Cancer Association of South Africa (CANSA)

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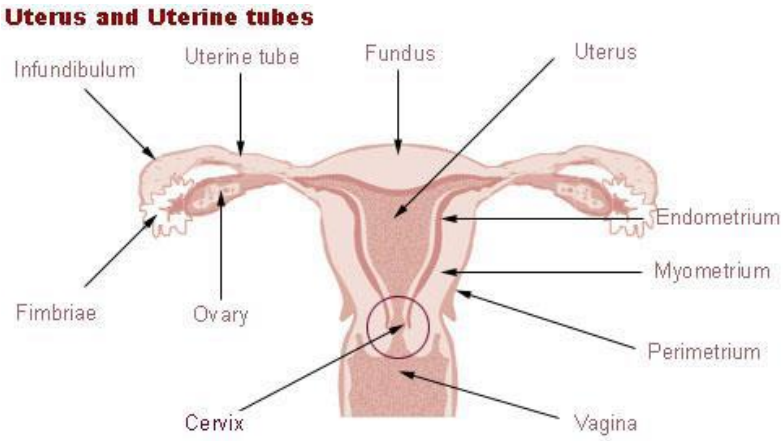
CANSA Fact Sheet on Cervical Cancer

Introduction

The cervix is the lower, narrow end of the uterus (the hollow, pear-shaped organ where a foetus can grow). The cervix leads from the uterus to the vagina (birth canal) below. The cervix is sometimes referred to as the *uterine cervix*. The part of the cervix closest to the body of the uterus is called the *endocervix*. The part next to the vagina is the *exocervix*.



[Picture credit: Female Reproductive System]

Worldwide, cervical cancer counts among the top five (5) female cancers in the world (Globocan statistics 2018). It is much less common in developed countries like the United States of America because of the routine use of Pap smears by most women.

The top five (5) female cancers, worldwide, are:

- Breast Cancer
- Colorectal Cancer
- Lung Cancer
- Cervical Cancer
- Thyroid Cancer.

Cervical cancer tends to appear during midlife. Over half of the women diagnosed are between the ages of 35 and 55. It rarely occurs in women under 20 and only 20% of the infected women are over 65 years of age (CervicalCancer.org).

Cervical Cancer

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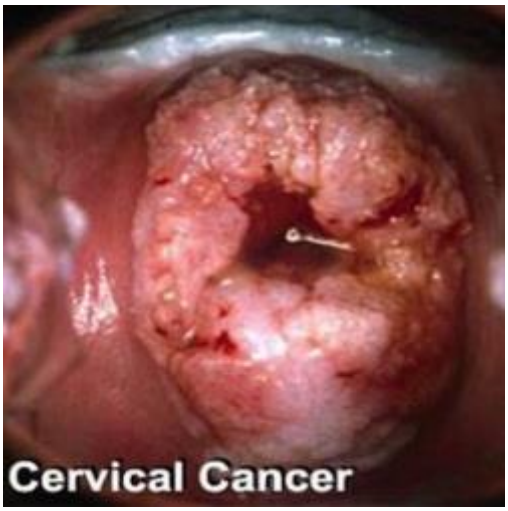
Cervical cancer is a malignant neoplasm arising from cells originating in the cervix. Cervical cancer is a disease in which cells in the cervix become malignant (cancerous). The two main types of cells covering the cervix are *squamous cells* (on the *exocervix*) and *glandular cells* (on the *endocervix*). The place where these two cell types meet is called the *transformation zone*. Most cancers start in the transformation zone of the cervix.

[Picture Credit: Cervical Cancer]



Cervical cancer is usually a slow-growing cancer that may not have immediate symptoms but can be found with regular Pap smear tests (a procedure in which cells are scraped from the cervix and looked at under a microscope). Cervical cancer is almost always caused by Human Papillomavirus (HPV) infection.

Cervical cancer starts as a pre-cancerous condition called dysplasia. This pre-cancerous condition can be detected by a Pap smear and is 100% treatable. That is why it is so important for women to get regular Pap smears done. Most women who are diagnosed with cervical cancer today have not had regular Pap smears or they have not followed up on abnormal Pap smear results.

Undetected pre-cancerous changes can develop into cervical cancer. From there is can spread to the bladder, intestines, lungs, and liver. It can take several years for pre-cancerous changes to turn into cervical cancer. Patients usually start experiencing problems when the cancer is already advanced and has spread.

Yadav, G., Srinivasan, G. & Jain, A. 2024.
"Cervical cancer poses a significant global public health issue, primarily affecting women, and stands as one of the four most prevalent cancers affecting woman globally, which includes breast cancer, colorectal cancer, lung cancer and cervical cancer. Almost every instance of cervical cancer is associated with infections caused by the human papillomavirus (HPV). Prevention of this disease hinges on screening and immunization of the patients, yet disparities in cervical cancer occurrence exist between developed and developing nations. Multiple factors contribute to cervical cancer, including sexually transmitted diseases (STDs), reproductive and hormonal influences, genetics, and host-related factors. Preventive programs, lifestyle improvements, smoking cessation, and prompt precancerous lesion treatment can reduce the occurrence of cervical cancer. The persistency and recurrence of the cases are inherited even after the innovative treatments available for cervical cancer. For patient's ineligible for curative surgery or radiotherapy, palliative chemotherapy remains the standard treatment. Novel treatment strategies are emerging to combat the limited effectiveness of chemotherapy. Nanocarriers offer the promise of concurrent chemotherapeutic drug delivery as a beacon of hope in cervical cancer research. The primary aim of this review study is to contribute to a thorough understanding of cervical cancer, fostering awareness and informed decision-making and exploring novel treatment methods such as nanocarriers for the treatment of cervical cancer. This manuscript delves into cutting-edge approaches, exploring the potential of nanocarriers and other innovative treatments. Our study underscores the critical need for global awareness, early intervention, and enhanced treatment options. Novel strategies, such as

nanocarriers, offer renewed optimism in the battle against cervical cancer. This research provides compelling evidence for the investigation of these novel therapeutic approaches within the medical field. Cervical cancer remains a formidable adversary, but with ongoing advancements and unwavering commitment, we move closer to a future where it is a preventable and treatable disease, even in the most underserved regions."

Conflict of interest statement

Declaration of Competing Interest There is no conflict of interest.

Crafton, S.M., Venkat, P.S. & Salani, R. 2024.

Purpose of review: To summarize the recent updates in cervical cancer from prevention and early detection to the management of early stage and recurrent disease as well as future areas of exploration.

Recent findings: The importance of the human papilloma virus vaccine and screening continue to make an impact in reducing the global burden of cervical cancer. In early-stage, low risk disease, new studies have demonstrated the role of less radical surgery with similar disease related outcomes. Efforts to improve outcomes in locally advanced cervical cancer have been reported. The incorporation of adjuvant chemotherapy, novel agents and checkpoint inhibitors, with the latter impacting disease free survival. In advanced/recurrent disease, the role of immunotherapy continues to make an impact and, in addition to recurrent disease, has now moved to the frontline for patients with programmed cell death ligand 1 expression. Tisotumab vedotin, an antibody drug conjugate, and other novel agents continue to be studied in this setting.

