14 Cervical Cancer Screening in Low-Resource Settings

Ashrafun Nessa, Begum Rokeya Anwar, and Shirin Akter Begum

14.1 Introduction

The incidence of cervical cancer (CC) varies greatly between developing and developed countries, where CC cases have been considerably reduced due to effective implementation of screening programs. CC is one of the most common cancers in women across the globe, with an estimated prevalence of 1,547,161 cases worldwide in 2012 [1]. A large fraction of the world's population lives in low- and middle-income countries (LMICs) and contributes to a significant burden of CC. This increase is mostly related to growing aging population, inadequate treatment facilities, and poor involvement of the community in cancer control [2]. Almost 80% of cervical cancer occurs in developing countries such as Southeast Asia, Western Pacific regions, India, and Africa, the regions of very high mortality rate [3]. LMICs have high burden of cervical cancer due to lack of screening; high prevalence of risk factors like early marriage, early initiation of sexual activity, multiparity, and sexually transmitted diseases (STDs) and low socioeconomic status. Treatment of CC is expensive and requires radical operative procedures and/or radiotherapy and prolonged hospital stay. In many low-resource countries, facilities for radical surgery and radiotherapy are inadequate and expensive.

Presently, several developing countries are trying to adopt a CC screening program to ensure wide coverage of the target population with on-site, low-cost screening with minimum infrastructure requirement. Management of screen-positive cases and adequate follow-up with proper linkage to immediate treatment are essential to make all these efforts successful.

Two main approaches have been adopted for cancer screening programs: organized and opportunistic [4]. An organized cancer screening program should be population-based, be managed through the public health delivery system, follow a uniform guideline, achieve a reasonable coverage of the target population, and have efficient linkage between screening and treatment of the positive cases. On the other hand, in opportunistic screening, a doctor or health professional offers the test when a woman visits health facilities for other reasons. In opportunistic screening, cases may not be checked or monitored. In LMICs, organized population-based screening needs to be introduced at national level with good population coverage to make the program successful.

A. Nessa · S. A. Begum
Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

B. R. Anwar (✉)
Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital, Dhaka, Bangladesh

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In LMICs, CC screening started sporadically in one or two tertiary health-care centers in the mid-1980s by conventional cervical cytology. However, the United Kingdom and some other developed countries developed a systemic call and recall system in the late 1980s and reduced the death rate of CC by conventional cytological test [5]. Tertiary centers of low-resource countries became familiar with cytological test and started opportunistic screening in the mid-1990s, but several difficulties were encountered in implementing the cytology-based screening program in a low-resource setting. As a result, the CC burden remained unchanged.

In the mid-1990s, developed countries initiated research on HPV DNA test, and by 2005 many developed countries started using HPV DNA test as the primary screening test [6]. In the meantime, liquid-based cytology (LBC) replaced conventional cytology in some developed countries due to its higher sensitivity and specificity [7]. Several studies in LMICs have suggested the feasibility of primary screening by HPV test in terms of decreased program costs and increased screening interval [8]. However, the test is too expensive for introduction in the screening program of many LMICs due to resource shortage at the present moment. LMICs need to adopt an affordable, accessible way of cervical cancer screening. The best available evidence supports visual inspection with acetic acid (VIA) testing as a primary screening modality for cervical precancer screening in low-resource countries, as it requires minimum infrastructure support, and the result of the procedure is available immediately.

In most LMICs, population-based cervical cancer screening is still nonexistent. In these countries, CC screening remains opportunistic due to competing health-care priorities, insufficient financial resources, and a limited number of trained providers. Hence, a significant number of cases are detected at advanced stages, leading to increased mortality. To implement successful CC screening program in LMICs, support and funding from the Ministry of Health are essential. The Middle East and North Africa have taken steps to implement national screening programs based on VIA [9].

India is carrying the largest burden of disease in the world. India developed guidelines for a population-based screening program for cervical cancer detection based on visual inspection tests more than 10 years ago. Despite introduction of the national guidelines, important demonstration projects, and a number of well-conducted research studies showing feasibility and cost-effectiveness, very little scale-up of CC screening services has been developed in the country [10]. The government of Bangladesh (GOB) evaluated the feasibility of screening with VIA in 2005 and initiated to scale up the program in 2006 to the district level and is now expanding the program to the sub-district level [11, 12]. In Bangladesh, screening is practiced currently by 411 centers at primary, secondary and tertiary health-care facilities [13].

14.2 Screening in LMICs

14.2.1 Choice of Screening Test in LMICs

Despite the attractiveness of the vaccination program, CC screening is still recognized as the most successful approach for CC control. The available methods of CC screening are cervical cytology (Pap smear), HPV test, VIA, visual inspection of the cervix with Lugol's iodine (VILI), and colposcopy. An ideal screening test should be simple, painless, less time-consuming, cost-effective, and accurate. Pap smear has been used most frequently in cervical cancer screening programs of different high-resource countries. However, cytology-based screening has several drawbacks that limit its usefulness. The technical and monetary constrains of implementing cytology-based screening programs in LMICs initiated the development of simple screening tests. VIA and HPV testing have been suggested as suitable tests for primary screening methods in low-resource countries.

14.2.1.1 Cytology-Based Screening

Cytology-based CC screening is the oldest and most widespread cancer screening technique.

It began in the United Kingdom in the 1960s as opportunistic screening. In 1988, a systemic call and recall program was developed that significantly reduced cervical cancer and subsequently has led to effective reduction in the incidence and mortality from CC in many developed countries [14, 15]. In the United Kingdom, from 1990 to 2008, women aged 35–64 years participating in a CC screening program had a reduced risk of CC of 60–80% and a reduced risk of developing an advanced CC of 90% over the next 5-year period [16].

Introduction of conventional cytology services in Cameroon, a low-resource country, reduced cervical cancer rates by 60–90% within 3 years of implementation [17]. However, the widespread opportunistic screening and the large-scale national or regional cytology screening programs in Brazil, Cuba, Costa Rica, Chile, and Mexico, among others, in Latin America and the Caribbean have been largely ineffective in reducing the CC burden compared with high-income developed countries [18].

A combination of suboptimal cytology testing, lack of quality assurance, poor coverage of women, and inadequate follow-up of screen-positive women were the main reasons for lack of success of cytology programs in low-resource countries which are mainly due to the inadequate health-care infrastructure, human resource, and program logistics.

