FOGSI GCPR
SCREENING AND MANAGEMENT OF PREINVASIVE LESIONS OF CERVIX
AND HPV VACCINATION

FOGSI GYNAECOLOGIC ONCOLOGY COMMITTEE
January, 2018
Introduction

India is a land of diversity and this is reflected also in the varied practices followed for cervical screening. For years we have followed guidelines of various foreign societies, simultaneously lamenting the lack of uniformity of resources in our country. Also, each one of us works across different scenarios, sometimes in a tertiary hospital with state of the art facilities and sometimes in an outreach clinic or camp setting. The FOGSI Gynaecologic Oncology Committee takes great pleasure in presenting Good Clinical Practice Recommendations (GCPR) for cervical cancer prevention in the Indian context. The first step is to identify which situation you are working in – good resource or low resource – and accordingly to identify the options for screening, triage for confirmation of diagnosis and management.

Recognising that the bulk of cervical cancer in India manifests after the age of 30 years, FOGSI recommends that screening should be started at 25 years for good resource and 30 years for low resource settings. FOGSI recognises that while HPV testing is the best method, all the screening tests, namely, HPV, cytology, co-testing with both HPV and cytology, and VIA, are all valid options. The critical steps are maintenance of quality control as well as follow-up and treatment of screen detected lesions. Single visit approach is to be practiced wherever possible to minimise non-compliance and loss to follow-up. The charts show the screening algorithms for each type of screening method and management of various grades of CIN. All options have been evaluated and recommended based on global evidence and international guidelines, resource based recommendations, e.g., WHO and ASCO, and Indian data and recommendations of the Ministry of Health & Family Welfare. These have been extensively reviewed by the group of experts and summarized in the GCPR. Acceptable options have been offered wherever it was felt necessary based on expert opinion.

Primary prevention with HPV vaccine is strongly recommended. FOGSI endorses the WHO recommendation that the preferred age group is under 15 years, where two doses can be administered at an interval of 6 months. The charts also outline the recommendations for older girls and women as well as for special situations. It is to be emphasised that screening must continue after vaccination too.

This work would not have been possible without the inspiration from our seniors and the hard work and commitment of the expert panel. I am grateful to each one of them for their untiring support and contributions. I am also thankful to PSI for their partnership and support to bring this work to fruition. The detailed document with references and explanations of levels of evidence can be accessed online at www.fogsi.org. I am confident that you will find the FOGSI GCPR useful in your day-to-day practice and helpful in our common battle to eliminate cervical cancer.

January 17, 2018
FOGSI Good Clinical Practice Recommendation

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<td>ASCUS in women aged ≥ 30 years</td>
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<td>LSIL in women aged ≥ 30 years</td>
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<td>ASC-H / HSIL in women aged &lt; 30 years and desirous of pregnancy</td>
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<td>Abnormal glandular cells: AGC-NOS / Atypical Endocervical Cells</td>
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<td>24</td>
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<td>Abnormal glandular cells: AGC-FN / AIS</td>
<td>10</td>
<td>25</td>
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<td>Unsatisfactory Smear</td>
<td>11</td>
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<td>Management of Histologically proven CIN/AIS</td>
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<td>Management of Women with CIN 2, 3 on Histology</td>
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<td>Newer modalities</td>
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<td></td>
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<td>Cytology-based screening</td>
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<td>HPV-based screening</td>
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<td>35</td>
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</table>
HPV VACCINATION
## FOGSI GCPR: HPV Vaccination

<table>
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<th>Types of vaccines</th>
<th>FOGSI RECOMMENDATION</th>
<th>STRENGTH OF RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent (Cervarix, GSK) Quadrivalent (Gardasil, Merck)</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

| License to use in India                 | 9 - 45 years                  | NA                          |

| Preferred target age group              | 9 - 14 years                  | Grade A                     |

| Number of doses for girls aged < 15 years, not immunocompromised or HIV infected | 2 doses                       | Grade A                     |

| Number of doses for girls aged ≥ 15 years or immunocompromised and/or HIV infected girls | 3 doses                       | Grade A                     |
## FOGSI GCPR: HPV Vaccination

