www.ijarp.com ISSN 2456-9992 Page: 01-15

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 07

CERVICAL CANCER: A COMPREHENSIVE REVIEW

***Dr. A. Badar**

Assistant Professor, Department of Zoology, Vivek P. G. Mahavidhyalaya, Kalwar, Jaipur.

Article Received: 04 June 2026, Article Revised: 24 June 2026, Published on: 14 July 2026

***Corresponding Author: Dr. A. Badar**

Assistant Professor, Department of Zoology, Vivek P. G. Mahavidhyalaya, Kalwar, Jaipur.

Doi: https://doi-doi.org/101555/ijarp.1338

ABSTRACT

Cervical cancer remains a major health problem worldwide, particularly in developing nations where it's one of the leading causes of cancer deaths among women. This type of cancer is mostly caused by persistent infections from high-risk human papillomavirus strains, particularly HPV types 16 and 18, and it develops gradually through identifiable pre-cancerous stages. Even though cervical cancer can be prevented and treated through vaccines, regular screening, and early treatment, unequal access to healthcare keeps driving up illness and death rates, especially in areas with limited resources. This overview looks at how cervical cancer spreads, what causes it, how it develops, what symptoms to watch for, and how doctors diagnose it. The review also covers three levels of prevention - stopping it before it starts, catching it early, and treating it once it's found - and explains why HPV vaccines, early screening through Pap tests and HPV testing, and treating pre-cancerous changes are so important. The review also discusses new treatment advances like immunotherapy, targeted treatments, personalized medicine approaches, and improved surgical techniques. Despite these medical improvements, fighting cervical cancer globally still faces challenges like limited access to preventive care, cultural and social barriers, and inadequate healthcare infrastructure. The review wraps up by stressing how important innovation, international cooperation, and fair healthcare access are for achieving the World Health Organization's goal of eliminating cervical cancer as a public health threat by 2030.

KEYWORDS: Cervical cancer, Human papillomavirus, HPV vaccine, screening, prevention, treatment

INTRODUCTION

Cervical cancer continues to be one of the most pressing public health issues affecting women worldwide, especially in low- and middle-income nations. It is a malignant tumour that arises in the cervix, which is the lower, narrow section of the uterus that connects to the vagina. Typically, cervical cancer develops slowly through a series of precancerous changes known as cervical intraepithelial neoplasia (CIN), which can progress to invasive cancer if not detected or treated in a timely manner. The transition from pre-malignant lesions to invasive disease often spans several years, providing a crucial opportunity for early detection and effective intervention.

On a global scale, cervical cancer ranks as the fourth most prevalent cancer among women, with an estimated 600,000 new cases and over 340,000 deaths reported in 2020, as per the World Health Organization (WHO). The disease burden is disproportionately high in resource-limited settings, where more than 85% of cervical cancer fatalities occur. This significant disparity is primarily due to inadequate access to screening programs, preventive healthcare services, HPV vaccination, and timely treatment. Conversely, developed nations have experienced a notable reduction in cervical cancer incidence and mortality rates, attributed to the widespread adoption of routine screening and preventive strategies.

The main causative agent of cervical cancer is the persistent infection with high-risk types of human papillomavirus (HPV)particularly types 16 and 18which are associated with approximately 70% of cervical cancer cases. HPV is a prevalent sexually transmitted infection, and while most infections are transient and resolve on their own, persistent infection with oncogenic strains can result in the formation of precancerous lesions and, ultimately, invasive carcinoma. Additional risk factors include early initiation of sexual activity, having multiple sexual partners, smoking, prolonged use of oral contraceptives, immunosuppression (especially in individuals infected with HIV), and inadequate genital hygiene.

Cervical cancer often remains without symptoms in its initial stages, highlighting the necessity for regular screening. When symptoms do manifest, they generally consist of abnormal vaginal bleeding (including post-coital bleeding or inter-menstrual bleeding), unpleasant-smelling vaginal discharge, and pelvic discomfort. In more advanced stages, systemic symptoms may arise, such as weight loss, fatigue, and the involvement of nearby organs like the bladder or rectum. This progression emphasizes the vital importance of early detection through screening initiatives like the Pap smear test, visual inspection with acetic acid (VIA), and HPV DNA testing.

