

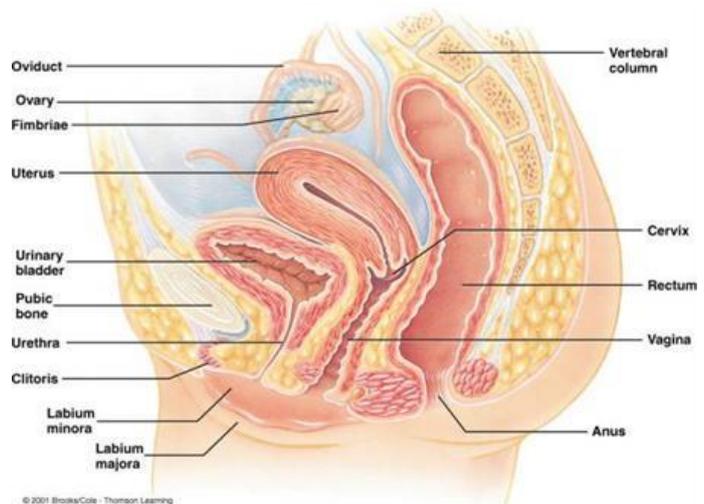


## Fact Sheet on Cancer of the Anus

### Introduction

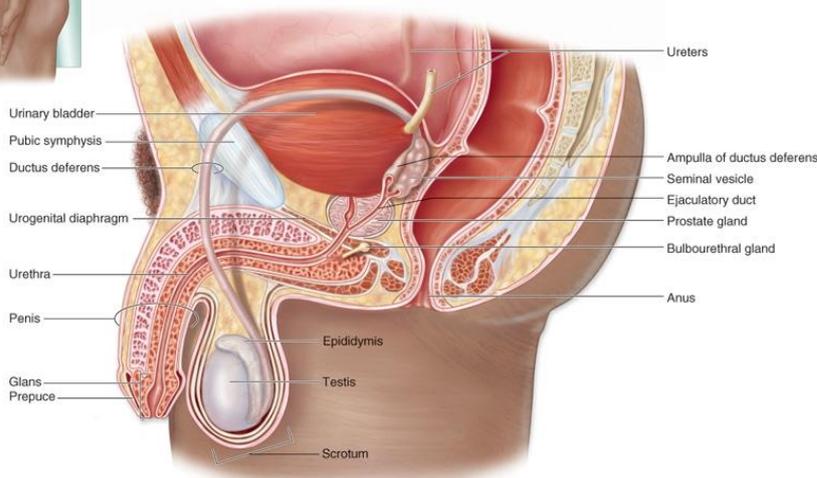
The human anus (from Latin *anūs* meaning 'ring', 'circle') is the external opening of the rectum. Like other vertebrates, its closure is controlled by sphincter muscles. Faeces are expelled from the body through the anus during the act of defaecation, the primary function of the anus.

[Picture Credit: Female Pelvis]



The anus is often considered a taboo part of the body, however, the anus is also the site of potential infections and other conditions, including cancer and, therefore, of great medical concern (Wikipedia).

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[Picture Credit: Male Pelvis]

The anus starts at the bottom of the rectum, the last portion of the colon (large intestine). The ano-rectal line separates the anus from the rectum. Tough tissue called fascia surrounds the anus and attaches it to nearby structures.

Circular muscles called the external *sphincter ani* form the wall of the anus and hold it closed. Glands

release fluid into the anus to keep its surface moist.

A plate-like band of muscles, called the *levator ani* muscles, surround the anus and form the floor of the pelvis. A network of veins lines the skin of the anus (WebMD).

## Anal Cancer

Anal cancer is an uncommon malignancy that starts in the anus - the opening at the end of the rectum. When it is found early, anal cancer is highly treatable.

### Incidence of Anal Cancer in South Africa

According to the National Cancer Registry (2012) the following number of anal cancer cases was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	99	1:1 781	0,27%
Asian males	6	1:838	0,74%
Black males	59	1:2 018	0,51%
Coloured males	11	1:1 109	0,26%
White males	22	1:1 733	0,11%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	120	1:2 105	0,32%
Asian females	4	1 : 1 938	0,41%
Black females	69	1:2 893	0,42%
Coloured females	21	1:752	0,50%
White females	25	1:1 774	0,16%

The frequency of histologically diagnosed cases of anal cancer in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	2	0	9	20	22	20	13	11
Asian males	0	0	0	1	1	2	1	1
Black males	2	0	7	13	14	8	5	6
Coloured males	0	0	1	3	2	2	3	1
White males	0	0	0	3	5	6	4	3

Group - Females 2012	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	0	5	20	23	22	18	18	11
Asian females	0	1	0	1	2	0	0	0
Black females	0	3	13	14	11	7	7	6
Coloured females	0	0	2	2	5	5	5	0
White females	0	1	1	2	2	5	6	5

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.