<table>
<thead>
<tr>
<th>Interval</th>
<th>FOGSI RECOMMENDATION</th>
<th>STRENGTH OF RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Two doses:</strong> 0 &amp; 6 months (second dose may be given at 5-15 months)</td>
<td>Grade A</td>
</tr>
<tr>
<td></td>
<td><strong>Three doses:</strong> 0, 1, 6 months (Bivalent) 0, 2, 6 months (Quadrivalent)</td>
<td></td>
</tr>
<tr>
<td>Catch-up vaccination</td>
<td>- 3 doses</td>
<td>Grade B</td>
</tr>
<tr>
<td>(15-26 years)</td>
<td>- Girls/ women who have been sexually active should be counselled regarding <strong>reduced efficacy</strong> and <strong>importance of screening</strong> from the age of 25-30 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Not to be considered in public programs unless resources are available after vaccinating and screening the respective target age groups)</td>
<td></td>
</tr>
<tr>
<td>Older age groups</td>
<td>- 3 doses</td>
<td>Grade B</td>
</tr>
<tr>
<td>(&gt; 26 years)</td>
<td>- Women aged &gt; 26 years who have been sexually active should be counselled regarding <strong>reduced efficacy</strong> in older age group and the <strong>importance of screening</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- In limited-resource settings, women in this age group should first invest in screening</td>
<td></td>
</tr>
<tr>
<td>Situation</td>
<td>FOGSI RECOMMENDATION</td>
<td>STRENGTH OF RECOMMENDATION</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>HIV positive or immunocompromised girls</td>
<td>- Same age recommendation</td>
<td>Grade A</td>
</tr>
<tr>
<td></td>
<td>- Three doses</td>
<td></td>
</tr>
<tr>
<td>Interrupted doses</td>
<td>- Continue with the remaining doses as per age-based recommendation, vaccination series need not be restarted</td>
<td>Grade B</td>
</tr>
<tr>
<td>Pregnancy and Lactation</td>
<td>- Not recommended in pregnancy (if inadvertently given, no need for MTP)</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td>- Can be given during lactation</td>
<td></td>
</tr>
<tr>
<td>Victims of sexual abuse</td>
<td>- Same age recommendation</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td>- Three doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Initiate preferably at the time of examination at health care facility</td>
<td></td>
</tr>
<tr>
<td>Women with history of abnormal screening reports</td>
<td>- Same age recommendation</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td>- Women should be counselled regarding <strong>reduced efficacy</strong> in older age group and the <strong>importance of regular follow-up</strong></td>
<td></td>
</tr>
</tbody>
</table>
SCREENING AND TREATMENT OF PREINVASIVE LESIONS OF CERVIX
Criteria of Various Single Visit Approach Strategies

See and Treat

- In Colposcopy Clinics
- Patient referred with abnormal cytology report
- Colposcopy scoring indicates a high grade lesion
- Simultaneous treatment done – excision or ablation
- Low probability of over-treatment because of high specificity of cytology
- Post-hoc analysis of biopsy report/excision specimen

Screen and Treat

- In Public Health Programs
- VIA detects abnormal lesion
- Criteria for ablation fulfilled
- Treat immediately, with or without biopsy
- Lower probability of over-treatment in high prevalence areas
- Post-hoc analysis is possible if biopsy taken
Choosing the Most Appropriate Screening Test for Your Practice

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Do you presently screen by Cytology?

- Yes
  - Does your lab meet quality indicators?  
    (Diagnostic accuracy, training, coverage, follow up, etc.)
    - No: Continue screening with Cytology
    - Yes: Can your hospital / patient afford HPV testing?

- No: Can your hospital / patient afford HPV testing?

