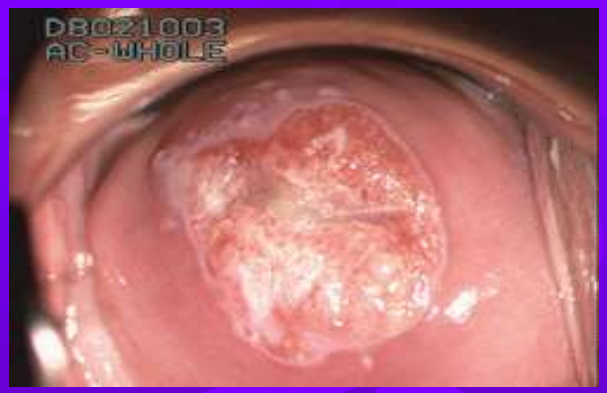
ΚΡΙΤΙΚΗ ΠΑΡΟΥΣΙΑΣΗ ΓΙΑ ΤΗΝ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΩΝ ΕΝΔΟΕΠΙΘΗΛΙΑΚΩΝ ΑΛΛΟΙΩΣΕΩΝ ΤΟΥ ΤΡΑΧΗΛΟΥ ΤΗΣ ΜΗΤΡΑΣ

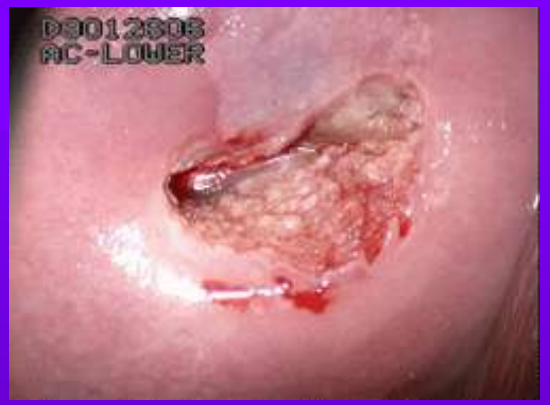
Ασημάκης Γ. Παππάς

Επικουρικός Επιμελητής

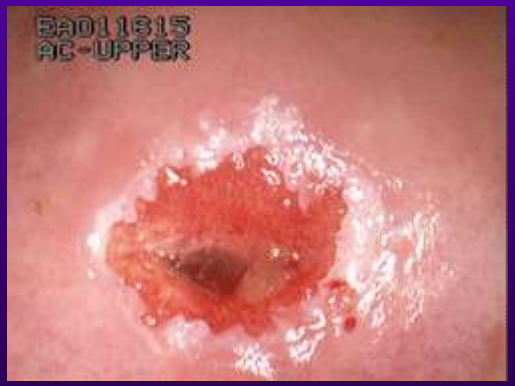
Διδάκτωρ Πανεπιστημίου Αθηνών

Γ΄ Μαιευτική Γυναικολογική Κλινική, Π.Γ.Ν. «ΑΤΤΙΚΟΝ»