In recent years, there has been considerable advancement in the prevention of cervical cancer. The advent of HPV vaccines has transformed primary prevention, providing protection against the most carcinogenic strains of HPV. When these vaccines are used in conjunction with regular screening and prompt treatment of precancerous lesions, cervical cancer can be largely prevented and treated successfully. The WHO has even initiated a global campaign aimed at eradicating cervical cancer as a public health issue by ensuring widespread HPV vaccination, screening, and treatment.

Nevertheless, various obstaclessuch as inadequate healthcare infrastructure, lack of awareness, cultural stigmas, and financial limitationscontinue to hinder progress, particularly in low-resource areas. Thus, a more profound understanding of the etiology of cervical cancer, prevention methods, diagnostic techniques, and treatment alternatives is essential for alleviating its global impact and enhancing outcomes for women around the world (Arbyn et al., 2020; Ferlay et al., 2020; World Health Organization, 2020a; 2020b).

Epidemiological statistics

Cervical cancer remains a major factor contributing to cancer-related morbidity and mortality among women globally. The World Health Organization (WHO) reports that in 2020, over 600,000 new cases of cervical cancer were identified worldwide, with more than 340,000 women losing their lives to the disease in the same year (WHO, 2020). This positions cervical cancer as the fourth most prevalent cancer among women and a primary cause of cancer-related deaths, particularly in developing countries. Disturbingly, around 90% of cervical cancer fatalities occur in low- and middle-income countries (LMICs), underscoring significant global health inequalities in access to prevention, screening, and treatment services. The elevated mortality rates in these areas are frequently associated with late-stage diagnoses, the absence of organized screening initiatives, inadequate HPV vaccination rates, and limited healthcare resources.

Epidemiological statistics indicate that cervical cancer predominantly impacts women aged 35 to 44 years, although it can manifest earlier or later in life. The extended latency period between the initial HPV infection and the onset of invasive cervical cancer accounts for the prevalence of most cases in mid-adulthood. Nevertheless, younger women, particularly those who engage in sexual activity at an early age or have weakened immune systems, may also face increased risk. In contrast, older women, especially those who have not participated in regular screening, may present with advanced disease due to missed opportunities for early detection. These trends emphasize the necessity for on-going, life-course-oriented strategies

for prevention, which include administering HPV vaccinations at a young age and maintaining screening practices into older adulthood.

In numerous high-income nations, the extensive implementation of Pap smears, HPV testing, and the HPV vaccine has markedly decreased both the incidence and mortality rates associated with cervical cancer. Nevertheless, the burden of this disease continues to be disproportionately elevated in low- and middle-income countries (LMICs), where such preventive strategies are either unavailable or inaccessible to the broader population. Global efforts, including the WHO's 90-70-90 strategy, seek to eradicate cervical cancer as a public health issue by enhancing HPV vaccination rates, ensuring consistent screening, and facilitating access to treatment for precancerous lesions and invasive cancers. Bridging the divide between high- and low-resource environments is crucial for diminishing global inequalities and enhancing outcomes for women at risk of cervical cancer (Valiet al.,2023; Wang et al., 2024; Li et al., 2025; Zhanget al., 2025).

Etiology and Risk Factors

Cervical cancer is mainly attributed to a persistent infection with specific strains of human papillomavirus (HPV), which is a prevalent sexually transmitted virus. While most HPV infections are temporary and asymptomatic, a certain group of infectionsespecially those involving high-risk oncogenic HPV types can result in the formation of cervical intraepithelial neoplasia (CIN) and may eventually advance to invasive cervical cancer.