- Yes: Do you have facilities for triage?
  - No: Switch to Primary HPV testing or Co-testing
  - Yes: VIA alone

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Colposcopy and Biopsy → Appropriate management

Ablation / Excision at the same sitting in a ‘Screen and Treat’ or ‘See and Treat Approach’ wherever feasible as per criteria

Adapted from WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention.
# Resource-Based Strategies for Cervical Cancer Screening and Management of CIN

<table>
<thead>
<tr>
<th>SETTING</th>
<th>SCREENING TOOLS</th>
<th>TRIAGE TOOLS</th>
<th>MANAGEMENT OPTIONS</th>
<th>SINGLE VISIT APPROACH</th>
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<tr>
<td>Good resource settings</td>
<td>Primary HPV test or Co-testing (HPV test + Cytology) or Cytology or VIA</td>
<td>Cytology ± newer modalities* HPV test HPV Genotyping-16/18 Colposcopy and biopsy** VIA and biopsy**</td>
<td>LEEP Conization Cryotherapy Thermal coagulation</td>
<td>See and Treat approach</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited resource settings#</td>
<td>VIA HPV#</td>
<td>Colposcopy, if available Biopsy**</td>
<td>Cryotherapy LEEP Conization Thermal coagulation</td>
<td>Screen and Treat or Screen, See and Treat approach</td>
</tr>
</tbody>
</table>

* Newer modalities (p16, Ki 67 testing, mRNA testing, E6,E7 protein testing).
** Biopsy from any abnormal area(s)
# Affordable HPV test (if available), including self-sampling, can be used.
### Resource-based Cervical Cancer Screening Recommendation

<table>
<thead>
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<th>GOOD RESOURCE SETTINGS</th>
<th>LIMITED RESOURCE SETTINGS</th>
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<tr>
<td><strong>Modalities</strong></td>
<td>HPV testing</td>
<td>VIA (Affordable HPV testing may be introduced if feasible)</td>
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<tr>
<td></td>
<td>• Primary HPV testing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Co-testing (HPV &amp; cytology)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytology</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VIA</td>
<td></td>
</tr>
<tr>
<td><strong>Target Age Group (years)</strong></td>
<td>25 - 65</td>
<td>30 - 65</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(N.B.: In postmenopausal women, screening with VIA may not be as effective)</td>
</tr>
<tr>
<td><strong>Age to start (years)</strong></td>
<td>Cytology at 25</td>
<td>VIA at 30</td>
</tr>
<tr>
<td></td>
<td>Primary HPV Testing / Co-testing at 30</td>
<td></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Primary HPV Testing or Co-testing – every 5 years</td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>Cytology – every 3 years</td>
<td>(at least 1-3 times in a lifetime)</td>
</tr>
</tbody>
</table>
## Resource-based Cervical Cancer Screening Recommendation

<table>
<thead>
<tr>
<th>Age to stop (years)</th>
<th>GOOD RESOURCE SETTINGS</th>
<th>LIMITED RESOURCE SETTINGS</th>
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<tr>
<td></td>
<td>• 65 with consistent negative results in last 15 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Women with no prior screening should undergo tests once at 65 years and, if negative, they should exit screening.</td>
<td></td>
</tr>
<tr>
<td>Follow-up method after treatment; interval</td>
<td>HPV testing (preferred) or cytology 12 months</td>
<td>VIA 12 months</td>
</tr>
<tr>
<td>Screening following abnormal reports ≥ CIN 2+, irrespective of method of treatment</td>
<td>20 years</td>
<td></td>
</tr>
<tr>
<td>Screening in hysterectomized women</td>
<td>• Following hysterectomy in which cervix was removed for benign causes: no need for screening, unless there is history of previous cervical intraepithelial neoplasia (CIN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Absence of cervix must be confirmed by clinical records or examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• If indications for hysterectomy unclear, screening may be performed at clinician’s discretion</td>
<td></td>
</tr>
<tr>
<td>Follow up in women with CIN in hysterectomy HPE report</td>
<td>Need to be screened with HPV at 6 months and 18 months</td>
<td></td>
</tr>
<tr>
<td>Screening of immunocompromised women</td>
<td>• Start within one year of initiation of sexual activity</td>
<td>• VIA / (Affordable HPV testing if available)</td>
</tr>
<tr>
<td></td>
<td>• HPV testing / Co-testing / Cytology / VIA</td>
<td>• Every 3 years (at least twice as often as general population)</td>
</tr>
<tr>
<td></td>
<td>• Every 2-3 years</td>
<td></td>
</tr>
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</table>
### The Bethesda System for Reporting Cytology

