.76 - 0.95)
Ihonor	0.80	(0.64 - 0.91)
Lee	0.63	(0.48 - 0.76)
Barker	0.83	(0.78 - 0.88)
Fambrini	0.93	(0.90 - 0.94)
Diakomanolis	0.90	(0.88 - 0.93)
Byrom	0.74	(0.66 - 0.82)
Weigl	0.80	(0.69 - 0.88)
Boonlikit	0.84	(0.78 - 0.88)

Inconsistency (I-square) = 95.0 %

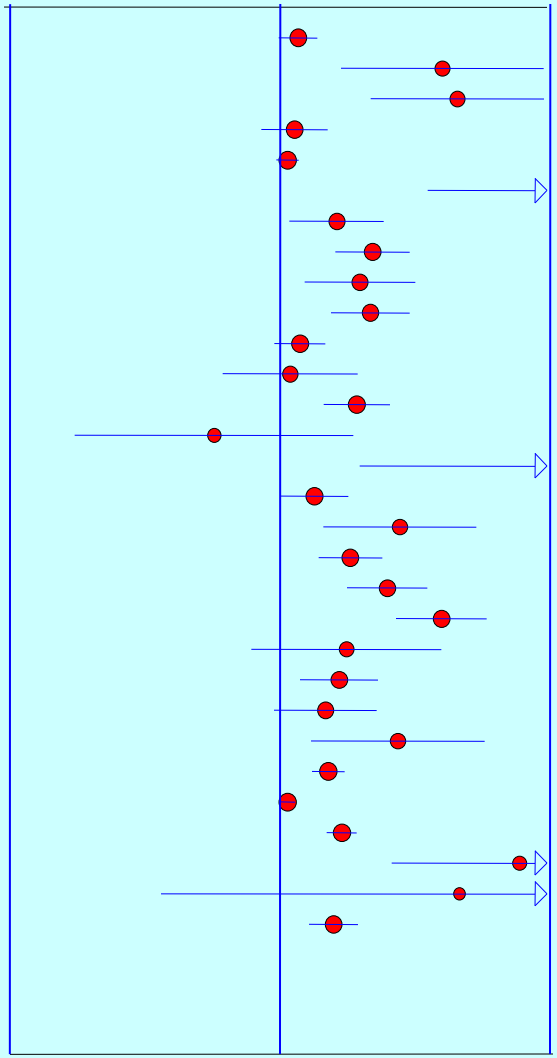
Specificity



	Specificity (95% CI)	
Ortiz	0.21	(0.09 - 0.36)
Savage	0.76	(0.50 - 0.93)
Hovadhanakul	0.85	(0.73 - 0.93)
Kirkup	0.18	(0.02 - 0.52)
Veridiano	0.10	(0.03 - 0.22)
Helmerhorst	1.00	(0.88 - 1.00)
McIndoe	0.56	(0.38 - 0.73)
Cinel	0.66	(0.55 - 0.76)
Skehan	0.63	(0.44 - 0.79)
Chappatte	0.56	(0.40 - 0.71)
Howe	0.37	(0.24 - 0.51)
Vergote	0.25	(0.01 - 0.81)
Buxton	0.65	(0.55 - 0.74)
Bonardi	0.91	(0.86 - 0.94)
Burger	1.00	(0.79 - 1.00)
Srisomboon	0.32	(0.14 - 0.55)
Massad	0.73	(0.54 - 0.88)
Ang	0.64	(0.54 - 0.73)
Powell	0.65	(0.52 - 0.76)
Baldauf	0.76	(0.66 - 0.85)
Heatley	0.50	(0.12 - 0.88)
Fung	0.49	(0.32 - 0.66)
Ihonor	0.48	(0.26 - 0.70)
Lee	0.78	(0.58 - 0.91)
Barker	0.47	(0.40 - 0.54)
Fambrini	0.16	(0.11 - 0.22)
Diakomanolis	0.48	(0.42 - 0.55)
Byrom	0.91	(0.75 - 0.98)
Weigl	1.00	(0.16 - 1.00)
Boonlikit	0.49	(0.38 - 0.60)

