Multicentric Study of Cervical Cancer Screening and Triage with Human Papillomavirus Testing
The ESTAMPA Study

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THE ESTAMPA STUDY

Multicentric study of cervical cancer screening with HPV testing and assessment of triage methods in Latin America

AIMS:

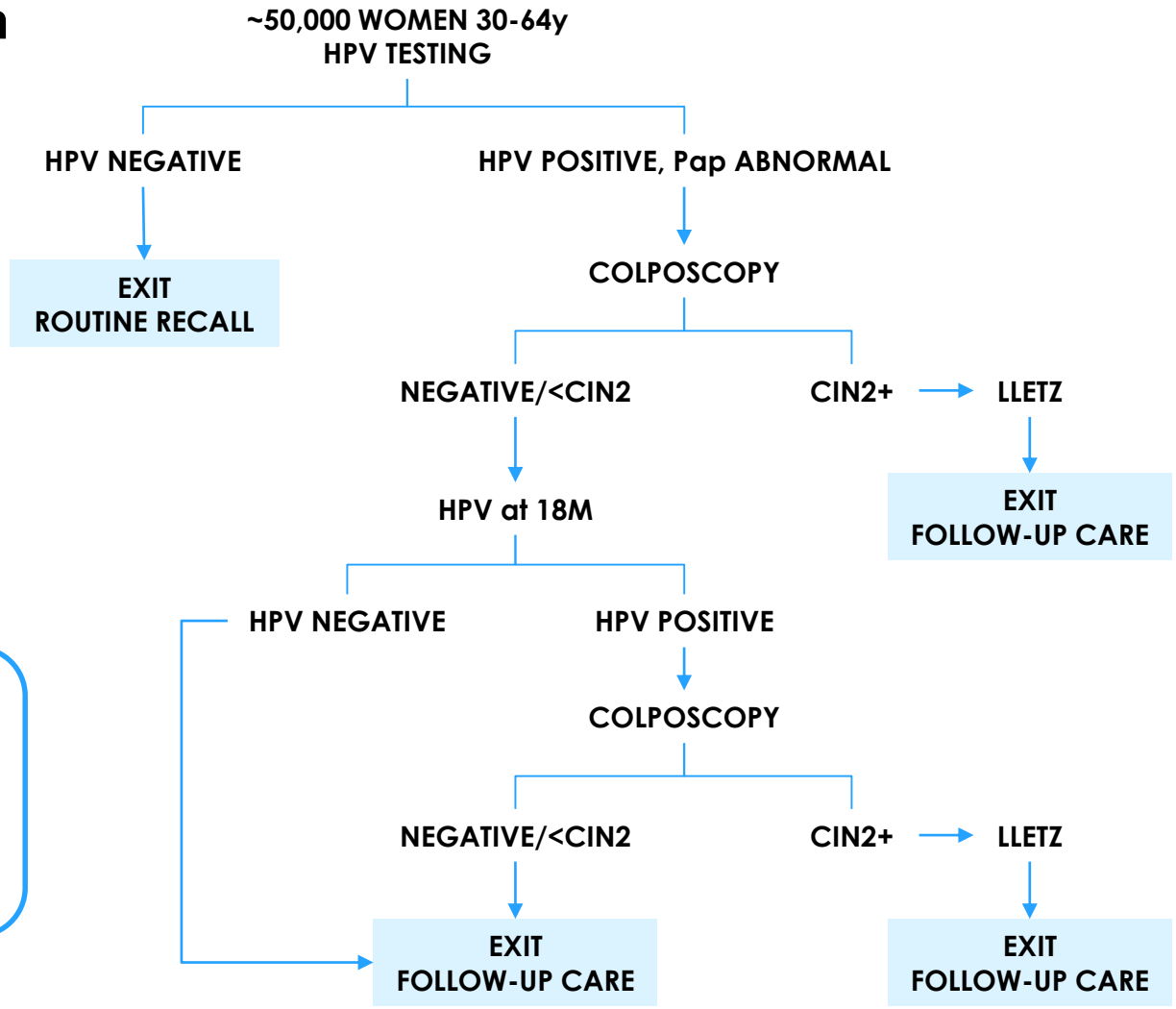
To investigate the performance of emerging cervical cancer screening and triage techniques among women 30 years and older