Drawbacks and limitations of cytology-based screening are as follows:

- Sensitivity is inadequate to detect cervical intraepithelial neoplasia (CIN) 2+ disease (approximately 50%).
- Needs expensive laboratory infrastructure and highly skilled manpower that may not be easily available.
- The strict quality control required for optimum performance of the test cannot be ensured.
- Does not provide the result immediately, and the positive women need to be recalled after the results are available.
- A repeat visit is inconvenient for the women and increases the dropout rates.

Table 14.1 Sensitivity and specificity of cytology-based screening in different LMICs

Author, year, country	Sensitivity (%)	Specificity (%)
Nessa et al., 2013, Bangladesh [19]	33.3	95.8
Sankaranarayanan et al., 2003, India [20]	81.9	87.8
Karimi et al., 2013, Iran [21]	51	66.6

Even if high-quality cytology programs were implemented in low-resource countries, the cytology-based programs would only be moderately effective. The cytology test misses approximately 50% of high-grade precursor lesion and cancers with a single screening [6]. In low-resource settings, women would probably only be screened once or twice in their lifetime making cytology screening less effective. Sensitivity and specificity of cytology-based screening in different low-resource settings are shown in Table 14.1.

14.2.1.2 Human Papillomavirus (HPV) Test

Infection by the high-risk (hr) HPV is needed for the development of CC. So detection of hrHPV DNA should be a good approach to identifying women with CIN. HPV causes cellular changes very slowly. The time from HPV infection to development of CC is about 10–20 years [22]. Therefore, a woman who is HPV negative is extremely unlikely to develop cervical cancer over the next 5–10 years, and infrequent screening would be safe. Thus, there are two potential uses for HPV testing: to identify those likely to have the disease presently and those who may develop the disease after few years. The HPV test has been proved more effective than cytology for CC screening, providing increased reassurance and allowing longer screening intervals [23]. Though many types of HPV tests are available, only several commercial HPV tests have documented clinical performance compared with the standard HPV test. According to guidelines, an ideal test should have at least 90% clinical sensitivity for CIN 2+ and clinical specificity of at

least 98% [24, 25]. However, too many options of HPV tests make selection of a suitable one difficult. Due to high sensitivity, HPV tests have replaced cervical cytology for primary screening in many countries.

Several studies have confirmed that HPV testing is feasible in low-resource settings and appears to be the best strategy for CC screening [26, 27]. A large-cluster randomized trial from rural India has shown approximately 50% reduction of CC after a single round of HPV screening (Hybrid Capture II) [28]. HPV testing is time-consuming, and expensive laboratory infrastructure is required, but development of new rapid molecular methods for detecting HPV DNA initiated a new horizon in CC screening in low-resource settings. As a result of introduction of rapid molecular methods with high sensitivity, HPV test became the most efficient and cost-effective strategy for use in low-resource settings [29]. Moreover, the use of "screen-and-treat" and "see-and-treat" approaches requiring minimum visits made HPV test more cost-effective. Even then, affordability and sustainability using HPV test for primary CC screening in some low-resource settings are difficult to implement.

14.2.1.3 Visual Inspection of the Cervix with Acetic Acid (VIA)

VIA, also known as "the acetic acid test," involves naked eye inspection of the cervix under bright light at least 1 min after the application of 3% to 5% dilute acetic acid using a cotton swab or a spray. It involves non-magnified visualization of the uterine cervix and search for the appearance of acetowhite areas in the transformation zone (TZ), close to the squamocolumnar junction (SCJ) or the external os. The identification of acetowhite lesions helps in early diagnosis of preinvasive disease and early preclinical, asymptomatic invasive cancer.

The test can be categorized as VIA positive or VIA negative. A positive test is the detection of well-defined, densely opaque dull acetowhite lesions in the TZ of the cervix. The faint, ill-defined, translucent acetowhite areas, faint acetowhitening of endocervical polyps, nabothian cysts, dot-like acetowhite appearance, and prominent SCJ are categorized as negative. However, immature squamous metaplasia and inflamed and regenerating cervical epithelium may appear as faint acetowhite areas, and therefore these are not specific to cervical neoplasia.

A major benefit of VIA is that the result of screening test is available without delay, and therefore additional investigations/management can be planned and carried out during the same visit. All these advantages lead to VIA being considered as the primary cervical screening tool.

The advantages of VIA in programmatic context are as follows:

- Sensitivity better than cytology (80% to detect CIN 2+ disease).
- Can be performed at primary and secondary health centers.
- Paramedical staff (nurses, female health workers) and nonspecialist doctors can be trained to do the test.
- The procedure is simple, and the test providers can be trained through a 1 to 2 weeks course.
- The equipment is inexpensive and the consumables can be made available very easily.
- The test result is available immediately.

Studies indicate that VIA is at least as sensitive as conventional cytology in detecting high-grade lesions, but its specificity is lower. VIA appears to be the most promising low-technology alternative to cytology [29, 30]. Table 14.2 compares the sensitivity and specificity of VIA in detecting CIN 2 and CIN 3 and invasive cancer in different low-resource countries.

For countries in resource-constrained settings, where screening with an HPV test is not feasible, the World Health Organization (WHO) recommends screening with VIA and treatment with cryotherapy. However, if the lesion is not eligible for treatment by cryotherapy, she should be referred to a higher center [39, 40].

Several countries in Asia, Africa, and Central America initiated scale-up of the program after gaining some experience from the pilot program.

Table 14.2 Accuracy of VIA in detecting CIN 2–3 and invasive cancer [38]

Author, year, country	Number of participants	Sensitivity (%)	Specificity (%)
Denny et al., 2000, South Africa [8]	2885	67	84
Nessa et al., 2010, Bangladesh [12]	104,098	93.6	58.3
University of Zimbabwe, 1999, Zimbabwe [31]	2148	77	64
Denny et al., 2002, South Africa [32]	2754	70	79
Sankaranarayanan et al., 2004, India [33]	54,981	79	86
Braganca et al., 2005, Brazil [34]	809	54	88
Ngoma et al., 2010, Tanzania [35]	10,378	60.6	98.2
Muwonge et al., 2010, Angola [36]	8851	70.7	94.5
Sauvag et al., 2011 [37]		80	92
Sankaranarayanan et al., 2011 [18]		80 (14–95)	92 (14–98)

The government of Zambia has initiated a large-scale screening program using VIA [41, 42]. Characteristics of the screening programs of the mentioned countries including the management algorithm for screen-positive women are given in Table 14.3 [42]. Bangladesh evaluated the feasibility of screening with VIA within the existing government health infrastructure in 16 districts in 2005 [11] and scaled up the program to all the districts and is now expanding the program to the sub-district level. In Bangladesh, screening is practiced currently by 411 centers at primary-, secondary-, and tertiary-level health-care facilities [13]. Bangladesh has adopted CC screening for the women of 30 years and above with VIA, and positive cases are being referred to the higher facilities, where colposcopy and management are carried out. In Bangladesh, colposcopy became an important part of this prevention program both for diagnosis and guiding the treatment [12, 43, 44]. However this is predominantly an opportunistic screening program [42, 43]. In India also the government has advocated VIA as the screening modality for women more than 30 years of age.