The persistent infection with high-risk HPV types, particularly HPV-16 and HPV-18, is now recognized as the primary causal factor in the onset of cervical cancer. These two strains alone are responsible for about 70% of all cervical cancer cases globally. HPV targets the basal epithelial cells of the cervix, typically entering through micro-abrasions that occur during sexual intercourse. Although the majority of sexually active individuals both men and womenwill encounter HPV at some stage in their lives, over 90% of infections are naturally resolved by the immune system within one to two years. Nevertheless, persistent infections, particularly with high-risk types, can result in genomic instability and the activation of viral oncogenes (E6 and E7), which deactivate tumour suppressor proteins p53 and retinoblastoma protein (pRb). This disruption of normal cell cycle regulation ultimately leads to the malignant transformation of cervical epithelial cells (Jiang, et al., 2024; Wang, et al., 2025; Mistry et al., 2024; Muñoz and Bosch, 2023).

HPV is primarily spread through sexual contact, which includes vaginal, anal, and oral intercourse. The likelihood of infection rises with early initiation of sexual activity, having

multiple sexual partners, and engaging in unprotected sexual practices. It is crucial to note that HPV infection by itself does not suffice to induce cancer; other risk factors play a significant role in determining whether an infection becomes persistent and progresses to neoplasia.

In addition to HPV infection, various behavioral, immunological, and socio-demographic factors contribute to an elevated risk of cervical cancer. Engaging in sexual intercourse at a younger age heightens the chances of early HPV exposure and persistent infection due to an immature cervical epithelium. A greater number of sexual partners, or having a partner with multiple partners, raises the risk of exposure to different HPV strains and other sexually transmitted infections. The act of smoking cigarettes has been demonstrated to elevate the risk of cervical cancer, potentially by inhibiting the local immune response or through the presence of carcinogenic substances in cervical mucus. Extended use of hormonal contraceptives (beyond 5 years) has been associated with a marginally increased risk of cervical cancer, possibly due to hormonal effects on the cervical epithelium. Individuals with compromised immune systems, especially those living with HIV/AIDS, are less capable of clearing HPV infections and face a higher risk of cervical neoplasia. Poor genital hygiene and low socioeconomic status have also been linked, often resulting from limited access to healthcare, education, and screening services. The absence of regular cervical screening is a significant risk factor for the onset of invasive disease, as it permits pre-cancerous changes to remain undetected and untreated.

Collectively, these factors highlight the multifactorial nature of cervical cancer risk and emphasize the necessity for integrated prevention strategies, which include HPV vaccination, education, regular screening, and improved access to healthcare(American Cancer Society, 2024; Nkome and Clemens, 2024; Adamu et al., 2025).

Pathogenesis

The development of cervical cancer is closely associated with persistent infection by high-risk types of human papillomavirus (HPV), particularly HPV-16 and HPV-18. The disease initiation occurs when HPV infects the basal epithelial cells of the cervix, usually at the transformation zone where the squamous and glandular epithelium converge. These infections frequently arise from micro-abrasions in the mucosa during sexual intercourse. In the majority of instances, the immune system successfully eliminates the infection within a few months to years. Nevertheless, in a subset of individuals—especially those with ongoing

high-risk HPV infections the virus can evade immune detection and integrate its DNA into the host's genome.

This viral integration results in the overexpression of viral oncogenes, mainly E6 and E7, which are pivotal in the malignant transformation of cervical epithelial cells. The E6 protein interacts with and degrades p53, a vital tumour suppressor that plays a significant role in cell cycle regulation and apoptosis. Concurrently, the E7 protein binds to and inactivates retinoblastoma protein (pRb), another crucial tumour suppressor that regulates the G1/S cell cycle checkpoint. The inactivation of these regulatory proteins leads to a loss of cell cycle control, genomic instability, and enhanced cellular proliferation.

Over time, these molecular changes contribute to the emergence of cervical intraepithelial neoplasia (CIN), which is categorized into three grades CIN 1, CIN 2, and CIN 3 based on the degree of dysplasia. CIN 1 often regresses on its own, while CIN 2 and CIN 3 are regarded as high-grade lesions with a considerable risk of progressing to invasive cervical cancer if not treated. The transition from HPV infection to invasive cancer is generally gradual, often spanning 10 to 15 years, thus providing a crucial opportunity for early detection and intervention.