To evaluate the feasibility of different approaches for implementation of organised HPV-based screening programmes

STUDY CENTRES

THE ESTAMPA STUDY

- ~50,000 women aged 30-64y screened with HPV testing (and Pap)
- HPV positives referred to colposcopy
  - 2-3 biopsies of observed lesions
- HPV positives with <CIN2 recall at 18m
  - HPV test, no other test
  - HPV positives referred to colposcopy
- CIN2+ treated with LLETZ

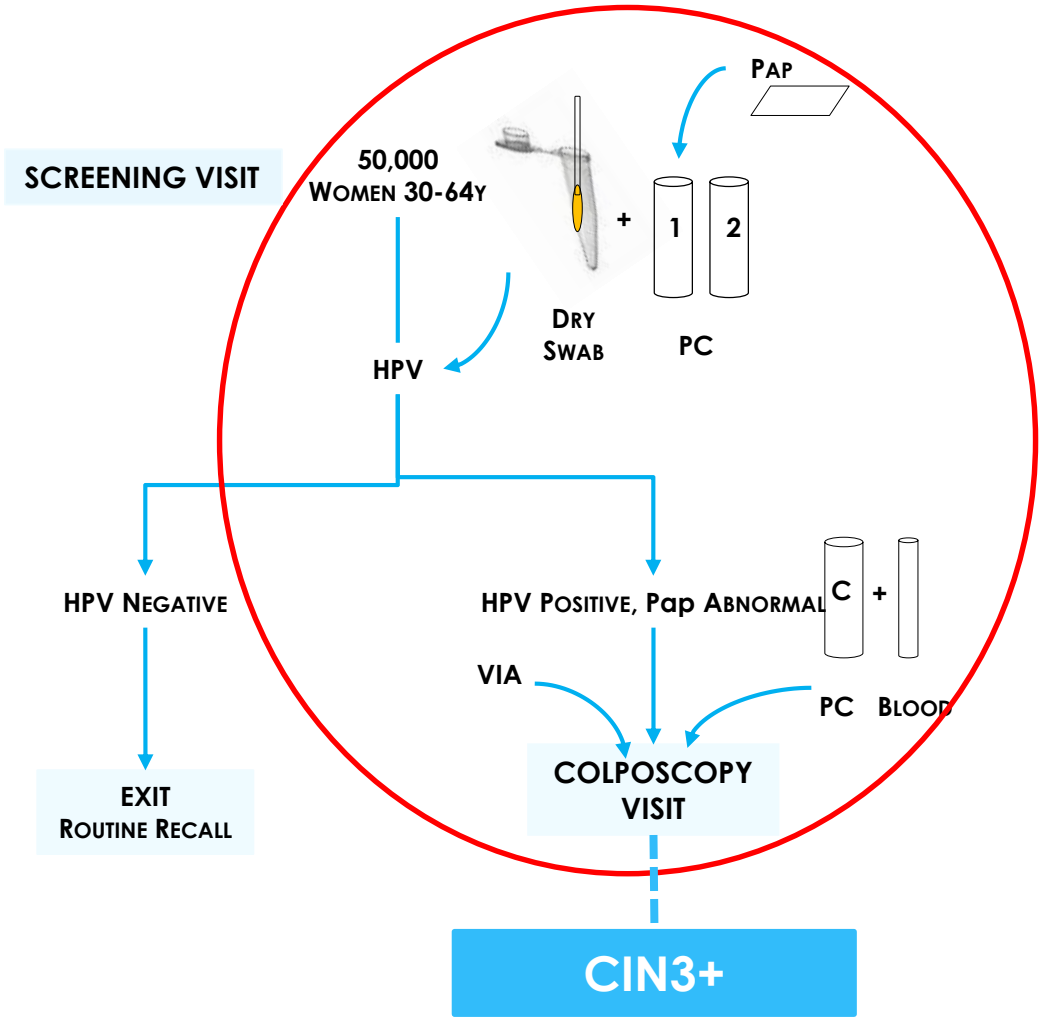


STUDY OUTCOMES

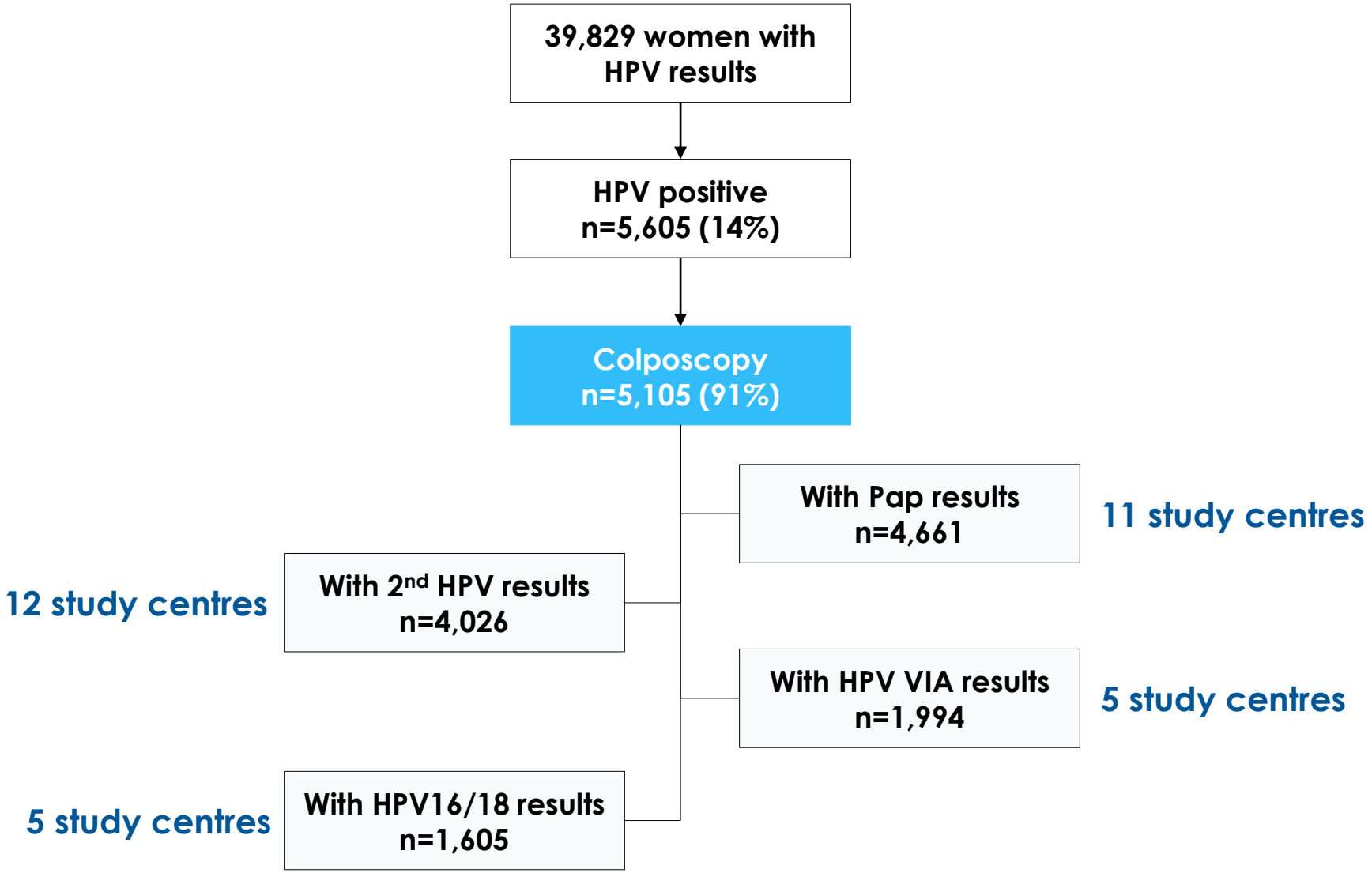
✓ CIN3+ detected at entry

THE ESTAMPA STUDY

- Triage tests: Pap, LBC, p16/ki67 dual-stained cytology, VIA, HPV genotyping, methylation, and triage strategies (e.g., short-term repeat HPV test)
- Specimens collected at initial screening used for triage evaluation simulating reflex-testing whenever possible
- Triage tests except Pap not used for clinical management
- Testing done locally, in regional hubs or in expert centres outside the region
- Not all tests/strategies evaluated in all centres (e.g, VIA: Bolivia, Colombia, Honduras, Paraguay, Peru; HPV 16/18 genotyping: centres that used COBAS)