Summary: In this review, we discuss prevention measures and the outcomes of recent trials in all stages of cervical cancer. As therapies continue to evolve, ongoing trials and new areas of exploration will continue to identify opportunities to improve survival in cervical cancer.

Tumour Grade and Tumour Stage

Tumour grade and stage are terms used to describe the severity of a tumour, while tumour grade describes the appearance of cancerous cells in the tissue by examining them under a microscope.

Tumour stage encompasses:

- The location of the tumour.
- The size and/or extent of the original tumour.
- Whether cancer cells have spread to lymph nodes or anywhere else in the body.
- The number of tumours present.

Doctors use tumour grade, cancer stage, and a patient's age and general health to decide the course of treatment for the patient and determine prognosis. Prognosis describes all factors including the disease course, cure rate, chances of survival, and risk of recurrence of cancer.

What are the cancer stages?

Different systems of cancer staging are used to describe the types of cancer. Below is a common method in which stages are ranged from 0 to IV.

- Stage 0: The tumour is confined to its place of origin (in situ) and has not spread to nearby tissue.
- Stage I: The tumour is located only in the original organ, is small, and has not spread.
- Stage II: The size of the tumour is large but has not spread.
- Stage III: The tumour has become larger and may have spread to surrounding tissues and/or lymph nodes.
- Stage IV: The tumour has spread to other distant organs of the body, which is known as the metastasis stage.

TNM staging

Another common staging method used for cancer is the TNM system, which stands for tumour, node (which means spread of the tumour to lymph nodes), and metastasis. When a patient's cancer is staged using the TNM system, a number will be present along with the letter. This number signifies the extent of the disease in each category - tumour, node, and metastases.

Another system of cancer staging divides cancer into five stages, which include:

- In situ: Abnormal cells are present but have not spread to nearby tissue.
- Localized: Cancer is located only in the original organ and shows no sign of its spread.
- Regional: Cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant: Cancer has spread to distant parts of the body.
- Unknown: The stage cannot be figured out due to a lack of enough information.

What are the cancer grades?

Cancer grades are based on examination of the suspected tissue sample under a microscope. This involves surgically removing a piece of the suspected cancerous tissue and sending it to the lab for analysis. The entire procedure is known as a biopsy.

A doctor who specializes in diagnostic tests (pathologist) examines the cells of the tissue and determines whether they are harmless (benign or noncancerous) or harmful (malignant or cancerous). They describe the microscopic appearance of the cells and assign a numerical "grade" to most cancers.

Generally, a lower grade indicates slow-growing cancer and a higher grade indicates fast-growing cancer.

The most commonly used grading system is as follows:

- Grade I: Cancer cells that look like normal cells but are not growing rapidly.
- Grade II: Cancer cells that don't look like normal cells with their growth being faster than normal cells.
- Grade III: Cancer cells that look abnormal and have the potential to grow rapidly or spread more aggressively.

Sometimes, the following system can be used:

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well-differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

The International Classification of Diseases 10th version (ICD-10)

The International Classification of Diseases (ICD) is designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics. This includes providing a format for reporting causes of death on the death certificate.

ICD serves a broad range of uses globally and provides critical knowledge on the extent, causes and consequences of human disease and death worldwide via data that is reported and coded with the ICD. Clinical terms coded with ICD are the main basis for health recording and statistics on disease in primary, secondary and tertiary care, as well as on cause of death certificates. These data and statistics support payment systems, service planning, administration of quality and safety, and health services research. Diagnostic guidance linked to categories of ICD also standardizes data collection and enables large scale research.

For more than a century, the International Classification of Diseases (ICD) has been the basis for comparable statistics on causes of mortality and morbidity between places and over time. Originating in the 19th century, the latest version of the ICD, ICD-11, was adopted by the 72nd World Health Assembly in 2019 and came into effect on 1st January 2022.

The ICD-10 Code for malignant neoplasm: Cervix uteri, unspecified, is C53.9.

Incidence of Cervical Cancer in South Africa

According to the latest edition of the National Cancer Registry (2022) the following number of cervical cancer cases was histologically diagnosed in South Africa during 2022:

Group - Females 2022	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	7 499	1:41	16,41%
Asian females	102	1:97	6,45%
Black females	6 287	1:36	30,08%
Coloured females	510	1:59	9,79%
White females	600	1:55	2,97%

The frequency of histologically diagnosed cases of cervical cancer in South Africa for 2022 was as follows (National Cancer Registry, 2022):

Group - Females 2022	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	4	143	1 197	2 288	1 921	1 180	593	191

Asian females	**0**	**1**	**19**	**23**	**27**	**16**	**13**	**3**
Black females	**3**	**120**	**1 004**	**1 952**	**1 594**	**962**	**473**	**179**
Coloured females	**1**	**8**	**85**	**153**	**133**	**89**	**39**	**2**
White females	**0**	**14**	**89**	**160**	**167**	**113**	**50**	**7**

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Causes of Cervical Cancer

Almost all cervical cancers are caused by the Human Papilloma Virus (HPV). HPV is a common virus that is spread through skin-to-skin contact, body fluids and sexual intercourse. There are many different types of HPV. Some strains lead to cervical cancer. Other strains may cause genital warts, while others do not cause any problems at all.

Human Papillomavirus (HPV) is the most common sexually transmitted infection in the world. More than 100 HPV types have been identified, over 40 of which can infect the genital area. HPV types are classified by their association with cancer:

Non-oncogenic (low-risk HPV) – such as HPV 6 and HPV 11
It can cause:

- Benign or low-grade abnormalities of cervical cells
- Anogenital warts
- Recurrent Respiratory Papillomatosis – a disease of the respiratory tract

Ongonenic (high-risk HPV) – such as HPV 16 and HPV 18
It can cause:

- Intraepithelial neoplasia of the anogenital region
- Cervical cancer
- Vulva cancer
- Vaginal cancer
- Penile cancer
- Anal cancer
- Oropharyngeal cancers

Cervical cancer counts among the top five (5) cancers in women worldwide, with about 500 000 new cases and 250 000 deaths each year, according to the World Health Organization (WHO). Virtually all cases are linked to genital infection with HPV, the most common viral infection of the reproductive tract.

The top five (5) cancers are (Globocan 2018 statistics):

- Breast Cancer
- Colorectal Cancer
- Lung Cancer
- Cervical Cancer
- Thyroid Cancer

Li, N., Yi, H., Sun, W., Sundquist, J., Sundquist, K., Zhang, X., Zheng, D. & Ji. J. 2024.

