

WHO GUIDANCE NOTE

Comprehensive cervical cancer prevention and control: a healthier future for girls and women



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INTRODUCTION

Women's cancers, including breast, cervical and ovarian cancer, lead to hundreds of thousands of premature deaths among women. Investments and programmes to prevent and treat women's cancers such as cervical cancer have improved and led to strong reductions in high income countries.

Cervical cancer is the second most common cancer in women worldwide. Yet, because of poor access to screening and treatment services, the vast majority of deaths occur in women living in low- and middle-income countries. Effective methods for early detection of precancerous lesions using cytology (Pap smear) exist and have been shown to be successful in high income countries. However, competing health care priorities, insufficient financial resources, weak health systems, and limited numbers of trained providers have made high coverage for cervical cancer screening in most low- and middle-income countries difficult to achieve.

New technological developments offer the potential to tackle cervical cancer in a more comprehensive way and build a healthier future for girls and women.

The increasing availability of an alternative screening technology called VIA¹, and new vaccines against the *Human papillomavirus* (HPV) may help prevent cervical cancer further. Moreover, because HPV vaccination targets 9-13 year old girls, there is the opportunity to catalyse a life course approach to cervical cancer prevention and control from childhood and through adulthood.

Implementation of cervical cancer prevention and control programmes contributes to the attainment of the Millennium Development Goals through universal access to sexual and reproductive health services to improve women's health, to the 2010 UN Secretary-General's *Global Strategy for Women and Children's Health* and to the 2011 Political Declaration of the UN General Assembly High level Meeting on Non-Communicable Diseases.

Cervical cancer is highlighted in the "Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases" as well as in the "comprehensive global monitoring framework" under development which includes key indicators, and a set of global targets for the prevention and control of non-communicable diseases.

This WHO Guidance Note, that is part of the overall guidance WHO is issuing on Women's cancers, is aimed at senior policy-makers and programme managers. It gives a broad vision of what a comprehensive approach to cervical cancer prevention and control means. It is not new guidance but summarizes existing WHO publications. In particular, it outlines the complementary strategies for comprehensive cervical cancer prevention and control, and highlights the need for collaboration across programmes, organizations, and partners.

KEY FACTS ABOUT CERVICAL CANCER

- Every year more than 270 000 women die from cervical cancer, more than 85% of these deaths are in low and middle income countries.
- Cervical cancer is caused by sexually-acquired infection with *Human papillomavirus* (HPV). Most people are infected with HPV shortly after onset of sexual activity.
- Vaccination against HPV in girls 9 to 13 years old combined with regular screening in women over age 30 for precancerous lesions followed by adequate treatment are key tools to prevent the 530 000 new cervical cancer cases diagnosed every year.
- Survival rates for cervical cancer can be further improved by establishing effective cancer treatment programmes.

¹ Visual inspection with acetic acid (VIA).