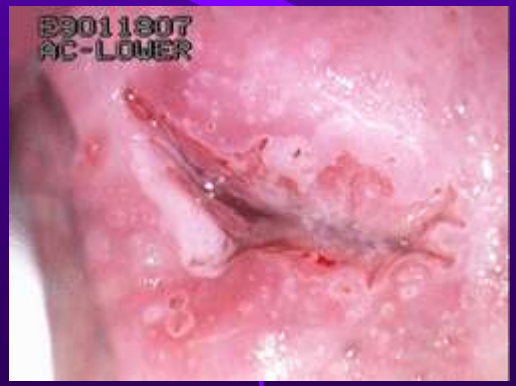




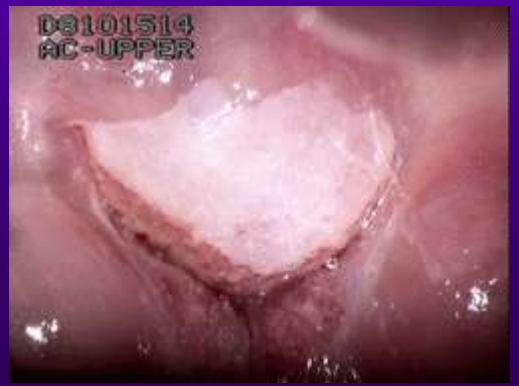
HPV infection of the cervix



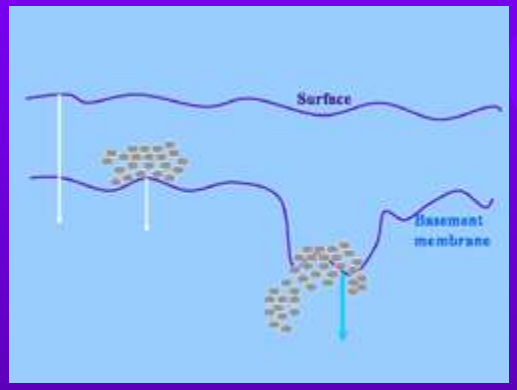
CIN1

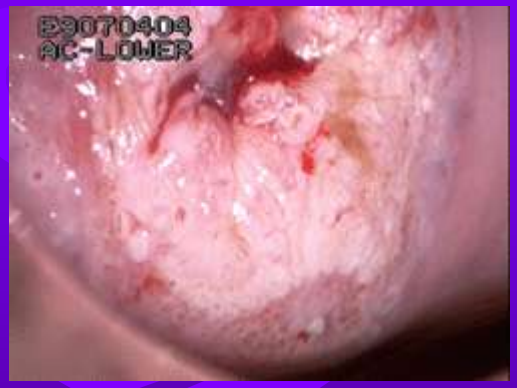


CIN2

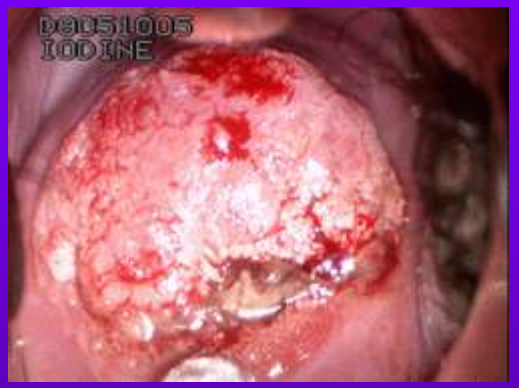


CIN3

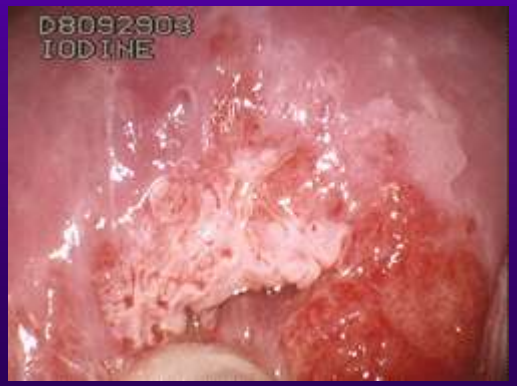




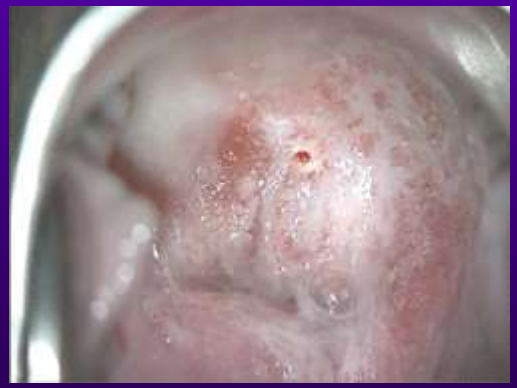
Micro-invasive lesions of the cervix



Invasive squamous carcinoma of the cervix

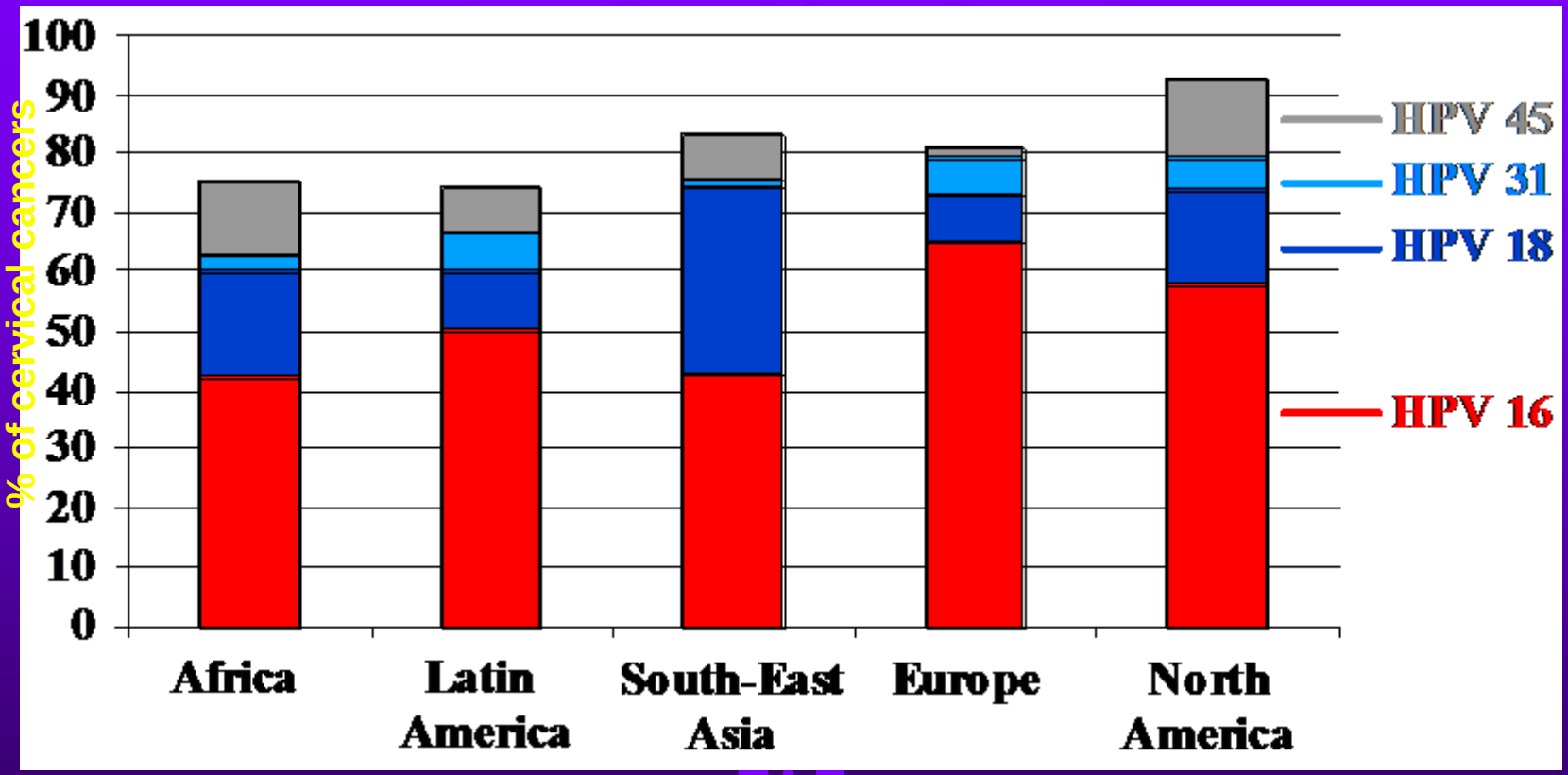


High grade CGIN



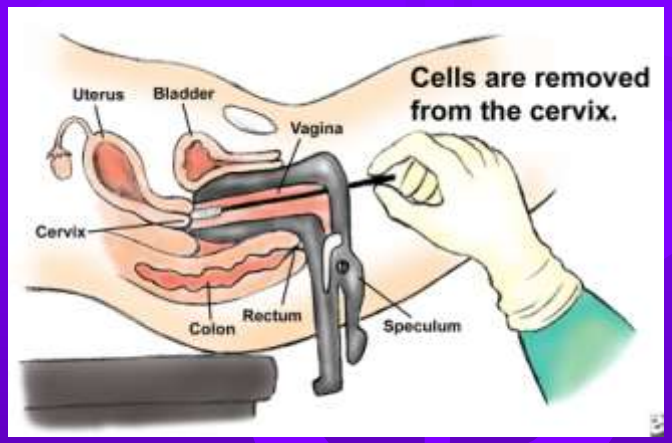
Adenocarcinoma of the cervix

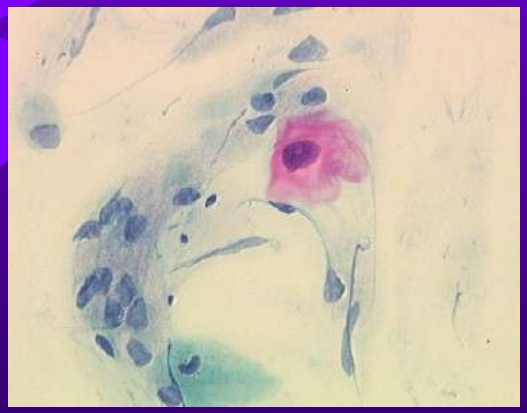
Distribution of HPV Types in Cervical Cancer by Geographical Region



