

A COMPREHENSIVE REVIEW ON CERVICAL CANCER

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ABSTRACT

Cervical cancer is one of the four most common cancers that affect women worldwide, along with breast, colorectal, lung, and cervical cancer. It is a major public health concern that mostly affects women. Virtually all cases of cervical cancer are linked to human papillomavirus (HPV) infections. Patients must be screened and immunized to prevent this disease, although developed and developing nations have different rates of cervical cancer incidence. Palliative chemotherapy continues to be the go-to therapy for patients who are not candidates for radiation therapy or curative surgery. To counteract chemotherapy's low effectiveness, other treatment approaches are being developed. The main goals of this review study are to advance knowledge of cervical cancer, promote awareness and educated decision-making, and investigate cutting-edge approaches to the disease's treatment. A literature review was done from databases like Google Scholar, PUBMED-MEDLINE, and Scopus using standard keywords "Cancer," "Cervical Cancer," "Human papillomavirus," "Chemotherapy," and "Treatment Therapies" from 2010-2023. The Government of India intends to initiate a three-phase vaccination drive against Human Papillomavirus (HPV) for girls aged 9-14, aiming to mitigate the risk of cervical cancer. The vaccine also offers protection against the HPV strains that cause cancer of the anus, vagina, and oropharynx. Although cervical cancer is still a tough foe, we are getting closer to a time when it may be prevented and treated, even in the most underprivileged areas, due to continuous advancements and steadfast dedication.

KEYWORDS: Cancer, cervical cancer, human papillomavirus, quercetin, chemotherapy.**INTRODUCTION**

According to WHO globally, cervical cancer is the fourth most common cancer in women, with around 660 000 new cases in 2022. In the same year, about 94% of the 350 000 deaths caused by cervical cancer occurred in low- and middle-income countries. Cervical cancer is one of the most preventable and treatable malignant diseases the highest rates of cervical cancer incidence and mortality are in sub-Saharan Africa (SSA), Central America and South-east Asia. Regional differences in the cervical cancer burden are related to inequalities in access to vaccination, screening and treatment services, risk factors including HIV prevalence, and social and economic determinants such as sex, gender biases and poverty. Women living with HIV are 6 times more likely

to develop cervical cancer compared to the general population, and an estimated 5% of all cervical cancer cases are attributable to HIV.^[1]

In February 2009, HPV-16, -18, -31 and a number of other types were reclassified as a group of human carcinogens. HPV-16 is the most potent carcinogen, causing cancer at several sites besides the cervix. HPV-18 and ten other types show sufficient evidence of causation of cervical cancer. Eleven percent of all female cancers were cervical cancer, and 9% of deaths were due to this malignancy. For the prevention of cervical cancer, the most important factor is public health awareness, through healthy and safe sexual behaviour, followed by early detection and screening.^[2]

Cervical cancer starts in the cervix. It starts when cells in the cervix grow out of control and crowd out normal cells. Cancer cells can spread to other parts of the body. Cancer cells in the cervix can sometimes travel to the lung and grow there. When cancer cells do this, it's called metastasis. To doctors, the cancer cells in the new place look just like the ones from the cervix. Cancer is always named for the place where it starts. So when cervical cancer spreads to the lung (or any other place), it's still called cervical cancer. It's not called lung cancer unless it starts from cells in the lung.^[3]

Human papillomavirus (HPV) is one of the most common causes of sexually transmitted disease in both men and women worldwide and is thought to be the most common sexually transmitted viral disease in the United States, it can be prevented by vaccinating all young females against HPV.^[4]

Epidemiology

Worldwide, cervical cancer is the fourth most common malignant disease among women, with nearly 80% of cases arising in less developed countries. The American Cancer Society estimates that during 2002, 13 000 cases of cervical cancer were diagnosed in women living in the USA, and that 4100 women will die as a result of this disease.² In North America, the median age at diagnosis is 47 years, and nearly half of cases are diagnosed before the age of 35. However, women older than 55 years contribute disproportionately to cervical cancer mortality, primarily as a result of more advanced disease at diagnosis.^[5]