CERVICAL CANCER PREVENTION AND CONTROL: A COMPREHENSIVE APPROACH

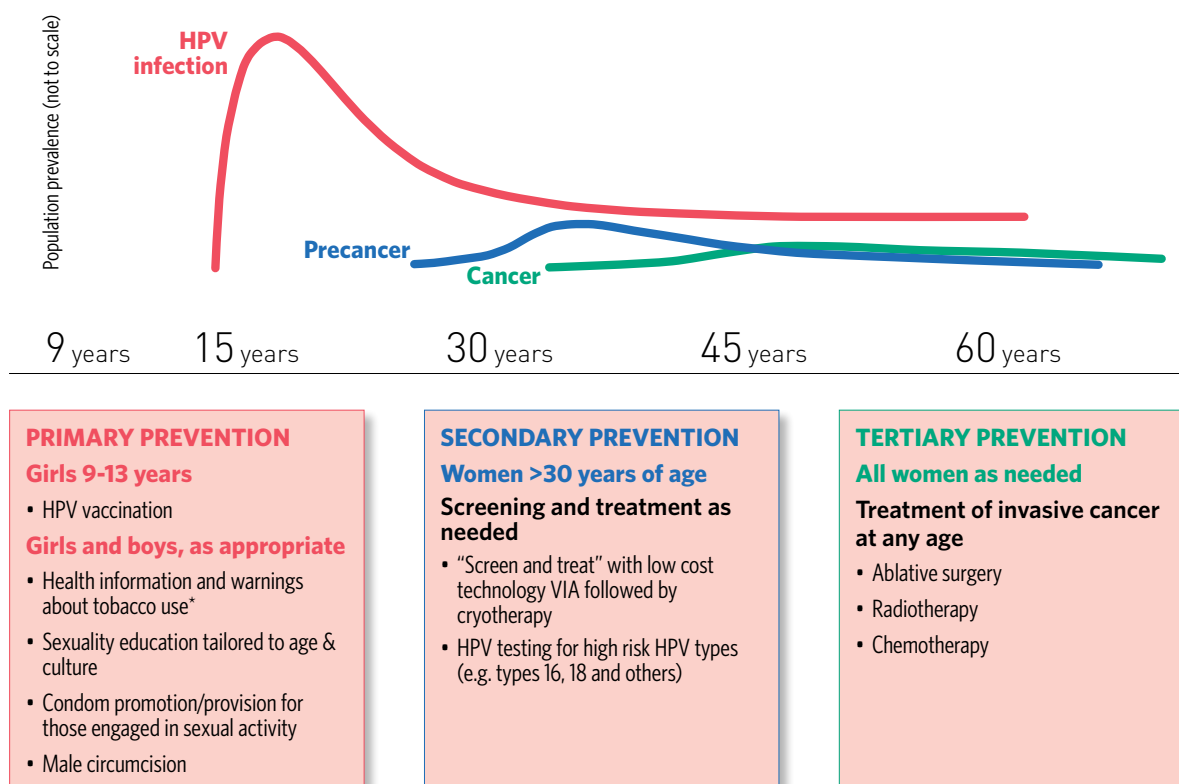
Cervical cancer is caused by the sexually transmitted HPV, which is the most common viral infection of the reproductive tract. Almost all sexually active individuals will be infected with HPV at some point in their lives and some may be repeatedly infected. The peak time for infection is shortly after becoming sexual active.

The majority of HPV infections resolve spontaneously and do not cause symptoms or disease. However, persistent infection with specific types of HPV (most frequently, types 16 and 18) may lead to precancerous lesions. If untreated, these lesions may progress to cervical cancer.

The core principle of a comprehensive approach to cervical cancer prevention and control is to act across the life course using the natural history of the disease to identify opportunities in relevant age groups to deliver effective interventions (Figure 1).

At the national level, a comprehensive approach to cervical cancer prevention and control benefits from being multidisciplinary. As this approach is made up of several key components ranging from community education, social mobilization, vaccination, screening, and treatment to palliative care, it is important to involve representatives from various disciplines and national health programmes such as immunization, reproductive health, cancer control and adolescent health. HPV vaccination does not replace cervical cancer screening. In countries where HPV vaccine is introduced, screening programmes will need to be developed or strengthened.

FIGURE 1: OVERVIEW OF PROGRAMMATIC INTERVENTIONS OVER THE LIFE COURSE TO PREVENT HPV INFECTION AND CERVICAL CANCER



* Tobacco use is an additional risk factor for cervical cancer.

PRIMARY PREVENTION

HPV VACCINATION: OPPORTUNITIES AND CHALLENGES

HPV vaccination is targeted at girls 9–13 years of age. The fact that this age group is a different target population from the infants who routinely receive vaccines through the national immunization programme presents both opportunities and challenges:

» **Choice of delivery strategy:** Effective, affordable and equitable delivery strategies to reach girls 9–13 years of age three times during a 6 month period are required. Where school enrolment of girls is high, school-based vaccination is a possibility; however, different approaches are needed to reach girls not in school and who may be particularly vulnerable (e.g. street children, migrants). Attracting young girls to repeatedly come to health facilities and outreach sessions is likely to take special efforts. Prior to national introduction, countries are encouraged to pilot and assess vaccine delivery strategies in order to determine how to achieve affordable and high HPV vaccination coverage. At the same time, reaching these girls with HPV vaccine offers a huge opportunity to provide them with other health interventions (Figure 1).