**Epithelial cell abnormalities**

<table>
<thead>
<tr>
<th>ABBREVIATION</th>
<th>TERMINOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>NILM</td>
<td>Negative for Intra-epithelial Lesion or Malignancy</td>
</tr>
<tr>
<td>ASCUS</td>
<td>Atypical Squamous Cells of Undetermined Significance</td>
</tr>
<tr>
<td>ASC-H</td>
<td>Atypical Squamous Cells: cannot exclude High grade Squamous Intra-epithelial Lesion</td>
</tr>
<tr>
<td>LSIL</td>
<td>Low-grade Squamous Intra-epithelial Lesion</td>
</tr>
<tr>
<td>HSIL</td>
<td>High grade Squamous Intra-epithelial Lesion</td>
</tr>
<tr>
<td>SCC</td>
<td>Squamous Cell Carcinoma</td>
</tr>
</tbody>
</table>

**Glandular cell abnormalities**

<table>
<thead>
<tr>
<th>ABBREVIATION</th>
<th>TERMINOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGC</td>
<td>Atypical Glandular Cells (specify endocervical, endometrial or NOS, i.e., Not Otherwise Significant)</td>
</tr>
<tr>
<td>AGC-FN</td>
<td>Atypical Glandular Cells – Favor Neoplastic</td>
</tr>
<tr>
<td>AIS</td>
<td>Endocervical Adenocarcinoma in Situ</td>
</tr>
<tr>
<td></td>
<td>Endometrial cells in a woman &gt; 40 years of age</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td>Others</td>
</tr>
</tbody>
</table>

**List of other abbreviations**

- **CIN**: Cervical Intraepithelial Neoplasia
- **ECC**: Endocervical Curettage
- **HPV**: Human Papillomavirus
- **LEEP**: Loop Electrosurgical Excision Procedure
- **TZ**: Transformation Zone
- **VIA**: Visual Inspection with Acetic Acid
Screening with Primary HPV Testing in women aged > 30 years

- **HPV Testing**
  - **HPV Negative**
    - VIA
      - Negative
        - Repeat HPV test at 1 year
      - Positive
        - Repeat HPV test at 1 year
    - HPV Negative
    - HPV Positive
      - Colposcopy ± biopsy
  - **HPV Positive**
    - HPV Negative
      - Normal
        - Repeat HPV test at 1 year
      - Abnormal
        - Follow FOGSI CIN management GCPR
    - HPV Positive
      - Colposcopy ± biopsy
        - Normal
          - Repeat HPV test at 1 year
        - Abnormal
          - Follow FOGSI CIN management GCPR

Other HR HPV Positive
- Repeat HPV test at 1 year
- Follow FOGSI CIN management GCPR

HPV genotyping
- Other HR HPV Positive
- HPV 16/18 Positive
- Repeat HPV test at 1 year
- Follow FOGSI CIN management GCPR

Preferred
Acceptable
Screening with Co-testing (HPV Test with Cytology) in women aged > 30 years

Available HPV Tests
The digene HPV test (Hybrid Capture 2, Qiagen) Cobas (Roche)
Affordable HPV test careHPV (Qiagen)
Screening with Cytology
Management of ASCUS in women aged ≥ 30 years

ASCUS in women aged ≥ 30 years

HPV test
- Negative
  - Return to routine 5 yearly screening with HPV test / Co-testing
- Positive
  - Colposcopy ± biopsy
    - Normal
    - Abnormal
      - Co-testing / HPV test at 1 year
      - Follow FOGSI CIN Management GCPR

Cytology at 1 year
- Negative
- ASCUS, LSIL
  - Colposcopy ± biopsy
    - Normal
    - Abnormal
      - CytoLOGY at 1 year
      - Follow FOGSI CIN Management GCPR
      - Follow Screening GCPR Chart 6
- ASC-H, HSIL
  - If patient non-compliant, Colposcopy / VIA ± biopsy (See-and-Treat)