Procedure of VIA

VIA has become the screening test of choice for the CC screening program in several low-resource countries due to its simplicity and affordability. If a woman wishes to undergo VIA test, she needs counseling along with taking a brief reproductive, contraceptive, and menstrual history including date of last menstrual period. The criteria to categorize the observations into negative, positive, or suspected cancer after VIA are given in Table 14.4.

The steps of VIA are as follows:

- Select a bivalve speculum of appropriate size to see the vagina and cervix adequately (Fig. 14.1).
- Use a good focusing light preferably with halogen or LED or 100 W tungsten bulb.
- The woman should be informed before inserting the speculum in the vagina.
- When inserting the speculum, ask the woman to breathe in deeply and then breathe out slowly through her mouth. This helps her to relax and not contract her vaginal muscles.
- Insert the blades fully or until resistance is felt.
- If difficulty is faced in exposing the cervix because of lax vaginal walls, a non-lubricated condom over the speculum blades can be used with cutting the tip of the condom.
- Examine the vagina. Note for inflammation, ulcers, or sores.
- Examine the cervix and locate the cervical opening (external os) (Fig. 14.2).
  - Note the color of the cervix. The surface should be smooth and pink. The area of the cervix where the color changes from pink to red is the squamocolumnar junction, which is usually close to the external cervical os (Fig. 14.3).
  - Note if there is bleeding or discharge from the cervix. Normal cervical secretions should be clear and odorless.
  - To perform VIA, apply 5% freshly prepared dilute acetic acid solution liberally on the cervix using a cotton swab (Fig. 14.4).

Table 14.3 Characteristics of country screening programs [42]

Country	Year pilot project initiated	Year program scale-up began	Screening policy and protocol	Screening test used	Target age	Management algorithm for screen-positive women	Health information system capabilities	Institution responsible for program coordination
Bangladesh	2004	2006	Cervical and Breast Cancer Screening Program: Standard & Guidelines (2005)	VIA	≥30 years	VIA+ women referred for colposcopy and treated immediately	Electronic template recently introduced; generates key system indicators; does not yet enable tracking of women	Ministry of Health and Family Welfare, Bangabandhu Sheikh Mujib Medical University and UNFPA
Guatemala	2015	2016	National Guidelines for Screening and Treatment of Precancerous Lesions for the Prevention of Cervical Cancer (2014)	HPV DNA	30–65 years	Varies by health facility • HPV screen-and-treat, using VIA to determine treatment eligibility only • HPV+ VIA+ women treated; HPV+ VIA− women rescreened in 1 year • HPV+ Pap ASCUS+ women referred for colposcopy and treatment; HPV+ normal Pap rescreened in 1 year	Electronic; generates key system indicators; limited functionality for tracking of women	Ministry of Public Health and Social Assistance
Honduras	2015	2016	Protocol for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention (2015)	HPV DNA	30–64 years	HPV+ VIA+ women treated; HPV+ VIA− women rescreened in 1 year	Electronic template recently introduced; generates key system indicators; limited functionality for tracking of women	Secretary of Health

Nicaragua	2015	2016	Norm and Protocol for Cervical Cancer Prevention and Control (not yet published)	HPV DNA	30–59 years	Varies by health facility • HPV+ VIA+ women treated; HPV+ VIA− women rescreened in 1 year • HPV+ Pap ASCUS+ women referred for colposcopy and treatment; HPV+ normal Pap rescreened in 1 year	Electronic; generates key system indicators; enables tracking of women	Ministry of Health
Zambia	2006	2012	Visual Inspection with Acetic Acid (VIA) and Cryotherapy: A Reference Manual for Trainers and Health Care Providers (2015)	VIA aided by digital cervicography	25–59 years	VIA+ women treated immediately	Electronic; generates key system indicators; enables tracking of women	Ministry of Health

Table 14.4 Criteria for categorizing VIA test results

VIA category	Description of the findings
Negative	No acetowhite area
	Transparent or faint patchy acetowhite areas without definite margins
	Nabothian cysts becoming acetowhite
	Faint line like acetowhitening at the junction of the columnar and squamous epithelium
	Acetowhite lesions far away from the transformation zone
Positive	Distinct, opaque acetowhite area
	Margin should be well-defined, may or may not be raised
	Abnormality close to the squamocolumnar junction in the transformation zone and not far away from the os
Suspected cancer	Obvious growth or ulcer on the cervix
	Acetowhite area may not be visible because of bleeding

– After at least 1 min, inspect the cervix to reconfirm the position of the SCJ and also to look for features of the transformation zone (TZ) (Fig. 14.5).
– Carefully look for any abnormality, especially an acetowhite area on the TZ (Figs. 14.6, 14.7, and 14.8).
– After completion of the test, wipe out the excess acetic acid, and gently remove the speculum, keeping the blades partially closed.
– Inform the woman of the test results and appropriately counsel her.
– Fill out appropriate forms and registers. Document the findings clearly.

