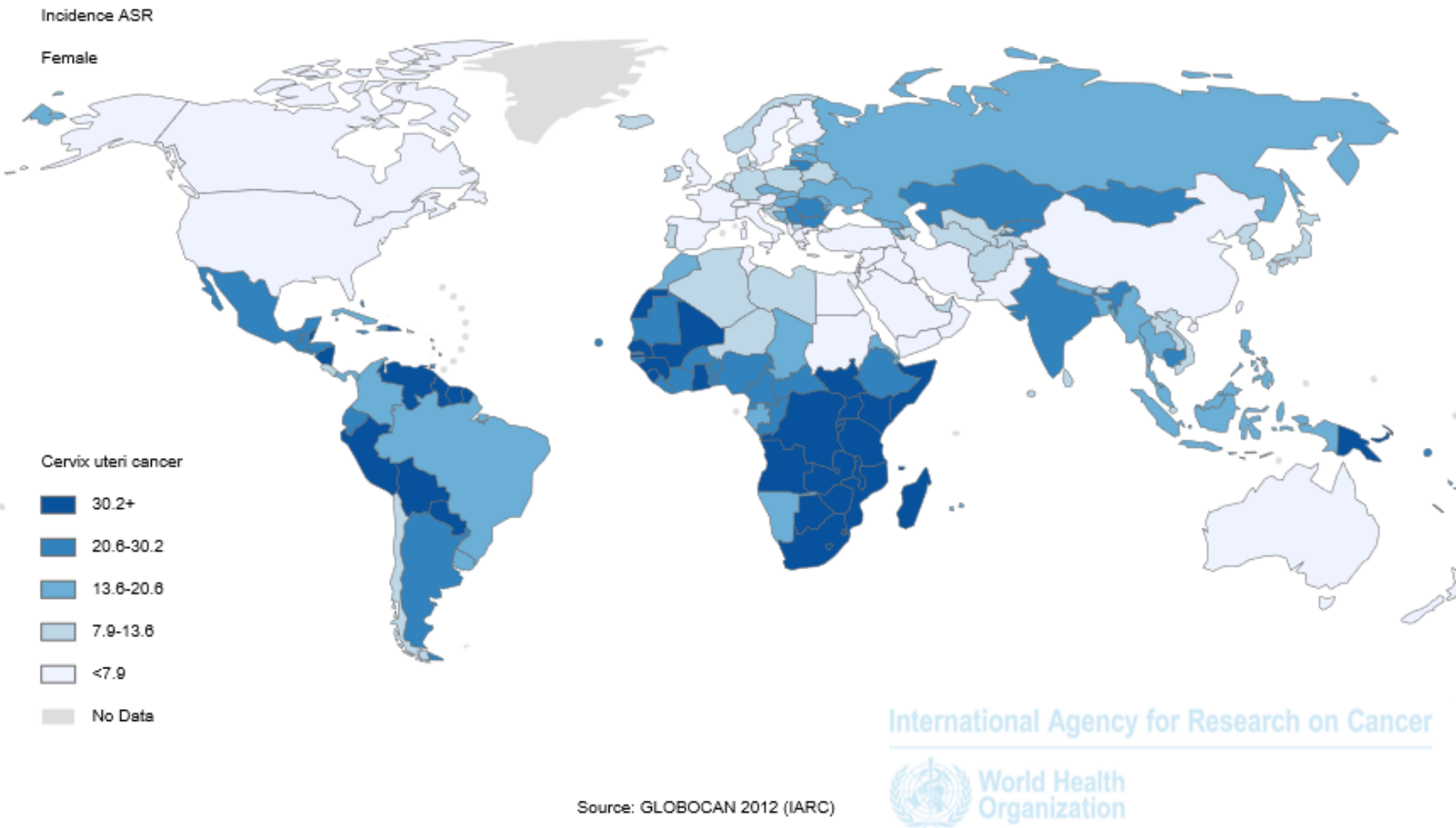
CANCER DU COL UTERIN:
70 ans de despistage et le développement

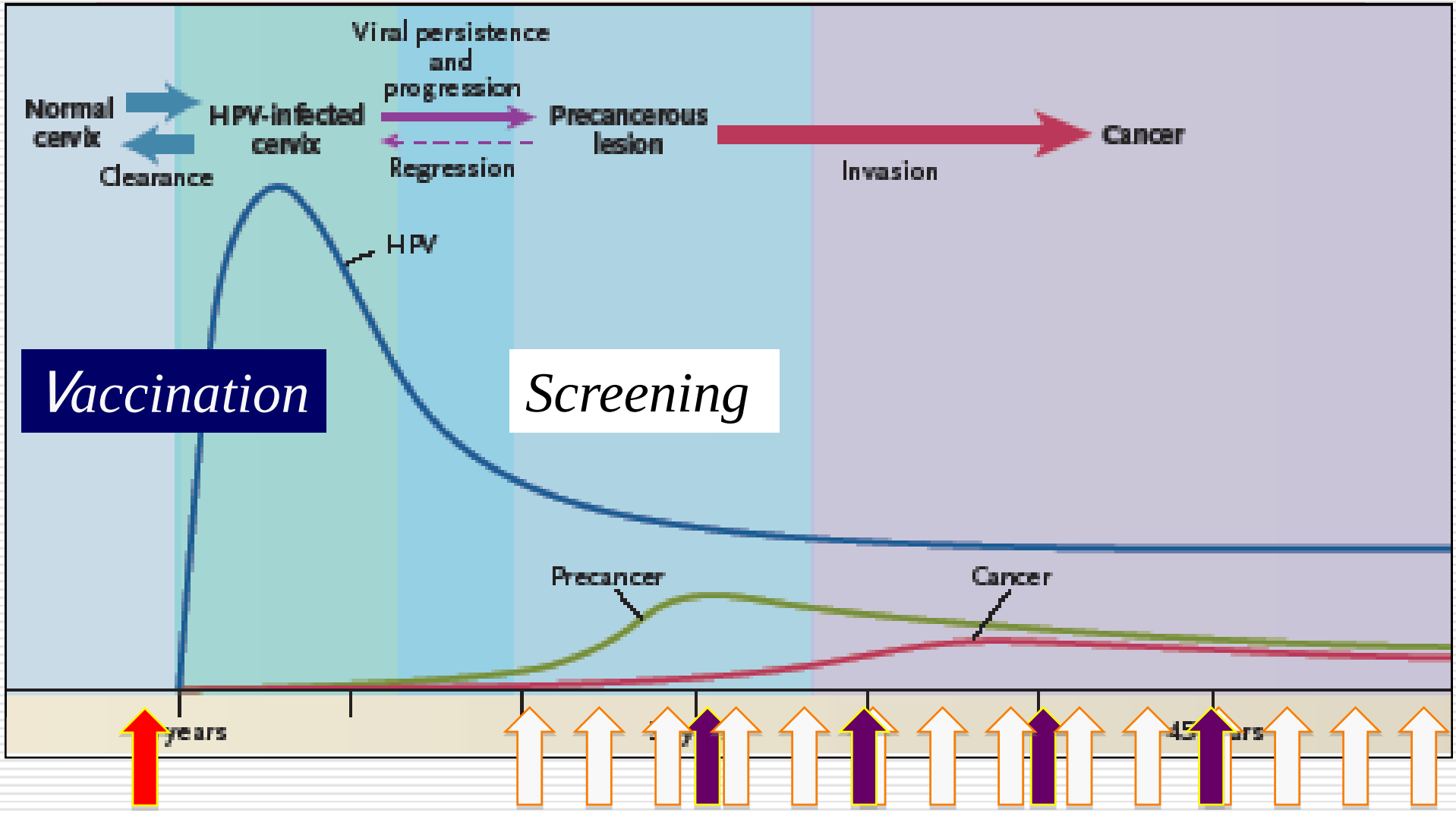
LÊ QUANG THANH
Bệnh viện Từ Dũ

GLOBOCAN 2012: Incidence du K col



http://globocan.iarc.fr/Default.aspx

Stratégies de prévention K col



Schiffman & Castle, NEJM, 2005

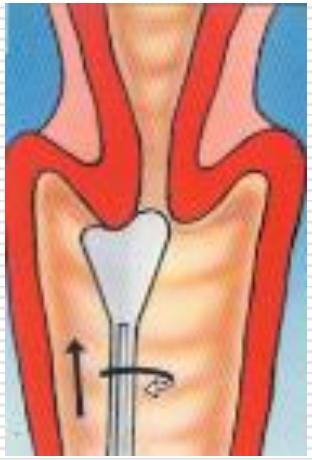
MÉTHODES DE DÉPISTAGE K col

- **Papsmear test- LBC**
- Observation du col:
  - VI (unaided Visual Inspection)
  - **VIA (Visual Inspection using Acetic acid)**
  - **VILI (Visual Inspection using Lugol's iodine)**
  - VIAM (VIA with low level of Magnification)
  - Colposcopy
  - Cervicography
- **HPV DNA test**

