



World Health  
Organization

REGIONAL OFFICE FOR

South-East Asia

**Regional  
implementation  
framework for  
elimination of  
cervical cancer  
as a public  
health problem  
2021–2030**



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Regional implementation framework for elimination of cervical cancer as a public health problem: 2021–2030

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# Foreword

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Cervical cancer is preventable and curable if detected early and adequately treated. And yet it is one of the most common causes of cancer-related death globally. In 2020 an estimated 604 000 women were diagnosed with cervical cancer worldwide. About 342 000 women died of the disease. The WHO South-East Asia Region accounts for an estimated 32% of incident cervical cancer cases globally, and 34% of cervical cancer deaths. Cervical cancer is the third most common cancer in the Region.

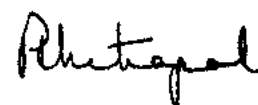
In 2020 the Seventy-third World Health Assembly adopted the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. The Strategy aims to ensure that by 2030 90% of girls are fully vaccinated with the HPV vaccine by 15 years of age; 70% of women have been screened using a high-performance test by 35 years of age and again by 45 years of age; and 90% of women identified with cervical disease are treated. The achievement of these targets will contribute to the global fulfilment of Sustainable Development Goal (SDG) 3, target 3.4, on reducing by one third premature mortality from noncommunicable diseases. In the Region, it will also help achieve our Flagship Priority on preventing noncommunicable diseases through multisectoral policies and plans with a focus on best buys.

The Region has in recent years prioritised a series of strategic interventions to prevent and treat cervical cancer, including improved access to HPV vaccination, increased cervical cancer screening, and enhanced management of precancers and advanced cancers. Among other achievements, the Region is the first WHO region globally to introduce a total training package of capacity building on screening and management of precancers, in addition to an online colposcopy training course, implemented amid the COVID-19 response. There nevertheless remains substantial Region-wide variation in availability of screening, diagnostic and imaging services, onco-surgery facilities, radiotherapy infrastructure, radiation oncologists, medical physicists, radiotherapy technologists, and palliative care physicians. To meet the Global Strategy and SDG targets and goals, these and other gaps must be identified and filled with rapid effect.

To help do that, this Regional Implementation Framework identifies five strategic actions that reflect the public health principles of primary prevention, secondary prevention and tertiary prevention, and which are aligned with existing WHO guidance: first, strengthening primary prevention through HPV vaccination; second, improving cervical cancer screening and precancer treatment through innovative approaches; third, enhancing access to services for early diagnosis, treatment of invasive cancer, rehabilitation, and palliative care; fourth, improving health system support for cervical cancer elimination; and fifth, strengthening information, education advocacy and social mobilization for cervical cancer elimination.

Reaching the ambitious yet achievable interim elimination targets will require robust political commitment, sustained international cooperation, and immediate and ongoing support for resource mobilization. In all countries of the Region, suitable financing mechanisms are required to ensure that vaccination, screening and treatment services are available to all women and girls, without financial hardship, in line with the Region's Flagship Priority on achieving universal health coverage. Services that support cervical cancer elimination must be integrated into all areas of health, especially sexual, reproductive and family planning services. Services for immunization, adolescent health and cancer control can also be strong enablers for implementing the elimination strategy, and should be harnessed and applied to maximum effect.

I am confident that this Regional Implementation Framework will be of immense benefit to Member States and partners across our Region, as together we strive to achieve the Global Strategy interim targets and eliminate cervical cancer as a public health problem. For the health and well-being of all women and girls, we must dare to be bold and achieve our vision.



Dr Poonam Khetrpal Singh  
Regional Director  
WHO South-East Asia Region



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The document has been developed under the overall guidance of Dr Neena Raina, Senior Adviser, Reproductive, Maternal, Newborn, Child, Adolescent health and Ageing. Dr Anoma Jayathilaka, Medical Officer, Maternal and Reproductive Health, coordinated this effort jointly with Dr Gampo Dorji, Technical Officer, Noncommunicable Diseases, and Dr Emmanuel Njambe T. Opute, Technical Officer, Immunization, and Dr Rajesh Mehta, Regional Adviser, Child and Adolescent Health.

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# Executive summary

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Cervical cancer continues to be a significant public health problem and a major cause of premature mortality among women, disproportionately affecting the socioeconomically disadvantaged population in low- and middle-income countries (LMICs). In the absence of implementing the known evidence-based, cost-effective interventions, the number of deaths per year is projected to reach approximately 416 000 globally in 2035. It was estimated in 2020 that 32% of incident cervical cancer cases and 34% of cervical cancer deaths in the world occurred in the 11 Member States of the WHO South-East Asia (SEA) Region. In 2020, 190 874 new cases and 116 015 deaths were estimated due to cervical cancer, which is the third commonest cancer in the Region.

Persistent infection with one of the 14 high-risk human papillomavirus (HPV) types is the necessary cause for cervical cancer. HPV16 and HPV18 are the two most oncogenic types and are responsible for 70% of cervical carcinomas reported globally. A small proportion (approximately 10%) of infections can persist for several years, progress to precancerous lesion, and, if left untreated, to invasive cancer over a 10–20-year period. Cervical cancer is a preventable disease. It is also curable if detected early and adequately treated.

Cognizant of the urgency that cervical cancer prevention deserves, Dr Tedros Adhanom Ghebreyesus, Director-General of WHO, made a call to action in May 2018 to eliminate cervical cancer.

The WHO Executive Board in February 2020 and the Seventy-third World Health Assembly in May 2020 adopted a Global Strategy to accelerate the elimination of cervical cancer as a public health problem, urging the Member States to reach the interim goals and targets by 2030 to eliminate cervical cancer as a public health problem. Globally, all countries must work together to bring down the incidence of cervical cancer to below 4 per 100 000 women-years by the end of the century.

To achieve cervical cancer elimination by the end of the century, the Strategy aims to ensure that by 2030 90% of girls are fully vaccinated with the HPV vaccine by 15 years of age; 70% of women have been screened using a high-performance test by 35 years of age and again by 45 years of age; and 90% of women identified with cervical disease are treated. These achievements will contribute to a 30% reduction of cervical cancer deaths by 2030.

The cervical cancer prevention and control strategy follows the critical public health principles of primary prevention, secondary prevention and tertiary prevention in the life-cycle approach. Primary prevention mainly refers to HPV vaccination and age-appropriate information on known risk factors such as tobacco use and safe sexual behaviour, including the age of sexual debut and condom use, which should be made readily available to bring behavioural changes. Secondary prevention involves screening and treating precancerous lesions before they advance to invasive cervical cancer. Tertiary prevention comprises stage-appropriate quality management of invasive cervical cancer to prevent deaths due to cancer, improve survival, and enhance health-related quality of life and palliative care.

The SEA Region implementation framework for elimination of cervical cancer identifies the following five strategic lines of action:

1. Strategic actions to strengthen primary prevention through HPV vaccination
2. Strategic actions to improve cervical cancer screening and precancer treatment through innovative approaches
3. Strategies to improve access to services for early diagnosis, treatment of invasive cancer, rehabilitation and palliative care
4. Strategic actions to improve health system support for elimination of cervical cancer
5. Strategic actions to strengthen information, education advocacy and social mobilization for elimination of cervical cancer.

The meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization in October 2018 affirmed that HPV vaccination is the most critical intervention for eliminating cervical cancer. As per the 2017 HPV position paper, WHO recommends a two-dose schedule for the primary target age group, girls aged 9–14 years. Bhutan (2010), Maldives (2019), Sri Lanka (2017), Thailand (2017) and Myanmar (2020) have introduced nationwide HPV vaccination that is integrated into the national immunization programmes. In India and Indonesia, HPV vaccination has been introduced in a few states and provinces. Vaccines are administered to target girls through a mix of school-based, health facility and community outreach strategies in Member States of the SEA Region.

To achieve the 90% coverage of HPV vaccination by 2030 would be a challenge that several Member States of the SEA Region would have to meet. Hence, the implementation framework proposes several approaches such as increasing the effectiveness of delivery by establishing multisectoral delivery platforms; dealing with vaccine short supply; securing adequate and affordable HPV vaccines; improving communication for vaccination; advocacy, social mobilization and information/education; innovating to improve the efficiency of vaccine delivery and increasing resource mobilization for HPV vaccine delivery.

Health information and education campaigns need to be strengthened, depending on the specific information needs of individuals and communities. This should be done by communicating up-to-date scientific information and messages about HPV infection, HPV vaccines, HPV testing, cervical cancer, and behaviour changes that can reduce risks and prevent cervical cancer. A communication strategy needs to be developed to cover all aspects of the elimination strategy.

The principal goal of cervical cancer screening is to reduce cervical cancer incidence and mortality by accurately detecting and treating high-grade cervical premalignant lesions such as cervical intraepithelial neoplasia (CIN) grade 2 and 3 (CIN2/3 lesions) and adenocarcinoma in situ (AIS). The interim 2030 target for this action is to screen 70% of target women using a high-performance test by 35 years of age and again by 45 years of age, and 90% of women with precancer treated.

The 2021 WHO recommendations on cervical cancer screening focused on the general population of women and women living with HIV (WLHIV). The same guideline proposed two approaches to screening and treatment: the screen-and-treat approach and the screen, triage and treat approach. Since screening and treatment can be done using different primary screening and triage tests, numerous possible combinations or algorithms are tested and proposed for inclusion in national programmes.

Women can be screened using various tests to identify those who have or are at risk of cervical precancer. In the past, cervical cytology was the most widely used screening test and has substantially reduced cervical cancer incidence and mortality in high-income countries. However, it is challenging to implement and would require comprehensive logistic management, substantial resources and organization to introduce and sustain a quality-assured and effective cytology-based screening programme de novo in most LMICs.

Consequently, different screening tests, including visual inspection with acetic acid (VIA) and HPV testing, have been developed and proven to prevent cervical cancer effectively. VIA has emerged as a screening tool for those who do not have access to cervical cytology and HPV testing in low-resource settings. The most significant advantage of VIA is that it is the only point-of-care (screen-and-treat) test available to date; it does not require a laboratory infrastructure and provides immediate results. However, it has several disadvantages, including scaling up in a programme where a large number of providers have to perform the test. There is considerable performance variability, and the sensitivity in real health-care settings is low to moderate. In addition, VIA has a very high false-positivity rate.

Recently introduced, clinically validated, high-risk HPV (hrHPV) testing is the most objective, highly reproducible and accurate cervical screening test with a high negative predictive value for high-grade CIN and cancer. The 2021 WHO screening guidelines recommend using HPV DNA detection rather than VIA or cytology as the primary screening test. If infrastructure and resources permit, HPV testing has a higher sensitivity to detect CIN2 or worse lesions and a higher negative predictive value than cytology. WHO current screening guidelines recommend that rapid transition should be made to replace VIA testing with HPV DNA testing as the primary screening modality to prevent cervical cancer. HPV DNA-based screening programmes have a much higher impact in reducing cervical cancer morbidity and mortality compared with VIA-based screening and is more cost-effective compared with VIA and Pap smear.

Cervical cancer screening programmes have been instituted in nine out of 11 Member States of the SEA Region beginning as early as 1990. Large-scale, population-based screening programmes with adequate coverage are largely an unmet need in the Member States of the SEA Region. In the SEA Region, five of 11 countries use VIA as a primary screening test followed by Pap smear in four countries of the Region. Thailand is the only country of the SEA Region that is scaling up HPV DNA testing and replacing Pap smear screening; and Sri Lanka has completed a feasibility study to move from Pap smear to HPV DNA testing. The overall screening coverage is low in many settings.

Most countries of the SEA Region either use a screen-and-treat approach or the screen, triage and treat approach using a country-specific algorithm. Colposcopy services are not widely accessible for the early treatment of cervical lesions in most countries of the Region. The implementation framework has proposed several actions to progress towards the 2030 targets on screening and management of precancers.

Cancer treatment can exert a significant psychosocial and financial impact on women and their families, a factor that should be considered when improving access to and coverage of cervical cancer treatment services. Adequate treatment of invasive cancer can achieve high survival rates and significantly improve patients' quality of life, particularly when patients with early disease (stages I and IIA) are treated. Surgery and/or concurrent chemoradiotherapy constitute primary treatment modalities depending on the stage and clinical extent of the disease. It is essential to address the issue of health literacy, improve referral pathways and ensure palliative care and survivor care. Understanding and addressing barriers to cancer care on both the fronts of patients and health-care systems is critical in planning cervical cancer prevention.

There is a substantial variation in the availability of diagnostic and imaging services, onco-surgery facilities, radiotherapy infrastructure, radiation oncologists, medical physicists, radiotherapy technologists and palliative care physicians in Member States of the SEA Region.

It is crucial to make planned investments in human resource generation, improving cancer care infrastructure, and appropriate health-care financing mechanisms to avoid catastrophic out-of-pocket (OOP) payments by women and families.

Cervical cancer prevention and management programmes should be situated within a holistic approach to health systems that are people-centred and responsive to the needs of women across the life course. Primary care should remain the preferred entry point for cervical cancer prevention interventions, but service structures need to accommodate women presenting at any point in the health-care system.

To coordinate infrastructure development, human resources, garnering resources, and phased implementation of interventions, it is essential to develop a policy framework for cervical cancer elimination integrated into the national immunization/cancer control/noncommunicable disease (NCD) control/reproductive health programmes.

Investing in the interventions to meet the 90-70-90 targets offers immense economic and societal benefits.

A suitable financing mechanism through universal health coverage (UHC), including innovative public health insurance schemes, should be in place to ensure that vaccination, screening and treatment services are available without catastrophic expenditure by the beneficiaries. Monitoring and evaluation through well-functioning health information systems, including population-based cancer registries, which generate reliable data on progress towards cervical cancer elimination, can support improved decision-making. Monitoring and evaluation also enable programme managers to identify gaps and take specific actions to improve coverage, quality and outcomes to reach the 2030 targets.

HIV and sexual and reproductive health (SRH) services, and family planning services, are natural platforms for synergies with cervical cancer prevention. Immunization services, adolescent health services, cancer control programmes, primary health care, access to medicines and technology can also be strong enablers for implementing the elimination strategy. Implementation should focus on a continuum of care to be followed up adequately after a positive screening test and reached effectively throughout their lives. Continuous capacity-building using available training packages and innovative approaches is essential to achieve high coverage and quality care for screening, management of precancers and new treatment options.

Active collaboration is essential with key international partners such as Gavi, UNFPA, UNICEF, the International Atomic Energy Agency (IAEA), the International Agency for Research on Cancer (IARC), and other United Nations partners, as well as voluntary/professional organizations such as the Union for International Cancer Control (UICC) and FIGO, and other relevant sectors.

It is critical to conduct implementation research to understand the barriers and facilitators of delivering HPV vaccination, cervical cancer screening and treatment services with high coverage, quality and equity. Understanding the local context will help the countries plan and implement more accessible, acceptable, feasible, affordable and sustainable services. Involving all relevant stakeholders is a key to successful implementation research.

The response to the current COVID-19 pandemic has pushed back the HPV vaccination and cervical cancer screening programmes that had gained momentum in the previous years and this needs to be re-focused by Member States.

Operationalization of the “Regional implementation framework for elimination of cervical cancer as a public health problem 2021–2030” will require a strong political commitment from national governments in Member States of the SEA Region. It will entail earnest allocation of resources to support investments in health systems, including committed human resources.

# 1. Introduction and background

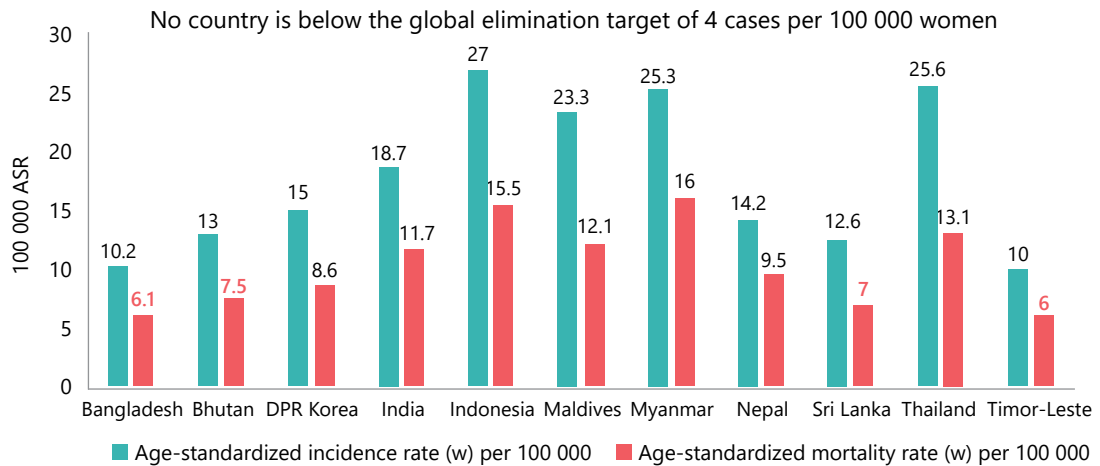
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Cervical cancer continues to be a major public health problem and major cause of premature mortality among women, disproportionately affecting socioeconomically disadvantaged population in low- and middle-income countries (LMICs). In 2020, an estimated 604 000 women were diagnosed with cervical cancer worldwide and about 342 000 women died from the disease. Cervical cancer is the most commonly diagnosed cancer in 23 countries and is the leading cause of cancer death in 36 countries. Many of these countries are in sub-Saharan Africa, Melanesia, South America and South-eastern Asia. In the absence of implementation of effective interventions, the number of deaths per year is projected to reach approximately 416 000 in 2035 (1).

## 1.1 Cervical cancer incidence and mortality in the SEA Region

It is estimated that 32% of incident cervical cancer cases and 34% of cervical cancer deaths in the world are contributed by the 11 Member States of the WHO South-East Asia (SEA) Region. In 2020, 190 874 new cases and 116 015 deaths (1) were estimated due to cervical cancer, which is the third commonest cancer in the Region. The age-standardized cervical cancer incidence rates range from a low of 10 per 100 000 population in Timor-Leste to a high of 23.4 per 100 000 in Indonesia; and the age-standardized cervical cancer mortality rates range from a low of 4.2 per 100 000 in the Democratic People's Republic of Korea to a high of 13.9 per 100 000 in Indonesia (Fig. 1) (1). A pragmatic framework of implementing the WHO's three pronged 90%-70%-90% strategy in Member States of the SEA Region is discussed, taking into consideration the ground realities and current status of cervical cancer control interventions (2).

The fact that nine out of 10 deaths due to cervical cancer occur in LMICs brings forth an important equity issue that needs to be addressed in right earnest with the urgency it deserves. Cognizant of this reality and the urgency that cervical cancer prevention deserves, Dr Tedros Adhanom Ghebreyesus, Director-General of WHO, made a call to action in May 2018 for the elimination of cervical cancer (3).

**Fig. 1.** Cervical cancer incidence and mortality in countries of the SEA Region

Source: Globocan 2020 (7)

## 1.2 Pathophysiology of cervical cancer

There are more than 100 types of human papillomavirus (HPV) among which at least 14 are known to be oncogenic (4). HPV16 and HPV18 are the two most oncogenic types and are responsible for 70% of cervical carcinomas reported globally (4). Nearly 80% of high-risk HPV infections clear up spontaneously without any intervention within 2 years. A small proportion (approximately 10%) of infections can persist for several years, progress to precancerous lesions and, if left untreated, to invasive cancer over a 10–20-year period (4).

Invasive cancer may progress further, forming a visible tumour that can invade adjacent organs and tissues (e.g. bladder, rectum, ureters, nerves, blood vessels, pelvic lymph nodes) and spread (metastasize) to distant sites and organs (e.g. supraclavicular and inguinal lymph nodes, liver, lungs, brain and bones) (5). Also notable is the disproportionate burden of cervical cancer borne by girls and women living with HIV (WLHIV), who are less likely to clear an HPV infection due to compromised immune systems and are six times more likely to develop cervical cancer, and at a younger age (6).

