VISUAL INSPECTION WITH ACETIC ACID AS A CERVICAL CANCER SCREENING TOOL FOR DEVELOPING COUNTRIES

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Cervical Cancer

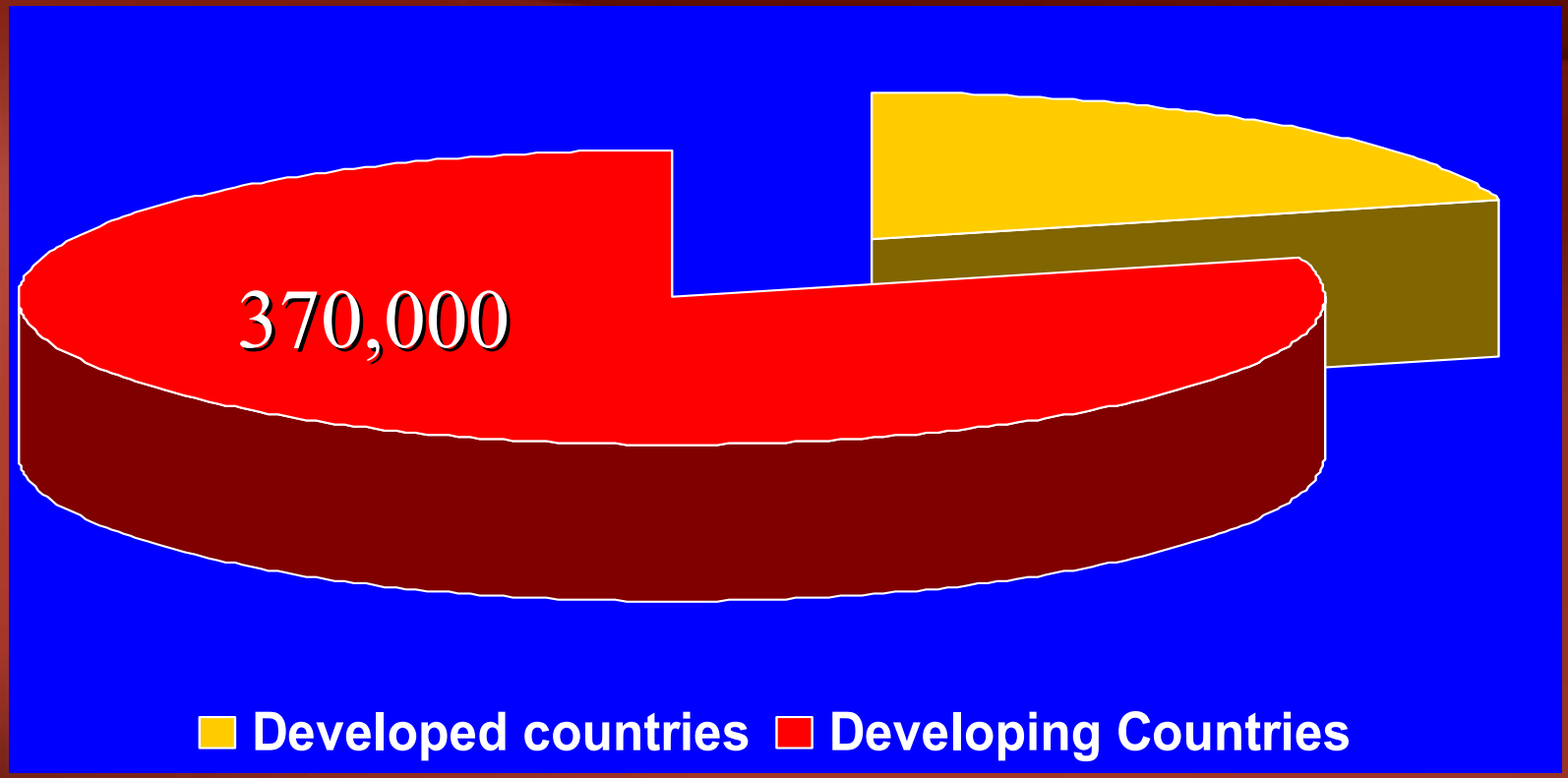
Worldwide

- 231,000 women die of cervical cancer every year
- 12 % of all cancers in women
- 80 % from developing countries