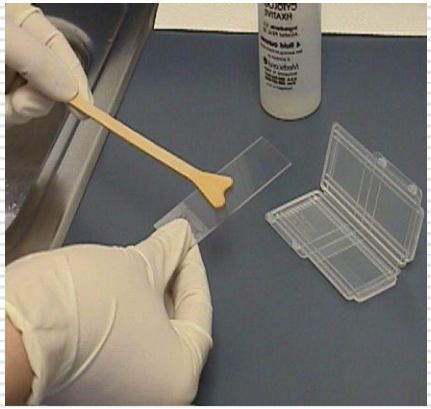
CYTOLOGIE DU COL

George Papanicolaou (1883-1962): Inventor of the Pap Smear

frottis conventionnel



Prelevement



étalement

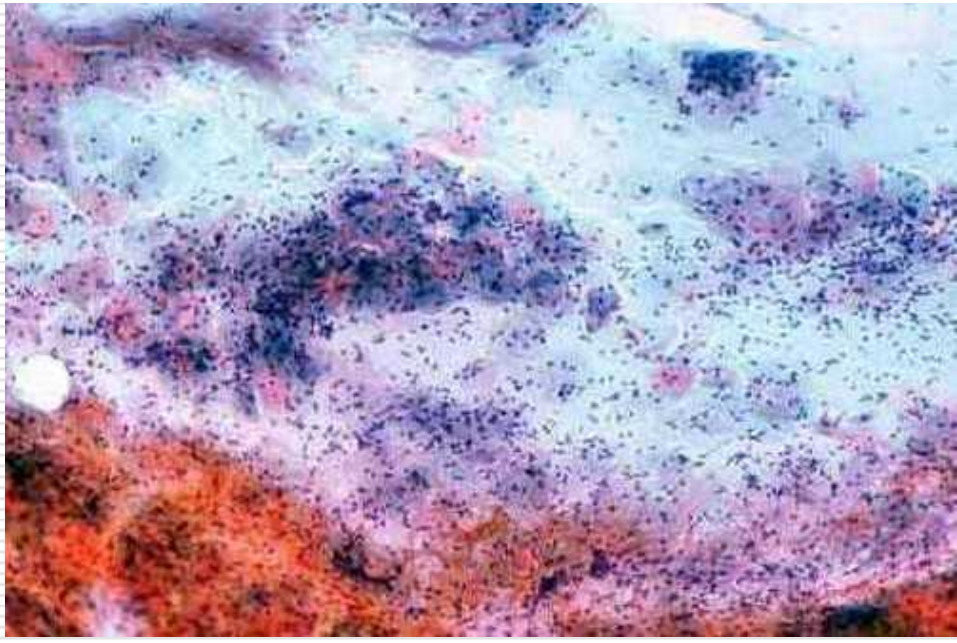
fixation

teinture

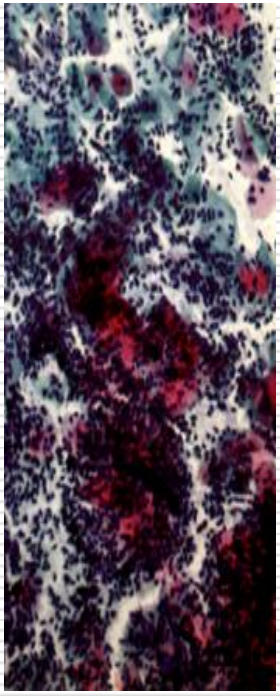
Interprétation

frottis conventionnel

- Se: 47 – 62%
- Sp: 60 – 95%
- Non interprétable :
  - Hématies
  - mucus
  - réaction inflammatoire
  - mauvais étalement: épais



Frottis: Faible Sens

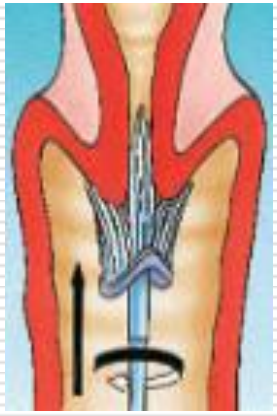


Pap slide – Poor quality

Journal Reference	Conclusions
Obstet & Gynecol, 2008; 111:167-77	HSIL Sensitivity = 55.2 % LSIL Sensitivity = 75.6 % ASCUS = 88.2 %
Wright, Clin. Obstet & Gynecol, 2007, Vol 50, No. 2, 313-323	CIN 2 / 3 Sensitivity = 44-59 %
Mayrand, Franco, NEJM, 2007; Oct 18, Vol 357, No 16	CIN 2 / 3 Sensitivity = 55.4%

Pap sensitivity can be as low as 55 % for detecting pre-cancer and disease cases

La cytologie en milieu liquide (LBC)



Prelevement

rince & fixation

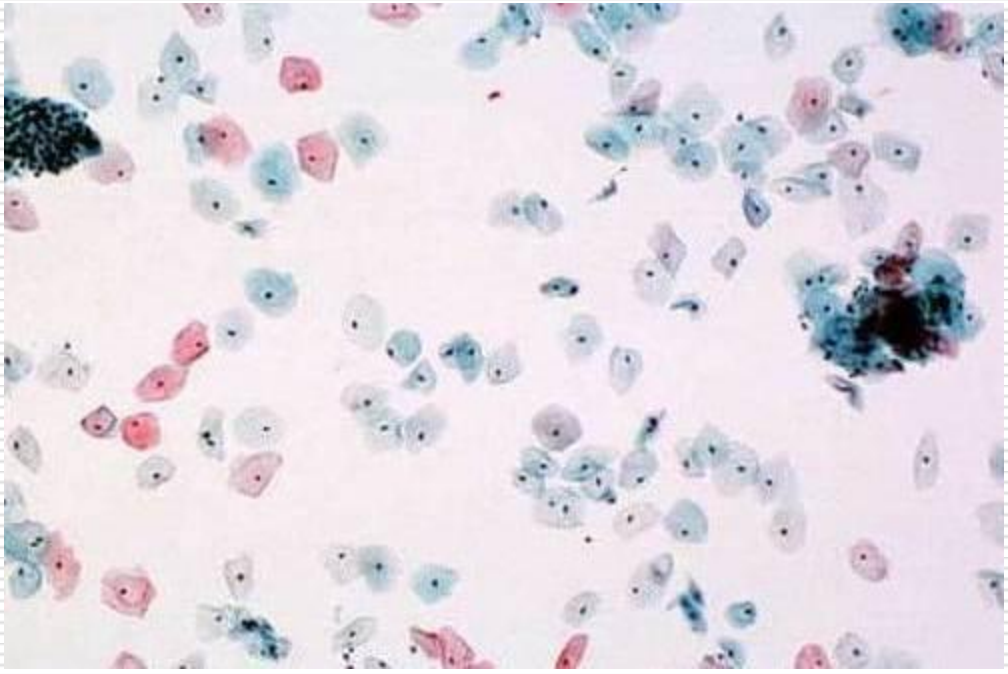
Filtre, étale

teinture

interpretation

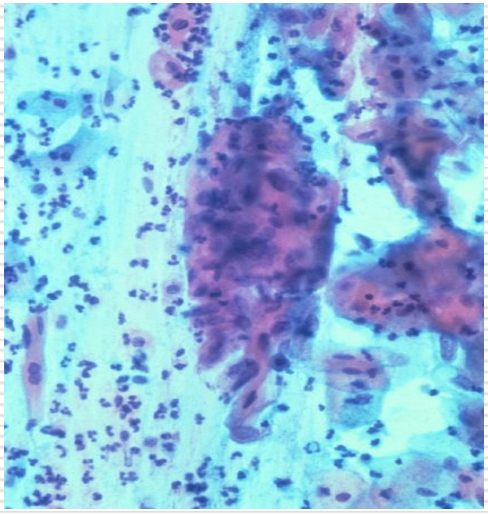
La cytologie en milieu liquide (LBC)

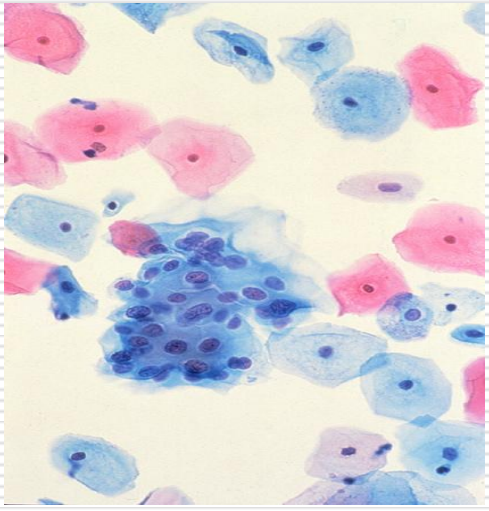
- bonne interprétation:
  - eliminer: Hematies, mucous réaction inflammatoire
  - lame en couche mince
  - Sens à 75%



Limitation de PAP et LBC

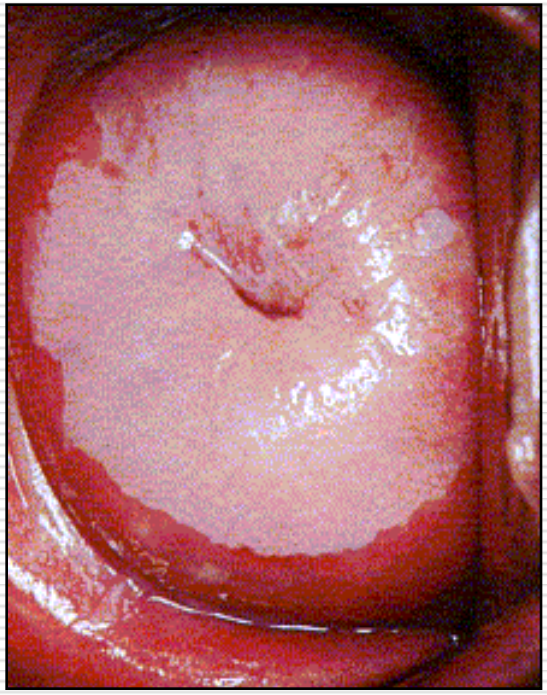
- Faible Sens
- Refait annuel
- Subjective
- Les erreurs d'échantillonnage
- **détection symptômes non la cause**



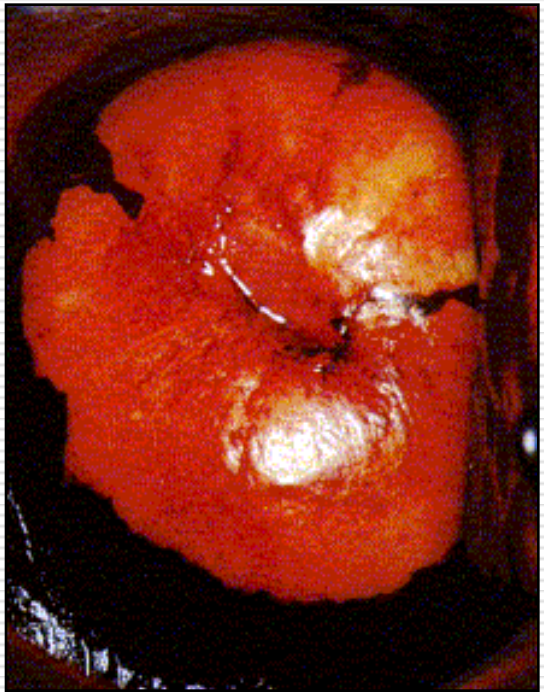


VIA - VILI

HSIL?



a



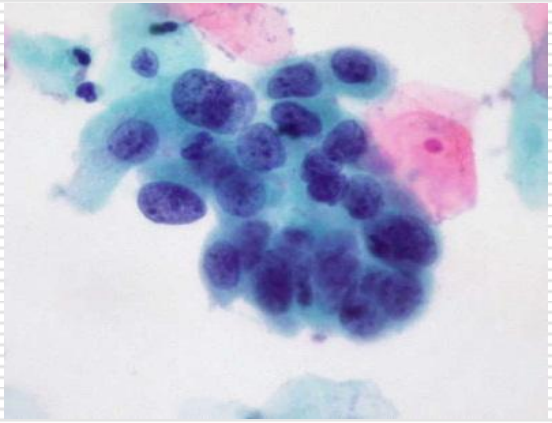
b

(a) VIA-positive:

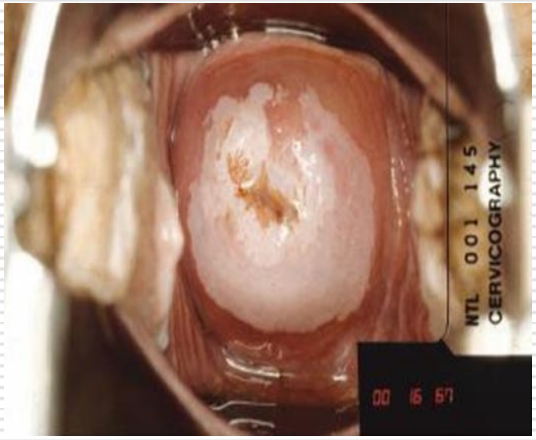
(b) VILI-positive

Dépistage conventionnel

- **Frottis**
  - Sens: 40 - 75%
  - Spe: 90 - 98%

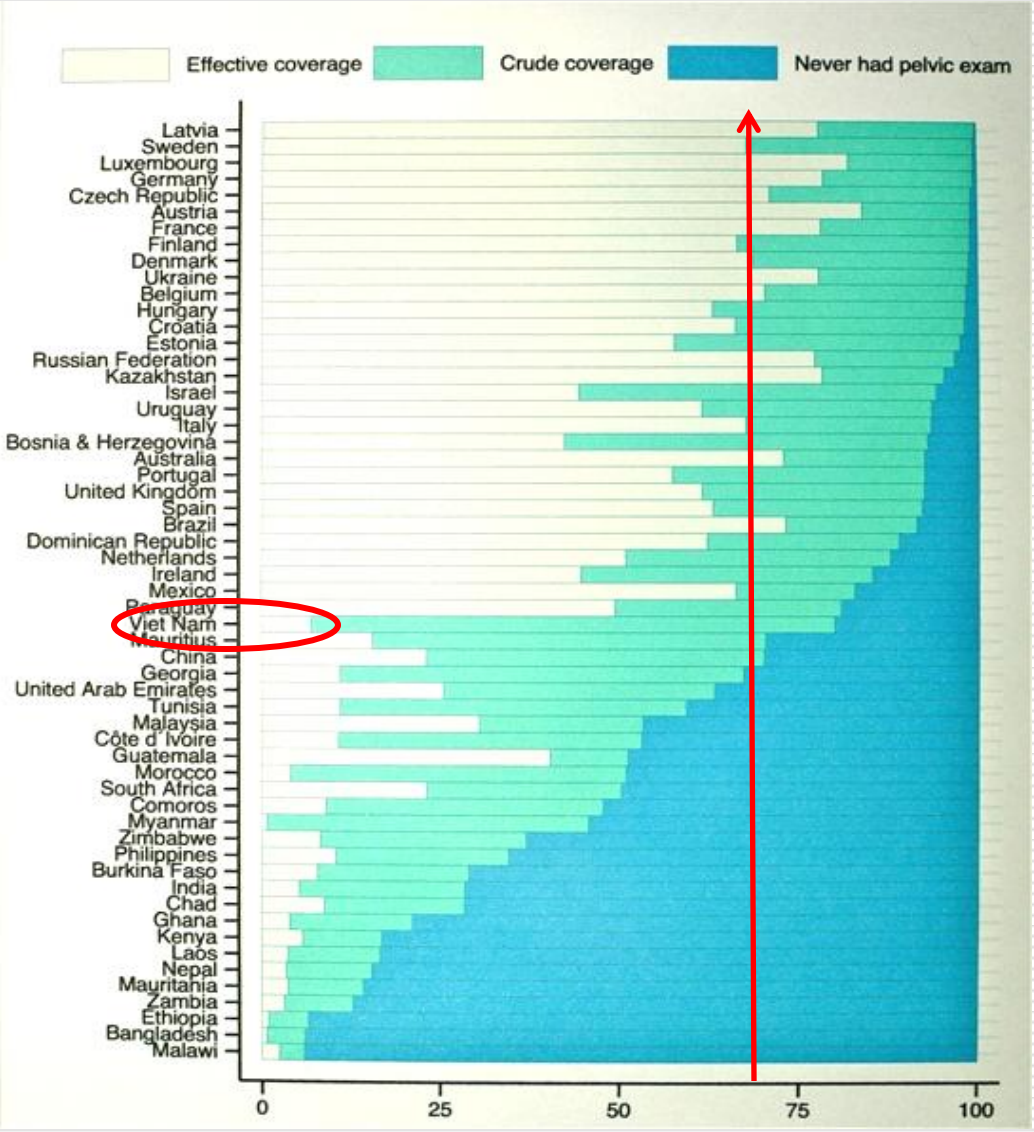


- **VIA - VILLI**
  - Sens: 40 - 70%
  - Spe: 40 - 70%



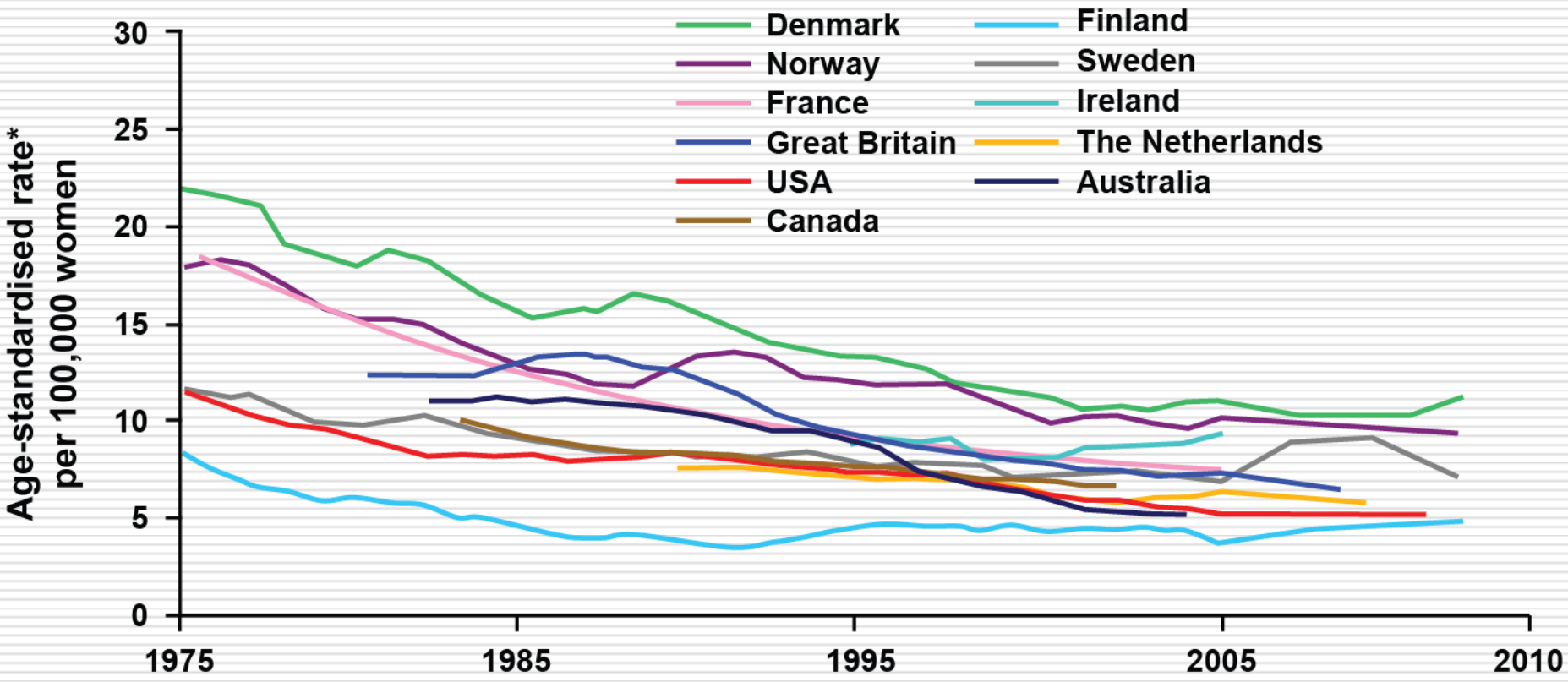
La couverture du programme de dépistage chez les femmes de 25-64 ans

- La couverture de la population à risque
- Minimum de 70% de couverture → incidence K Col
- Qualité de test de dépistage: essentielle



Gakidou E et al. PLoS Med 2008;5:e132.
World Health Organization (WHO); 2003.

Incidence de K col: mondiale



Cytologie ne peut plus réduire l'incidence de K col

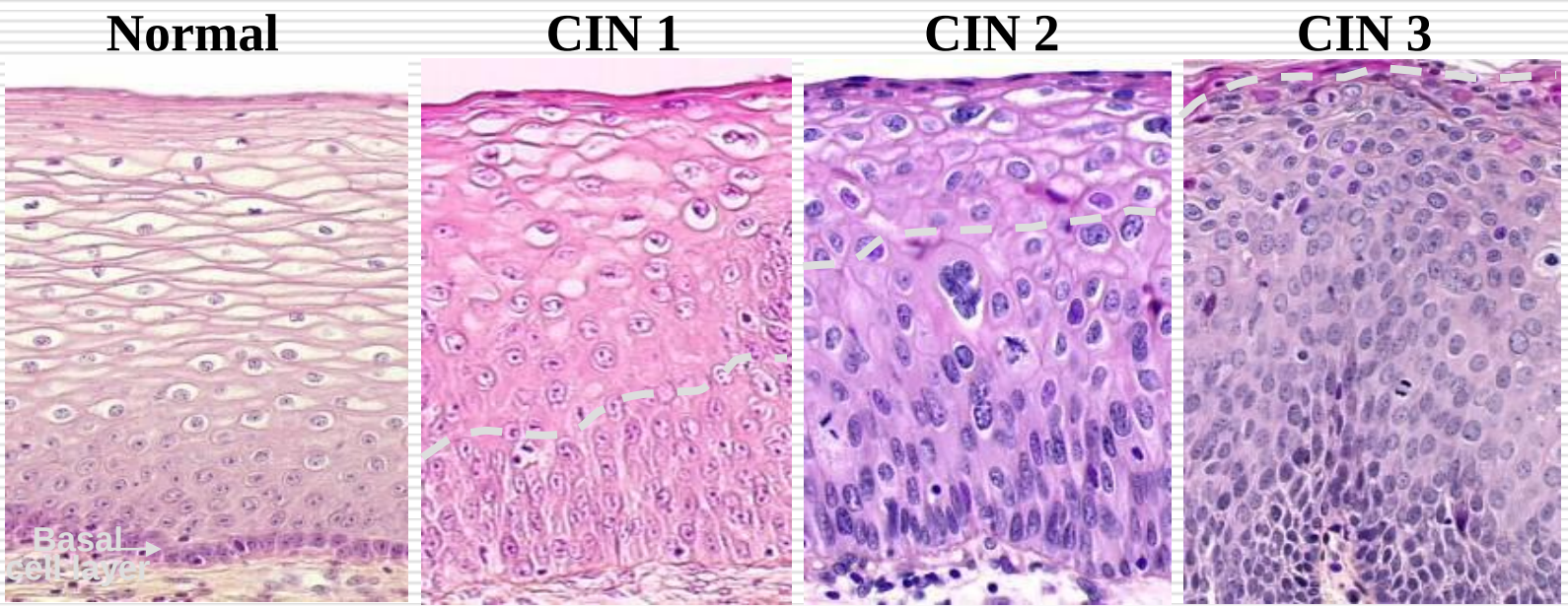
Ferlay J, *et al.* GLOBOCAN 2008. Available at: http://globocan.iarc.fr/factsheets/cancers/cervix.asp (accessed March 2012). IARC CancerBase. Lyon; 2010.