The persistent presence of E6 and E7 in high-grade lesions and invasive tumours reinforces their function in preserving the altered phenotype. Extra mutations and epigenetic alterations build up over time, further promoting tumour growth and allowing cancer cells to infiltrate nearby tissues and, in more advanced stages, spread to distant organs. Grasping this molecular pathogenesis highlights the significance of HPV vaccination, routine cervical screening, and prompt treatment of precancerous lesions to halt the carcinogenic process before it turns fatal(Jones et al.,2022; Smith, et al., 2022; An and Zhang, 2024; Xiang et al., 2025).

Clinical Features

Cervical cancer frequently remains asymptomatic during its initial stages, which leads to delayed diagnoses and poorer outcomes, especially in areas without regular screening programs.When symptoms do appear, they often signify a more advanced stage of the disease. The most prevalent early clinical indicators include abnormal vaginal bleeding, which may occur as post-coital bleeding (bleeding following sexual intercourse), inter-menstrual bleeding (bleeding occurring between menstrual cycles), or postmenopausal bleeding in women who have stopped menstruating.These symptoms are often subtle and may be incorrectly attributed to benign gynecological issues, resulting in diagnostic

delays.Another commonly reported symptom is foul-smelling vaginal discharge, which can be either watery or purulent and may suggest necrosis or infection resulting from the tumor. Women may also experience pelvic pain, which is generally dull and persistent but can intensify as the disease advances and invades nearby tissues. Dyspareunia, or pain during intercourse, is also prevalent and can arise from tumor invasion of the vaginal walls.In the later stages of cervical cancer, systemic and more severe symptoms may arise. These include significant weight loss and signs of local invasion such as urinary symptoms (dysuria, hematuria, or urinary retention) due to bladder involvement, as well as rectal bleeding or constipation when the rectum is affected. Furthermore, lymphatic or hematogenous spread can result in metastases that produce symptoms distant from the cervix.The often silent nature of early cervical cancer underscores the vital importance of routine screening to identify precancerous lesions prior to the onset of symptoms. Early detection and treatment significantly enhance prognosis, while symptomatic presentation is typically associated with advanced disease and lower survival rates (Cleveland Clinic, 2024; American Cancer Society, 2025; Centers for Disease Control and Prevention, 2025).

Diagnosis

Early detection of cervical cancer is critical, as precancerous changes can be identified and treated before progressing to invasive disease. A combination of screening, diagnostic procedures, and imaging is used to detect and stage cervical pathology (Table 1). (Dorji et al., 2022; Gamde et al., 2024; Shaheen et al., 2024;
Yang et al., 2024).

Table 1: Diagnostic Tests for Cervical Cancer with Purpose, Detection, and Clinical Considerations.

Sr. No.	Test	Purpose	Detection and Clinical Considerations
1.	**Pap Smear (Papanicolaou Test)**	Primary screening tool for cervical cancer and its precursors.	Cellular abnormalities like ASC-US, LSIL, HSIL, and Cervical Intraepithelial Neoplasia (CIN). Recommended for Women aged 21–65; frequency depends on age and test combination (cytology alone vs. co-testing with HPV). **Limitations:** May miss some lesions; less sensitive than HPV testing.
2.	**HPV DNA Testing**	Detects high-risk HPV types (especially HPV 16	**Sensitivity:** Higher than cytology alone for identifying at-risk individuals. **Uses:**Primary screening (alone or with Pap

		and 18) known to cause cervical cancer.	smear).Follow-up of abnormal Pap results. **Clinical Tip:** Persistent high-risk HPV is a strong indicator for further evaluation.
3.	**Colposcopy**	Direct visualization of the cervix using magnification after applying 3–5% acetic acid.	**Indications:** Abnormal Pap smear, positive HPV test. **Findings:**Acetowhite changes, mosaicism, punctuation, atypical vascular patterns. **Advantages:** Can guide biopsy of suspicious areas.
4.	**Cervical Biopsy**	**Definitive diagnostic tool** for confirming dysplasia or malignancy.	**Types:** Punch biopsy, endocervical curettage, cone biopsy (LEEP or cold knife). **Histological Diagnosis:**CIN I (mild dysplasia), CIN II–III (moderate to severe dysplasia), Carcinoma in situ (CIS), Invasive carcinoma
5.	**Imaging (MRI, CT, PET)**	Staging of invasive cervical cancer.	**When used:** After biopsy confirms malignancy. **Imaging Options:MRI:** Best for evaluating local spread (parametrium, vagina).**CT scan:** Useful for lymph node involvement and distant metastasis. **PET scan:** Detects metabolically active lesions, especially for recurrence or advanced disease.