"Human papillomavirus can be contracted by sexually active women. However, only a small proportion of these infections persist and have the potential to progress into cervical cancers, indicating a significant involvement of the immune system in cervical cancer development. Despite this, our understanding of the precise contributions of genes from different immune cell types in cervical cancers remains limited. Therefore, the primary objective of our study was to investigate the potential causal relationships between specific immune cell genes and the development of cervical cancers. By accessing expression quantitative trait loci datasets of 14 distinct immune cell types and genome wide association study of cervical cancers, we employed the summary data-based Mendelian randomization (SMR) along with multi-single nucleotide polymorphism (SNP)-based SMR to identify significant genes associated with cervical cancers. Colocalization analysis was further conducted to explore the shared genetic causality. A total of 10 genes across 11 immune cell types (26 significant gene-trait associations) were found to be associated with cervical cancers after false discovery rate correction. Notably, the ORMDL3, BRK1 and HMGN1 gene expression levels showed significant association with cervical cancer in specific immune cell types, respectively. These associations were supported by strong evidence of colocalization analyses. Our study has identified several genes in different immune cells that were associated with cervical cancer. However, further research is necessary to confirm these findings and provide more comprehensive insights into the association between these gene expressions and cervical cancer risk."

High and Low Risk Human Papilloma Viruses

Most people infected with HPV never develop any symptoms, however, there are a number of conditions that can result from an HPV infection.

HPV Research Scientists have separated HPV types into those that are more likely to develop into cancer and those that are less likely. The so-called 'high-risk' types are more likely to lead to the development of cancer, while 'low-risk' viruses rarely develop into cancer.

The sexually transmitted varieties of 'high-risk' HPV types include:

HPV-16	HPV-18	HPV-31	HPV-33	HPV-35	HPV-39
HPV-45	HPV-51	HPV-52	HPV-56	HPV-58	HPV-59
HPV-68	HPV-69				

A few other HPV types are also sometimes included on this list. These 'high-risk' HPV types cause growths that are usually flat and nearly invisible as compared to the warts caused by types HPV-6 and HPV-11. Up to 70% of cervical cancer cases are caused by HPV-16 and HPV-18.

'Low-risk' HPV types can cause no symptoms or may cause conditions such as genital warts, but do not cause cervical cancer. Warts can form weeks, months, or even years after sexual contact with a person who has genital HPV. It is also possible that warts may never appear. In fact, most people with 'low-risk' HIV types never know they are infected because they do not get warts or any other symptoms.

The following table lists various conditions along with their associated types of HPV:

Disease	HPV Type
Cervical cancer	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58
Precancerous changes	16, 18, 34, 39, 42, 55
Laryngeal papillomas	6, 11, 30
Genital Warts	6, 11, 30, 40, 41, 42, 43, 44, 45, 51, 54
Common warts	1, 2, 4, 26, 27, 29, 41, 57
Flat warts	3, 10, 27, 28, 41, 49
Plantar warts	1, 2, 4

CANSA's Position:

CANSA:

- is in favour of vaccinating all prepubescent girls against HPV.
- commends and requests the South African Government, National Department of Health, and National Department of Basic Education to continue the HPV vaccination programme started in 2014 whereby every girl in Grade 4 (9 years) to be vaccinated against HPV at no cost.
- CANSA further recommends that the HPV vaccination programme be extended to also include prepubescent boys as men are carriers of the HPV.

Signs and Symptoms of Common Gynaecologic Problems

Early on, cervical cancer may not cause signs and symptoms. Advanced cervical cancer may cause bleeding or discharge from the vagina that is not normal, such as bleeding after sex. If any of these signs are present, a medical doctor should be consulted. The cause may be something other than cancer, but the only way to know is to consult a medical doctor.

Gynaecologic Cancer Symptoms

Symptom	Cervical Cancer	Ovarian Cancer	Uterine Cancer	Vaginal Cancer	Vulva Cancer
Abnormal vaginal bleeding or discharge	▪	▪	▪	▪	
Pelvic pain or pressure		▪	▪		
Abdominal or back pain		▪			
Bloating		▪			
Having to pass urine often		▪		▪	
Itching or burning of the vulva					▪
Changes in vulva colour or skin such as a rash, sores or warts					▪

Risk Factors for Cervical Cancer

Even though HPV infection is the major cause of cervical cancer, several risk factors are linked to the development of cervical cancer.

Risk factors for cervical cancer include:

- Having sex at an early age
- Having many sexual partners
- Having first sexual intercourse at a young age
- Smoking tobacco products
- Using oral contraceptives
- Having a weakened immune system
- Poor economic status (may not be able to afford regular Pap smears or have limited access to screening services)
- Sexual partners who have multiple partners or who participate in high-risk sexual activity
- parity – HPV is less common among women with decreased parity
- women who smoke are more susceptible to cervical cancer than women who do not smoke
- failure to always use barrier methods during sexual intercourse, and
- ineffective management and treatment of sexually transmitted infections (STI's)
- Women whose mothers took the drug DES (diethylstilbestrol) during pregnancy in the early 1960's to prevent miscarriage

Urbute, A., Frederiksen, K., Thomsen, L.T., Kesmodel, U.S. & Kjaer, S.K. 2024.

Objective: Obesity is a known risk factor for many types of cancer. However, there is no clear evidence whether overweight and obesity increases the risk of cervical cancer. We investigated the association between body mass index (BMI) and detection of squamous and glandular cervical cancer and precancer.

Methods: Based on the Medical Birth Registry, we conducted a nationwide cohort study in Denmark of 384,559 women with BMI ≥18.5 kg/m^2 (pre-pregnancy BMI reported at the start of the pregnancy) having a cervical cytology screening at age 23-49 years within 5 years following the date of childbirth. The cohort was followed for 10 years from the first cervical cytology screening after the childbirth. We assessed absolute risks of cervical lesions according to BMI with the Aalen-Johansen estimator. We conducted Cox proportional hazards regression analyses to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Analyses were adjusted for age, calendar year, parity, oral contraception use, HPV vaccination, smoking, country of origin, and education.

Results: Overweight and obesity were associated with higher rates of cervical cancer (HR = 1.24, 95% CI 1.04-1.49 and HR = 1.14, 95% CI 0.91-1.43, respectively) and lower rates of cervical precancer detection (HR = 0.88, 95% CI 0.84-0.92 and HR = 0.67, 95% CI 0.63-0.71, respectively).

Conclusions: Higher than normal BMI was associated with higher incidence rates of cervical cancer and lower rates of precancer detection, emphasizing the importance of further research in possible mechanisms behind this association.

Conflict of interest statement

Declaration of Competing Interest: AU, LTT, USK and KF report no potential conflicts of interest. SKK has received research grants through her research institution from Merck.

Cottrell-Daniels, C., Hoogland, C.E., Fennell, B.S., Simmons, V.N., Vidrine, D.J. & Vidrine, J.I. 2024.

Introduction: Continued smoking following a cancer diagnosis is associated with poorer cancer treatment outcomes and survival times. Little is known about how cancer treatment status at the time of tobacco treatment enrollment impacts long-term smoking cessation outcomes. Using data

from a smoking cessation RCT, this study compared long-term cessation outcomes of women undergoing active treatment for cervical cancer at trial enrollment (n=40) to outcomes of women with a history of cervical cancer or cervical intraepithelial neoplasia (CIN) who were not undergoing active cancer treatment at enrollment (n=154).

