Chapter

Cervical Cancer Prevention and Control

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Abstract

Cervical cancer is caused by HPV (human papilloma virus). It is the second most common cancer in women living low developed countries. The components of cervical cancer prevention and control comprises primary prevention, secondary prevention and tertiary prevention. Primary prevention of cervical cancer encompasses prevention of infection with HPV. Giving HPV vaccine for girls aged 9–14 years before they initiate sexual activity is one of the interventions of primary prevention of cervical cancer. Screening and treatment is needed in secondary prevention of cervical cancer. Screening of cervical cancer encompasses testing a target group (women) who are at risk for a cervical pre-cancer. Tertiary prevention of cervical cancer comprises treatment of cervical cancer and palliative care. The components of tertiary care comprise surgery, radiotherapy, chemotherapy and palliative care. Community mobilization, health education and counseling on cervical cancer prevention and control is vital to make ownership on cervical prevention. Monitoring and evaluation of cervical cancer prevention and control on key program indicators should be done regularly.

Keywords: cervical cancer, primary prevention, secondary prevention, tertiary prevention, control, vaccination

1. Introduction

Cervical cancer is caused by sexually acquired infection with certain types of HPV (human papilloma virus). HPV is a group of viruses that are extremely common worldwide. There are more than 100 types of HPV, of which at least 14 are cancer-causing [1]. Worldwide, cervical cancer is the fourth most frequent cancer in women. There were 570 000 new cases of cervical in 2018. More than 311 000 deaths from cervical cancer occur every year. More than 85% of these deaths occur in low and middle income countries. Seventy-percent of cervical cancers worldwide are caused by only two HPV types (16 and 18) [1, 2].

Abnormal vaginal bleeding is the common symptom of cervical cancer. The bleeding can occur after sexual intercourse. Bleeding after menopause or increased vaginal discharge may also be symptoms [3].

There are numerous risk factors the can cause cervical cancer. Educational status, place of residence, using old sanitary napkins, younger age at marriage, sexual transmitted infections, number of partners and health service utilization are associated with cervical cancer. Bathing daily and during menstruations is found to be preventive factors for cervical cancer [4, 5]. Women who have HIV infection

have an increased risk for cervical cancer than women who have no HIV infection [3, 6]. Non access to cervical cancer screening, commence sexual intercourse at early age, cigarette smoking and long term use of oral contraceptives are also related with higher risk of cervical cancer [3, 5]. History of genital warts, immunosuppression, multiparty, diet low in folates, carotene and vitamin C are also included in risk factors of cervical cancer [7].

The component of cervical cancer prevention and control comprise primary, secondary and tertiary prevention. Cervical cancer can often be prevented by having regular screenings with pap tests and HPV tests to find any pre-cancers and treat them. It can also be prevented by receiving the HPV vaccine [8]. World health organization (WHO) recommended vaccine that can protect HPV 16 and 18 and the vaccine is approved for use in many countries [9]. Avoiding exposure to risk factors is additional actions to prevent cervical cancer [8].

WHO put new cervical elimination targets of 90% HPV vaccination coverage, 70% screening coverage, 90% access to treatment for cervical pre-cancer and cancer and access to palliative care by 2030. Attaining these targets can decrease more than 40% of new cervical cancer cases and 5 million associated mortality by 2050. To achieve this targets efforts should be increased [6]. Availing updated evidence based information on cervical cancer prevention and control is important to increase the information coverage and to develop best strategies that focus on cervical cancer prevention and control. The aim of this chapter is providing the best available information on cervical cancer prevention and control. The chapter described three components of cervical cancer prevention, community mobilization, education and counseling on cervical cancer prevention and monitoring and evaluating cervical cancer prevention and control.

2. Prevention and control of cervical cancer

The goal of any comprehensive cervical cancer prevention and control programme is to decrease the burden of cervical cancer. This can be done by reducing HPV infections, detecting and treating cervical, pre-cancer lesions, and providing timely treatment and palliative care for invasive cancer [9].