* Standardised using the world reference population

Colposcopie

Dysplasie cervicale: CIN[1]

- CIN 1: légère; condyloma [2]
- CIN 2: moderé[2]
- CIN 3: sévère; CIS[2,3]



All figures reprinted with permission from Frappart, et al. Histopathology and Cytopathology of the Uterine Cervix. Digital Atlas, Lyon, France: IARC *Press*, 2004.

Images de hístologie[4]

1. Frappart L, Fontaniere B, Lucas E, Sankaranarayanan R, eds. Lyon, France: International Agency for Research on Cancer; 2004. 2.Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. Washington, DC: American Society for Microbiology Press; 2002:557–596. 3. Canadian Cancer Society. Available at: http://www.cancer.ca/vgn/images/portal/ cit_86751114/ 63/40/151140772cw_library_wyntk_cervical_en.pdf. Accessed March 13, 2006. 4. Wright TC Jr, Cox JT, Massad LS, et al. *JAMA.* 2002;287:2120–2129.

Images de CIN sous Colposcopie

Hístologie sous la Colposcopie[1]

- CIN 1: légère; condyloma [2]
- CIN 2: moderé[2]
- CIN 3: sévère; CIS[2,3]

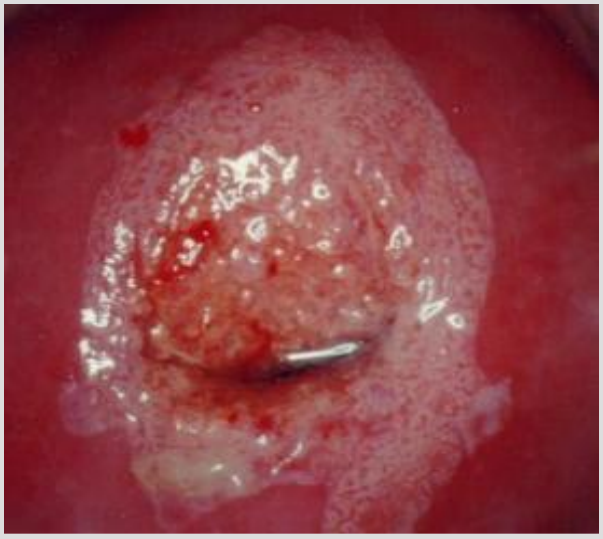
CIN 1

Photo courtesy of Dr. J. Monsonego

CIN 2

Photo courtesy of Dr. J. Monsonego

CIN 3



From IARC, 2003.[4]

1. Wright TC Jr, Cox JT, Massad LS, et al. *JAMA*. 2002;287:2120–2129. 2. Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. Washington, DC: American Society for Microbiology Press; 2002:557–596. 3. Canadian Cancer Society. Cervical Cancer: Available at: http://www.cancer.ca/vgn/images/portal/cit_86751114/63/40/151140772cw_library_wyntk_cervical_en.pdf. Accessed March 13, 2006. 4. Reprinted with permission from Sellors JW, Sankaranarayanan R, eds. Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual. Lyon, France: International Agency for Research on Cancer; 2003.

Colposcopie: Adénocarcinome du Col

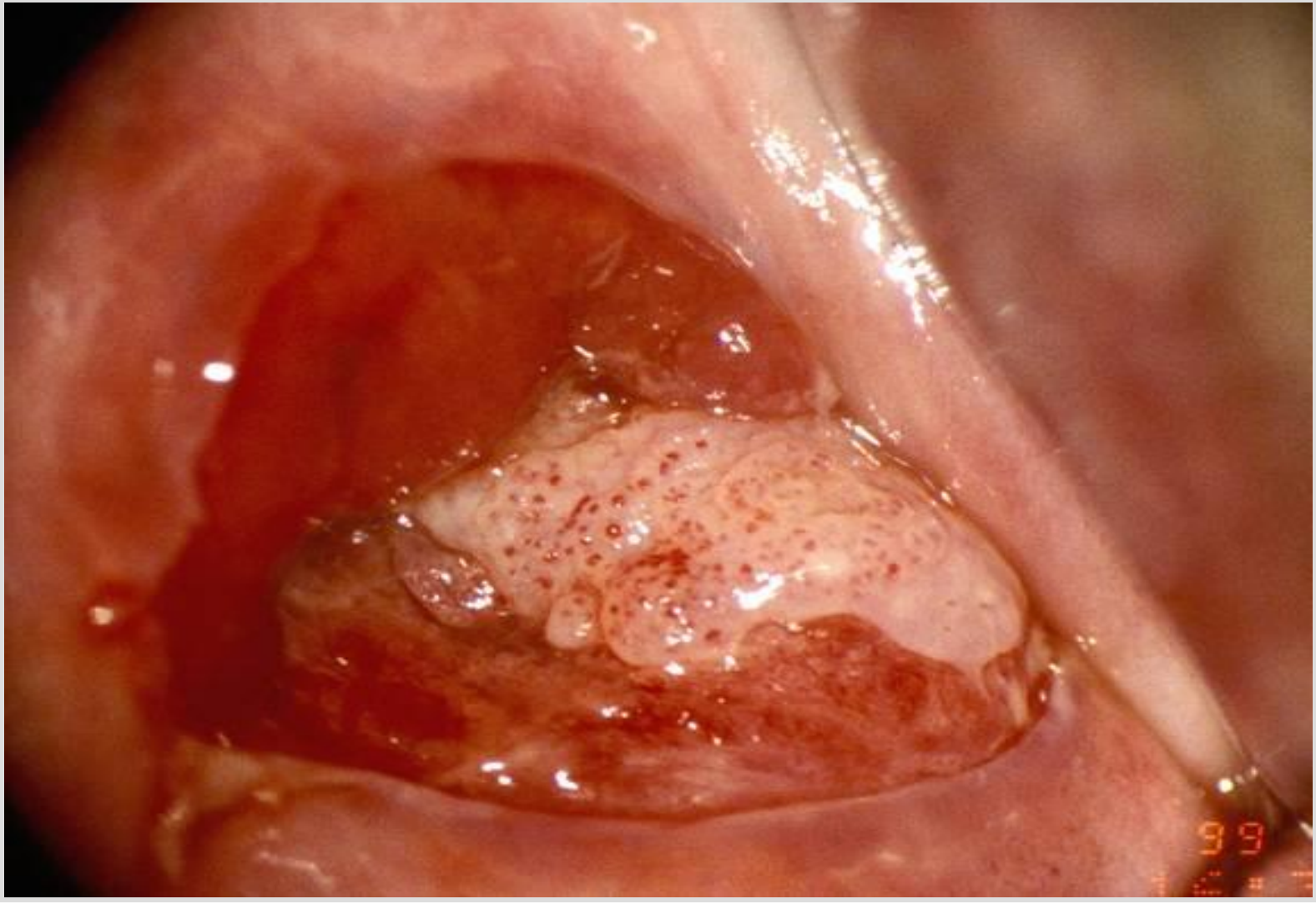
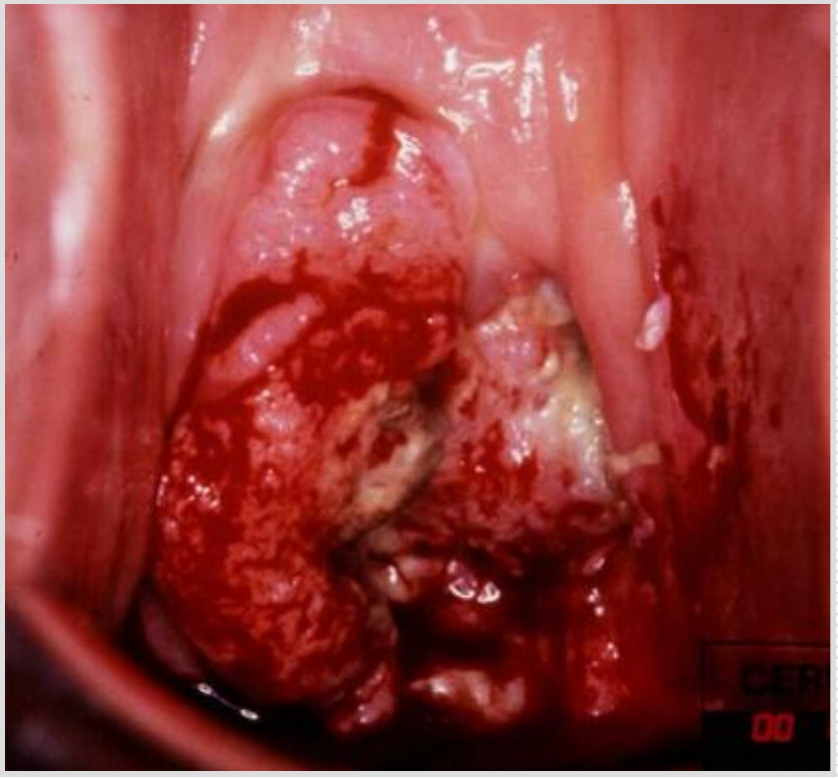
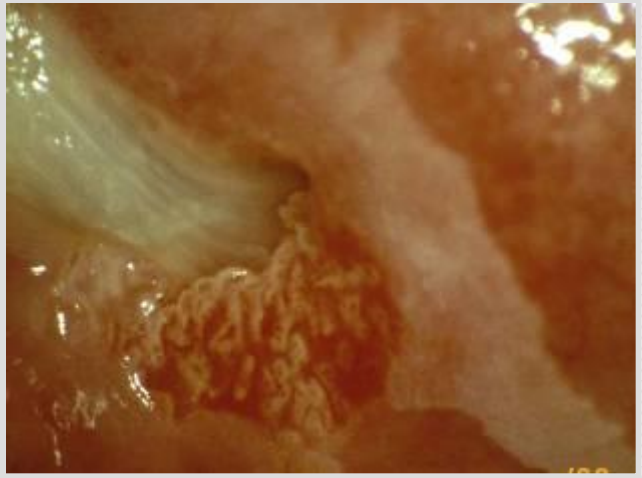