World Health Organization. Cervical Cancer Screening in Developing Countries. Report of a WHO Consultation. 2001(unpublished)

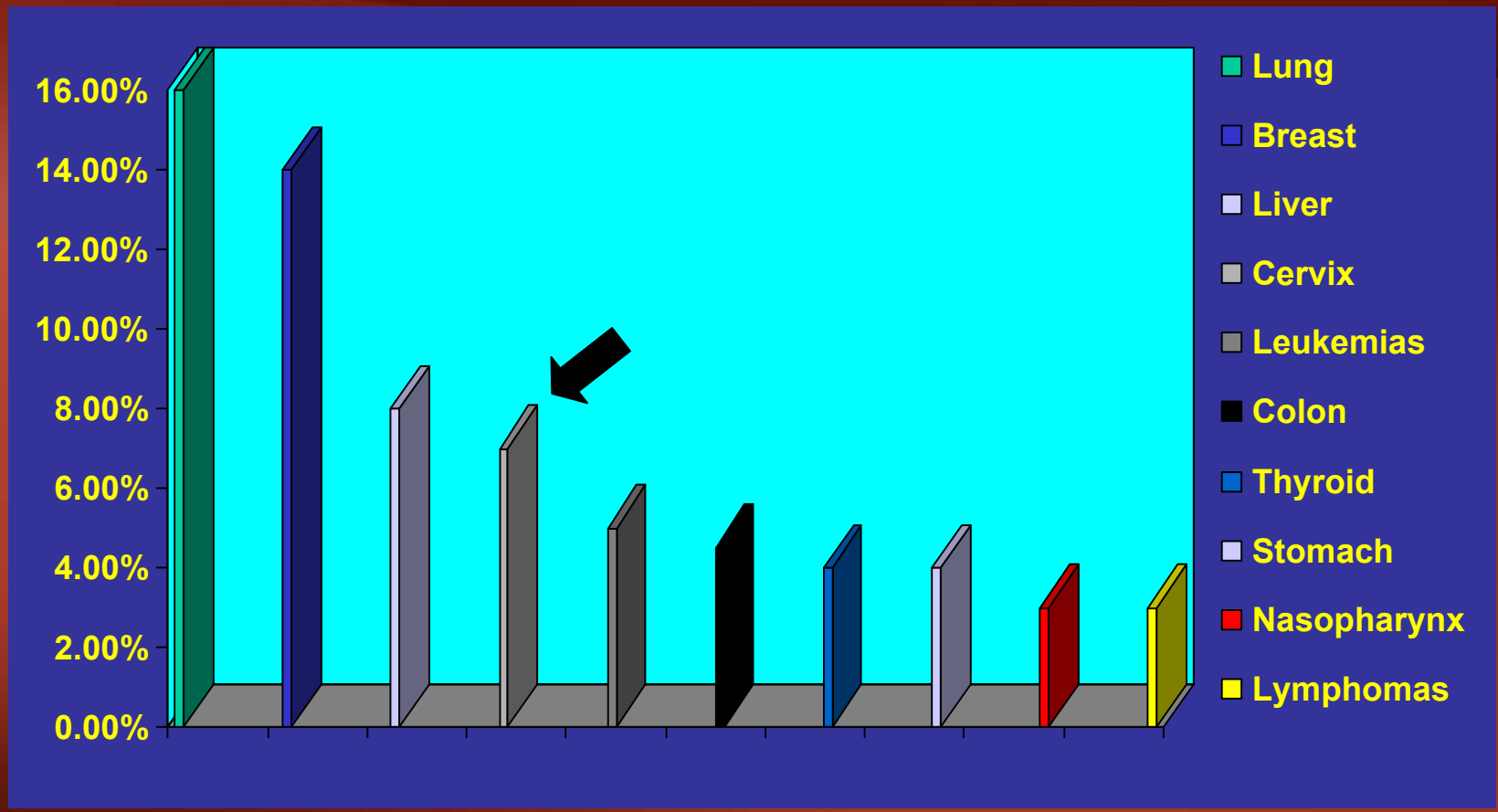
Cervical Cancer

466,000 New Cases Year 2002



Ferlay J et al. Globocan 2000. Cancer Incidence, Mortality and Prevalence Worldwide , Version 1.0. International Agency for Research on Cancer , 2001 (IARC Cancer Base No. 5)

THE TEN LEADING CANCER SITES IN THE PHILIPPINES



Philippine Cancer Facts and Estimates, 1998

TEN LEADING CANCER SITES IN WOMEN

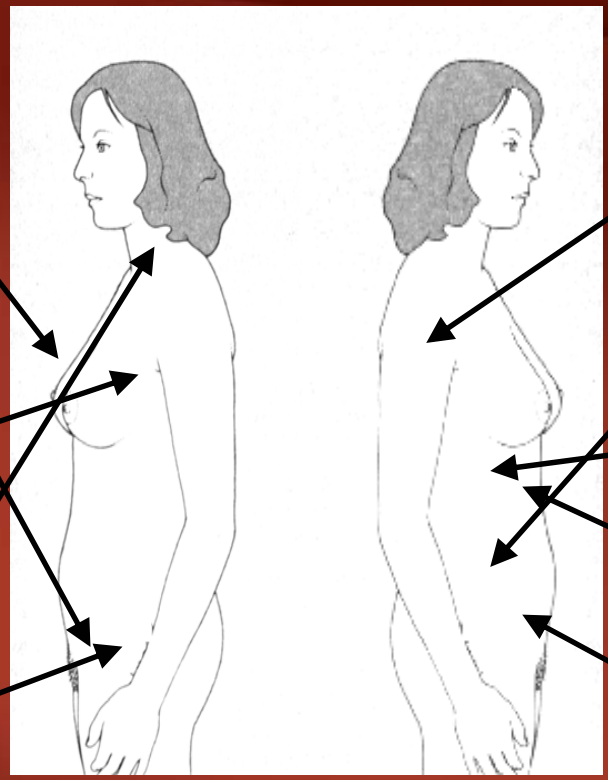
BREAST (1)

CERVIX (2)

LUNG (3)

THYROID (4)

OVARY (5)



LEUKEMIAS (6)

COLON (7)

LIVER (8)

STOMACH (9)

UTERUS (10)

Philippine Cancer Facts and Estimates, 1998

Cervical Cancer Problem in the Philippines

- Incidence rate remains unchanged from 1980-1995 – 22 per 100,000 women
- 56 % of Filipino women with cervical cancer will die within 5 years (44% overall survival rate)
  - About 2/3 of cervical cancer is diagnosed in the advanced stage, where mortality is high.

Cervical Cancer is PREVENTABLE

- Screening detects PREINVASIVE STAGE
- Developed countries with well-organized screening programs – invasive cervical cancer incidence reduced by as much as 90%
- Community based screening programs require sophisticated infrastructure, highly trained personnel, adequately equipped laboratories, good referral systems

In the Philippines

- Geographic limitation- 7,100 islands
- Lack of cytological facilities and expertise
- Lack of treatment facilities in rural areas
- Lack of patient's compliance in rural areas
- Lack of knowledge among women on symptoms associated with cervical cancer
- A fatalistic attitude toward cancer in general

Philippine Knowledge, Attitude and Practices Behavior Modification Study ,2000

Cervical Cancer Screening Situation in the Philippines

389 of 946 Philippine Hospitals surveyed

(118 primary; 167 secondary; 104 tertiary)