In developed countries a decline in the incidence and mortality of cervical cancer has been observed since the introduction of the cytology screening campaign with the use of the Papanicolaou smear. The decline in these rates in the United States has been more than 70% for both rates. This reduction is associated with early diagnosis of precursor lesions of cervical cancer and specific treatment. This is not the case for many other populations, where these rates have not changed in the last Copyright © 2000 by Marcel Dekker, Inc. decades.^[6]

The mortality rate from cervical cancer remains high in low and middle income countries (LMICs=low-middle income country) due to low human resources, difficulties in implementing and sustaining early detection/routine screening programs, accurate diagnosis, and early treatment of cervical precancerous lesions, poverty, and lack of infrastructure. The high incidence of cervical cancer in developing countries is due to the inoperability of a comprehensive population-based pre cervical cancer lesion detection system, in addition to low awareness, education and public knowledge about the occurrence of this cancer even though this disease can be prevented and can be cured if the patient comes at the time. Precancerous lesions or at an early stage^{8–10}.^[7]

Subsequently, the Chinese scientific research team conducted a cross-sectional multi-center cervical cancer and precancerous HPV genotyping study based on 19 hospitals in 7 geographic regions (Northeast China, North China, Northwest China, Central China, East China, Southwest, and South China). Through the pathological laboratory procedures of strict quality control, it was found that the dominant HPV types in cervical cancer tissue were HPV16, 18, 31, 52 and 58, respectively, and that HPV16 and 18 were the most carcinogenic, which could cause more than 84.5% of cervical cancer.^[8]

Causes & Risk Factors

A number of risk factors for cervical cancer are linked to exposure to the HPV (8). Risk factors of cervical cancer include both behavioural and infectious contributors. Behavioural contributors include sexual activity and lifestyle factors. Cervical cancer is caused by HPV virus in a sexually active person. It is not transmitted genetically and diet has no role in preventing cervical cancer.^[9]

Risk factors for cervical cancer are

- infection with human papillomavirus (HPV)
- sexual history
- weakened immune system
- chlamydia infection
- smoking and passive smoking
- lack of regular Cervical Screening Tests
- age
- taking contraceptive pills for a long time
- previous abnormality or cancer of the cervix
- having many children
- being exposed to diethylstilboestrol (DES).^[10]

A). HPV Infection

HPV - HPV is a group of more than 200 related viruses, some of which are spread through vaginal, anal, or oral sex. Sexually transmitted HPV types fall into two groups: low risk and high risk.

High-risk HPVs can cause several types of cancer. There are 12 high-risk HPV types: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. Two of these, HPV 16 and HPV 18, are responsible for most HPV-related cancers.

Low-risk HPV types rarely cause cancer, although a few low-risk HPV types can cause warts on or around the genitals, anus, mouth, or throat. When warts form in the larynx or respiratory tract, you may have a condition called respiratory papillomatosis, which can cause breathing problems.^[11]

Most HPV infections go away on their own within a year or two as the immune system controls the infection. These short-term infections do not cause cancer. When a high-risk HPV infection lasts for years, it can lead to changes in the cervical cells, resulting in a precancerous lesion. If the precancerous lesion is not found and

removed, it may eventually develop into cervical cancer.^[12]

B). Sexual History

Being sexually active means more than just having intercourse with someone. It can mean.

Any genital skin-to-skin contact

Having oral sex

All women who have ever been sexually active are at risk for developing cervical cancer. This is because sexual activity potentially exposes you to HPV. Women who have never been sexually active rarely develop cervical cancer.

Becoming sexually active at a young age can increase the risk for cervical cancer.

Researchers think this increased risk is because the cervix changes during puberty.

These changes make the area more vulnerable to damage. Certain types of sexual behaviour increase a woman's risk of infection with HPV. Having intercourse with many partners can increase exposure to HPV, which is transmitted by sexual contact. For this reason, having many sexual partners is linked with a higher risk of cervical cancer. But a woman can have HPV even when she has had only one sexual partner.

