FOGSI-ICOG
Good Clinical Practice Recommendations (GCPR)
Prevention and Management of Cervical Cancer

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Fogsi Good Clinical Practice Recommendations

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SCOPE

GCPR has been formulated in a structured manner using simple understandable language with easy adoptable flow charts, algorithms, and tables covering the topic of cervical cancer in the most holistic manner from prevention to cure. It is designed to be used as a ready reckoner by FOGSIANS for adopting vaccination, screening in their day-to-day clinical practice. Also, it provides an up-to-date knowledge about cancer management protocols.

METHODOLOGY

Extensive literature search of randomized controlled trials (RCTs), meta-analysis, and systemic review studies has been done by the core team and the document has been reviewed by national and international expert group.

Grade Practice Recommendations

Grade	*Descriptor*	*Qualifying Evidence*	*Implications for Practice*
A	Strong recommendation	Level I evidence or consistent findings from the multiple studies of levels II, III, or IV	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is sack present
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role
D	Option	Level V evidence: little or no systematic empirical evidence	Clinicians should consider all options in their decision-making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role

Levels of Evidence

Level	*Type of evidence*
I	High quality prospective cohort study with adequate power or systematic review of these studies
II	Lesser quality prospective cohort, retrospective cohort study, untreated controls from an RCT, or systematic review of these studies
III	Case-control study or systematic review of these studies
IV	Case series
V	Expert opinion; case report or clinical example; or evidence-based on physiology, bench research or "first principles"

PART 1: PRECANCEROUS

INTRODUCTION

Cervical cancer is a leading cause of mortality among women. In 2020, an estimated 604,000 women were diagnosed with cervical cancer worldwide, with India contributing to almost one- fourth of the global burden of cervical cancers. In India, the number of new cases in 2020 were 123,907 and deaths due to cervical cancer were estimated at 77,348 and 5 year prevalence was 283,842.[1]

In 2018, the Federation of Obstetric and Gynecological Societies of India (FOGSI) released the good clinical practice recommendations on the screening and management of the preinvasive lesions of the cervix and human papillomavirus (HPV) vaccination and same was subsequently published in 2020.[2] In November 2020, the global strategy to accelerate the elimination of cervical cancer by 2030 was launched by the World Health Organization (WHO), with the targets of 90% HPV vaccination coverage of eligible girls, 70% screening coverage of the target population with a high-performance test and 90% of women with a positive screening test or a cervical lesion managed appropriately.[3] According to the United Nations Sustainable Development (SD) Goals, there is need to reduce mortality due to cancer by 30% by 2030. This is possible by offering diagnostic work-up at district hospitals and ensuring an early and systematic referral to tertiary care treatment center.

Human papillomavirus is the most common viral infection of the reproductive tract and causes a range of conditions in men and women, including precancerous lesions that may progress to cancer. In addition to cervical cancer, in both men and women, HPV infection is associated with cancers of the head, neck, oropharynx, and anogenital area, as well as with anogenital warts and respiratory papillomatosis. Most HPV infections (70–90%) are asymptomatic and resolve spontaneously within 1–2 years. Persistent infection with high-risk types may progress to precancerous lesions which, if not detected and treated appropriately, can progress to invasive carcinoma at the site of infection.

VACCINATION

Storage of HPV Vaccines

- All HPV vaccines are stored at 2–8°C, not frozen but protected from light.
- They should be administered immediately after removal from the refrigerator.

Dosage Schedule

The vaccine is available as 0.5 mL dose. It should be given intramuscularly in the deltoid region. The individual should be seated during vaccination and observed for 15 minutes after vaccination **(Table 1)**.

Table 1 FOGSI HPV vaccine recommendations[4-6]

	Schedule	***Evidence level and grade of recommendation***
Optimal dose	• Two doses 9–14 years at least 6 months apart • Three doses above 15–26 years (0, 1–2 months, 6 months) • Three doses for older women till 45 years Regular screening as per guidelines has to be followed in this age group	Level I, Grade A Level II, Grade B
Reduced dose* A. Two doses WHO SAGE Recommendation B. Alternative single dose (Off label)	• One or two doses for 9–14 years • One or two doses for 15–20 years • Two doses for 21 years and above • Single dose schedule can be used for girls and boys aged 9–20 years	Level II, Grade B Level II, Grade B
Boys	Boys can be vaccinated from 9–26 years • 9–14 years 2 doses 0, 6 months • 15–26 years 3 doses 0, 2, 6 months	Level II, Grade C

*Reduced dose schedule of HPV vaccine awaits Drug Controller General of India (DCGI) approval.

HPV vaccines available in India:[7-9]

- Bivalent (CERVARIX by GSK) licensed for girls 10–45 years.
- Quadrivalent (Gardasil by MERCK) licensed for girls 9–45 years.
- Nonavalent (Gardasil by MERCK) licensed for girls 9–45 years.
- Quadrivalent (Cervavac by SIL) licensed for girls and boys 9–26 years.

Vaccine Safety[10]

- No serious safety issues to date except rare reports of anaphylaxis.
- The Global Advisory Committee for Vaccine Safety (GACVS) has not identified any safety concerns.
- Among males and females of all ages receiving HPV vaccine, injection site reactions included pain (35–88%), redness (5–40%), and swelling (4–35%).
- Mild systemic adverse events included headache, dizziness, myalgia, arthralgia, and gastrointestinal symptoms (nausea, vomiting, and abdominal pain).
- HPV vaccines are safe and well tolerated and can be used in persons who are immunocompromised or human immunodeficiency virus (HIV) infected.
- Adverse events following HPV vaccination are generally mild and of short duration.