» **Communication:** National educational campaigns for vaccine introduction should be used to increase community awareness about cervical cancer and its prevention. Carefully designed messages are essential to educate communities, parents, teachers, adolescents and other stakeholders about the HPV vaccine, HPV infection and cervical cancer and the availability of services. Programmes can be quickly undermined by rumours and misinformation if the reasons for targeting girls only are not fully and sensitively communicated. Educating men, including fathers and boys, about HPV vaccines and cervical cancer is particularly important in this regard. Providing cervical cancer information to older women and mothers of the girls being offered vaccination is a potential way to involve parents. Informed consent for HPV vaccination can be another communication opportunity to educate parents and girls about adolescent health issues or cervical cancer screening.

» **Monitoring and evaluation:** It is important to have strong systems in place to monitor national vaccination programmes. Existing systems for monitoring vaccine coverage need to be adapted for HPV vaccines. HPV vaccine coverage data need to be collected by dose number and by year of age of the girl receiving the vaccine. This requires the redesign of tally sheets and registers. As for any new vaccine, WHO recommends that a post-introduction evaluation (PIE) of an HPV vaccination programme be undertaken 6–12 months after the vaccine has been introduced.

KEY FACTS ABOUT HPV VACCINES

- Seventy-percent (70%) of cervical cancers worldwide are caused by only two HPV types (16 and 18).
- Three vaccines against HPV are licensed in most countries.
- The vaccines prevent over 95% of HPV infections caused by HPV types 16 and 18, and some cross-protection against other less common HPV types which cause cervical cancer. One of the vaccines also protects against HPV types 6 and 11 which cause anogenital warts.
- Both vaccines work best if administered prior to exposure to HPV.
- The vaccines cannot treat HPV infection or HPV-associated disease.
- The WHO recommended target group for vaccination is 9–14 year old girls who have not yet become sexually active.
- HPV vaccines require 2 doses administered over a period of 6 months.
- Safety of these vaccines is being closely monitored, and thus far, is very reassuring.
- HIV-infected individuals can be vaccinated and need 3 doses



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» **Affordability and sustainability:** Current market prices of HPV vaccines range from more than US\$100 to below US\$10 a dose. In addition to vaccine costs, there are operational costs for delivery that need to be calculated and financed. Careful analysis of the financial costs of both the vaccine and the delivery strategy will be a critical step in the decision-making process. Support by GAVI and industry donation² programmes provide opportunities for some of the poorest countries to access HPV vaccine, but many low- and middle-income countries are not able to benefit from these mechanisms. To be affordable and sustainable in low income countries, WHO estimates a negotiated price considerably less than US\$5 per fully vaccinated girl will be necessary. However, this does not include the full vaccine delivery costs (see box for more details) that require substantial additional financial resources which countries need to secure.

HPV VACCINE DELIVERY COSTS (EXCLUDING VACCINE COSTS)

Costs vary by country and whether HPV vaccine is administered monthly or in campaign mode; in urban, rural, or mountainous areas; via health facility, school or integrated community outreach; and by the number of girls per vaccination session.

Currently available data suggest that for GAVI-eligible countries:

- Start-up costs for HPV vaccine introduction are ~US\$3/girl.
- Operational costs for delivering 3 doses is ~US\$4.20/girl.
- During the first year, total start-up and operational costs for delivering 3 doses of HPV vaccine is ~US\$7.20/girl (not including the cost of the vaccine).