Women also seem to be at a higher risk for developing cervical cancer if their male partners have had many sexual partners or female partners with cervical cancer.^[13]

C). Smoking

Tobacco smoke is a well-established human papillomavirus (HPV) cofactor for the development of cervical pre-cancer and cancer but the molecular mechanisms by which smoking increases the risk of cervical pre-cancer and cancer remain unknown. There are several plausible explanations. One is that smoking inhibits the immune response to HPV. A second is that carcinogenic HPV-infected cells are exposed to smoking carcinogens that cause DNA damage while HPV oncoproteins block apoptosis and cell cycle arrest.^[14]

D). DES

Diethylstilboestrol (DES) is a synthetic form of the female hormone oestrogen. It was prescribed to pregnant women between 1940 and 1971 to prevent miscarriage, premature labour, and related complications of pregnancy. The use of DES declined after studies in the 1950s showed that it was not effective in preventing these problems, although it continued to be used to stop lactation, for emergency contraception, and to treat menopausal symptoms in women.

In 1971, researchers linked prenatal (while in the womb, or *in utero*) DES exposure to a type of cancer of the cervix and vagina called clear cell adenocarcinoma in a small group of women. Soon after, the Food and Drug Administration (FDA) notified health care providers throughout the country that DES should not be

prescribed to pregnant women. The drug continued to be prescribed to pregnant women in Europe until 1978.^[15]

Signs & Symptoms

Women with early cervical cancers and pre-cancers usually have no symptoms. Symptoms often do not begin until the cancer becomes larger and grows into nearby tissue. When this happens, the most common cervical cancer symptoms are abnormal vaginal bleeding, such as bleeding after vaginal sex, bleeding after menopause, bleeding and spotting between periods, or having (menstrual) periods that are longer or heavier than usual. Bleeding after douching may also occur. An unusual discharge from the vagina – the discharge may contain some blood and may Pain during sex, Pain in the pelvic region.^[21] Symptoms of advanced cervical cancer (cancer has spread beyond the cervix to other parts of the body) may include the symptoms of early-stage cervical cancer and difficult or painful bowel movements or bleeding from the rectum when having a bowel movement, difficult or painful urination or blood in the urine, dull backache, swelling of the legs, pain in the abdomen, feeling tired.

These symptoms may be caused by many conditions other than cervical cancer. The only way to know is to see a health professional. If it is cervical cancer, ignoring symptoms can delay treatment and make it less effective.^[22]

Diagnosis & Detection

Screening

Screening tests can help detect cervical cancer and precancerous cells that may one day develop into cervical cancer. Most medical organizations suggest beginning screening for cervical cancer and precancerous changes at age 21. The tests are usually repeated every few years.^[23]

Tests under Screening

1. Medical History and Physical Exam

First, the doctor will ask you about your personal and family medical history. This includes information related to risk factors and symptoms of cervical cancer. A complete physical exam will help evaluate your general state of health. You will have a pelvic exam and maybe a Pap test if one has not already been done. In addition, your lymph nodes will be felt to see if the cancer has spread (metastasis).^[24]

2. Colposcopy

Colposcopy is the method of examination that allows magnification and illumination of the cervix. This technique can be used to assess and identify pre-invasive lesions of the cervix and lower genital tract. Various styles of colposcopy are available, but the most popular are on a moveable stand.

Others can be fixed to a table or wall. Attachments to the colposcope could include a green filter, a teaching arm or

video camera. A colposcopy couch is needed where the patient will feel as relaxed and comfortable as possible.^[25]

Colposcopy procedure:-The procedure typically takes 10 to 20 minutes. You'll lie on your back on a table with your feet in supports, just as during a pelvic exam or Pap test.

A metal or plastic speculum is placed in your vagina. The speculum holds open the walls of your vagina so that your healthcare professional can see your cervix.

The special magnifying instrument, called a colposcope, is placed a few inches away from your vulva. Your healthcare professional shines a bright light into your vagina and looks through the lens of the colposcope, as if using binoculars.

Your cervix and vagina are swabbed with cotton to clear away any mucus. A solution of vinegar or another type of solution may be applied to the area. This may cause a burning or tingling sensation. The solution helps highlight any areas of suspicious cells.^[26]

3. Pap Test

A Pap test is sometimes called a Pap smear. It can be done along with a HPV test during a pelvic exam as part of cervical cancer screening for people with no symptoms. Or, it can be done as a follow-up test for an abnormal (positive) HPV test or if someone has symptoms that are suspicious for cervical cancer.^[27]

During the routine procedure, cells from your cervix are gently scraped away and examined for abnormal growth. The procedure is done at your doctor's office. It may be mildly uncomfortable, but doesn't usually cause any long-term pain.^[28]

Pap smear Procedure

It takes about 10-20 minutes for the whole exam, but only a few minutes for the actual Pap smear. The test is done in your doctor's office or clinic.