## 1.3 Impact of cervical cancer elimination on the Sustainable Development Goals

Elimination of cervical cancer would contribute to the attainment of several Sustainable Development Goals (SDGs) (2) as given in Box 1.



### **Box 1. Prevention and control of cervical cancer contributes to the attainment of several SDGs and targets**

**Goal 1:** End poverty in all its forms everywhere.

**Goal 3:** Ensure healthy lives and promote well-being for all at all ages:

- Target 3.4: By 2030, reduce by one third premature mortality from noncommunicable diseases (NCDs) through prevention and treatment and promote mental health and well-being.
- Target 3.7: By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes.
- Target 3.8: Achieve universal health coverage (UHC), including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

**Goal 5:** Achieve gender equality and empower all women and girls.

**Goal 10:** Reduce inequality within and among countries.

## 1.4 Cervical cancer elimination strategy

The WHO Executive Board in February 2020 and the World Health Assembly in November 2020 have adopted the global strategy to accelerate the elimination of cervical cancer as a public health problem and urged the Member States to reach the implementation goals and targets by 2030 (2).

To eliminate cervical cancer as a public health problem globally, all countries must work towards an age-adjusted incidence rate of below 4 per 100 000 women-years by the end of the century (2). To achieve that goal, high coverage for HPV vaccination, screening and treatment of precancerous lesions, and management of cancer, must be reached by 2030 and maintained at this high level for decades.

By reaching an incidence threshold of 4 cases or less of cervical cancer per 100 000 women-years (2), a country for all practical purposes would have eliminated cervical cancer as a public health problem. An expert committee convened by WHO in 2018–2019 recommended this threshold that is commonly used to designate a cancer as a “rare” one. The committee also considered this target feasible to be achieved globally.

To achieve cervical cancer elimination within the timeline, every country must reach the global interim targets by 2030 (2) as given in Box 2.

### Box 2. The 2030 interim targets towards elimination of cervical cancer

Meeting the following 90-70-90 targets by 2030 will put all countries on the path to elimination of cervical cancer by the end of the century.

# 90-70-90

**90% of girls fully vaccinated with HPV vaccine by 15 years of age**

**70% of women screened using a high-performance test by 35 years of age and again by 45 years of age**

**90% of women identified with cervical disease are treated:**

- **90% of women with precancer treated**
- **90% of women with invasive cancer managed**

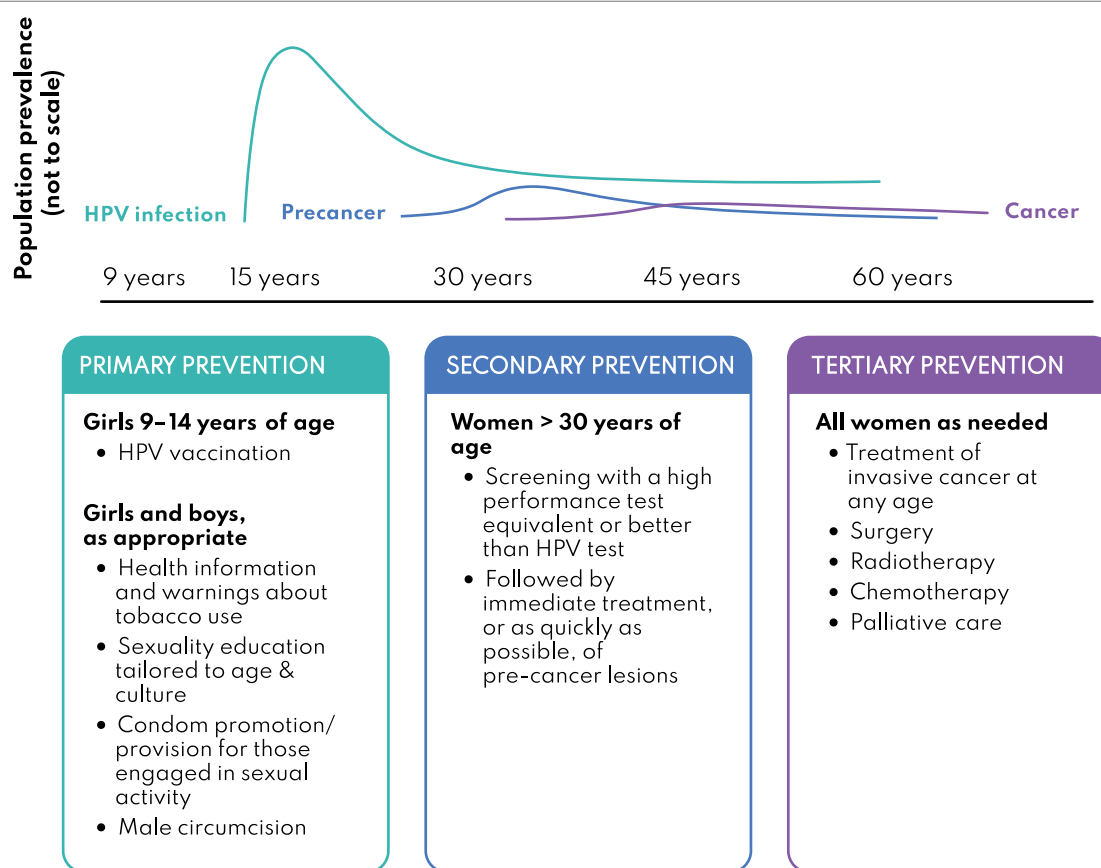
This will contribute to a 30% reduction of cervical cancer deaths by 2030.

**For maximum impact, interventions to meet the three targets must be implemented simultaneously and at scale.** Implementing all three pillars of the strategy will contribute to the immediate and accelerated reduction in mortality rates, which results from the treatment of invasive cervical cancers. Incidence rates will gradually decrease as a result of wide-scale implementation of population-based screen-and-treat services; and vaccination against HPV offers protection against cervical cancer for girls and future generations

The triple-intervention strategy has been chosen for elimination as it would accelerate elimination by 11–31 years and prevent an additional 12 million cervical cancer cases over the next century compared with vaccination alone (2,6). A mathematical model illustrates that the median cervical cancer rate will decline by 42% by 2045 and by 97% by 2120, avoiding more than 74 million incident cases of cervical cancer following the achievement of the 90-70-90 targets by 2030 in LMICs; it also indicates that the median cumulative number of cervical cancer deaths averted will be 300 000 by 2030, over 14 million by 2070, and over 62 million by 2120 (2).

Fig. 2 shows that over the life-course of women three preventative strategies can bring down the prevalence of HPV infection, precancer and invasive disease (2). It also highlights the periods during this life-course when the control strategies are recommended to be applied.

**Fig. 2.** WHO comprehensive approach to cervical cancer prevention and control



Source: Global Strategy to accelerate the elimination of cervical cancer as a public health problem 2020

The cervical cancer prevention and control strategy follows the critical public health principles of primary prevention, secondary prevention and tertiary prevention in the life-cycle approach.

Primary prevention mainly refers to HPV vaccination. Currently, WHO recommends prioritizing HPV vaccination for girls aged between 9 and 14 years, prior to becoming sexually active. In addition to vaccination, age-appropriate information should be made readily available on known risk factors such as tobacco use and safe sexual behaviour including age of sexual debut and condom use.

Secondary prevention involves screening and treatment of precancerous lesions before they advance to invasive cervical cancer. For maximum benefit, screening must cover at least 70% of the target population, be conducted with a high-performance test, and linked to timely and effective treatment of detected cervical disease.

Tertiary prevention comprises stage-appropriate quality management of invasive cervical cancer to prevent cancer deaths, improve survival and enhance health-related quality of life.

Preventative cancer strategies, which are embedded in the targets and indicators of the WHO global action plan for the prevention and control of NCDs 2013–2020 (7), are “best buys” and have high return on investments for health-care systems. When implemented to scale with adequate coverage in a person-

centred and rights-based approach, comprehensive cancer control upholds the principles of UHC. The newly launched global strategy to accelerate the elimination of cervical cancer as a public health problem (2) has reinforced the strategy.

Biomedical and clinical interventions alone will not be enough for reaching the targets and outcomes of cervical cancer elimination, as many of the implementation challenges are related to weaknesses of the health-care system, which commonly plague LMICs where disease burden is the highest. Strategic actions must be customized by each country to take into consideration its unique health system deficiencies and level of readiness to implement, as well as the other barriers to care (e.g. sociocultural, gender, myths and misconceptions about the disease and its prevention and treatment).

Approaches to scaling up interventions in urban settings may differ from those in remote and rural areas. Inequities in health outcomes among vulnerable or underserved populations, including women with HIV, call for focused approaches. In addition, the current focus on UHC stressed by the United Nations General Assembly in September 2019 offers a unique opportunity for countries to strengthen interventions for the management of invasive cervical cancer (8).

**The cervical cancer elimination strategy as a public health advance will require**

(i) political support and effective resource mobilization from national authorities; (ii) cooperation among multisectoral partners for interventions scaled up to the population level; (iii) mechanisms including universal health care to ensure equitable access to elimination interventions; (iv) health system strengthening; (v) active health promotion at all levels; and (vi) adapting innovative models of service delivery, training methods and digitalized data and information systems. Modern forms of communications technology including m-Health approaches must be integrated into all aspects of service delivery. **The key is implementation at scale rather than incremental approaches**

## 1.5 Scope and feasibility of cervical cancer elimination in Member States of the SEA Region

### ***Contribution of the SEA Region on cervical cancer prevention***

The SEA Region gives high importance to cervical cancer prevention and it focuses under the Regional Director's Flagship Priority of "prevention of NCDs through multisectoral policies and plans with focus on best buys". In 2015, a resolution was passed in the Sixty-eighth session of the Regional Committee (SEA/RC68/R5) on cancer prevention and control as the way forward in the context of comprehensive NCD prevention and control. It broadly urges the Member States to focus on primary prevention (vaccination), secondary prevention (screening and treatment), treatment and palliative care of cervical cancer.

The Regional Strategic Framework for the comprehensive control of cervical cancer was developed in 2015 (9) to guide the Member States to strengthen their national programmes on cervical cancer

prevention and control. A Regional Vaccine Action Plan (2016–2020) (10) was developed in line with the Global Vaccine Action Plan. This plan is being revised for the period 2021 to 2030. The initiation and scale-up of HPV vaccination in the Region continues to be one of the goals of the regional plan.

The Regional Strategic Framework for accelerating universal access to sexual and reproductive health (SRH) in the WHO SEA Region 2020–2024 (11) has included major strategic directions on cervical cancer prevention in the Member States. The Seventy-second session of the WHO Regional Committee for South-East Asia noted the proposed elimination threshold and interim targets in the draft Global Strategy on Elimination of Cervical Cancer.

The current and future trends of cervical cancer burden in Member States of the SEA Region indicate that the elimination initiative is worth pursuing and will be feasible and effective if implemented in right earnest. Elimination is within the reach of all countries in the SEA Region and the time is right for a concerted and inclusive strategy to accelerate the elimination of cervical cancer as a public health problem.

The WHO SEA Region Technical Advisory Group on Women’s and Children’s Health (SEAR-TAG) also gave recommendations on cervical cancer prevention in the Region (Annex 2). The Regional Office for South-East Asia launched an advocacy and educational video in 2021 on elimination of cervical cancer in Region.

Nonetheless, significant gaps and challenges persist in reducing incidence and mortality and paving the way towards the elimination of cervical cancer as a public health problem is discussed in different sections of the document. This implementation framework sets forth a blueprint to guide Member States in strengthening their capacity for evidence-based, innovative and effective strategies that will accelerate reductions in cervical cancer incidence and mortality.

## 2. Strategic actions to eliminate cervical cancer in the SEA Region

The SEA Region implementation framework envisions a future with the elimination of cervical cancer as a public health problem as a result of universal access to sexual reproductive health and prevention services for sexually transmitted infections (STIs), HPV vaccines, effective screening and precancer treatment services, treatment of invasive cervical cancer, and palliative care. It foresees that all women and girls, regardless of age, race, ethnicity, socioeconomic status, HIV status, or disability, will have timely access to quality cervical cancer prevention, care and treatment so that they can live in good health throughout the life course and enjoy the health-related human rights.

This regional framework has been developed to facilitate the implementation of the Global Strategy to accelerate the elimination of cervical cancer (2) by Member States of the South-East Asia (SEA) Region. The framework takes into consideration the WHO Global Report, resolutions and decisions, strategies and action plans, as well as WHO regional guidance documents, following the adoption of the World Health Assembly resolution (WHA73.2) on the Global strategy to accelerate the elimination of cervical cancer as a public health problem for the period 2020–2030. It describes the priority strategies and actions, in line with the Global Strategy to address the high burden of cervical cancer in the SEA Region.

The framework is based on the recognition of Member States' diverse contexts, priorities and needs, while adapting the global mandates and initiatives relevant to cervical cancer to the regional context; and involves cooperating with Member States on the implementation of comprehensive strategies to strengthen cervical cancer programmes. The implementation framework identifies the following goal and five strategic actions.

### 2.1 The goal of the implementation framework

The goal is to accelerate progress towards the elimination of cervical cancer as a public health problem in Member States of the WHO SEA Region by reducing incidence and mortality rates by one third by 2030. This goal is aligned with target 3.4 of the SDGs and the 2030 interim targets towards the elimination of cervical cancer (Box 2)

## 2.2 Strategic actions

### **The implementation framework identifies the following strategic actions:**

1. Strategic actions to strengthen primary prevention through HPV vaccination
2. Strategic actions to improve cervical cancer screening and precancer treatment through innovative approaches
3. Strategies to improve access to services for early diagnosis, treatment of invasive cancer, rehabilitation and palliative care
4. Strategic actions to improve health system support for elimination of cervical cancer
5. Strategic actions to strengthen information, education advocacy and social mobilization for the elimination of cervical cancer

## 2.3 Strategic actions to strengthen primary prevention through HPV vaccination

The discovery that almost all cervical cancers are caused by persistent infection with one of the 14 high-risk types of HPV (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) and the HPV types 16 and 18 account for around 71% of cervical cancer globally (12,13), has advised the use of HPV vaccination and HPV screening as the key preventive strategies for cervical cancer. In the meeting of the Strategic Advisory Group of Experts (SAGE) in October 2018, it was affirmed that HPV vaccination is the most critical intervention for eliminating cervical cancer (14).

The characteristics of HPV vaccines, their WHO prequalification status, HPV types targeted, dosage and cross-protection details are given in Table 1. Currently available HPV vaccines target high-risk HPV types 16 and 18 that cause about 71% of all cervical cancers. Bivalent and quadrivalent HPV vaccines have some cross-protective efficacy against HPV31, 33 and 45, which are associated with 13% of cervical cancers. The nonavalent vaccine also protects against high-risk HPV types 31, 33, 45, 52 and 58, which are associated with 18% of all cervical cancers. The bivalent and quadrivalent vaccines thus protect against HPV high-risk types associated with 84% of cervical cancers, while nonavalent HPV vaccine will protect against those high-risk types associated with 90% of cervical cancers.

The quadrivalent and nonavalent vaccines also protect against HPV6 and 11, the types responsible for nearly 90% of anogenital warts and recurrent respiratory papillomatosis (RRP). In a recent modelling study, HPV vaccination targeting girls-only was predicted to reduce the median age-standardized cervical cancer incidence rate in LMICs from 19.8 (range 19.4–19.8) to 2.1 (2.0–2.6) cases per 100 000 women-years over the next century (89.4% [95% CI 86.2–90.1%] reduction), and to avert 61 million (95% CI 60.5–63.0%) cervical cancer cases during this period (15). Adding once or twice in a lifetime screening with a high-performance test will significantly accelerate the impact of vaccination alone in achieving cervical cancer elimination (6).

### 2.3.1 HPV vaccine – dosage and schedule

As per the 2017 position paper, WHO recommends a two-dose schedule with the vaccine administered intramuscularly in the upper arm (deltoid region), for all three HPV vaccines for the primary target age group, girls aged 9–14 years (16). The recommended interval between the two doses is at least 6 months. There is no maximum recommended interval between doses. However, an interval no greater than 12–15 months is suggested in order to complete the schedule promptly and before the girls become sexually active.

If the interval between doses is shorter than 5 months, then a third dose should be given at least 6 months from the first dose. For girls aged 15 years and above and for those younger than 15 years known to be immunocompromised or living with HIV, a three-dose schedule (0, 1, 6 months for bivalent and 0, 2 and 6 months for quadrivalent and nonavalent (nine valent) vaccines is recommended by WHO (16). It is recommended that HPV vaccine should be first introduced into the national immunization programme as a multi-age cohort (MAC) vaccination, targeting girls of many age groups between 9 and 14 years, followed by single-age vaccination of a target group in subsequent years. However, the feasibility of implementing this depends on the availability of HPV vaccines and/or the capacity of the country to procure enough HPV vaccine doses for the targets to conduct a MAC vaccination.

**Table 1.** Currently available HPV vaccines, target HPV types, recommended dosage

Vaccine type	HPV types targeted#	Cross-protection against HPV types	Manufacturer	WHO prequalification
Bivalent (Cervarix)	HPV16 and HPV18	31, 33 and 45 <sup>#</sup>	GlaxoSmithKline	2009
Bivalent (Cecolin) (currently licensed in China only)	HPV16 and HPV18	31, 33 and 45 <sup>*</sup>	Innovax, Xiamen, Fujian province, People's Republic of China	Under review
Quadrivalent (Gardasil)	HPV6, 11, 16 and 18	31, 33 and 45 <sup>#</sup>	Merck	2009
Nonavalent (Gardasil 9)	HPV6, 11, 16, 18, 31, 33, 45, 52 and 58		Merck	2018

<sup>#</sup>Source: HPV. WHO position paper, May 2017.

<sup>\*</sup>Source: Gavi HPV vaccine characteristics document 2020 and Cecolin insert.

### 2.3.2 Status of HPV vaccination in the SEA Region

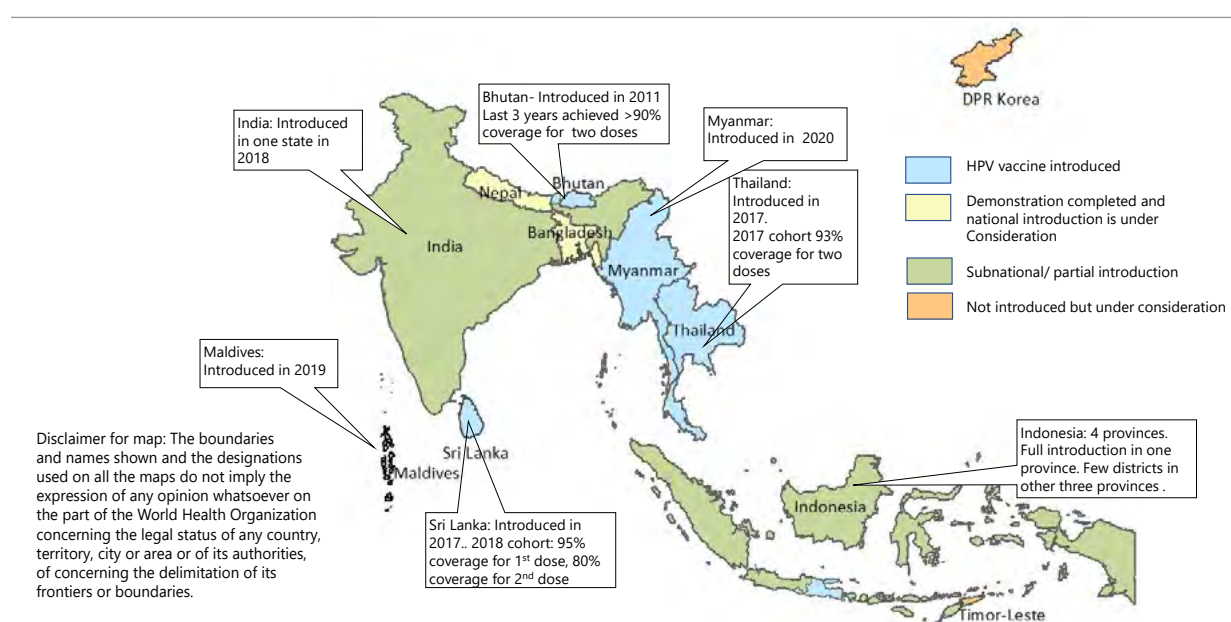
The current status of HPV vaccination in countries of the Region is given in Table 2 and Fig. 3. Bhutan (2010), Maldives (2019), Sri Lanka (2017), Thailand (2017) and Myanmar (2020) have introduced nationwide HPV vaccination. In India, Sikkim state initiated a statewide vaccination since 2017. In Indonesia, subnational introduction was effective in the province of Jakarta in 2016, in Yogyakarta province, partly in 2017 and in all districts in 2019, in East Java province in 2017, in Central Java, South Sulawesi and in North Sulawesi provinces in 2018. The HPV vaccination is integrated in the national immunization programme and vaccines are administered to target girls through a mix of school-based, health facility and community outreach strategies.



