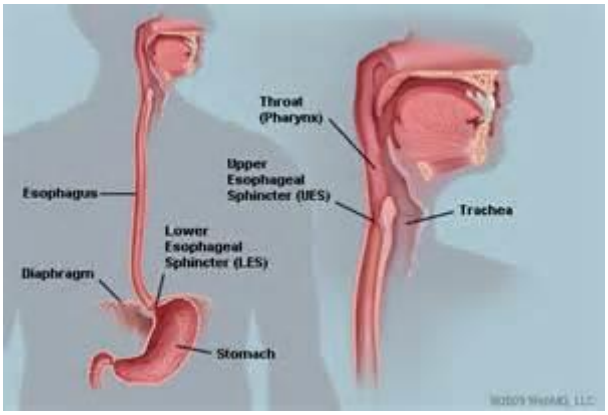
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet On Oesophageal Cancer

Introduction

The oesophagus (commonly known as the gullet) is an organ in humans (and other vertebrates) which consists of a muscular tube through which food passes from the pharynx to the stomach. During swallowing, food passes from the mouth through the pharynx into the oesophagus and travels via peristalsis to the stomach.



[Picture Credit: Oesophagus picture]

This Latin word 'oesophagus' is derived from the Greek word *oisophagos*, literally meaning 'entrance for eating'. In humans the oesophagus is continuous with the laryngeal part of the pharynx at the level of the 6th cervical (neck) vertebra. The 0esophagus passes through the posterior mediastinum in the thorax (chest) and enters the abdomen through a hole in the diaphragm at the level of the 10th thoracic (chest) vertebrae. It is usually about 25cm long, but variations have been recorded depending on the individual's height. It is divided into the cervical, thoracic and abdominal parts. Due to the lower pharyngeal constrictor muscle, the entry of the oesophagus to the stomach, opens only when swallowing or vomiting.

Oesophageal Cancer

Oesophageal cancer is malignancy of the oesophagus. There are various subtypes, primarily squamous cell cancer and adenocarcinoma. Squamous cell cancer arises from the cells that line the upper part of the oesophagus. Adenocarcinoma arises from glandular cells that are present at the junction of the oesophagus and stomach.

Oesophageal cancers are typically carcinomas which arise from the epithelium or surface lining of the oesophagus. A general rule of thumb is that a cancer in the upper two-thirds of the oesophagus is a squamous cell carcinoma and a cancer in the lower one-third of the oesophagus is an adenocarcinoma.

Incidence of Oesophageal Cancer in South Africa

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

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	1 122	1:124	3,04%
Asian males	16	1:374	1,92%
Black males	808	1:113	6,92%
Coloured males	105	1:112	2,42%
White males	193	1:154	0,96%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	702	1:271	1,86%
Asian females	12	1:645	1,11%
Black females	544	1:239	3,30%
Coloured females	67	1:217	1,61%
White females	78	1:481	0,49%

The frequency of histologically diagnosed cases of oesophageal cancer in South Africa for 2012 were 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	0	2	16	87	324	358	200	68
Asian males	0	0	1	1	2	5	4	1
Black males	0	1	11	71	239	238	126	53
Coloured males	0	0	1	5	37	44	13	2
White males	0	1	2	10	43	66	54	13

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	7	37	175	216	148	83
Asian females	0	1	0	1	3	2	3	1
Black females	0	4	6	28	130	170	110	67
Coloured females	0	0	1	5	20	23	13	4
White females	0	0	0	2	22	20	21	11

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 Oesophageal Cancer

While risk factors for squamous cell carcinoma (SCC) of the oesophagus have been identified, namely tobacco use, alcohol use, malnutrition, and infection with human papillomavirus (HPV), the risk factors associated with oesophageal adenocarcinoma (AC) are less well defined. The most important epidemiological difference between squamous cell cancer and adenocarcinoma of the oesophagus is the strong association between gastro-oesophageal reflux disease (GERD) and adenocarcinoma.