Bosch et al, JNCI, 1995

Screening Test: Κυτταρολογία Τραχήλου





- Ευαισθησία: Το ποσοστό των γυναικών που πάσχουν από τη νόσο, τις οποίες το τεστ σωστά αναγνωρίζει και είναι θετικό.
- Ειδικότητα: Το ποσοστό των γυναικών που είναι υγιείς , για τις οποίες το τεστ είναι αρνητικό.

Η αποτελεσματικότητα του Pap test :

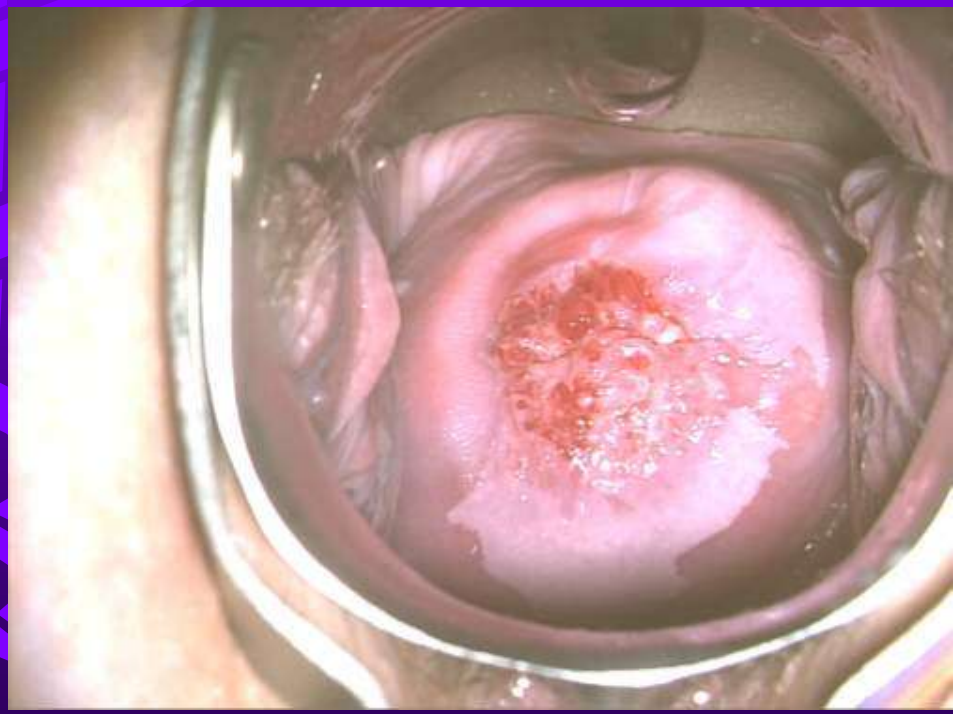
- Ευαισθησία= 51% για CIN I ή παραπάνω
  - Εύρος 37% έως 84%
- Ειδικότητα = 98% για CIN I ή παραπάνω

  Εύρος 86% to 100%
- Οι μελέτες αυτές είναι από μετα-ανάλυση μελετών cross-sectional (AHCPR 1999).
- Πολλές μελέτες από το ACCP έχουν επίσης ανακαλύψει μια ευαισθησία του Pap test σε επίπεδα του 50% στην καλύτερη περίπτωση.