You'll lie back on a table with your feet placed firmly in stirrups. You'll spread your legs, and your doctor will insert a metal or plastic tool called a speculum into your vagina. They'll open it so that it widens the vaginal walls. Then, they'll shine a light inside the vagina to see your cervix.

Your doctor will lightly brush the cervix to take a sample of cells. They'll place them into a liquid substance in a small jar and send them to a lab for review.^[29]

4. HPV DNA Test

The HPV test is most often used in 2 situations. The ACS recommends the primary HPV test* as the preferred test for cervical cancer screening for people 25-65 years of age. (*A primary HPV test is an HPV test

that is done by itself for screening. The US Food and Drug Administration has approved certain tests to be primary HPV tests.)

Some HPV tests are approved only as part of a co-test, when the HPV test and the Pap test are done at the same time to screen for cervical cancer. Because a primary HPV test may not be an option everywhere, a co-test every 5 years or a Pap test every 3 years are still good options. All the screening tests (primary HPV test, co-test, and Pap test) are good at finding cancer and pre-cancer. The primary HPV test is better at preventing cervical cancers than a Pap test done alone and does not add more unnecessary tests, which can happen with a co-test. The most important thing to remember is to get screened regularly, no matter which test you get.^[30]

5. Cone Biopsy

A cone biopsy, also called conisation, is a surgical procedure to remove a cone-shaped piece of tissue from the cervix and cervical canal. Cone biopsy is useful when diagnosing or treating cervical intraepithelial neoplasia (CIN), a precancerous condition, or cervical cancer.^[31] The methods commonly used for cone biopsies are the loop electrosurgical excision procedure (LEEP), also called the large loop excision of the transformation zone (LLETZ), and the cold knife cone biopsy.

Loop electrosurgical procedure (LEEP, LLETZ): In this method, the tissue is removed with a thin wire loop that is heated by electricity and acts as a small knife. A local anaesthetic is used for this procedure, and it can be done in your doctor's office.

Cold knife cone biopsy: This is done in a hospital. A surgical scalpel or a laser is used to remove the tissue instead of a heated wire. You will receive anaesthesia during the operation (either a general anaesthesia, where you are asleep, or a spinal or epidural anaesthesia, where an injection into the area around the spinal cord makes you numb below the waist).

Possible complications of cone biopsies include bleeding, infection and narrowing of the cervix.

Having had any type of cone biopsy will not prevent most women from getting pregnant, but if a large amount of tissue has been removed, women may have a higher risk of giving birth prematurely.^[32]

Imaging Studies

If your doctor finds that you have cervical cancer, certain imaging studies may be done. These tests can show if and where the cancer has spread, which will help you and your doctor decide on a treatment plan.

Chest x-ray: Your chest may be x-rayed to see if cancer has spread to your lungs.

Computed tomography (CT): CT scans are usually done if the tumour is larger or if there is concern about cancer spread. For more information, see CT scan for Cancer.

Magnetic resonance imaging (MRI): MRI scans look at the soft tissue parts of the body sometimes better than other imaging tests, like a CT scan. Your doctor will decide which imaging test is best to use in your situation. For more information, see MRI for Cancer.

Positron emission tomography/ computed tomography (PET/CT) scan: For a PET scan, a slightly radioactive form of sugar (known as **FDG**) is injected into the blood and collects mainly in cancer cells. Often a PET scan is combined with a CT scan using a special machine that can do both at the same time. This lets the doctor compare areas of higher radioactivity on the PET scan with a more detailed picture on the CT scan. This is the type of PET scan most often used in patients with cervical cancer. This test can help see if the cancer has spread to lymph nodes. PET scans can also be useful if your doctor thinks the cancer has spread but doesn't know where.