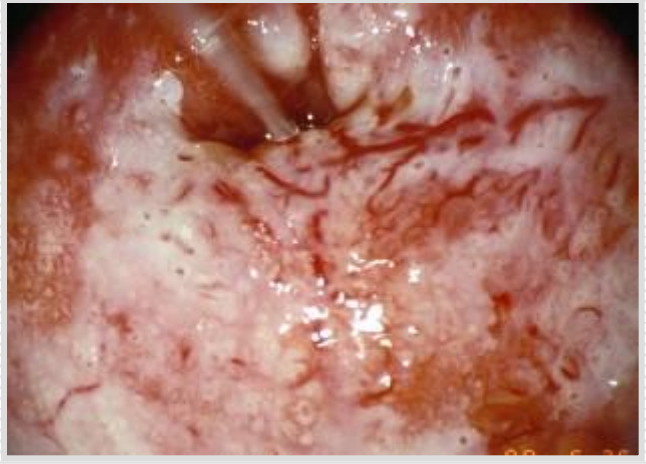
Photo courtesy of Dr. J. Monsonego

Colposcopie: K Col invasif



From IARC, 2003.[1]



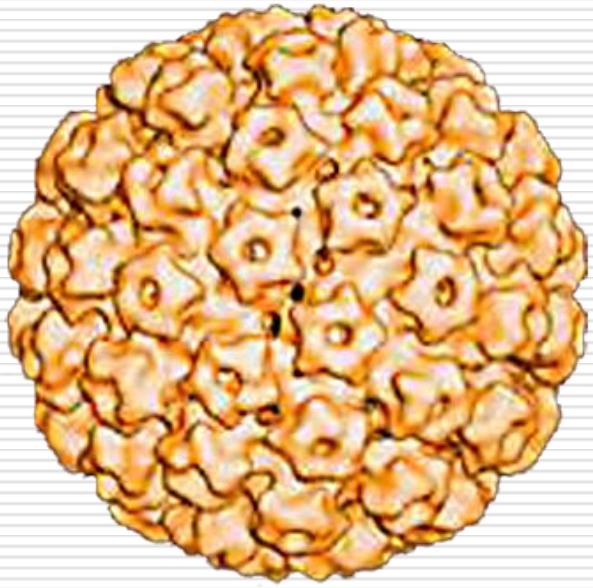


Photos courtesy of Dr. J. Monsonego

1. Reprinted with permission from Sellors JW, Sankaranarayanan R, eds. Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual. Lyon, France: International Agency for Research on Cancer; 2003.

HPV & Cancer du Col

VPH ?

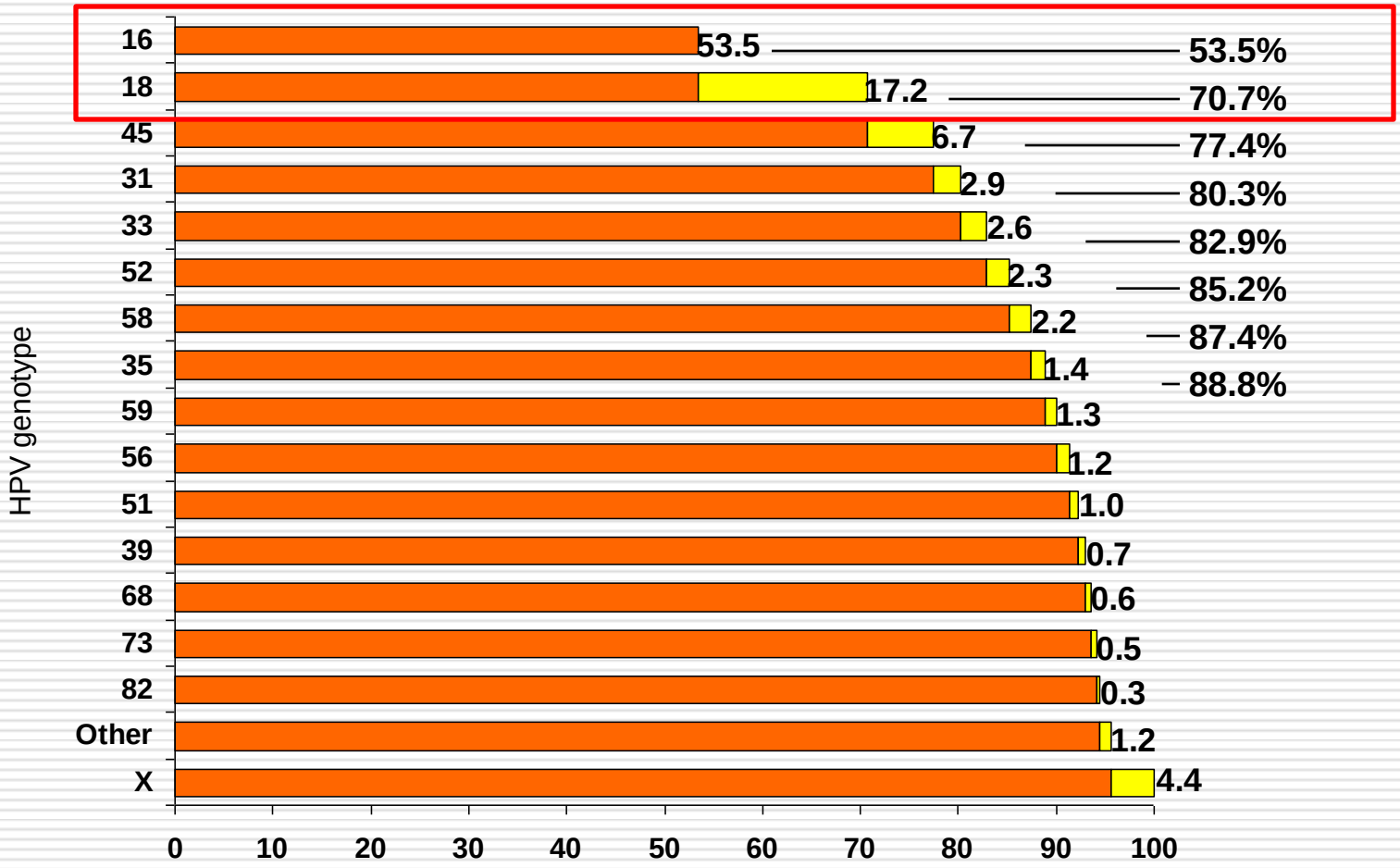


Virus à ADN, sans capsule

- Le virus du papillome humain (VPH)
- infectent les muqueuses génitales et la peau.
- ~100 génotypes de VPH[3]
- plus 13 types VPH liés K col [4]
- K Col: VPH 16 et 18.

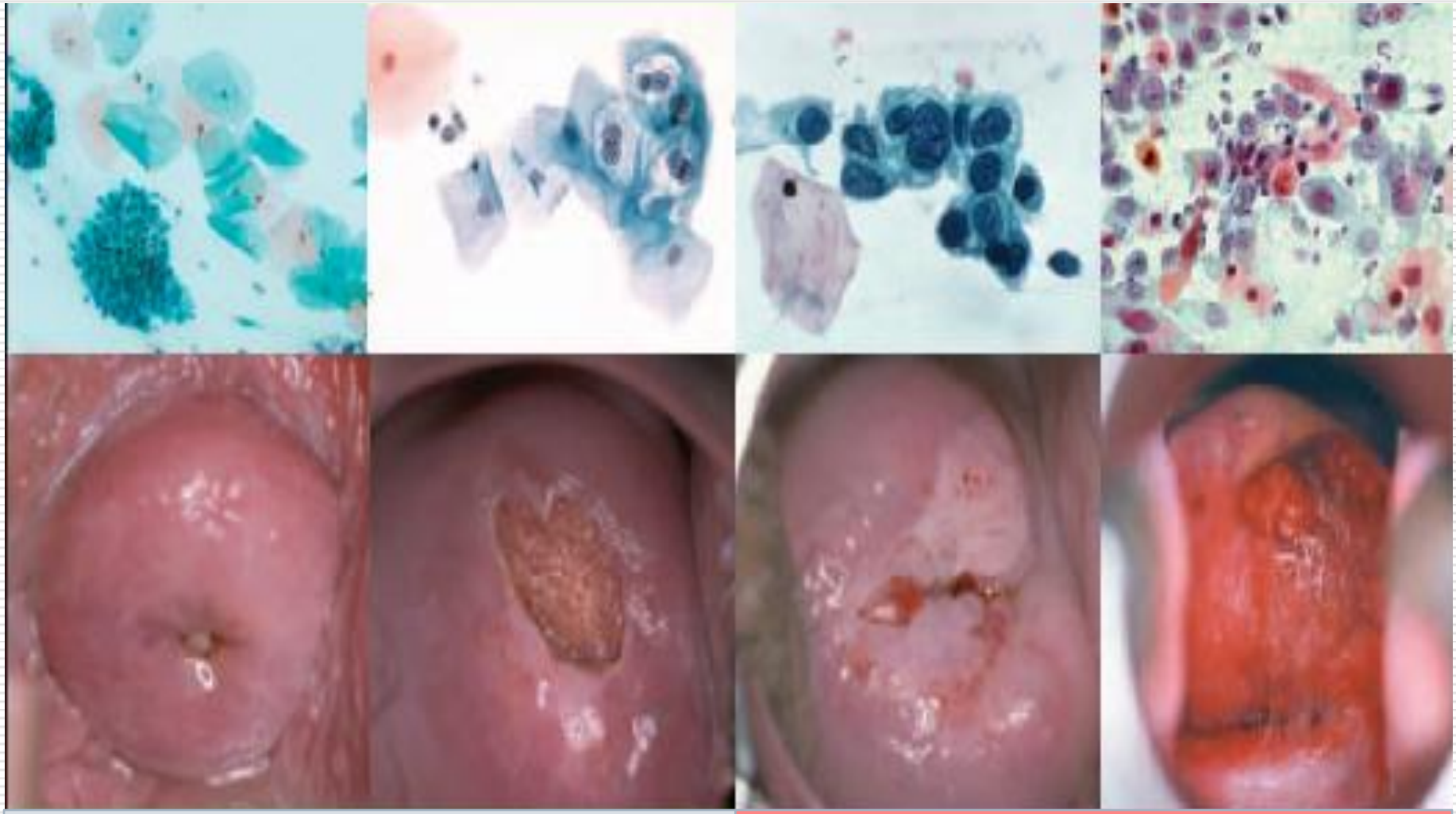
Early detection of HPV saves lives!

