Epidemiology, Prevention & Early detection of Carcinoma cervix

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Cervical Cancer Facts

- Cervical cancer affects an estimated 490,000 women worldwide each year and leads to more than 270,000 deaths.

- About 85 percent of women who die from cervical cancer reside in developing countries. Each year, 75,000 women die from the disease in India alone.

- If current trends continue, by the year 2050 there will be over one million new cases annually.
• Considerable uncertainty with respect to estimates of the global burden of cervical cancer.

• Tumor registries in these regions are frequently inadequate, making estimates difficult (cases may be greater than estimated)
Figure 1.1 Age-standardized incidence rates of cervical cancer in developed and developing countries (2005)


Figure 1.2 Age-standardized mortality rates of cervical cancer in developed and developing countries (2005)

INCIDENCE OF CERVICAL CANCER WORLD WIDE

Numbers indicate cases per 100,000 population. Data are from the International Association of Cancer Registries, GLOBOCAN 2002.
Figure 1.3 Worldwide incidence rates of cervical cancer per 100,000 females (all ages), age-standardised to the WHO standard population (2005)
CERVIX (ICD-9: 180)

Numbers and Incidence

<table>
<thead>
<tr>
<th>Registry</th>
<th>No.</th>
<th>%</th>
<th>R</th>
<th>AAR</th>
</tr>
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<tbody>
<tr>
<td>Bangalore</td>
<td>2523</td>
<td>21.5</td>
<td>1</td>
<td>26.1</td>
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<tr>
<td>Barshi</td>
<td>388</td>
<td>50.7</td>
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<td>Bhopal</td>
<td>537</td>
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<tr>
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<tr>
<td>Delhi</td>
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<tr>
<td>Mumbai</td>
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<td>15.2</td>
<td>2</td>
<td>17.2</td>
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</table>
International Comparisons of Age Adjusted Incidence Rates with that of PBCRs under NCRP CERVIX UTERI (ICD-10 : C53) - Females

Source: NCRP, Bangalore

<table>
<thead>
<tr>
<th>Location</th>
<th>Rate per 100,000</th>
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<tbody>
<tr>
<td>Zim., Har.: African</td>
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<tr>
<td>Brazil, Goiania</td>
<td>38.2</td>
</tr>
<tr>
<td>Chennai</td>
<td>30.6</td>
</tr>
<tr>
<td>Vietnam, Ho Chi Minh City</td>
<td>28.8</td>
</tr>
<tr>
<td>Bhopal</td>
<td>24.5</td>
</tr>
<tr>
<td>Delhi</td>
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</tr>
<tr>
<td>Barshi</td>
<td>22.4</td>
</tr>
<tr>
<td>Bangalore</td>
<td>21.7</td>
</tr>
<tr>
<td>Popland, Cracow</td>
<td>19.6</td>
</tr>
<tr>
<td>USA, Cali, LA, His: White</td>
<td>19.5</td>
</tr>
<tr>
<td>Mumbai</td>
<td>18.0</td>
</tr>
<tr>
<td>Aust., Nor. Terri.</td>
<td>16.3</td>
</tr>
<tr>
<td>Algeria, Algiers</td>
<td>12.5</td>
</tr>
<tr>
<td>USA, Puerto Rico</td>
<td>8.3</td>
</tr>
<tr>
<td>Singapore: Indian</td>
<td>8.2</td>
</tr>
<tr>
<td>USA, Cali., LA: Jap.</td>
<td>5.1</td>
</tr>
<tr>
<td>USA, Haw.: Chi.</td>
<td>3.8</td>
</tr>
<tr>
<td>Spain, Cuenca</td>
<td>3.4</td>
</tr>
<tr>
<td>China, Jiashan</td>
<td>1.2</td>
</tr>
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</table>
Districtwise Comparisons of Age Adjusted Incidence Rates with that of PBCRs under NCRP CERVIX UTERI (ICD-10 : C53) - Females
Cervical cancers

• CERVIX UTERI (ICD-10 : C53) - Females Chennai PBCR has had the highest incidence rate of cervical cancer among the Indian PBCRs. The districtwise MAARs indicate a belt of high incidence rates even higher than that in Chennai PBCR, in the North Eastern districts of Tamil Nadu State including Pondicherry which had the highest MAAR of 39.2/100,000.