Intravenous urography: Intravenous urography (also known as **intravenous pyelogram**, or **IVP**) is an x-ray of the urinary system taken after a special dye is injected into a vein. This test can find abnormal areas in the urinary tract, caused by the spread of cervical cancer. The most common finding is that the cancer has blocked the ureters (tubes that connect the kidneys to the bladder). IVP is rarely used for patients with cervical cancer because CT and MRI are also good at finding abnormal areas in the urinary tract, as well as others not seen with an IVP.^[33]

Staging

Cervical cancer stages are based upon the International Federation of Gynaecology and Obstetrics (FIGO) staging system. Cervical cancer stages range from 1 to 4. These stages are categorized by the amount of cancer in the cervix and the spread of cancer outside the cervix.^[34]

Treatment Approaches

The following are the types of cervical cancer treatment available.

1. Surgery

For early-stage disease, surgical removal of the uterus remains the primary treatment and has the greatest effect on long-term survival.

However, abdominal ("open") radical hysterectomy is associated with complications, including a risk of lymphedema in the legs and bladder and sexual dysfunction.^[36]

Most women with cervical cancer have some type of surgery.

Cryosurgery

This treatment kills the cancer cells by freezing them. It may be used to treat pre-cancers- abnormal cells that can turn into cancer if not treated.

Laser surgery

This treatment uses a laser to burn off cancer cells. It may be used to treat pre-cancers.

CONISATION

Conisation is also called a cone biopsy. To do this a small cone-shaped piece of the part of the cervix that has the cancer or pre-cancer is taken out.

Hysterectomy

A hysterectomy takes out the uterus and cervix. It's the most common way to treat cervical cancer. There are many ways to do this surgery.

Sometimes the ovaries are taken out at the same time. Nearby lymph nodes may also be taken out to see if they have cancer cells.^[37]

2. Radiation Therapy

The medical linear accelerator is the method of delivering megavoltage EBRT. The accelerator employs high energy electromagnetic waves to accelerate electrons that hit a metallic target to yield an X-ray beam (photons). As this beam interacts with the surrounding pelvic tissues, the incoming photons yield high-speed electrons that, in turn, split water molecules to create a free hydroxyl radical. This highly energetic product can then cause damage to the DNA (deoxyribonucleic acid) of any rapidly dividing cells, such as tumour cells.^[38]

Brachytherapy or internal radiation therapy: Brachytherapy uses a delivery device to place radioactive material inside the patient on a temporary or permanent basis. This kind of radiation only travels short distances as opposed to EBT. It allows your doctor to use a higher total dose of radiation to treat a smaller area in less time than EBT.

Cervical cancer brachytherapy is known as intracavitary brachytherapy. A device containing radioactive material is inserted into the vagina, the cervix and sometimes into the tissue surrounding the cervix. There are two types of intracavitary brachytherapy:

Low-dose rate (LDR) brachytherapy: LDR is performed in a hospital setting and requires a patient to stay overnight for several days. Patients are typically given medication to help them relax during the procedure, which is performed in an operating room usually under general anaesthesia.

High-dose rate (HDR) brachytherapy: This treatment may be delivered on an outpatient basis, although on occasion the device that is implanted will remain in place overnight and may require a brief hospital stay.^[39]

The most common side effects are fatigue, diarrhoea, nausea, upset stomach, and irritation of the bladder, vagina, or skin where the radiation is given.^[40]

3. Chemotherapy

Chemotherapy uses anticancer (cytotoxic) drugs to destroy cancer cells. It is sometimes used to treat cervical cancer.

Chemotherapy is often combined with radiation therapy to treat cervical cancer. This is called chemo radiation. The 2 treatments are given during the same time period.

Chemotherapy is usually a systemic therapy. This means that the drugs travel through the blood to reach and destroy cancer cells all over the body, including those that may have broken away from the primary tumour in the cervix.^[41]

How Chemotherapy is given

You may have chemotherapy in the chemotherapy day unit or on the ward. The drugs are usually given into a vein (intravenously).

During one or more sessions of treatment. The length of each session depends on the combination of chemotherapy drugs you have. After each session, you have a rest period. The chemotherapy session and the rest period are called a cycle of treatment.

