Multicentric study of HPV testing screening and triage (ESTAMPA)

International Agency for Research on Cancer
Lyon, France
Cytology-based screening programs have proven ineffective in developing countries.
Some reasons for limited impact of cervical cancer screening in Latin America

- Poor screening coverage
- Specimen collection and handling
- Inherent limitation of cytology
- Lack of SOPs and quality assurance at the labs
- Loss to follow-up
- Lack of information systems
- Geographic and economic barriers
- Lack of organization of program
Recent knowledge of natural history and biology of HPV infection and cervical cancer have resulted in new primary and secondary prevention methods.
Newly available primary and secondary prevention tools

- HPV vaccination of adolescents
  - Modified schedules <3 doses
- HPV testing of women over 30 years old
  - Self collection
  - CareHPV
- Visual inspection with acetic acid
  - See and treat
## Characteristics of HPV testing

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Objective</td>
<td>Limited specificity</td>
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<tr>
<td>Robust</td>
<td>High cost</td>
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<td>Reproducible</td>
<td>Follow up of positives</td>
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<td>Accurate</td>
<td>Technical requirements</td>
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<td>Effective</td>
<td>Social stigma</td>
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<td>Extension of intervals</td>
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<td>Self-collection</td>
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<td>OK for post vaccination</td>
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ESTAMPA Background

- HPV detection will soon become standard for primary screening
- However, viral detection has low positive predictive value
- Many women with HPV do not have a lesion and do not require treatment
New algorithms for cervix screening

- ve

Repeat test 5-10 years

+ ve

Cytology

ASCUS +

Colposcopy Diagnosis Treatment

Negative

Repeat HPV testing After 1 year BIOMARKERS

+ ve

- ve
HPV testing not recommended before age 30 due to high prevalence

% Prevalence, Guanacaste 1993

Tipos no oncogénicos
Tipos oncogénicos

Age group

International Agency for Research on Cancer
Herrero JID 2005
Prevalent infections, all carcinogenic types

N = 777          Mean age = 34.7 ( 15.1) years

68.7% clearance @ 12 months
Background

- New methods are required to select women at risk who require evaluation and treatment
- Multiple methods under development but more data required on their performance
General Objective

• To establish the most effective strategy for HPV screening and triage

• Primary: To estimate performance of different triage techniques alone or in combination to detect CIN3+ among HPV positive women
Study design

• Multicentric screening study
• 50,000-100,000 women 30-64 years old
• Primary screening with HPV test and collection of specimens for triage
• Referral to colposcopy of all HPV positive women and 2% of negatives, with diagnostic histology as needed
• Second round for HPV positives 18-24 months later
Primary HPV testing

- Hybrid capture
- COBAS 4800
- Cervista
- Aptima
Possible triage tests
(on all colposcopy patients)

- VIA
- Cytology (liquid vs conventional)
- Aptima (RNA 14 types)
- COBAS/ABBOTT (DNA HPV 16, 18)
- PreTec Proofer (RNA, HPV 16, 18, 31, 33, 45)
- p16 ki67 IHC
- E6 strip (oncoprotein HPV 16, 18, 45)
- Biobank for evaluation of future methods
Model for organized screening

- Population based
- Conducted within public health services
- Standardized procedures
- Assurance of follow-up
- Training and QA of colposcopy, cytology, pathology
- Performance assessment
Collection of pathology specimens and review

• Biopsy slides will be collected from biopsies and LEEPs
  – Quality assurance of staining process
• Paraffin blocks for HPV and other studies
  – Quality assurance of histologic preparations
• Local interpretation for clinical management
• Panel review for final endpoint definition
Evaluation of psychosocial impact of HPV testing

- Personal interviews after notification of results
- Survey of knowledge and attitudes of medical personnel on HPV and cervical cancer
- Determinants in non participation in follow-up procedures
- Survey of knowledge and attitudes of males in the community
Participating centers and investigators

WHO, PAHO, RINC