Inconsistency (I-square) = 94.1 %

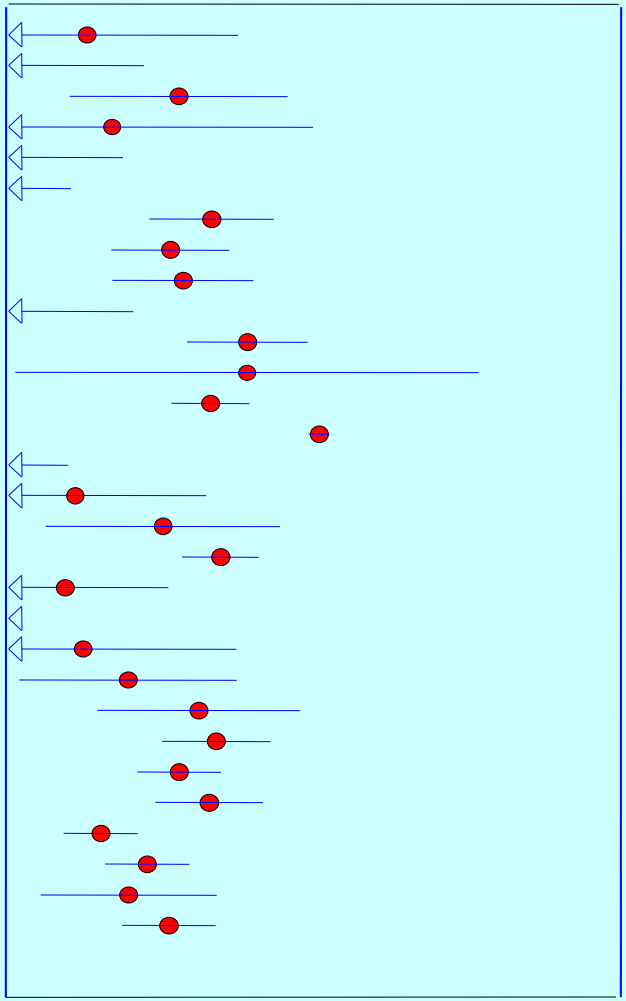
Positive Likelihood Ratio



	Positive LR (95% CI)
Ortiz	1.21 (1.03 - 1.43)
Savage	4.12 (1.75 - 9.73)
Hovadhanakul	4.67 (2.24 - 9.75)
Kirkup	1.17 (0.89 - 1.55)
Veridiano	1.11 (1.01 - 1.22)
Helmerhorst	56.88 (3.64 - 889.79)
McIndoe	1.68 (1.13 - 2.50)
Cinel	2.28 (1.66 - 3.12)
Skehan	2.04 (1.28 - 3.27)
Chappatte	2.24 (1.60 - 3.12)
Howe	1.23 (0.99 - 1.53)
Vergote	1.13 (0.64 - 2.00)
Buxton	1.99 (1.51 - 2.64)
Bonardi	0.59 (0.18 - 1.93)
Burger	31.30 (2.04 - 480.54)
Srisomboon	1.39 (1.04 - 1.85)
Massad	2.87 (1.50 - 5.49)
Ang	1.89 (1.44 - 2.47)
Powell	2.58 (1.84 - 3.63)
Baldauf	4.08 (2.78 - 5.99)
Heatley	1.82 (0.82 - 4.08)
Fung	1.71 (1.23 - 2.38)
Ihonor	1.53 (0.99 - 2.36)
Lee	2.82 (1.35 - 5.90)
Barker	1.56 (1.36 - 1.80)
Fambrini	1.11 (1.04 - 1.18)
Diakomanolis	1.75 (1.54 - 1.99)
Byrom	7.91 (2.68 - 23.36)
Weigl	4.76 (0.38 - 59.95)
Boonlikit	1.64 (1.33 - 2.02)