The key components of comprehensive cervical cancer prevention and control contains three interdependent components: primary, secondary and tertiary prevention (**Figure 1**). In **Figure 1**, programmatic interventions to prevent HPV infections and cervical cancer is also illustrated.

Even though, effective cervical cancer methods such as HPV vaccination, screening and safe sex practice exists, affordability and putting into practice remain challenge for most countries [5].

Unless cervical cancer prevention and control measures are effectively executed, it is estimated that by 2030, nearly 800,000 new cases of cervical cancer will be annually diagnosed. The huge majority of these cases will be in developing countries [10]. To reduce this burden, community mobilization, education and counseling on cervical cancer prevention should be implemented at all levels. Monitoring and evaluation of cervical cancer prevention and control on key program indicators should also be done on a regular basis.

2.1 Primary prevention of cervical cancer

Prevention of HPV infection is included in primary cervical prevention and control. There are different subtypes of HPV that can cause cervical cancer but, the major subtypes are 16 and 18 [9].

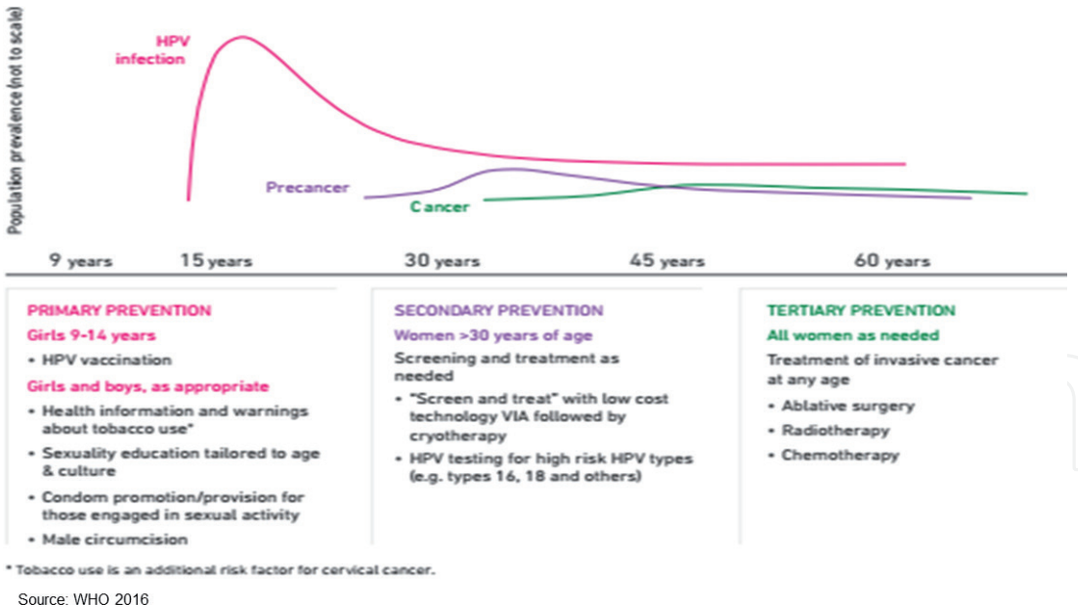

Figure 1.
Programmatic interventions to prevent HPV infections and cervical cancer.

The public health goal of primary prevention of cervical cancer is to reduce HPV infections. Primary prevention can be realized through behavioral change approaches and the use of biological mechanisms, including HPV vaccination. The interventions for primary prevention of cervical cancer include: providing immunization for girls aged 9–14 years before the start sexual intercourse, health education on healthy sexuality for both boys and girls and promotion of condom use. HPV vaccines are not intended to treat women with past or present HPV infection [9, 11].

The target age group for HPV vaccination is 9–14 years earlier to becoming sexual active. Two doses of HPV vaccine with six month interval is required. There is no maximum interval between the two doses. But, the interval of not greater than 12–15 months is suggested to allow girls to complete the schedule on time prior to becoming sexually active. If the interval between doses is shorter than 5 months, then a third dose should be offered at least six months after the first dose. A three dose schedule (at 0, 1–2, and 6 months) is recommended for females 15 years and older and for those known to be immunocompromised and/or HIV-infected [10, 12, 13].