Coadministration Interchangeability

- As per licensing indications, specific HPV vaccine may be administered concomitantly with other routine vaccines containing diphtheria (d), tetanus (T), and acellular pertussis (pa), with no clinically relevant interference with antibody response to any of the components of either vaccine.
- Efforts should be made to administer the same vaccine for all doses when using a multidose schedule.
- However, if the vaccine used for the prior dose(s) is unknown or unavailable, any HPV vaccine administered to complete the recommended schedule.

Primary and Secondary Target Groups

- For the prevention of cervical cancer, the WHO-recommended primary target population for HPV vaccination is girls aged 9–14 years before they become sexually active.
- Achieving over 80% coverage in girls also reduces the risk of HPV infection for boys.
- Vaccination of secondary target populations, e.g. females aged ≥15 years, boys, older males or men who have sex with men (MSM), is recommended only if this is feasible and affordable, and does not divert resources from the vaccination of the primary target population.

Special Situations

HPV vaccine can be safely coadministered with other age appropriate vaccines.

- It is not recommended for use in pregnancy. If the patient conceives after the first dose, it is advisable to give further doses after pregnancy.
- If inadvertent vaccination during pregnancy, no need for the medical termination of pregnancy.
- Lactating women can receive HPV vaccine. Available evidence does not indicate an increased risk of adverse events in either the mothers or their baby after the administration of HPV vaccine to lactating mothers.
- Sexual assault survivors should be given age appropriate HPV vaccination,with the first dose at the time of initial examination.
- Women with abnormal Pap/Positive HPV test/previous HPV lesions: Can be vaccinated if they desire; however, they should be counseled that it is not a therapeutic vaccine and will not treat existing pathology and there is reduced efficacy in older women.
- HPV vaccination is a primary prevention intervention and does not eliminate the need for screening, since the existing vaccines do not protect against all high-risk HPV. The screening of the cervical cancer should be done as per the guidelines.

SCREENING TESTS

Cervical Cytology

Cervical cytology can be done by conventional method on a glass slide or liquid-based cytology (LBC) and results are interpreted according to the Bethesda 2001 System of reporting.

Visual Inspection after Application of Acetic Acid (VIA)

About 5% of acetic acid is applied on the cervix for one minute using a cotton swab and findings are interpreted as per **Table 2**.

Table 2 Interpretation of findings of visual inspection with acetic acid (VIA)

Parameters of aceto white lesion	*VIA positive*	*VIA negative*
Speed of appearance	Appears rapidly and may last for 1–2 minutes	Appears late and quickly disappears (within a minute)
Color intensity	Shiny and cloudy white, more dense, thick and opaque	Pale or dull white, less dense, thin, often translucent
Borders and demarcation	Well demarcated, regular, raised from surrounding epithelium	Patchy with ill-defined, diffuse margins
Location	Restricted to transformation zone mostly, lesions close to or abutting the squamocolumnar junction	Distributed widely in the cervix, not restricted to the transformation zone (TZ)
Color uniformity	Uniformly white	Color intensity varies across the lesion

High-risk Human Papilloma Virus (HPV) DNA Testing

- Both healthcare provider and self sampling is acceptable.
- Clinically validated polymerase chain reaction (PCR)-based hrHPV DNA are recommended for primary screening **(Tables 3 and 4)**.

Signal-amplification-based HPV test has been found to be lower on self versus the provider collected specimens; hence, these tests could be considered acceptable if validated PCR-based assays are not available or affordable.[11] The Indian tests are available but are awaiting approval by the WHO prequalification diagnostic program.

Table 3 List of validated HPV tests[12]

HPV DNA signal amplification	*PCR-based test*	*mRNA-based E6/E7*
Hybrid Capture 2 (HC2; Qiagen, Hilden, Germany)	Cobas® HPV test (Roche, Pleasanton, USA) BD Onclarity HPV assay (Becton Dickinson, Sparks, MD)	Aptima® HPV assay (Hologic, San Diego, CA)
Cervista HPV HR Test (Hologic Inc., Bedford, MA, USA)	Abbott Real-Time High-Risk HPV test PapilloCheck (Greiner Bio-One, Frickenhausen)	
careHPV test (Qiagen Gaithersburg Inc., MD, USA)	Pretect™ HPV-Proofer (Nor Chip Norway) Anyplex II HPV HR (Seegene Inc, Seoul, Korea) Xpert HPV (Cepheid, Sunnyvale, CA, USA)	

Table 4 Accuracy of cervical cancer screening tests[13,14]

Test	*Sensitivity (%)*	*Specificity (%)*
Cytology	62.5–72.9%	90.3–96.6%
Visual inspection with acetic acid	74.2–79.4%	85.2–85.8%
HPV* DNA testing	94%	88%