**Table 2.** HPV vaccination scenario in countries of the SEA Region

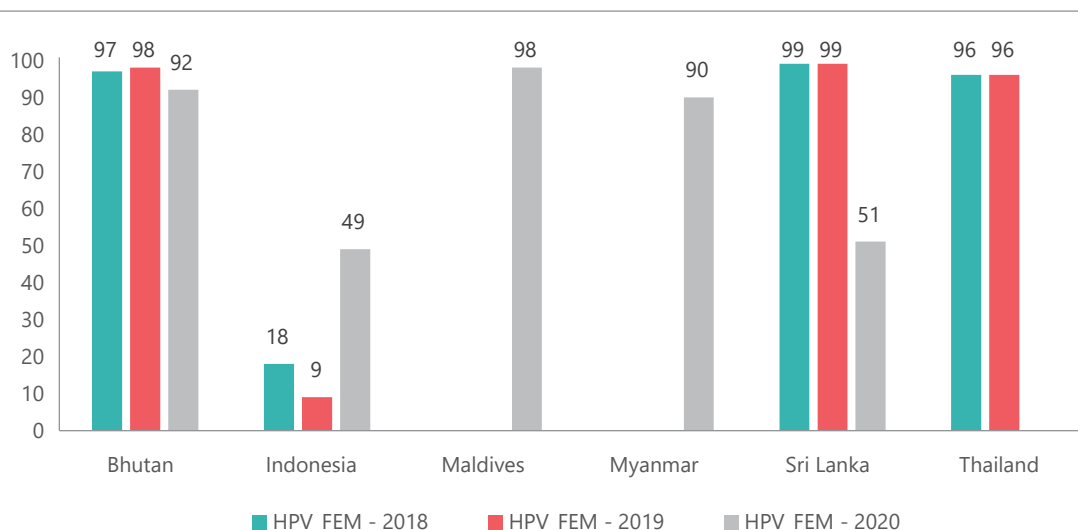
Item	BAN	BHU	DPR Korea	IND	INO	MDV	MMR	NEP	SRL	THA	TLS
Ongoing national/subnational HPV vaccination programme	N	Y National	N	Y Sub-national	Y Sub-national	Y National	Y National	N	Y National	Y National	N
Year of Introduction of HPV vaccination	NA	2010	NA	2017	2016	2019	2020		2017	2017	NA
Type of HPV vaccine used	NA	Quad-rivalent	NA	Quad-rivalent	Quad-rivalent	Bivalent	Quad-rivalent	NA	Quad-rivalent	Bivalent	NA
Dosage schedule	NA	2 D/6 M	NA	2 D/6 M	2 D/12 M	2 D/6 M	2 D/12 M	NA	2 D/6 M	2 D/6 M	NA
Whether introduced as single- or multi-age target	NA	Multi-age	NA	Multi-age	Single-age	Multi-age	Single-age	NA	Single-age	Single-age	NA
Target age for HPV vaccination in routine	NA	11	NA	11	11	10	9	NA	10	11	NA

Y: yes; N: no; M: month apart between doses; NA: not applicable; \*As on February 2021.

**Fig. 3.** HPV vaccination in countries of the SEA Region in June 2021

The vaccine programmes in these countries are supported by a sustained information education programme to tackle vaccine misinformation on safety and efficacy, vaccine hesitancy and to sustain the high participation rates (at least >90% for the last dose) by encouraging parents and girls. However, given the effects of the COVID-19 pandemic, special consideration should be given to minimize dropout for the second dose with a well-organized tracking system and organizing catch-up sessions for missed girls.

**Fig. 4.** HPV vaccine final dose coverage (official data) among girls (9–14 yrs) from 2018 to 2020 in the SEA Region



Source: WHO/UNICEF HPV vaccine coverage estimates 2020<sup>1</sup>

Fig. 4 shows the official reported HPV vaccine final dose coverages among women targets from 2018 to 2020. Bhutan and Thailand have maintained a high level of HPV coverage during this period. Maldives and Myanmar introduced HPV vaccination in 2019 and 2020, respectively, and also achieved the target. Sri Lanka had attained the target in 2018 and 2019. However, in 2020, an adverse impact of the COVID-19 situation is seen in Sri Lanka with a sudden drop in the HPV final coverage. In Indonesia, HPV introduction has been gradually expanded to more provinces, and the coverage shows a marked increase in 2020, after a slight drop from 2018 to 2019.

### 2.3.3 Strategic actions needed to attain at least 90% HPV vaccination coverage

One needs to consider the strategic actions to reach 90% HPV vaccination coverage in Member States of the SEA Region (Table 2). There is an important need for improving awareness about HPV vaccine and its efficacy and safety, through educational programmes, communication techniques, m-Health strategies and by involving voluntary agencies interested in primary prevention of cervical cancer.

Active collaboration and cooperation between public health services, the education department and social welfare services is critical. Strengthening health systems, particularly cold chain capacity, vaccine distribution to vaccination centres, reducing vaccine wastage, improving staff training and health system readiness to manage side-effects and complications if any, are all important for the success of the programme

<sup>1</sup> HPV estimates data published on 15 July 2021 and available at <https://immunizationdata.who.int/pages/coverage/hpv.html>.

## 1. Increasing effectiveness of delivery by establishing multisectoral delivery platforms

Adopting sustainable multisectoral delivery platforms (such as school-based immunization platforms) and tailored community-based approaches are necessary to reach targets and hard-to-reach populations (such as adolescent girls who are not in school). Monitoring systems or registers should track vaccinations and contribute to improve coverage and equity.

## 2. Dealing with vaccine short supply

For a country targeting cervical cancer elimination, long-term high routine vaccination coverage is necessary to achieve this goal. Therefore, the current worldwide shortage of vaccine supply is a matter of concern as it could result in failure to introduce or sustain HPV vaccination programmes in some countries, and especially in those with a high burden of cervical cancer. In the context of a limited supply of HPV vaccine, WHO's SAGE on immunization reaffirmed in June 2019 the following recommendations for the use of HPV vaccines:

- The primary target population for HPV vaccination should continue to be girls aged 9–14 years, prior to becoming sexually active, with a two-dose schedule (16). If pertinent, a three-dose schedule (0, 1–2, 6 months) should be used for all vaccinations initiated among those  $\geq 15$  years of age, including in those younger than 15 years known to be immunocompromised and/or human immunodeficiency virus (HIV)-infected (regardless of whether they are receiving antiretroviral therapy [ART]). The Working Group reiterates that all three licensed HPV vaccines have excellent safety, efficacy, immunogenicity and effectiveness profiles and offer comparable immunogenicity, efficacy and effectiveness for the prevention of cervical cancer.

The SAGE also noted and welcomed the ongoing and planned trials of single-dose schedules, as they will inform future policy recommendations. Additional SAGE recommendations can be found in the SAGE working document at [https://www.who.int/immunization/sage/meetings/2019/october/1\\_HPV\\_SAGE2019WG\\_for\\_SAGE.pdf](https://www.who.int/immunization/sage/meetings/2019/october/1_HPV_SAGE2019WG_for_SAGE.pdf)

To optimize the use of the available vaccine supply, SAGE also proposed in October 2019 an off-label use of HPV vaccines, stating that countries could adopt an extended interval of 3–5 years between the two doses, with the first dose being given to younger girls, such as those aged 9 or 10 years or in the equivalent lower school grade, and the second dose to 13–14-year-old girls or in the equivalent higher school grade<sup>2</sup>

As far as increasing the portfolio of HPV vaccines is concerned, one low-cost bivalent vaccine has been approved for use in the People's Republic of China and is in the process to obtain WHO prequalification. In addition, there is currently a nonavalent HPV vaccine under clinical trial in India. This vaccine is expected to reach the market by 2025–2030.

<sup>2</sup> Available at <https://apps.who.int/iris/bitstream/handle/10665/329963/WER9447-541-559-eng-fre.pdf?sequence=1&isAllowed=y>.

### **3. Securing adequate and affordable HPV vaccines**

A concerted effort is needed between partners and the private sector to overcome vaccine procurement constraints. Additionally, through appropriate negotiations more affordable prices can be achieved while ensuring a healthy market for HPV vaccines. As mentioned, the introduction of more affordable HPV vaccines, such as the bivalent from China, into the market is also an opportunity and would contribute to increased affordability and sustainability of HPV vaccines, especially for self-financing countries. Countries should ensure commitment to advance vaccine forecasting, ensure annual allocation for procurement, procurement planning, and maintaining buffer stocks to ensure uninterrupted supply at each level.

### **4. Improving communication for vaccination: advocacy, social mobilization and information/education**

As HPV vaccination programmes are introduced and expanded, they need nationwide, evidence-based communication and social mobilization efforts. Addressing the social, cultural, societal and other barriers that may affect the acceptance and uptake of the vaccine is critical. Special attention is needed to overcome vaccine hesitancy and to counter misinformation regarding vaccines.

Countries need to develop a communication strategy and simple messages on target age and dose, with a view to achieving greater than 90% national coverage of HPV vaccines as part of national immunization.

Health information and education campaigns need to be strengthened, depending on the specific information needs of individuals and communities, by communicating up-to-date scientific information and messages about HPV disease and cervical cancer, effectiveness and safety of HPV vaccines, addressing misinformation and rumours that inhibit acceptance of HPV vaccination, and promoting behaviour changes that can reduce the risks and prevent progression to cervical cancer. These must be presented in a simple gender-sensitive, culturally appropriate, easy-to-understand language.

While communicating around HPV vaccination, comprehensive information, education and communication (IEC) activities should be implemented and campaigns such as adolescent health days should be undertaken, including interventions such as micronutrient supplementation (iron and folic acid [IFA]), deworming and menstrual management among girls. Some countries are using peer-peer approach under adolescent health programmes that could include IEC for HPV vaccines.

### **5. Innovating to improve efficiency of vaccine delivery**

National guidelines, policies and strategies should be updated as new evidence and innovations become available, on better and more efficient approaches to HPV vaccination. Some of these are currently under study and results are awaited, such as the ongoing clinical trials to assess the efficacy and immunogenicity of single-dose HPV vaccination compared with the currently recommended schedules.

### **6. Increasing resource mobilization for HPV vaccine delivery**

Dedicated funding will be necessary to secure the HPV vaccine doses, to ensure operational costs for delivery including vaccination sessions and specific communication activities, given that the target for HPV vaccination is different from the target of other routine vaccination programmes and the necessary strategies may demand additional delivery sites or sessions, in comparison with routine childhood vaccinations.

## 2.4 Strategic actions to improve cervical cancer screening and precancer treatment through innovative approaches

The principal goal of cervical cancer screening is to reduce cervical cancer incidence and mortality by identifying and treating women with precancerous lesions. **The interim 2030 target for this action is to screen 70% of target women using a high-performance test by 35 years of age and again by 45 years of age and 90% of women with precancer treated (2).**

### 2.4.1 Cervical cancer screening

Effective screening is an important method to prevent cervical cancer by accurately detecting high-grade cervical lesions such as cervical intraepithelial neoplasia grade 2 and 3 (CIN2/3 lesions) and adenocarcinoma in situ (AIS) and effectively treating them to avoid development of cervical cancer. A key requirement for any programme for screening and treatment to prevent cervical cancer is that the screening approach and the tests used should be of the highest quality and standards to produce accurate and reliable results and beneficial outcomes.

To prevent and treat cervical cancer and reduce mortality, programmes are encouraged to implement population-based screening and treatment strategies. All programmes should ensure that women who have screened positive are treated or managed adequately. Screening without providing treatment is not ethical and this is an essential aspect of the programme that needs to be addressed.

### 2.4.2 WHO recommendations for cervical cancer screening

The 2021 WHO recommendations for cervical cancer screening for the general public and WLHIV are given in Box 3 (17).

There are a total of 23 recommendations and seven good practice statements. Among the 23 recommendations, six are identical for both the general population of women and for WLHIV, and 12 are different and specific for each population. Among the seven good practice statements, three are identical for both the general population of women and for WLHIV, and two are different and specific for each population (17).

### Box 3. 2021 WHO recommendations for cervical cancer screening for the general population of women and women living with HIV (WLHIV)

Recommendations for the general population of women	Recommendations for WLHIV
<p>1. WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and WLHIV.</p>	<p>1. WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and WLHIV.</p>
<p><i>Remarks: Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance.</i></p>	<p><i>Remarks: Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance.</i></p>
<p>2. WHO suggests using an HPV DNA primary screening test either with triage or without triage to prevent cervical cancer among the general population of women.</p>	<p>2. WHO suggests using an HPV DNA primary screening test with triage rather than without triage to prevent cervical cancer among WLHIV.</p>
<p>3.3a. In a screen-and-treat approach using HPV DNA detection as the primary screening test, WHO suggests treating women who test positive for HPV DNA among the general population of women.</p>	<p>3. In a screen, triage and treat approach using HPV DNA detection as the primary screening test among WLHIV, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (Annex 3).</p>
<p>3b. In a screen, triage and treat approach using HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (Annex 3).</p>	<p><i>Remarks: The benefits, harms and programmatic costs of the triage options are similar; therefore, the choice of triage method will be dependent on feasibility, training, programme quality assurance and resources in countries. HPV16/18 genotyping could be integrated into the HPV DNA test for specific details of the algorithms) (Annex 3).</i></p>
<p><i>Remarks: The benefits, harms and programmatic costs of the triage options are similar; therefore, the choice of triage method will be dependent on feasibility, training, programme quality assurance and resources in countries. HPV16/18 genotyping could be integrated into the HPV DNA test (refer to Annex 3 for specific details of the algorithms).</i></p>	<p>4. When providing HPV DNA testing, WHO suggests using either samples taken by a health-care provider or self-collected samples among both the general population of women and WLHIV.</p>
<p>4. When providing HPV DNA testing, WHO suggests using either samples taken by a health-care provider or self-collected samples among both the general population of women and WLHIV.</p>	<p>5. WHO suggests starting regular cervical cancer screening at the age of 25 years among WLHIV.</p>
<p>5. WHO recommends starting regular cervical cancer screening at the age of 30 years among the general population of women.</p>	<p><i>Remarks: Low-certainty evidence found that there are likely to be small numbers of WLHIV with cervical cancer who are below the age of 25 years. This recommendation applies to WLHIV regardless of when they first tested positive for HIV.</i></p>
<p>6. For women above the age of 50 years, WHO suggests that screening should be stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and WLHIV.</p>	<p>6. For women above the age of 50 years, WHO suggests that screening should be stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and WLHIV.</p>
<p><i>Remarks: Neither VIA nor ablative treatment is suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after the menopause.</i></p>	<p><i>Remarks: Neither VIA nor ablative treatment is suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after the menopause.</i></p>

Recommendations for the general population of women	Recommendations for WLHIV
<p>7. Priority should be given to screening women aged 30–49 years in the general population. When tools are available to manage women aged 50–65 years, those in that age bracket who have never been screened should also be prioritized.</p>	<p>7. Priority should be given to screening WLHIV aged 25–49 years. When tools are available to manage WLHIV aged 50–65 years, those in that age bracket who have never been screened should also be prioritized.</p>
<p>8. WHO suggests a regular screening interval of every 5–10 years when using HPV DNA detection as the primary screening test among the general population of women.</p>	<p>8. WHO suggests a regular screening interval of every 3–5 years when using HPV DNA detection as the primary screening test among WLHIV.</p>
<p>9. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and WLHIV.</p>	<p>9. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and WLHIV.</p>
<p>10. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and WLHIV.</p>	<p>10. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and WLHIV.</p>
<p>11. WHO suggests that the general population of women who have screened positive on an HPV DNA primary screening test and then negative on a triage test are retested with HPV DNA testing at 24 months and, if negative, move to the recommended regular screening interval.</p>	<p>11. WHO suggests that WLHIV who have screened positive on an HPV DNA primary screening test and then negative on a triage test, are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.</p>
<p>12. WHO suggests that women from the general population and WLHIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.</p>	<p>12. WHO suggests that women from the general population and WLHIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.</p>
<p>13. WHO suggests that women from the general population who have been treated for histologically confirmed CIN2/3 or AIS, or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing, and, if negative, move to the recommended regular screening interval.</p>	<p>13. WHO suggests that WLHIV who have been treated for histologically confirmed CIN2/3 or AIS, or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing, and, if negative, are retested again at 12 months and, if negative again, move to the recommended regular screening interval.</p>
<p>14. As programmes introduce HPV DNA testing, use this test at the woman's next routine screening date regardless of the test that was used at prior screening. In existing programmes with cytology or VIA as the primary screening test, rescreening with the same test should be continued until HPV DNA testing is operational among both the general population of women.</p>	<p>14. As programmes introduce HPV DNA testing, use this test at the woman's next routine screening date regardless of the test that was used at prior screening. In existing programmes with cytology or VIA as the primary screening test, rescreening with the same test should be continued until HPV DNA testing is operational among both the general population of women.</p>

### 2.4.3 Screening tests

To prevent cervical cancer, women can be screened using various tests to identify those who have or are at risk of cervical precancer (Table 3).

#### 1. Cytology (the Papanicolaou test/Pap smear or smear test)

The traditional method to screen women for cervical cancer has been cytology (the Papanicolaou test, also known as the Pap smear or smear test). When cytology results are positive, the diagnosis is confirmed by colposcopy, and appropriate treatment is informed by biopsy of suspicious lesions for histological diagnosis. In countries with effective cytology-based cervical cancer screening and treatment programmes, the mortality from cervical cancer has been reduced five-fold over the past 50 years (18). However, this approach has proven less effective in LMICs (17), mainly because of requirements for laboratory infrastructure, equipment and logistic challenges associated with the screening process; as well as the performance of the Pap test itself, which has shown sensitivity of approximately 50% or less (17).

The screening tests introduced in the past 15 years include VIA, and molecular tests, mainly high-risk HPV DNA-based tests (17), which are suitable for use in all settings (Table 3). More recently, even newer tests and techniques have been developed: (i) other molecular tests such as those based on HPV mRNA, oncoprotein detection or DNA methylation; (ii) more objective tests performed on cytological samples such as p16/Ki-67 dual staining; and (iii) more advanced visual inspection tests based on artificial intelligence/machine learning platforms (e.g. automated visual evaluation of digital images) (17).