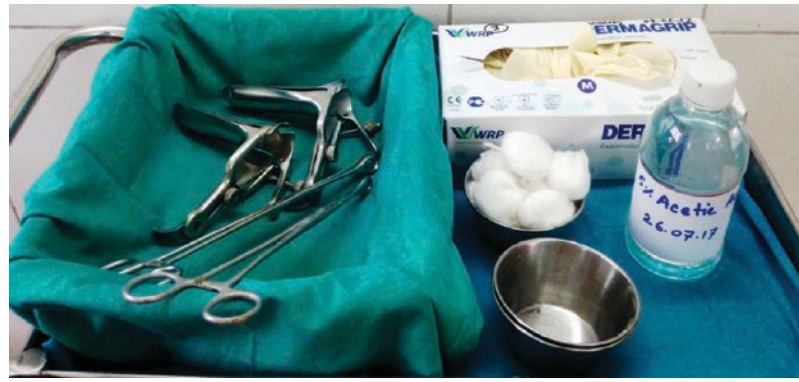


Fig. 14.1 Instrument tray for VIA

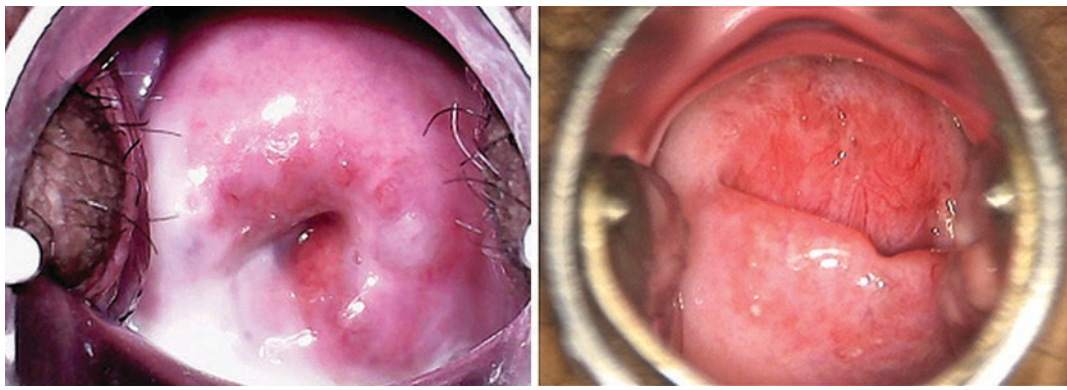


Fig. 14.2 Exposing the cervix and noting the type of vaginal discharge if any

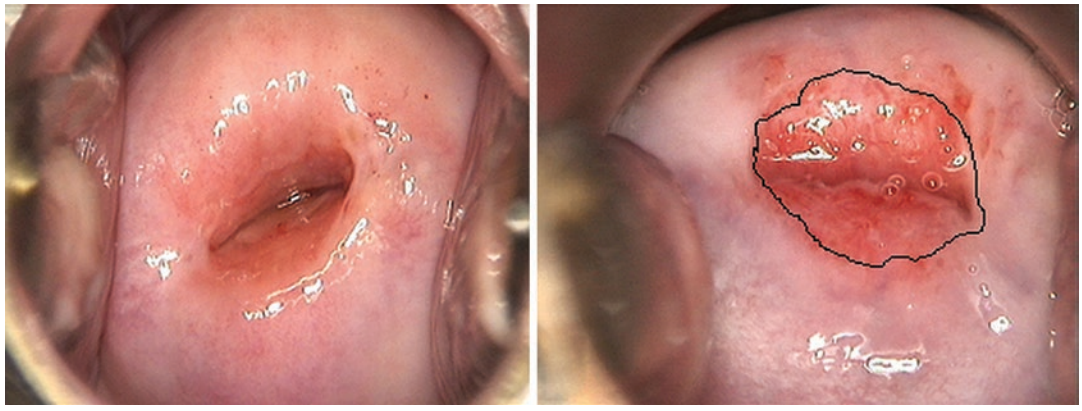


Fig. 14.3 Identifying the squamocolumnar junction

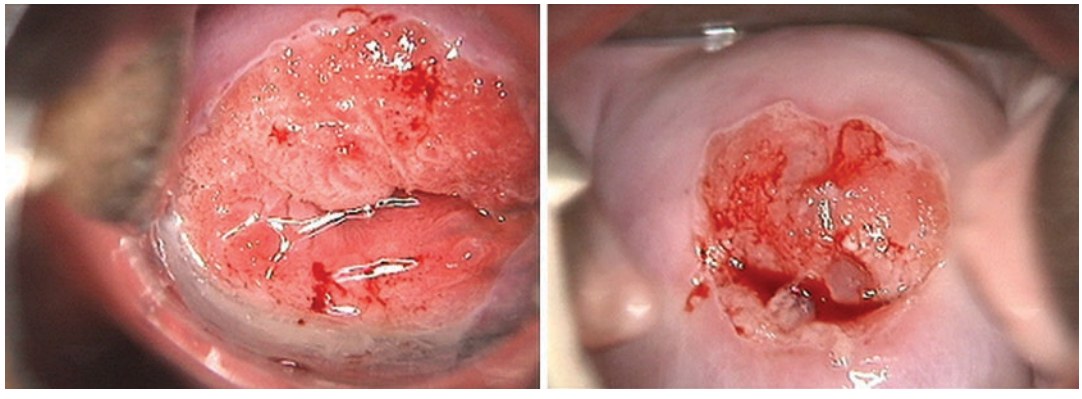
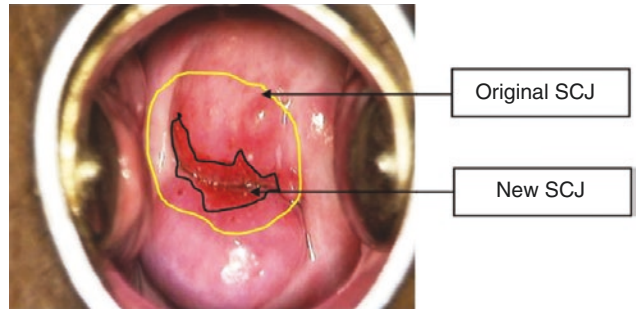


Fig. 14.4 The cervix after application of acetic acid

Fig. 14.5 Identifying the TZ



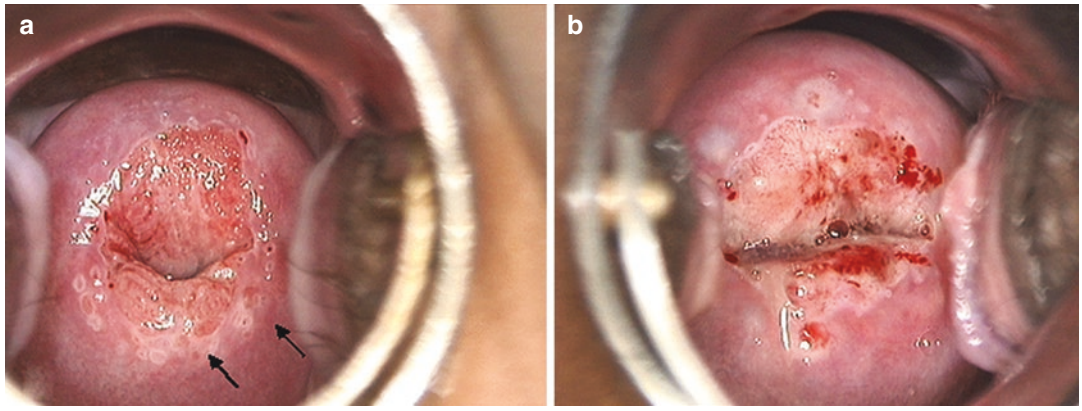


Fig. 14.6 VIA category—negative. (**a**) Blanching of the columnar epithelium noted. Crypt openings are seen prominently. (**b**) The columnar epithelium temporarily becomes patchy acetowhite

