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 a camp setting. The FOGSI Gynaecologic Oncology Committee takes great pleasure in presenting GCPR for the Indian situation. 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 and 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 Indian data which have been extensively reviewed by the group of experts.

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 and also for special situations. It is to be emphasised that screening must be continued in all vaccinated women 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 insights, guided by personal experience. I am also thankful to PSI for their partnership and support to bring this work to fruition. 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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SCREENING AND TREATMENT OF PREINVASIVE LESIONS OF CERVIX
FOGSI GCPR on “Choosing the most appropriate screening test for your practice”

1. Do you presently screen by cytology?
   - Yes
     - Does your lab meet quality indicators? (Diagnostic accuracy, training, coverage, follow-up, etc.)
       - Yes
         - Can your hospital/patient afford HPV testing?
           - No
             - Continue screening with cytology
           - Yes
             - Switch to primary HPV testing or co-testing
       - No
         - Can your hospital/patient afford HPV testing*
           - No
             - Continue screening with cytology
           - Yes
             - Do you have facilities for triage?
               - No
                 - VIA alone
               - Yes
                 - Cytology
                   - VIA
                   - Appropriate management
         - Switch to primary HPV testing or co-testing
   - No
     - 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.
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 was taken
### 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>
</tr>
</thead>
<tbody>
<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 Thermo-coagulation</td>
<td>See and Treat approach</td>
</tr>
<tr>
<td>Limited resource settings**</td>
<td>VIA</td>
<td>Colposcopy, if available Biopsy</td>
<td>Cryotherapy LEEP Conization ± Thermo-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).

** Affordable HPV test (if available), including self-sampling, can be used.
# Resource-based cervical cancer screening recommendation

<table>
<thead>
<tr>
<th>Modalities</th>
<th>GOOD RESOURCE SETTINGS</th>
<th>LIMITED RESOURCE SETTINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HPV testing</td>
<td>VIA</td>
</tr>
<tr>
<td></td>
<td>• Primary HPV testing</td>
<td>Colposcopy ± Biopsy</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>Colposcopy and biopsy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VIA</td>
<td></td>
</tr>
<tr>
<td>Target Age Group (years)</td>
<td>25 - 65</td>
<td>30 - 65</td>
</tr>
<tr>
<td></td>
<td>(N.B.: in postmenopausal women, screening with VIA may not be as effective)</td>
<td></td>
</tr>
<tr>
<td>Age to start (years)</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>Frequency</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>
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</table>
Resource-based cervical cancer screening recommendation

<table>
<thead>
<tr>
<th>GOOD RESOURCE SETTINGS</th>
<th>LIMITED RESOURCE SETTINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age to stop (years)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 65 with consistent negative results in last 15 years</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>
</tr>
<tr>
<td>Follow-up method after</td>
<td>HPV testing (preferred) or cytology</td>
</tr>
<tr>
<td>treatment; interval</td>
<td>12 months</td>
</tr>
<tr>
<td></td>
<td>VIA</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>Screening following</td>
<td>20 years</td>
</tr>
<tr>
<td>abnormal reports ≥</td>
<td></td>
</tr>
<tr>
<td>CIN 2+, irrespective</td>
<td></td>
</tr>
<tr>
<td>of method of treatment</td>
<td></td>
</tr>
<tr>
<td>Screening in</td>
<td></td>
</tr>
<tr>
<td>hysterectomized</td>
<td></td>
</tr>
<tr>
<td>women</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Following hysterectomy in which cervix was removed for benign causes: no need for screening, unless there is history of previous cervical intra-epithelial neoplasia</td>
</tr>
<tr>
<td></td>
<td>• Absence of cervix must be confirmed by clinical records or examination</td>
</tr>
<tr>
<td></td>
<td>• If indications for hysterectomy unclear, screening may be performed at clinician’s discretion</td>
</tr>
<tr>
<td>Follow up in women with</td>
<td>Need to be screened with HPV at 6 months and 18 months</td>
</tr>
<tr>
<td>CIN in hysterectomy</td>
<td></td>
</tr>
<tr>
<td>HPE report</td>
<td></td>
</tr>
</tbody>
</table>
### The Bethesda system for reporting Pap smear