- 42% claimed they offer screening & early detection services for cervical cancer; only 8% have clinics dedicated to cervical cancer screening
- Cotton swab – common smear collection tool
- MD – usual person performing Pap smear
- Cytology technician is available in only 21% of hospitals

University of the Philippines-Department of Health Cervical Cancer Screening Study Group. Delineation of an Appropriate and Replicable Cervical Cancer Screening Program for Filipino Women. Manila. 2001

Cervical Cancer Screening Situation in the Philippines

389 of 946 Philippine Hospitals surveyed

(118 primary; 167 secondary; 104 tertiary)

- Pathologist available (part-time) in 45% hospitals
- Colposcopy in 22% tertiary hospitals, 16 % of secondary hospitals, none in primary hospitals
- Only 11 % of hospitals with treatment facilities for cervical cancer

University of the Philippines-Department of Health Cervical Cancer Screening Study Group. Delineation of an Appropriate and Replicable Cervical Cancer Screening Program for Filipino Women. Manila. 2001

Cervical Cancer Screening Situation in the Philippines

- 47 +/- 11 days (mean/sd) days – for a patient to travel from her residence to the clinic for a Pap smear to the time she is told of the result

University of the Philippines-Department of Health Cervical Cancer Screening Study Group. Delineation of an Appropriate and Replicable Cervical Cancer Screening Program for Filipino Women. Manila. 2001

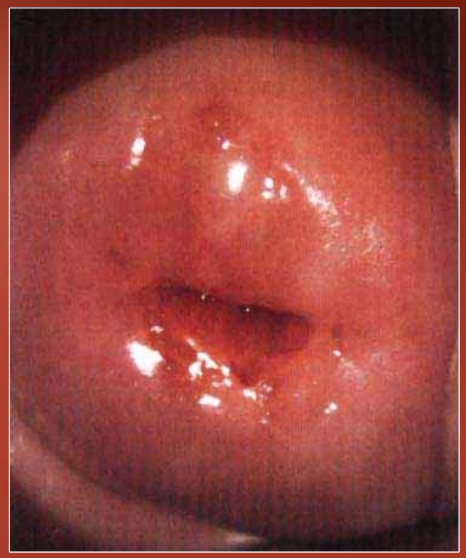
Cervical Cancer Screening

- Alternatives to cervical cytology
  - Automated pap screening
  - VIA (visual inspection with acetic acid)
  - HPV testing
  - Polar probe

VIA

- Inexpensive
- Requires supplies locally obtainable
- Can be competently performed by non physicians with proper training
- Result is immediate

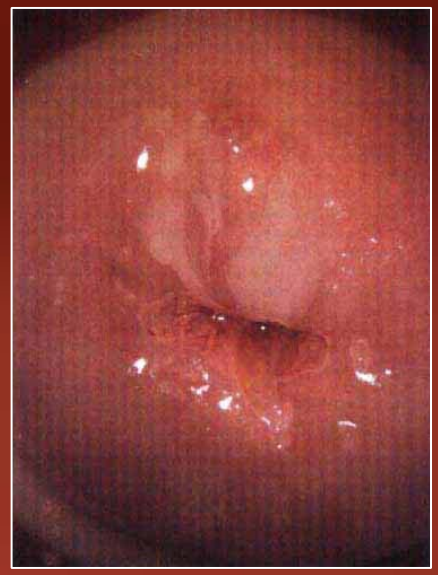
Visual Inspection with Acetic Acid



3-5 %
Acetic acid

Inspection with naked eye

With 100 watt lamp as light source



Colposcopy

Objectives

- To review the evidence on VIA as a cervical cancer screening tool in terms of its sensitivity and specificity in detecting pre-invasive lesions compared to cervical cytology , which is the standard of screening at present.
- To evaluate how this evidence can be used to implement a feasible screening program in a low resource setting like the Philippines.