² For guidance on "Good Donations Practice" see WHO-UNICEF Joint Statement on Vaccine Donations August 7, 2010 http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.09_eng.pdf

SECONDARY PREVENTION

SCREENING AND TREATMENT OF PRECANCEROUS LESIONS

Cervical cancer screening is the systematic application of a test to identify cervical abnormalities in an asymptomatic population. Women targeted for screening may actually feel perfectly healthy and see no reason to visit health facilities.

Screening services may be provided either as organized or opportunistic (i.e. taking advantage of a woman's visit to the health facility for another purpose) services or a combination of both. It is generally accepted that organized screening is more cost-effective than opportunistic screening, making better use of available resources and ensuring that the greatest number of women will benefit.

For treatment of precancerous lesions, the technology of choice is loop electrosurgical excision procedure (LEEP). For settings where LEEP cannot be performed or in low resource settings, recent WHO guidelines recommend cryotherapy as a good alternative treatment for eligible VIA positive lesions. In high-resource settings, other techniques such as cold knife conisation can be used.



The current options for providing services for screening and treatment of precancerous lesions include the following:

- » 'Screen and treat' – using a screening test that gives immediate results (like visual methods, VIA) followed by “on the spot” treatment (e.g. using cryotherapy) of detected lesions, without any further tests unless a suspected cancer is found.
- » 'Sequential testing' – carrying out a second screening test (triage test) for those who had a positive first screening test result, and if pre-cancer lesion is re-confirmed this is followed by treatment.
- » Screening and, for those women who tested positive, carry out colposcopy and biopsy with treatment based on the biopsy result.

The first option can be provided as a 'single visit approach', while the others need a 'multi visit' approach, which has important programmatic implications. Women in many countries, particularly women living in rural and remote areas, have limited access to health services due to long distances, transportation and other costs, family and work responsibilities and other access barriers.

Strategies that reduce the number of clinic visits required for screening and treatment make it easier for women to receive the care they need, to increase follow-up and reduce programme costs. Single visit and multiple visit approaches both have their limitations and “trade-offs” based on the screening test and treatment used. In some settings, it may be important to accept a screening test with lower performance characteristics if it reduces barriers to access and leads to increased screening test coverage. Any positive test has to be followed by adequate treatment.

Availability of, and access to, health services, may mean that countries decide to use more than one approach for screening and treatment of pre-cancer.

KEY FACTS ABOUT CERVICAL CANCER SCREENING AND TREATMENT

- Cervical cancer screening is the testing for precancer and cancer of women at risk, most of whom will be without symptoms.
- At a minimum, screening is recommended for every woman 30–49 years of age at least once in a life time.
- Globally, in 2012, there were nearly a billion women between 30 and 49 years old, most of whom have never been screened even once in their life.
- Early detection and treatment of precancerous lesions can prevent the majority of cervical cancers.
- Three different types of tests are currently available:
 - Conventional (Pap) and liquid based cytology (LBC)
 - Visual inspection with Acetic Acid (VIA)
 - HPV testing for high risk HPV types (e.g. types 16 and 18).
- HPV vaccination does not replace cervical cancer screening. In countries where HPV vaccine is introduced, screening programmes may need to be developed or strengthened.

CRITERIA FOR AGE AND FREQUENCY OF CERVICAL CANCER SCREENING

- Women younger than 30 years of age should not undergo screening except for women known to be HIV-infected or living in a high HIV prevalence area.
- At a minimum, a national programme should prioritize women who are between 30–49 years old for screening.
- The screening interval (frequency) should not be less than 5 years (and not less than 10 years, if using an HPV test).
- Priority should be given to maximizing coverage within the at-risk target age group and assuring complete follow-up of those women with abnormal screening test results rather than maximizing the number of tests performed in a woman's lifetime.
- In high HIV prevalence countries, women who screen positive for cervical cancer should be offered HIV testing and counselling.

TERTIARY PREVENTION

TREATMENT OF CERVICAL CANCER AND PALLIATIVE CARE

Each year, some 530 000 new cases of cervical cancer are diagnosed globally that need treatment. Invasive cervical cancer is treated by surgery and/or radiotherapy. Chemotherapy can complement the treatment regime in late stages.