• Incidence rates begin to rise in the early twenties in all registries and reach a peak in the 50-54 age group and only slowly thereafter.

• 90% of cases of cancer of the cervix were squamous cell carcinomas. Adenocarcinomas constituted 2-4% of all cervical cancers.
The main reasons for the higher incidence and mortality in developing countries are:

• Lack of awareness of cervical cancer among the population, health care providers and policy-makers

• Absence or poor quality of screening programmes for precursor lesions and Early-stage cancer.

• Cancer tends to be diagnosed in its later stages, when it is less easily treatable.

• Limited access to health care services

• Lack of functional referral systems.
Natural History of Cervical Cancer:

- **HPV Infection**
  - Normal Epithelium
  - Persistent infection with high risk HPV
  - 80% HPV clearance
  - 20% HPV infection

- **HPV-related Changes**
  - Low-Grade SIL (Atypia, CIN I)
    - About 60% regress within 2-3 yrs
  - High-Grade SIL (CIN II, III/CIS)
    - About 15% progress within 3-4 yrs
    - 30% - 70% progress within 10 yrs
  - Invasive Cancer

Birth  On set of sexual activity

Average Age 13  18

Dysplasia  Carcinoma insitu  Invasive Cancer  Death

Detectable preclinical phase (DPCP)

-8% of cancers  -92% of cancers

Screening here encounters the Dysplasia Swamp

Screening here has maximum Cost-effectiveness
HPV

- Human papillomavirus (HPV), a common sexually transmitted infection, is the primary underlying cause of cervical cancer.

- HPV infection is a necessary but not sufficient precursor to cervical cancer.

- Detection of high risk HPV DNA is an indicator of development of high grade lesion.

- Preventing HPV transmission is very difficult. Barrier contraceptive methods are only partially effective because the virus can exist throughout most of the anogenital area (including areas not covered by male condoms) and can remain infectious for years.

- HPV cannot be treated, but infection becomes undetectable in the majority of cases.

- Prevalence varies among regions, it generally reaches a peak of about 20 percent among women aged 20 to 24, with a subsequent decline to approximately 3 percent among women over age 30.6
HPV

- Double stranded DNA virus of Papovaviridae family.
- >114 types described; 40 infect ano-genital tract.
- High risk types-16,18,31,33,35,39,45,51,52,58,59,68,73
- Low risk types- 6,11, 42, 43 and 44.
HPV and Cervical Neoplasia

- Virus encodes for 6 early or regulatory proteins (E1, E2, E4, E5, E6E and E7) and 2 late or structural proteins (L1 and L2).

**Early region:**
- Controls Viral replication
- Maintains a high intracellular viral copy number
- Produces onco-proteins which transfer the normal cell into a neoplastic cell.
The conditions or cofactors that lead HPV infection to persist and progress to cancer are not well understood.
**HPV-related cofactors:**
- Viral type;
- Simultaneous infection with several oncogenic types;
- High virus load.

**Host-related cofactors**
- Immune status: people with immunodeficiency have more persistent HPV infections and a more rapid progression
- Parity.

**Exogenous cofactors:**
- Tobacco smoking;
- Coinfection with HIV or other sexually transmitted agents such as *herpes simplex virus 2 (HSV-2), Chlamydia trachomatis* and *Neisseria gonorrhoeae* increase persistence.
- Long-term (> 5 years) use of oral contraceptives.
Natural history of HPV infections

• The eight most common HPV types detected in descending order of frequency are: HPV 16, 18, 45, 31, 33, 52, 58, and 35. These eight types of HPV are responsible for about 90% of all cervical cancers worldwide.

• The fraction of squamous cell carcinomas or adenocarcinomas attributable to HPV-16 and -18 was 70% and 86%, respectively.