Materials and Methods

All relevant articles were retrieved from 1980 to March 2003. Studies were identified by a MEDLINE search.

- **Manual searches of relevant journals,**
- **Reference lists of retrieved articles,**
- **Direct communication with other researchers**
  - **Unpublished data from the**
    - **World Health Organization (WHO)**
    - **International Agency for Research on Cancer (IARC)**

Table 1 Description of Studies Reviewed

	Authors/ Year (Reference)	Type of study	Purpose	No of women screened	Setting	Technique	Intervention (VIA) done by	Independence of assessments	Key Statistics	Reference Standard	Comments
1	Megevand et al 1996 (20)	Cross sectional	VIA as an alternative to cytology	2426	Community-based (Mobile clinics in a squatter area in Cape Town, South Africa)	described	Trained Nurses, Community Health workers	Cytotecnologist not blinded to result	Positive Predictive Value	Colposcopy with or without a biopsy	Cytotechnologist not blinded to study results, limited by lack of information on those patients negative on VIA and cytology
2	Sankaranarayanan et al 1998 (21)	Cross sectional	Compare performance of VIA and cytology	3000	Community-based (Open access cancer detection clinics in Karala, India)	described	Trained cytotechnologists	blinded	Sensitivity ratio, approximate sensitivity, approximate specificity	Colposcopy with or without a biopsy	Reference test not applied to women who were screening test negative
3	Sankanarayanan et al 1999 (22)	Cross sectional	Compare performance of VIA and cytology	1351	Community-based (In Ernakulam, India)	described	Trained nurses	blinded	Sensitivity ratio, approximate sensitivity, approximate specificity	Colposcopy with or without a biopsy	Reference test not applied to women who were screening test negative
4	University of Zimbabwe/ JHPIEGO 1999 (26)	Cross sectional	Test qualities of VIA	10934 phase 1- 8731 phase 2- 2203	Community-based (151 clinics Chitungwiza and Greater Harare Area, Zimbabwe)	described	Trained nurse-midwife	blinded	Sensitivity/Specificity	Colposcopy with or without a biopsy	Phase 1- work up bias, Phase 2- all women underwent gold standard
5	Denny et al 2000 (23)	Cross sectional	Compare performance of cytology, VIA, VIA with magnification and HPV DNA in detecting HGSIL	2944	Community based (clinics in Khagelitska, South Africa)	described	Trained nurses	blinded	Sensitivity ratio, approximate sensitivity, approximate specificity	Colposcopy with or without a biopsy	Reference standard not applied to the women who were screening test negative

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Authors/ Year (Reference)	Type of study	Purpose	No of women screened	Setting	Technique	Intervention (VIA) done by	Independence of assessments	Key Statistics	Reference Standard	Comments
Cronje et al 2000 (27)	Cross sectional	Compare cytology, cervicography, VIA	6301	Community based (Volunteers throughout Free State Province of South Africa)	described	Trained Nurses	blinded	Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value	Colposcopy with biopsy	Gold standard done on all women
Belinson , Quia et al 2001 (28)	Cross-sectional	Determine accuracy of 6 screening tests: conventional cytology, liquid based cytology, VIA, colposcopy, HPV testing, fluorescence spectroscopy	1997	Community-based (Rural Shanxi Province, China)	described	Gynecologic Oncologists	blinded	Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value	Colposcopy with biopsy	Gold standard done on all women Result may not be reproducible VIA performed by Gynecologic Oncologists
Ngelangel et al 2001 (29)	Cross sectional	VIA alone, VIA with magnification compared to cytology	13,710	Hospital based (6 Metro Manila Hospitals and 6 regional Hospitals Philippines)	described	Tained nurses, midwives, physicians from community centers	blinded	Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value	Colposcopy with or without a biopsy	Reference standard used was colposcopy not applied to the women who were screening test negative
Denny et al 2002 (24)	Cross Sectional	Compare VIA and VIA with magnification to cytology	2754	Community based (Periurban settlement in Cape Town, South Africa)	described	Trained Nurses	blinded	Sensitivity ratio, approximate sensitivity, approximate specificity	Colposcopy with or without a biopsy	Reference standard not applied to the women who were screening test negative