Génotypes du VPH associés au K col



Muñoz N *et al*. *Int J Cancer* 2004; 111: 278–85.

évolution



Transient infection

Persistent HPV

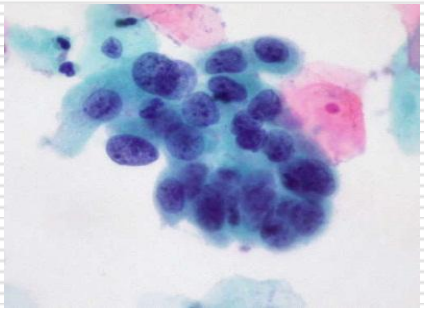
Normal cervix —INFECTION→ **HPV-infected cervix** —PROGRESSION→ **Precancer** —INVASION→ **Cancer**

HPV-infected cervix —CLEARANCE→ **Normal cervix**

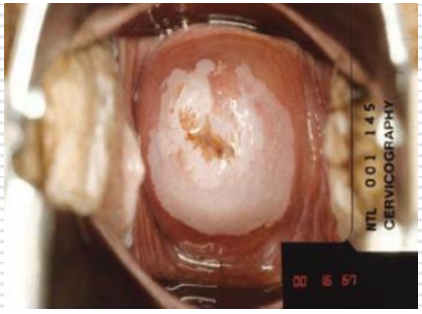
Precancer —REGRESSION?→ **HPV-infected cervix**