Inconsistency (I-square) = 91.9 %

Negative Likelihood Ratio



	Negative LR (95% CI)	
Ortiz	0.18	(0.06 - 0.57)
Savage	0.04	(0.01 - 0.28)
Hovadhanakul	0.36	(0.16 - 0.82)
Kirkup	0.22	(0.05 - 1.00)
Veridiano	0.07	(0.02 - 0.24)
Helmerhorst	0.08	(0.04 - 0.16)
McIndoe	0.46	(0.29 - 0.74)
Cinel	0.34	(0.22 - 0.53)
Skehan	0.37	(0.22 - 0.64)
Chappatte	0.02	(0.00 - 0.26)
Howe	0.61	(0.38 - 0.96)
Vergote	0.61	(0.11 - 3.48)
Buxton	0.46	(0.34 - 0.61)
Bonardi	1.04	(0.96 - 1.13)
Burger	0.08	(0.04 - 0.16)
Srisomboon	0.17	(0.06 - 0.45)
Massad	0.32	(0.13 - 0.78)
Ang	0.49	(0.37 - 0.66)
Powell	0.15	(0.07 - 0.33)
Baldauf	0.05	(0.03 - 0.08)
Heatley	0.18	(0.06 - 0.56)
Fung	0.25	(0.11 - 0.56)
Ihonor	0.42	(0.20 - 0.90)
Lee	0.48	(0.32 - 0.72)
Barker	0.36	(0.26 - 0.50)
Fambrini	0.45	(0.30 - 0.68)
Diakomanolis	0.20	(0.15 - 0.27)
Byrom	0.28	(0.21 - 0.39)
Weigl	0.25	(0.13 - 0.48)
Boonlikit	0.34	(0.24 - 0.48)

Inconsistency (I-square) = 97.0 %

Interpreting the findings

- Small number of studies identified
- Study quality generally poor
- Wide sensitivity
- Wide specificity

Comments

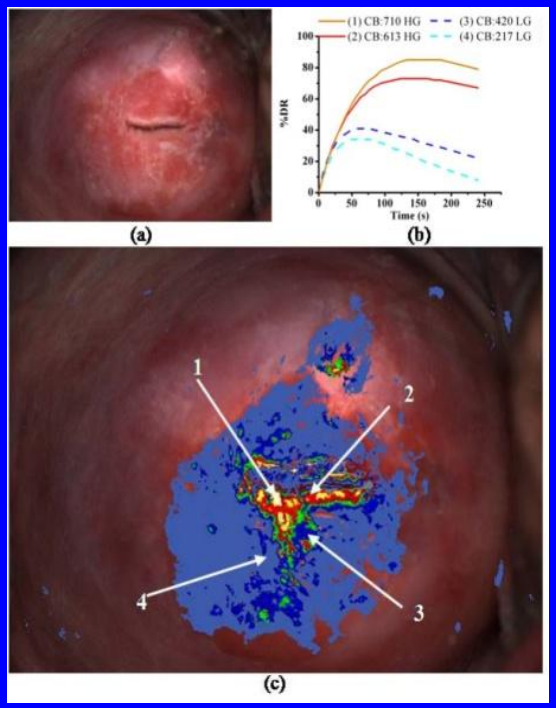
Accuracy as diagnostic test is questionable

Further prospective studies required

Considerations of new technology

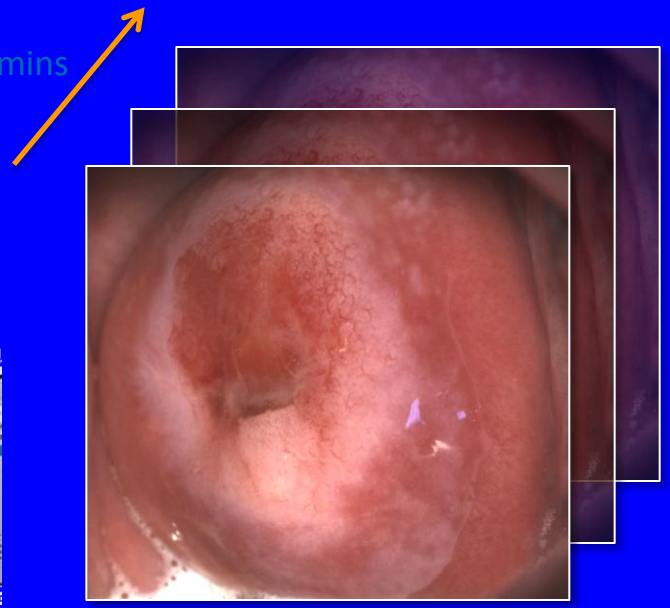
DySIS: A New Standard of Care in Cervical Cancer