**Table 3.** Three approaches to cervical cancer screening and future tests

Molecular	Cytologic	Visual inspection
<b>Nucleic acid amplification tests (NAAT)<sup>a</sup></b> <ul style="list-style-type: none"> <li>high-risk HPV DNA/ NAAT</li> <li>mRNA</li> </ul>	<b>Conventional Pap smears</b> <b>Liquid-based cytology (LBC)<sup>a</sup></b> <b>Dual staining to identify p16 and Ki-67<sup>a</sup></b>	<b>Visual inspection with acetic acid or with Lugol's iodine (VIA/VILI)<sup>a</sup></b> <ul style="list-style-type: none"> <li>naked eye</li> <li>magnified by colposcope or camera</li> </ul>
<b>DNA methylation<sup>b</sup></b> <b>Protein biomarkers<sup>b</sup></b> <ul style="list-style-type: none"> <li>HPV antibodies</li> <li>oncoproteinsA</li> </ul>		<b>Automated visual evaluation of digital images<sup>b</sup></b>

a Current tests

b Tests under evaluation (future tests).

#### 2. Visual inspection with acetic acid (VIA)

VIA using 3–5% dilute acetic acid has emerged as a screening tool for low-resource settings. The biggest advantage of VIA is that it is the only truly point-of-care test available till date. VIA is provided by trained health workers, auxiliary nurse midwives (ANMs), nurses and medical officers. VIA has been evaluated for its accuracy to detect CIN2 or worse lesions in cross-sectional studies and has been shown to have comparable sensitivity, but lower specificity, compared with cytology in settings where both tests have been evaluated (19). VIA's sensitivity to detect CIN2 or worse lesions ranged from 16.6% to 82.6% and



specificity ranged from 82.1% to 96.8% to detect CIN2 or worse lesions in different studies (20). VIA screening was followed by a 30–35% reduction in cervical cancer mortality in two randomized trials in India (21, 22).

Another advantage is that VIA can be combined with simple ablative treatments provided by trained health workers such as thermal ablation or cryotherapy for early cervical precancerous lesions in a single visit “screen-and-treat” approach as recommended by WHO (17,18). However, it has several disadvantages including the challenges of scaling up in a programme where large number of providers have to perform the test. There is a huge variability of performance and the sensitivity in real health-care settings is low to moderate. The 2021 WHO screening guidelines indicated cost-effectiveness of VIA screen-and-treat over HPV screen-and-treat and the latter was found to be more cost-effective due to higher sensitivity, higher negative predictive value and the requirement of less frequent screening.

Neither VIA nor ablation treatment is suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after menopause (17). HPV DNA-based screening programmes have a much higher impact in reducing cervical cancer morbidity and mortality compared with VIA-based screening and is more cost-effective.

The 2021 WHO screening guidelines recommended that existing screening programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance (17).

### 3. High-risk HPV DNA tests

The high-risk HPV (hrHPV) testing is the most objective, highly reproducible and accurate cervical cancer screening test (24). These tests identify a group of high-risk carcinogenic HPV genotypes, typically including up to 14 types (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, 66 and 68) (27, 28). HPV16 and 18 are the highest-risk genotypes and are the most common pathogen for cervical cancers. Some of the HPV DNA tests available in the market provide information about specific HPV genotypes, such as HPV16 and 18.

The evidence indicates that HPV testing shows a high negative predictive value for high-grade CIN and cancer. It has a higher sensitivity to detect CIN2 or worse lesions and a higher negative predictive value compared with cytology (24, 25, 26, 27). Primary hrHPV screening increased the detection rate of CIN2 or worse lesions and cancer by approximately 30–40% compared with cytology. HPV-negative women were significantly less likely to have CIN2+ or CIN3+ or cancer at 48 months or more compared with those who had negative Pap smear or VIA results at baseline.

Modelling studies have shown that adding twice-lifetime screening with HPV testing reduced the incidence to 0.7 (0.6–1.6) cases per 100 000 women-years (96.7% [91.3–96.7] reduction) and averted an extra 12.1 million (9.5–13.7) cases (15).

The very low frequency of CIN3 or cancer following a negative hrHPV test supports the extension of screening intervals up to 10 years or a minimum of two rounds of screening at a maximum of 10 years apart. The HPV DNA test is much more accurate and effective in identifying women at greater risk of

developing precancerous cervical lesions, and that screening intervals can be longer than those with other tests. HPV test samples can be taken by a health provider or the woman herself (self-sampling). Processing of HPV tests is automated, results do not require subjective interpretation, and thus more objective results are given with HPV testing than with other screening tests. HPV testing is more cost-effective than VIA or Pap smears, although it may require higher upfront costs for supplies and equipment. This has a very good programmatic advantage of choosing an HPV DNA test as a primary screening test in population-based cervical cancer screening programmes (17).

Some disadvantages, which should be weighed against all the advantages, are the costs of HPV testing, and that HPV test results are currently not immediate and may require several visits to the health centre by women, which can result in loss to follow-up for treatment.

**WHO recommends using HPV DNA detection rather than VIA or cytology as the primary screening test for screening, management and treatment approaches if infrastructure allows (17).** When providing HPV DNA testing, WHO suggests using either provider- or self-collected samples. Self-sample HPV testing appears to be highly accepted and perceived as convenient, comfortable and safe by women (17). Women may feel more comfortable taking their own samples rather than going to see a provider for cervical cancer screening.

Whereas existing programmes with quality-assured cytology should be continued until HPV DNA testing is operational; and programmes using VIA should transition rapidly towards the use of HPV tests because of inherent challenges with quality assurance.

Given the performance profile of different screening tests, the high accuracy, objectivity, reproducibility and negative predictive value, HPV testing is the most preferred test to be considered for implementation in new and upcoming screening programmes in countries of the SEA Region. With bulk purchase, it should be possible to buy a clinically validated hrHPV test with genotyping for HPV16 and 18 for about US\$ 7–10 (as Thailand has done) (Box 4). Countries of the SEA Region may choose to perform twice-a-lifetime HPV screening to introduce HPV screening in health services.

#### Box 4. Pilot HPV testing demonstration programmes in Sri Lanka and Thailand

##### Pilot HPV testing demonstration programme in one district in Sri Lanka (29)

- ⊙ A community-based descriptive cross-sectional study was conducted in one district of Sri Lanka. The study population comprised ever-married women 35 years of age. A total of 918 women were recruited. HPV/DNA cervical specimen collection (n=822) was carried out. Cervical specimens were tested with the cobas 4800 PCR-based screening machine. Clients' perceptions and prevalence were assessed. The follow-up of women with positive HPV/DNA screening results was carried out. The operational and technical feasibility of the screening test were assessed. Results: Overall response rate was 91.1% (n=836). Clients' perception was highly positive for HPV/DNA screening test procedure (99.9%, n=821) and 99.6% (n=819) of clients had mentioned that the HPV/DNA screening test is worthwhile to be incorporated into the National Cervical Cancer Screening Programme. The prevalence of HPV was 6.2% (95% CI 6.18–6.22%).
- ⊙ Conclusions: Implementation of the HPV/DNA test as a primary cervical cancer screening method is feasible among the 35-year age cohort of ever-married women in Kalutara district of Sri Lanka. It is necessary to explore alternative methods of the cobas 4800 HPV/DNA test, which would be more suitable for resource-limited settings.

##### Pilot HPV testing demonstration programme in Ubon Ratchthani province, Thailand (30, 31)

- ⊙ The National Cancer Institute (NCI), Thailand, conducted a pilot project to test the feasibility of using HPV testing and liquid-based cytology (LBC) techniques to screen for cervical cancer in Ubon Ratchathani province; 185 of 5004 women were positive on cytology or HPV testing, 176 (95.1%) underwent colposcopy, and 21 were detected with CIN2 or worse lesions.
- ⊙ This pilot project clearly showed the high sensitivity and objectivity of HPV testing than cytology in detecting CIN2/3 lesions.
- ⊙ HPV testing substantially reduced the workload, repeat smear taking due to inadequate smears, and overcame the shortage of skilled personnel for cells collecting and slide preparing for the cytology test.
- ⊙ The economic evaluation of HPV testing as primary screening for the national programme in Thailand was evaluated by the Health Intervention and Technology Assessment Programme (HITAP) and was found to be cost-effective for Thailand.
- ⊙ The above findings indicated the poor performance of cytology screening and showed the potential and utility of using HPV testing in public health services in Thailand as well as the utility of primary HPV testing and LBC triage in screening for cervical neoplasia.
- ⊙ The Thai government has now approved HPV testing as the most suitable primary screening method when the vaccinated girls reach the screening age group; thus the planned implementation of HPV testing as primary screening replacing Pap smear is an appropriate decision to improve the performance of the Thai National Cervical Cancer Programme.

## 2.4.4 Status of cervical cancer screening in countries of the SEA Region

The current status of cervical cancer screening and treatment of cervical precancerous lesions in countries of the SEA Region as reported by country authorities to a recent questionnaire survey is summarized in **Tables 4 and 5**.

**Table 4.** Status of cervical cancer screening in the SEA Region

Item	BAN	BHU	DPR Korea	IND	INO	MDV	MMR	NEP	SRL	THA	TLS
Availability of a national cervical cancer screening programme	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N
Initiated in year	2005	2006	2010	1990	2007	2014	NA	2010	1998	2005	NA
Type of programme	Opportunistic	Opportunistic	Opportunistic	Population-based	Population-based	Opportunistic	NA Planned population-based	Opportunistic	Population-based	Population-based-based	NA
Target age group for screening	30–60	25–65	35–45	30–65	30–50	21–65	NA	30–60	35 and 45	30–60	NA
Screening test used	VIA	Pap	VIA	VIA	VIA	Pap	NA	VIA	Pap Piloting done for HPV DNA	HPV DNA testing	NA
Screening coverage (%)	6.1 (2018)	66.1 (2019)	88.4 (2016)	2.3 (2017-2018)	7.7 (2016)	NK	4.4 (2014)	8.2 (2019)	23 (2015)	50.4 (2014)	1 (2014)
Screen positivity rate	4.1%	NK	10.8%	NK	1.7%	NK	NA	NK	3.3%	NK	NA

Source: Country reported survey 2019; NA: not applicable; Y: yes; VIA: visual inspection with acetic acid; Pap: cytology; NK: not known.

Screening data: Calculated from WHO STEP surveys. Geneva and New Delhi: World Health Organization; 2014–2019 (respective years in parentheses by country) and for Indonesia (Sirkenas 2016 Health indicator survey report) and Thailand (NHES, 2014)

WHO suggests a regular screening interval every 5–10 years when using HPV DNA detection as the primary screening test among the general population of women. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and WLHIV (17)

The cervical cancer screening programmes have been instituted in nine out of 11 Member States of the SEA Region beginning as early as 1990. Large-scale, population-based screening programmes with adequate coverage are largely an unmet need in the Member States of the SEA Region, despite several policy initiatives in this regard. The policy initiatives in most countries with the exception of Bhutan, Bangladesh, Sri Lanka and, to a certain extent, Thailand, have not been accompanied by allocation of sufficient resources to build up screening infrastructure and trained human resources to cater to the needs of large-scale, population-based cervical screening programmes.

Although the programmes in many countries of the SEA Region are population-based, they lack many key elements of an organized screening programme. Most countries (five of 11) use VIA as a primary screening test. The 2021 WHO recommendation on screening of cervical cancer indicated that existing screening programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance. The Pap smear as a primary screening method is in use by four countries in the Region, although challenges continue to impede the effectiveness of screening services in many countries.

Thailand is the only country in the SEA Region which is scaling up HPV DNA testing and replacing Pap smear screening, and Sri Lanka has completed a feasibility study to move from PAP smear to HPV DNA testing.

The overall screening coverage is low in many settings and screening test positivity is highly variable. Compliance of screen-positive women with downstream investigations and diagnosis is rather low. However, target groups for screening vary widely in countries of the SEA Region. This area needs attention by Member States of the SEA Region keeping in mind the rational use of available resources to achieve high coverage in their screening programme.

### 2.4.5 Screening frequency

The screening frequency varies in countries of the SEA Region and the majority have screened only once or twice in their lifetime. The SEA Region health system response in terms of test providers, infrastructure for diagnosis and treatment, and access to follow-up services needs immediate attention.

WHO recommends starting regular cervical cancer screening at the age of 30 years among the general population of women. For women above the age of 50 years, WHO suggests that screening should be stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and WLHIV. Priority should be given to screening women aged 30–49 years in the general population. When tools are available to manage women aged 50–65 years, those in that age bracket who have never been screened should also be prioritized (17)

Screening alone is not sufficient to prevent cervical cancer. Follow-up treatment of women with abnormal screening results is required, but it has been reported to be very low in most countries of the Region and continues to be a challenge (Tables 4 and 5).

### 2.4.6 Interim target by 2030: 90% of women identified with cervical disease are treated

The following good practices are promoted by the Global Strategy on elimination of cervical cancer as a public health problem. Once a decision to treat a woman is made, it is good practice to treat her as soon as possible within 6 months to reduce losses to treatment. However, in women who are pregnant, good practice includes deferral of treatment until the pregnancy ends. In circumstances when treatment is not provided within this time frame, it is good practice to evaluate the woman before initiating treatment.

### 2.4.7 Screening and treatment of precancerous lesions

WHO screening guidelines (17) propose two approaches to screening and treatment: (i) the screen-and-treat approach, and (ii) the screen, triage and treat approach (Box 5). Since screening and treatment can be done using different primary screening and triage tests, there are numerous possible combinations or algorithms tested and proposed (Annex 3). Based on their individual situation, countries may choose a relevant algorithm (17).

#### Box 5. Screening and treatment approaches

- ⊙ In the “screen-and-treat approach”, the decision to treat is based on a positive primary screening test only.
- ⊙ In the “screen, triage and treat approach”, the decision to treat is based on a positive primary screening test followed by a positive second test (a “triage” test), with or without histologically confirmed diagnosis.

**(a) In the screen-and-treat approach**, treatment is provided based on a positive primary screening test alone, without triage (i.e. no second screening test and no histopathological diagnosis).

VIA and HPV DNA (self- or clinician-collected) and Pap smear are considered as the primary screening tests, followed by treatment. When the patient is eligible for ablative treatment, this should ideally be done immediately, at the same visit as the screening test (the single-visit approach). At some facilities, this is not feasible, and a second visit is needed (the multiple-visit approach). Women who are not eligible for ablation can have excisional treatment on the same day if the clinic has the capacity for large-loop excision of the transformation zone (LLETZ)<sup>3</sup> (17). If LLETZ is not available onsite, women need to be referred for the excisional treatment or for further evaluation.

3 In this guideline, the term LLETZ refers to excision of the transformation zone. In some countries, this terminology was changed to LEEP (loop electrosurgical excision procedure), and the two terms are often used interchangeably.

**(b) In the screen, triage and treat approach**, the triage test is done if the primary screening test is positive, and the decision to treat is made when both the primary test and the triage test are positive. In the screen, triage and treat approach using HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test. Depending on their context, countries may choose an appropriate algorithm for triage and management of screened positive patients.

A positive triage test can lead to colposcopy with biopsy and histopathological examination for diagnosis to determine the appropriate treatment. The implementation of colposcopy and biopsy can be challenging; however, the 2021 WHO guideline also considers triage strategies that are not dependent on the availability of colposcopy. When the primary screening test is positive, and the triage test is negative, women need appropriate follow-up evaluation at a specified date according to the recommendations.

## 2.4.8 Treatment considerations

In the screen-and-treat approach, women who screen positive are treated without histological diagnosis. The treatment aims to destroy or remove the transformation zone of the cervix or remove areas of the cervix that have been identified as abnormal by screening. Methods of treatment may be ablative (destroying abnormal tissue by heating it with thermal coagulation or freezing it with cryotherapy) or surgically removing abnormal tissue with loop electrosurgical excision procedure also known as LLETZ (17). Ablative treatments do not result in a tissue specimen for histological evaluation.

WHO has published technical specifications for ablative therapy and LLETZ (32). Before treatment, all women who have screened positive with any test other than VIA should be visually inspected with acetic acid by a trained health worker to determine the transformation zone type (17), rule out suspected cervical cancer and determine eligibility for ablative therapy.

As shown in Table 5 most countries of the SEA Region either use the screen-and-treat approach or the screen, triage and treat approach using a country-specific algorithm. Colposcopy services are not widely accessible for early treatment of cervical lesion in most countries of the Region.

**Table 5.** Treatment of precancerous lesions in countries of the SEA Region

Item	BAN	BHU	DPR Korea	IND	INO	MDV	MMR	NEP	SRL	THA	TLS
Nationally approved SOP/ guidelines	Y	Y	Y	Y	Y	Y	Y	Y	In process	Y	No
Screen-and-treat with cryo/TA	Y	Y	NK	Y	Y	NK	NK	NK	No	No	No
Triage with colposcopy/ biopsy and treatment	Y	Y	Y	Y	NK	NK	Y	Y	Y	Y	No

Item	BAN	BHU	DPR Korea	IND	INO	MDV	MMR	NEP	SRL	THA	TLS
Treatment methods carried out in screening programmes	TA; LEEP	Cryo/ TA; LEEP CC	Cryo/ LEEP CC	Cryo/ TA; LEEP CC	Cryo/ LEEP CC	Cryo/ TA; LEEP	Cryo/ TA; LEEP	Cryo/ TA; LEEP; CC	TA; LEEP; CC	Cryo/ LEEP/ CC	No
Coverage rate of treatment of women with lesions	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Treatment included in UHC package	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No

Source: Country reported survey 2019

SOP: standard operating procedure; Y: yes; NA: not available; Cryo: cryotherapy; TA: thermal ablation; LEEP: loop electrosurgical excision procedure; CC: cold knife conization.

**The Global Strategy to accelerate the elimination of cervical cancer as a public health problem proposed several strategic actions needed to ensure 70% coverage for cervical screening and 90% coverage for treatment of cervical precancerous lesions (Annex 4).**

However, the HPV test, given its superior performance, followed by ablative treatment, is recommended over other screening tests and approaches whenever it is feasible (2,17). Yet countries, regardless of the screening test, treatment method, or approach adopted and health services delivery, need to be organized to ensure high screening coverage in the target group, a high treatment rate for women with abnormal test results, and high quality in testing and treatment.

### 2.4.9 Strengthen screening and precancer treatment services in Member States of the SEA Region

The actions suggested to strengthen screening and precancer treatment are mentioned in Box 6.