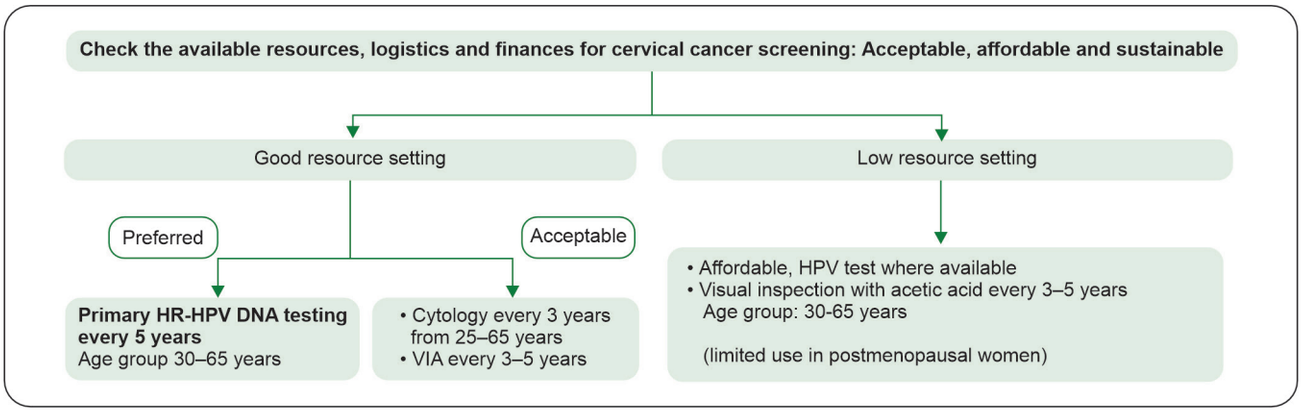
*HPV-Human Papilloma Virus

Table 5 FOGSI screening recommendations

	Recommendation	***Level of evidence, Grade of recommendation***
Age to start screening	25 years in good resource setting, universal recommendation: 30 years	Level 1, Strong recommendation
Age to end screening	65 years with 3 consecutive negative cytology results, or 2 consecutive negative HPV test within 10 years. The most recent test should have been performed within 5 years	Level 1, Strong recommendation
Tests with screening interval	Primary hrHPV testing every 5–10 years; In limited resource settings at least twice in a life time, i.e. 35 years and 45 years Cytology every 3 years VIA every 3–5 years	Level 1, Strong recommendation
Screening after hysterectomy with removal of cervix	Not recommended. If hysterectomy was done for cancer or precancer, screening to be continued	Level 1, Strong recommendation
Screening for immunocompromised women	Start at 25 years and to be screened more frequently, duration between two screenings should not extend beyond 3 years, preferable to screen with HPV tests	Level 1, Strong recommendation

Screening recommendations according to resource settings are summarized in **Table 5 and Algorithm 1**.

Algorithm 1: Screening recommendations according to resource settings



FOGSI MANAGEMENT RECOMMENDATIONS OF CERVICAL PRECANCERS IN THE GENERAL POPULATION

Treatment strategies of cervical precancers may be based on either on screen-triage- and-treat approach or screen-and-treat approach (Level 1, Strong recommendation)[15,16]

Screen-triage-and-treat approach: HPV DNA testing is used as the primary screening test. Once it is positive, triaging will be done using partial genotyping, colposcopy, VIA or cytology, depending on the availability of resources, training, and feasibility. In this approach, cytology can also be used as primary screening test with colposcopy triage.

In screen-and-treat, HPV test is considered as the best test for screening with high sensitivity and almost 100% negative predictive value (NPV). In case of single visit approach (SVA), HPV positives can undergo treatment at the same visit depending on the eligibility criteria ascertained by VIA. Albeit the fact in this approach, the chances of overtreatment is high, yet, this will ensure providing treatment to all the screen positives whose revisit for follow-up is doubtful due to varied sociodemographic conditions. Wherever possible it is advisable to triage HPV-positive patients with colposcopy or VIA to as certain the lesion and then treat, this will ensure the avoidance of overtreatment. In a low-resource setting, VIA can be used as a screening modality to ascertain lesion. If lesion positive, treatment can be offered at the same sitting.

Management (Level 1, Strong Recommendation)

- In colposcopy, if lesion is cervical intraepithelial neoplasia 1 (CIN1), rescreening after 1–2 years with cytology should be done. If lesion is CIN2+ and satisfies eligibility criteria for ablative therapy, ablation with cryotherapy or thermal ablation should be done and follow-up after 1 year with HPV DNA testing or cytology should be done.
- Criteria for ablative treatment for screen-positive women includes type 1 transformation zone (TZ), no suspicion of invasive cancer or glandular disease. Type 2 or type 3 TZ are not suitable for ablative treatment and, the whole lesion is visible and does not extend into the endocervix.
- Patients should be counseled for excessive white discharge postprocedure for minimum 2 weeks in case of cryotherapy.
- If lesion is CIN2+ and does not satisfy eligibility criteria for ablative therapy, excisional procedure with large loop excision of the transformation zone (LLETZ)/loop electrosurgical excision procedure (LEEP) or cold-knife conization (CKC) should be done. Histopathology should include information on the status of margin, whether involved or uninvolved. If margins are involved, on relook colposcopy at 6 months done and lesion treated with repeat LLETZ, and CKC. If the lesion is suggestive of invasive cancer, further evaluation and management based on stage should be done.
- Once a decision to treat a woman is made, the patient should be treated within 6 months in order to reduce the risk of loss to follow-up. In case treatment was not possible within 6 months, the woman should be re-evaluated before treatment.
- Treatment of women with histologically confirmed adenocarcinoma in situ (AIS), CKC is preferred. However, LLETZ with top hat excision can be used depending on availability and expertise. The treatment of AIS is hysterectomy in the older women.
- Hysterectomy may be considered in the older women, who wish to go for definitive surgery or in noncompliant women in whom follow-up is doubtful.
- The presence of disease should be measured beyond 6 months after treatment and 1–3 years is preferred.
- Women with any suspicion of invasive cancer or glandular disease (adenocarcinoma or AIS) and women with types 2 and 3 TZ should be referred in a screen-and-treat-program.