In many countries there is insufficient capacity to provide these services or the existing services are not accessible and affordable to the majority of affected women. The main challenges faced in establishing well-functioning treatment systems are:

- » **Establishing and maintaining a treatment referral network:** The main challenge faced in the provision of treatment is to establish and maintain an effective referral network to enable timely access and continuity of care by linking the service facility to the referral facility, laboratory, diagnostic and treatment centres for cervical cancer. A referral protocol and functioning communication system need to be in place to ensure an effective referral system. Referral networks can vary from country to country and depend on the structure of the health system in the country.
- » **Compliance with treatment:** Another important challenge is ensuring completion of treatment which requires a long stay at a treatment centre located at the regional or national level. Geographic, financial, and social barriers often result in non-compliance with treatment, especially for radiotherapy. Providing support for housing, cost of travel and/or disability grants for lost work hours can play an important role in enabling the woman and her family to cope during the treatment period. In countries which do not have the capacity to provide cancer treatment services, it is useful to be aware of intergovernmental arrangements for referral to neighbouring countries and avail of this arrangement.
- » **Palliative care:** Ensuring that patients with life-threatening cervical cancer are provided with relief from pain and suffering (both physical and psychological) requires resources, special skills, and supervision. Effective palliative care engages a team of doctors, nurses, other specialists, and community members who work together in health facilities, the community, and homes.



MONITORING AND EVALUATING COMPREHENSIVE CERVICAL CANCER PREVENTION AND CONTROL



It is important to monitor and assess progress of the objectives and targets of the overall national strategy.

Key programme indicators for primary, secondary and tertiary prevention within the cervical cancer prevention and control approach are:

- » **HPV vaccination:** Vaccination coverage, by year of age and by dose.
- » **Screening and treatment of precancers:** Screening coverage, screening test positivity rate, and treatment rate.
- » **Treatment of cancers:** Proportion of curable cancer patients who get adequate treatment and survival rates.
- » **Palliative care:** Opioid access for women with advanced cervical cancer.

Essential impact indicators are incidence and mortality of cervical cancer. Given that the aim of a comprehensive cervical cancer prevention and control programme is to reduce the incidence of cervical cancer deaths, countries are advised to establish or improve reporting to cancer registries to monitor long-term trends in disease incidence and mortality rate. This registry will enable countries to assess the long-term impact of both HPV vaccination and cervical cancer screening and treatment programmes.

INTRODUCTION OF HPV VACCINES: A CATALYST FOR PROGRAMME SYNERGY

Introducing and scaling up delivery of HPV vaccine to girls who are 9 to 13 years old is a unique opportunity to develop synergies between national programmes of immunization, cancer control, sexual and reproductive health, HIV and other sexually transmitted infections, adolescent health, and women's health.

HPV vaccine introduction can be a potential catalyst for action in the following ways:

- » Development of a National Cervical Cancer Prevention and Control Strategy:
 - HPV vaccine introduction can serve as an impetus for governments to design and cost a comprehensive approach to cervical cancer prevention and control and to develop national policies and guidelines based on WHO standards.
 - Continued screening will be needed for older women who are unable to benefit from vaccination due to previous HPV infection, as well as for vaccinated women to prevent cancer from HPV types not included in the current vaccines. Therefore, a comprehensive approach to cervical cancer prevention and control across the life-course involves health education to all age groups, vaccinating girls 9 to 13 years old before initiation of sexual activity, screening women for precancerous lesions, and treatment before progression to invasive disease.
 - In order to be able to monitor cancer incidence and mortality, establishing cancer registries is a key area for collaboration between national immunization and cancer control programmes. Strengthened cancer registries can provide an opportunity to strengthen National Cancer Control Programmes to more broadly address other cancers.