Methods: Participants (n=194) were randomized to Standard Treatment (ST) or ST plus a 6-session Motivation And Problem Solving (MAPS) telephone counseling protocol (data collected: 2017-2021; analyzed: 2023). Sociodemographic differences between participants undergoing (versus not undergoing) active cancer treatment at enrollment were examined. Significant covariates were included in a logistic regression analysis comparing the 2 groups' smoking cessation outcomes at 12 months, the end of the tobacco treatment period.

Results: Participants in active cancer treatment at enrollment were significantly younger and less educated than those not in active cancer treatment. Race/ethnicity, relationship status, household income, nicotine dependence, and tobacco treatment condition did not vary by cancer treatment status. After adjusting for tobacco treatment condition, age, and education, being in active cancer treatment at the time of enrollment was associated with lower odds of abstinence at 12 months (5% vs 20%, aOR=0.22, 95% CI [0.05-0.998]).

Conclusions: Further research is necessary to identify and overcome barriers to abstinence among cancer survivors undergoing active treatment.

CANSA supports:

- all efforts to assist women to quit smoking or preferably never to start smoking
- promotion of the use of barrier methods during intercourse to prevent the spread of HPV and other sexually transmitted infections (STI's) including HIV
- the promotion of the postponement of sexual activity to older age
- the effective management and treatment of sexually transmitted infections (STI's) and
- decreasing parity.

Types of Cervical Cancer

There are two main types of cervical cancer: squamous cell carcinoma and adenocarcinoma. Each one is distinguished by the appearance of cells under a microscope.

- Squamous cell carcinomas begin in the thin, flat cells that line the bottom of the cervix. This type of cervical cancer accounts for 80 to 90 percent of cervical cancers.
- Adenocarcinomas develop in the glandular cells that line the upper portion of the cervix. These cancers make up 10 to 20 percent of cervical cancers.

Sometimes, both types of cells are involved in cervical cancer. Other types of cancer can develop in the cervix, but these are rare.

- Metastatic cervical cancer is cancer that has spread to other parts of the body.

Referral Criteria

For any primary health care service to operate effectively a referral system needs to be in place.

The referral system must make provision for:

- Clients with a normal Pap smear to be informed of their next Pap smear date
- Any client with a microscopically suspicious lesion, whatever the cytological result, should be referred for colposcopy

CANSA's Position:
CANSA supports the above referral criteria.

CANSA has an organised cervical screening programme that services many women in rural and previously disadvantaged areas in South Africa. This service is offered using mobile health clinics manned by professional nurses. They work in close collaboration with the National Department of Health (NDoH), National Health Laboratory Services (NHLS) and private laboratories on agreement.

Staging of Cervical Cancer

A very important factor in determining the prognosis (outcome) of cervical cancer is how early the cancer is detected to determine how far it has spread.

The various stages of cervical cancer also affect the chance of recovery or prognosis of the patient.

FIGO stages for cervical cancer

Doctors assign the stage of the cancer by evaluating the tumo0r and whether the cancer has spread
to other parts of the body.

Staging is based on the results of a physical exam, imaging scans, and biopsies.

Stage I: The cancer has spread from the cervix lining into the deeper tissue but is still just found in the uterus. It has not spread to other parts of the body. This stage may be divided into smaller groups to describe the cancer in more detail (see below).

- **Stage IA:** The cancer is diagnosed only by viewing cervical tissue or cells under a microscope. Imaging tests or evaluation of tissue samples can also be used to determine tumor size.
  Stage IA1: There is a cancerous area of less than 3 millimetres (mm) in depth.
  Stage IA2: There is a cancerous area 3 mm to less than 5 mm in depth.
- **Stage IB:** In this stage, the tumour is larger but still only confined to the cervix. There is no distant spread.
  Stage IB1: The tumour is 5 mm or more in depth and less than 2 centimetres (cm) wide. A centimetre is roughly equal to the width of a standard pen or pencil.
  Stage IB2: The tumour is 2 cm or more in depth and less than 4 cm wide.
  Stage IB3: The tumour is 4 cm or more in width.

Stage II: The cancer has spread beyond the uterus to nearby areas, such as the vagina or tissue near the cervix, but it is still inside the pelvic area. It has not spread to other parts of the body. This stage may be divided into smaller groups to describe the cancer in more detail (see below).

- **Stage IIA:** The tumour is limited to the upper two-thirds of the vagina. It has not spread to the tissue next to the cervix, which is called the parametrial area.
  Stage IIA1: The tumour is less than 4 cm wide.
  Stage IIA2: The tumour is 4 cm or more in width.
- **Stage IIB:** The tumour has spread to the parametrial area. The tumour does not reach the pelvic wall.

Stage III: The tumour involves the lower third of the vagina and/or: has spread to the pelvic wall; causes swelling of the kidney, called hydronephrosis; stops a kidney from functioning; and/or involves regional lymph nodes. Lymph nodes are small, bean-shaped organs that help fight infection. There is no distant spread.

- **Stage IIIA:** The tumour involves the lower third of the vagina, but it has not grown into the pelvic wall.
- **Stage IIIB:** The tumour has grown into the pelvic wall and/or affects a kidney.
- **Stage IIIC:** The tumor involves regional lymph nodes. This can be detected using imaging tests or pathology. Adding a lowercase "r" indicates imaging tests were used to confirm lymph node involvement. A lowercase "p" indicates pathology results were used to determine the stage.
  Stage IIIC1: The cancer has spread to lymph nodes in the pelvis.
  Stage IIIC2: The cancer has spread to para-aortic lymph nodes. These lymph nodes are found in the abdomen near the base of the spine and near the aorta, a major artery that runs from the heart to the abdomen.

Stage IVA: The cancer has spread to the bladder or rectum, but it has not spread to other parts of the body.

Stage IVB: The cancer has spread to other parts of the body.

Cervical Cancer Survival Rates

There are many different factors that affect the prognosis (outlook) of cervical cancer including the stage of the cancer, the age of the patient, and general health of the patient.

Signs and Symptoms of Cervical Cancer

Early signs and symptoms of cervical cancer

In women who receive regular Pap screening, the first finding of the disease is usually an abnormal Pap test result.

