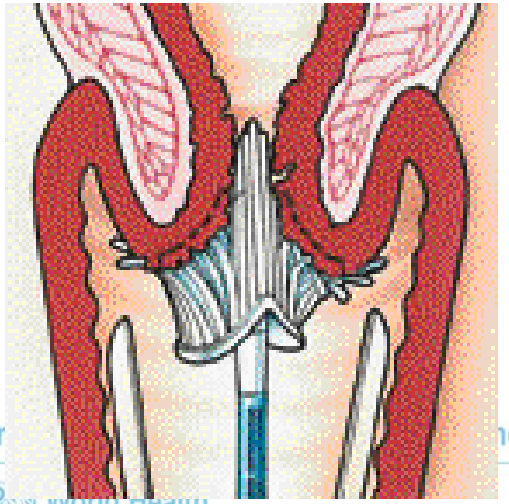
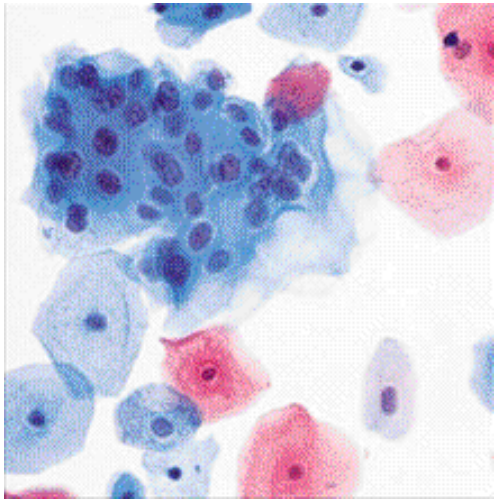
Multicentric study of HPV testing screening and triage (ESTAMPA)

International Agency for Research on Cancer
Lyon, France

Pan American Health Organization
Regional Office of the World Health Organization

Cytology-based screening programs have proven ineffective in developing countries