Factors that cause irritation in the cells of the oesophagus which increases the risk for oesophageal cancer include:

- Drinking alcohol - smoking and drinking combined increase the risk of squamous cell carcinoma (SCC) of the oesophagus 20-fold
- Having bile reflux
- Chewing tobacco (smokeless tobacco) - The International Agency for Research on Cancer (IARC) classifies smokeless tobacco and betel quid* (with or without tobacco) as a cause of oesophageal cancer. Studies into smokeless tobacco and oesophageal cancer risk in the west have mainly been conducted in the Nordic countries, showing a 60% increase in risk of oesophageal cancer for smokeless tobacco users
- Having difficulty swallowing because of an oesophageal sphincter that will not relax (achalasia)
- Drinking very hot liquids
- Other potential risk factors for oesophageal cancer include oesophageal burns due to accidental or intentional swallowing of caustic materials such as bleach
- Barret's Oesophagus - One of the strongest risk factors for adenocarcinoma of the oesophagus is an acquired premalignant condition known as Barrett's oesophagus (BO, or Barrett's metaplasia)
- Eating few fruits and vegetables - A recent meta-analysis of case-control and cohort studies reported a significant reduction in risk with higher consumption of fruit and a non-significant protective role of vegetable consumption. A study published in December 2011 estimated that more than 46% of oesophageal cancer cases overall in men and around 45% in women in the UK in 2010 were linked to people eating fewer than five portions a day (400g/day) of fruit and vegetables (Cancer Research UK)
- Eating foods preserved in lye, such as lutefisk, a Nordic recipe made from aged stockfish (air-dried whitefish) or dried/salted whitefish (klippfisk) and lye (*lut*) whitefish. Lye-cured olives is another food type in this category
- Certain asthmatic medicines - drugs given to asthmatics such as ?-agonists and aminophyllines also have the effect of relaxing the sphincter and this is the likely reason for the higher incidence of AC observed in asthmatics
- Having gastro-oesophageal reflux disease (GERD)
- Being obese
- Undergoing radiation treatment to the chest or upper abdomen
- Smoking - European studies showed a four-fold risk increase for oesophageal cancer overall among smokers. The effect of smoking is stronger for SCC than adenocarcinoma (AC), with a recent cohort study showing that current smokers have a nine-fold risk increase for oesophageal SCC and a four-fold risk increase for oesophageal AC
- Race - squamous cell cancer of the oesophagus is more common among blacks than whites. Adenocarcinoma is more common in white men than men of other races
- Vitamin Deficiencies - some studies have linked oesophageal cancer with deficiencies in beta carotene, vitamin E, selenium, and iron
- History of other Illnesses - a variety of other illnesses and medical conditions have been associated with an increased risk of oesophageal cancer. These include:

    - Cancers of the head, neck, or lungs
    - Human papillomavirus (HPV) infection
    - Tylosis, a very rare inherited disease that causes excess skin growth on the palms of the hands and the soles of the feet. People with this disease have a high risk of developing oesophageal squamous cell cancer and should be screened regularly
    - Oesophageal webs - abnormal bands of tissue that extend inward into the oesophagus making it difficult to swallow

Other risk factors include:

- Being male
- Age - being between the ages of 45 and 70

(*) Betel quid is a combination of betel leaf, areca nut, and slaked lime. In many countries, tobacco is also added, and the product is known as *gutka*, *ghutka*, or *gutkha*. Other ingredients and flavourants are also added according to local preferences and customs (e.g., sweeteners; catechu; or spices such as cardamom, saffron, cloves, anise seeds, turmeric, and mustard). The following cancers have been associated with betel quid use: lip, mouth, tongue, pharynx and oesophagus. (Centers for Disease Control and Prevention).

(Mayo Clinic; Memorial Sloan-Kettering Cancer Center; National Foundation for Cancer Research; Cancer Research UK; Cancer.Net; MedicineNet.com).