Early symptoms that may occur can include

- Abnormal vaginal bleeding between periods, after intercourse, or after menopause
- Any bleeding after menopause

- Continuous vaginal discharge, which may be pale, watery, pink, brown, bloody or foul-smelling
- Periods becoming heavier and lasting longer than usual

Signs and symptoms of progressed cervical cancer
Some of the common symptoms observed during the later stages of cervical cancer are:

- Vaginal bleeding after sexual intercourse
- Pelvic pain
- Pain during sexual intercourse
- Offensive vaginal discharge may occur (pink, pale, brown, blood streaked, and foul-smelling)
- Abnormal bleeding between menstrual periods
- Heavy bleeding during menstrual period
- Increased urinary frequency
- Bleeding after menopause
- Painful urination
- Pelvic pain that is not related to the normal menstrual cycle
- Low back pain
- Leg pain
- Single swollen leg
- Bone fractures
- Weight loss
- Urethritis or urinary infection can be a sign of cervical cancer

Diagnosis of Cervical Cancer
The following procedures may be used:

Papanicolaou 'PaP' smear – This is a procedure whereby cells from the surface of the cervix are collected. The cells are viewed under a microscope, after staining, to find out if the cells are abnormal. This procedure is also called a Pap test. It is short for Papanicolaou (1947) with reference to George Nicholas Papanicolaou (1883-1962), a Greek-born United States anatomist who developed the technique of staining and examining collected cells to test for cervical cancer.

Cooper, D.B. & McCathran, C.E. 2024.
"The pap smear is responsible for decreasing the incidence of and mortality rates from cervical cancer. The Papanicolaou (Pap) smear is a collection of cells from the squamocolumnar junction of the cervix where the columnar epithelium is juxtaposed to the smooth squamous epithelium. In this area, squamous metaplasia is causing squamous cells to replace columnar cells. This cell growth and change can allow the entrance of human papillomavirus (HPV), the cause of more than 90% of cervical cancer. The Pap smear is a sample of cells from this area to screen a patient for abnormalities such as cervical dysplasia."
Conflict of interest statement
Disclosure: Danielle Cooper declares no relevant financial relationships with ineligible companies.

Disclosure: Charles McCathran declares no relevant financial relationships with ineligible companies.

Human Papillomavirus (HPV) Test – A laboratory test used to check DNA for certain types of HPV infection. Cells are collected from the cervix and checked to find out if an infection is caused by a type of HPV that is linked to cervical cancer. It is also called the HPV DNA Test.

Colonetti, T., Rodrigues Uggioni, M.L., Meller Dos Santos, A.L., Michels Uggioni, N., Uggioni Elibio, L., Balbinot, E.L., Grande, A.J. & Rosa, M.I. 2024.
"Cervical cancer is the third most common gynecological cancer worldwide. Its origin is linked to intraepithelial lesions caused by high-risk Human Papillomavirus (HPV) types, detected in 99.7% of cases. Early screening is essential to prevent cancer development from these lesions. Molecular methods are more specific and offer the possibility of being performed through a self-collected sample by the patient, thus contributing to increasing screening coverage for this pathology. This study aim was to map the medical-scientific literature on existing protocols for self-sampling for HPV testing in cervical cancer screening. A search strategy was developed using the following keywords and their synonyms: "self-sampling," "professional sampling," and "HPV", on the databases: MEDLINE, Cochrane Library, Virtual Health Library - BVS, Scopus, National Institute for Health Research NHS EED, Web of Science, and EMBASE. The search strategy was formulated to identify relevant studies and describe their main characteristics, such as patient acceptance of self-sampling, cost differences between the tests used, and the accuracy of self-sampling compared to the gold standard test. A total of 876 studies were found, and 33 of those studies were included in this review. Out of these, 10 studies were domized clinical trials involving 46,751 patients, and 23 observational studies included 142,795 patients. Regarding acceptance, most studies reported a preference for self-sampling. Sensitivity analyses from various studies also showed that the low cost of self-sampling kits generally increased cost-effectiveness. The study concluded that using HPV testing on self-collected samples is a viable strategy for monitoring women with HPV."
Conflict of interest statement
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The cobas® HPV Test - is the only clinically validated, FDA-approved assay that simultaneously provides pooled results on high-risk genotypes and individual results on the highest-risk genotypes, HPV 16 and HPV 18. This test is a qualitative *in vitro* test for the detection of Human Papillomavirus (HPV) in patient specimens. The test utilises amplification of target DNA by the Polymerase Chain Reaction (PCR) and nucleic acid hybridisation for the detection of 14 high-risk (HR) HPV types in a single analysis.

The test specifically identifies (types) HPV 16 and HPV 18 while concurrently detecting the rest of the high risk types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) at clinically relevant infection levels. Specimens are limited to cervical cells collected in cobas® PCR Cell Collection Media (Roche Molecular Systems, Inc.), PreservCyt® Solution (Cytyc Corp.) and SurePath® Preservative Fluid (not approved in the US) (BD Diagnostics-TriPath).

White, C., Reynolds, S., Murphy, K., Keegan, H., Naik, P., O'Brien, R., Pilkington, L., Sharkey Ochoa, I., Glesson, G., Russell, N., Nuttall, D., Tewari, P., Wright, F., O'Toole, S., Sharp, L., Flannelly, G., O'Leary, J.J., Martin, C.M.; CERVIVA the Irish Cervical Screening Research Consortium. 2024.

"There are currently several validated HPV tests. However, longitudinal data which spans appropriate age ranges, as well as evaluation of potential screening algorithms are necessary for screening programmes choice of test. The objective of our study was to evaluate the performance of HPV mRNA and HPV DNA testing, including partial genotyping, in routine cervical screening. As part of the CERVIVA HPV Primary Screening Study, ThinPrep samples from 10 150 women were tested for HPV mRNA using the Aptima HPV assay and HPV DNA using the Cobas 4800 HPV test. HPV mRNA-positive women were further assessed with the Aptima genotyping assay for HPV 16/18/45. Baseline cytology and prospective follow-up data were collected. The performance of the two tests was examined over 42 months (to date). HPV mRNA demonstrated equivalent sensitivity to HPV DNA testing for detection of CIN2+ (93.2% [92.4-93.9] vs 92.8% [92.0-93.6], respectively) and CIN3+ (94.6% [93.8-95.3] vs 94.6% [93.8-95.3]). HPV mRNA testing had significantly higher specificity compared to HPV DNA for detection of CIN2+ (84.0% [83.5-84.5] vs 80.8% [80.2-81.4], respectively) and CIN3+ (88.44% [88.2-88.6] vs 85.62 [85.4-85.9]). The proportion of CIN2+ and CIN3+, over 3 years (42 months), in HPV-negative women was comparable for both RNA (0.20% and 0.10%) and DNA (0.22% and 0.11%). Genotyping data was comparable across both assay platforms. In the context of HPV primary screening HPV mRNA testing has potential to reduce triage tests and follow-up tests at 12 months compared to DNA testing, with no significant difference in detection of CIN2+ and CIN3+."

Colposcopy – A procedure in which a colposcope (a lighted, magnifying instrument) is used to check the vagina and cervix for abnormal areas.