ESTAMPA Study Population as of April 2020



PAP AS TRIAGE OF HPV POSITIVES

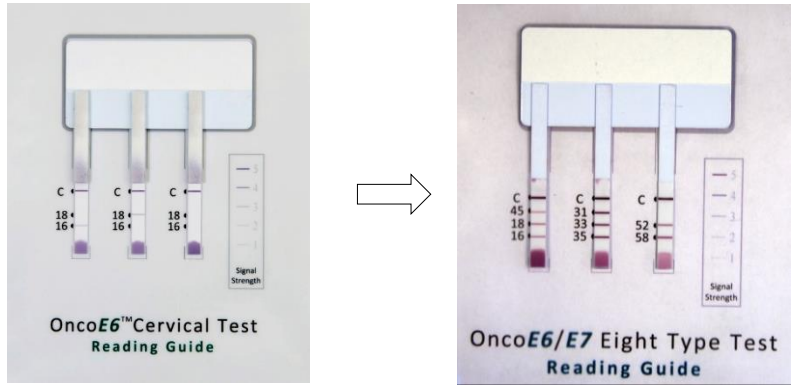
- Pap was done at all study centres
  - HPV testing not yet included in national cervical screening guidelines or not yet implemented
  - HPV status was unknown when smears arrived at laboratories
- Laboratories were classified by:
  - Type of organization: public or private
  - Pap interpretation protocol: cytotechnician interpreting all followed by pathologist confirming abnormal Paps or pathologists interpreting all preparations
- In one centre, only Paps from HPV positives were prepared and interpreted
  - But as a public health laboratory, ESTAMPA smears were prepared and interpreter within a larger number of smears provided by many health clinics

VALIDATION OF THE 8-HPV TYPE ONCOE6/E7 CERVICAL TEST

HYPOTHESIS

Adding detection of other high-risk HPV types oncoproteins might increase the sensitivity of the 16/18 oncoprotein test (OncoE6, Arbor Vita) without losing much specificity

- Under an NCI Affordable Cancer Technologies Award we teamed-up with Arbor Vita to develop/validate a new oncoprotein test



