

Cancer Association of South Africa (CANSA)

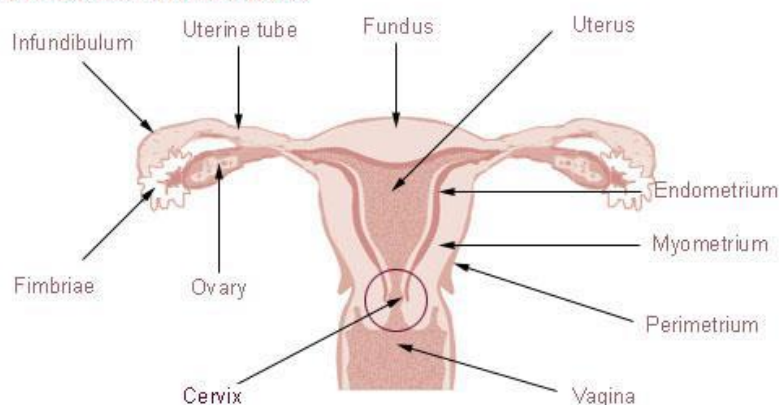


Fact Sheet and Position Statement on Cervical Cancer

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*.

Uterus and Uterine tubes



[Picture credit: Female Reproductive System]

Worldwide, cervical cancer is the third most common type of cancer in women. 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 (PubMed).

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

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.

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[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 it 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.

Incidence of Cervical Cancer in South Africa

According to the outdated National Cancer Registry (2016), known for the under reporting of cancer statistics, the following number of cervical cancer cases was histologically diagnosed in South Africa during 2016:

Group - Females 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	7 327	1:35	17,33%
Asian females	94	1:89	7,56%
Black females	6 190	1:29	31,69%
Coloured females	470	1:58	9,92%
White females	573	1:57	3,37%

The frequency of histologically diagnosed cases of cervical cancer in South Africa for 2016 was as follows (National Cancer Registry, 2016):

Group - Females 2016	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	10	156	1 369	1 943	1 834	1 205	565	245
Asian females	0	3	10	26	29	17	8	1
Black females	9	124	1 170	1 659	1 508	1 015	485	220
Coloured females	0	15	79	125	124	85	33	9
White females	1	14	110	133	173	88	39	15

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.

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According to **Bruni, et al.**, (2019), the burden of cervical cancer for South Africa for 2018 is estimated as:

- | | |
|---|--------|
| • Annual number of cervical cancer cases | 12 983 |
| • Annual number of cervical cancer deaths | 5 595 |

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

Oncogenic (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

(Centres for Disease of Control and Prevention)

Cervical cancer is the second most common cancer 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.

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.

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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

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					■

(Centers for Disease Control and Prevention)

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

Staples, J.N. & Duska, L.R. 2019.

“The Pap smear is the only proven screening intervention in the field of gynecologic oncology. Women should receive treatment for precancerous conditions of the cervix, vulva, vagina, and endometrial lining. Women with inherited conditions should consider having a risk-reducing surgery once they have finished childbearing. The human papilloma virus vaccination should be offered to all girls and boys aged 11 to 12 years, and can also be given as early as age 9 and through 26 years of age.”

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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.

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:

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.

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.

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 (Cytoc Corp.) and SurePath® Preservative Fluid (not approved in the US) (BD Diagnostics-TriPath).

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

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*.

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

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)

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.

Staples, J.N. & Duska, L.R. 2019.

"The Pap smear is the only proven screening intervention in the field of gynecologic oncology. Women should receive treatment for precancerous conditions of the cervix, vulva, vagina, and endometrial lining. Women with inherited conditions should consider having a risk-reducing surgery once they have finished childbearing. The human papilloma virus vaccination should be offered to all girls and boys aged 11 to 12 years, and can also be given as early as age 9 and through 26 years of age."

CANSA's Position:

CANSA Supports the *Cervical Cancer Prevention and Control Policy* of the National Department of Health regarding Screening Intervals for Pap 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.

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- 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

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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.

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

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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

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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: www.sanctr.gov.za/

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

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