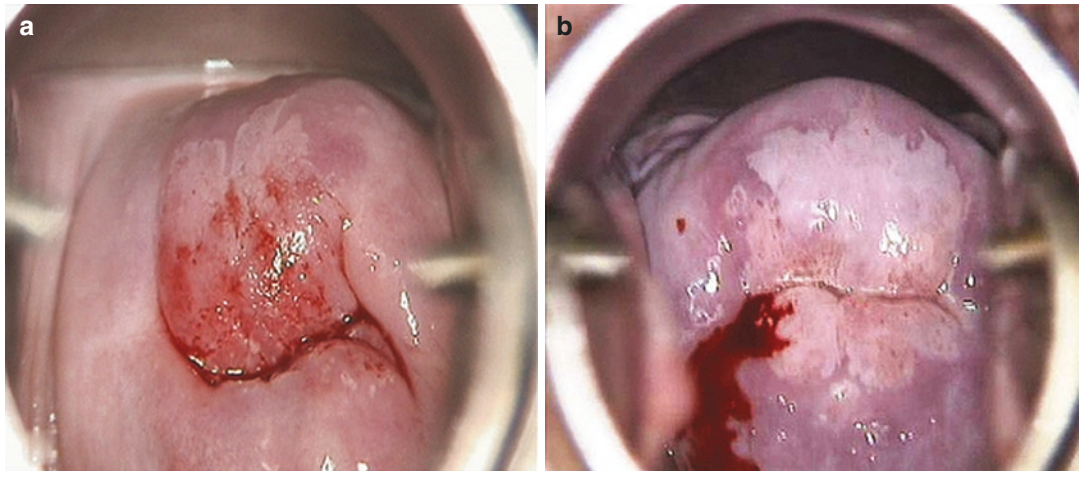


Fig. 14.7 VIA category—positive. (**a**) Thin acetowhite area seen on the anterior lip in the transformation zone attached to the SCJ. (**b**) Dense acetowhite area seen on both the anterior and posterior lip in the transformation zone

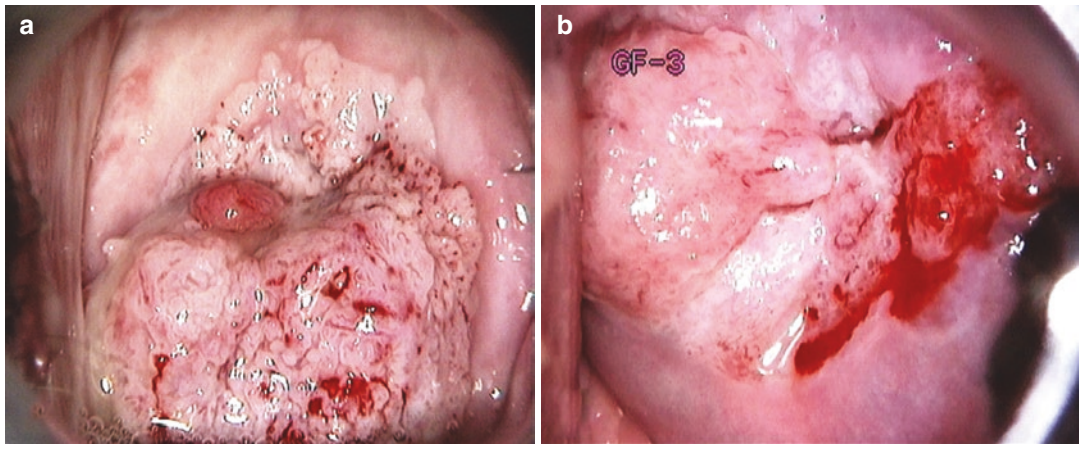


Fig. 14.8 VIA category—suspected cancer. (**a**) Dense acetowhite area with surface irregularity and bleeding points seen mostly on the posterior lip. (**b**) Raised nodular growth with dense acetowhite area and contact bleeding

14.2.2 Components of Screening Program

14.2.2.1 Defining the Target Population, Frequency of Screening, and Population Coverage

The target age group for CC screening and the frequency of screening should be based on the reasonable estimation of the capabilities and resources available for the program. In LMICs, utilization of the limited resources should be planned to provide benefit to the maximum number of women who are at risk of the disease. CC screening should be started at the age of 30 years in programs with limited resources as this disease is rare before the age of 30 years and screening women at a younger age detects many low-grade lesions that never progress to cancer.

WHO recommends screening from 30 years of age, with population screening coverage of women aged 30–49 years of age [39, 40]. Best utilization of the resources is possible if screening is limited to the age group with maximum possibility of detecting the high-grade precancer lesions (CIN 2 and 3), which is between 30 and 49 years of age. Individual countries may adopt variations depending on the government's attitude and political will, stakeholder's view, economic situation, budgetary allocation, etc.

The screening should be performed every 5 years. All efforts should be made to achieve high coverage of the target population. For test-negative women on VIA or cytology, the screening interval for repeat screening should be every 3–5 years. However, in case of HPV test, women with negative result should have rescreening after a minimum interval of 5 years. In women who are HIV-positive or with unknown HIV status in areas with endemic HIV infection, the screening interval should be more frequent [40].

Too frequent screening of women such as every year or every 2 years causes a heavy burden on the limited manpower and financial resources of low-resource settings. Frequent screening does not add extra benefit over 3-yearly or 5-yearly screening. It has been estimated that screening women with VIA even twice in their lifetime is highly cost-effective. In countries of low-resource settings, achieving a good coverage (more than 70%) of the target women determines the success of the screening program rather than too frequent screening.