DIAGNOSTIC ACCURACY OF COLPOSCOPY

Mitchell MF. *Obstetrics & Gynecology* 1998

- Gold standard
- Limitations :
  - Specificity 48 - 69%
  - Sensibility 85 - 96%



THE LONG ROAD TO COLPOSCOPY

The human eye may be wrong…

It takes some time and experience to properly analyze what you see

- American Society for Colposcopy and Cervical Pathology
- Australian Society for Colposcopy and Cervical Pathology
- Brasilian Society of Cervical Pathology and Colposcopy
- European Federation for Colposcopy and Cervical Pathology
- The Hong Kong Society for Colposcopy and Cervical Pathology
- International Federation for Cervical Pathology & Colposcopy (IFCPC)
- Society for Colposcopy and Cervical Pathology of Singapore
- CancerHelp UK
- Cervical Screening Wales website
- **NHSCSP:** Standards and quality in colposcopy - publication 20.
- European Guidelines for Quality Assurance in Cervical Cancer Screening
- **ECCA** - European Cervical Cancer Association
- **IARC** - International Agency for Research on Cancer.

Bethesda, etc.

DESCRIPTION	DEGREES OF SEVERITY	EXPLANATION
Descriptive System	Mild dysplasia, Moderate dysplasia, Severe dysplasia	
CIN System	CIN 1, CIN 2, CIN 3	CIN stands for cervical intraepithelial neoplasia
Bethesda System (2001)	•ASC-US (Atypical Squamous Cells of Undetermined Significance) •ASC-H (Atypical Squamous Cells-can not exclude HSIL) •Low-Grade SIL (LSIL) •High-Grade SIL (HSIL)	•Means the results look borderline between "normal" and "abnormal" • Borderline results, but may really include High-Grade lesions • SIL stands for squamous intraepithelial lesion
Class System	Class 1, Class 2, Class 3, Class 4	This system is no longer widely used

2006

- The American Society for Colposcopy and Cervical Pathology (ASCCP) has offered to share consensus clinical guidelines and educational resources with International Gynecological Cancer Society (IGCS).
- 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests
- A group of 146 experts representing 29 organizations and professional societies met September 18-19, 2006, in Bethesda, MD, to develop revised evidence-based,consensus guidelines for managing women with abnormal cervical cancer screening tests.

Definitions of Terms Utilized in the Consensus Guidelines

- Colposcopy is the examination of the cervix, vagina, and, in some instances the vulva, with the colposcope after the application of a 3-5% acetic acid solution coupled with obtaining colposcopically-directed biopsies of all lesions suspected of representing neoplasia.
- Endocervical sampling includes obtaining a specimen for either histological evaluation using an endocervical curette or a cyto brush or for cytological evaluation using a cyto brush.
- Endocervical assessment is the process of evaluating the endocervicalcanal for the presence of neoplasia using either a colposcope or endocervical sampling.
- Diagnostic excisional procedure is the process of obtaining a specimen from the transformation zone and endocervical canal for histological evaluation and includes laser conization, cold-knife conization, loop electrosurgical excision (i.e., LEEP), and loop electrosurgical conization.
- Satisfactory colposcopy indicates that the entire squamo columnar junction and the margin of any visible lesion can be visualized with the colposcope.
- Endometrial sampling includes obtaining a specimen for histological evaluation u sing an endometrial biopsy or a “dilatation and curettage” or hysteroscopy.

ASCUS / LGSIL

- Recommendations for managing atypical squamous cells of undetermined significance and low-grade squamous intraepithelial lesion (LSIL) are essentially unchanged.
- Changes were made for managing these conditions in adolescents for whom cytological follow-up for 2 years was approved.
- HPV DNA testing and colposcopy are unacceptable for adolescents with ASC-US.

HGSIL

- Recommendations for managing high-grade squamous intraepithelial lesion (HSIL) and atypical glandular cells(AGC) also underwent only minor modifications.
- More emphasis is placed on immediate screen-and-treat approaches for HSIL.
- An immediate loop electrosurgical excision or colposcopy with endocervical assessment is an acceptable method for managing women with HSIL

HPV testing

- Human papillomavirus (HPV) testing is incorporated into the management of AGC after their initial evaluation with colposcopy and endometrial sampling.
- The 2004 Interim Guidance for HPV testing as an adjunct to cervical cytology for screening in women 30 years of age and older was formally adopted with only very minor modifications.
- HPV DNA testing and colposcopy are unacceptable for adolescents with ASC-US.
- Most newly acquired HPV infections clear spontaneously and the prevalence of HPV DNA positivity drops with age from a peak in adolescents and women in their 20s.

RECOMMENDED MANAGEMENT DIFFERENT COMBINATIONS OF RESULTS
General recommendations

- For women 30 years of age and older who have a cytology result of “negative for an intraepithelial lesion or malignancy” but test positive for HPV, repeat cytology and HPV testing at 12 months is preferred. If on repeat testing HPV is detected, colposcopy is recommended.

RECOMMENDED MANAGEMENT DIFFERENT COMBINATIONS OF RESULTS
General recommendations

- It is recommended that HPV DNA testing target only high-risk (oncogenic) HPV types. There is no clinical utility in testing for other (nononcogenic) types.

- Testing for other (nononcogenic) HPV types when screening for cervical neoplasia, or during the management and follow-up of women with abnormal cervical cytology or cervical neoplasia, is unacceptable.

Colposcopy and Programme management, NHSCSP No 20, April 2004
Referral Guidelines for Colpocsopy in UK

Squamous cell changes

- after 3 borderline smear test

- ideally after one mild dyskaryotic smear or after 2 mild smear tests

Frequency of screening

Age group (years)	Frequency of screening
25	First invitation
25–49	Three yearly
50–64	Five yearly
65+	Only screen those who have not been screened since age 50 or those who have had recentabnormal tests

Why not under 25?