It is not essential to screen for HPV infection or HIV infection prior to HPV immunization. Pre-immunization assessments (e.g., HPV testing of any kind, cervical cancer screening or Pap testing, pregnancy testing, or "virginity testing") are not mandatory [10, 13].

If girls are age ≥ 15 years and received their first dose before age 15 years, they may complete the three doses. If no doses were taken before age 15 years, three doses should be administered. In both scenarios, immunization can be given up to 26 years. If adequate resources remain after immunizing girl's age 9 to 14 years, girls who received one dose may take extra doses between age 15 and 26 years. If there is ≥50% coverage in the priority female target population, sufficient resources and cost effectiveness, boys may be immunized to prevent other non-cervical human papillomavirus related cancers and diseases [12].

The HPV vaccines prevent over 95% of HPV infections caused by HPV types 16 and 18. It may have some cross-protection against other less common HPV types which cause cervical cancer [14]. There are three various vaccines, which vary in the number of HPV types they comprise and target. However, not all are obtainable in everywhere.

- Quadrivalent HPV vaccine (Gardasil®) targets HPV types 6, 11, 16 and 18.
- 9-valent vaccine (Gardasil 9®) targets the same HPV types as the quadrivalent vaccine as well as types 31, 33, 45, 52 and 58.
- Bivalent vaccine (Cervarix ®) targets HPV types 16 and 18 [5].

Cervarix is the best cost effective vaccine with proved efficacy in one dose. The WHO commends two doses for either Gardasil 9 or Cervarix for those up to 15 years of age and three doses for women 15 years or older. The WHO commends are grounded on induced antibody titers at month 7 for Gardasil and Gardasil 9 as there are at present no efficacy data for these vaccines in fewer than three doses. The WHO recommendations for Cervarix are built on efficacy information in addition to immunogenicity information. Three dose efficacy prevents cervical intraepithelial neoplasia (CIN) 2 or worse by any HPV type is around 62% for both Cervarix and Gardsail9. The three dose efficacy prevents CIN 3 or worse by any HPV type is 93% for Cervarix and 43% for Gardasil, with no information for ardasil9 [10, 15] (**Table 1**).

There are numerous HPV vaccination distribution approaches. The followings are commonly used distribution approaches:

- Vaccine distribution at health care facilities
- Vaccine distribution through outreach
- Vaccine distribution through campaigns [9, 10, 16].

Educational interventions announcing the risk of HPV and the benefits of vaccines are important, especially in low and middle income countries [17]. Education and effective communication is vital in attaining successful immunization programme [18].

2.2 Secondary prevention of cervical cancer

In secondary prevention of cervical cancer, screening and treatment as desired is included. Screening comprises testing women who are at risk for a cervical precancer. The aim of screening is to detect and treat those people identified as having early signs of the illness, usually by means of inexpensive, precise, and reliable test that can be practical widely. The other aim of screening is to decrease the death related with cervical cancer through identifying the illness when still at an early treatable stage or through detecting precursor lesions. The systematic removal of CIN lesion during screening also leads to reductions of the incidence of invasive cervical cancers of all stages.

There are numerous cervical cancer screening tests in use or being studied around the world. Cervical cytology has been in use for the past 50 years. Newer screening tests are HPV DNA testing and visual screening tests [19]. Increasing the acceptance of screening has many sigfinaces in preventing cervical cancer through early detection and treatment of pre-cancerous changes before malignancy grows. Approaches of inspiring women to start cervical cancer screening include inviting, reminding, teaching, communication framing, counseling, risk factor identification and financial interventions. Use of invitations and to a lesser degree educational resource are supported by evidence as a good methods of encouraging women to undertaken cervical cancer screening [20].