14.2.2.2 Screening Test Facilities

The CC screening program of low-resource settings should be integrated into the existing government health-care delivery system. This is convenient and cost-effective. For convenience and to ensure better compliance, the screening tests should be done close to the residence of the women. Primary and secondary health-care facilities are best suited for this purpose. However, if the health facilities are too far from a particular locality or are in hard-to-reach areas, mobile clinics (screening camps) can be set up on a temporary basis at a suitable place in the village.

14.2.2.3 Capacity Building of Test Providers

The nurses, female health workers, and other paramedical staff or the physicians at the primary and secondary health-care level can do the screening test. They require training and certification before they start the procedure. One essential component is the development of a strong screening implementation infrastructure.

Adequate number of trained manpower for service delivery should be developed at all levels of the health-care system to achieve optimum screening coverage. Competency-based training for service providers at designated training centers should be ensured with proper resource persons and training materials. Good-quality training with appropriate post-training follow-up should be ensured. Only certified providers should perform the tests. After training, the service providers need to be supervised until they achieve a satisfactory level of competency. All test providers should receive a short refresher training, initially every year and later every alternate year.

14.2.2.4 Ensuring Management of the Screen-Positive Women

All screen-positive women should have adequate counseling, further evaluation, and treatment at appropriate facilities. In low-resource settings, equipment for evaluation and treatment (colposcope, electrosurgical equipment, cryotherapy equipment, thermocoagulator) and trained expertise (colposcopists, gynecologists) are less available. Therefore "screen-and-treat" and "see-and-treat" strategy is being introduced as alternative approach of management. Women should have easy access to treatment services to ensure high compliance. In low-resource settings, an approach requiring fewer visits should be adopted to achieve better compliance for the screen-positive cases. They can be managed during the first visit with or without evaluation by colposcopy/histopathology report. However, selected cases need referral to the colposcopy clinics/higher-level health-care facilities (secondary/tertiary level) where further evaluation and management can be carried out.

14.2.2.5 Screen-and-Treat Protocol

The purpose of a "screen-and-treat protocol" is to link screening test to appropriate treatment of precancer with less adverse effects. However, women who are not eligible to receive treatment at the respective facility need referral to higher centers. WHO mentions cryotherapy as the preferred method of treatment in the "screen-and-treat" protocol. WHO algorithm for screen-and-treat strategy at the program level is shown in Fig. 14.9. Using this chart, program managers and decision-makers can determine the best option for screen and treat, in context to their country. Cryotherapy has fewer side effects and nurse/paramedics can perform the procedure at

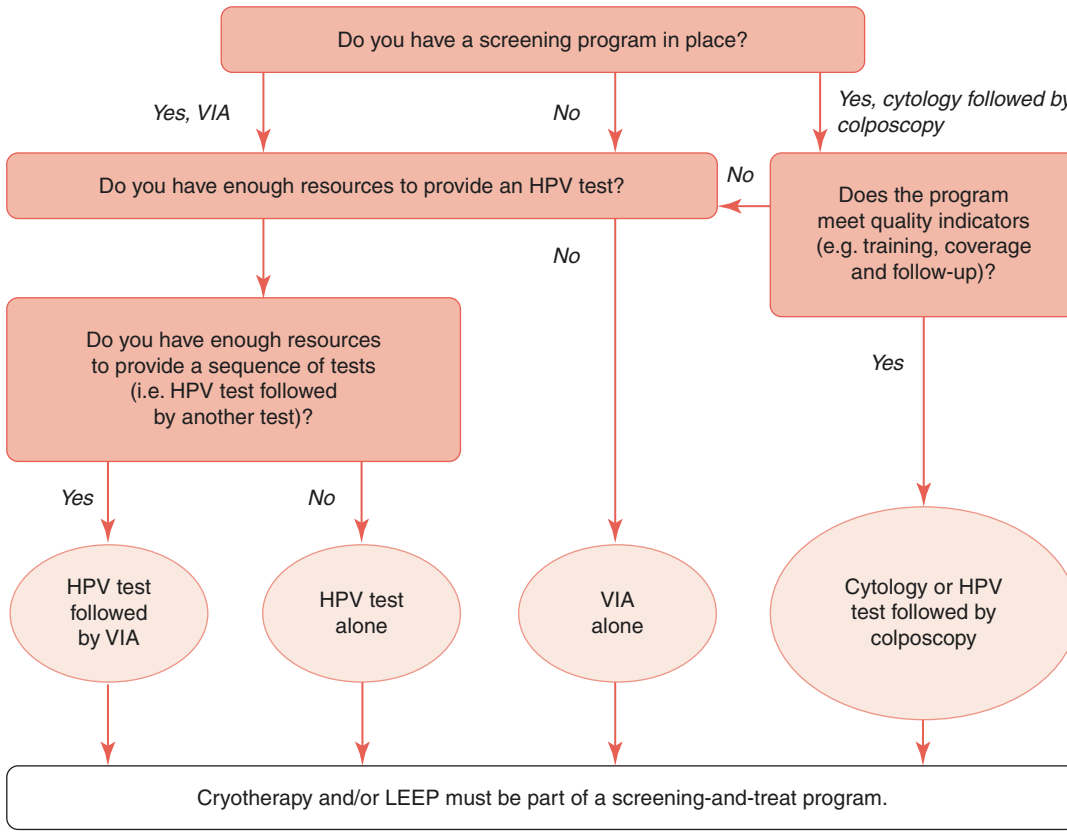


Fig. 14.9 Decision-making flowchart for program managers [39]

the lower level of the health-care system [39]. However, when women are not eligible for cryotherapy, loop electrosurgical excision procedure (LEEP) is the preferred method of treatment.

All HPV-positive women should be treated, and VIA should be used to determine eligibility for treatment with cryotherapy or LEEP [39]. A demonstration project on "prevention of cervical cancer through screening using VIA and treatment with cryotherapy" involving seven sites in six African countries (Madagascar, Malawi, Nigeria, Uganda, United Republic of Tanzania, and Zambia), from 2005 to 2009, revealed that the "screen-and-treat" approach can be introduced in the existing reproductive health services in low-resource countries. Screening for precancerous lesions using VIA and treatment with cryotherapy were well accepted by women and have been incorporated into the cervical cancer-prevention services in existing reproductive health services in these countries [45]. However, though cryotherapy is the primary treatment option for many countries, procuring the gas required for freezing is a significant obstacle. Low quality of carbon dioxide gas also damages equipment. To overcome the barriers, different low-resource countries are trying to adopt use of thermocoagulator to treat CIN. The Guatemalan government has taken steps to introduce thermocoagulation, which needs only electricity [42]. Thermocoagulation is safe, simple, and an effective technique to treat selected CIN lesions of any grade, and it can be used in the single-visit "screen-and-treat" approach and "see-and-treat" approach in the management of CIN in the cervical cancer control program [46].