- Recently published research and experience from the cervical screening programme have shown that screening women under the age of 25 years may do more harm than good.

- Cervical cancer is very rare in women under 25.

  In 2002, five deaths from cervical cancer were registered amongwomen aged between 15 and 24.

- In total, 26 cases of cervical cancer were registered. By contrast, there were 55 000 women aged 20–24 with abnormal (borderline or worse) smears.

Why not after 65?

- The prevalence of CIN 3 and invasive cancer in women over the age of 50 is low: 11 in 100 000 in well screened women compared with a prevalence rate of 59 in 100 000 women in the population as a whole.

- Women who were diagnosed with invasive cancer after the age of 50 had not participated adequately in the cervical screening programme.

Summary of standards I

- Women should be referred for colposcopy after three consecutive inadequate samples.
- Women should be referred for colposcopy after three tests reportedas borderline nuclear change in squamous cells in a series, without the woman being returned to routine recall.
- Women should be referred for colposcopy after one test reported as borderline nuclear change in endocervical cells.
- Women should be referred for colposcopy if they have had three tests reported as abnormal at any grade in a 10-year period.

Summary of standards II

- Ideally, women should be referred for colposcopy after one test reported as mild dyskaryosis, but it remains acceptable to recommend a repeat test.
- Women must be referred after two tests reported as mild dyskaryosis without a return to routine recall.
- Women must be referred for colposcopy after one test reported as moderate dyskaryosis (**100%**).
- Women must be referred for colposcopy after one test reported as severe dyskaryosis (**100%**).
- Women must be referred for colposcopy after one test reported as possible invasion (**100%**). They should be seen urgently within two weeks of referral (**90%**).

Summary of standards III

- Women must be referred for colposcopy after one test reported as glandular neoplasia (**100%**). They should be seen urgently within two weeks of referral (**90%**).
- Women should be referred for colposcopy if they have been treated for CIN and have not been returned to routine recall and a subsequent test is reported as mild dyskaryosis or worse (**100%**).
- At least **90%** of women with an abnormal test result should be seen in a colposcopy clinic within eight weeks of referral.
- At least **90%** of women with a test result of moderate or severe dyskaryosis should be seen in a colposcopy clinic within four weeks of referral.

Summary of standards IV

- An excisional form of biopsy is recommended (**95%**):

-when colposcopic appearances indicate high grade abnormality –

-when low grade colposcopic change is associated with severe dyskaryosis or worse

-when a lesion extends into the canal

- All patients must have a biopsy or biopsies taken prior to local destructive treatment (**100%**).

- Biopsy should be carried out unless an excisional treatment is planned, when the cytology indicates persisting moderate dyskaryosis or worse, and always when a recognisably atypical transformationzone is present (**100%**). Pregnancy is an exception.

- Of all biopsies taken (directed and excisional), **> 90%** should be suitable for histological interpretation.

- For those with satisfactory colposcopic examination, the predictive value of a colposcopic diagnosis of a high grade lesion (CIN 2 or worse) should be at least **65%**.

Age range & screening interval

- WHO (2006) recommendation for new programmes:
  - no screening women <25 yrs
  - 3 year interval for women 25-49 yrs
  - 5 year interval for women >50 yrs.

Review of the Guidelines for Cervical Screening in New Zealand

Update 1999 guidelines

The introduction of HPV testing (from 1 July 2009)

Age range and screening interval

- All women aged 20 years who have ever been sexually active should be invited to have a smear.
- Women 20-69 years should be offered a smear test every 3 years.
- Women under 20 years **must not** be routinely screened
  - the risk of cervical cancer is extremely low in this age group
  - can cause more harm than benefit

Management of women with unsatisfactory smears

- Repeat the smear within 3 months
- *There may be situations where LBC offers some advantage over conventional smears, such as women with:*
  - *excessive cervical mucus, discharge or blood*
  - *recurrent inflammatory smears*
  - *recurrent unsatisfactory smears*