### Risk Factors for Anal Cancer

Several factors have been found to increase the risk for anal cancer, including:

- older age – most cases of anal cancer occur in people aged 50 and older
- many sexual partners – men and women who have many sexual partners over their lifetimes have a greater risk for anal cancer

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- unprotected anal sex – men and women who engage in unprotected anal sex have an increased risk for anal cancer
- smoking – smoking may increase the risk for anal cancer. Former smokers have only a slightly elevated risk for anal cancer
- human papillomavirus (HPV) – HPV infection increases the risk for several cancers, including anal cancer and cervical cancer. HPV infection is a sexually transmitted infection that can also cause genital warts. HPV may cause cells in the anal canal to appear abnormal – a condition called anal squamous intraepithelial lesions (ASIL). The abnormal cells associated with AIL are not cancer but it may develop into anal cancer, however, some people with ASIL never develop anal cancer
- 95% of anal cancers are caused by the human papillomavirus (HPV). There are many types of HPV. Some HPV types cause benign warts, but some cause lesions (also called dysplasia) that can progress to invasive cancer. HPV-16 and HPV-18 are the high-risk strains responsible for the majority of HPV-associated cancers.
- drugs or conditions that suppress the immune system – people who take drugs to suppress their immune system (immunosuppressive drugs), including people who have received organ transplants may have an increased risk for anal cancer. Long-term use of corticosteroids, such as those prescribed to control autoimmune disorders also may increase the risk for anal cancer. HIV (the virus that causes AIDS) suppresses the immune system and increases the risk for anal cancer
- fistulas – presence of abnormal openings in or around the anus
- history of cervical, vaginal or vulval cancer – some studies show that women who had cervical, vulval or vaginal cancer have a higher risk of developing abnormal cells in the anus or anal cancer than the general population. The risk is also increased for women with a history of abnormal cells in the cervix (cervical intraepithelial neoplasia), vulva (vulval intraepithelial neoplasia) or vagina (vaginal intraepithelial neoplasia).

(Mayo Clinic; About.Com Cancer; Cancer Research UK; Roswell Park Cancer Institute).

### **Screening for Anal Cancer**

Ongoing research is being done on the value of screening tests for anal cancer, especially in people with major risk factors. The test studied most is anal cytology, sometimes called the *anal Pap test*. This test may be useful in early diagnosis of anal cancer and pre-cancer (called *anal intraepithelial neoplasia*, or AIN).

In this test, cells are gently scraped from the lining layer of the anus and checked under a microscope. Some doctors already recommend this test for people at high risk for anal cancers, such as those who are HIV positive.

Research is also in progress on treating AIN to help prevent cancer from developing. (American Cancer Society).

### **Signs and Symptoms of Anal Cancer**

Signs and symptoms of anal cancer include:

- rectal bleeding - the patient may notice blood on faeces or toilet paper
- pain in the anal area
- lumps around the anus. These are frequently mistaken for piles (haemorrhoids)

- mucus discharge from the anus
- jelly-like discharge from the anus
- anal itching
- change in bowel movements. This may include diarrhoea, constipation, or thinning of stools
- faecal incontinence (problems controlling bowel movements)
- bloating
- women may experience lower back pain as the tumour exerts pressure on the vagina
- women may experience vaginal dryness
- a sense of fullness and constant need to go to the bathroom, or both, which may occur as tumours grow and begin to invade the sphincter muscle
- change in the diameter of stool
- swollen lymph nodes in the anal or groin areas
- ulcers around the anus that can spread to the skin of the buttocks

(Medical News Today; Mayo Clinic; University of California San Francisco; Caring4Cancer; American Cancer Society; MacMillan Cancer Support).

### Diagnosis of Anal Cancer

Anal cancer is often fairly easy to diagnose because it is in a fairly easy-to-reach area. Some cases of anal cancer in people at high risk for that disease are diagnosed by screening tests, such as the digital rectal exam and/or anal Pap test, but most people are diagnosed after their cancer starts to cause symptoms (American Cancer Society).