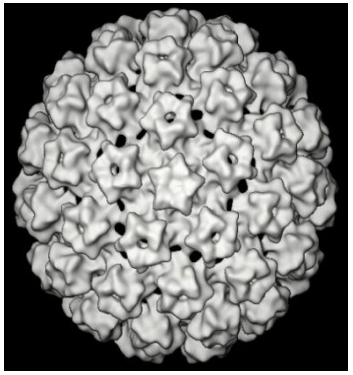




Some reasons for limited impact of cervical cancer screening in Latin America

- 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

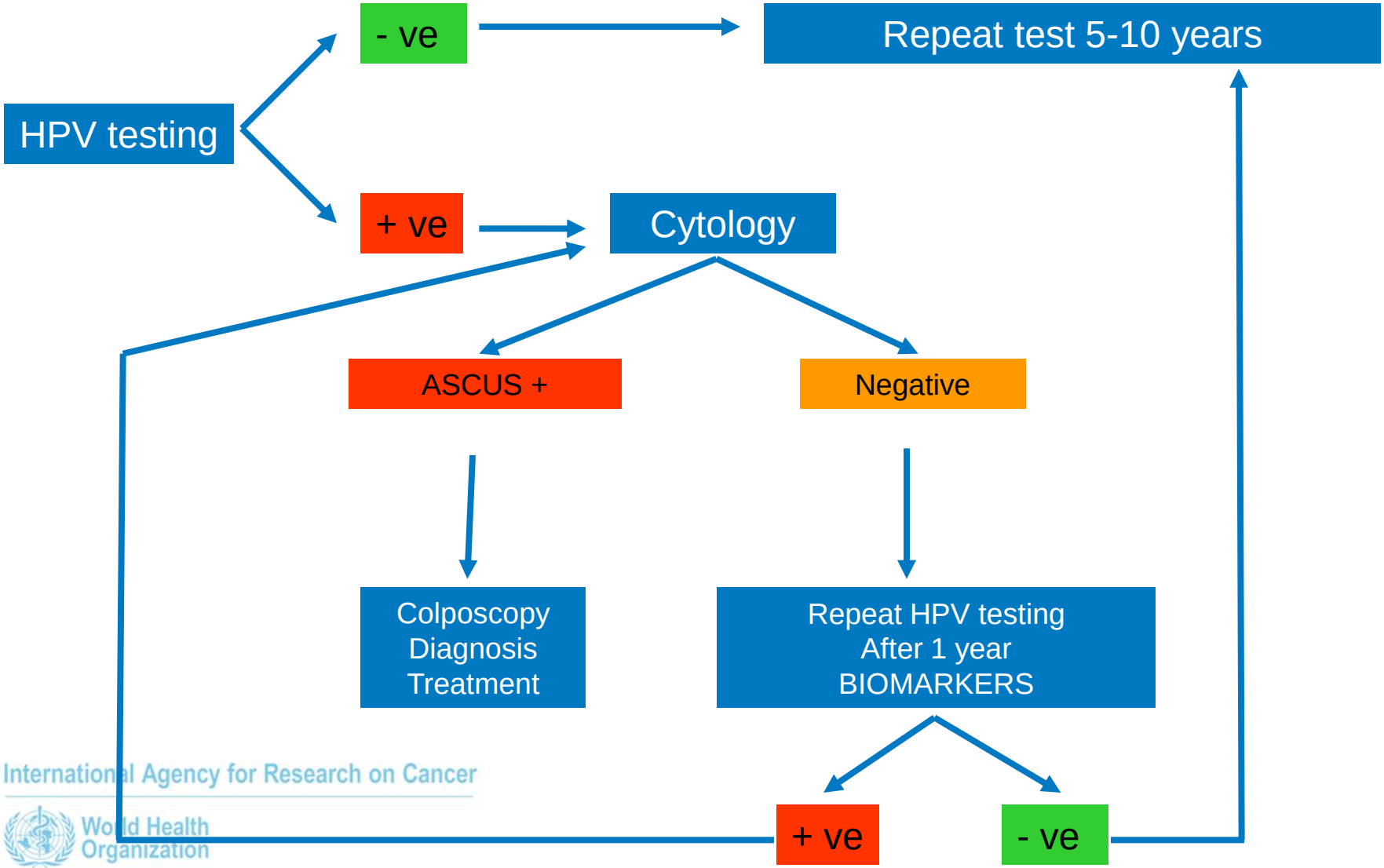
Characteristics of HPV testing

Advantages	Disadvantages
Objective	Limited specificity
Robust	High cost
Reproducible	Follow up of positives
Accurate	Technical requirements
Effective	Social stigma
Extension of intervals	
Self-collection	
OK for post vaccination	