Residual Recurrent Disease[15]

- Persistent or residual disease is defined as the detection of a histopathological high-grade intraepithelial lesion (HSIL) - CIN2 and 3, or AIS excluding cancer diagnosed from a punch biopsy or a subsequent surgical specimen (including hysterectomy, CKC, and LLETZ/LEEP) at any time interval after the initial treatment was performed with no intervening documented absence of disease.
- Recurrent disease or new disease is defined as the detection of a histopathological high-grade lesion that was diagnosed from a biopsy or a subsequent surgical specimen following a documented absence of high-grade lesions at any time interval after the initial treatment was performed.
- In a screen-and-treat-approach persistence or residual disease follow the same criteria except that it may be defined as a positive follow-up screening test (VIA, HPV test, or cytology), preferable the one used initially, and histopathological verification is not essential. HPV type- specific persistence/recurrence (detection of same HPV genotype at different time points) may be studied with an appropriate HPV detection test. The presence of disease should be measured beyond 6 months after treatment and 1–3 years is preferred.
- Both persistent/residual disease and recurrent disease are taken as treatment failures and need retreatment. Recurrent or persistent HSIL/CIN2/CIN3 is treated using LLETZ or ablation (depending on the eligibility for ablation and the availability of treatment techniques). LLETZ or CKC is recommended for AIS.

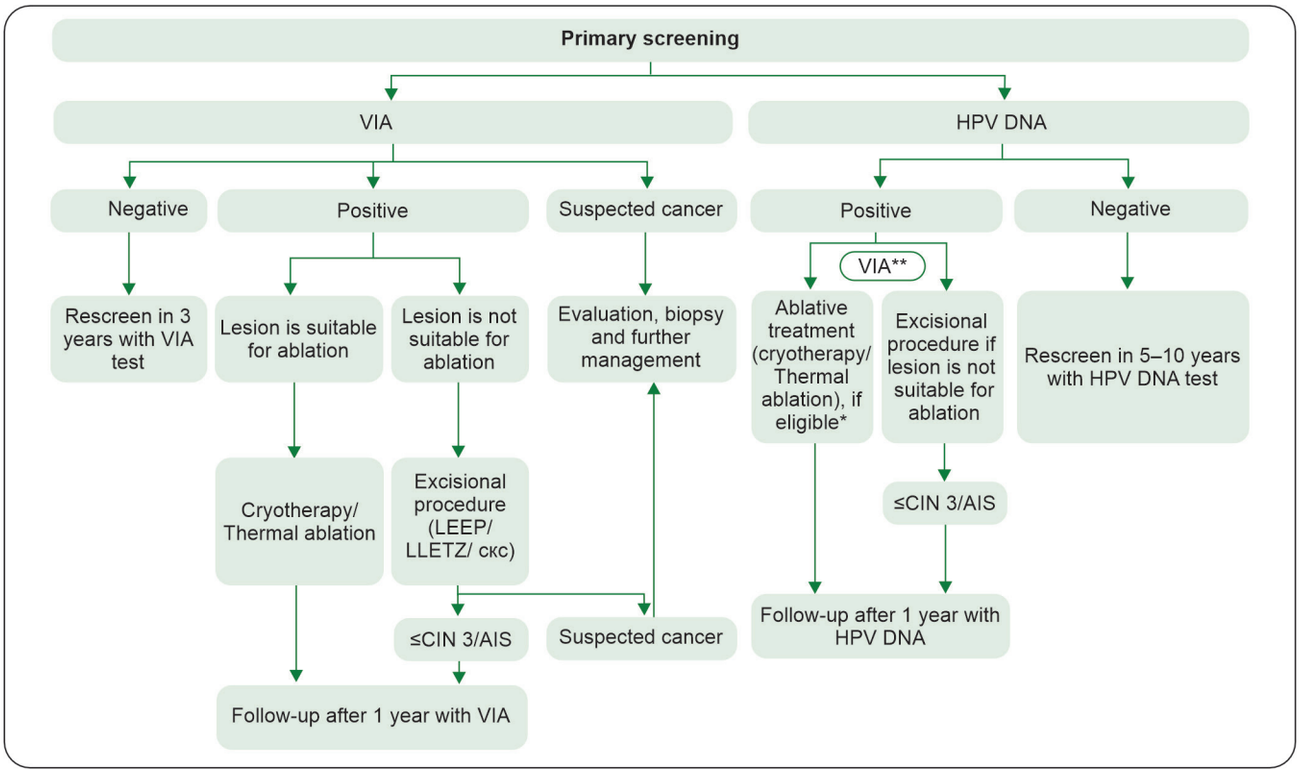
Follow-up after Treatment

Post-treatment follow-up should be after 1 year with HPV DNA test (preferred). In case HPV DNA testing is not available, cytology can be done. Follow-up should be after 1 year with HPV DNA test (preferred). In case HPV DNA testing is not available, cytology can be done.

MANAGEMENT RECOMMENDATIONS OF CERVICAL PRECANCERS IN SPECIAL GROUPS[15]

- In women living with HIV, immunocompromised women or organ transplant recipients: Screen-triage-and-treat approach should be used from the age of 25 years with regular screening every 3–5 years. After a positive HPV DNA primary screening test and following a negative triage test, retesting with HPV DNA should be done at 1 year.
- Post-treatment follow-up: Immunocompromised cases, e.g. HIV, organ transplant recepients should have more frequent follow-ups at 12 months and 24 months with HPV DNA testing and if negative, routine follow-up every 3–5 years.
- In women who are screen positive and pregnant, good practice for treatment includes deferral until after pregnancy. **Algorithms 2 to 4** discuss the screen-and-treat and screen-triage-and-treat approach