• There is some data to suggest that HPV 16 persists longer, on average, than do other types of HPV.
Age-specific HPV prevalence among women with normal cytology. Crude and adjusted estimates are presented based on the meta-analysis of 78 studies.
<table>
<thead>
<tr>
<th>Bethesda System</th>
<th>Cervical Intraepithelial Neoplasia (CIN) system</th>
<th>Common Dysplasia Terminology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical Squamous cell of undetermined significance (ASCUS)</td>
<td>Cellular atypia</td>
<td>Unspecified cellular changes</td>
</tr>
<tr>
<td>Low grade Squamous intraepithelial lesions (LSIL)</td>
<td>CIN I</td>
<td>Mild Dysplasia</td>
</tr>
<tr>
<td>High grade Squamous intraepithelial (HSIL)</td>
<td>CIN II</td>
<td>Moderate Dysplasia</td>
</tr>
<tr>
<td></td>
<td>CIN III includes carcinoma insitu (CIS)</td>
<td>Severe Dysplasia</td>
</tr>
</tbody>
</table>
Metaplastic Epithelium

- Found at S-C junction.
- Originates from sub-columnar reserve cells under the influence of low vaginal pH.
- Eventually matures into 4-layered normal squamous epithelium and replaces columnar epithelium.
Dysplastic epithelium

- Cytologic atypia.
- Nuclear atypia.
- Increased mitotic activity.
- Cellular disorganization and loss of polarity.
- Extent of these abnormalities identifies the degree of dysplasia.
Various screening tests are available.

Regardless of the screening test used, the focus should be to maximize coverage and link screening and treatment services.
Cervical cancer screening is justified according to the listed criteria because:

» • Cervical cancer is an important public health problem in many resource-poor settings.

» • There is a recognized precursor stage that can be treated in a safe, effective, and acceptable way.

» • The time between the appearance of precancerous lesions and the occurrence of cancer is long (about ten years), leaving ample time for detection and treatment.

» • Treatment of early lesions is very inexpensive compared to the management of invasive cancer.
Qualities of a Good Screening Test?

- Effective
- Safe
- Practical
- Affordable
- Available
Screening for cervical neoplasia

CYTOLOGY

- Cervical Cytology (PAP Test)

NONCYTOLOGY METHODS

- HPV-DNA testing
- VIA (Visual inspection of cervix with Acetic acid)
- VILI (Visual inspection of cervix with Lugol’s Iodine)
- Cervicography

- Key Point is to detect precancerous lesions – “Down staging”

- Answer: A good screening method
  - PAP smear test is considered to be the gold standard – Has limitations?
  - Alternatives to Pap Smear – What are they?
Traditional screening methods: Conventional cervical cytology

*Strengths of cytology*

- Historical success in developed countries.
- High specificity, meaning women with no cervical abnormalities are correctly identified by the test with normal test results.
- A well characterized screening approach.
- May have the potential to be cost-effective in middle-income countries.
Minimum requirements for establishing cytology based screening program

- Well-trained Pap smear providers (including non-physicians).

- Initial and ongoing access to supplies and equipment.

- Linkages, including transportation, to a reliable cytology laboratory.

- Proven systems for timely communication of test results to screened women.

- Effective referral systems for diagnosis and treatment.
Well-organized and well-implemented cytology-based screening programs that screen women at regular intervals have been associated with measurable reductions in cervical cancer incidence and mortality when screening coverage and the treatment rate of women with abnormal findings are high.

Cytology-based programs can be implemented effectively only if infrastructure and laboratory quality assurance requirements are consistently met.
Limitations of Pap Smears for National Screening Programs

- Pap smear-based programs require complex logistics, advanced training, and well managed program implementation for adequate testing to occur.

- These elements are not available outside large cities in many low-resource settings.

- Even in large cities, quality pap smears are possible but ongoing supervision, refresher training and continued supplies are necessary.

- Cytology is not viable as a nationally accessible screening method in many developing countries in Low Resource Settings.
Liquid-based cytology (LBC)

» Liquid-based cytology (LBC) testing is a new technique that provides a uniform thin layer of cervical cells without debris.

» It is a more expensive test than conventional cytology and requires additional supplies and sophisticated equipment to process the smear.