Preferred — Acceptable
Screening with Cytology
Management of LSIL in women aged ≥ 30 years

LSIL in women aged ≥ 30 years

- Positive HPV test:
  - Colposcopy ± biopsy
    - Follow FOGSI CIN Management GCPR

- Negative HPV test:
  - Co-testing at 1 year
    - Cytology normal and HPV negative:
      - Co-testing at 3 years
        - Cytology normal and HPV negative:
          - Return to 5 yearly routine screening protocol
        - Cytology ≥ ASCUS or HPV positive:
          - Colposcopy ± biopsy
            - Follow FOGSI CIN Management GCPR
    - Cytology ≥ ASCUS or HPV positive:
      - Colposcopy ± biopsy
        - Follow FOGSI CIN Management GCPR

- If patient non-compliant, See-and-Treat Follow Chart 11
Screening with Cytology
Management of ASCUS / LSIL in women aged < 30 years

ASCUS / LSIL in women aged < 30 years

Repeat cytology annually x 2

NILM

Repeat cytology at 3 years

Return to routine screening by age-specific modality

Preferred

≥ ASCUS

Colposcopy ± biopsy

Normal

Repeat cytology at 1 year

Acceptable

Abnormal

Follow FOGSI CIN management GCPR

If patient non-compliant, Colposcopy / VIA ± biopsy
Screening with Cytology
Management of ASC-H / HSIL in women aged > 30 years

ASC-H / HSIL

Colposcopy with cervical biopsy & endocervical assessment

Adequate, entire transformation zone seen

≤ CIN 1
- Co-testing at 1 year
- Follow FOGSI Screening GCPR

CIN 2,3
- Ablation
- LEEP / ablation* of transformation zone (See-and-Treat*)

Inadequate, TZ not completely seen

Diagnostic excision procedure - Conization
- Follow FOGSI CIN Management GCPR

* Ablation can be considered in selected small lesions of CIN 2+

Eligibility for See-and-Treat Excision Procedures
1. Lesion should be entirely visible limited to cervix
2. Entire lesion should be located on ectocervix without any vaginal and/or endocervical extension
3. There is no suspicion of invasive cancer
4. Not pregnant
5. See Chart 11 for criteria for ablation
Screening with Cytology
Management of ASC-H / HSIL in women aged < 30 years and desirous of pregnancy

ASC-H / HSIL in women desirous of pregnancy

Colposcopy ± biopsy

No CIN 2, 3

Repeat cytology and colposcopy 6 monthly for 2 years

HSIL persisting for 1 year

Cervical biopsy

CIN 2, 3

Follow FOGSI CIN management GCPR

No CIN 2, 3

No high grade abnormalities in cytology and colposcopy

Return to age-specific routine screening

6 monthly follow-up

ASC-H / HSIL persisting for 2 years

Diagnostic excisional procedure
Screening with Cytology
Management of Abnormal Glandular Cells: Atypical Endometrial Cells

Cytology report-
Atypical endometrial cells

Endometrial and endocervical curettage

Endometrial pathology

Manage accordingly

No endometrial pathology

Colposcopy ± biopsy

Normal

Return to age-specific routine screening

Follow FOGSI CIN Management GCPR
Screening with Cytology
Management of Abnormal Glandular Cells: AGC-NOS / Atypical Endocervical Cells

AGC-NOS / Atypical endocervical cells

Colposcopy ± biopsy & endocervical sampling & endometrial sampling*

No CIN 2+, AIS or cancer

Co-test / cytology at 1, 2 years

Tests negative

Return to routine screening

Any test positive

Colposcopy ± biopsy

≥ CIN 2+, AIS or cancer

Follow FOGSI CIN Management GCPR

*Age > 35 yrs, high risk factors, e.g., obesity, chronic anovulation
AGC - NOS: Atypical Glandular Cells - Not Otherwise Specified; AIS - Adenocarcinoma in Situ
Screening with Cytology
Management of Abnormal Glandular Cells: AGC-FN / AIS