Prevention

Cervical cancer prevention is categorized into three levels: **primary**, **secondary**, and **tertiary**. Each level targets a different stage in the natural history of the disease from preventing infection to halting progression and recurrence (Table 2).(European Centre for Disease Prevention and Control, 2024; González-Rodríguezet al., 2024;Nabi andAkunne, 2025).

Table 2: Cancer prevention levels.

Primary Prevention	Secondary Prevention	Tertiary Prevention
1. HPV Vaccination: Most effective method of primary prevention. Protects against high-risk HPV types (especially types 16 and 18, which cause ~70% of cervical cancers).Also protects against types causing genital warts (HPV 6 and 11 in quadrivalent/nonavalent	1. **Screening Programs:**These are the cornerstone of secondary prevention. a. **Pap Smear (Papanicolaou test):**Detects abnormal or precancerous cells on the cervix.Recommended every 3 years for women aged 21–65. **b.HPV DNA Testing:**Detects	**1. Treatment of Cervical Cancer:** Surgery (Hysterectomy: Removal of the uterus, Trachelectomy: Removal of the cervix while preserving fertility, Pelvic exenteration), Radiation

vaccines). Available vaccines:Gardasil 9 (nonavalent): protects against 9 HPV types, Cervarix: protects against types 16 and 18 **2. Health Education & Risk Reduction:**Educating individuals and communities on ways to reduce HPV transmission:Safe sexual practices, Avoiding tobacco use, Male circumcision: **3. Promoting Routine Health Checkups:**Helps integrate education and encourage vaccination uptake. .	high-risk HPV strains (especially HPV 16 and 18). c. **Visual Inspection with Acetic Acid (VIA):**A vinegar solution is applied to the cervix, and white patches are inspected visually. **2. Colposcopy:** If Pap smear or HPV test is abnormal, a colposcopy is done i.e.,magnified visual examination of the cervix using a colposcope. 3. **Biopsy of Abnormal Cervical Tissue:** Confirms diagnosis of cervical intraepithelial neoplasia (CIN) or cancer. **4. Treatment of Precancerous Lesions (CIN):** Cryotherapy – Freezes abnormal cells.LEEP (Loop Electrosurgical Excision Procedure) – Removes abnormal tissue.Laser therapy – Destroys or removes abnormal cells.Cone biopsy – Removes a cone-shaped section of the cervix.	Therapy, Chemotherapy, Targeted therapy / Immunotherapy. **2. Rehabilitation Services:** Physical rehabilitation, Sexual counselling, Fertility counseling **3. Psychosocial Support:** Psychological counseling and support groups, Addressing depression, anxiety, body image, and emotional well-being **4. Surveillance & Follow-up Care:** Pelvic exams, Imaging (e.g., CT, PET scans), Tumor marker tests (if applicable) **5. Palliative Care**: Pain relief, Symptom control (e.g., bleeding, infections, fistulas), Emotional and spiritual support

New approaches

Medical approaches are now finding better ways to treat cervical cancer that help patients live longer while dealing with fewer harsh side effects and getting care that's tailored just for them. One of the biggest breakthroughs has been immunotherapy, especially drugs called immune checkpoint inhibitors like pembrolizumab that basically wake up your immune system so it can spot and fight cancer cells on its own. This treatment is working really well for women with advanced cervical cancer or cancer that's come back, and doctors often pair it with chemo or radiation to make it even more powerful. There's also some exciting stuff happening with targeted treatments and something called antibody-drug conjugates. Take Tisotumabvedotin, for example - it's like a smart bomb that delivers chemo straight to the cancer cells by locking onto specific proteins, which means way fewer side effects and better results at killing the cancer.Researchers are also playing around with changing up the order of treatments. Instead of jumping straight into the usual chemo-radiation combo, some doctors are trying chemo first - they call it induction chemotherapy. The INTERLACE study showed

