

# Conventional cervical smears were better than monolayer cytology or human papillomavirus testing for detecting cervical intraepithelial neoplasia

Coste J, Cochand-Priollet B, de Cremoux P, et al. Cross sectional study of conventional cervical smear, monolayer cytology, and human papillomavirus DNA testing for cervical cancer screening. *BMJ* 2003;326:733-6.

**QUESTION:** In women referred for colposcopy or presenting for routine smears, is monolayer cytology (MLC) or human papillomavirus (HPV) testing more accurate than the conventional cervical smear (CCS) test for detecting cervical neoplasia?

## Design

Blinded comparison of the CCS test, MLC, and HPV testing with colposcopy and histology as the reference standard.

## Setting

2 university centres and 2 private practices in France.

## Participants

828 women (mean age 38 y) who had been referred for colposcopy and 1757 women (mean age 33 y) who presented for routine smears.

## Description of tests and diagnostic standard

All women were evaluated by the 3 methods (CCS test, MLC, and HPV testing), and by colposcopy followed by biopsy if abnormalities were detected. After the CCS test, the remaining portion of the sample was used for the monolayer slide and for HPV testing. Smear abnormalities were classified into 5 ordered categories (negative, atypical squamous/glandular cells of undetermined significance, low or high grade squamous intraepithelial lesions, and invasive cancer), and the reference standard was classified into 4 ordered categories (normal colposcopy or negative biopsy result; cervical intraepithelial neoplasia [CIN] grades I, II, and III; and invasive carcinoma). The clinical readings and optimised interpretations (2 blinded readings followed, if necessary, by consensus) were done by experienced cytopathologists.

## Main outcome measures

Sensitivity and specificity, and positive and negative likelihood ratios.

## Main results

65% of women referred for colposcopy and 5.8% of women presenting for routine smears had cervical intraepithelial neoplasia ( $\geq$  CIN I). Sensitivity and specificity, and positive and negative likelihood ratios for the 3 methods are in the table.

*Diagnostic properties of the conventional cervical smear (CCS) test, monolayer cytology (MLC), and human papillomavirus (HPV) testing for detecting cervical intraepithelial neoplasia\**

Test	Women referred for colposcopy				Women presenting for routine smears			
	Sensitivity (95% CI)	Specificity (CI)	+LR	-LR	Sensitivity (CI)	Specificity (CI)	+LR	-LR
CCS test†	95% (93 to 97)	60% (55 to 66)	2.4	0.1	72% (63 to 80)	94% (93 to 95)	11.5	0.3
MLC†	92% (90 to 95)	58% (52 to 64)	2.2	0.1	66% (56 to 75)	91% (90 to 93)	7.5	0.4
HPV testing	82% (77 to 86)	74% (67 to 80)	3.1	0.3	69% (58 to 79)	83% (81 to 85)	4.1	0.4

\*Abnormality threshold = atypical squamous cells or glandular cells of undetermined significance for CCS test and MLC, and relative light units  $>1$  for HPV testing. Diagnostic terms defined in glossary. †Clinical reading.

## Conclusion

In women referred for colposcopy or presenting for routine smears, the conventional cervical smear test was more accurate than monolayer cytology or human papillomavirus testing for detecting cervical neoplasia.

## COMMENTARY

Coste *et al* compared cytological results from the CCS test, MLC, and high risk HPV testing with the gold standard (colposcopy and biopsy if indicated) in women referred for colposcopy or presenting for routine smears. Thus, they performed a standard diagnostic study that avoided verification bias.

It should be noted, however, that the cytologists were initially inexperienced in MLC and that the MLC smear was prepared from the sample that remained after producing the CCS test. Such a fixed sequence may introduce some bias at the expense of MLC.

The authors conclude that the CCS test consistently had better sensitivity and specificity than MLC for detecting CIN  $\geq$  I or CIN  $\geq$  II. However, an overlap of the confidence intervals weakens the strength of this claim. In our view, these results do not support any meaningful differences in diagnostic indicators between the 2 cytology systems. They support worse results for HPV testing at detecting CIN  $\geq$  I (in women referred for colposcopy) but better results for detecting CIN  $\geq$  II in women who presented for screening (sensitivity for HPV testing was 96%, whereas that for the CCS test at a threshold  $\geq$  high grade squamous intraepithelial lesions was only 51%; although HPV testing had considerably lower specificity). It might be interesting to document this finding in different age groups.

Although the study was rigorously done, its results will have to be considered together with findings from other studies. The evidence to support any firm choice between the CCS test and MLC is still insufficient. For HPV testing, the picture may be different. The initial expectations of good performance with respect to initial screening are not being confirmed. However, interest as well as the supporting evidence that favours triage with HPV testing in women with equivocal papanicolaou smears is growing.<sup>1</sup>

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1 Cox JT. American Society for Colposcopy and Cervical Pathology. The clinician's view: role of human papillomavirus testing in the American Society for Colposcopy and Cervical Pathology Guidelines for the management of abnormal cervical cytology and cervical cancer precursors. *Arch Pathol Lab Med* 2003;127:950-8.