AGC-FN / AIS

Colposcopy + endocervical sampling + endometrial sampling*

Endometrial pathology
Hysterectomy

Endocervical pathology
Diagnostic excisional procedure - Conization
(Intact specimen with non-fragmented margins)
Hysterectomy
(Type as per the disease extent)

Both endocervical and endometrial sampling negative
Evaluate for ovarian, Fallopian tube pathology by imaging
If no pathology detected, Conization

If any pathology detected, treat accordingly
Follow FOGSI CIN Management GCPR

*Age > 35 yrs, high risk factors, e.g., obesity, chronic anovulation
AGC-FN - Atypical Glandular Cells favouring Neoplasia; AIS - Adenocarcinoma in Situ
Chart 11: Unsatisfactory Smear

- **Unsatisfactory**
  - Review HPV report if available
    - Negative: Return to Routine Screening
    - Positive: Follow FOGSI Screening GCPR
  - Repeat Cytology in 2-4 months*
    - Unatisfactory: Colposcopy
    - ASCUS: Follow FOGSI Screening GCPR
    - NILM: Return to Routine Screening
  - If HPV test NA/ < 30 years
    - Negative: Return to Routine Screening
    - Positive: Follow FOGSI Screening GCPR
  - VIA
    - Negative: Return to Routine Screening
    - Positive: Follow FOGSI Screening GCPR

*consider LBC if facilities available
*In postmenopausal female local estrogen x 3 weeks, and stop 1 week prior to testing
Screening with VIA in women aged 30-65 years

VIA between 30-65 years* (preferable upto 50 years)

VIA negative

VIA positive

Normal

Colposcopy ± biopsy

Return to routine 5 yearly screening protocol

CIN 1

CIN 2, 3

Invasive cancer

Lesion eligible for Ablation*

Screen-and-treat approach*

Observation / Ablation

LEEP / Ablation

Refer to tertiary care center

Cryotherapy / Thermal coagulation

Rescreen after 1 year

* Eligibility for Screen-and-treat (Ablative Procedures)
1. Lesion should be entirely visible and occupy not more than two quadrants of cervix
2. Entire lesion should be located on ectocervix without any vaginal and/or endocervical extension
3. Lesion can be adequately covered by largest cryotherapy probe available (Multiple overlapping applications with thermocoagulation)
4. There is no suspicion of invasive cancer
5. Screen-and-treat by cryotherapy is contraindicated in cases of postcoital or postmenopausal bleeding, obvious cervical growth, irregular surface or bleeds on touch

N.B. Biopsy can be taken prior to ablation, if feasible, for post-hoc correlation

* Recommendation of Ministry of Health & Family Welfare, Government of India
Management of Women with CIN 1 on Histology

1. **HPV positive or ASCUS / LSIL or VIA positive**
   - Co-testing / HPV / Cytology / VIA at 1, 2 years
     - Any test positive
       - Colposcopy ± biopsy
         - CIN 1
   - Test negative
     - Return to routine screening

2. **Any test positive**
   - Repeat Co-test / HPV / cytology / VIA after 1 year
     - Test positive
       - Colposcopy ± biopsy
         - CIN 1

3. **Test negative**
   - Return to routine screening

4. **ASC-H, HSIL**
   - Co-testing at 1 & 2 years or cytology at 6 months
     - Any test positive
       - Diagnostic excisional procedure - LEEP
         - Assess adequacy of excision
         - Follow-up

5. **CIN 1 persisting for 2 years**
   - Ablative procedure*, excisional procedure
     - If lesion not amenable for ablation or persisting CIN 1 after ablation consider excision procedure

---

* Eligibility for Ablative Procedures
1. Lesion should be entirely visible and occupy not more than two quadrants of cervix
2. Entire lesion should be located on ectocervix without any vaginal and/or endocervical extension
3. Lesion can be adequately covered by largest cryotherapy probe available
4. There is no suspicion of invasive cancer
Management of Women Desirous of Pregnancy with CIN 1 on Histology