Attributes	**Bivalent(CERVARIX®)**	**QUADRIVALENT (GARDASIL®/ SILGARD®)**	**9-VALENT (GARDASIL 9®)**
Vaccine	Recombinant L1-capsid virus-like particles (VLP)	Recombinant L1-capsid virus-like particles (VLP)	Recombinant L1-capsid virus-like particles (VLP)
HPV types in vaccine	16,18	6,11,16,18	6,11,16,18 31,33,45,52,58
Disease protection	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina)	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina) Genital warts	Cervical cancer (and premalignant genital lesions of cervix, vulva and vagina) Genital warts
Cross-protection against HPV-types	31, 33	31, 45	Not necessary
Number of doses required	2	2	2
Dosing interval (flexibility)	0 and 6 months (No maximum interval but suggested not more than 12–15 months)	0 and 6 months (No maximum interval but suggested not more than 12–15 months)	0 and 6 months (No maximum interval but suggested not more than 12–15 months)
Method of administration	Intramuscular injection	Intramuscular injection	Intramuscular injection
Presentation and Type of Vaccine Vial Monitor (VVM)	1-dose vial; VVM 30 2-dose vial; VVM 30	1-dose vial; VVM 30	1-dose vial; VVM TBD
Shelf-life	48 months at 2–8 °C for 1-dose vial; 36 months at 2–8°C for 2-dose vial; vaccine is freeze sensitive	36 months at 2–8°C, vaccine is freeze sensitive	36 months at 2–8°C, vaccine is freeze sensitive
Contraindications	Severe allergic reaction to any vaccine component after first dose • Severe febrile illness • Known to be pregnant	Severe allergic reaction to any vaccine component after first dose • Severe febrile illness • Known to be pregnant	Severe allergic reaction to any vaccine component after first dose • Severe febrile illness • Known to be pregnant

Source: WHO [10].

Table 1.
Characteristics of HPV vaccines.

Screening of cervical cancer is identifying for pre-cancer. Cervical cancer screening is recommended for woman aged 30 up to 49 years at least one in life time. Early detection and treatment of precancerous lesions can prevent the majority of cervical cancers.

HPV vaccination does not substitute cervical cancer screening. In countries where HPV vaccine is introduced, screening programs may need to be developed or strengthened [21]. Visual inspection of the cervix without magnification was the first technique of screening of the cervix. Nowadays, three types of tests are encouraged:

- Conventional Pap smear (or cytology) and liquid-based cytology
- Visual inspection with Acetic Acid (VIA) or with lugol iodine (VILI)
- HPV testing for high risk HPV types (types 16 and 18).

The randomized trial studies done in different places on cervical cancer screening have shown the efficacy of visual inspection, cytology screening and HPV screening [22–24]. Many studies have acknowledged that in countries where the resources exist to confirm high value and good coverage of the people, cytology screening provides to decreasing the incidence of advanced stage cancers and death related with cervical cancer [25–27].

The treatment methods mostly used are cryotherapy, loop electrosurgical excision procedure or cold-knife conisation [5].

There are two kinds of HPV tests:

- The test that identify if 13 up to 14 HPV subtypes are present or not. But this test cannot help to identify which subtypes are present.
- The tests performed to identify HPV genotyping and identify if HPV 16 or 18 is present or not.

HIV infected women should undergo cervical cancer screening twice in the first year after diagnosis of HIV infection and then annually. For women with two successive normal cytological examinations, the recommendation is that annual follow up includes a detailed visual inspection of the anus, vulva, and vagina, as well as the cervix [5].

Cervical screening based on HPV testing can prevents more invasive cervical cancer and precancerous lesions. It can offers innovative options such as self-collection of specimens to improve screening uptake broadly [28].

2.3 Tertiary prevention of cervical cancer

Tertiary prevention of cervical cancer comprises treatment of cervical cancer and palliative care. Surgical treatment, chemotherapy, radiotherapy and palliative are included in tertiary cervical cancer prevention [16]. The public health goal of tertiary prevention of cervical cancer is to reduce the number of mortality due to cervical cancer.

The interventions for tertiary prevention of cervical cancer comprise:

- A referral mechanism from primary care providers to facilities that offer cancer diagnosis and treatment
- Accurate and timely cancer diagnosis by exploring the extent of invasion
- Treatment, appropriate to each stage based on the diagnosis [9].