Algorithm 2: Screen-and-treat approach

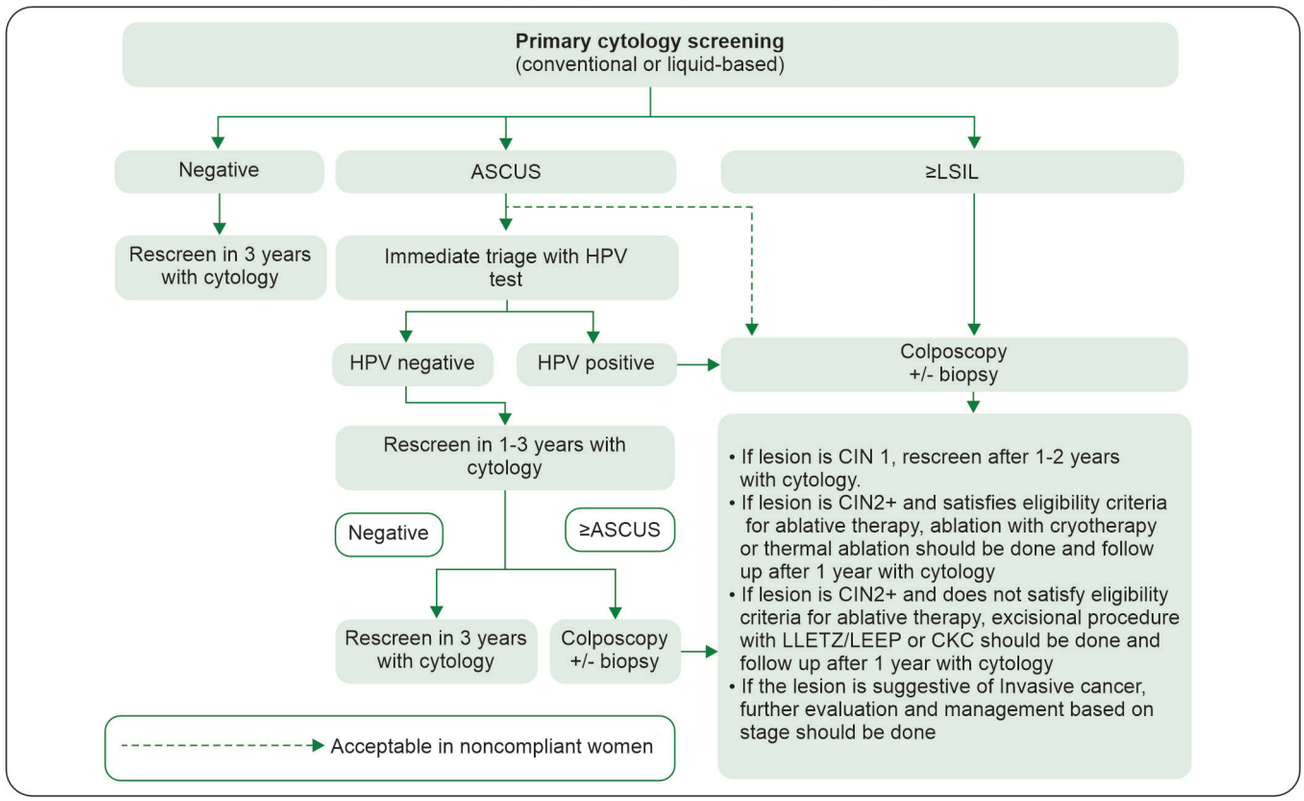


**VIA—Visual Inspection with Acetic Acid. VIA is used to identify new SCJ, type of TZ thereby to determine eligibility criteria for treatment

Abbreviations: AIS, adenocarcinoma in situ; CIN, Cervical intraepithelial neoplasia; CKC, cold-knife conization; DNA, deoxyribonucleic acid; HPV, human papillomavirus; LEEP, loop electrosurgical excision procedure; LLETZ, large loop excision of the transformation zone; VIA, visual inspection with acetic acid

Algorithm 3: Screen-Triage-and-Treat Approach

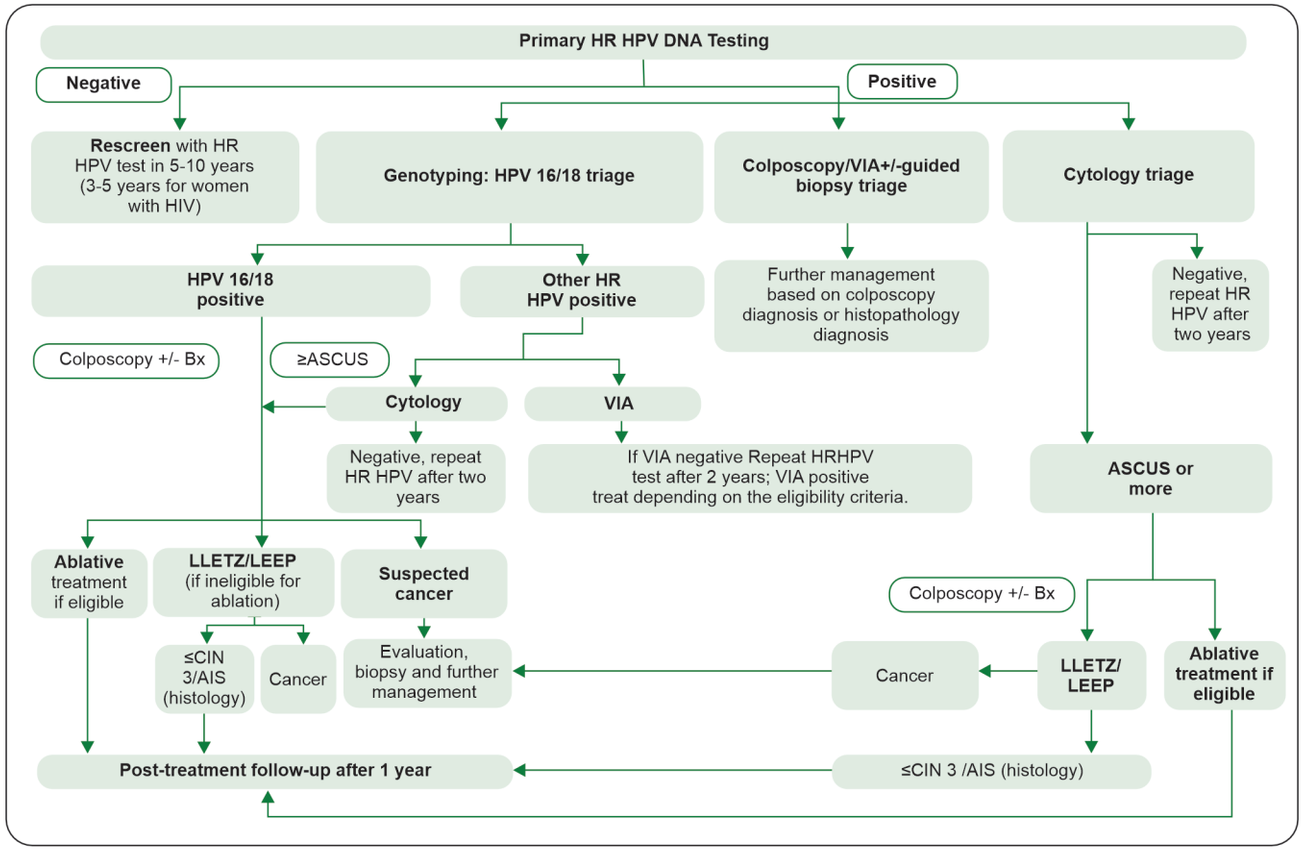
Primary cytology screening and colposcopy triage