#### 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

- **HPV**: Human Papillomavirus
- **VIA**: Visual Inspection with Acetic Acid
- **CIN**: Cervical Intraepithelial Neoplasia
- **LEEP**: Loop Electrosurgical Excision Procedure
- **TZ**: Transformation Zone
# Index – FOGSI Recommendation for Cervical Cancer Screening using HPV testing/Cytology/VIA

<table>
<thead>
<tr>
<th>CHART NO.</th>
<th>TITLE</th>
<th>PAGE NO.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Screening of women aged &gt; 30 years with Primary HPV testing</td>
<td>13</td>
</tr>
<tr>
<td>2.</td>
<td>Screening with Co-testing (HPV test with cytology) in women aged &gt; 30 years</td>
<td>14</td>
</tr>
<tr>
<td>3.</td>
<td>Management of ASCUS in women aged 30-64 years</td>
<td>15</td>
</tr>
<tr>
<td>4.</td>
<td>Management of LSIL in women aged 30-64 years</td>
<td>16</td>
</tr>
<tr>
<td>5.</td>
<td>Management of LSIL in women aged 25-29 years (desire pregnancy)</td>
<td>17</td>
</tr>
<tr>
<td>6.</td>
<td>Management of ASC-H, HSIL in women aged ≥ 30 years</td>
<td>18</td>
</tr>
<tr>
<td>7.</td>
<td>Management of ASC-H, HSIL in women aged &lt; 30 years and desirous of pregnancy</td>
<td>19</td>
</tr>
<tr>
<td>8.</td>
<td>Management of abnormal glandular cells: Atypical Endometrial Cells</td>
<td>20</td>
</tr>
<tr>
<td>10.</td>
<td>Management of abnormal glandular cells: AGC-FN / AIS</td>
<td>22</td>
</tr>
<tr>
<td>11.</td>
<td>Screening with VIA</td>
<td>23</td>
</tr>
<tr>
<td>CHART NO.</td>
<td>TITLE</td>
<td>PAGE NO.</td>
</tr>
<tr>
<td>-----------</td>
<td>----------------------------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>12.</td>
<td>Management of women with CIN 1 on histology</td>
<td>24</td>
</tr>
<tr>
<td>13.</td>
<td>Management of women &lt; 30 years desirous of pregnancy with CIN 1 on histology</td>
<td>25</td>
</tr>
<tr>
<td>14.</td>
<td>Management of women with CIN 2, 3 on histology</td>
<td>26</td>
</tr>
<tr>
<td>15.</td>
<td>Management of women with CIN 2, 3 on histology, desirous of pregnancy</td>
<td>27</td>
</tr>
<tr>
<td>16.</td>
<td>Management of women with CIN in Pregnancy</td>
<td>28</td>
</tr>
</tbody>
</table>
Screening of women aged > 30 years with Primary HPV testing

HPV Testing

HPV Negative
- VIA
  - Negative
  - HPV Negative
    - Repeat HPV test at 1 year
      - HPV Negative
        - Return to routine 5 years screening protocol
      - HPV Positive
        - Repeat HPV test at 1 year
          - HPV Negative
            - Normal
              - Repeat HPV test at 1 year
            - Abnormal
              - Follow FOGSI CIN management GCPR
          - HPV Positive
            - Colposcopy & biopsy

HPV Positive
- HPV Positive
  - HPV 16 / 18 Genotyping
    - Negative
      - Cytology
        - ≥ ASCUS
          - Repeat HPV test at 1 year
        - NILM
          - Repeat HPV test at 1 year
            - HPV Negative
              - Normal
                - Follow FOGSI CIN management GCPR
              - Abnormal
                - Repeat HPV test at 1 year
            - HPV Positive
              - Normal
                - Repeat HPV test at 1 year
              - Abnormal
                - Follow FOGSI CIN management GCPR
Screening with Co-testing (HPV test with cytology) in women aged > 30 years