#### Box 6. Actions to strengthen screening and precancer treatment

1. Review/evaluate the national cervical cancer prevention programme to understand the strengths and weaknesses of the programme to achieve the 2030 targets.
2. Review/update national screening and precancer treatment protocols to ensure that they are based on the most recent WHO recommendations.
3. Encourage the cervical cancer screening programmes to implement population-based strategies.
4. Tailor the cervical cancer prevention programmes to the needs of priority populations, including those living with HIV who need more frequent screening. The target age should be determined based on the likelihood of reaching the largest group of women, focusing on those between the ages of 30 and 49 years in the general population, and between 25 and 49 years in the



5. Identify a country-specific screening strategy after considering the health system's capacity by selecting the most appropriate screening test/s based on current evidence and the strength of the health system. (*note that WHO recommends to transit to highly precise screening test*).
6. Constitute a multidisciplinary team of ministries of health (MoH), which can consider different factors and make informed decisions on selecting primary screening tests and approaches (screen-and-treat or screen, triage and treat) chooses appropriate algorithm/s (Annex 3) to include in a national programme. The choice of algorithm will vary by country and in different settings within country programmes and depend on available resources, feasibility and acceptability.
7. Ensure an affordable supply of high-performance screening tests and treatment devices: introducing innovations is crucial. Countries should anticipate and plan ahead for transitions between technologies. Member States of the SEA Region are encouraged to develop common approaches to procuring affordable, high-performance tests, sharing regulatory data, improving supply planning and evaluating new technologies. Pooled procurement and common quality assurance mechanisms and processes could help Member States to achieve these goals.
8. Assess the infrastructure capacity and needs, including laboratory capacity to process screening tests in a timely and accurate manner, and ensure the provision of the necessary infrastructure, supplies and equipment to enable timely screening and precancer treatment services. Design efficient, integrated networks of laboratory services to maximize the impact of limited human and financial resources, which should be adapted to the volumes and capacity of each testing facility. Leverage the existing installed base of multiplex analysers that may be used for other forms of molecular testing (such as TB, HIV, viral hepatitis).
9. Assess health service capacity and needs to increase equitable access, screening coverage and treatment rates through clinical outreach services and static health services while tailoring the service delivery model to the needs of women living in vulnerable and disadvantaged communities. Consider ways to minimize the loss in follow-up care. Ensure that cervical cancer screening and management of precancer are part of the essential benefits offered by health systems and services at the first level of care with a clear strategy for referrals to secondary and tertiary care.
10. Strengthen integrated service delivery approaches to better address women's health, sexual and reproductive health, STI/HIV services, and the prevention of other cancers and other NCDs.
11. Introduce a robust quality assurance system that requires the collection of performance data using WHO-recommended key performance indicators, comparing performance with accepted standards and taking corrective actions to address the deficiencies.
12. Ensure that all health-care providers are trained and competent in carrying out the procedures for screening and precancer treatment, in assuring high-quality care for women, and in providing comprehensive care through multidisciplinary teams that include community health workers who have been trained to address the clinical, psychosocial and gender needs of women with persistent HPV infections or cervical precancerous lesions, as well as the elimination of stigma and discrimination in the health services.

- Encourage to do the training need assessment and develop a training plan for the country.
  - Strengthen partnerships with professional associations and academic institutions to contribute to the capacity building and elimination process. Encourage skills transfer and strengthening the existing south to south collaboration among countries.
  - The WHO Regional Office for South-East Asia is the first to develop a training package for cervical cancer screening and management of precancers in 2017 (37) and completed an IFCPC-IARC online training course on colposcopy for 100 trainees in 10 Member States in 2020–2021.
13. Promote cryotherapy or thermal ablation to treat screen-positive women eligible for ablative treatment in a screen-and-treat approach during a single or double visit.
  14. Use surgical removal of abnormal tissue with LEEP, also known as LLETZ, to treat lesions not eligible for ablation, preferably under colposcopy guidance.
  15. Implement effective advocacy and communication strategies to overcome the many challenges that impede access to and use of cervical cancer prevention and care, if culturally relevant, context-specific content and should reflect the national policy and be integrated into all levels of the health system.
  16. This strategy should aim to create demand for screening and address misbeliefs and misinformation] of disease, screening and treatment.
  17. Ensure the engagement of civil society, women’s groups, nongovernmental organizations (NGOs) and a wide range of local networks to the successful uptake of services at the community level.

## 2.5 Strategies to improve access to services for early diagnosis, treatment of invasive cancer, rehabilitation and palliative care

Cancer treatment can exert a significant psychosocial and financial impact on women and their families, a factor that should be taken into account when improving access to and coverage of cervical cancer services. Vaccination and screening will prevent invasive cancer and avoid mortality due to cervical cancer. Adequate treatment of invasive cancer prevents death from disease.

The “WHO framework for strengthening and scaling-up services for the management of invasive cervical cancer” is published in 2021 (33). Besides giving details on the management of advanced cancers, the document highlights each aspect of invasive cancer management – diagnosis, staging, treatment, palliative care and survivor care.

### 2.5.1 Cervical cancer detection pathways

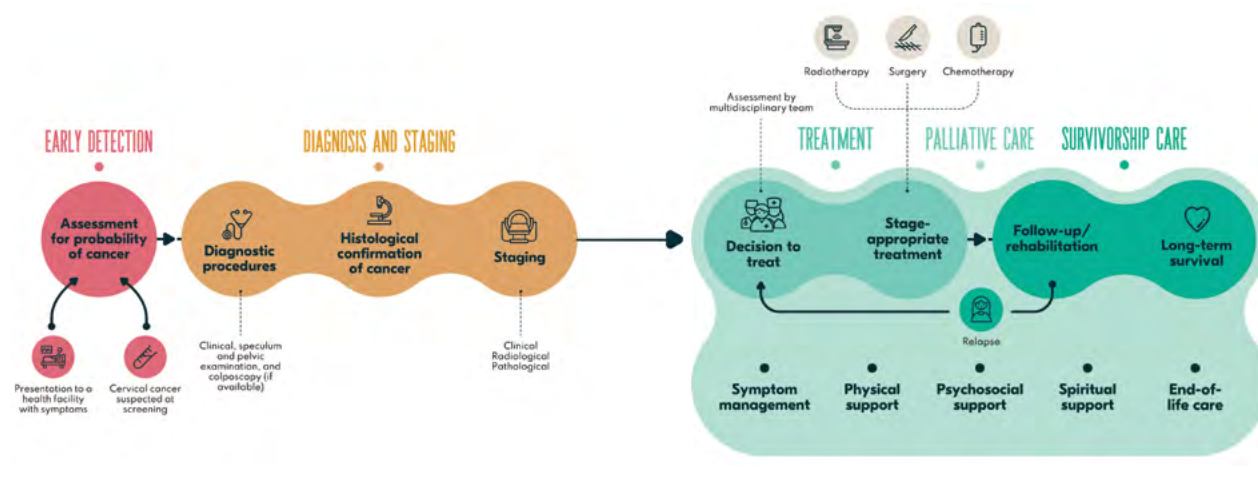
There are two possible pathways for women to access cervical cancer management services.

These are: the **screening pathway** in which invasive cervical cancer is detected through a cervical cancer screening programme.

The **symptomatic pathway**: Non-acute (early diagnosis) invasive cervical cancer is detected when a woman presents for a consultation at a health-care facility because of symptoms such as postcoital vaginal spotting. Early-stage cervical cancer can be diagnosed through appraisal of screening history (33).

The total care pathway is shown in Fig. 5.

**Fig. 5.** The total care pathway (33)



Physical examination, histopathology services and imaging facilities are vital for diagnosis and staging of invasive cancer. Whereas vaccination and screening will prevent invasive cancer and avoid mortality due to cervical cancer, adequate treatment of invasive cancer prevents mortality from disease, particularly when early disease (stages I and IIA) is treated by a single modality. Only early-stage disease can be treated with surgery; radiotherapy and chemotherapy can be used to treat any-stage disease; a combination of surgery and radiotherapy should be avoided. Member States can follow the treatment protocols based on current evidence.-

There are substantial variations in Member States of the SEA Region in the availability of diagnostic and imaging services, radiation infrastructure, cancer surgery services and skilled human resources such as cancer surgeons, gynaecology oncologists, radiation oncologists, medical physicists, palliative care physicians and radiotherapy technologists. The country-specific context is crucial in terms of the degree of centralization and decentralization of diagnostic and treatment services based on existing capacities (infrastructure and human resources) and geographical barriers. Each country should develop solutions based on individual context for strengthening of referral pathways, especially for potentially curable cervical cancers; and for researching and understanding barriers to care (patient and health-care system perspective).

It is important to make planned investments in human resource generation, improving cancer care infrastructure, appropriate health-care financing mechanisms to avoid catastrophic out-of-pocket payments, and for establishing both sentinel population-based and hospital-based cancer registries to support monitoring inputs, evaluation of outcomes and make mid-course corrections.

Strategic actions proposed in the Global Strategy for elimination of cervical cancer to achieve 90% coverage of cervical cancer treatment are given in Annex 4.

## 2.5.2 Strengthen diagnosis, treatment and palliative care services in Member States of the SEA Region

The actions suggested to strengthen diagnosis, treatment and palliative care are given Box 7.

### Box 7. Actions to strengthen diagnosis, treatment and palliative care

1. Develop/update and implement evidence-based protocols for treatment and palliative care of cervical cancer based on the current scientific evidence and considering the existing capacities to diagnose and treat cervical cancer.
2. Promote the early diagnosis approach and reduce the access delay, diagnostic delay and treatment delay for women with symptoms suggestive of cervical cancer and draw synergies with breast cancer initiatives.
3. Improve equitable access to diagnostic radiology, pathology, radiation therapy, surgery, chemotherapy, rehabilitation and palliative care services by ensuring that they are part of UHC schemes. The use of affordable telepathology platforms can improve services for countries with limited or no capacity to interpret samples.
4. Build capacity to perform gynaecological oncology surgery for improving access to surgical treatment of cervical cancer and bringing broader benefits to the health system; optimize cancer surgery capacity and ensure availability of critical resources for blood banking, anaesthesia, surgical instruments and consumables; leverage innovative solutions, such as tele mentoring, eLearning, and low-cost virtual reality surgical simulation; provide adequate hospital infrastructure, such as operating room space and hospital beds; and apply principles of management science to facilitate more efficient use of constrained resources.
5. Provide comprehensive treatment plans incorporating only end-of-life care and pain relief for patients and psychological support, family support and other services from the outset. Where possible, home-based models of palliative care should be integrated into primary health care for maximizing the outcomes.
6. Ensure that sufficient numbers of trained health-care workers in place, especially pathologists, gynaecologist-oncologists, radiologists, medical physicists and oncology nurses (based on each country's human resource plan).
7. Ensure appropriate competencies and skills for cervical cancer control through appropriate human resource planning, recruitment, continuing education and training, deployment and retention strategies, including career development opportunities.
8. Ensure access to and supply of quality-assured and essential cancer diagnostics, medicines and treatment technologies. Ensure that these are included in the essential medicine list (EML) in concordance with the national EML and national cervical cancer management guidelines. Ensure maintenance of supply chain management structures and processes (forecasting, procurement, warehousing and distribution).
9. Improve access to morphine tablets; review the regulatory landscape in the country that may restrict the use of morphine; train primary care providers and other health professionals dealing with advanced stage cancer patients.
10. Strengthen medical devices regulatory infrastructure for effective and efficient procurement practices; also strengthen radiation protection policies and practices.
11. Ensure financial protection for treatment for cervical cancer.

## 2.6 Strategic actions to improve health system support for the elimination of cervical cancer

Cervical cancer programmes should be situated within a holistic approach to health systems, which is people-centred and responsive to the needs of women across the life course. Primary care should remain the preferred entry point for cervical cancer prevention interventions, but service structures need to accommodate women presenting at any point in the system.

Such efforts should be mutually reinforcing and facilitate the integration of cervical cancer services with other specific programmes. For example, within the health sector, interventions should transcend common dividing lines – between immunization programmes, adolescent health services, HIV and sexual and reproductive health services, and communicable disease and noncommunicable disease (NCD) programmes, including cancer prevention and control.

### 2.6.1 Policy issues

To coordinate technical assistance, development of infrastructure, human resources, garnering resources and phased implementation of interventions developing policy frameworks such as the national cancer control programmes, national cervical cancer control plans and national cervical cancer elimination policies are important.

### 2.6.2 Investment case for eliminating cervical cancer in high-burden countries

Investing in the interventions to meet the 90-70-90 targets by 2030 offers immense economic and societal benefits. An estimated US\$ 3.20 will be returned to the economy for every dollar invested through 2050, owing to increases in women's workforce participation; this figure will rise to US\$ 26 when societal benefits are incorporated (34). It is estimated that about 250 000 women will remain productive members of the workforce, adding an estimated US\$ 28 billion to the world's economy: US\$ 700 million directly through increased workforce participation and almost US\$ 27.3 billion through indirect socioeconomic benefits of good health.

High socioeconomic benefits would accrue if the 78 low- and lower-middle-income countries achieve the 90-70-90 targets by 2030, by mobilizing and spending the estimated US\$ 10.5 billion needed to scale up cervical cancer prevention and treatment interventions between 2018 and 2030 (35). Sustaining interventions requires mobilization and proper allocation of domestic resources. For long-term sustainability, the financing of cervical cancer interventions should be supported from domestic resources

Primary health care system support for cervical cancer programmes should be reinforced to ensure higher coverage for vaccination and screening, thus contributing to increased follow-up of women with abnormal screening test results. Cumulatively, these steps make a greater impact on cervical cancer incidence and mortality.

### 2.6.3 Strengthen health systems to support cervical cancer elimination

The actions suggested to improve the organization and implementation of cervical cancer programmes are mentioned in Box 8.

#### **Box 8. Actions to strengthen cervical cancer programme planning governance and financing**

1. Coordinate several programmes for elimination of cervical cancer by creating a task force led by the Ministry of Health (MoH), with representatives of different health programmes (sexual reproductive health, adolescents, NCD, cancer control, immunization, HIV/AIDS), also including finance, health economists, and NGOs, civil society and patient advocacy groups.
2. Review/develop/strengthen national cervical cancer policies based on current evidence, in line with the Regional Implementation Framework on Cervical Cancer Elimination 2021–2030 and the Global Strategy for elimination of cervical cancer.
3. Review and align national cervical cancer programme strategies and plans with targets and milestones for 2030, in line with regional and global objectives of cervical cancer elimination. The WHO Cervical Cancer Prevention and Control Costing (C4P) Tool (36) will allow countries to do a budget estimate depending on the interventions they select.
4. Complete the country needs assessment for technical assistance and financial support to achieve the 2030 interim targets.
5. Implement the recommendations of the WHO Regional Office for the South-East Asia Technical Advisory Group 2020 (Annex 2).
6. Create/strengthen the managerial structure for elimination of cervical cancer in the MoH to ensure implementation, monitoring and attainment of the national programme's goals and targets.
7. Strengthen multidisciplinary partnerships between the public sector and the private sector to improve the coverage of screening and management of precancer and advanced cancer.
8. Reinforce primary health care-oriented service delivery models of care.
9. Reorient country programmes towards models of care that promote high-quality, people-centred primary health care throughout the life course.
10. Develop a sufficiently sized health workforce, with staff who have an optimal mix of skills and who are competent and equitably distributed, to support the delivery of new cervical cancer prevention and treatment interventions, as well as palliative care services.
11. Identify the need for task shifting.
12. Ensure continuous capacity-building to achieve high coverage and quality care for screening, management of precancers and new treatment options by using available training packages.

- ◉ *Capacity-building: In 2017, the SEA Region became the first among WHO regions to publish a training package for health workers on screening of cervical cancers and management of precancers and completed several capacity-building programmes. The topic of cervical cancer is included in the Package of Essential NCD (PEN) interventions for primary health care teams (37, 38, 39, 40, 41).*
13. Improve access to medicines and other health products and ensure availability and affordability of appropriate, safe, effective, quality medicines and other health products that are central to the elimination targets and include these in essential service packages. All essential medicines including chemotherapeutic agents commonly used for cervical cancer treatment (especially cisplatin) and morphine tablets should be included in the EML.
  14. Ensure UHC and protection from catastrophic costs –
    - ◉ Sustainable financing should be secured through domestic resource mobilization, increased efficiencies in the health system and by allocating separate budget lines where possible for information and education initiatives and HPV vaccination, screening, diagnosis, treatment and palliative care.
    - ◉ Cervical cancer programmes must be fully integrated into UHC and essential health packages to reduce out-of-pocket expenditure.
    - ◉ Cervical cancer diagnosis and treatment need to be incorporated into the existing insurance schemes to help improve coverage and reduce out-of-pocket expenditure.

## 2.6.4 Surveillance, monitoring and evaluation

The scale-up of cervical cancer prevention activities cannot proceed without the monitoring framework and tools to assess and evaluate progress towards cervical cancer elimination. It is fundamental that robust surveillance and monitoring systems are developed at the national or subnational levels to determine the baseline and monitor and evaluate the impact.

Monitoring and evaluation through well-functioning health information systems that generate reliable data are significant to monitor progress towards cervical cancer elimination and enabling programme managers to identify gaps and take specific actions to improve coverage, quality and outcomes.

## 2.6.5 Programme monitoring

The monitoring of the elimination strategy requires a comparative assessment of the quality and coverage of the different preventive interventions. Vaccination coverage, screening coverage, quality of screening and diagnostic services, and the extent of timely and effective treatment modalities will help in monitoring the effectiveness of programmes in achieving a reduction in the disease burden. Cervical cancer service coverage should be included as a core health-care performance measure and progress should be monitored at the health facility catchment population, provincial and national levels.

The cervical cancer prevention programmes present unique challenges to monitoring and evaluation. Information systems need to span primary through to tertiary prevention measures, requiring the recording and tracking of data on individual women across multiple touch points in the continuum of care. According to the recommended set of processes and outcome indicators, countries are encouraged to select indicators. Overall, WHO recommends monitoring the following key indicators (2).

### **1. Proposed performance indicators**

- ⊙ HPV vaccination coverage disaggregated by age at vaccination and the number of doses
- ⊙ Screening rate of the target population (women aged 30–49 years)
- ⊙ Percentage of women aged 30–49 years who have been screened for the first time in the previous 12-month period
- ⊙ Positivity rate: percentage of screened women aged 30–49 years with a positive screening test result in the previous 12-month period
- ⊙ Treatment rate: percentage of screening test-positive women receiving treatment in the previous 12-month period.

### **2. Result indicators**

#### **Coverage indicators**

- ⊙ Percentage of women aged 30–49 years who have been screened with a high-performance test at least once between the ages of 30 and 49 years
- ⊙ Percentage of women aged 30–49 years who have been screened with a high-performance test at least twice.

#### **Impact indicators**

- ⊙ Cervical cancer age-specific incidence
- ⊙ Cervical cancer age-specific mortality

### **3. Programme monitoring situation in the SEA Region**

Almost all Member States have developed health information platforms, which include information on health programmes. The completeness and accuracy of data collected through health management information systems (HMIS) at health facilities and communities and their reporting is a significant concern. The District Health Information System-2 (DHIS-2), a web-based information system, is used in almost all Member States (tailored to local country needs in most situations). However, it is not known how well the cervical cancer data are incorporated, especially those related to HPV vaccination, screening, management of precancers and treatment of advanced cancers and palliative care, and used for programme planning. In most Member States, HMIS data are not used for monitoring coverage of interventions due to incompleteness; the DHS is the primary source of coverage data, which means missed opportunities to monitor coverage annually. Most countries of the SEA Region are currently using estimated data to assess incidence and mortality.



#### **4. Strengthen monitoring and evaluation to support cervical cancer elimination**

The actions suggested to strengthen surveillance, monitoring and evaluation are mentioned in Box 9.

##### **Box 9. Actions to strengthen surveillance, monitoring and evaluation**

1. Strengthen governance and accountability of programmes related to cervical cancer and conduct regular reviews to help ensure that national strategies, plans and resource allocations reflect actual country needs; select country-specific targets, milestones and indicators for monitoring and evaluating the national cervical cancer elimination programme.
2. Ensure the availability of reliable population-based cancer registration covering entire populations in small countries, and sentinel registries in representative regions of large countries that will help monitor trends in disease burden to evaluate the journey of countries towards cervical cancer elimination.
3. Identify the core cervical cancer indicators based on global and regional monitoring frameworks.
4. Review and revise the HMIS related to cervical services, to include indicators on cervical cancer in health information systems that permit data generation and monitoring of cervical cancer programmes across the continuum of prevention, care and treatment services from a programmatic perspective, including reporting on HPV vaccination coverage, cervical cancer screening coverage and treatment rates.
5. Establish a mechanism to collect cause-of-death data to evaluate cervical cancer mortality in a population. The number of deaths provides a measure of the outcome or impact of cancer. The evolution of cervical cancer mortality trends is relevant for monitoring the effectiveness of screening programmes. In countries with no nationwide death registration, governments should prioritize establishing vital registration, beginning with a well-defined geographical area or population.