2.4 Community mobilization, education and counseling on cervical cancer prevention

Community mobilization is a process of engaging communities and generating support for all those in need of health services, resulting in sustainable community ownership and involvement. Effective communication can increase rates of vaccination

and screening and save women's lives. Health care workers and others involved in cervical cancer control at all levels should be trained in basic counseling skills, so that they can communicate effectively with clients. The content of the counseling encounter will vary according to the client's problems or concerns and her individual situations. It can address prevention, screening, follow-up, referral, diagnosis, treatment of precancerous lesions, treatment of invasive cancer and/or palliative care [9].

2.5 Monitoring and evaluating (M & E) cervical cancer prevention and control

Monitoring and assessing the improvement of objectives and targets at country level is crucial. The followings are crucial indicators of cervical cancer preventions and control:

- Immunization coverage by year of age and by dose.
- Screening coverage, screening test positivity rate and treatment rate.
- Proportion of curable cancer patients who get adequate treatment and survival rates.
- Opioid access for women with advanced cervical cancer.

Essential impact indicators of cervical cancer are incidence and death. Establishing cancer register is important to monitor the incidence and death rate of cervical cancer. The register will help to assess long term impacts of cervical cancer screening, treatment and vaccination [21]. The main recording and reporting tools that are used for immunization should be adapted to include HPV vaccine. The recording and reporting tools comprises: immunization register, tally sheet, immunization card, defaulter tracking system, stock record and integrated monthly report [10].

M & E helps the management team to determine the extent to which the program is meeting the stated goals, objectives, targets and make corrections accordingly [16].

An effective program of prevention and control of cervical cancer must address several issues, including the coverage and quality of screening services, availability of diagnosis, treatment and monitoring [29].

Depending on the country setting and resources available, M & E of cervical cancer prevention can be done by using different approaches.

The approaches includes:

- Site visits
- Peer assessment
- Client and community assessment
- Use of new information and communication technology [30].

3. Conclusion

Cervical cancer prevention and control components are primary prevention, secondary prevention and tertiary prevention. Primary prevention comprise HPV

vaccination of girls 9–14 years old. Secondary prevention include screening and treatment with low technology VIA followed by cryotherapy. Tertiary prevention of cervical cancer incorporates treatment of invasive cancer and providing palliative care. Mobilizing community, giving health education and counseling is very important in prevention and control of cervical cancer. M & E of cervical cancer prevention and control on key program indicators should also be done regularly.

4. Terminology

Bivalent: a vaccine that works by stimulating an immune response against two different antigens; e.g. Cervarix is a bivalent vaccine that helps protect the body against infection with HPV types 16 and 18.

Chemotherapy: The term that usually describes the use of drugs to treat cancer but which may also describe the use of antibiotics to treat infectious diseases.

Cervical intraepithelial neoplasia (CIN): abnormalities in the cells of the cervix which may become cancerous.

Cryotherapy: the use of cold or freezing in treatment.

Cytology: the study of individual cells. Cytology's main use in medicine is to detect abnormal cells. It is widely used to screen for cancer (as in the cervical smear test) or to confirm a diagnosis of cancer.

DNA (**deoxyribonucleic acid**): the principal molecule carrying genetic information in almost all organisms.

Immunogenicity: the property of eliciting an immune response.

Neoplasia: the pathological process that results in the formation and growth of a tumor.

Palliative treatment: treatment that relieves the symptoms of a disorder but does not cure it.

Opioid: a type of drug used to relieve strong pain, e.g. morphine.

Quadrivalent: a vaccine that works by stimulating an immune response against four different antigens; e.g. Gardasil is a quadrivalent vaccine that helps protect the body against infection with HPV types 6, 11, 16 and 18.

Screening: The application of a test to people who are as yet asymptomatic for the purpose of classifying them with respect to their likelihood of having a particular disease. It is not undertaken to diagnose a disease, but to identify individuals with increased probability of having either the disease itself or a precursor of the disease.

Prognosis: An assessment of the probable course and outcome of a disease.

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