- Verification bias
- Non-independence of assessments

Table 2 Data from Studies Reviewed (VIA)

Authors/ Year (Reference)	No of women screened	Age range	Key results (Sensitivity,Specificity,PPV,NPV when available)	Reference Standard	Comments
Megevand et al 1996 (20)	2426	20-83	Sensitivity of VIA 65 % vs 100 % for cytology Specificity 97 % vs 89 % for cytology PPV 72.4 % vs 88.9 % for cytology	Colposcopy with or without a biopsy	Cytotechnologist not blinded to study results, limited by lack of information on those patients negative on VIA and cytology
Sankaranarayanan et al 1998 (21)	3000	25-70	Sensitivity ratio to cytology= 1.05, p=0.25 Estimated Sensitivity 90 % for VIA vs 86 % for cytology Estimated specificity 92 % for VIA vs 91 % for cytology PPV 17.0 % vs 17.2 % NPV 99 % vs 99 %	Colposcopy with or without a biopsy	Reference test not applied to women who were screening test negative
Sankanarayanan et al 1999 (22)	1351	22-70	Sensitivity ratio to cytology= 1.54, p<0.001 Estimated Sensitivity 96 % for VIA vs 62 % for cytology Estimated specificity 68 % for VIA vs 90 % for cytology PPV 15 % vs 25 % NPV 99 % vs 97 %	Colposcopy with or without a biopsy	Reference test not applied to women who were screening test negative
University of Zimbabwe/ JHPIEGO 1999 (26)	10934 phase 1-8731 phase 2-2203	25-55	Sensitivity of VIA 77 % (70.3-82.3) vs 44 % (37.3-51.4) for cytology Specificity 64 % (61.9-66.2) vs 91 % (89.2-91.9) for cytology PPV 19 % vs 33 % NPV 96 % vs 94 %	Colposcopy with or without a biopsy	Phase 1- work up bias, Phase 2- all women underwent gold standard
Denny et al 2000 (23)	2944	35-65	Sensitivity ratio to cytology= 0.85, p=0.16 Estimated Sensitivity 67 % for VIA vs 78 % for cytology Estimated specificity 83 % for VIA vs 94 % for cytology PPV 11 % vs 27 % NPV 99 % vs 99 %	Colposcopy with or without a biopsy	Reference standard not applied to the women who were screening test negative

Table 2 Data from Studies Reviewed (VIA)

Authors/ Year (Reference)	No of women screened	Age range	Key results (Sensitivity,Specificity,PPV,NPV when available)	Reference Standard	Comments
Cronje et al 2000 (27)	6301	Ave age 34.4	Sensitivity 49.4 %(44.1-54.7) for VIA vs 19.3 % (15.1-23.5)for cytology specificity 48.5 %(45.9-51.2) for VIA vs 99.3 % (98.7-99.7) for cytology PPV 18.9 % vs 86.8 % NPV 99 % vs 97 %	Colposcopy with biopsy	Reference standard done on all women
Belinson , Quia et al 2001 (28)	1997	35-45	Sensitivity 71 for VIA % vs 77 % for cytology Specificity 74 % vs 98 % for cytology PPV 11 % vs 61 % for cytology NPV 98 % vs 98 % for cytology	Colposcopy with biopsy	Reference standard done on all women Result may not be reproducible VIA performed by Gynecologic Oncologists
Ngelangel et al 2001 (29)	13,710	20-65	Estimated Sensitivity 50.3 %(45.2-55.5) for VIA vs 8.5 % (5.5-11.5) for cytology Estimated specificity 94.1 %(93.4-94.9) for VIA vs 97.3 % (97.1-98.2) for cytology	Colposcopy with or without a biopsy	Reference standard used was colposcopy not applied to the women who were screening test negative
Denny et al 2002 (24)	2754	35-65	Sensitivity 69.8 %(59.4-78.5) for VIA vs 57.4 %(46.8-67.4) for cytology specificity 79.3 %(77.6-80.8) for VIA vs 96.3 % (95.5-97.0) for cytology PPV 12.9 % vs 34.5 % NPV 96.3 % vs 95.8 %	Colposcopy with or without a biopsy	Reference standard not applied to the women who were screening test negative