» The impact of LBC on cancer incidence and mortality remains to be established, as does its cost-effectiveness.
Cervical Cancer Screening

Alternatives

- Visual inspection with acetic acid (VIA)
- Visual inspection with acetic acid and magnification (VIAM): Gynescope or Aviscope
- Colposcopy
- Molecular (HPV/DNA) tests
HPV Testing Methods

- Non-amplified tests commercially available in U.S. since late 80s
  - Virapap/Viratype (dot blot assay for HPV 6/11, 16/18, 31/33/35)
  - HPV Profile (dot blot assay for HPV 6/11/42/43/44, and 16/18/31/33/35/45/51/52/56)
  - Hybrid Capture-I (tube-based solution hybridization assay for same HPV types as Profile, sensitivity threshold, >10pg/ml)
  - Hybrid Capture-II (microtiter-based solution hybridization assay; same HPV types as HC-I plus 39/58/59/68)

- Amplified tests (polymerase chain reaction--PCR) using various primers (most commonly MY09/MY11) are more sensitive but not available in standardized formats
Testing Methodologies

- Southern blotting
- Dot blot
- Filter in situ hybridisation (FISH)
- In situ hybridisation
- Hybrid capture HCI / HC II
- Polymerase chain reaction (PCR)
- Others: LCR, NASBA, in situ PCR
Limitations of HPV testing as a basis for screening programmes:

- The current costs of the equipment and reagents.

- The requirement to modify the paradigm of cervical screening with some implications in:
  a) the adoption of new clinical protocols for the diagnosis and treatment of precancerous lesions and
  b) training health professionals.

- Transfer of the HPV testing technology to middle-income countries has to be proven and may require country-specific evaluations.
Disadvantages of HPV DNA testing

- High costs of equipments and reagents

- Dependence on reagents currently produced by only a single commercial manufacturer.

- Requirement for a molecular diagnostic laboratory and its low specificity in younger women and populations with significant rates of HIV seropositivity.

- Does not provides results at the time of the visit or soon afterwards, thus many of the traditional barriers to cytological screening remain.

- The need to transport specimens to a laboratory for evaluation.

- The need to recall women to undertake diagnostic tests and provide treatment.
**Visual inspection with acetic acid (VIA):**

Performing a vaginal speculum exam during which a health care provider applies dilute (3-5%) acetic acid (vinegar) to the cervix

↓

Abnormal tissue temporarily appears white when exposed to vinegar

↓

Viewing the cervix with the naked eye (with or without magnification) to identify colour changes

↓

Determining whether the test result is positive or negative for possible pre-cancerous lesions or cancer.
AIDED VISUAL SCREENING TEST IS A PROMISING APPROACH

- Is simple, non invasive & inexpensive test
- Has easy to learn approach
- Does not require laboratory involvement
- Is a real time test; Plan management during the same visit.
- Non-physicians can perform the procedure

As a result, Visual screening tests has the potential for greater population coverage than other screening approaches.
PATHOPHYSIOLOGICAL CONCEPT OF VISUAL SCREENING TESTS-TRANSFORMATION ZONE, SQUAMOUS METAPLASIA
VISUAL INSPECTION OF CERVIX WITH ACETIC ACID (VIA)

Visualization of the acetic acid- washed cervix using a good light source to facilitate cervical cancer screening & possibly to guide biopsy & treatment of pre-invasive lesions
VISUAL INSPECTION WITH LUGOL’S IODINE

Visualization of Lugol’s iodine washed cervix using a good light source to differentiate mat. Sq. epithelium from imm. Sq.ep or dysplastic ep to facilitate cervical cancer screening & possibly to guide biopsy & Rx of pre-invasive lesions.
# Cervix Cancer Screening Trials in India

<table>
<thead>
<tr>
<th>Authors</th>
<th>Place</th>
<th>Location</th>
<th>Method</th>
<th>Provider</th>
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<tbody>
<tr>
<td>Sankaranarayanan R et al (2003)</td>
<td>TVM</td>
<td>Community</td>
<td>VIA, VILI, Pap</td>
<td>HW</td>
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<td>Sankaranarayanan R et al (2003)</td>
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<td>VIA, VIAM, VILI Pap, HPV</td>
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## Cervix Cancer Screening Trials in India

<table>
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<th>Authors</th>
<th>Place</th>
<th>Location</th>
<th>Method</th>
<th>Provider</th>
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Figure 2. Sensitivity and specificity of VIA (%) for CIN II or worse, by study
### Appendix 1.1. Characteristics of Screening Tests