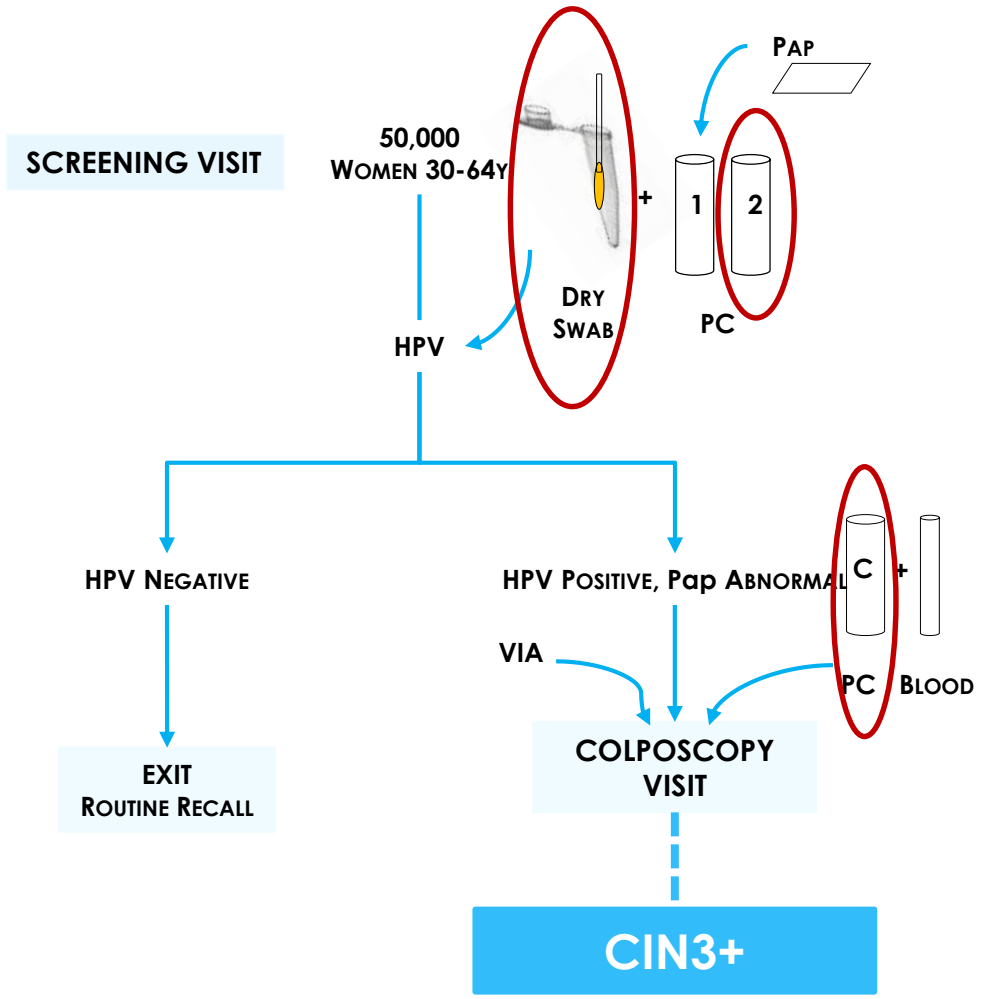
OBJECTIVE

- **Develop and validate the 8-HPV Type OncoE6/E7 for CIN3+ and cancer detection within the ESTAMPA study (convenient sub-sample)**

VALIDATION OF THE 8-HPV TYPE ONCOE6/E7 CERVICAL TEST

Convenient sample of 872 women

STATUS AT INITIAL SCREENING	N
HPV Negative	123
Colposcopy Negative	124
Biopsy Negative	125
CIN1	129
CIN2	120
CIN3	153
Cancer	98
TOTAL	872



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Conclusions and Next Steps

- **Results from evaluations of Pap, VIA, Repeat HPV test and HPV16/18 as triage for HPV positives for CIN3+ detection:**
  - **Pap and HPV16/18 having limited sensitivity ≤ 60%, while the repeat HPV testing strategy and VIA show moderate sensitivity (~86%)**
    - **Pap sensitivity was significantly higher in the laboratory with smears only from HPV positives**
    - **Adding Pap ASCUS+ to triage by HPV non-16/18 positives increased the sensitivity by ~10-15%**
    - **VIA high sensitivity possibly due to examiners with large expertise**
  - **Pap had the highest specificity (~85%) followed by HPV16/18 (~77%), while the other two had limited specificity of ≤50%**
- **The new 8-HPV Type OncoE6/E7 Test preliminary validation showed limited sensitivity but high specificity for individual oncoprotein HPV types**
  - **Six HPV oncoproteins (16,18, 31, 33, 45, 52) contributed to reach overall test sensitivity for CIN3+ and cancer threshold; HPV oncoproteins 35 and 58 not relevant in this population**

Conclusions and Next Steps

- No single triage test/strategy offers a final answer yet, but further evaluation is ongoing/planning:
  - Pap when HPV status is known
  - VIA at screening clinic and at colposcopy to account for potential correlation between VIA and colposcopy results
  - Dual-stained cytology (p16/ki67), HPV full genotyping & methylation
  - Colposcopy as triage of HPV positives, using 18m visit to confirm disease
- Using a convenient sample, the first results of the new 8-HPV Type OncoE6/E7 showed limited sensitivity (60%) but high single oncoprotein specificity (>95%) to detect CIN3+
  - 93% negative in HPV negatives (no colposcopy), 79% in negative colposcopy (no biopsy), 76% in histology<CIN2
  - A further refined version of the test will be evaluated in the ESTAMPA screening population: stand alone and triage

- All screening techniques/strategies will be evaluated alone/combination using HSIL (main study outcome under LAST), including cases detected at initial and 18m screening visits

ESTAMPA INVESTIGATORS

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