Wang, P., Gao, D., Yu, X. & Zhu, G. 2024.
"In the present study, the diagnostic value of high risk-human papillomavirus (HR-HPV) combined with colposcopy for the detection of cervical cancer and precancerous lesions was evaluated. A total of 397 patients with confirmed cervical disease were enrolled between August 2020 and December 2021. According to the pathological diagnosis, the patients were divided into cervical intraepithelial neoplasia grade I (CIN I; n=153 cases), CIN II (n=101 cases), CIN III (n=86 cases) and cervical cancer (n=57 cases) groups. The HR-HPV-positive rate of the patients with different lesion types was compared, and the consistency of colposcopy and pathological examination results were assessed. For cervical cancer and precancerous lesions, the diagnostic value and efficacy of HR-HPV testing, colposcopy and combined HR-HPV testing and colposcopy examination were compared using pathological examination results as the gold standard. The results of the present study demonstrated that in patients with cervical cancer, the positive rate of HR-HPV (100.00%; n=57/57) was higher than that in patients with precancerous lesions, and the positive rate of HR-HPV in patients with CIN I type (36.60%, n=56/153) was lower than that in patients with CIN II (83.17%, n=84/101) and CIN III (82.56%, n=71/86) types ($P<0.05$). There was no significant difference in the HR-HPV-positive rate between patients with CIN II and CIN III ($P>0.05$). Cohen's κ coefficient for colposcopy examination and pathological examination of patients with cervical cancer and precancerous lesions was 0.622, the diagnostic accuracy was 90.43% (n=359/397), the positive predictive value was 65.57% (n=40/61), and the negative predictive value was 94.94% (n=319/336). Receiver operating characteristic curve analysis demonstrated that the area under the curve of the combined examination in the diagnosis of cervical cancer and precancerous lesions was 0.904, which was higher than that of colposcopy (0.820) or HR-HPV testing (0.802) alone ($P<0.05$). The results of the present study indicated that HR-HPV detection combined with colposcopy has diagnostic value for cervical cancer and precancerous lesions."
Conflict of interest statement
The authors declare that they have no competing interests.

Biopsy – A sample of tissue is cut from the cervix and viewed under a microscope by a pathologist to check for signs of cancer, often referred to as *cone biopsy*.

Bianchi, T., Grassi, T., Di Martino, G., Negri, S., Trezzi, G., Fruscio, R. & Landoni, F. 2024.
"The implementation of sentinel lymph node (SLN) biopsy is changing the scenario in the surgical treatment of early-stage cervical cancer, and the oncologic safety of replacing bilateral pelvic lymphadenectomy with SLN biopsy is currently under investigation. Part of the undisputed value of SLN biopsy is its diagnostic accuracy in detecting low-volume metastases (LVM) via pathologic ultrastaging. In early-stage cervical cancer, the reported incidence of LVM ranges from 4 to 20%. The prognostic impact and the role of adjuvant treatment in patients with LVM is still unclear. Some non-prespecified analyses in prospective studies showed no impact on the oncologic outcomes compared to node-negative disease. However, the heterogeneity of the studies, the differences in the disease stage and the use of adjuvant treatment, and the concomitant pelvic lymphadenectomy (PLND) make reaching any conclusions on this topic hard. Current guidelines suggest considering micrometastases (MIC) as a node-positive disease, while considering isolated tumor cells (ITC) as a node-negative disease with a low level of evidence. This review aims to highlight the unanswered questions about the definition, identification, and prognostic and therapeutic roles of LVM and to underline the present and future challenges we are facing. We hope that this review will guide further research, giving robust evidence on LVM and their impacts on clinical practice."
Conflict of interest statement
The authors declare no conflicts of interest.

Endocervical curettage (ECC) - to examine the opening of the cervix

Alqabbani, R., Chan, J. & Goldberg, A. 2024.
Objectives: In another publication, we concluded endocervical curettage (ECC) should have a minimum number of squamous cells for adequacy, similar to the requirements for adequate cervical Papanicolaou smears. Here, we investigate if also, similar to cervical Papanicolaou smears, the presence of at least 10 cells from the endocervical/transformation zone (EC/TZ) in ECCs should be used as a quality assurance measure or if, instead, at least 10 EC/TZ cells should be part of the adequacy criteria for ECC, with an emphasis on diagnosis of at least high-grade squamous dysplasia (HGD).
Methods: All patients with at least HGD diagnosed on an excisional biopsy specimen (loop electrosurgical excision procedure [LEEP]) from May 1, 2018, to December 31, 2019, and an ECC in the preceding 6 months at our institution were included. Number of EC/TZ cells present in ECCs was counted visually and categorized as less than or greater than 10 TZ cells. A $\chi 2$ test was used to evaluate the proportion of ECCs with and without HGD and the presence or absence of at least 10 EC/TZ cells. Given our recent work encouraging at least 1000 squamous cells in an ECC to be considered adequate, we also evaluated only ECCs with greater than 1000 squamous cells with and without HGD and the presence or absence of at least 10 EC/TZ cells. P value was <.05.
Results: Fifty-one LEEPs with HGD and a preceding ECC in the previous 6 months were identified. Of the 51 ECCs, 6 had fewer than 10 EC/TZ cells and 45 had at least 10 EC/TZ cells. A similar proportion of the ECCs with HGD had at least 10 EC/TZ cells as those without HGD (93% vs 86%, P = .53). Using only ECCs with greater than 1000 squamous cells, we still found no statistical difference in the

proportion of ECCs with HGD having greater than 10 EC/TZ cells compared to those without HGD (91% vs 100%, P = .49).
Conclusions: We found that the presence of at least 10 EC/TZ cells does not increase the likelihood of finding HGD in an ECC performed in the 6 months prior to a LEEP with HGD. Similar to the use of the TZ component in cervical Papanicolaou smears, the presence or absence of at least 10 TZ cells in an ECC should only be considered a quality assurance measure and not be used as a criterion for adequacy of the specimen.

Pelvic Examination – An examination of the vagina, cervix, uterus, fallopian tubes, ovaries, and rectum.

Once a woman is diagnosed with cervical cancer, the medical practitioner may order more tests to determine how far the cancer has spread. This is part of staging and may include:

- Chest X-ray
- Computed Tomography (also called Computerised Axial Tomography or CT scan)
- Cystoscopy
- Intravenous Pyelogram (IVP)
- Magnetic Resonance Imaging (MRI)

Bethesda Classification of Cervical Cytology*

Category	Specifics	Comments
Specimen type	Conventional (Papanicolaou [Pap]), liquid-based preparation, or another	Type of test is noted.
Adequacy of the specimen	Satisfactory for evaluation	Any quality indicators (eg, presence or absence of endocervical or transformation zone component, partially obscuring blood, inflammation) are described.
	Unsatisfactory for evaluation (rejected and not processed)	Reason is specified.
	Unsatisfactory for evaluation but processed and evaluated	Reason is specified.