VPH vs PAP test

Comparaison des méthodes de dépistage



- **Pap**
  - Se: 40-75%
  - Sp: 90-98%

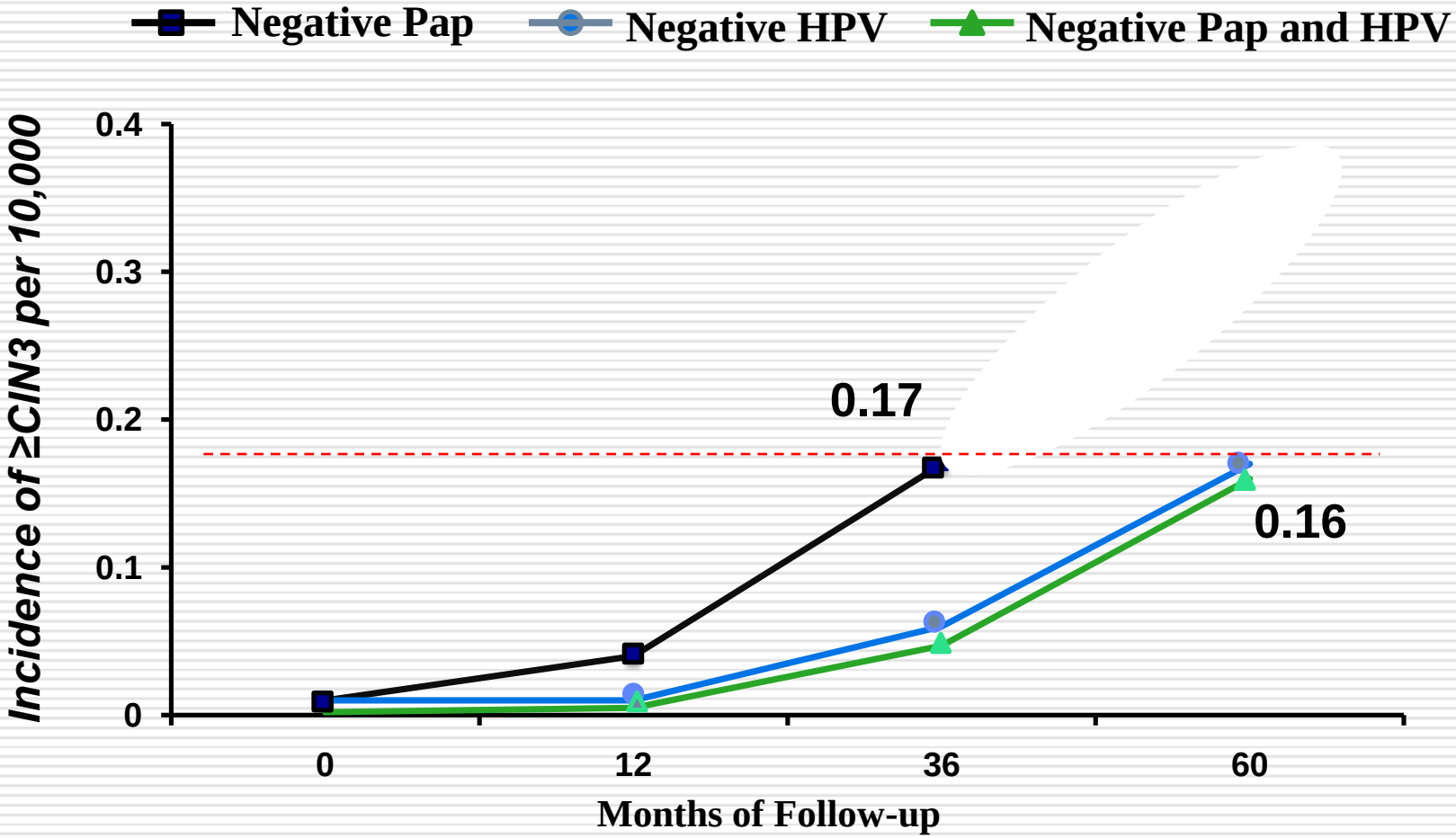


- **VIA**
  - Se : 40-70%
  - Sp: 40-70%

- **HPV testing**
  - Se : 90 – 100%
  - Sp: 92 – 96%

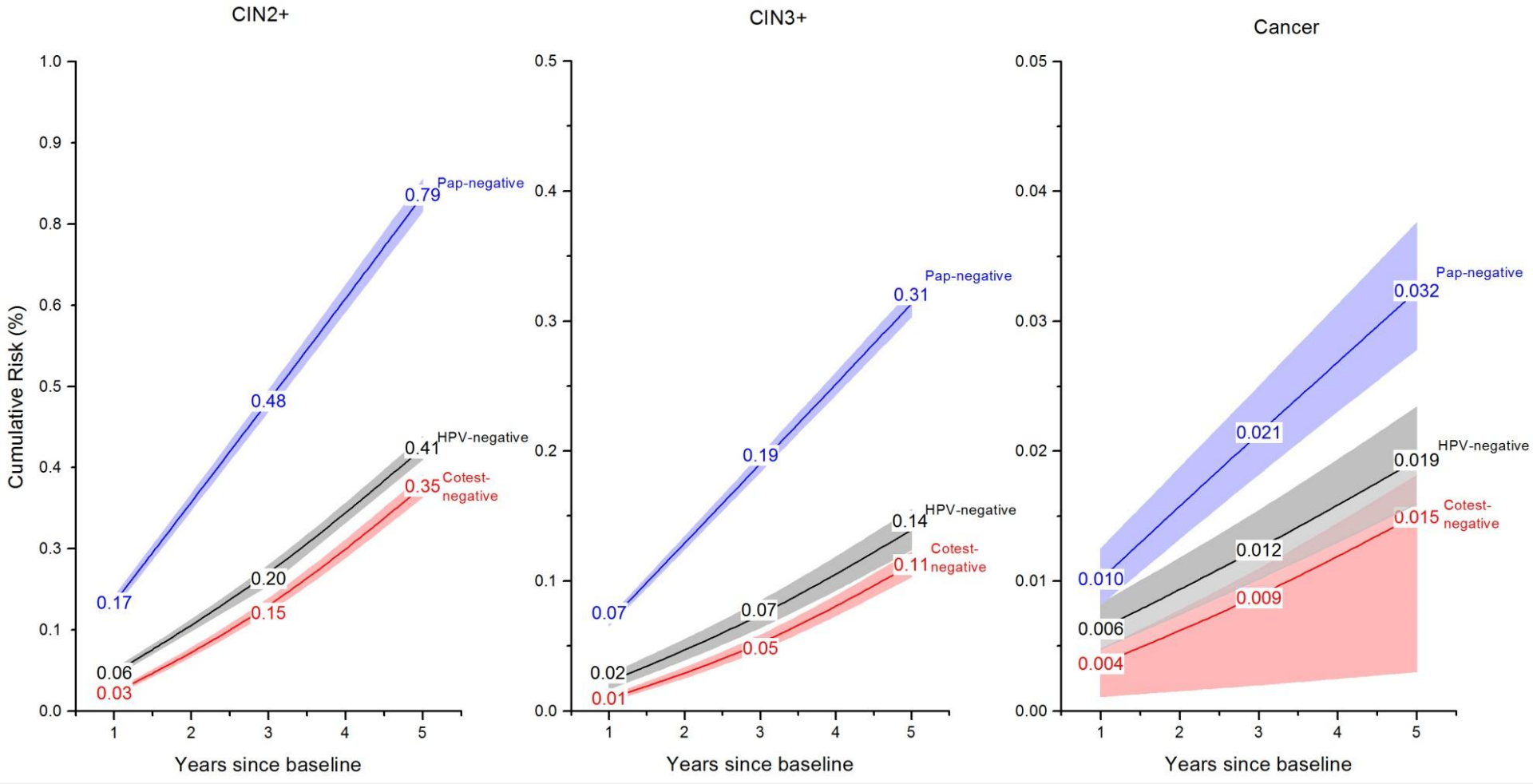
Risque ≥ CIN3 post test (-) 5 ans

Étude de Kaiser > 300.000 femmes



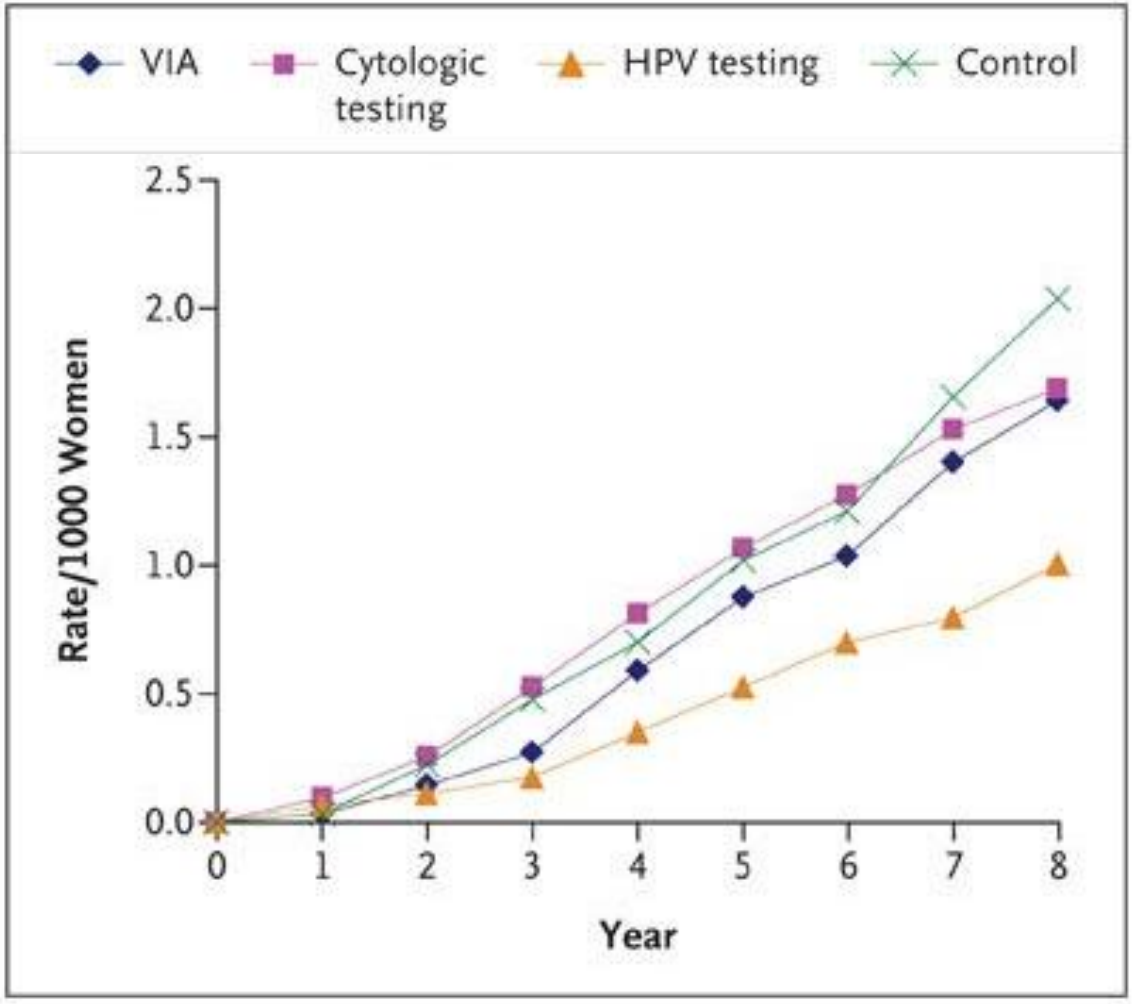
Katki HA. et al. Lancet Oncol. 2011 12:663

Risque post test (-) de 1 000 000 femmes ont fait test de depistage



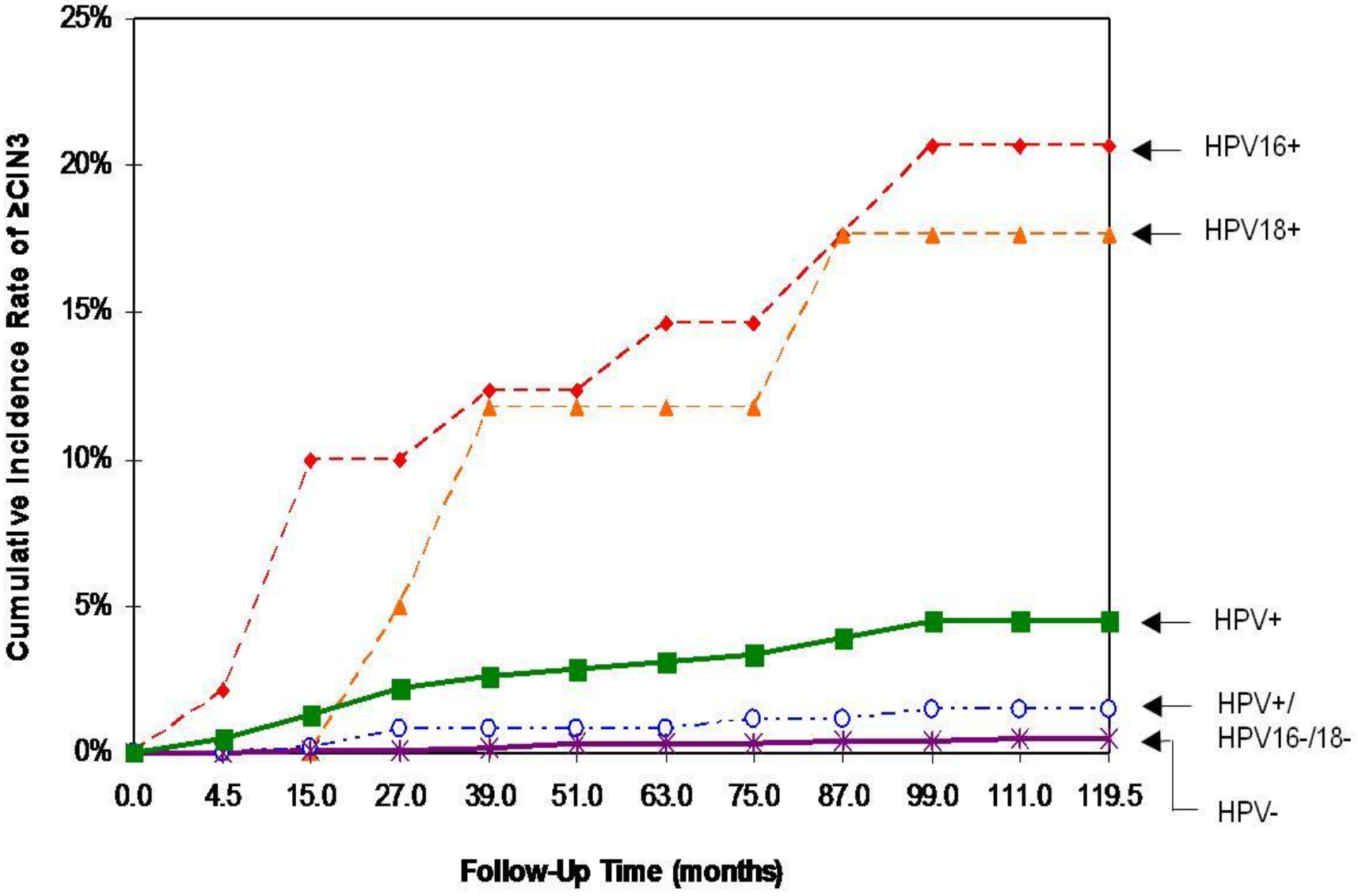
Gage *et al*., JNCI, Accepted

VPH test réduite le mortalité de K Col (Inde)



Sankaranarayanan *et al*., NEJM, 2009

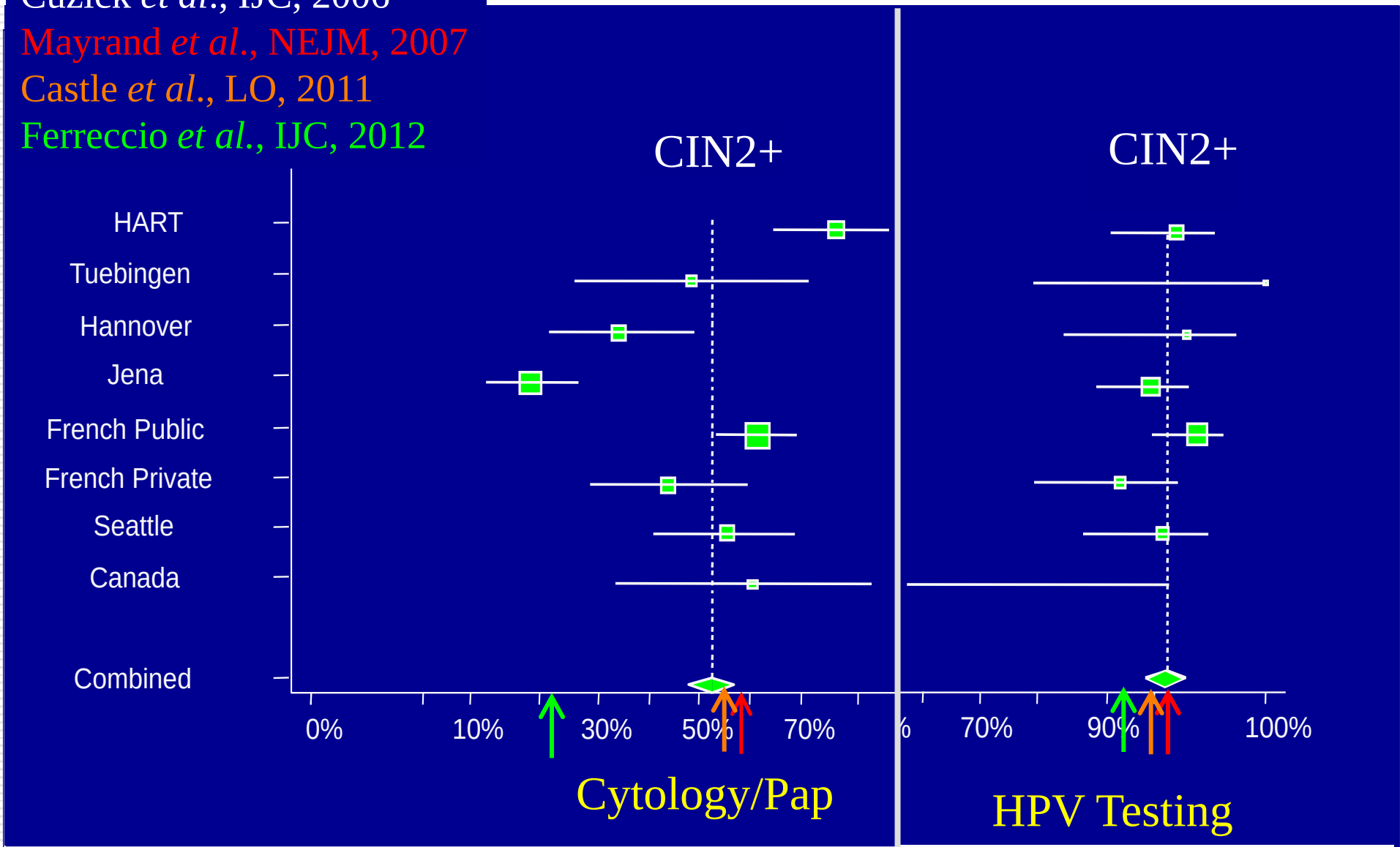
Stratification le risque quand HPV+/Pap-