CIN 1 on histology in women desirous of pregnancy

- Check preceding cytology report
  - ASCUS, LSIL
    - Repeat Cytology at 1 year
      - Cytology ≥ ASCUS
        - Colposcopy ± biopsy
          - Follow FOGSI CIN management GCPR
        - Manage according to standard of care
      - Not suggestive of invasive disease
        - Repeat cytology and colposcopy at 6 monthly interval
    - Cytology NILM
      - Repeat Cytology at 1 year
      - ASC-H, HSIL
        - Repeat cytology and colposcopy at 1 year
        - Not suggestive of invasive disease
          - Repeat cytology and colposcopy at 1 year
        - ASC-H, HSIL or high grade lesion in colposcopy persisting for 1 year
          - Diagnostic excision procedure (See-and-Treat)
            - Follow FOGSI CIN management GCPR
        - ASCUS / LSIL
          - Follow FOGSI screening GCPR
Management of Women with CIN 2, 3 on Histology

CIN 2 / 3 on histology

- Review colposcopy report

  - Adequate
    - LEEP / ablation*
  - Inadequate / ECC positive / recurrent CIN
    - Conization
      - Margin negative
        - Repeat cone biopsy. Consider hysterectomy if repeat cone not feasible, e.g., postmenopausal, or patient non-compliant for follow-up
        - Return to routine screening
      - Margin positive
        - Repeat Co-test / HPV / Cytology and ECC at 6 months, 1 & 2 years
          - Positive
            - Return to routine screening
          - Negative
Management of Women with CIN 2, 3 on Histology, Desirous of Pregnancy

CIN 2 / 3 young women desirous of pregnancy

- Cytology & colposcopy at 6 months
  - Negative
  - Adequate colposcopy
    - CIN 2 lesions, triage with p16, Ki 67
    - CIN 3 with inadequate colposcopy
      - Excisional procedure
  - Inadequate colposcopy
    - High grade cytology / colposcopy worsens at 1 year
      - Treat using excision procedure or ablation if eligible
    - Follow FOGSI CIN management GCPR

- Lesion persists
  - Repeat cytology & colposcopy at 1 year
    - Cytology negative / improving & normal colposcopy
      - Repeat Co-testing / cytology after 1 year
        - Normal reports - follow-up with Co-test / cytology at 3 years
          - Preferred
        - Any abnormal reports
          - Colposcopy ± biopsy
            - If normal, return to routine 5 yearly screening

- Lesion persists
  - Repeat cytology & colposcopy at 1 year
    - Cytology negative / improving & normal colposcopy
      - Repeat Co-testing / cytology after 1 year
        - Normal reports - follow-up with Co-test / cytology at 3 years
          - Preferred
        - Any abnormal reports
          - Colposcopy ± biopsy
            - If normal, return to routine 5 yearly screening

- Lesion persists
  - Repeat cytology & colposcopy at 1 year
    - Cytology negative / improving & normal colposcopy
      - Repeat Co-testing / cytology after 1 year
        - Normal reports - follow-up with Co-test / cytology at 3 years
          - Preferred
        - Any abnormal reports
          - Colposcopy ± biopsy
            - If normal, return to routine 5 yearly screening

Management of Cervical Preinvasive Lesions
Management of Women with CIN in Pregnancy

CIN in Pregnancy

Review colposcopy report for adequacy*

Low grade lesion
- Follow-up with colposcopy at 6 weeks postpartum

High grade lesion on colposcopy
- Repeat colposcopy at every trimester to rule out invasive disease
- Review & treat at 6 weeks postpartum

Invasive cancer
- Offer treatment according to the period of gestation

* ECC should be avoided in pregnant women
Management of Women with AIS

AIS on biopsy or ECC

Conization to rule out invasive disease

Hysterectomy (Type depending on extent of disease)