## **2.7 Strategic actions for cervical cancer prevention through advocacy, social mobilization and information/education**

### **2.7.1 Social mobilization and information/education**

Health education and awareness are key components of a comprehensive cervical cancer control programme. Health education should be targeted towards high acceptance of the services by the community and improved compliance with various interventions related to cervical cancer control. All activities should be sustained by implementing robust communication activities. Countries need to develop or strengthen and implement gender-sensitive education and awareness on cervical cancer prevention initiatives to inform people, both girls and boys, as well as priority populations with higher HPV infection prevalence and populations in situations of vulnerability.

Communication should include information about HPV infection, increase awareness of signs and symptoms of cervical cancer and other HPV-related cancers, their causes and natural history, education on sexual health, tailored to age and culture, with a view to reducing high-risk sexual behaviour. The communication should also emphasize the importance of prevention of HIV and STI, including increased access to and use of condoms, promote screening for age-eligible women, address ignorance, fear, embarrassment and stigma related to HPV infection and cervical cancer.

Patient awareness, health literacy and education initiatives, especially through survivor groups, contribute to addressing stigmatization associated with cervical cancer. Health awareness can be done at community or health facilities, or both. Health workers and volunteers at community or primary health facilities are the first point of contact with the community. The awareness on screening can be integrated with several programmes such as maternal, child health, immunization, family planning and NCD control. The telehealth options need to be explored.

### **2.7.2 Advocacy**

The purpose of advocacy is to empower policy-makers to make informed decisions on programme needs, implementation and service utilization. Advocacy is also essential to ensure community participation and acceptance and generate demand for the services from within the community. The targets for advocacy and communication efforts should include high-level decision-makers in relevant government sectors; administrators and managers at the health ministry and curative institutions; members of civil society organizations; members of academic institutions and professional associations; health-care providers including physicians, nurses, midwives and school health workers; as well as community leaders and media representatives.

## 3. Implementation of the framework

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Country leadership is the key to operationalizing the “Regional Implementation Framework for eliminating cervical cancer” or adding its elements to the existing national strategies and plans for immunization, SRH or overall cancer management. It is the driver for the major outcomes related to health systems, especially for financing and community engagement, and is also critical for changing policies and laws to operationalize the implementation framework. To further strengthen country leadership, it is crucial to work with stakeholders in other government sectors and beyond, such as development partners, civil society organizations, professional associations, the private sector, and research and training institutes.

Countries need to invest in and lead implementation research to address barriers, ensure acceptability, feasibility and equity in screening and management of cervical precancers.

Intercountry and inter-programmatic collaboration is also vital for the implementation process. Active collaboration is essential with key international partners such as Gavi, UNFPA, UNICEF, the International Atomic Energy Agency (IAEA), the International Agency for Research on Cancer (IARC), and other United Nations partners, as well as voluntary/professional organizations such as the Union for International Cancer Control (UICC) and FIGO, SAFOG and other relevant sectors.

Implementation of this framework will require the inclusion of relevant activities in WHO biennial work plans aligned with the WHO South-East Asia biennial planning cycle. It will also require multisectoral, multiagency, intercountry, and inter-programmatic cooperation and collaboration.

From a resource, planning and implementation perspective, a phased scaling up is a pragmatic approach to cover the entire countries, particularly large countries such as India and Indonesia. Phased scaling up of HPV vaccination and HPV screening in Thailand is a standard example in the SEA Region. If no action is taken, cervical cancer deaths will rise by almost 50% by 2030 and thus planned and timely investment in mechanisms to deliver the WHO triple intervention strategy is vital.

Depending on the country structure, the national programme manager/s should lead in strategy development with key stakeholders. Most Member States have a functioning national TAG on SRH, cancer control/NCD control, and National Immunization Technical Advisory Groups (NITAGs), which will be the ideal forums to work on the strategy development/adaptation and policy dialogues. If a TAG is not available, it should be created, or an existing mechanism should be used, consisting of representatives of the immunization/SRH/cancer control divisions of the MoH, and relevant professional associations, NGOs and development partners.

In countries where the H6 partnership exists, the forum can work with the TAG to develop/adapt the national cervical cancer elimination strategy. The regional implementation framework is a generic document with proposed strategies and major activities for the Member States to achieve the 2030 interim targets for eliminating cervical cancer by the end of the century.



# Annexes

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## Annex 1: WHO recommendations on screening (17)

Recommendations for the general population of women <sup>a</sup>	Strength of recommendation and level of evidence	Recommendations for women living with HIV (WLHIV) <sup>a</sup>	Strength of recommendation and level of evidence
<p>1. WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and WLHIV.</p> <p><i>Remarks: Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance.</i></p>	Strong recommendation, moderate-certainty evidence	21. WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and WLHIV.	Strong recommendation, moderate-certainty evidence
<p>2. WHO suggests using an HPV DNA primary screening test either <b>with triage</b> or <b>without triage</b> to prevent cervical cancer among the general population of women.</p> <p>3a. In a screen-and-treat approach using HPV DNA detection as the primary screening test, WHO suggests treating women who test positive for HPV DNA among the general population of women.</p>	Conditional recommendation, moderate-certainty evidence	22. WHO suggests using an HPV DNA primary screening test <b>with triage</b> rather than without triage to prevent cervical cancer among WLHIV.	Conditional recommendation, moderate-certainty evidence
	Conditional recommendation, moderate-certainty evidence	23. In a screen, triage and treat approach using HPV DNA detection as the primary screening test among WLHIV, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (Annex 3).	Conditional recommendation, moderate-certainty evidence

Recommendations for the general population of women <sup>a</sup>	Strength of recommendation and level of evidence	Recommendations for women living with HIV (WLHIV) <sup>a</sup>	Strength of recommendation and level of evidence
<p><b>3b. In a screen, triage and treat approach using HPV DNA detection as the primary screening test among the general population of women, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test (Annex 3).</b></p> <p><i>Remarks: The benefits, harms and programmatic costs of the triage options are similar; therefore, the choice of triage method will be dependent on feasibility, training, programme quality assurance and resources in countries. HPV16/18 genotyping could be integrated into the HPV DNA test (refer to Annex 3 for specific details of the algorithms).</i></p>	<p>Conditional recommendation, moderate-certainty evidence</p>	<p>24. When providing HPV DNA testing, WHO suggests using either samples taken by a health-care provider or self-collected samples among both the general population of women and WLHIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>
<p>4. When providing HPV DNA testing, WHO suggests using either samples taken by a healthcare provider or self-collected samples among both the general population of women and WLHIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>	<p>25. WHO suggests starting regular cervical cancer screening at the age of 25 years among WLHIV.</p> <p>Remarks: Low-certainty evidence found that there are likely to be small numbers of WLHIV with cervical cancer who are below the age of 25 years. This recommendation applies to WLHIV regardless of when they first tested positive for HIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>
<p>5. WHO recommends starting regular cervical cancer screening at the age of 30 years among the general population of women.</p>	<p>Strong recommendation, moderate-certainty evidence</p>	<p>26. For women above the age of 50 years, WHO suggests that screening should be stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and WLHIV.</p> <p>Remarks: Neither VIA nor ablative treatment is suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after the menopause.</p>	<p>Conditional recommendation, very low-certainty evidence</p>

Recommendations for the general population of women <sup>a</sup>	Strength of recommendation and level of evidence	Recommendations for women living with HIV (WLHIV) <sup>a</sup>	Strength of recommendation and level of evidence
<p>6. For women above the age of 50 years, WHO suggests that screening should be stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and WLHIV.</p> <p><i>Remarks: Neither VIA nor ablative treatment is suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after the menopause.</i></p>	<p>Conditional recommendation, low-certainty evidence</p>	<p>27. Priority should be given to screening WLHIV aged 25–49 years. When tools are available to manage WLHIV aged 50–65 years, those in that age bracket who have never been screened should also be prioritized.</p>	<p>Good practice statement</p>
<p>7. Priority should be given to screening women aged 30–49 years in the general population. When tools are available to manage women aged 50–65 years, those in that age bracket who have never been screened should also be prioritized.</p>	<p>Good practice statement</p>	<p>28. WHO suggests a regular screening interval of every 3–5 years when using HPV DNA detection as the primary screening test among WLHIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>
<p>8. WHO suggests a regular screening interval of every 5–10 years when using HPV DNA detection as the primary screening test among the general population of women.</p>	<p>Conditional recommendation, low-certainty evidence</p>	<p>29. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and WLHIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>
<p>9. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and WLHIV.</p>	<p>Conditional recommendation, low-certainty evidence</p>	<p>30. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and WLHIV.</p>	<p>Good practice statement</p>
<p>10. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and WLHIV.</p>	<p>Good practice statement</p>	<p>31. WHO suggests that WLHIV who have screened positive on an HPV DNA primary screening test and then negative on a triage test are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.</p>	<p>Conditional recommendation, low-certainty evidence</p>



Recommendations for the general population of women <sup>a</sup>	Strength of recommendation and level of evidence	Recommendations for women living with HIV (WLHIV) <sup>a</sup>	Strength of recommendation and level of evidence
11. WHO suggests that the general population of women who have screened positive on an HPV DNA primary screening test and then negative on a triage test are retested with HPV DNA testing at 24 months and, if negative, move to the recommended regular screening interval.	Conditional recommendation, low-certainty evidence	32. WHO suggests that women from the general population and WLHIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.	Conditional recommendation, low-certainty evidence
12. WHO suggests that women from the general population and WLHIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.	Conditional recommendation, low-certainty evidence	33. WHO suggests that WLHIV who have been treated for histologically confirmed CIN2/3 or AIS, or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing, and, if negative, are retested again at 12 months and, if negative again, move to the recommended regular screening interval.	Conditional recommendation, low-certainty evidence
13. WHO suggests that women from the general population who have been treated for histologically confirmed CIN2/3 or adenocarcinoma in situ (AIS), or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing, and, if negative, move to the recommended regular screening interval.	Conditional recommendation, low-certainty evidence	34. As programmes introduce HPV DNA testing, use this test at the woman's next routine screening date regardless of the test that was used at prior screening. In existing programmes with cytology or VIA as the primary screening test, rescreening with the same test should be continued until HPV DNA testing is operational among both the general population of women and WLHIV.	Good practice statement
14. As programmes introduce HPV DNA testing, use this test at the woman's next routine screening date regardless of the test that was used at prior screening. In existing programmes with cytology or VIA as the primary screening test, rescreening with the same test should be continued until HPV DNA testing is operational among both the general population of women and WLHIV.	Good practice statement		

### **Recommendations and good practice statements for treatment not covered in previous guidelines**

For both the general population of women and WLHIV	Strength of recommendation and certainty of evidence
<p>41. Once a decision to treat a woman is made – whether from the general population of women or WLHIV – it is good practice to treat as soon as possible within 6 months to reduce the risk of loss to follow-up. However, in women who are pregnant, good practice includes deferral of treatment until after pregnancy. In circumstances when treatment is not provided within this time frame, it is good practice to re-evaluate the woman before treatment.</p>	Good practice statement
<p>42. WHO suggests large-loop excision of the transformation zone (LLETZ) or cold knife conization (CKC) for women from the general population and WLHIV who have histologically confirmed AIS. <i>Remarks: Loop excision may be preferred in women of reproductive age, in settings with greater availability of LLETZ and by providers with greater expertise in performing LLETZ. CKC may be preferred when interpretation of the margins of the histological specimen is imperative.</i></p>	Conditional recommendation, low-certainty evidence

### **Additional recommendations for treatment not covered in previous guidelines**

Recommendations for the general population of women	Strength of recommendation and level of evidence	Recommendations for WLHIV	Strength of recommendation and level of evidence
<p>a. Once a decision to treat a woman is made, it is good practice to treat as soon as possible within 6 months to reduce losses to treatment. However, in women who are pregnant, good practice includes deferral of treatment until after pregnancy. In circumstances when treatment is not provided within this time frame, it is good practice to evaluate the woman before treatment.</p>	Good practice statement	<p>a. Once a decision to treat a woman is made, it is good practice to treat as soon as possible within 6 months to reduce losses to treatment. However, in women who are pregnant, good practice includes deferral of treatment until after pregnancy. In circumstances when treatment is not provided within this time frame, it is good practice to evaluate the woman before treatment.</p>	Good practice statement

Recommendations for the general population of women	Strength of recommendation and level of evidence	Recommendations for WLHIV	Strength of recommendation and level of evidence
<p>b. WHO suggests LLETZ or CKC for women who have histologically confirmed AIS.</p> <p><b>Remarks:</b> Loop excision may be preferred in women of reproductive age, in settings with greater availability of LLETZ, and by providers with greater expertise in performing LLETZ. CKC may be preferred when interpretation of the margins of the histological specimen is imperative.</p>	<p>Conditional recommendation, low-certainty evidence for effects</p>	<p>c. WHO suggests LLETZ or CKC for women who have histologically confirmed AIS.</p> <p><b>Remarks:</b> Loop excision may be preferred in women of reproductive age, in settings with greater availability of LLETZ, and by providers with greater expertise in performing LLETZ. CKC may be preferred when interpretation of the margins of the histological specimen is imperative.</p>	<p>Conditional recommendation, low-certainty evidence for effects</p>

## Annex 2: SEAR-TAG committee recommendations for elimination of cervical cancer

The SEAR-TAG and SRHR Subcommittee deliberated and provided recommendations on mitigation strategies for COVID-19 impact and to ensure continuation of essential health services in the Region. The focus was on preventing and reducing stillbirths and neonatal mortality, access to and provision of safe abortion services and prevention and elimination of cervical cancer.

The TAG and SRHR Subcommittee appreciated the progress in the Region so far, but urged acceleration in efforts acknowledging that cancer cervix is a preventable and treatable human tragedy especially for economically disadvantaged women. The TAG and SRHR subcommittee emphasized that several aspects need to be addressed as recommended below:

### 1. Countries to work towards the global targets to be achieved by 2030

The global targets were endorsed by the TAG as 30% reduction of NCDs including cervical cancer by 2030 and the following interim elimination targets for 2030 for the Region:

- ◉ 90% girls vaccinated by age 15 years with HPV vaccine
- ◉ 70% women between ages 35 and 45 years are screened for cervical cancer
- ◉ 90% of women with cervical disease – precancerous lesion receive treatment; with invasive cancer receive treatment.

The countries should strengthen the national cancer control plans to align with the recent WHO call for elimination of cervical cancer and the SEA Region implementation framework on elimination of cervical cancer as a public health problem.

#### 1.1 High-level advocacy

The WHO Regional Director to advocate to the health ministers at the Regional Committee to give priority to cervical cancer and adopt the targets, engage with professional associations and stakeholders of countries to advocate to national governments to give priority to prevention, management, accelerate progress towards the global targets and observe the week annually designated for cervical cancer.

#### 1.2 90% target girls fully vaccinated with HPV vaccine by age 15 years

- ◉ The members noted with concern that only Bhutan, Maldives, Myanmar, Sri Lanka and Thailand have introduced HPV vaccine at the national level
- ◉ In collaboration with the vaccine programmes, Member States that have already introduced HPV vaccination to maintain quality and coverage and others should scale up their pilot projects or subnational introductions with strong advocacy involving community and religious leaders
- ◉ Member States must align with the recommendation of the TAG on immunization on procurement of HPV vaccine and HPV vaccination programme (regional vaccine action plan).

### **1.3 Capacity-building; 70% women screened with high precision tests between 35–45 years 10 years apart**

The WHO Regional Office for South-East Asia to facilitate countries to implement affordable, high precision point-of-care diagnostics and build capacity of health workers for screening and treatment, incorporating quality assurance mechanisms. Use the opportunities created through development of COVID-19 and use innovative measures such as the teaching and education of health workforce to build back better and stronger.

### **1.4 90% of women with cervical lesions receive treatment and palliative care**

- ⊙ MoH of countries to ensure that screening and treatment including palliative care are part of UHC plans to make the services accessible to the marginalized high-risk populations.

## **2. Health system-related**

### **2.1 Data systems**

- ⊙ WHO to support countries to develop their population-based cancer registry and also undertake analysis of data at intervals to improve planning and monitoring the progress.

### **2.2 Implementation research**

- ⊙ WHO to support countries on implementation research.

## Annex 3: Seven algorithms prioritized for phase 1 of the guideline update (17)

### Screening and treatment approaches

1. In the “**screen-and-treat approach**”, the decision to treat is based on a positive primary screening test only
2. In the “screen, triage and treat approach”, the decision to treat is based on a positive primary screening test followed by a positive second test (a “triage” test), with or without histologically confirmed diagnosis.

### Screen-and-treat approaches

1. **Visual inspection with acetic acid (VIA)** as the primary screening test, followed by treatment
2. **HPV DNA** (self- or clinician-collected) as the primary screening test, followed by treatment.

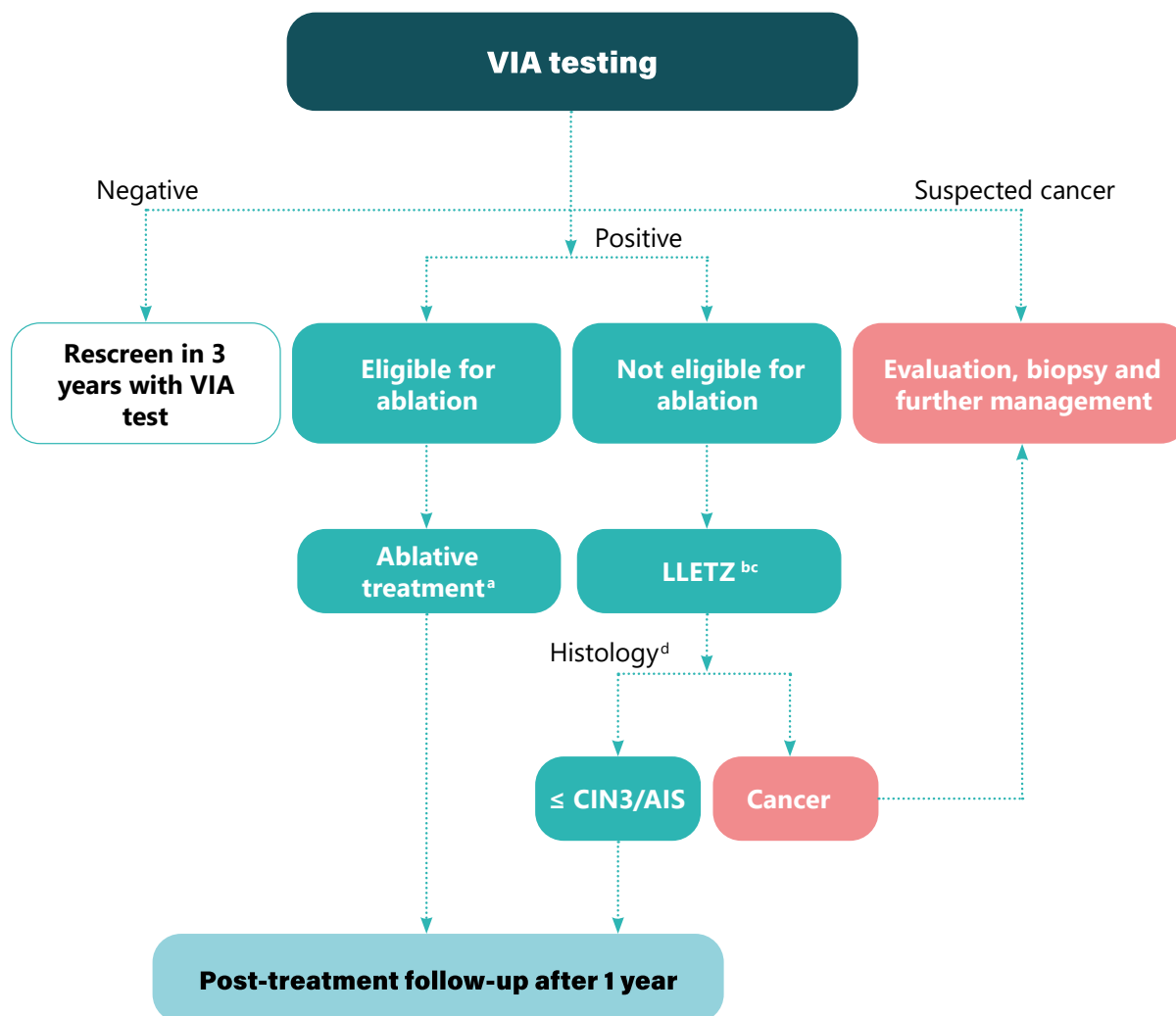
### Screen, triage and treat approaches

1. **Cytology** as the primary screening test, followed by **colposcopy triage**, followed by treatment
2. **HPV DNA** as the primary screening test, **followed by HPV16/18 triage** (when already part of the HPV test), followed by treatment, and using **VIA triage** for those who screen negative for HPV16/18
3. **HPV DNA** as the primary screening test, followed by **VIA triage**, followed by treatment
4. **High-risk HPV DNA** as the primary screening test, followed by **colposcopy triage**, followed by treatment
5. **HPV DNA** as the primary screening test, followed by **cytology triage**, followed by **colposcopy** and treatment.