Sequential testing with VIA and VILI is the most feasible screening approach for cervical cancer screening for HIV-infected women in low-resource countries. When HPV testing becomes feasible and affordable, HPV testing followed by VIA/VILI may be considered [47].

14.2.2.6 See-and-Treat Protocol

In LMICs, where facilities are available, the screen-positive women can be further evaluated following "see-and-treat protocol," and diseased cases can be treated during the same visit for better compliance of treatment. Women with VIA-, HPV-, or Pap-positive report can have further evaluation using colposcopy through addition of a second visit at a higher referral system where colposcopy facilities are available. The women suspected to have high-grade CIN on colposcopy may be treated at the same visit without any histopathological confirmation of the disease. This strategy is called "see-and-treat" or also "colposcopy-and-treat" approach. The "see-and-treat" approach is convenient for the woman; it reduces her anxiety, it improves compliance to treatment, and it is cost-effective for the program. LEEP has been used as the treatment modality for such protocols. A population-based large randomized screening trial in Osmanabad district in Maharashtra, India, was conducted during 2000–2004. The study confirmed that a "see-and-treat" approach using cryotherapy by nurses is acceptable to women, is safe, and ensures satisfactory participation of screen-positive women for diagnosis and treatment [48–50]. Another randomized trial in India has shown a significant reduction in cervical cancer mortality following a single round of screening with HPV testing or VIA screening [51].

In Bangladesh, the government has adopted "see-and-treat" approach combining VIA with colposcopy and LEEP since the year 2010 to improve compliance to treatment [52]. The program is also using thermocoagulation in "see-and-treat" protocols in selected centers. Pooled data from five sites in Asia and South America for women treated for CIN with thermocoagulation from 2010 to 2015, and followed up within 6–12 months of treatment, showed cure after thermocoagulation treatment was 88% (475/543) for CIN 1, 83% (113/137) for CIN 2, and 83% (79/95) for CIN 3 lesions. No serious adverse effect or complications were observed throughout the follow-up period. Thermocoagulation was effective, safe, and accepted in treatment of women diagnosed with CIN and can be used in the single-visit "screen-and-treat" approach or "see-and-treat" approach in management of CIN in the cervical cancer control program [46]. The major benefits are shorter treatment time, easy portability of the equipment to field, use of easily

available electricity than gas refills, is noiseless and produces less smoke, and there is no need for general anesthesia.

14.2.2.7 Posttreatment Follow-up

The treated women should receive posttreatment follow-up screening at 1 year to ensure effectiveness of treatment [39]. Follow-up of treated patients can be continued at all levels of facilities by available methods. VIA, colposcopy, or HPV DNA test can be used during follow-up on an annual basis for 3 years. Women tested negative on three consecutive rounds should be returned to the routine screening protocol applicable to the normal population.

14.2.2.8 Record-Keeping and Data Management

Maintenance of records, storage of data related to various components of screening, and periodic reports are essential for an organized screening program. For population-based organized screening, countries need to develop an electronic database for all women of target age. This database should include women's basic information, screening, colposcopy, treatment, and follow-up records. The computerized database should be maintained at each screening center and all colposcopy centers. A mechanism to check the compliance of screen-positive women to colposcopy and/or treatment should be established by the government.

14.2.2.9 Monitoring, Evaluation, and Quality Assurance

Reduction of CC incidence and death from the disease can be assessed by impact indicators. It can be obtained through a population-based cancer registry or organized health information system. Outcome indicators should be monitored on a regular basis to identify gaps and to identify ways of improvement.

14.2.3 Overcoming Challenges for Cancer Screening Services in LMICs

The main challenges to improve CC screening services include:

- Lack of initiation of a demonstration /pilot program and scale-up of program
- Low level of community awareness on the importance of screening for this cancer
- Poor health system in low-resource settings with insufficient number of skilled manpower and inadequate treatment facilities when there is precancer or cancer diagnosis
- Lack of an effective health information system to facilitate referral and tracking of non-compliant women
- Lack of well-coordinated monitoring and evaluation plan, especially for data collection and management

14.2.3.1 Initiation of a Pilot Program and Scaling Up CC Screening Strategies in LMICs

A pilot program should be initiated by the government and can be supported by nonprofit or international organizations. An advocacy meeting to initiate a pilot program should be organized by the government in countries where piloting has not been performed. The advocacy document should include focused country-specific messages and data on CC incidence and deaths. It should also clearly identify strategies and service delivery guidelines based on the country's needs and priorities. Advocacy meetings should focus on the elimination of policy barriers, allotment of adequate monetary, and human resources for the CC control program. Working with other government sectors and nongovernmental agencies, developing materials to increase public awareness on CC and its prevention, mobilizing eligible women to utilize CC control services, and encouraging communities to assist women with cervical cancer are important.

Although pilot or demonstration programs have taken place in several LMICs, only a few countries have experienced scale-up of evidence-based screening strategies. These countries selected screening modalities recommended by the WHO to avoid budgetary constraints and other health system bottlenecks [42]. The gathered experience may help other countries plan for large-scale implementation. In Bangladesh scale-up efforts began in 2006. About 411 VIA centers are

operational throughout the country, and 1,386,887 VIA tests were performed from 2005 to 2016 at different service centers. Among them 65,247 (4.7%) women were found VIA-positive. The coverage of the screening tests is increasing every year. VIA+ve cases are referred to the colposcopy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) and different medical college hospitals. In Bangladesh, LEEP acquired acceptability as a commonly used outpatient treatment procedure for CIN under local anesthesia and thermocoagulation without local anesthesia.

In Central America, governments are implementing HPV testing using a low-cost assay. HPV testing enables women to collect their own vaginal samples in a variety of settings. Several common challenges remain for continued scale-up in these countries such as training and maintaining a manpower to carry out screening and treatment activities and monitoring and improving the quality of screening and treatment services to bring an impact on CC mortality rates. Governments must begin to move beyond pilot testing and opportunistic efforts to implementing large-scale, population-based approaches where possible.