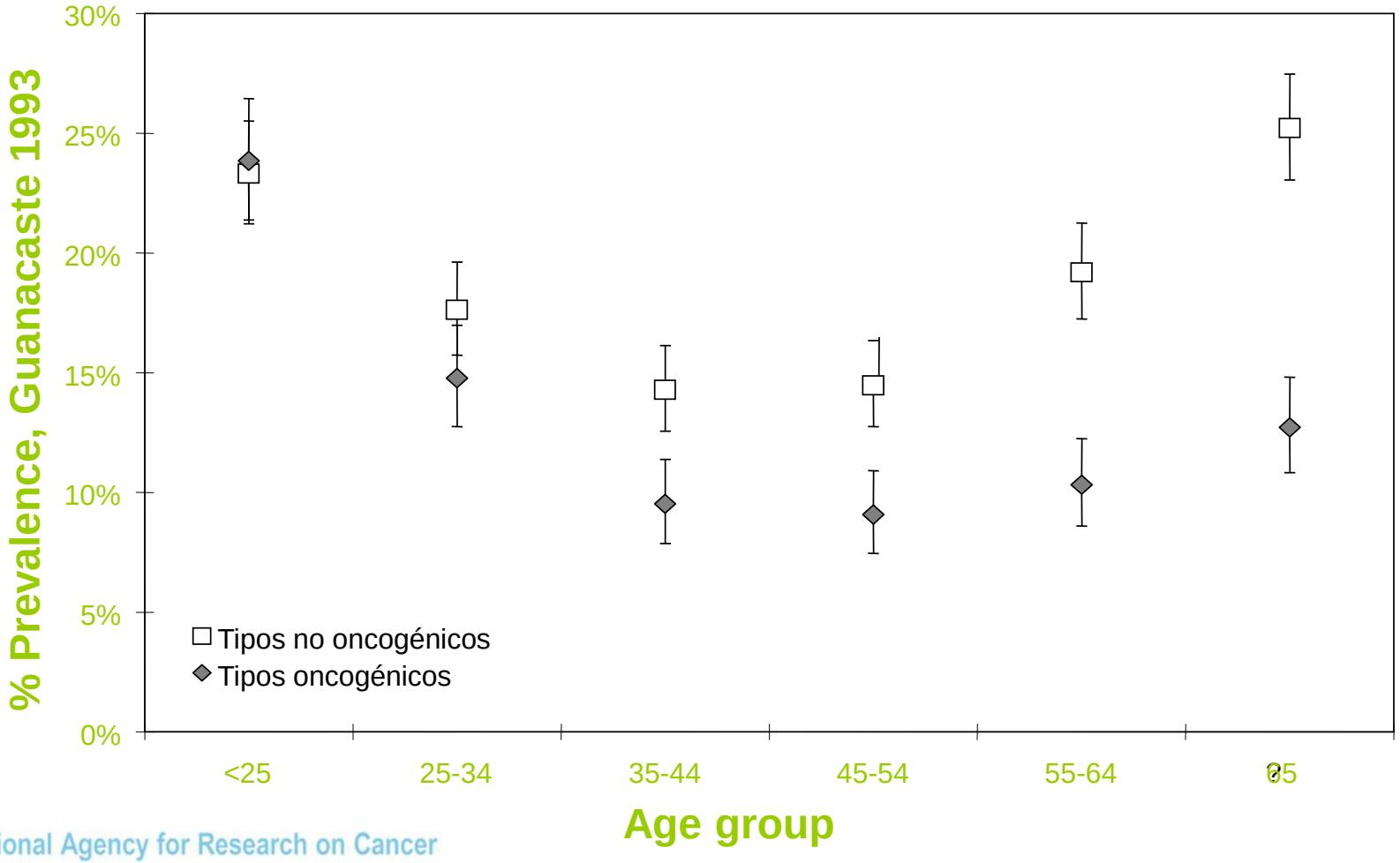
ESTAMPA Background

- 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



HPV testing not recommended before age 30 due to high prevalence