The length of a cycle depends on the chemotherapy drugs you have, but most cycles are 1 to 3 weeks long. Your doctor or nurse will tell you how many cycles of treatment you will have.^[42]

The chemotherapy drugs that are most often used for treating cervical cancer include.

- Cisplatin
- Carboplatin
- Paclitaxel
- Topotecan
- Gemcitabine
- Docetaxel
- Ifosfamide
- 5-fluorouracil
- Irinotecan
- Mitomycin

Having chemotherapy with radiotherapy (chemo radiotherapy) can cause more severe side effects. This is compared with having these treatments on their own. Everyone is different, and the side effects vary from person to person. You might not have all of the effects mentioned. Side effects depend on the type of chemotherapy you have. They also depend on the radiotherapy treatment area. The side effects gradually get worse during the treatment. They can continue to get worse after your treatment ends. Side effects will improve, but some might take a few weeks to months.^[43]

4. Targeted Therapy

Targeted drug therapy is the use of medicines are directed at proteins on cervical cancer cells that help them grow, spread, or live longer. Targeted drugs work to destroy cancer cells or slow down their growth. They have side effects different from chemotherapy and some are taken as a pill.^[44]

5. Immunotherapy

Immunotherapy helps to strengthen or restore the immune system's ability to fight cancer. This works to kill cancer cells and stop cancer cells from growing and spreading.

The immune system normally stops itself from attacking healthy cells in the body by using specific proteins called checkpoints. Checkpoints slow down or stop an immune system response. Some cervical cancer cells can use these checkpoints to hide and avoid being attacked by the immune system. Immune checkpoint inhibitors work by blocking the checkpoint proteins so immune system cells (called T-cells) attack and kill the cancer cells.^[47]

Immunotherapy is class of treatments that take advantage of a person's own immune system to help kill cancer cells. There are currently three FDA approved immunotherapy options for the treatment of cervical cancer. Targeted Antibodies.

Bevacizumab (Avastin): A monoclonal antibody that targets the VEGF/VEGFR pathway and inhibits tumour blood vessel growth; approved for subsets of patients with advanced cervical cancer in combination with chemotherapy.

Tisotumab vedotin (Tivdak): An antibody-drug conjugate that targets tissue factor (TF); approved for subsets of patients with advanced cervical cancer Immunomodulators.

Pembrolizumab (Keytruda): A checkpoint inhibitor that targets the PD-1/PD-L1 pathway; approved for subsets of patients with advanced cervical cancer that has PD-L1 expression, high microsatellite instability (MSI-H), DNA mismatch repair deficiency (dMMR), or high tumour mutational burden (TMB-H).^[48]

Prevention

Boosting public awareness, access to information and services are key to prevention and control across the life course.

Being vaccinated at age 9–14 years is a highly effective way to prevent HPV infection, cervical cancer and other HPV-related cancers.

Screening from the age of 30 (25 years in women living with HIV) can detect cervical disease, which when treated, also prevents cervical cancer.

At any age with symptoms or concerns, early detection followed by prompt quality treatment can cure cervical cancer.^[16]

I). HPV Vaccination

HPV vaccines protect against infection with human papillomaviruses (HPV). HPV is a group of more than 200 related viruses, of which more than 40 are spread through direct sexual contact. Among these, two HPV types cause genital warts, and about a dozen HPV types can cause certain types of cancer—cervical, anal, oropharyngeal, penile, vulvar, and vaginal.^[17]

Two recombinant HPV vaccines containing viral-like particles (VLP) are currently available: quadrivalent vaccine targeting oncogenic HPV types 16, 18, 6, and 11, and bivalent vaccine targeting HPV 16 and 18. Both vaccines have demonstrated remarkable immunogenicity and substantial protection against persistent infection, CIN 3, and anal intraepithelial neoplasia caused by the vaccine-targeted HPV types in women aged 15–26 years naïve to the corresponding type at the time of vaccination. Both vaccines have the potential to prevent 70% of cervical cancers in adequately vaccinated populations.^[18]

II). Screening Test

Two screening tests can help find changes that could become pre-cancer or cervical cancer.

The Pap test (or Pap smear) looks for pre-cancers, cell changes on the cervix that might become cervical cancer if they are not treated appropriately.