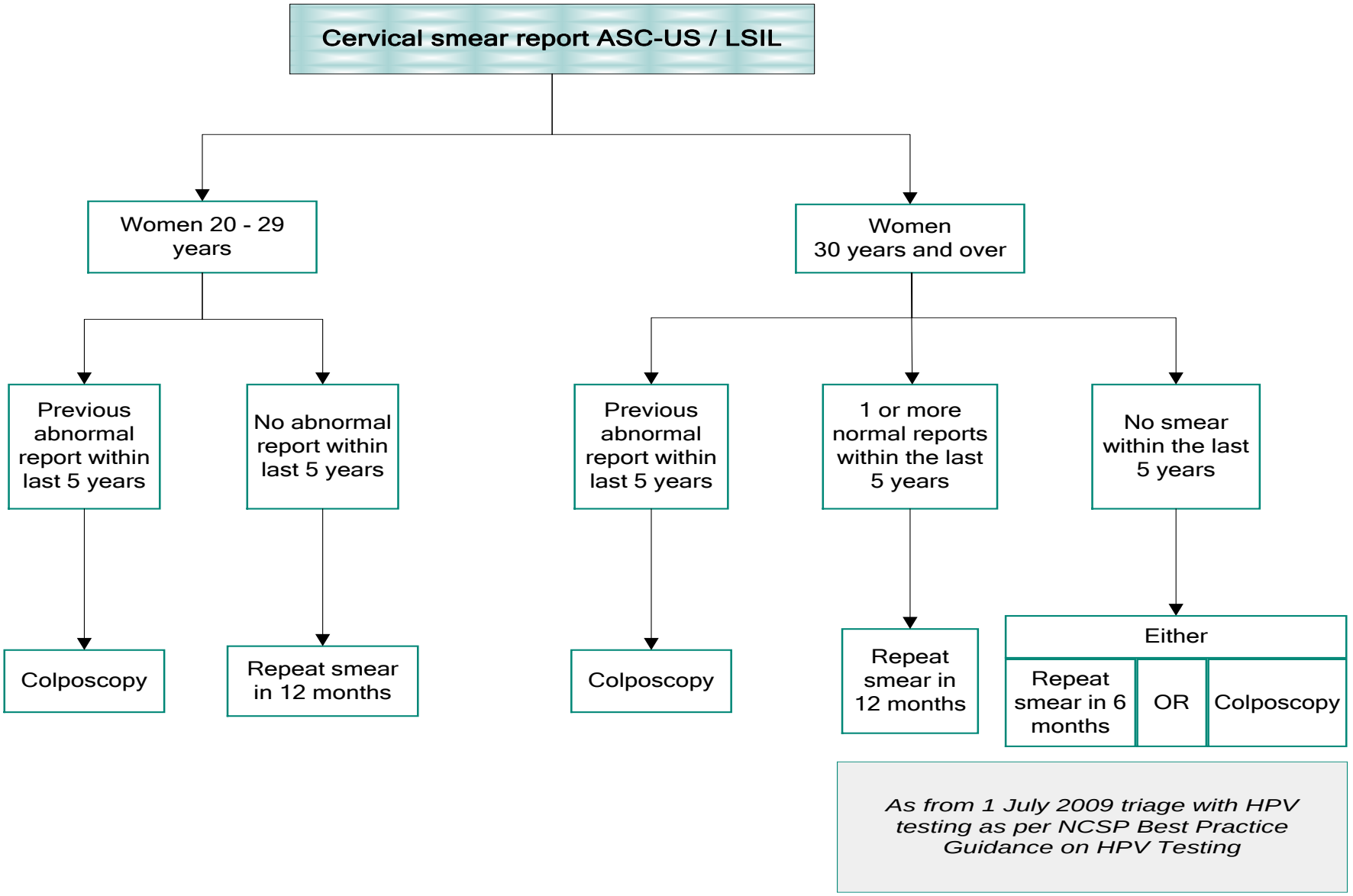
Liquid Based Cytology Policy (2006)

Low Grade:
ASC-US or LSIL smear report

CERVICAL SMEAR REPORT	GUIDELINE
ASC-US or LSIL	Women aged 20 - 29 years with no abnormal smear reports within the last 5 years Repeat cervical smear in 12 months
	Until 1 July 2009: Women aged 30 years and over with one (or more) normal smear reports in the last 5 years Repeat cervical smear in 12 months Women aged 30 years and over who haven't had a smear in the last 5 years should be offered either a repeat smear within 6 months or a referral to colposcopy. *HrHPV testing as from 1 July 2009*

ie. extends time for repeat smear from 6 to 12 months
- HrHPV testing from 1 July 2009