Abbreviations: ASCUS, atypical squamous cells of undetermined significance; CIN, Cervical intraepithelial neoplasia; CKC, cold-knife conization; HPV, human papillomavirus; LEEP, loop electrosurgical excision procedure; LLETZ, large loop excision of the transformation zone; LSIL, low-grade squamous intraepithelial lesion

Algorithm 4: Screen-Triage-and-Treat Approach

Primary HPV DNA Screening and HPV16/18 or colposcopy or VIA triage



Abbreviations: AIS, adenocarcinoma in situ; ASCUS, atypical squamous cells of undetermined significance; CIN, Cervical intraepithelial neoplasia; DNA, deoxyribonucleic acid; HIV, human immunodeficiency virus; HPV, human papillomavirus; LEEP, loop electrosurgical excision procedure; LLETZ, large loop excision of the transformation zone; VIA, visual inspection with acetic acid

PART 2: MANAGEMENT OF INVASIVE DISEASE

Confirmation of diagnosis by histopathology. Pathologists should give diagnosis as per recent the WHO histopathological classification and especially mentioning HPV-associated and HPV-independent cervical cancer.

Proper clinical evaluation including per speculum and bimanual examination is mandatory to stage the disease. Once the diagnosis is confirmed, management should be done by trained gynecologist/oncologist.

INVESTIGATIONS

- Routine investigations including hemogram, and liver and kidney function tests
- Chest radiograph
- Magnetic resonance imaging (MRI) or contrast-enhanced computed tomography (CECT) abdomen and pelvis if available, is preferred to tailor treatment
- Ultrasonography as a basic imaging modality for cervical cancer, if MRI/CECT not available
- For early lesion, MRI is superior over CECT in identifying tumor size and parametrial invasion, with equivalent performance in identifying nodal disease.
- Positron emission tomography–computed tomography (PET-CT) may be used in advanced cases
- Cystoscopy and/or proctosigmoidscopy are recommended only if clinically or radiologically indicated.

FIGO STAGING OF CARCINOMA OF THE CERVIX UTERI 2018 (ANNEXURE 1)[1]

Treatment Recommendations[17-19]

All efforts should be made for proper staging in order to avoid the dual modality of treatment to prevent complications and increased morbidity.

Stage I A1

- Type I/class A (extrafascial hysterectomy)
- Conisation/Trachelectomy may be an alternative for stage I A1 squamous cell and adenocarcinoma of the cervix if fertility preservation is needed
- Radical brachytherapy (BT) with a dose of up to 65 Gy equivalent dose in 2Gy to point A is a good alternative for medically inoperable patients
- Sentinel lymph node (SLN) biopsy/Lymphadenectomy if lymph-vascular space invasion (LVSI) positive.

Stage I A2

- Type II/class B radical hysterectomy and pelvic lymphadenectomy is recommended.
- Conization with extraperitoneal or laparoscopic lymph adenectomy or radical trachelectomy are fertility preserving options.
- Brachytherapy alone or external beam radiation therapy (EBRT) and brachytherapy to a dose of up to 70 Gy to point A should be considered for medically inoperable patients.
- Salpingectomy is done along with hysterectomy. Ovarian preservation can be done in younger patient. But young patients with non-HPV-related adenocarcinoma should be counseled carefully regarding bilateral oophorectomy, due to the higher risk of metastases and/or relapse in the adnexa compared to squamous cell histology.

Stage I B1

- Type III/class C radical hysterectomy with or without bilateral salpingo-oophorectomy is recommended.
- In patient desirous of fertility, radical trachelectomy with bilateral pelvic lymph node (BPLND)/SLN biopsy/pelvic lymph node dissection (PLND) may be considered.
- Open abdominal route is the standard of care. Minimally invasive surgery (MIS) is currently not recommended.

Stage I B2 and Stage II A1

Abdominal Type III/C1 radical hysterectomy with bilatera lpelvic lymphadenectomy+/-bilateral oophorectomy is the preferred modality of treatment.

Patients unfit or unwilling for surgery: Radical radiotherapy (RT)

FOR TYPES OF HYSTERECTOMY, REFER ANNEXURE 2[20,21]

Stage I B3, II A2 to Stage IV A

- Definitive platinum-based chemoradiotherapy and brachytherapy is the standard of care.
- Treatment strategy should aim to avoid the combination of radical surgery and postoperative EBRT, due to a significant increase of morbidity and no impact on survival.
- Pelvic exenteration is an option in selected cases with stage IV A disease. This should be especially considered when need for symptom control applies, e.g. for fistulae.
- Neoadjuvant chemotherapy is not indicated to downstage the disease.