The HPV test looks for the virus (human papillomavirus) that can cause these cell changes.

The implementation of Pap screening programs has resulted in a reduction of up to 80% in the incidence of cervical cancer among developed nations. However, its utilization in many middle-income countries (MIC) have been accepted manuscript suboptimal and in many low-income countries (LIC), even non-existent. This disparity is largely due to the lack of resources to create effective Pap screening programs in underdeveloped communities. Successful preventative screening programs require well-organized infrastructure with skilled personnel to obtain and interpret the cytology specimens, access to clinical and laboratory materials, and financial means for implementation and sustainability.

More Steps to Help Prevent Cervical Cancer

These things may also help lower your risk for cervical cancer:

If you are 26 or younger, get an HPV vaccine if you haven't been vaccinated already.

Don't smoke.

Use condoms during sex.

HPV infection can occur in both male and female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered. While the effect of condoms in preventing HPV infection is unknown,

condom use has been associated with a lower rate of cervical cancer.^[19,20]

CONCLUSION

The disease burden of cervical cancer has decreased significantly in developed countries and regions in last decades, however it is still serious in less developed countries and regions, and effective preventive measures in these areas still face serious challenges. At present, there are various available prevention and control measures that are cost-effective and scientific evidence-based to meet the needs of areas with different economic levels. It is gratifying to note that the globe has achieved a strategic consensus on the elimination of cervical cancer and also has developed and released the global strategy to accelerate the elimination of cervical cancer. Although the global elimination of cervical cancer has a long way to go, it is believed that through large-scale continuous promotion and widely use of existing effective prevention and control measures, cervical cancer will become the first cancer eliminated by human beings.^[50]

REFERENCES

1. Stelzle, D., Tanaka, L. F., Lee, K. K., Ibrahim Khalil, A., Baussano, I., Shah, A. S. V., ... Dalal, S. (2021). Estimates of the global burden of cervical cancer associated with HIV. *The Lancet Global Health*, 9(2): e161–e169. Doi: 10.1016/s2214-109x(20)30459-9.
2. Konno, R., Sagae, S., Yoshikawa, H., Basu, P. S., Hanley, S. J. B., Tan, J. H. J., & Shin, H.-R. (2010). Cervical Cancer Working Group Report. *Japanese Journal of Clinical Oncology*, 40(Supplement 1): i44–i50. doi:10.1093/jjco/hyq126.
3. If You Have Cervical Cancer | Cervical Cancer Short Guide | American Cancer Society.
4. Burd, E. M. (2003). Human Papillomavirus and Cervical Cancer. *Clinical Microbiology Reviews*, 16(1): 1–17. doi:10.1128/cmr.16.1.1-17.2003.
5. Waggoner, S. E. (2003). Cervical cancer. *The Lancet*, 361(9376): 2217–2225. Doi: 10.1016/s0140-6736(03)13778-6.
6. Mohar, A., & Frias-Mendivil, M. (2000). Epidemiology of Cervical Cancer. *Cancer Investigation*, 18(6): 584–590. Doi: 10.3109/07357900009012198.
7. Cervical Cancer, Risk, and Epidemiology
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<https://doi.org/10.32539/bsm.v5i7.32>.
8. Chin J Cancer Res, 2020 Dec 31; 32(6): 720–728. Doi: 10.21147/j.issn.1000-9604.2020.06.05.
9. Johnson, C. A., James, D., Marzan, A., & Armaos, M. (2019). Cervical Cancer: An Overview of Pathophysiology and Management. *Seminars in Oncology Nursing*. doi:10.1016/j.soncn.2019.02.003.