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cervical cytology</th>
<th>Newer screening tests</th>
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<tbody>
<tr>
<td></td>
<td>Sensitivity = 47-62%**</td>
<td>HPV DNA test</td>
</tr>
<tr>
<td></td>
<td>Specificity = 60-95%**</td>
<td>Visual Inspection Tests</td>
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<tr>
<td>Sensitivity and specifity for high-grade lesions and</td>
<td>Cytology has been assessed over the last 50 years in a wide range of setting in</td>
<td>Visual Inspection with acetic acid (VIA)*</td>
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<tr>
<td>invasive cancers</td>
<td>both developed and developing countries.</td>
<td></td>
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<tr>
<td></td>
<td>HPV DNA testing has been assessed over the last decade in many setting in</td>
<td></td>
</tr>
<tr>
<td></td>
<td>developed countries and relatively few setting in developing countries.</td>
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<tr>
<td></td>
<td>VIA testing has been assessed over the last decade in many setting in</td>
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<tr>
<td></td>
<td>developing countries.</td>
<td></td>
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<tr>
<td>Number of visits required for screening and treatment</td>
<td>Requires 2 or more visits.</td>
<td>Can be used in a single-visit approach in setting where outpatient treatment is</td>
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<tr>
<td></td>
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<td>available.</td>
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<tr>
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<td>Can be used in a single-visit approach in setting where outpatient treatment is</td>
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<tr>
<td></td>
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<td>available.</td>
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</table>

**Source: Sankaranarayanan et al. forthcoming**

Sensitivity is the proportion of individual correctly identified by the test as having disease. Higher sensitivity means that fewer lesions will be missed (i.e., there will be fewer negatives). Specificity is the proportion of individuals correctly identified by the test as NOT having disease. Higher specificity means that there will be fewer false positives.
ROLE OF COLPOSCOPY IN SCREEN POSITIVE CASES

• To confirm the screening tests
• To locate, evaluate the extent of lesion and thus to grade the lesion
• To direct the diagnostic biopsy – at SCJ on the worst appearing area
• Triage the management of CIN in the OPD settings and also for See & treat option for screen positives in single sitting at the screening camp.
# Approaches to Cervical Cancer Prevention in Low-resource Settings

<table>
<thead>
<tr>
<th>Method</th>
<th>Effective</th>
<th>Safe</th>
<th>Practical</th>
<th>Affordable</th>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Visual Screening: Unaided</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Automated Pap Screening</td>
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<td>Yes</td>
<td>?</td>
<td>No</td>
<td>No</td>
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<tr>
<td>HPV Screening</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>Cervicography</td>
<td>Yes?</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>HPV Vaccine</td>
<td>?</td>
<td>?</td>
<td>Yes</td>
<td>?</td>
<td>No</td>
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</tbody>
</table>

Source: Program for Appropriate Technology in Health (PATH) 1997.
SCREENING GUIDELINES FOR CERVIX CANCER

- 30-65 years – Once in 3-5 years
- Primary screening with VIA-VILI
- Test positives should receive Pap or HPV followed by Colposcopy, Diagnostic confirmation and treatment

Routinely Look For

- Post menopausal bleeding PV.
- Intermenstrual bleeding PV.
- Post-Coital bleeding PV.
Linking screening and treatment

Regardless of the screening test used, screening must be linked to treatment to ensure program effectiveness.

This can be done using:

- Traditional approach (screen, diagnose, confirm, and treat)
- Intermediate approach (screen, diagnose, and treat with post-treatment biopsy confirmation)
- Screen-and-treat approach (treatment is based on the results of screening test alone).
TREATMENT OPTIONS FOR CIN

There are several outpatient treatment options available for treating precancerous lesions

In general treatment options are:

1. No treatment- close follow-up

2. Ablative methods:
   Cryotherapy ..... outpatient Trt
   Electrocautery.... outpatient Trt
   LASER vaporization

3. Excisional methods:
   LEEP..... outpatient Trt
   Conisation
   Hysterectomy
Cryotherapy

» Cryotherapy is the most practical treatment approach for most low-resource settings given its simplicity and low cost.

» Cryotherapy is a relatively simple procedure that destroys precancerous cells by freezing the cervix, using compressed carbon dioxide (CO2) or nitrous oxide (N2O) gas as the coolant.

» Cryotherapy is performed using a single-freeze or double-freeze technique.

» Cryotherapy is an outpatient procedure that can be performed easily and quickly (in 15 minutes or less) without anesthesia.