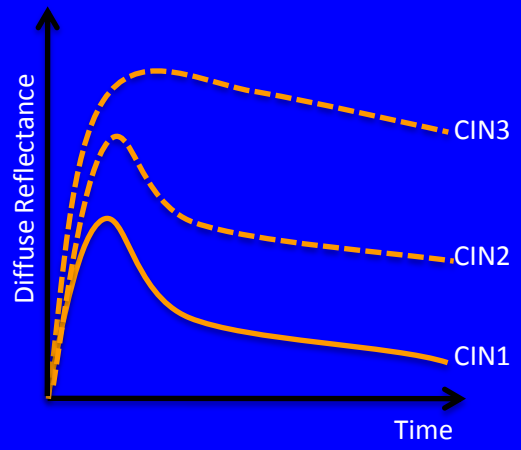
DySIS in non-16 HPV +ve women



Greater sensitivity than conventional colposcopy

DySIS: Technology





- Standard examination process
- High Resolution imaging
- Acetic acid used as normal

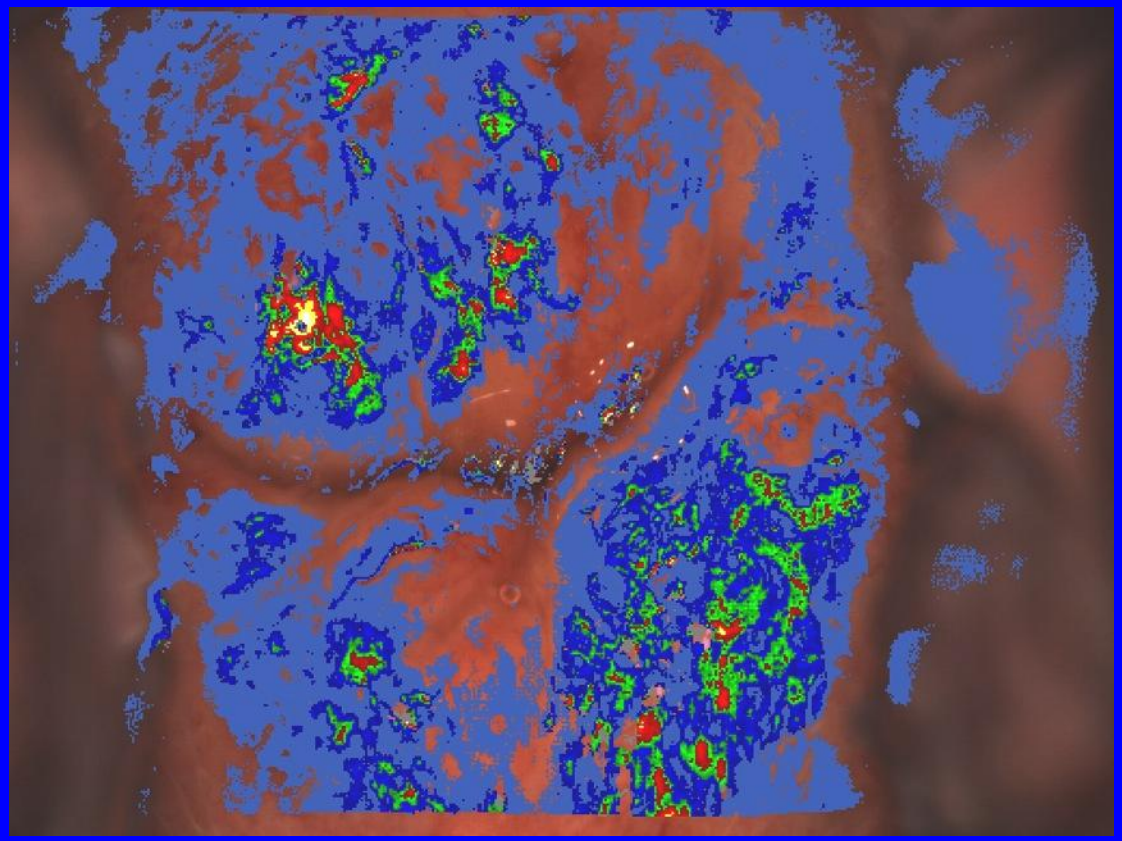
- Sequential images captured
- Dynamic Spectral analysis performed on each pixel (proprietary algorithms)

- Cellular response is measured
- Characteristic curves relate to tissue status at each pixel
- DySISmap is generated