## Algorithm

### 1 Primary via screening (screen-and-treat approach)

For both the general population of women and women living with HIV



a Ablative treatment includes cryotherapy and thermal ablation.

b Cold knife conization (CKC) if LLETZ not available.

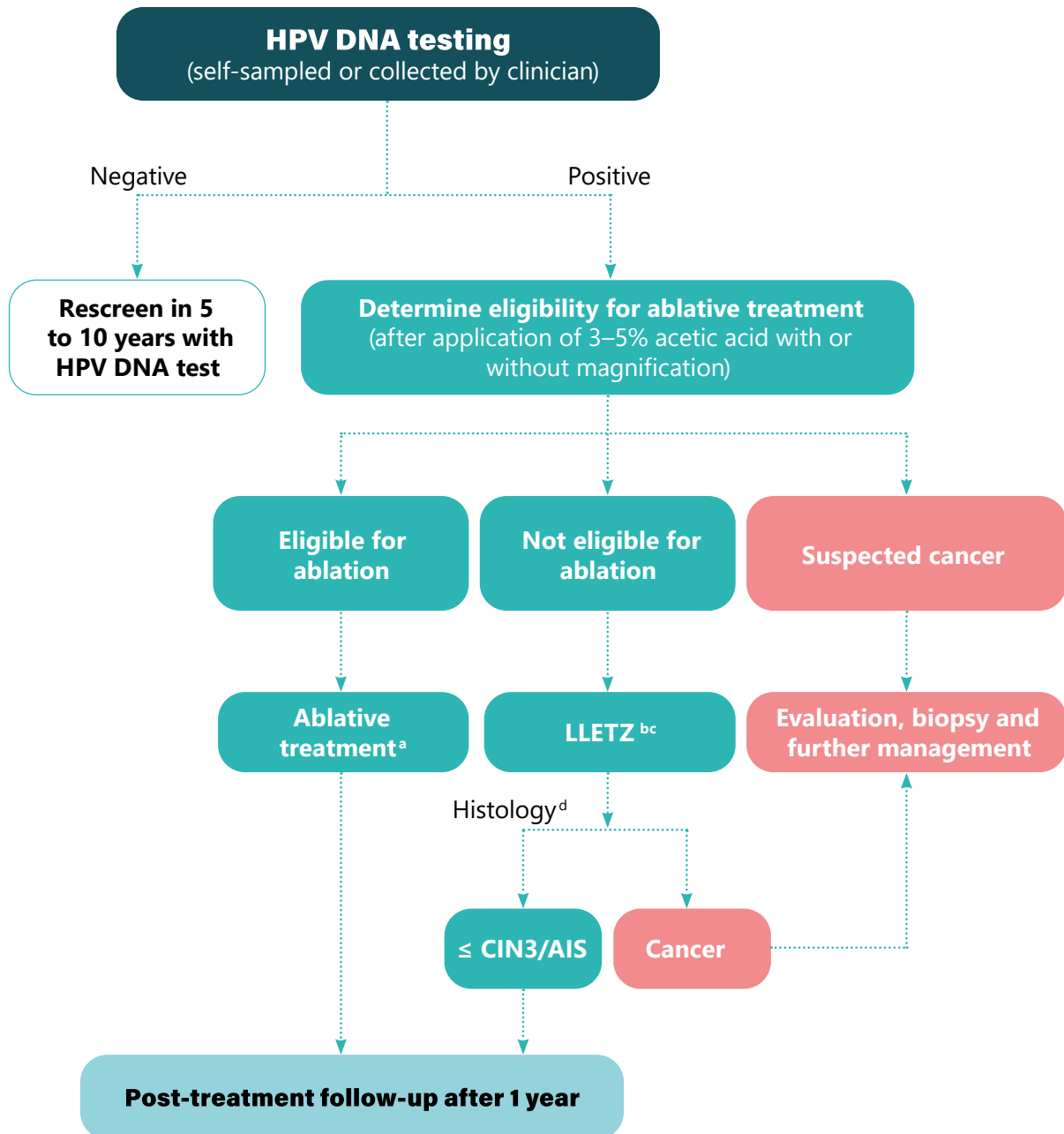
c LLETZ and LEEP (loop electrosurgical excision procedure) indicate the same procedure.

d Histology may not be available in certain settings; women should be advised to attend follow-up after 1 year or to report earlier, if they have any of the symptoms of cervical cancer.

AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; LLETZ: large-loop excision of the transformation zone; VIA: visual inspection with acetic acid.

## 2 Primary HPV DNA test screening (screen-and-treat approach)

For the general population of women



a Ablative treatment includes cryotherapy and thermal ablation.

b Cold knife conization (CKC) if LLETZ not available.

c LLETZ and LEEP (loop electrosurgical excision procedure) indicate the same procedure.

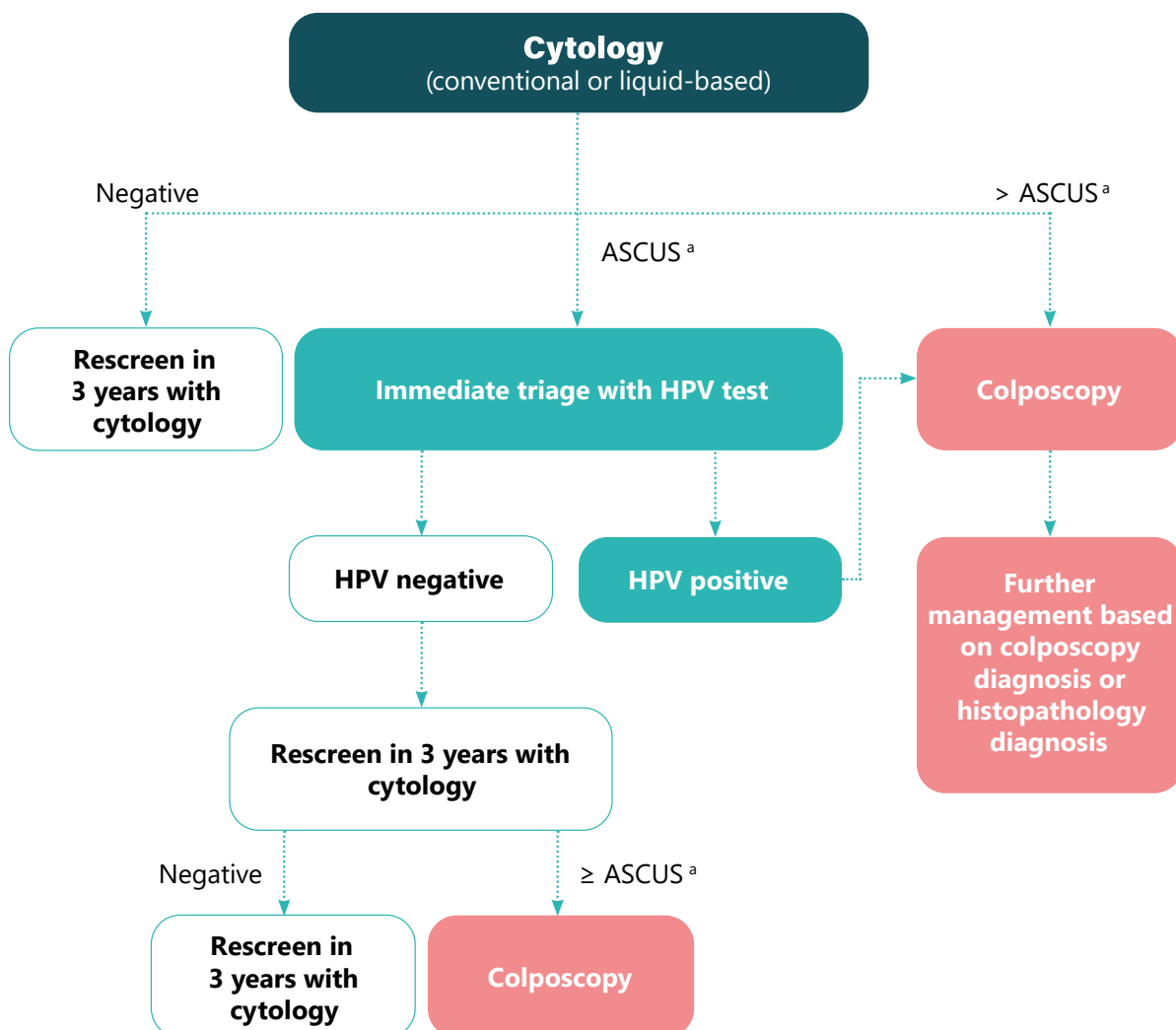
d Histology may not be available in certain settings; women should be advised to attend follow-up after 1 year or to report earlier, if they have any of the symptoms of cervical cancer.

AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; HPV: human papillomavirus; LLETZ: large-loop excision of the transformation zone.



### 3 Primary cytology screening and colposcopy triage (screen, triage and treat approach)

For both the general population of women and women living with HIV (WLHIV)

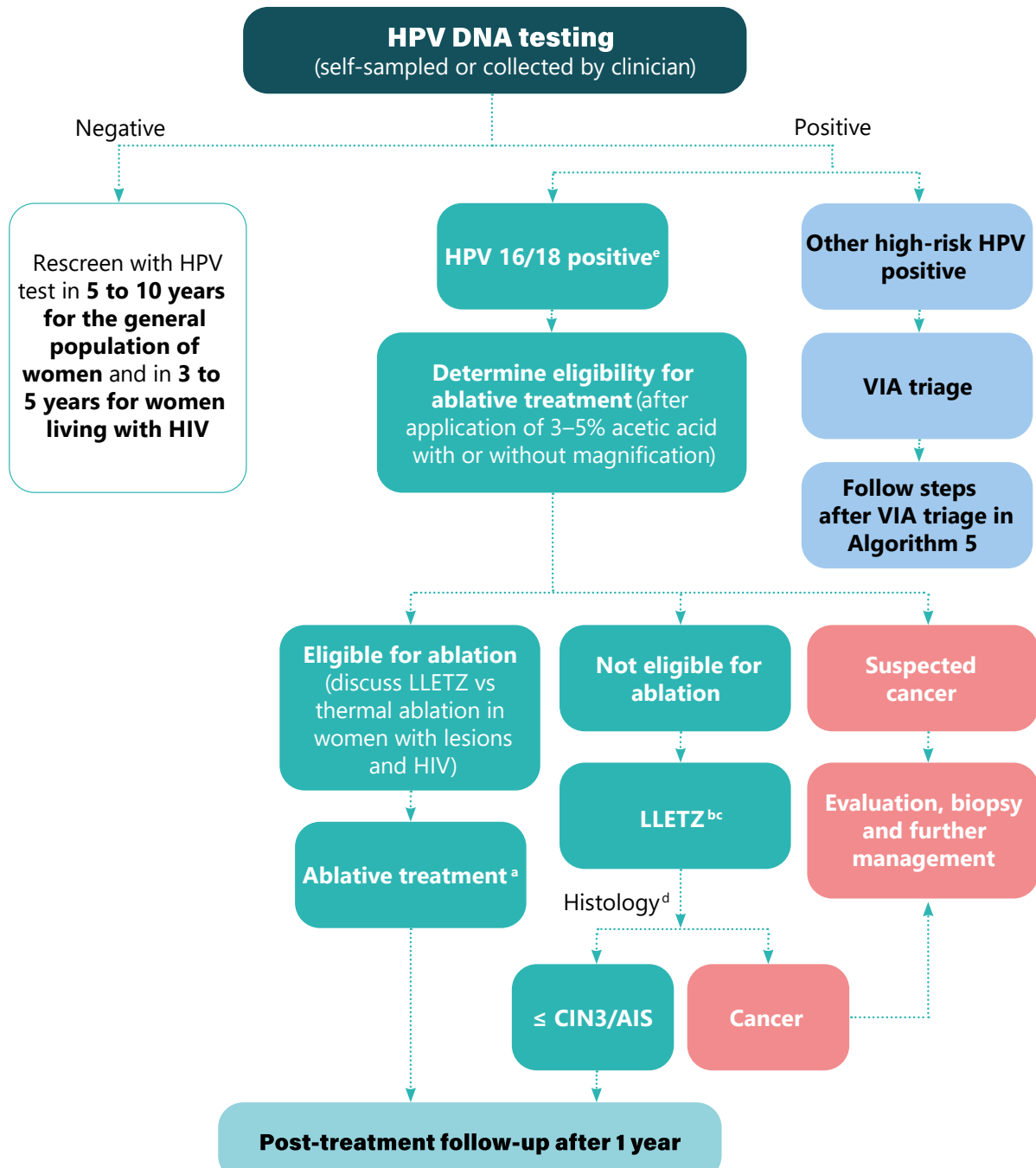


<sup>a</sup> Some programmes prefer to use LSIL threshold.

ASCUS: atypical squamous cells of undetermined significance; HPV: human papillomavirus; LSIL: low-grade squamous intraepithelial lesion.

#### 4 HPV DNA screening and HPV16/18 triage (screen, triage and treat approach)

For both the general population of women and women living with HIV (WLHIV)



a Ablative treatment includes cryotherapy and thermal ablation.

b Cold knife conization (CKC) if LLETZ not available.

c LLETZ and LEEP (loop electrosurgical excision procedure) indicate the same procedure.

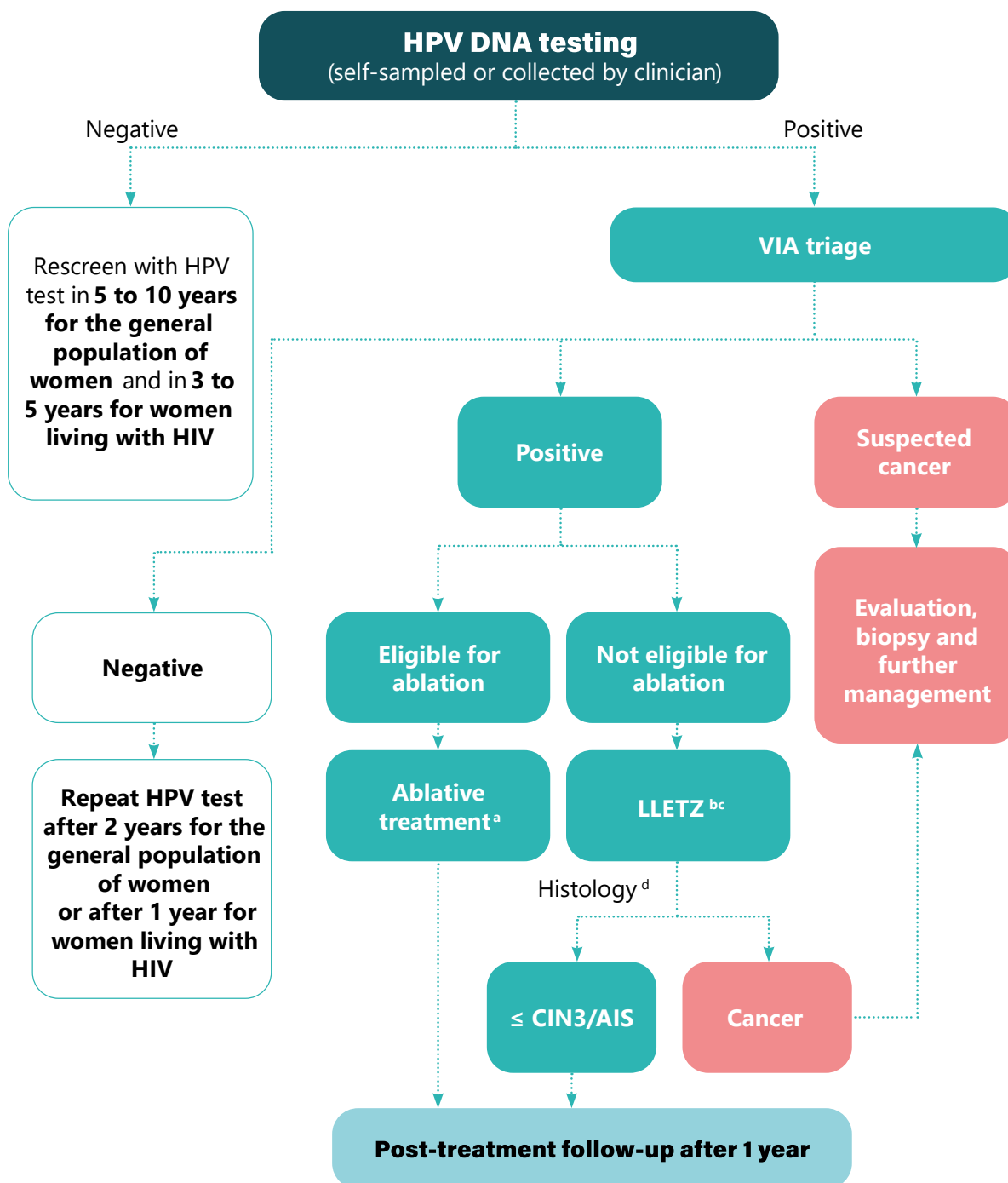
d Histology may not be available in certain settings; women should be advised to attend follow-up after 1 year or to report earlier, if they have any of the symptoms of cervical cancer.

e May or may not be positive for HPV 45.

AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; LLETZ: large-loop excision of the transformation zone; VIA: visual inspection with acetic acid.

## 5 Primary HPV DNA screening and via triage (screen, triage and treat approach)

For both the general population of women and women living with HIV (WLHIV)



a Ablative treatment includes cryotherapy and thermal ablation.

b Cold knife conization (CKC) if LLETZ not available.