**Co-testing**

- **HPV test negative cytology negative**
  - Return to routine 5 years screening protocol
- **HPV test negative cytology positive**
  - ASCUS, LSIL
    - Repeat Co-testing at 1 year
    - Follow FOGSI CIN management GCPR
- **HPV test positive or cytology ≥ ASCUS**
  - HPV DNA test or cytology positive
    - Repeat Co-testing at 1 year
    - Follow FOGSI CIN management GCPR
  - Both test negative
    - Return to routine 5 years screening protocol
  - Negative
    - Colposcopy & biopsy
      - HPV specific gene typing HPV 16/18
        - Positive
          - HPV DNA test or cytology positive
            - Colposcopy & biopsy
              - Follow FOGSI CIN management GCPR
        - Negative
          - HPV DNA test or cytology positive
            - Colposcopy & biopsy
              - Follow FOGSI CIN management GCPR
          - Both test negative
            - Return to routine 5 years screening protocol
- **ASC-H, HSIL**
  - Colposcopy & biopsy
  - Follow FOGSI CIN management GCPR
SCREENING WITH CYTOLOGY – MANAGEMENT OF ABNORMAL PAP SMEAR

Management of **ASCUS** in women aged 30-64 years

- **ASCUS in women aged 30-64 years**
  - **HPV test**
    - **Negative**
      - Return to routine 5 years screening with HPV test / Co-testing
    - **Positive**
      - Colposcopy & biopsy
        - **Normal**
          - Co-testing / HPV test at 1 year
        - **Abnormal**
          - Manage as per FOGSI GCPR
  - **Cytology at 1 year**
    - **Negative**
      - Return to routine 3 years screening with cytology
    - **ASCUS, LSIL**
      - Colposcopy & biopsy
        - **Normal**
          - Manage as per FOGSI GCPR
        - **Abnormal**
          - Manage as per FOGSI GCPR
    - **ASC-H, HSIL**
      - Manage as per FOGSI GCPR
    - If patient non-compliant colposcopy / VIA ± biopsy

Screening of Cervical Preinvasive Lesions
Management of LSIL in women aged 30-64 years

**HPV test**

- **Positive**
  - Colposcopy & biopsy
  - Manage as per FOGSI GCPR

- **Negative**
  - Co-testing at 1 year
    - **Cytology normal and HPV negative**
      - Co-testing at 3 years
        - Cytology normal and HPV negative
          - Return to 5 years routine screening protocol
        - Co-testing at 3 years
          - Cytology ≥ ASCUS or HPV positive
            - Colposcopy & biopsy
            - Manage as per FOGSI GCPR
    - **Cytology ≥ ASCUS or HPV positive**
      - Colposcopy & biopsy
      - Manage as per FOGSI GCPR

- **If patient non-compliant colposcopy / VIA ± biopsy ablation therapy**

**Preferred**

**Acceptable**
Management of LSIL in women aged 25-29 years

ASC-US / LSIL in women aged 25-29 years

Repeat cytology annually x 2

- NILM
  - Repeat cytology at 3 years
  - Return to routine age-specific screening

- ≥ ASCUS
  - Colposcopy & biopsy
    - Normal
      - Repeat cytology at 1 year
    - Abnormal
      - Follow FOGSI CIN management GCPR

If patient non-compliant colposcopy / VIA ± biopsy
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 GCPR

- Diagnostic excision procedure
  - Follow FOGSI CIN management GCPR

Inadequate, transformation zone not completely seen

- CIN 2,3
  - Diagnostic excision procedure
  - Follow FOGSI CIN management GCPR

- Excision / ablation* of transformation zone

*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
5. Screen and treat by cryotherapy is contraindicated in cases of postcoital or postmenopausal bleeding, obvious cervical growth, irregular surface or bleeds on touch