In young women desirous of fertility

Margins / ECC Positive

Margins Negative

Re excise

Follow-up

Co-testing / Cytology colposcopy and ECC at 6 months

Preferred

Acceptable
# Newer modalities: Cytology-based screening

<table>
<thead>
<tr>
<th>LIQUID-BASED CYTOLOGY (LBC)</th>
<th>BIOMARKERS</th>
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<tbody>
<tr>
<td><strong>Options</strong></td>
<td>p16INK4a : CINtec (Roche), CINtec PLUS (p16INK4a + Ki-67)</td>
</tr>
<tr>
<td><strong>Advantage</strong></td>
<td>Identify transforming HPV infection</td>
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<tr>
<td></td>
<td>Detect CIN 2 + disease</td>
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<tr>
<td></td>
<td>Triage low-grade smears</td>
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<td>Can be done with histology and cytology slides</td>
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<td></td>
<td>Reduce colposcopy referrals</td>
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<tr>
<td><strong>Efficacy</strong></td>
<td>Sensitivity:64-92%, Specificity: 41-96% for low-grade smears</td>
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<tr>
<td></td>
<td>Sensitivity not better than conventional (RR 1.1); 11% more sensitivity for LSIL + lesions</td>
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<tr>
<td><strong>Limitations</strong></td>
<td>Wide variation in reported sensitivity, lack of standardized reporting</td>
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<td></td>
<td>Need for substantial expertise</td>
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<td>False positive rates high</td>
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<tr>
<td></td>
<td>More expensive, not cost-effective</td>
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<td></td>
<td>Automated not effective</td>
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</table>
## Newer modalities: HPV-based screening

<table>
<thead>
<tr>
<th>VAGINAL SELF - COLLECTION</th>
<th>E6 E7 MRNA</th>
<th>DNA METHYLATION (DNAME)</th>
<th>MARKERS OF ABERRANT S-PHASE INDUCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Options</td>
<td>APTIMA, APTIMA HPV GT (Hologic) Oncotect (Incell Dx)</td>
<td>QIAsure Methylation Test (Qiagen)</td>
<td>Topoisomerase IIA (TOP2A) and MCM2 (BD)</td>
</tr>
<tr>
<td>Advantage</td>
<td>Acceptable, eliminates cost of visiting a clinician</td>
<td>Effective triage for low-grade smears</td>
<td>Alternative triage for hrHPV Automated, objective test</td>
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<td>Reduce colposcopy referral by 68% compared to 30% by HPV DNA testing</td>
<td>Run on the same sample as the HPV assay</td>
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<td>Identify transforming HPV infection</td>
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<tr>
<td>Efficacy</td>
<td>Sensitivity variable: 60-90% Overall 3.4 (95% CI=2.4-4.9) times more CIN 2+ detected by self-collected HPV samples than by routine cytology.</td>
<td>Sensitivity: 90-95%, Specificity: 42-61%, PPV: 67%</td>
<td>CADM1-m18 combined with MAL-m1 methylation: Sensitivity: 60.5%- 100%, Specificity: 22.7% to 83.3% (95% CI: 78.4-87.4).</td>
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<td>Sensitivity: 67-99% , Specificity: 61- 85%.</td>
</tr>
<tr>
<td>Limitations</td>
<td>Inadequate sample possible, Woman- dependent, reluctance to use medical devices</td>
<td>Expensive</td>
<td>Expensive, wide variation in reported sensitivity</td>
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<td>Research settings</td>
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ABOUT PSI

PSI India is a non-profit, non-governmental organisation enabling people of India to lead healthier lives and plan the families they desire by marketing affordable products and services. We assist and complement the efforts of the Government of India (GoI) in the priority areas – Family Planning, Non Communicable Diseases including Cervical Cancer Prevention, Maternal and Child Health, Sanitation and Gender-based Violence. We use social marketing models and enable quality products and services to reach people at a price they can afford. We apply commercial strategies to the non-profit health sector, allowing women to access care in a place that is convenient, and in a way, they can understand. We are one of the largest organisations in India with many human assets working in several States and Union Territories across India. We believe in creating healthy communities and working conditions.

Management and Coordination: Ms. Deepti Mathur, Senior Specialist, Knowledge Management, PSI
Dr. Parul Saxena, Assistant Manager, PSI