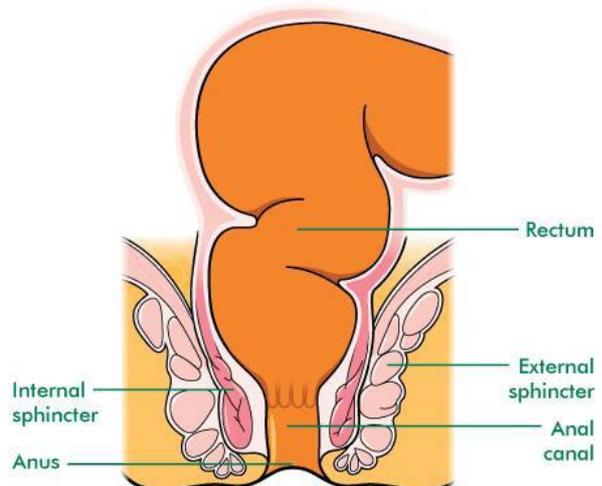
### Types of Anal Cancer

About 80% anal cancers are squamous cell cancers, sometimes called epidermoid cancers. There are 3 types of squamous cell anal cancer, namely:

- large cell keratinising cancer
- large cell non keratinising (also called transitional) cancer
- basaloid cancer

[Picture Credit: Anal Canal]

A keratinising cancer has keratin (the protein that forms one's hair and nails) in the cancer cells. This type of anal cancer starts in the lower part of the anus. Non-keratinising types start from the transitional zone of the anal canal, where the squamous cells meet the glandular cells. Many anal cancers will have a mix of these cell types. All these squamous cell types of anal cancer are treated in the same way.



### Non-epidermoid cancer

The other 2 out of 10 anal cancers (20%) are:

- adenocarcinoma - this is a rare type of anal cancer that affects the glandular cells that produce mucus in the anal canal. Only 5% of anal cancers are this type. This type of anal cancer is treated in the same way as rectal cancer
- small cell cancers - small cell carcinoma affecting the anal canal is a rare and poorly understood entity which can, in its early stages, masquerade as benign cells
- undifferentiated cancers - undifferentiated cells are cells that have become so abnormal that often we cannot tell what types of cells they started from
- basal cell carcinoma - This is a type of skin cancer and it develops in the area around the anus. You can find information about treatment of basal cell cancers in the skin cancer section
- melanomas - this is another type of skin cancer. These cancers develop from the cells that produce melanin, the pigment or colour for the skin. Treatment is the same as for other melanomas

This group is known as non epidermoid cancers. They behave differently to squamous cell anal cancers, so the treatment is different.

Cancers that start at the anal margin, usually look more like normal cells (they are well differentiated). Anal margin tumours are more common in men than women. Cancers that start higher up in the anal canal are more common in women.

(Cancer Research UK; Oncolink; Cancer.Net).

### **Lowering the Risk for Anal Cancer**

Since the cause of many cases of anal cancer is unknown it is not possible to prevent this disease completely.

The best way to reduce the risk of developing anal cancer is to avoid infection with HPV or HIV. The risk of these infections is higher for those who have sex with multiple partners and those who have unprotected anal sex (American Cancer Society).

- always use a condom - wearing a condom may provide protection against HPV. HPV is a virus transmitted through sexual contact that is linked to several types of cancer
- limit the number of sexual partners - when a person has multiple sexual partners they are at an increased risk for both HPV and anal cancer
- avoid unprotected anal intercourse – unprotected anal intercourse increases the risk factor for anal cancer for both men and women
- quit smoking and/or using other tobacco products - smokers are 4 times more likely to develop anal cancer than non-smokers. Smoking puts individuals at a higher risk for many other types of cancer as well like lung cancer
- avoid sex with people with sexually transmitted infections (STI) or those who have or have had multiple sexual partners
- get an HPV vaccine - Gardasil® and Cervarix® help protect against certain types of HPV. Individuals who already have HPV will not be cured by having these vaccines (About.Com Cancer; MD Anderson Cancer Center; Mayo Clinic).

## Staging of Anal Cancer

Staging is the process of finding out how far a cancer has spread. This is important because treatment options and outlook for recovery and survival depend on the cancer's stage.