Category	Specifics	Comments
General categorization (optional)	Negative for intraepithelial lesion or cancer Epithelial cell abnormalities Other findings	Findings are stated or described under Interpretation, below.
Interpretation of negative (nonmalignant) abnormalities†	Organisms	Possible findings include the following: • *Trichomonas vaginalis* • Fungi morphologically consistent with *Candida* species • Shift in vaginal flora suggesting bacterial vaginosis • Bacteria morphologically consistent with *Actinomyces* species • Cellular changes consistent with herpes simplex virus • Cellular changes consistent with cytomegalovirus
	Nonneoplastic findings (reporting is optional)	Possible findings include the following: • Nonneoplastic cellular variations (squamous metaplasia, keratotic changes, tubal metaplasia, atrophy, or pregnancy-associated changes) • Reactive cellular changes associated with inflammation (lymphocytic cervicitis), radiation, or IUD use • Glandular cell status after hysterectomy
Interpretation of epithelial cell abnormalities	Squamous cell	Possible findings include the following: • Atypical squamous cells of undetermined significance (ASC-US) • Atypical squamous cells for which a high-grade lesion cannot be excluded (ASC-H) • Low-grade squamous intraepithelial lesion encompassing HPV‡ infection or mild dysplasia (CIN 1) • High-grade squamous intraepithelial lesion encompassing moderate (CIN 2) and severe dysplasia (CIN 3/CIS), noting whether the lesion has features

Category	Specifics	Comments
		suggesting invasion • Squamous cell carcinoma
	Glandular cell	Possible findings include the following: • Atypical cells: Endocervical, endometrial, or glandular • Atypical cells likely to be cancerous: Endocervical or glandular • Adenocarcinoma in situ: Endocervical • Adenocarcinoma: Endocervical, endometrial, extrauterine, or NOS
Interpretation of other abnormalities	Endometrial cells (in a woman ≥ 45)*	Whether sample is negative for squamous intraepithelial lesion is specified.
Other cancers	—	Type is specified.

* Use of an automated device for scanning should be reported, as should adjunctive tests (eg, HPV) and their results.

† If there is no cellular evidence of neoplasia, clinicians should state negative for intraepithelial lesion or malignancy here or in the general categorization.

‡ Cellular changes of HPV infection—previously called koilocytosis, koilocytotic atypia, and condylomatous atypia—are included in the category of low-grade squamous intraepithelial lesion.

CIN = cervical intraepithelial neoplasia; CIS = carcinoma in situ; HPV = human papillomavirus; IUD = intrauterine device; NOS = not otherwise specified.

Adapted from the Bethesda System 2014, National Institutes of Health.

CANSA's Position Regarding Pap Smears

CANSA believes that it is ideal to have a Pap smear done 10-20 days after the start of the last period. It is not recommended to plan one's Pap smear during a period. Menstrual fluid and blood may make it difficult for the pathologist to interpret results. However, if the flow is light, some doctors will perform a Pap smear. Newer, liquid based Pap smears can separate cervical cells from mucus and blood, allowing a more accurate reading.

If a woman has started her period unexpectedly or finds that she has scheduled a Pap smear during a time when she may have her period, she should call her doctor's office. Ask to speak to a nurse or

the doctor and inform them that the Pap smear will coincide with her period. It is best to reschedule an appointment.

The World Health Organization (WHO) and Cervical Cancer Screening:

Summary recommendation for the general population of women	Summary recommendation for women living with HIV
World Health Organization (WHO) - 2021 - suggests using either of the following strategies for cervical cancer prevention:	**World Health Organization (WHO) - 2021 - suggests using the following strategy for cervical cancer prevention among women living with HIV:**
• HPV DNA detection in a screen-and-treat approach starting at the age of 30 years with regular screening every 5 to 10 years. • HPV DNA detection in a screen, triage and treat approach starting at the age of 30 years with regular screening every 5 to 10 years.	• HPV DNA detection in a screen, triage and treat approach starting at the age of 25 with regular screening every 3 to 5 years.

CANSA's Position:
CANSA Supports the *Cervical Cancer Prevention and Control Policy* of the World Health Organization (2021) including that of the National Department of Health regarding Cervical Screening Intervals for cervical smears in the Public Health Sector:

Women in the Low Risk Target Group

- Women in the low risk target group will be offered screening three (3) times in their lifetime, assuming no abnormalities were found during screening.
- Screening will be offered first at age 30 and then at 10-year intervals (i.e. at ages 40 and 50).
- If a woman is first screened at an age older than 30, her last screen may be after age 50.
- All low risk women who are found to have an abnormality during routine screening should subsequently be screened at 3-year intervals until the screen result is negative.
- When the result is negative, the woman will return to the 10-year schedule.
- Pregnancy will not preclude screening for cervical cancer as screening can be safely performed up to 20 weeks of gestation to avoid missed opportunity.

Women who Fall into the High Risk Population or who are HIV+.

- Women who are recipients of organ transplants are considered to be at high risk.

- All women with immunosuppressive disease are also considered to be at high risk.
- All women on chronic immune suppressing treatment are also considered to be at high risk.
- Screening for HIV+ women will be done irrespective of CD4 count and antiretroviral (ARV) treatment and will be screened annually as per below.
- All HIV+ women are considered to be at high risk for cervical cancer whether they are receiving antiretroviral (ARV) treatment or not.
- All HIV+ women will be screened immediately for cervical cancer at diagnosis.
- All HIV+ women will be subsequently screened annually if the screening test is positive.
- All HIV+ women will be subsequently screened every 3 years if the screening test is negative.
- Because of the high incidence of HIV among younger women and girls, screening services will be provided routinely to younger women (i.e. younger than 30 years) from the time that HIV diagnosis is confirmed provided that the young women have previously had sex (i.e. putting them at risk of acquiring HPV).

CANSA further suggests that women avoid having anything in the vagina 24-48 hours prior to a Pap smear.

This includes:

- sexual intercourse
- spermicides, foams, or jellies
- douching
- vaginal inserts
- tampons

All of the above can make it difficult for the pathologist to accurately interpret results.

CANSA further believes that:

- every eligible woman should preferably have a Pap smear at least every 3 years
- it is better to have a Pap smear at a less-than-optimal time than not at all
- routine cervical screening is not required for women under 18 years of age, even if they are sexually active as there is no evidence to support encouraging women under 18 years of age to have a Pap smear
- all women who have ever been sexually active should start having Pap smears between the ages of 18 and 20 years, or two years after first having sexual intercourse, whichever is later
- a decision to screen a woman below the age of 18 years is at the discretion of the clinician and would depend on the individual circumstances of the patient
- Pap smears may cease at the age of 70 years for women who have had two normal Pap smears within the last five years
- Women over 70 years who have never had a Pap smear, or those who request a Pap smear, should be screened

Treatment of Cervical Cancer

Treatment of cervical cancer depends on:

- The stage of the cancer
- The size and shape of the tumour
- The woman's age and general health
- The woman's desire to have children in the future

Treatment of early-stage cervical cancer may include:

- Cervical Conisation – it involves removing a cone-shaped piece of tissue from the cervix and cervical canal. The overall size of the tissue removed will vary depending on the severity of the cancer
- Loop Electrosurgical Excision Procedure (LEEP) – use is made of a thin, low-voltage electrified wire loop to cut out abnormal tissue
- Cryosurgery – used for cervical dysplasia or abnormal cells on the cervix. If left untreated, these abnormal cells may develop into cervical cancer. Cryosurgery kills pre-cancerous and cancerous cells by freezing them
- Total hysterectomy (removal of the uterus)
- Internal Radiation Therapy (Brachytherapy)

Treatment for more advanced cervical cancer may include:

- Radical hysterectomy – where the uterus and much of the surrounding tissues,, including lymph nodes and the upper part of the vagina is removed surgically
- Pelvic exenteration – an extreme type of surgery in which all of the organs of the pelvis, including the bladder and rectum, are removed surgically

Radiation Therapy may be used to treat cancer that has spread beyond the pelvis, or cancer that has returned:

- Internal radiation therapy
- External radiation therapy

Chemotherapy

The treatment of cancer by means of cytotoxic and other drugs.