Stage IVB: Treatment should be individualized. Palliative systemic therapy (chemotherapy and/or immunotherapy and/or targeted therapy) and/or palliative radiation therapy should be considered. Hemostatic radiotherapy can be given to control intractable bleeding. Symptom-directed care and pain relief is an integral part of palliative care. Psychosocial support must be incorporated in patient management.

MANAGEMENT OF RECURRENT CERVICAL CANCER

Inadvertent Simple Hysterectomy in Undiagnosed Cervical Cancer

Patients with stage 1 A1 without LVSI should be kept under regular follow-up. Rest all should be evaluated for revision surgery (radical parametrectomy/vaginectomy and lymphadenectomy) or radiation therapy with or without chemotherapy.

ADJUVANT TREATMENT POST SURGERY

According to postoperative histopathology report, patients regrouped in the following:

High-risk (Anyone factor):[22]
- Positive pelvic/para-aortic lymph nodes
- Parametrial involvement
- Positive surgical margin(microscopic)

  Patients with high-risk factors should be offered adjuvant concurrent chemoradiotherapy.

Intermediate-risk (Any two factors):[23]
- Presence of LVSI
- Tumor maximum diameter >4 cm at final pathology
- Deep cervical stromal invasion.

  Patient should receive adjuvant radiotherapy.

Low Risk: All other patients.

No adjuvant treatment required, only proper follow-up as per schedule

Definitive Chemoradiotherapy and Brachytherapy

- Definitive management consists of concomitant pelvic radiotherapy (platinum based) and brachytherapy
- Overall treatment time for the definitive treatment should not exceed 7–8 weeks. Overall treatment time for EBRT should not exceed **5–6 weeks**.
- There is evidence that overall treatment time (OTT) including brachytherapy, should be as short as possible and should not exceed 56 days.

CERVICAL CANCER IN PREGNANCY: REFER TO ANNEXURE 3

Follow-up: Follow-up should be every 3–4 monthly for 2 years, every 6 monthly for next 3 years and every yearly thereafter. At each follow-up visit, a detailed history should be taken, clinical examination should be done including the assessment of vault/cervix, vagina, and vulva.

Investigations including imaging should be tailored according to clinical findings. Pap smear or biopsy should be taken if a lesion is suspected. No routine cervical smear should be taken if the patient has received RT.

Management of recurrent cervical cancer:[24] Refer to **Annexure 4**.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.
2. Bhatla N, Singhal S, Saraiya U, et al. Screening and management of preinvasive lesions of the cervix: Good clinical practice recommendations from the Federation of Obstetrics and Gynaecologic Societies of India (FOGSI). J Obstet Gynaecol Res. 2020;46(2):201-14.
3. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Available from: https://www.who.int/publications/i/item/9789240014107. Accessed on 13th February 2023.
4. Human papillomavirus vaccines: WHO position paper (2022 update), 16 DECEMBER 2022. Available from: https://www.who.int/publications/i/item/who-wer9750-645-72.
5. SAGE evidence to recommendations framework. Geneva: World Health Organization. Available from: https://cdn.who.int/media/docs/default-source/immunization/position_paper_documents/human- papillomavirus-(hpv)/hpv-gender-recommendation-table.pdf?sfvrsn=40027bd2_2

6. Options for linking health interventions for adolescents with HPV vaccination. Geneva: World Health Organization; 2014. Available from: https://www.who.int/publications/m/item/options-for-linking-health-interventions-for-adolescents-with-hpv-vaccination
7. Gardasil. Available from: https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/downl oad_file_division.jsp?num_id=NDIyNw==
8. Cervarix. Available from: https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/down load_file_division.jsp?num_id=NDE3OA==
9. Cervavac. Available from: https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=OTg4Mg==
10. Global Advisory Committee on Vaccine Safety. Safety of HPV vaccines. Geneva: World Health Organization. Available from: https://www.who.int/publications/i/item/WER9428
11. Human papillomavirus (HPV) nucleic acid amplification tests (NAATs) to screen for cervical pre-cancer lesions and prevent cervical cancer. 2022. Available from: https://www.who.int/publications/i/item/9789240045248
12. Bhatla N, Singhal S. Primary HPV screening for cervical cancer. Best Pract Res Clin Obstet Gynaecol. 2020;65:98-108.
13. Koliopoulos G, Nyaga VN, Santesso N, et al. Cytology versus HPV testing for cervical cancer screening in the general population. Cochrane Database Syst Rev. 2017;8(8):CD008587.
14. Mustafa RA, Santesso N, Khatib R, et al. Systematic reviews and meta-analyses of the accuracy of HPV tests, visual inspection with acetic acid, cytology, and colposcopy. Int J Gynaecol Obstet. 2016;132(3):259-65.
15. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. World Health Organization. 2021. Available from: https://www.who.int/publications/i/item/9789240030824
16. Operational Framework – Management of Common Cancers. Ministry of Health and Family Welfare, Government of India. 2016. Available from: https://main.mohfw.gov.in/sites/default/files/Operational%20Framework%20Management%20of%20Common%20Cancers_1.pdf
17. Bhatla N, Aoki D, Sharma DN, et al. Cancer of the cervix uteri: 2021 update. Int J Gynaecol Obstet. 2021;155(Suppl 1):28-44.
18. Chopra SJ, Mathew A, Maheshwari A, et al. National Cancer Grid of India Consensus Guidelines on the Management of Cervical Cancer. J Glob Oncol. 2018;4:1-15.
19. Indian Council of Medical Research: Consensus document for the management of cancer cervix. Available from: https://main.icmr.nic.in/sites/default/files/guidelines/Consensus%20Document%20for%20The%20Management%20of%20Cancer%20Cervix_0.pdf
20. Querleu D, Cibula D, Abu-Rustum NR. 2017 Update on the Querleu–Morrow Classification of Radical Hysterectomy. Ann Surg Oncol. 2017;24(11):3406–12.
21. Piver MS, Ghomi A. The twenty-first century role of Piver-Rutledge type III radical hysterectomy and FIGO stage IA, IB1, and IB2 cervical cancer in the era of robotic surgery: a personal perspective. J Gynecol Oncol. 2010;21(4):219–24.
22. Peters WA 3rd, Liu PY, Barrett RJ 2nd, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol. 2000;18(8):1606-13.
23. Sedlis A, Bundy BN, Rotman MZ, et al. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. Gynecol Oncol. 1999;73(2):177-83.
24. Reed N, Balega J, Barwick T, et al. British Gynaecological Cancer Society (BGCS) cervical cancer guidelines: Recommendations for practice. Eur J Obstet Gynecol Reprod Biol. 2021;256:433-65.