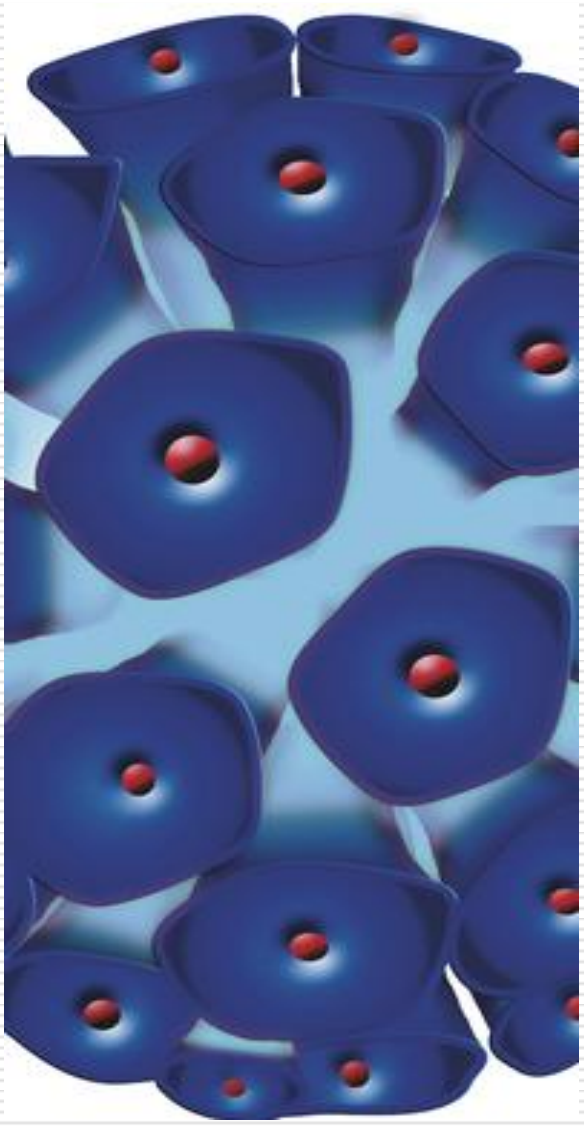
Khan *et al*., JNCI, 2005

Sensibilité: CIN2+

Cuzick *et al.*, IJC, 2006
Mayrand *et al.*, NEJM, 2007
Castle *et al.*, LO, 2011
Ferreccio *et al.*, IJC, 2012



VPH test et K col

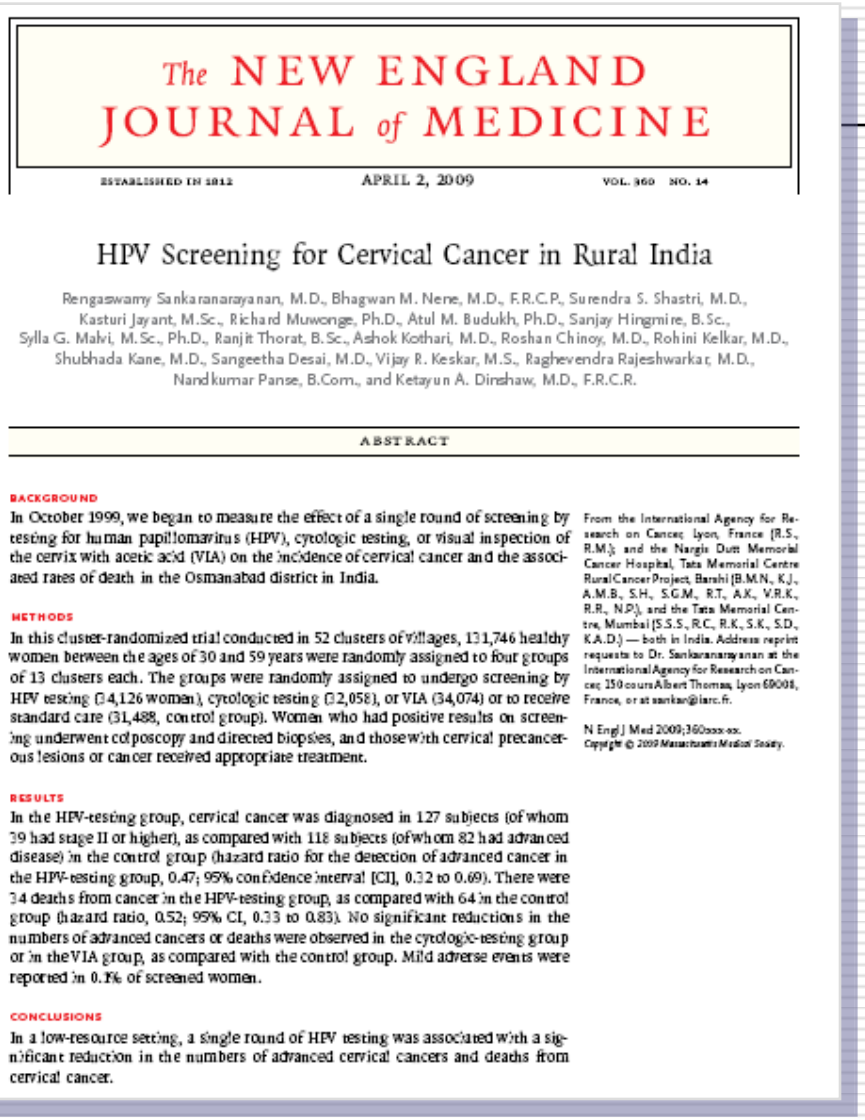


- Test dépistage du VPH chez les femmes de 25-65 ans réduit les décès par K col de l'utérus(2004, IARC).

- “Même une fois VPH [ADN] positives chez les femmes ont Pap négative est également un prédicteur important de CIN de haut niveau” (Kjaer 2005, Cancer Research).

International Agency for Research on Cancer
Centre International de Recherche sur le Cancer

Réduire la morbidité et la mortalité K Col



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 2, 2009 VOL. 360 NO. 14

HPV Screening for Cervical Cancer in Rural India

Rengaswamy Sankaranarayanan, M.D., Bhagwan M. Nene, M.D., F.R.C.P., Surendra S. Shastri, M.D., Kasturi Jayant, M.Sc., Richard Muwonge, Ph.D., Atul M. Budukh, Ph.D., Sanjay Hingmire, B.Sc., Sylla G. Malvi, M.Sc., Ph.D., Ranjit Thorat, B.Sc., Ashok Kothari, M.D., Roshan Chinoy, M.D., Rohini Kelkar, M.D., Shubhada Kane, M.D., Sangeetha Desai, M.D., Vijay R. Keskar, M.S., Raghevendra Rajeshwarkar, M.D., Nandkumar Panse, B.Com., and Ketayun A. Dinshaw, M.D., F.R.C.R.

ABSTRACT

BACKGROUND

In October 1999, we began to measure the effect of a single round of screening by testing for human papillomavirus (HPV), cytologic testing, or visual inspection of the cervix with acetic acid (VIA) on the incidence of cervical cancer and the associated rates of death in the Osmanabad district in India.

METHODS

In this cluster-randomized trial conducted in 52 clusters of villages, 131,746 healthy women between the ages of 30 and 59 years were randomly assigned to four groups of 13 clusters each. The groups were randomly assigned to undergo screening by HPV testing (34,126 women), cytologic testing (32,058), or VIA (34,074) or to receive standard care (31,488, control group). Women who had positive results on screening underwent colposcopy and directed biopsies, and those with cervical precancerous lesions or cancer received appropriate treatment.

RESULTS

In the HPV-testing group, cervical cancer was diagnosed in 127 subjects (of whom 39 had stage II or higher), as compared with 118 subjects (of whom 82 had advanced disease) in the control group (hazard ratio for the detection of advanced cancer in the HPV-testing group, 0.47; 95% confidence interval [CI], 0.32 to 0.69). There were 34 deaths from cancer in the HPV-testing group, as compared with 64 in the control group (hazard ratio, 0.52; 95% CI, 0.33 to 0.83). No significant reductions in the numbers of advanced cancers or deaths were observed in the cytologic-testing group or in the VIA group, as compared with the control group. Mild adverse events were reported in 0.1% of screened women.

CONCLUSIONS

In a low-resource setting, a single round of HPV testing was associated with a significant reduction in the numbers of advanced cervical cancers and deaths from cervical cancer.

From the International Agency for Research on Cancer, Lyon, France (R.S., R.M.); and the Nargis Dutt Memorial Cancer Hospital, Tata Memorial Centre Rural Cancer Project, Barshi (B.M.N., K.J., A.M.B., S.H., S.G.M., R.T., A.K., V.R.K., R.R., N.P.), and the Tata Memorial Centre, Mumbai (S.S.S., R.C., R.K., S.K., S.D., K.A.D.) — both in India. Address reprint requests to Dr. Sankaranarayanan at the International Agency for Research on Cancer, 150 cours Albert Thomas, Lyon 69008, France, or at sankar@iarc.fr.

N Engl J Med 2009;360:xxx-xx.

- “Test dépistage du VPH réduit l’incidence et mortalité du K col...”
- “ Test HPV est plus objective et facile à mettre en œuvre que d'autres tests de dépistage”

Recommandation du test de dépistage du K col par VPH ADN

2013

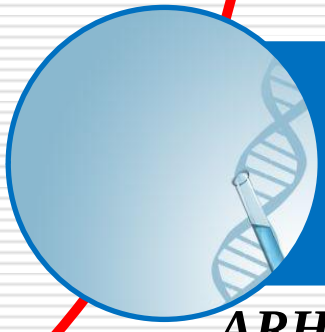
Le dépistage du VPH ne devrait détecter les types à haut risque oncogénique (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59)

ASCCP: *American Society for Colposcopy and Cervical Pathology*

2012

Le test HPV orienté vers type à haut risque. Tests pour les groupes de HPV à faible risque devraient pas être menées.

ACOG: *American College of Obstetricians and Gynecologists*



ARHP, CDC… ont même recommandations

ARHP: *Association of Reproductive Health Professionals* ***CDC:*** *Centers for Disease Control and Prevention*

Les principaux points

1. L'infection persistante types VPH à potentiel cancérigène élevé provoquant K col.
2. La sensibilité du test VPH est plus élevée que Pap et VIA.
3. 1er test dépistage VPH pour lé lesions du col.
4. Orientation clinique uniquement sur ceux qui ont les raisons nécessaires causant K Col
5. Identifier les genotypes (16, 18, 45) VPH pour la stratification du risque.
6. Identifier les causes et non les symptômes.

Merci de votre attention