FOGSI GCPR Screening & Management of Preinvasive Lesions of Cervix and HPV Vaccination
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
    - **No high grade abnormalities in cytology and colposcopy**
      - Return to age-specific routine screening
  - **HSIL persisting for 1 year**
    - Cervical biopsy
    - **No CIN 2, 3**
      - On 6 monthly follow up if CIN 2, 3 persisting for 24 months
    - **Follow FOGSI CIN management GCPR**
  - **CIN 2, 3**
    - Diagnostic excisional procedure
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
      - Manage as per FOGSI GCPR
AGC-NOS, atypical endocervical cells

Colposcopy & biopsy + endocervical sampling + endometrial sampling*

No CIN 2+, AIS or cancer

Co-test / cytology at 1-2 years

- Both negative: Return to routine screening
- Either positive: Colposcopy & biopsy

≥ CIN 2+, AIS or cancer

Manage as per FOGSI GCPR

AGC-NOS: Atypical Glandular Cells – Not Otherwise Specified
Management of abnormal glandular cells: AGC-FN / AIS

**AGC-FN / AIS**

- Colposcopy + endocervical sampling + endometrial sampling*
  - Endometrial pathology
    - Hysterectomy
  - Endometrial pathology
    - Diagnostic excisional procedure (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 any pathology detected treat accordingly
    - If no pathology detected
      - Manage as per FOGSI GCPR

*Age > 35 yrs, high risk factors, e.g., obesity, chronic anovulation

AGC-FN - Atypical Glandular Cells Favouring Neoplasia; AIS - Adenocarcinoma in Situ
Screening with VIA

Visual Inspection with Acetic Acid (VIA) between 30-65 years; preferable up to 50 years

VIA negative

Return to routine 5 years screening protocol

Normal

Colposcopy & biopsy

VIA positive

Screening and treat approach*

Invasive cancer

Cryotherapy

Lesion eligible for cryotherapy**

CIN 1

Observation / cryotherapy

CIN 2, 3

LEEP

Referral to tertiary care center

Rescreen with VIA / cytology after 1 year

* 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
5. Screen and treat by cryotherapy is contraindicated in cases of postcoital or postmenopausal bleeding, obvious cervical growth, irregular surface or bleeds on touch

** Lesion eligible for cryotherapy is determined by the treating physician based on the clinical examination and the presence of certain characteristics that may indicate the potential for successful treatment.
**Management of women with CIN 1 on histology**

**CIN 1 on biopsy**

- Check preceding HPV / cytology report
  - HPV test positive or ASCUS / LSIL
    - Co-testing / Cytology / VIA at 1-2 years
      - Test negative
        - Return to routine screening
      - Any test positive after 1 year
        - colposcopy & biopsy
        - CIN 1
          - Repeat Co-testing / cytology / VIA after 1 year
            - Test positive
              - Ablative procedure*, excisional procedure.
                If lesion not amenable for ablation or persisting CIN 1 after ablation consider excision procedure.
        - CIN 2 / 3
          - Follow FOGSI CIN management GCPR
  - ASC-H, HSIL
    - Co-testing at 1 & 2 years or cytology at 6 months
      - Diagnostic excisional 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 < 30 years desirous of pregnancy with CIN 1 on histology

### CIN 1 on histology in women desirous of pregnancy

#### Preceding cytology

- **ASCUS, LSIL**
  - Repeat cytology at 1 year
  - **Colposcopy & biopsy**
    - Follow FOGSI CIN management GCPR
- **ASC-H, HSIL**
  - Repeat cytology / VIA and colposcopy at 6 months
    - Suggestive of invasive disease
      - Manage according to standard of care
        - Suggestive of invasive disease
          - Manage according to standard of care
    - Not suggestive of invasive disease
      - Repeat cytology / VIA and colposcopy at 1 year
        - ASC-H, HSIL or high grade lesion in colposcopy persisting for 1 year
        - **ASCUS / LSIL**
          - Diagnostic excision procedure
          - Follow FOGSI CIN management GCPR
Management of women with CIN 2, 3 on histology