ANNEXURES

ANNEXURE 1: FIGO-STAGING OF CARCINOMA OF THE CERVIX UTERI 2018

Stage I: The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)

- IA: Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm.
- IA1: Measured stromal invasion<3 mm in depth.
- IA2: Measured stromal invasion>3 mm and ≤5 mm in depth.
- IB: Invasive carcinoma with measured deepest invasion>5 mm(greater than Stage IA), lesion limited to the cervix uteri.
- IB1: Invasive carcinoma>5 mm depth of stromal invasion, and ≤2 cm in greatest dimension.
- IB2: Invasive carcinoma >2 cm and ≤4 cm in greatest dimension.
- IB3: Invasive carcinoma >4 cm in greatest dimension.

Stage II: The carcinoma invades beyond the uterus but has not extended on to the lower third of the vagina or to the pelvic wall.

- IIA : Involvement limited to the upper two-thirds of the vagina without parametrial involvement.
- IIA1: Invasive carcinoma ≤4 cm in greatest dimension.
- IIA2: Invasive carcinoma >4 cm in greatest dimension.
- IIB: With parametrial involvement but not up to the pelvic wall.

Stage III: The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes.

- IIIA: The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall.
- IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- IIIC: Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r and p notations)
- IIIC1: Pelvic lymph node metastasis only
- IIIC2: Para-aortic lymph node metastasis.

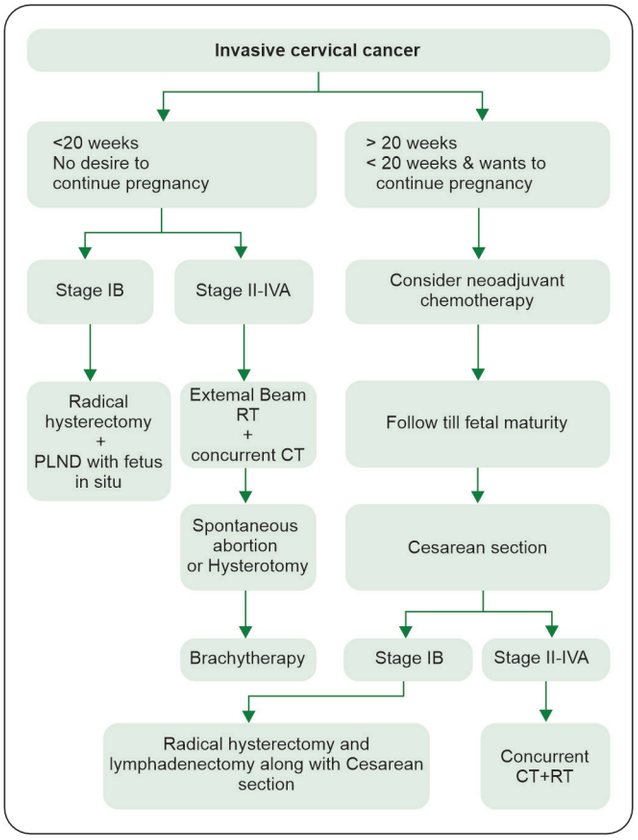
Stage IV: The carcinoma as extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. (Bullous edema does not upstage to Stage IV)

- IVA: Spread to adjacent pelvic organs
- IVB: Spread to distant organs.

ANNEXURE 2: TYPES OF HYSTERECTOMY

	Extrafascial Hysterectomy	***Modified Radical Hysterectomy***	***Radical Hysterectomy***
Piver-Rutledge Type	Type I	Type II	Type III
Querleu–Morrow Type	Type A	Type B	Type C
Indication	Stage IA1	Type IA1 with lymph-vascular space invasion (LVSI), IA2	Stage IB1 and IB2, selected Stage IIA
Cardinal ligaments	Divided at uterine and cervical border	Divided where ureter crosses uterine artery	Divided at pelvic side wall
Uterosacral ligaments	Divided at cervical border	Partially removed	Divided near sacral origin
Vaginal margin	None	1–2 cm	Upper one-quarter to one- third
Uterosacral ligaments	Divided at cervical border	Partially removed	Divided near sacral origin
Urinary bladder	Mobilized to base of bladder	Mobilized to upper vagina	Mobilized to middle vagina
Rectum	Not mobilized	Mobilized below cervix	Mobilized below cervix

ANNEXURE 3: ALGORITHM FOR MANAGEMENT OF CERVICAL CANCER IN PREGNANCY



Abbreviations: CT, computed tomography; PLND, pelvic lymph node dissection; RT, radiotherapy

ANNEXURE 4: MANAGEMENT OF RECURRENT CERVICAL CANCER