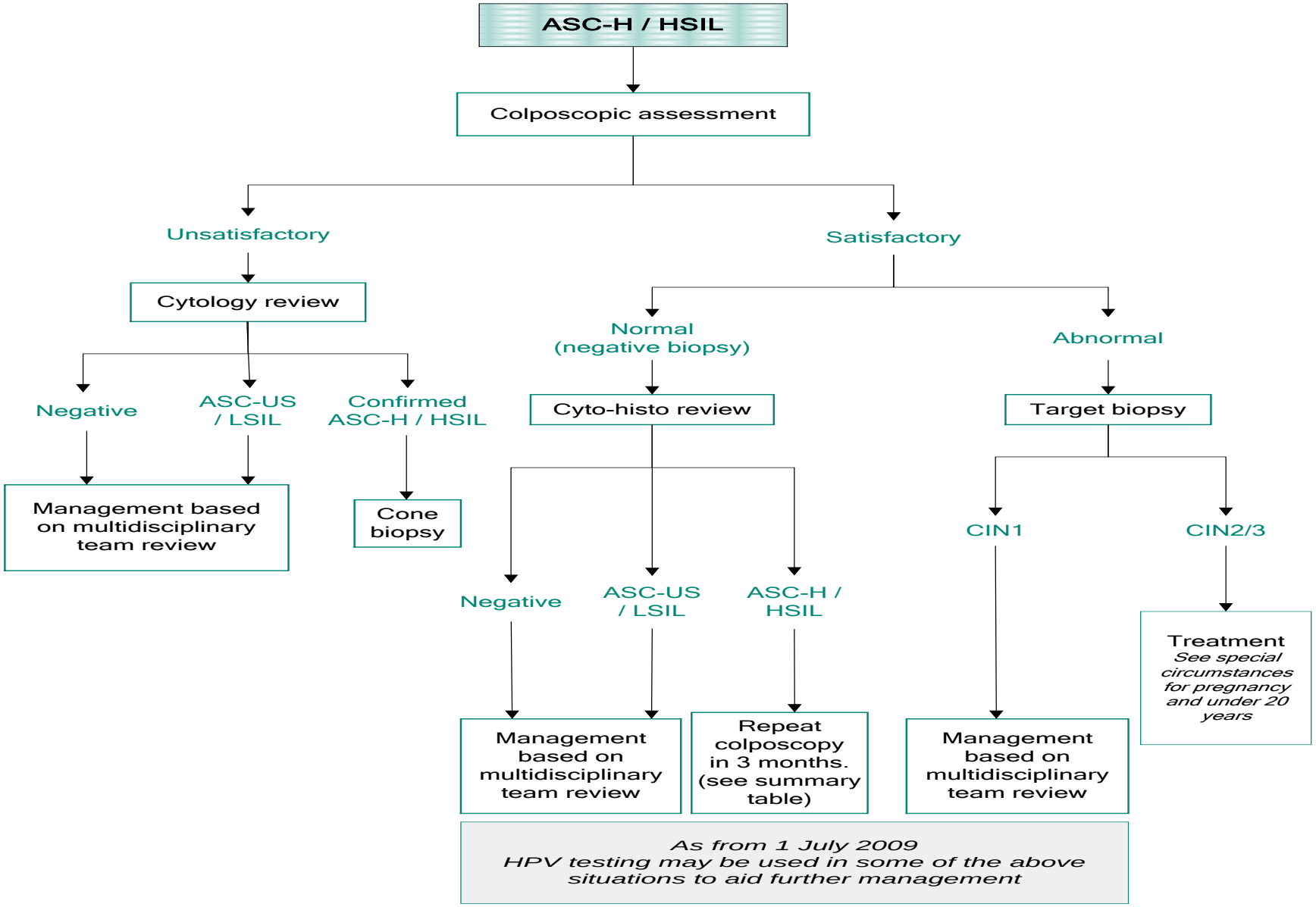
Low Grade: flowchart



High Grade: ASC-H/HSIL

CERVICAL SMEAR REPORT	GUIDELINE
ASC-H	Refer for colposcopy
HSIL	Refer for colposcopy and targeted biopsy where indicated.
HSIL with suspected invasion	Urgent referral to a colposcopist or oncologist

High Grade: ASC-H /HSIL



High Grade: glandular AGC/AIS/AC - cytology

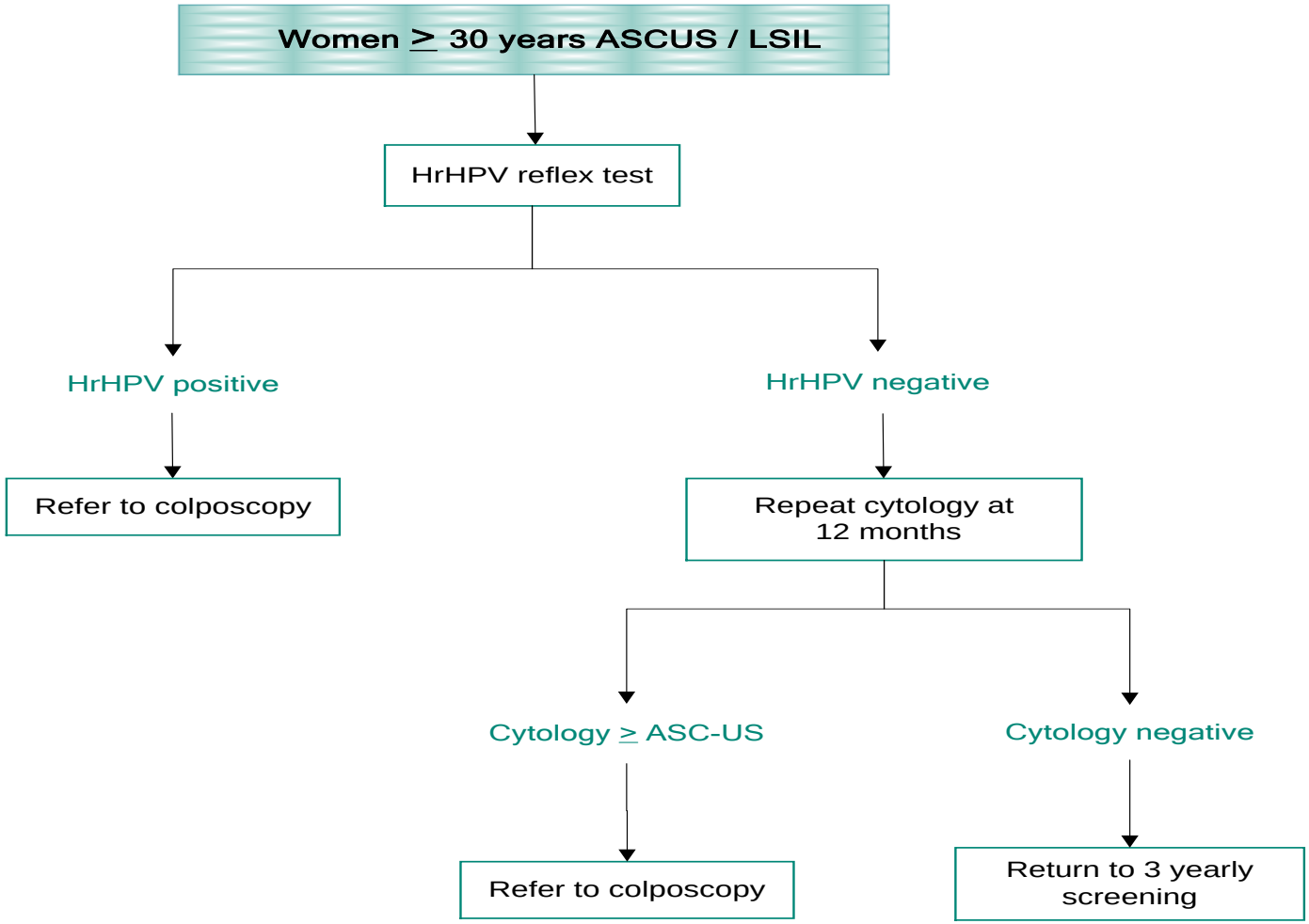
- Proportionally, cervical adenocarcinomas are increasing.
- Glandular lesions carry a significant risk of cancer.
- Colposcopic assessment is mandatory for cytology suggesting glandular abnormalities.