- DySISmap for improved diagnosis and sensitivity

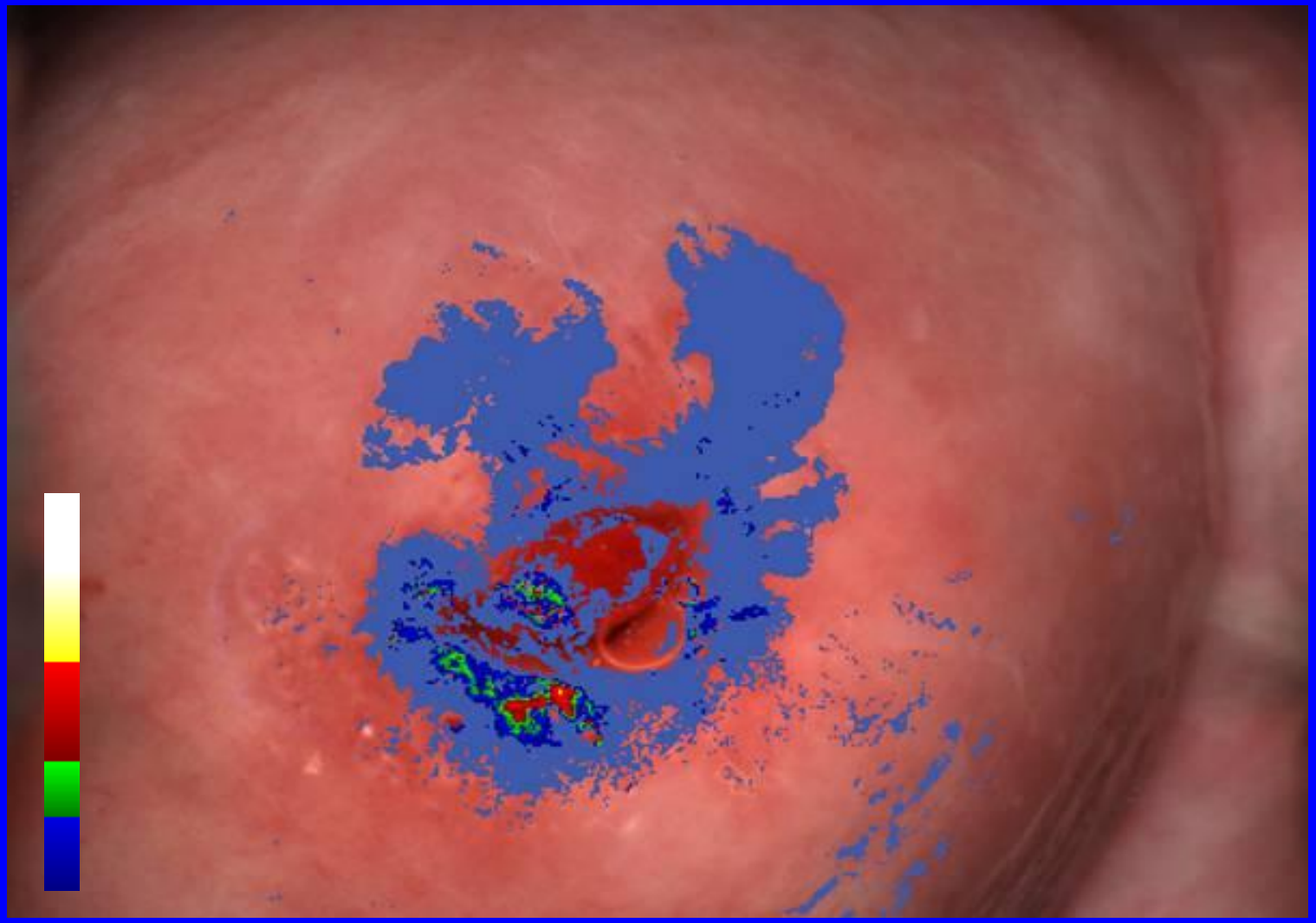
DySISmap colour	Aceto-whitening Level	Cervical Neoplasia	PAP Smear Grade
	Extreme	CIN3	High-grade
	Strong	CIN2	
	Moderate	CIN1	Low-grade
	Mild	HPV Inflammation	