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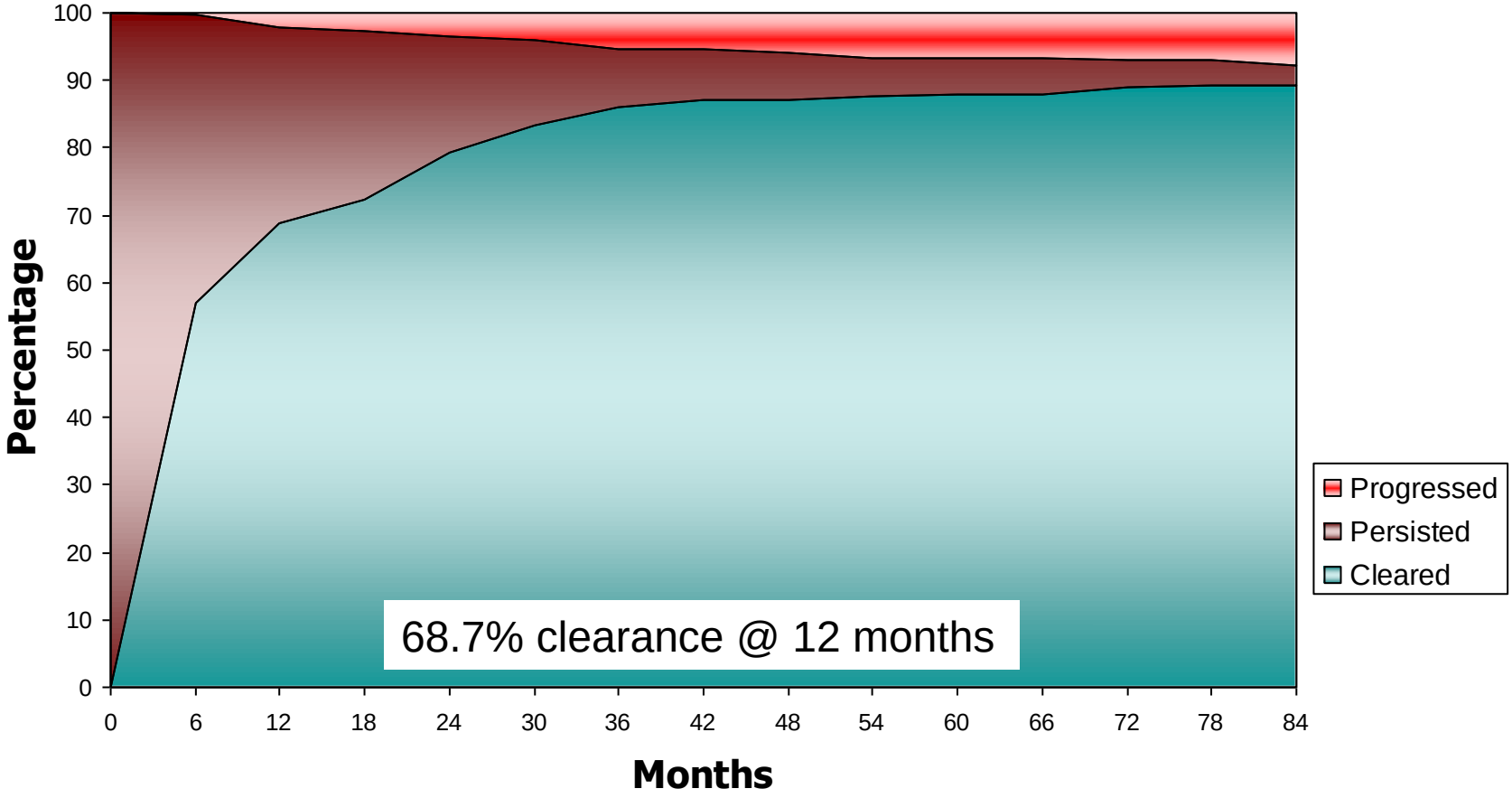
Herrero JID 2005

Prevalent infections, all carcinogenic types



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N = 777 Mean age = 34.7 (15.1) years