» It can be safely and effectively performed by general practitioners and non-physicians
Cryotherapy:

All the following criteria should be fulfilled-

- Fully visible CIN lesions (of any grade on the ectocervix occupying less than 75% of the TZ).
- No extension into endocervical canal
- SCJ fully visible
- Invasive cancer has been excluded
- Biopsy has taken
Cryotherapy equipment

Cervix immediately after cryotherapy
Complications

» Complications associated with cryotherapy are minimal.

» Severe bleeding and pelvic inflammatory disease, two of the most serious.

» Potential complications, are extremely rare in women treated with cryotherapy.

» No evidence that cryotherapy is linked to cervical stenosis or has any long-term impact on women’s fertility or pregnancy outcomes.
Disadvantages of cryotherapy

» Destroys the tissue, no tissue sample is available to confirm that the entire lesion has been removed.

» Not possible to establish whether it is an early invasive lesion requiring further treatment.

» Cryotherapy is not appropriate for treating large lesions that cannot be covered by the probe or lesions located in the endocervical canal.
Loop electrosurgical excision procedure (LEEP)

LEEP utilizes a thin electric wire in the form of a loop to remove the abnormal area of the cervix.

Advantages

» Simple surgical procedure and that the excised tissue can be sent for histopathological confirmation,

» Allows the exact nature of the lesion to be determined and unsuspected microinvasions to be detected.

Disadvantages

» Severe bleeding is a possible complication both during and after the procedure, occurring in 1% to 4% of patients

» More sophisticated equipment is required compared with cryotherapy.
Loop ElectroSurgical Excision Procedure (LEEP)
**LEEP/ Cold knife conisation:**

One of the following criteria should be fulfilled

- Fully visible CIN lesion of any grade occupying >75% or TZ.
- CIN lesion of any size extending into the endocervical canal.
- CIN lesion associated with unsatisfactory Colposcopy.
## Comparision of cryotherapy and LEEP

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Cryotherapy</th>
<th>LEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>86-95%*</td>
<td>91-98%*</td>
</tr>
<tr>
<td>Potential side effects</td>
<td>Watery discharge</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>None required</td>
<td>Local anesthesia necessary</td>
</tr>
<tr>
<td>Tissue sample for histopathology</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Power required</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Relative cost</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Level of provider</td>
<td>Physician and non-physicians</td>
<td>Mostly by physicians</td>
</tr>
</tbody>
</table>

Source: Adapted from Bishop 1995

*ACCP 2003, Martin-Hirsch et al. 2004
Vertical versus integrated programs

- They include political commitment to integration in the existing health structure,

- competing health priorities,

- existing national policy on cervical cancer prevention,

- availability of personnel and material resources,

- requirements for a shift in resources, and donor preferences and commitment of resources.
Effectiveness of a screening programme

Reduction in incidence and mortality from cervical cancer screening programme are affected by factors such as

- Access to screening,
- Participation,
- Compliance to investigations, treatment and follow-up
- Quality of treatment,

*Do not depend only on the accuracy of screening*
HPV Vaccines

• The US Food and Drug Administration (FDA) approved Gardasil [Quadrivalent HPV (Types 6, 11, 16, 18) Recombinant Vaccine], the first HPV vaccine for children and young adults, female, ages 9-26 years.

  • **Gardasil** is manufactured by Merck & Co., Inc: vaccine, protects against HPV types 16 and 18, which are responsible for about 70% of all cervical cancers,

  • GlaxoSmithKline has also developed its bivalent HPV vaccine, **Cervarix** for HPV types 16 and 18. It will be submitted for regulatory approval in Europe and countries outside the USA.

  • Clinical research has shown that both vaccines are safe and effective in preventing infection with the HPV 16 and 18 types.

  • The two HPV vaccines under consideration are considered “prophylactic” rather than “therapeutic” vaccines and optimally should be administered prior to natural exposure to the vaccine HPV types.
Unresolved issues

• Target populations

  Optimal age groups for vaccination: logistics of administering a series of three injections to adolescents or preadolescent girls, and the relative benefits of also vaccinating males.