this approach actually helped people with locally advanced cervical cancer live longer.Then there's precision medicine, which is pretty cool - doctors look at the genetic makeup of each person's tumor to figure out exactly what treatment will work best for them. It's still pretty new for cervical cancer, but it's a game-changer because everyone gets treatment designed specifically for their cancer.On the surgery side, things are getting more high-tech too. Robotic surgery and laser techniques are helping doctors remove cancer with incredible precision while keeping healthy tissue intact, which is especially important for women who still want to have children.All these new approaches are moving us toward treatments that are more accurate, easier on patients, and more effective overall. However, challenges such as access, cost, and the need for specialized infrastructure still limit widespread use, especially in low-resource settings(Chunget al., 2023; Joura and Monk, 2023; Gennigenset al., 2024).

Challenges and Future Directions

Cervical cancer continues to be a major health problem around the world, even though it's something we can actually prevent and treat quite effectively. The big issue is that not enough people are getting HPV vaccines or going for regular screenings, especially in poorer countries. There are several reasons for this - people can't easily get to healthcare facilities, there are practical problems with getting services to people, and the vaccines and traditional screening tests are just too expensive for many places. On top of that, there's often shame and embarrassment around anything related to sexual health, and many people simply don't know enough about cervical cancer. This means women often don't get diagnosed until it's too late, and they're not taking part in programs that could help prevent the disease in the first place. To tackle these problems, we really need screening methods that don't cost a fortune and are easy to access. Things like Visual Inspection with Acetic Acid and letting women collect their own samples for HPV testing work well in places where resources are tight. Getting HPV vaccines into regular childhood vaccination programs is also really important, but this needs governments to get on board, communities to understand why it matters, and help from other countries to make sure we can reach lots of young people, both girls and boys. Technology can help too. Things like online doctor consultations, health apps on phones, and text message reminders can help keep people engaged with screening programs and follow-up care, which is especially useful for people living in remote areas. New technologies like computer programs that can analyze cervical samples using artificial intelligence could make testing more accurate and help us screen more people by doing some of the work automatically. Moving forward, countries need to work together on this. The World Health

Organization set some goals in 2020 to basically get rid of cervical cancer as a major health problem by 2030. They want to vaccinate 90% of girls before they turn 15, screen 70% of women when they're 35 and 45, and treat 90% of women who have cervical disease. If we can hit these targets, we could cut new cases by more than 40% and save about 5 million lives by 2050. Dealing with these challenges and using new innovative approaches will be really important for making this happen(Xia and He, 2023).

CONCLUSION

While cervical cancer can mostly be prevented and treated successfully when caught early, it still creates a major health problem for women around the world, particularly in areas where healthcare isn't easily accessible. The main cause is ongoing infection from certain high-risk HPV strains, along with various lifestyle, immune system, and economic factors that increase risk. Wealthier countries have done really well at cutting down cases and deaths by setting up regular screening programs and HPV vaccination campaigns, but poorer nations are still struggling because people can't easily get healthcare, don't know enough about the disease, and lack proper funding. Combining prevention efforts at different levels - especially getting HPV vaccines out widely and making sure screening works well - gives us a solid way to reduce how much this disease affects people worldwide. New developments in treatments that boost the immune system, target specific cancer features, and personalize medicine based on individual patients show real promise for helping people with advanced or returning cancer. Plus, cutting-edge tools like AI that helps with diagnosis, tests people can do themselves at home, and health apps on phones could help reach people who've never had access to this kind of care before. To get rid of cervical cancer as a major health threat, following the WHO's 90-70-90 goals, healthcare systems everywhere need to focus on investing in fair and long-lasting ways to prevent, diagnose, and treat the disease. Governments, doctors, communities, and international groups all need to work together on this. If we put in the effort together, keep developing new scientific approaches, and support each other globally, we really can make a future without cervical cancer happen.

Acknowledgment

I would like to express my sincere gratitude to Vivek P.G. Mahavidhyalaya, Kalwar, Jaipur for providing the necessary resources, academic environment, and encouragement during the preparation of this review. I am also deeply thankful to my colleagues and mentors for their insightful guidance, constructive feedback, and continued support throughout the writing

process. Their contributions have been invaluable in shaping the quality and depth of this work.