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

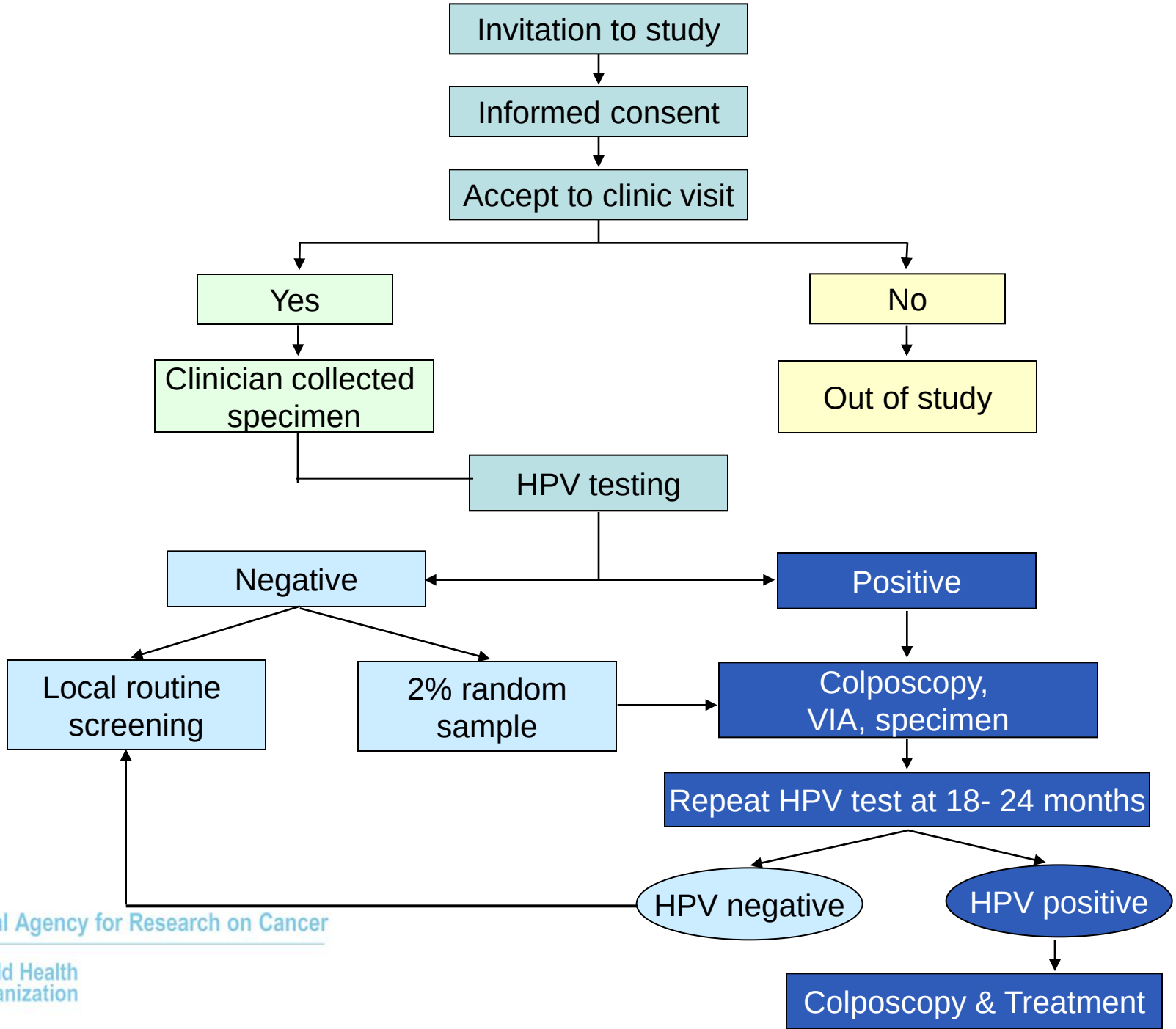
General Objective

- 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



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Primary HPV testing

- Hybrid capture
- COBAS 4800
- Cervista
- Aptima

Possible triage tests (on all coloposcopy 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

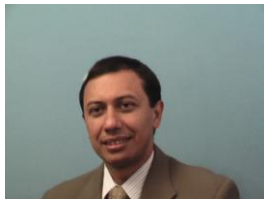
Evaluation of psychosocial impact of HPV testing

- 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

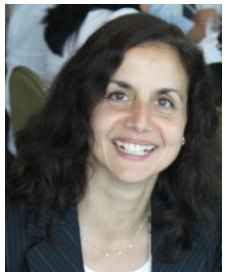
Participating centers and investigators









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WHO, PAHO, RINC