Immunotherapy

Treatment or prevention of cancer that involves the stimulation, enhancement, suppression, or desensitisation of the immune system.

Kobayashi, O., Taguchi, A., Nakajima, T., Ikeda, Y., Saito, K. & Kawana, K. 2024.

"Cervical cancer and its precursor lesion, cervical intraepithelial neoplasia (CIN), are caused by high-risk human papillomavirus (HPV) viral infection and are highly susceptible to host immunity targeting of HPV viral proteins, which include both foreign antigens and cancer antigens expressed by tumors. Immunotherapy that induces Th1 immunoreactivity against viral proteins is expected to take advantage of this immunological regression mechanism. However, although cancer immunotherapies for cervical cancer and CIN have been developed over the past several decades, none have been commercialized. Most of these immunotherapies target the viral cancer proteins E6

and E7, which are generally the same. The reasons for the underdevelopment of HPV-targeted immunotherapy differ depending on whether the target is invasive cancer or CIN. We here summarize the developmental history of cancer immunotherapy for CIN and discuss strategies for solving the problems that led to this underdevelopment. We note that CIN is a mucosal lesion and propose that inducing mucosal immunity may be the key."

Conflict of interest statement

GLOVACC Inc. gifted GLBL101c, IGMKK16E7, and placebo, and partially supported this clinical trial.

Therapeutic Vaccines

Utilising a patient's own immune system to fight an existing disease rather than immunising for protection against future disease.

Adoptive Cell Therapy

T cells are collected from a patient and grown in the laboratory. This increases the number of T cells that are able to kill cancer cells or fight infections. These T cells are given back to the patient to help the immune system fight disease. Also called cellular adoptive immunotherapy.

Monoclonal Antibodies

An antibody produced by a single clone of cells. Monoclonal antibodies can be made in large quantities in the laboratory and are a cornerstone of immunology. Monoclonal antibodies are increasingly coming into use as therapeutic agents.

Follow-up Treatment

Follow-up checks will continue for some years after treatment. At first follow-up checks may be conducted every few months, becoming gradually less and less frequent.

Follow-up checks may include:

- Having a physical examination by the medical practitioner
- Pap smear
- Colposcopy
- Blood tests for tumour markers
- X-rays
- CT Scan or MRI scan

Lowering the Risk for Cervical Cancer

Cancer prevention is action taken to lower the risk for getting cancer. The risk for cervical cancer can be lowered by:

- Having regular Pap smear tests – Current guidelines recommend that women should have a Pap test every 3 years beginning at age 21. These guidelines further recommend that women aged

30 to 65 should have HPV and Pap co-testing every 5 years or a Pap test alone every 3 years. Women with certain risk factors may need to have more frequent screening or to continue screening beyond age 65

- Having a Human Papilloma Virus (HPV) test - In women older than age 30, the Pap smear may be combined with a test for human papillomavirus (HPV) — a common sexually transmitted infection that can cause cervical cancer in some women
- Getting an HPV vaccine before becoming sexually active
- Not using tobacco products
- If smoking, to quit smoking
- Not having unprotected sexual intercourse
- Limiting the number of sexual partners
- Not becoming sexually active at a young age

Individuals Often Ask Whether a "Booster" HPV Vaccine is Required

The answer is "yes" depending on the following. In a 2-dose schedule of HPV vaccine, the recommended interval is 6–12 months, and the minimum interval is 5 months between the first and second dose. If the second dose is given earlier than 5 months, a third dose should be given.

HPV Vaccine Schedule and Dosing

If an HPV vaccine is given to individuals between the ages of 9 and 14 years of age, a 2-dose schedule is advised.

If and HPV vaccine is given to individuals between the ages of 15 and 26 years of age, a 3-dose schedule is advised.

Immunogenicity studies have shown that 2 doses of HPV vaccine given to 9–14 year-old individuals at least 6 months apart provided as good or better protection than 3 doses given to older adolescents or young adults.

Current studies have followed HPV vaccinated individuals for ten years, and the results show that there is no evidence of weakened protection over time.

According to the US Centers for Disease Control and Prevention (CDC) HP Vaccine Recommendations are:

- HPV vaccine is recommended for routine vaccination at age 11 or 12 years. (Vaccination can be started at age 9.)
- ACIP also recommends vaccination for everyone through age 26 years if not adequately vaccinated previously. HPV vaccination is given as a series of either two or three doses, depending on age at initial vaccination.
- Vaccination is not recommended for everyone older than age 26 years. However, some adults ages 27 through 45 years may decide to get the HPV vaccine based on discussion with their clinician, if they did not get adequately vaccinated when they were younger. HPV vaccination of people in this age range provides less benefit, for several reasons, including that more people in this age range have already been exposed to HPV.

- For adults ages 27 through 45 years, clinicians can consider discussing HPV vaccination with people who are most likely to benefit. HPV vaccination does not need to be discussed with most adults over age 26 years.

Keep in mind that HPV vaccination prevents new HPV infections but does not treat existing HPV infections or diseases. HPV vaccine works best when given before any exposure to HPV.

Most sexually active adults have already been exposed to HPV, although not necessarily all of the HPV types targeted by vaccination. At any age, having a new sex partner is a risk factor for getting a new HPV infection. People who are in a long-term, mutually monogamous relationship are not likely to get a new HPV infection.

Cervical Cancer and HIV

There are approximately 5,7 million HIV+ people in South Africa of which 60% are women. They are at higher risk of HPV infection and persistence. Research shows that they are infected with a broader range of HPV strains. Research has also found that those who are treated with Highly Active Antiretroviral Therapy (HAART), have a longer lifespan and are at a significantly higher risk to develop cancer of the cervix.

CANSA's Position:

CANSA supports a non-discriminating approach and calls for the equal treatment of all individuals.

CANSA further supports:

- The education of health personnel concerning the importance of cervical screening;
- The training of health personnel in the correct taking of Pap smears;
- The training of professional nurses in cytology so that they can be used for the staining and screening of Pap smears;
- Ensuring that good records are kept concerning the quality and outcome of Pap smears, including a client recall system;
- Effective follow-up and referral of clients;
- Educating the community about the importance of vaccination of all girls against HPV.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: https://pactr.samrc.ac.za/

Medical Disclaimer

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