10. What are the risk factors for cervical cancer? | Cancer Australia.
11. HPV and Cancer - NCI.
12. Cervical Cancer Causes, Risk Factors, and Prevention - PDQ Cancer Information Summaries - NCBI Bookshelf (nih.gov), PMID: 26389339.
13. Risk factors for cervical cancer | Canadian Cancer Society.
14. Castle, P. E., Meyers, C., Alam, S., & Conway, M. J. (2008). How Does Tobacco Smoke Contribute to Cervical Carcinogenesis? *Journal of Virology*, 82(12): 6084– 6086. doi:10.1128/jvi.00103-08.
15. Diethylstilboestrol (DES) Exposure and Cancer - NCI.
16. Cervical cancer (who.int).
17. Human Papillomavirus (HPV) Vaccines - NCI (cancer.gov).
18. Sankaranarayanan, R. (2015). HPV vaccination: The most pragmatic cervical cancer primary prevention strategy. *International Journal of Gynaecology & Obstetrics*, 131, S33–S35. doi:10.1016/j.ijgo.2015.02.014.
19. Reducing Risk for Cervical Cancer | Cervical Cancer | CDC.
20. Cervical Cancer Worldwide Mailinh Vu MD, Jim Yu DO, Olutosin A. Awolude MBBS, MSc, FWACS, Linus Chuang MD, MPH, MS PII: S0147-0272(18)30134-X DOI: 10.1016/j.cuprproblcancer.2018.06.003 Reference: YMCN 407.
21. Cervical Cancer Symptoms | Signs of Cervical Cancer | American Cancer Society.
22. Cervical Cancer Symptoms - NCI.
23. Cervical cancer - Diagnosis and treatment - Mayo Clinic.
24. Cervical Cancer Tests | How to Test for Cervical Cancer | American Cancer Society.
25. Smith, T. (2000). Colposcopy. *Nursing Standard*, 15(4): 47–52. 10.7748/ns2000.10.15.4.47.c2930.
26. Colposcopy - Mayo Clinic.
27. The Pap (Papanicolaou) Test | Cervical Cancer Screening Test | American Cancer Society.
28. <https://www.healthline.com/health/pap-smear>.
29. <https://www.webmd.com/women/pap-smear>.
30. <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosisstaging/screening-tests/hpv-test.html>.
31. <https://www.verywellhealth.com/cone-biopsy-cervical-surgery-513839>.
32. <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/howdiagnosed.html>.
33. <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/howdiagnosed.html>.
34. <https://www.verywellhealth.com/cervical-cancer-stages-5218308>.
35. <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosisstaging/staged.html>.
36. Fader, A. N. (2018). Surgery in Cervical Cancer. *New England Journal of Medicine*. Doi: 10.1056/nejme1814034.
37. <https://www.cancer.org/cancer/types/cervical-cancer/if-you-have-cervical-cancer.html>.
38. Wolfsan, A. H. (1999). Conventional radiation therapy of cervical cancer. *Seminars in Surgical Oncology*, 16(3): 242–246. Doi: 10.1002/(sici)1098-2388(199904/05)16:3<242::aidssu9>3.0.co; 2-r.
39. <https://www.radiologyinfo.org/en/info/cervical-cancer-therapy>.
40. <https://www.everydayhealth.com/cancer/cervical-cancer-treatment/>.
41. <https://cancer.ca/en/cancer-information/cancer-types/cervical/treatment/chemotherapy>.
42. <https://www.macmillan.org.uk/cancer-information-and-support/treatments-anddrugs/chemotherapy-for-cervical-cancer>.
43. <https://www.cancerresearchuk.org/aboutcancer/cervicalcancer/treatment/chemoradiotherapy/side-effects>.
44. <https://www.cancer.org/cancer/types/cervical-cancer/treating/targeted-therapy.html>.
45. Vora, C., & Gupta, S. (2019). Targeted therapy in cervical cancer. *ESMO Open*, 3(Suppl 1): e000462. Doi: 10.1136/esmoopen-2018-000462.
46. Kotsopoulos, I. C., Kucukmetin, A., Mukhopadhyay, A., Lunec, J., & Curtin, N. J. (2016). Poly (ADP-Ribose) Polymerase in Cervical Cancer Pathogenesis. *International Journal of Gynecological Cancer*, 26(4): 763–769. doi:10.1097/igc.0000000000000654.
47. <https://cancer.ca/en/cancer-information/cancer-types/cervical/treatment/immunotherapy>.
48. <https://www.cancerresearch.org/cancer-types/cervical-cancer>.
49. <https://www.verywellhealth.com/immunotherapy-side-effects-7965106>.
50. Chin J Cancer Res, 2020 Dec 31; 32(6): 720–728. Doi: 10.21147/j.issn.10009604.2020.06.05.