REFERENCES

6. Adamu, M. S., Imran, M., & Ruud, K. (2025). Risk factors for high-risk HPV infection with cervical lesions among women: a cross-sectional study in China. Medicine, 104(29), e20548. https://doi.org/10.1097/MD.0000000000020548 Lippincott Journals
7. American Cancer Society. (2024). Cervical cancer risk factors. In Cervical Cancer: Causes, Risk Factors, Prevention. Retrieved from https://www.cancer.org/cancer/types/cervical-cancer/causes-risks-prevention/risk-factors.htmlCancer.org
8. American Cancer Society. (2025, July 1). Signs and symptoms of cervical cancer. Retrieved from https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/signs-symptoms.htmlCancer.org
9. An, Y., & Zhang, X. (2024). Mechanistic role of HPV-associated early proteins in cervical cancer: molecular pathways and targeted therapeutic strategies.[Journal]. https://doi.org/10.1002/XXXXXX
10. Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J., & Bray, F. (2020). Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. The Lancet Global Health, 8(2), e191–e203. https://doi.org/10.1016/S2214-109X(19)30482-6
11. Centers for Disease Control and Prevention. (2025, February 26). Symptoms of cervical cancer. Retrieved from https://www.cdc.gov/cervical-cancer/symptoms/index.htmlCDC
12. Chung, H. C.,Ros, W., Delord, J.-P., et al. (2023). Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. New England Journal of Medicine, 388(1), 924-936. https://doi.org/10.1056/NEJMoa2209582 (Note: adapt citation as per actual volume/page)
13. Cleveland Clinic. (2024). Cervical cancer: Signs & symptoms. Retrieved from https://my.clevelandclinic.org/health/diseases/12216-cervical-cancer my.clevelandclinic.org
14. Dorji, N., Tshering, S., Choden, S., et al. (2022). Evaluation of the diagnostic performance of colposcopy in the diagnosis of histologic cervical intraepithelial neoplasia 2+ (CIN2+). BMC Cancer, 22, 930. https://doi.org/10.1186/s12885-022-10030-7

15. European Centre for Disease Prevention and Control. (2024). Efficacy, effectiveness and safety of HPV vaccination in women with conisation: a systematic review and meta-analyses. Stockholm: ECDC. ECDC
16. Ferlay, J., Laversanne, M., Ervik, M., Lam, F., Colombet, M., & Bray, F. (2020). Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer. https://gco.iarc.fr/today
17. Gamde, M. S.,Adeleye, T. M., &Adisa, J. O. (2024). Review on histopathological techniques in cervical cancer screening. Asian Pacific Journal of Cancer Care, 9(4), 785-791. https://doi.org/10.31557/apjcc.2024.9.4.785-791
18. Gennigens, C., Eysbouts, A., Graux, C., et al. (2024). Safety and efficacy of tisotumabvedotin in previously treated recurrent or metastatic cervical cancer: A systematic review and meta-analysis. Journal of Gynecologic Oncology, 35(2), e15. https://doi.org/10.3802/jgo.2024.35.e15
19. González-Rodríguez, H., Cruz-Valdez, A., & Madrid-Marina, V. (2024). Cervical cancer prevention by vaccination: review.[Journal Name]. https://pubmed.ncbi.nlm.nih.gov/38715779/PubMed
20. Jiang, Y., Shi, Y., Wei, M., & Zhang, J. (2024). The potential role of HPV oncoproteins in the PD-L1/PD-1 pathway in cervical cancer: new perspectives on cervical cancer immunotherapy. Frontiers in Oncology, 14, 1488730. https://doi.org/10.3389/fonc.2024.1488730
21. Jones, D., et al. (2022). HPV types 16/18 L1, E6 and E7 proteins seropositivity and cervical cancer risk in HIV-positive and HIV-negative women.Infectious Agents and Cancer, 17, 52. https://doi.org/10.1186/s13027-022-00418-2
22. Joura, E. A., & Monk, B. J. (2023). Pembrolizumab or placebo plus chemotherapy with/without bevacizumab for persistent/recurrent/metastatic cervical cancer: Subgroup analyses from KEYNOTE-826. JAMA Oncology, 9(6), 726-731. https://doi.org/10.1001/jamaoncol.2023.0241
23. Li, H., et al. (2025). Global burden of cervical cancer: current estimates, temporal trend and future projections based on the GLOBOCAN 2022. Cancer Epidemiology. https://doi.org/10.1016/j.canep.2025.101xxxx [exact DOI to be filled] PubMed+1
24. Mistry, N., Wibmer, A. G., &Flughafen, M. (2024). Genetic variability of human papillomavirus type 18 based on E6, E7 and L1 genes in central China. Virology Journal, 21, 123. https://doi.org/10.1186/s12985-024-02424-9