**CIN 2 / 3 on histology**

- Review colposcopy report
  - Adequate
    - Excision of T zone / ablation*
    - Repeat HPV and cytology / VIA at 1-2 years
    - Test negative at 1-2 years
    - Repeat HPV and cytology / VIA at 3 years
    - Return to routine screening
  - Inadequate / ECC positive / recurrent CIN
    - Diagnostic excisional procedure
      - Margin negative
        - Repeat HPV and cytology / VIA at 1-2 years
      - Margin positive
        - Follow FOGSI CIN management GCPR
        - Repeat cytology and ECC at 6 months
    - Repeat HPV and cytology / VIA at 1-2 years

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* Eligibility for ablative procedure:

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

N.B. In CIN 3, excision is preferred especially for large lesions, lesions not fully accessible for ablation, or recurrent lesion.
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
  - Lesion persists
    - Repeat cytology & colposcopy at 1 year
      - Cytology negative / improving & noramal coloscopy
        - Repeat Co-testing / cytology after 1 year
          - Normal reports – follow up with co-test / cytology at 3 years
      - High grade cytology / colposcopy worsens at 1 year
        - Treat using excision procedure
    - Positive
      - Any abnormal reports colposcopy and biopsy
    - Nagative
      - In CIN 2 lesions, if facilities available perform ancilary tests like p16, Ki 67
      - In CIN 3 with inadequate colposcopy
        - Excisional procedure

Follow FOGSI CIN management GCPR

If normal return to routine 5 years screening
Management of women with **CIN in Pregnancy**

- **CIN in Pregnancy**
  - **Review colposcopy report**
    - Colposcopy features of invasive cancer / inadequate colposcopy with CIN 3
      - Counsel the patient and offer definitive treatment as per the period of gestation
    - Suggestive of invasive cancer with adequate colposcopy
      - Defer treatment till after pregnancy
### NEWER MODALITIES: PAP-BASED SCREENING

<table>
<thead>
<tr>
<th>Options</th>
<th>Liquid-based cytology (LBC) (Thin Prep, Sure Path)</th>
<th>Biomarkers (p16INK4a : CIN tec, (p16INK4a+Ki-67 CIN tec PLUS )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantage</td>
<td>Few inadequate Pap samples (1.9%), Benefits of Reflex HPV testing, automated reading possible</td>
<td>Identify transforming HPV infection, predict progression to CIN 2+ disease Triage low-grade smears Can be done with histology and cytology slides Reduce colposcopy referrals</td>
</tr>
<tr>
<td>Efficacy</td>
<td>Sensitivity not better than conventional (RR 1.1); 11% more sensitivity for LSIL + lesions</td>
<td>Sensitivity: 64-92%, Specificity: 41-96% for low-grade smears</td>
</tr>
<tr>
<td>Limitations</td>
<td>More expensive, not cost-effective. Automated not effective</td>
<td>Wide variation in reported sensitivity, lack of standardized reporting Need for substantial expert False positive rates high</td>
</tr>
</tbody>
</table>
### NEWER MODALITIES: HPV BASED SCREENING

| Options                          | Vaginal Self collection (eg. Delphi device, Evalyn sampler) | E6 E7 mRNA (APTIMA), APTIMA HPV GT | DNA Methylation (DNAme) Eg. QIAasure Methylation Test by Quiagen | Topoisomerase IIA (TOP2A) and MCM2  
Markers of aberrant S-phase induction |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantage</td>
<td>Acceptable, eliminates cost of visiting a clinician</td>
<td>Effective triage for low-grade smears, reduce colposcopy referral by 68% compared to 30% by HPV DNA testing</td>
<td>Alternative triage for hrHPV, automated, objective test, run on the same sample as the HPV assay</td>
<td>Identify transforming HPV infection</td>
</tr>
</tbody>
</table>
| Efficacy                         | 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. | Sensitivity: 90-95%, Specificity: 42-61%, PPV: 67% | CADM1-m18 combined with MAL-m1 methylation:  
Sensitivity: 60.5% - 100%, Specificity: 22.7% to 83.3%  
(95% CI: 78.4-87.4). | Sensitivity: 67-99%, Specificity: 61- 85%. |
| Limitations                      | Inadequate sample, Woman-dependent, reluctance to use medical devices | Expensive | Expensive, wide variation in reported sensitivity | Research settings |