14.2.3.2 Development of Organized CC Screening Program

In LMICs, a mass screening policy should be taken along with developing a population-based screening program. Low-resource countries should have an organized screening program, in which all eligible women would be systematically invited to have the screening test through extensive community mobilization.

The essential components of an organized screening program:

- A protocol and guideline that will clearly spell out the target population, frequency of screening, screening test, and management of screen-positive population.
- A definite plan for broad-based community mobilization to ensure high participation rate of the target population.
- Ensuring access to screening as well as detection services at the grassroot level so that a high coverage (at least 70% of the target population) can be achieved.
- Linkage between screening and treatment to ensure that the positive cases detected through the program are treated appropriately.
- All categories of service providers should be trained and certified.
- A plan for supportive supervision and quality assurance should be inbuilt in the program.

14.2.3.3 Health Education and Awareness Creation

In low-resource countries, awareness programs conducted by NGOs and government are inadequate to increase awareness among women about CC and its risk factors. Awareness programs remain out of reach of target groups, because they live in villages and rural and urban slums. Programs conducted on special dates, like World Cancer Day, World Health Day, CC Awareness Day, etc., may create more awareness.

Health education and awareness are important elements of a cervical cancer control program, particularly in LMICs where education and health service-seeking attitude is low. Awareness should be created to develop service-seeking behavior among the community. Health education should be delivered both at the community and health facilities. In many LMICs, the existing health infrastructure has manpower and volunteers to increase public awareness, and health education messages in such situations can be imparted through direct face-to-face meetings. Health workers at community or primary health facilities are the first point of contact with the community, and this is particularly true for LMICs where a large number of women do not have access to the electronic media, and the government has less allocation on these expensive media.

At health facilities, health education and counseling can be given by trained service providers. Service providers can develop special skills on counseling techniques and should be well conversed with methods to ask and answer questions about CC screening in a well-informed, honest, and culturally sensitive way. Health educators need to realize that most precancerous lesions of the cervix and early cervical cancer do not have clinical symptoms. Thus, most women being tested need to be informed that the disease may

be silent for a long time without causing any problem, and the tests are for preventing CC and better treatment of the disease.

Flip charts should be developed for use by the health-care providers for counseling both at the screening center and in the community using their own language with consideration of cultural factors.

Posters in the local language aided by pictures, diagrams, and charts should be used to propagate the messages. A broad-based media campaign utilizing print and electronic media will be used to improve the visibility of the program and enhance participation rates.

Some basic principles and suggestions are listed below:

- Inform the community about the risk factors and common signs and symptoms of CC.
- Promote screening for women aged 30 to 60 years.
- Reduce ignorance, fear, embarrassment, and stigma related to cancer.
- Inform the community of available services and where to get them.
- Involvement of community leaders is critical to gain support for the outreach efforts and for adequate allocation of local resources.
- Male partners and other community members must support women's decisions to seek screening and to go for treatment when required.
- Multi-sectorial involvement of governmental and nongovernmental agencies is imperative for the success of this strategy.

14.2.3.4 Strengthening the Health Infrastructure

Patients are reluctant to attend the primary health-care centers in due time for many reasons. The main reasons are lack of awareness, poor knowledge, bad communication and transport facility, financial constrain, etc. In many centers health-care professionals poorly follow the referral system, mostly due to weak coordination with tertiary health-care center. Most of the South Asian countries and some countries of sub-Saharan Africa have insufficient number of pathologists, laboratories, colposcopists, and other health-care providers, which limits the services. Poor resource allocation and suboptimal infrastructure also hinder screening programs.

Strengthening various services within the existing health infrastructure, ensuring supply and maintenance of equipment, and uninterrupted supply of consumables are important factors for success of the screening program in LMICs. Appropriate referral system for screening and management within the existing health system should be organized. Development of a strong screening implementation infrastructure is an essential component for success in LMICs. The number of trained manpower for CC screening, including community health workers and administrators, should be increased. Improvement of coverage is important for the success of the program. Policies should be reviewed from time to time to reduce obstacles to improving coverage. Outreach clinics and health camps should be arranged to improve coverage, particularly at hard-to-reach and/or low-performing areas.

14.2.3.5 Strengthening Record-Keeping and Data Management

For population-based organized screening, countries need to develop an electronic database for all women of target age. The computerized database should be maintained at each screening center and all colposcopy centers. A mechanism to check the compliance of screen-positive women to colposcopy and/or treatment should be established by the government.

14.2.3.6 Strengthening Monitoring, Evaluation, and Quality Assurance

Reduction of CC incidence and death from the disease can be assessed by impact indicators. It can be obtained through a population-based cancer registry or organized health information system. Outcome indicators should be monitored on a regular basis to identify gaps and to identify ways of improvement. Head of the respective health facilities, gynecology consultants, and program managers should be responsible for

implementation of services, coordination between various levels of service delivery, and quality assurance.

The indicators to be used for monitoring and quality assurance of the program, and how they will be monitored periodically, should be clearly defined. The performance indicatos are coverage of the target population, screening test positivity, compliance to treatment, and detection rate of CIN 2 or worse.

14.3 Conclusion

In order to improve screening programs for cervical cancer in low-resource countries, it is imperative to increase access to accurate and timely information on CC, mobilize the community through a specific action plan, generate more trained human resources on priority basis, strengthen partnerships between stakeholders, mobilize resources for long-term continuity of the program, and establish a monitoring and evaluation framework.

Key Points

- CC can be prevented through implementing population-based organized CC screening program along with development of electronic data tracking for all women of target age group.
- HPV DNA test has proved more effective than other screening methods as it has a high negative predictive value.
- VIA is accepted as a method of screening in many countries with low-resource settings as it needs minimum infrastructure support and the results are available immediately.
- LMICs need to organize a stakeholders meeting to choose a method of screening suitable for the country's socioeconomic status wherever necessary, followed by a demonstration program and gradual nationwide scale-up.
- All low-resource countries need to develop national CC control strategies focusing age of initiation of screening, mechanism of awareness creation, method of screening, and mechanism of population coverage.
- All screen-positive cases should be treated following "screen-and-treat" strategy or "see-and-treat" strategy.
- Strengthening health infrastructure, ensuring supply and maintenance of equipment, and uninterrupted supply of consumables are important factors for CC screening program in LMICs.
- Strengthening monitoring, evaluation, and quality assurance and monitoring outcome indicators on a regular basis to identify gaps are important factors to reduce CC death.
- Multi-sectorial involvement of governmental and nongovernmental agencies is imperative for the success of this strategy.

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