Staging of anal cancer uses a system created by the American Joint Committee on Cancer (AJCC). The staging description that follows applies only to tumours in the anal canal, not to cancers that involve only the anal margin or perianal skin.

## The TNM system

The *TNM system* for staging contains 3 key pieces of information:

- **T** describes the size of the primary tumour, measured in centimetres (cm), and whether the cancer has spread to organs next to the tumour
- **N** describes the extent of spread to nearby (regional) lymph nodes
- **M** indicates whether the cancer has metastasised (spread) to other organs of the body

Numbers or letters appear after *T*, *N*, and *M* to provide more details about each of these factors:

- the numbers 0 through 4 indicate increasing severity
- the letter X means "cannot be assessed" because the information is not available
- the letters 'is' mean 'carcinoma in situ', which means the tumour is contained within the top layer of anal tissue and has not yet reached deeper layers of tissue

## T categories for anal cancer

**TX:** primary tumour cannot be assessed

**T0:** no evidence of primary tumour

**Tis:** carcinoma in situ

**T1:** the tumour is 2 cm across or smaller

**T2:** tumour is between 2 and 5 cm in size

**T3:** tumour is larger than 5 cm

**T4:** Tumour of any size that is growing into nearby organ(s), such as the vagina, urethra (the tube that carries urine out of the bladder), prostate gland, or bladder

## N categories for anal cancer

**NX:** regional lymph nodes cannot be assessed

**N0:** no regional lymph node spread

**N1:** spread to lymph nodes near the rectum

**N2:** spread to lymph nodes on one side of the groin and/or pelvis

**N3:** spread to lymph nodes near the rectum and in the pelvis or groin, or to both sides of the groin or pelvis

## M categories for anal cancer

**M0:** no distant spread

**M1:** distant spread to internal organs or lymph nodes of the abdomen

## Stage Grouping

To make this information more helpful, these TNM descriptions can be grouped together into a simpler set of stages, labelled stage 0 through stage IV

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- Stage 0:** Tis, N0, M0: Stage 0 is very early cancer (or pre-cancer) that exists only in the top layer of anal tissue. This stage is also known as carcinoma in situ
- Stage I:** T1, N0, M0: The cancer cells have spread beyond the top layer of anal tissue and is no longer carcinoma in situ. The tumour is less than 2 cm in size. It has not spread to lymph nodes or distant sites
- Stage II:** T2 or 3, N0, M0: The cancer is larger than 2 cm in size, but it has not spread to nearby organs or lymph nodes. It has not spread to distant sites
- Stage IIIA:** (T1-3, N1, M0) *or* (T4, N0, M0): The cancer can be any size and either has spread to the lymph nodes around the rectum(N1), *or* it has grown into nearby organs (T4), such as the vagina or the bladder without spreading to nearby lymph nodes. It has not spread to distant sites
- Stage IIIB:** (T4, N1, M0), *or* (Any T, N2-3, M0): Either the cancer has grown into nearby organs, such as the vagina or the bladder, and has also spread to lymph nodes around the rectum, *or* it can be of any size but has spread to lymph nodes in the groin, with or without spread to lymph nodes around the rectum. It has not spread to distant sites
- Stage IV:** Any T, Any N, M1: The cancer has spread to distant organs or tissues. It can be any size and may or may not have spread to lymph nodes  
(American Cancer Society; MacMillan Cancer Support).

### Spread of Cancer of the Anus

Cancer from the anus metastasises (spreads) mostly to:

- lymph nodes of your abdomen, it may cause bloating, a swollen abdomen, loss of appetite, or a feeling of fullness
- the liver, it may cause pain on the upper right side of your abdomen, bloating, loss of appetite, or a feeling of fullness
- the lungs, it may cause you to cough, spit up blood, or have a hard time breathing
- the bones, it may cause bone pain, especially in your back, hips, and pelvis
- the brain, it may cause problems with memory, concentration, balance, or movement (Web.MD).

### Prognosis (Outlook)

As with many types of cancer, the outcome of anal cancer depends on how advanced it is when diagnosed - in other words, the stage of the cancer. Because anal cancer is rare, it is harder to draw conclusions from the statistics because they are based on a small number of people. Generally the outlook is much better for people with anal cancer compared to many other types of cancer.

Overall, between 60% and 75% of people with anal cancer will live for at least 5 years. For people diagnosed with stage 1 and 2 anal cancer more than 80% will live for at least 5 years.