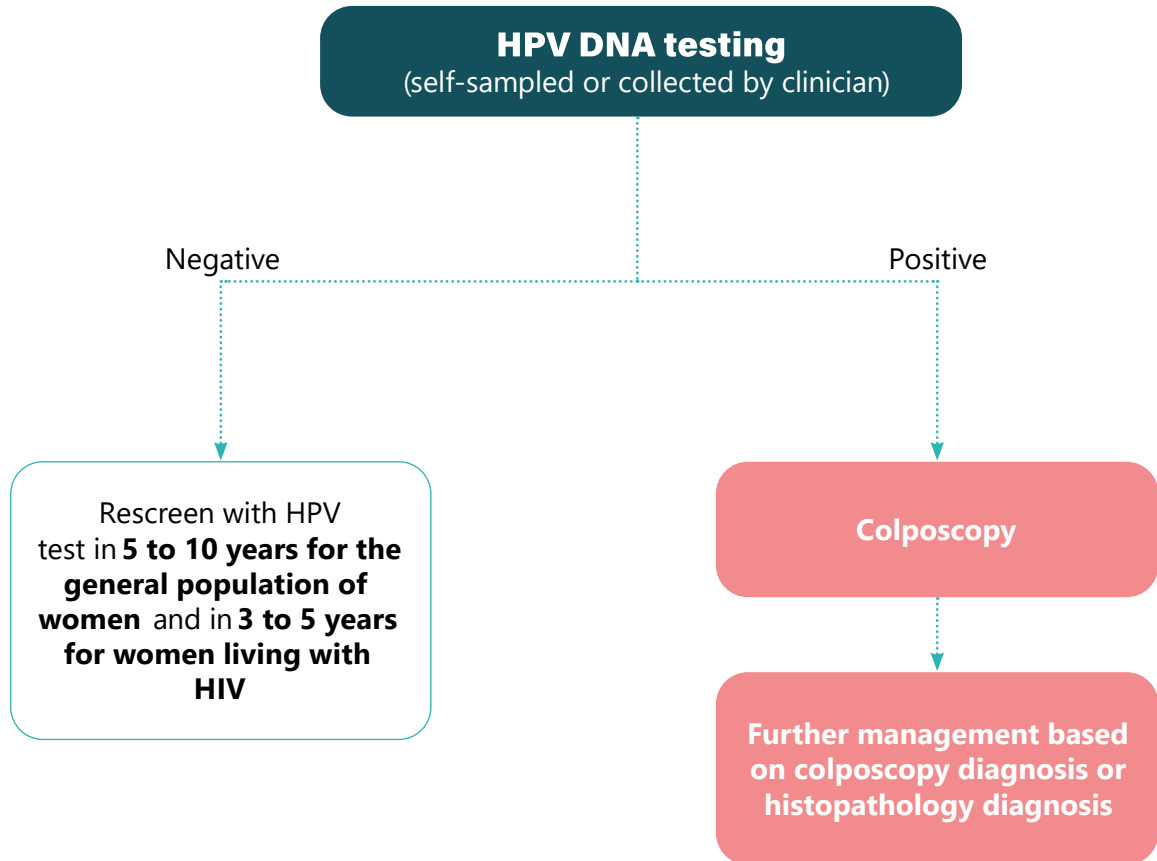
c LLETZ and LEEP (loop electrosurgical excision procedure) indicate the same procedure.

d Histology may not be available in certain settings; women should be advised to attend follow-up after 1 year or to report earlier, if they have any of the symptoms of cervical cancer.

AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; HPV: human papillomavirus; LLETZ: large-loop excision of the transformation zone; VIA: visual inspection with acetic acid.

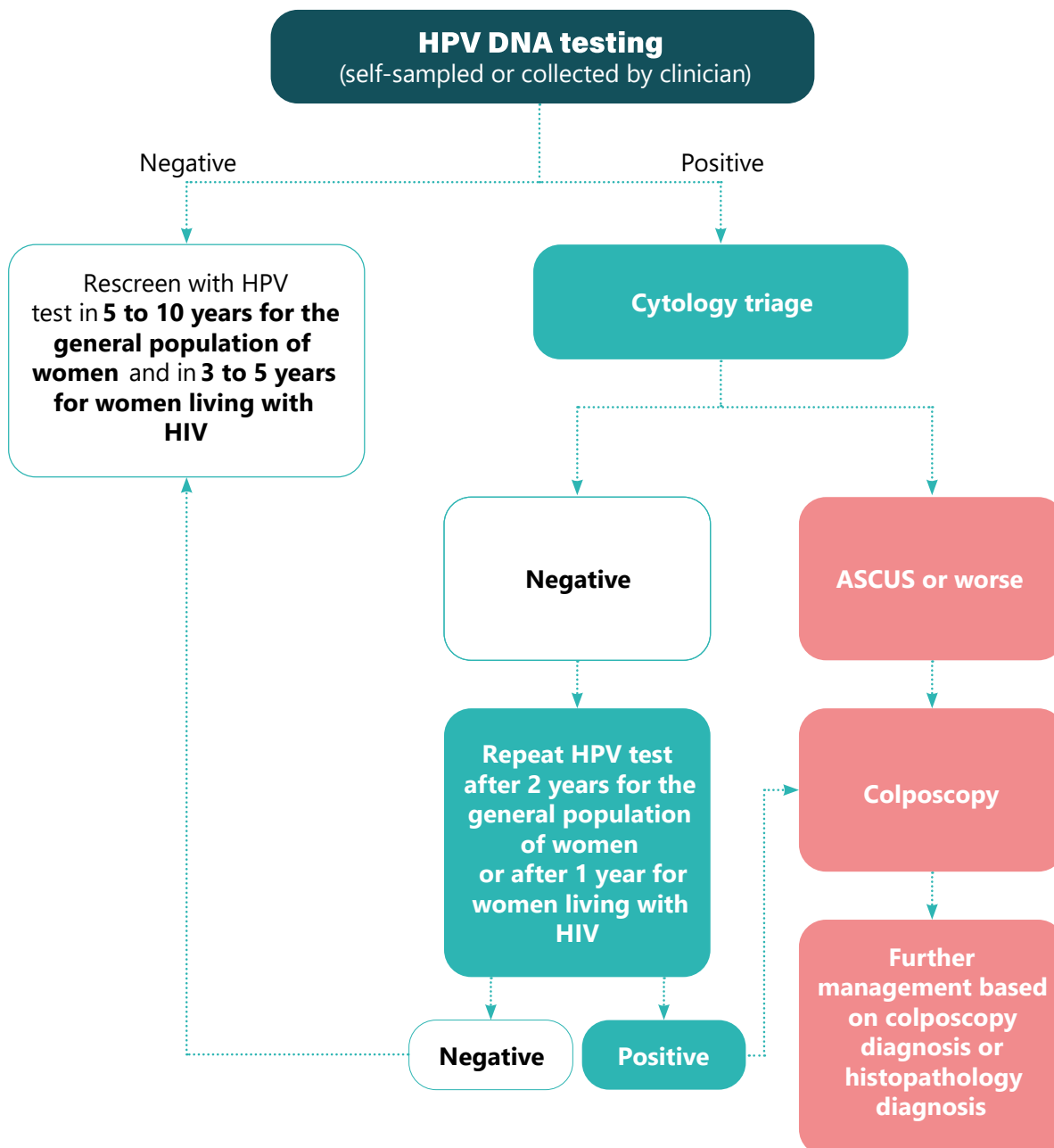
## 6 Primary HPV DNA screening and colposcopy triage (screen, triage and treat approach)

For both the general population of women and women living with HIV (WLHIV)



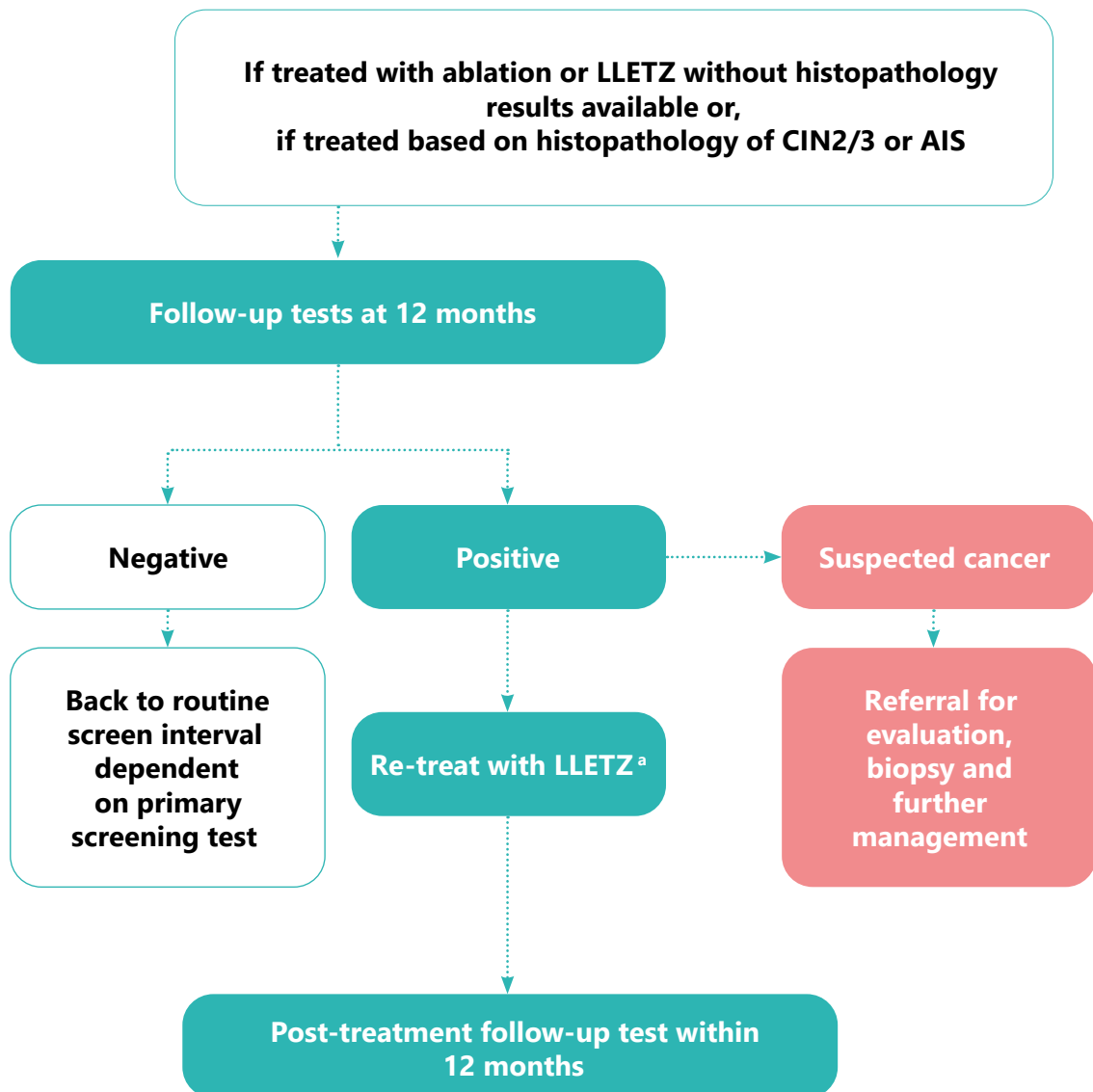
## 7 Primary HPV screening and cytology triage followed by colposcopy (screen, triage and treat approach)

For both the general population of women and women living with HIV (WWLHIV)



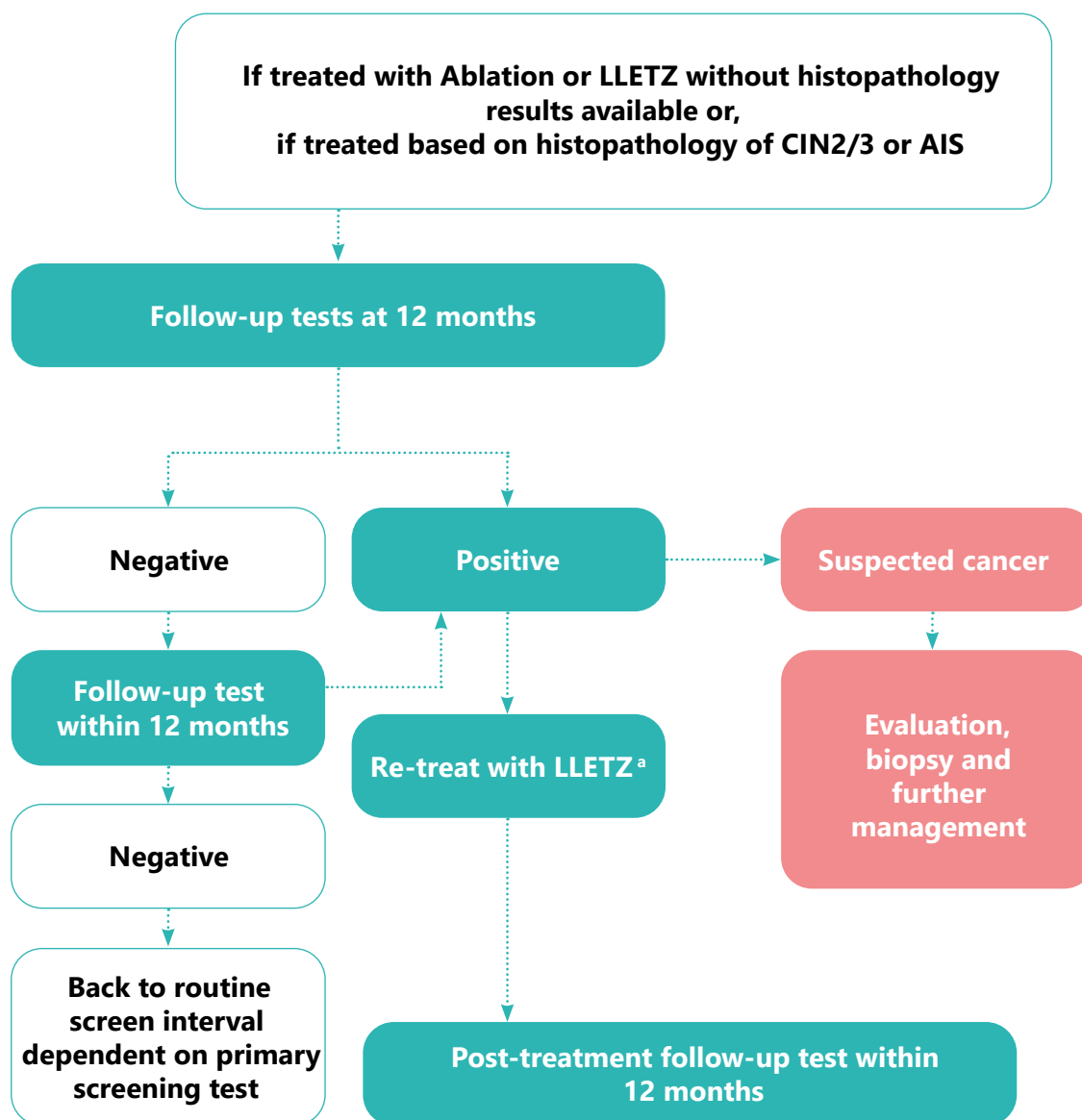
## Follow-up

### 1: Tests at 12 months post-treatment for the general population of women



<sup>a</sup> In circumstances where LLETZ not available, use cryotherapy or thermal ablation for retreatment, if eligible.  
 AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; LLETZ: large-loop excision of the transformation zone.

## 2: Tests at 12 months post-treatment for women living with HIV (WLHIV)



<sup>a</sup> In circumstances where LLETZ not available, use cryotherapy or thermal ablation for retreatment, if eligible.

AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; LLETZ: large-loop excision of the transformation zone.

## Annex 4: Strategic actions to achieve 70% coverage for screening and 90% treatment of precancerous lesions (2)

<p><b>Understand barriers to accessing services and create an enabling environment</b></p>	<p>A robust understanding of the social, cultural, societal and structural barriers to the uptake of services is crucial. Such knowledge will inform the development of context-specific and culturally appropriate demand creation strategies and the design of acceptable, accessible service delivery platforms. Local communities, especially women, must be engaged and empowered to lead the development of these critical programmes, serve as allies, counter misinformation or stigmatization, and support those needing more complex treatment. Increasing health literacy, knowledge of rights and awareness of cervical cancer prevention and control will help to mobilize, empower and engage communities and civil society, and women in their diversity.</p>
<p><b>Integrate screening and treatment services into the primary care package</b></p>	<p>Services integrated into existing sexual and reproductive health services, HIV care and treatment clinics, antenatal care, well women clinics and school-based health outreach are points of entry for reaching women and girls. People-centred referral mechanisms should minimize inconvenience to patients and reduce opportunity costs.</p>
<p><b>Promote a screen and treat approach</b></p>	<p>Countries will need to expand the number of facilities where a single-visit screen and treat approach could be implemented. Single-visit screen and treat approaches will not be feasible everywhere; however, they should be promoted and implemented as appropriate.</p>
<p><b>Ensure an affordable supply of quality assured, high performance screening tests and treatment devices</b></p>	<p>Prompt registration and market shaping for cervical cancer diagnostics and treatment devices will lead to improved access and affordability. WHO will strengthen its prequalification capacity, as appropriate, to remain abreast of emerging technologies. Post-market surveillance for all medical devices, including in vitro diagnostics, will ensure that safety monitoring is in place as programmes scale up.</p>
<p><b>Strengthen laboratory capacity and quality assurance programmes</b></p>	<p>Efficient, integrated networks of laboratory services will maximize the impact of limited human and financial resources. Strong quality assurance programmes are crucial to ensuring that services meet the requisite standards. Training and supervision must be an integral component of service delivery.</p>



## Annex 5: Strategic actions to achieve 90% treatment and care for cervical cancer cases (2)

<b>Implement cervical cancer management guidelines</b>	Developing and implementing national cervical cancer management guidelines, adapted to the national context, is central to ensuring high-quality care.
<b>Establish referral pathways and peoplecentred linkages throughout the continuum of care</b>	Streamlining care pathways and referral networks linking all levels of care will ensure timely management of patients.
<b>Strengthen pathology services</b>	Access to high-quality pathology services is crucial for management of invasive cancer. The development of regional pathology centres, making use of affordable telepathology platforms, is possible for countries with limited or no capacity to interpret samples. Where telepathology networks are already being used for complex cases, they could be used for routine ones.
<b>Expand surgical capacity</b>	Cervical cancer can often be cured by surgery alone, if diagnosed and treated in its early stages. However, of the cancer patients who live in the world's poorest countries, less than 5% have access to safe, effective and timely cancer surgery. In high-income countries the predominant model of postgraduate surgical oncology education consists of multiyear specialty training within accredited programmes, supported by experienced board-certified oncological surgeons and a sophisticated, highly functional surgical infrastructure characterized by readily available anaesthetic services, intensive care units, ubiquitous blood banking and modern laboratory platforms. In most low- and middle-income countries the health-care providers performing oncological procedures are generalists (general surgeons, gynaecologists, general practitioners and medical officers) without formal, certified subspecialty training, who provide cancer care out of necessity. Novel attempts to scale up surgical capacity in these environments using focused, competency-based training and North-South twinning partnerships have met with success and should be expanded.
<b>Improve access to radiotherapy and chemotherapy</b>	Most patients with cervical cancers in low- and middle-income countries present at stages that require radiation, so sustainable capacity for curative radiation therapy (external beam and brachytherapy) is critical.

<b>Strengthen and integrate palliative care services</b>	Treatment plans should incorporate not only end-of-life care and pain relief for patients but also psychological support, family support and other services from the outset. Where possible, home-based models of palliative care should be integrated into primary health care.
<b>Optimize health workforce competencies throughout the continuum of care</b>	A strategy for long-term national health workforce education and training, recruitment and retention is the key to ensuring sustainable multidisciplinary team-based care. The WHO Global Strategy on Human Resources for Health: Workforce 2030 provides a blueprint for countries to address workforce challenges. In addition, a wide range of regional observatories on human resources in health systems provide valuable resources for planning and policy development. More options include twinning programmes, regional training hubs located in centres of excellence, telementoring, e-learning, mobile learning, and low-cost virtual reality surgical simulation. Remote training may be appropriate for areas such as surgery, radiology, pathology and patient consultation.
<b>Reduce cancer stigmatization</b>	Patient awareness, health literacy and education initiatives, especially through survivor groups, contribute to addressing stigmatization associated with cancer.
<b>Provide comprehensive support designed to enhance quality of life and address physical, psychological, social and spiritual challenges faced by survivors</b>	Such programmes are best developed locally, tailored to the sociocultural context of affected communities and engaging advocates of sexual and reproductive health and rights.

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