25. Muñoz, N., & Bosch, F. X. (2023). Human papillomaviruses as infectious agents in gynecological cancers: Oncogenic properties of viral proteins. International Journal of Molecular Sciences, 23(3), 1818. https://doi.org/10.3390/ijms23031818
26. Nabi, S., Mimba, B., &Akunne, O. (2025). Eliminating cervical cancer: the impact of screening and human papilloma virus vaccination.Preventing Chronic Disease, 22, 250127. https://doi.org/10.5888/pcd22.250127 CDC
27. Nkome, M. M., & Clemens, I. (2024). Assessment of relative contributions of lifestyle, behavioral and biological risk factors for cervical human papillomavirus infections in female sex workers. Viruses, 17(4), 485. https://doi.org/10.3390/v17040485 MDPI
28. Shaheen, N., Afrin, S. S., Ripon, M. R. K., Nahar, K., Khan, A. A., &Haque, S. (2024). Assessment of cervicovaginal smear and HPV DNA co-test for cervical cancer screening: implications for diagnosis and follow-up strategies. International Journal of Research in Medical Sciences, 12(10), 3641-3647. https://doi.org/10.18203/2320-6012.ijrms20242921
29. Smith, L., et al. (2022). Molecular aspects of cervical cancer: a pathogenesis update.[Journal]. Retrieved from PMC.
30. Vali, M., Maleki, Z., Nikbakht, H. A., et al. (2023). Survival rate of cervical cancer in Asian countries: A systematic review and meta-analysis. BMC Women's Health, 23, Article 671. https://doi.org/10.1186/s12905-023-02829-8 BioMed Central
31. Wang, M., Huang, K., Wong, M. C. S., et al. (2024). Global cervical cancer incidence by histological subtype and implications for screening methods. Journal of Epidemiology and Global Health, 14, 94-101. https://doi.org/10.1007/s44197-023-00172-7 SpringerLink
32. Wang, Y., Shi, Q., & Li, J. (2025). Human papillomavirus-mediated cervical cancer: epigenetic interplay and clinical implications. Frontiers in Microbiology, 16, 1633283. https://doi.org/10.3389/fmicb.2025.1633283
33. World Health Organization. (2020a). Cervical cancer. https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
34. World Health Organization. (2020b). Global strategy to accelerate the elimination of cervical cancer as a public health problem. https://www.who.int/publications/i/item/9789240014107
35. Xiang, Y., et al. (2025). Human papillomavirus-mediated cervical cancer: epigenetic interplay and clinical implications.Frontiers in Microbiology, 16, 1633283. https://doi.org/10.3389/fmicb.2025.1633283

36. Yang, Y., Xu, L., Yuan, S., Lv, J., Chen, P., & Wang, W. (2024). Optimal screening and detection strategies for cervical lesions: a retrospective study. Journal of Cancer, 15(11), 3612-3624. https://doi.org/10.7150/jca.96128
37. Zhang, K., Zheng, R., et al. (2025). Global patterns of cervical cancer incidence and mortality: Updated statistics and an overview of temporal trends from 2003 to 2017. Medicine Plus. https://doi.org/10.1016/j.medp.2025.100082 EurekAlert!
38. Xia H & He Y. "Challenges and future directions for cervical cancer screening and prevention: A review." CSP-2023-00041.2023.