In those whose cancer has spread to the lymph nodes or nearby body structures, such as the bladder (stage 3), between 60% to 80% will live for at least 5 years.

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Unfortunately the outlook is much poorer if the cancer has spread to distant organs (stage 4). In this situation, only about 10% will live for at least 5 years. (Cancer Research UK; American Cancer Society).

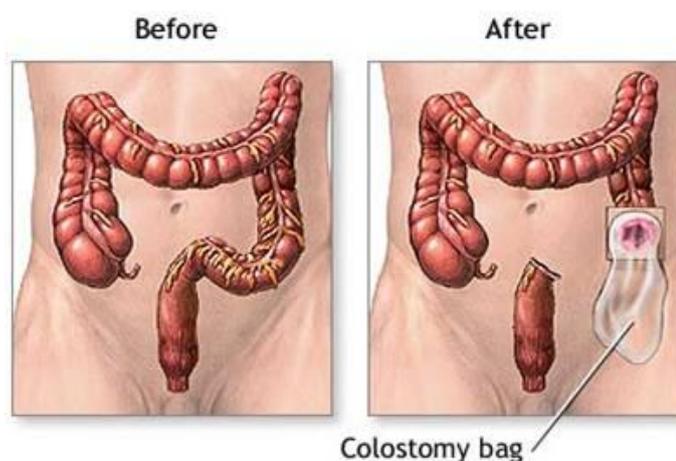
### **Treatment of Anal Cancer**

Most patients with anal cancer can have their cancer treated successfully with a combination of external beam radiation therapy and anticancer drugs known as chemotherapy. Preserving function of the anal sphincter muscles (ring-shaped muscles surrounding the opening) is one potential advantage of using a combination of therapies.

Chemotherapy - chemotherapy is drug treatment to kill cancer cells. Some chemotherapy drugs work because they kill any rapidly dividing cells, and many cancer cells grow and multiply more rapidly than normal cells. Other chemotherapy drugs attack cancer cells by targeting specific differences between cancer cells and normal cells (targeted therapies).  
Radiation therapy - the goal of radiation therapy is to destroy cancer cells while minimising the damage to surrounding tissue. An external beam therapy known as intensity modulated radiation therapy (IMRT) uses precisely shaped radiation beams to accurately deliver high-dose treatment. IMRT yields positive outcomes with fewer side effects than older forms of external radiation therapy.

Intraoperative radiation therapy - (IORT) delivers a concentrated beam of radiation to cancerous tumours while they are exposed during surgery. This technique allows doctors to administer high doses of radiation to tumours while sparing nearby healthy organs from radiation. IORT is still considered experimental in the treatment of anal cancer.

[Picture Credit: Colostomy Following Resection of Anus]



Surgery - surgical removal of the cancer is performed only when radiation and chemotherapy are not completely effective. Surgery may be used to treat small anal tumours or be used in combination with chemotherapy or radiotherapy for advanced anal cancer. Surgeons use several techniques to remove the cancer. The surgeon may remove the cancer and a small amount of adjacent healthy tissue (local resection). This procedure can often be used when doctors diagnose the cancer early. If more extensive surgery is needed, an abdominoperineal resection (APR) may be done. During this procedure, the surgeon removes the anus and the lower part of the rectum and creates an opening (stoma) on the outside of the body to pass waste. This is known as a colostomy. (Mayo Clinic; MacMillan Cancer Support).

## **Lifestyle Changes Following a Diagnosis of Anal Cancer**

In the event of a patient having had a colostomy, several lifestyle changes will be required. Please refer to CANSA's Fact Sheet on Colorectal Cancer for additional information on colostomy and colostomy care.

### **About Clinical Trials**

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

### Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

**Treatment** - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

**Prevention** - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer

**Screening** - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

**Diagnostic** - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

**Quality of life or supportive care** - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

### Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

### Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

### Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

### National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

### Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in

writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different “phase” in the clinical research process. The following phases are used for cancer treatment trials:

### Phases of a Clinical Trial

**Phase 0.** These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

**Phase I (also called phase 1).** These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

**Phase II (also called phase 2).** These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

**Phase III (also called phase 3).** These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for

a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

### Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

### Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

### Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

### Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

### When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care. (National Cancer Institute).

### **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 (CANSAs) 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.

Whilst CANSAs has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

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