- » Delivery of a broader set of health interventions for 9 to 13 year old children and adolescents:
 - Traditionally, few health services are provided to this age group. Linking HPV vaccination to the delivery of a broader set of effective health interventions could serve as a platform to increase the coverage of adolescent and school health programmes.
 - Interventions that address risk factors for the health of adolescents³ such as nutritional status, physical inactivity, under- and over-nutrition, tobacco use, and early and unprotected sexual activity, also deal with some of the co-risk factors for cervical cancer.
 - The delivery of these interventions requires new partnerships with adolescent and school health programmes involving ministries of health and education, as well as non-governmental organizations.

- » Experience gained with HPV vaccine introduction targeting 9 to 13 year old children and adolescents can serve as a model for future vaccines against sexually transmitted infections that are under development, such as HIV and *Herpes simplex virus* (HSV2) vaccines.

³ WHA 64.25 (2011) Youth and health risks.

COLLABORATION WITH PARTNERS

- » Address cervical cancer prevention and control in a comprehensive manner that also promotes the sexual and reproductive health of girls and women over the life course and together with a package of other key health interventions.
- » Support countries to:
 - Develop National Cervical Cancer Prevention and Control strategic plans.
 - Undergo a decision-making process to determine if introducing HPV vaccination is programmatically feasible, financially sustainable, and cost-effective, and to determine which screening and treatment algorithms will be the most appropriate and cost-effective.
 - Conduct HPV vaccine demonstration projects to determine best delivery strategy and estimate cost.
 - Make better use of sexual and reproductive health and HIV services to initiate or increase coverage of cervical cancer screening.
 - Develop culturally specific communication campaigns, social mobilization and education efforts to raise awareness of cervical cancer, risk factors and methods of prevention.
- » Ensure coordination between immunization, health education and cancer control programmes as well as other relevant public health programmes, with collaboration between the public and private sector as appropriate.
- » Generate support and advocacy for new financing mechanisms and resource mobilization for cervical cancer prevention and control.

A CHECKLIST FOR A COMPREHENSIVE CERVICAL CANCER PREVENTION AND CONTROL PROGRAMME

1	A functional multi-disciplinary platform to foster partnership and collaboration and set the national agenda	✓
2	A comprehensive national policy or plan on cervical cancer prevention and control	✓
3	National guidelines for health workers for all components of comprehensive cervical cancer prevention and control	✓
4	Financial and technical resources to implement the policy/plan and ensure that services are accessible and affordable to girls and women	✓
5	Communication strategies to educate the community and advocate for support of national policies	✓
6	A training plan in place, as well as supervisory mechanisms for quality control and assurance of the programme	✓
7	HPV vaccination as a population based strategy to an appropriate cohort in the target age group of 9 and 13 year old girls	✓
8	Cervical cancer programme to 'screen and treat' every women between 30 and 49 years old at least once in her life time	✓
9	A functioning referral system that links screening services with the treatment of precancerous lesions and invasive cancer	✓
10	Functioning monitoring systems to track coverage of HPV vaccination, screening and follow-up treatment	✓
11	Existence of a cancer registry as part of the health information system to monitor cervical cancer incidence and mortality	✓

FURTHER INFORMATION AND RESOURCES

Burden of cervical cancer disease by country

<http://www.who.int/hpvcentre/>

<http://globocan.iarc.fr/>

HPV vaccination

<http://www.who.int/nuvi/hpv/resources/en/index.html>

GAVI web link

<http://www.gavialliance.org/support/nvs/human-papillomavirus-vaccine-support/>

Reproductive Health/Cervical cancer

<http://www.who.int/reproductivehealth/topics/cancers/en/index.html>

<http://www.who.int/reproductivehealth/publications/cancers/9789241502856/en/index.html>

Adolescent health

http://www.who.int/maternal_child_adolescent/topics/adolescence/en/index.html

<http://www.who.int/reproductivehealth/topics/adolescence/en/index.html>

Cancer control

<http://www.who.int/cancer/detection/en/>

Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, and the Report of the Formal Meeting of Member States on the comprehensive global monitoring framework

<http://www.who.int/nmh/en/>