VIA

- Range of sensitivity: 49.4 % - 96 %
- Range for specificity: 48.5 % - 97 %
- Positive predictive value: 11% - 26 %
- Negative predictive value: 95.5% - 99 %.

Variations

- Definitions for a positive VIA test
- Personnel who performed VIA
- Age range among study participants: 20-83
  - Less than 35 vs older than 35
    - Sensitivity of pap smear and VIA increased

Conclusions

- VIA has better or similar sensitivity to that of cervical cytology in detecting pre-invasive disease but has lower specificity
- VIA should be evaluated further with regard to
  - improving specificity, without compromising sensitivity
  - standardization of criteria as to disease categories
  - a comprehensive competency based training of personnel involved in screening must be done
  - long term follow up of women and the consequent impact on disease burden deserve further research

Table 3: On-going IARC collaborative studies on VIA for cervical cancer screening

Program design	Interventions evaluated	Location of the study	Number of participants	End points of the program
Randomised, controlled intervention study	VIA, cervical cytology, HPV testing	Osmanabad district, India	160,000 women 30-59 years	Cervical cancer incidence/ mortality; Cost-effectiveness; establishment of a service and training platform for cervical cancer prevention.
Randomised, controlled intervention study	VIA	Dindigul District, India	73,000 women aged 30-59 years	Detection rates of CIN2-3Cervical cancer incidence/mortality; Cost-effectiveness; establishment of a service and training platform for cervical cancer prevention.
Cross-sectional study	VIA, VILI	Burkina Faso, Republic of Congo, Guinea, Hyderabad, India, Laos, Mali, Niger, Mauritania, Tanzania	5000 women aged 30-59 in each location	Test characteristics; Acceptability, efficacy, complications of cryotherapy; establishment of a service and training platform for cervical cancer prevention.
Cross-sectional study	VIA, cytology	Nigeria	2000 women aged 30-64 years	Test characteristics; Acceptability, efficacy, complications of cryotherapy; establishment of a service and training platform for cervical cancer prevention.
Cross-sectional study	VIA, VILI, cervical cytology	Trivandrum and Jaipur India;	6000 women 30-59 years in each location	Test characteristics; Acceptability, efficacy, complications of cryotherapy; establishment of a service and training platform for cervical cancer prevention.
Cross-sectional study	VIA, VIAM, VILI, cervical cytology, HPV testing	Calcutta, India	12,000 women aged 30-64 years	Test characteristics; Acceptability, efficacy, complications of cryotherapy; establishment of a service and training platform for cervical cancer prevention.
Cross sectional study	Cervical cytology, HPV testing, VIA, VIAM, VILI	Bombay, India	5000 women aged 30-59 years	Test characteristics; Acceptability, efficacy, complications of cryotherapy; establishment of a service and training platform for cervical cancer prevention.

VIA: Visual inspection with acetic acid; VIAM: Magnified visual inspection with acetic acid; VILI: Visual inspection with Lugol's iodine

Sankaranarayanan R .The current work of the International Agency for Research on Cancer (WHO/IARC) in cervical cancer control in developing countries. (Unpublished; Personal communication with the author)

In areas where resources are scarce, VIA may find a place as a low technology, low cost method of screening; particularly in regions like the Philippines - without extensive cytology laboratory facilities.

Good Morning.