CERVICAL SMEAR REPORT	GUIDELINE
AGC or AIS or adenocarcinoma	Refer to a colposcopist or to an oncologist.

Triage with HPV testing

- For:
  - Women 30 years and over
  - No abnormal smear reports in the last 5 years
  - Low-grade smear result (ASCUS/LSIL)
- Use of 'reflex testing' – LBC or co-collection
- Women who test positive for HPV will be referred to colposcopy. Women who are HPV negative return to 3 yearly recall (following another negative smear).

HPV triage ASC-US/LSIL



HPV testing: post treatment

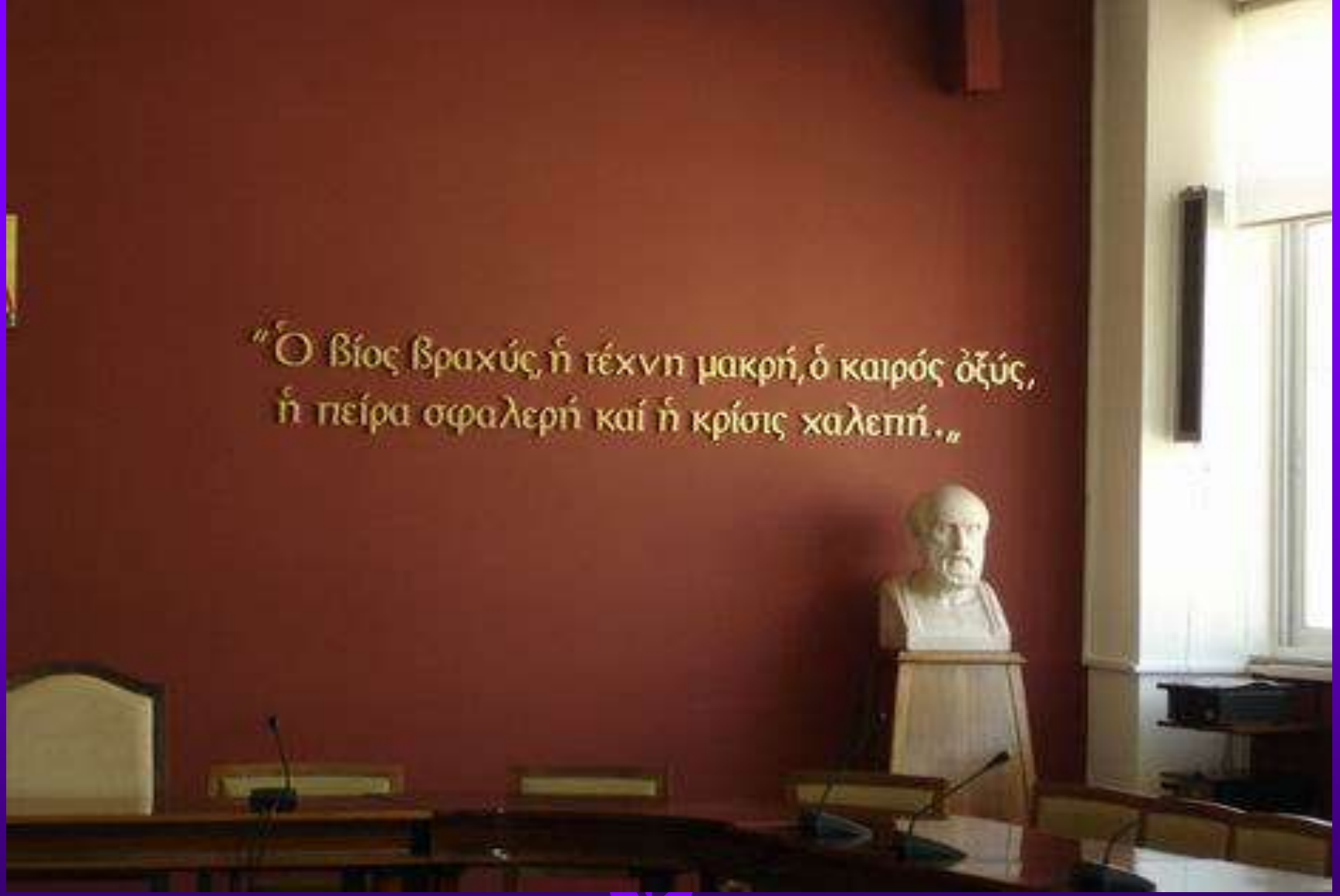
- Following treatment for pre-cancerous lesions
- Substitutes for annual smears for life
- 2 negative HPV and smear tests - return to normal screening
- Will require close monitoring of long term safety

For more information on cervical cancer prevention:

- The Alliance for Cervical Cancer Prevention (ACCP) www.alliance-cxca.org
- ACCP partner organizations:
  - EngenderHealth www.engenderhealth.org
  - International Agency for Research on Cancer (IARC) www.iarc.fr
  - JHPIEGO www.jhpiego.org
  - Pan American Health Organization (PAHO) www.paho.org
  - Program for Appropriate Technology in Health (PATH) www.path.org

Συμπεράσματα

- Οργανωμένη εκπαίδευση γυναικολόγων
- Δημιουργία πρωτοκόλλων στην Ελλάδα καθολικά αποδεκτά
- Σεβασμό στη γυναίκα
- Ενημέρωση του πληθυσμού



Ευχαριστώ πολύ!!!!