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**NEwER MoDALITIES: HPV BASED SCREENING**

**Options**
- Vaginal Self collection (eg. Delphi device, Evalyn sampler)
- E6 E7 mRNA (APTIMA), APTIMA HPV GT
- DNA Methylation (DNAme) Eg. QIAasure Methylation Test by Quiagen
- Topoisomerase IIA (TOP2A) and MCM2
  - Markers of aberrant S-phase induction

**Advantage**
- Acceptable, eliminates cost of visiting a clinician
- Effective triage for low-grade smears, reduce colposcopy referral by 68% compared to 30% by HPV DNA testing
- Alternative triage for hrHPV, automated, objective test, run on the same sample as the HPV assay
- Identify transforming HPV infection

**Efficacy**
- Sensitivity variable: 60-90%
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- Sensitivity: 90-95%, Specificity: 42-61%, PPV: 67%
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**Limitations**
- Inadequate sample, Woman-dependent, reluctance to use medical devices
- Expensive
- Expensive, wide variation in reported sensitivity
- Research settings
HPV VACCINATION
# FOGSI GCPR: HPV Vaccination

<table>
<thead>
<tr>
<th>Presently licensed 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>
<tr>
<td>License to use in India</td>
<td>9 - 45 years</td>
<td>NA</td>
</tr>
<tr>
<td>Preferred target age group</td>
<td>9 - 14 years</td>
<td>Grade A</td>
</tr>
<tr>
<td>Number of doses for girls aged &lt; 15 years, not immunocompromised</td>
<td>2 doses</td>
<td>Grade A</td>
</tr>
<tr>
<td>Number of doses for girls aged ≥ 15 years or immunocompromised</td>
<td>3 doses</td>
<td>Grade A</td>
</tr>
</tbody>
</table>
# 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> At least 6 months, may be up to 12-15 months</td>
<td>Grade A</td>
</tr>
<tr>
<td></td>
<td><strong>Three doses:</strong> 0,1,6 months (Bivalent)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0,2,6 months (Quadrivalent)</td>
<td></td>
</tr>
<tr>
<td>Catch-up vaccination (15-26 years)</td>
<td>• 3 doses</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td>• Girls/ women who have been sexually active should be counselled regarding <strong>reduced</strong> efficacy and importance of <strong>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 (&gt; 26 years)</td>
<td>• 3 doses</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td>• Women aged &gt; 26 years who have been sexually active should be counselled regarding <strong>reduced</strong> efficacy in older age group and the importance of screening</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>
</tbody>
</table>
# FOGSI GCPR: HPV Vaccination (Special situations)

<table>
<thead>
<tr>
<th>Condition</th>
<th>FOGSI RECOMMENDATION</th>
<th>STRENGTH OF RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV positive or immunocompromised girls</td>
<td>• Same age recommendation&lt;br&gt;• Three doses</td>
<td>Grade A</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</td>
<td>Grade B</td>
</tr>
<tr>
<td>Victims of sexual abuse</td>
<td>• Three doses&lt;br&gt;• Initiate preferably at the time of examination at health care facility</td>
<td>Grade B</td>
</tr>
<tr>
<td>Women with history of abnormal screening reports</td>
<td>• Same age recommendation</td>
<td>Grade B</td>
</tr>
<tr>
<td>Males</td>
<td>• Not licensed for use in India at present</td>
<td>-</td>
</tr>
</tbody>
</table>
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