  - Other age groups for vaccination
  - Vaccination of males

• Need for boosters

• Introduction in developing countries

• Impact of vaccination on screening programs
Introduction in developing countries

• Assuring a mechanism for service delivery,
• Providing funding for vaccination,
• Surveillance of vaccine coverage and safety,
• Sustaining and improving coverage rates,
• Creating awareness of the need for vaccination in the professional, public, and political communities through advocacy efforts in order to generate the political will to support vaccination are all critical for a successful vaccination system
Introduction in developing countries

- What do the various audiences know about cervical cancer?
- What sociocultural barriers may impede acceptance of HPV vaccine?
- What current policies may support or constrain health care for adolescents?
- In the opinions of the respondents, how can the vaccine be delivered most effectively to girls aged 10 to 14?
- How can HPV vaccine be integrated into (and strengthen) existing health programs,
- What aspects of the current medical system may need to be altered in order to reach older children and young adolescents?
- The importance of collaboration between reproductive health, immunization, child and adolescent health and cancer control programmes.
Impact of vaccination on screening programs

- 9–13 year old --impact will be seen 20-40 yrs later.

- “Catch-up” vaccination of older, sexually active women -- lower rates of coverage.

- Screening and treatment services will still be required, because the vaccines only prevent about 70% of cervical cancer cases.

- Cross-protection against other “high-risk” types possible but the extent and duration of cross-protection is currently unclear.
Second generation vaccines

Second generation vaccines that address the limitations of the current VLP vaccines are under development. Examples include:

- Mucosal deliver of VLPs,
- Chimeric VLPs containing E7 polypeptides to function as combined prophylactic/therapeutic vaccines, and
- L2 minor capsid protein-based vaccines to induce protection against more HPV types.

However, none of these strategies is sufficiently advanced to warrant large-scale efficacy trials at the present time.
Service Programmes
Tata Memorial Centre
Rural Outreach Program (TMCROP)

B.K.L.. Walawalkar Hospital, Dervan
TMCROP (2003-2007)  
(Tata Memorial Centre Rural Outreach Program)  
DAE Xth Plan Project  

Oral, Cervix and Breast Cancer Screening Program
Project Implemented in four stages

1- Household Survey
2- Health Awareness
3- Screening Camp
4- Definitive T/t & Follow Up

1526 villages from Ratnagiri District & 742 villages from Sindhudurg District
HEALTH AWARENESS PROGRAMME
SELECTION OF CAMP SITES
Screening Camp

Female Registration Counter

Male Registration Counter
SCREENING FOR ORAL BREAST & CERVICAL CANCERS
Progress till June 2007

- Household surveys covered **10,75,589** population spanning 1057 villages in 8 Tehsils.

- **2,27,204** no. of persons were listed as eligible for screening.

- **1,01,050** population was covered under Health Awareness Programme in Ratnagiri District

- **7,10,078** population (Male & Female) covered till date under community Cancer Screening Services.

- Total **438** frank malignancies (Breast **88**, Cervix **56**, and Head & Neck **293**) have been detected and treated till date.
National level Training Programme in Preventive Oncology

February 6-7, 2005.
Human Resource Development

Training programme on the practice of evidence based screening for common cancers in India and in the planning & management of rural community based cancer screening and treatment strategies.
BLUE PRINT FOR A DISTRICT CANCER CONTROL PROGRAMME

- PROGRAM GOALS
- DISTRICT SELECTION
- PLANNING OF LOGISTICS & RESOURCES
- RECRUITMENT & TRAINING OF HEALTH CARE STAFF
- COLLECTION OF BASELINE AND CANCER DATA
- COMMUNITY INFORMATION AND EDUCATION PROGRAMME
- PLANNING OF EFFECTIVE CANCER SCREENING SERVICES
- SETTING UP DIAGNOSTIC & TREATMENT SERVICES
- DYNAMIC DATA MANAGEMENT AND SERVICES EVALUATION
- QUALITY ASSURANCE, MONITORING AND EVALUATION
Global strategy to eliminate cervical cancer

through appropriate research, such as

- Economic analysis and acceptability studies,
- Training,
- Education,
- Communication,
- Building and strengthening political will through advocacy,
- Legislation and evidence-based policy formulation.
Primary prevention

• Education and awareness-raising to reduce high-risk sexual behaviours

• Implementation of locally appropriate strategies to change behaviour

• The development and introduction of an effective and affordable HPV vaccine

• Efforts to discourage tobacco use, including smoking.