DySISmap



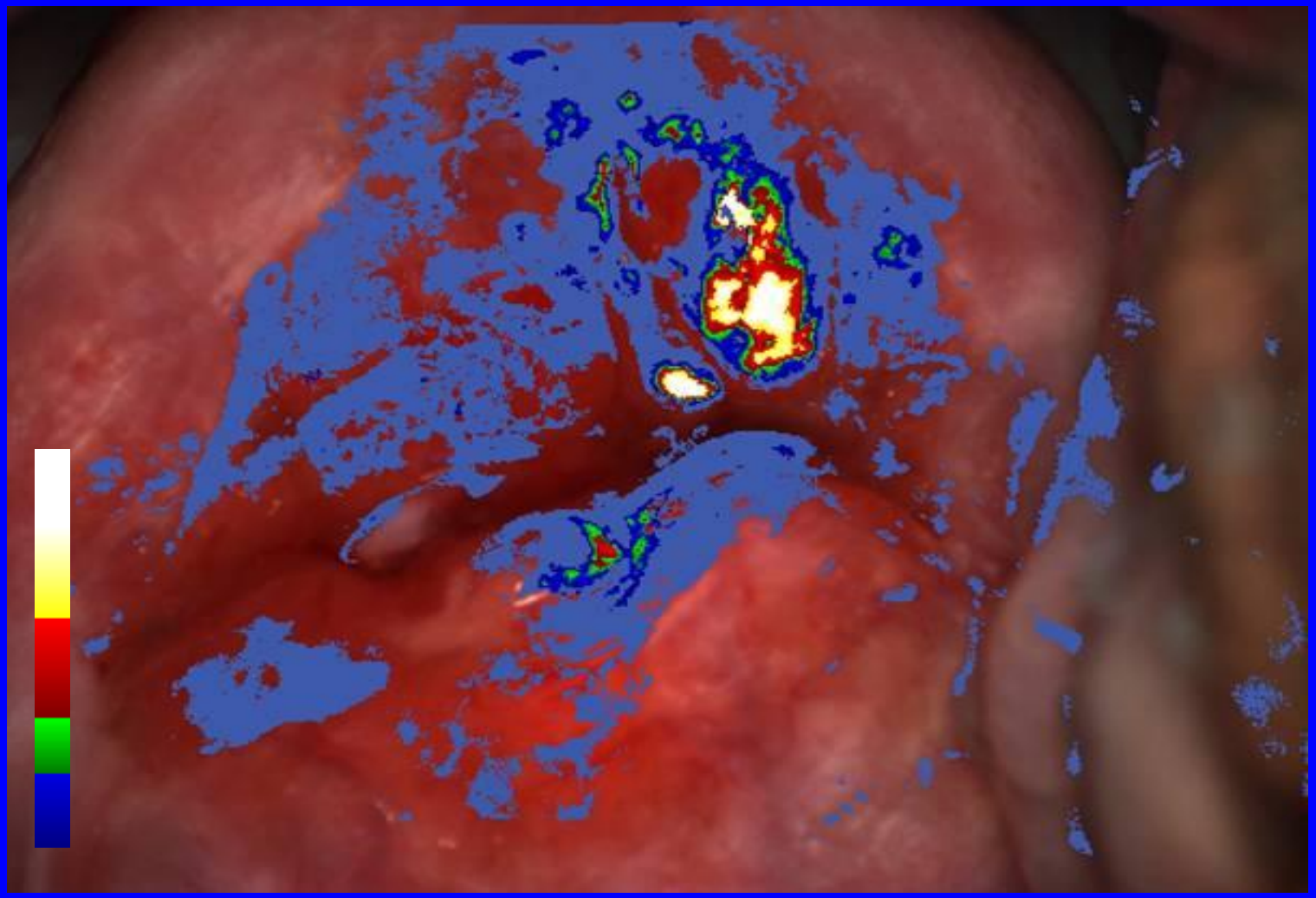
- Quantifies the aceto-whitening effect.
- Removes subjectivity from colposcopic interpretation of aceto-whitening.
- Provides accurate AW information to be used in conjunction with all other colposcopic indicators
- Assists in the identification of appropriate biopsy locations.
- Provides live feedback on biopsy accuracy.
- Creates automatic electronic documentation of the disease state, extent and margins.

DySIS: Acetowhitening mapping



Red, yellow and white areas indicate intense/long lasting acetowhitening

DySIS: Acetowhitening mapping



Red, yellow and white areas indicate intense/long lasting acetowhitening

Colposcopic diagnosis

Effective when contexual and multifactorial

Performs well in suspected HG disease

Lacks sensitivity in LG referrals

How Good a Diagnostic Tool is Colposcopy?

?