Signs and Symptoms of Oesophageal Cancer

The following are important signs and symptoms of oesophageal cancer:

- Unintentional weight loss - unintentional weight loss can mean many things, but it is better to have it checked out
- Pain when swallowing (odynophagia) - pain when swallowing is one of the most common symptoms of oesophageal cancer. The throat feels irritated or with pressure. This symptom is not associated with flu or flu-related illnesses. The pain or difficulty swallowing related with oesophageal cancer does not go away. Pain with swallowing is an ominous sign
- Hoarseness - if the voice is hoarse, or the person feels like he/she has to often clear their throat, it should get checked out by a doctor
- Persistent cough - having a cough that does not go away
- Heartburn - having heartburn - pain or burning sensation behind the breast bone. Heart burn that occurs often or increasingly warrants a consultation with a doctor
- Feeling like food is stuck in throat or chest - In certain cases of oesophageal cancer, the oesophagus narrows, thus reducing the amount of space foods have to travel down to the stomach. The sensation of food being stuck in the throat or chest is typical of oesophageal cancer. It is generally not noted until the oesophageal lumen is narrowed to one-half to one-third of normal
- Hiccups with pain – The presence of regular incidents of hiccups requires a visit to a doctor
- Coughing up of blood – the blood is bright red in colour and only a small quantity is vomited at any given time
- Dysphagia - the most common presenting complaint is dysphagia (difficulty in swallowing) which, due to oesophageal elasticity, is generally not noted until the oesophageal lumen is narrowed to one-half to one-third of normal
- Cough - cough that is induced by swallowing is suggestive of local extension into the trachea with resultant trachea-oesophageal fistula and may be a sign of oesophageal cancer
- Hoarseness - hoarseness may be a sign of recurrent laryngeal nerve involvement due to extra-oesophageal spread of cancer
- Metastatic disease - metastatic disease may present as malignant pleural effusion (fluid collection in the lungs) or ascites (fluid collection in the abdomen). Bone metastasis (cancer that has spread to the bones) can be identified by pain involving the affected site or by associated hypercalcaemia

(About.Com Cancer; CancerNetwork.Com; WebMD; National Foundation for Cancer Research; Cancer.Net; VCU Massy Cancer Center; Fred Hutchinson Cancer Research Center).

Diagnosis of Oesophageal Cancer
Screening - Regular screening tests to find oesophageal cancer in people without symptoms are not often used. People with Barrett's oesophagus (see above) may be advised to have endoscopic examinations (looking inside the oesophagus through a flexible, lighted tube) and biopsies (removal of a small amount of tissue for examination under a microscope) regularly to help find cancer early or to find changes that could become cancerous over time.

A diagnosis of oesophageal cancer is usually made following:

- Laboratory studies which focused on the evaluation of nutritional status
- Imaging studies that may include the following:
- Barium swallow (very sensitive for helping detect strictures and intraluminal masses, but now rarely used)
- Oesophagogastroduodenoscopy
- Endoscopic ultrasonography (most sensitive test for T and N staging)
- Computed tomography of the abdomen and chest (for M staging and assessing invasion of adjacent structures)
- Bronchoscopy (to help exclude invasion of the trachea or bronchi)
- Bone scan (for patients with complaints suggestive of bone metastases)
- Laparoscopy and thoracoscopy (for staging regional nodes)
- Positron emission tomography (PET for elucidating hypermetabolic foci of disease activity)
  (Medscape Reference; Cancer.Net).

Types of Oesophageal Cancer
There are two main types of oesophageal cancer. Both types are diagnosed, treated, and managed in similar ways.

The two most common types are named for how the cancer cells look under a microscope. Both types begin in cells in the inner lining of the oesophagus:

- Adenocarcinoma (AC) of the oesophagus: This type is usually found in the lower part of the oesophagus, near the stomach.
- Squamous cell carcinoma (SCC) of the oesophagus: This type is usually found in the upper part of the oesophagus.

(National Cancer Institute).

Reducing the Risk for Oesophageal Cancer
The following can assist in reducing the risk for oesophageal cancer:

- Quit smoking or chewing tobacco. Join the CANSA E-KickButt Programme
- Drink alcohol in moderation, if at all. The risk of various types of cancer — including cancer of the breast, colon, lung, kidney, liver and oesophagus — increases with the amount of alcohol one drinks and the length of time one has been drinking regularly. Alcohol was classified as a Group 1 carcinogen by IARC in 1980
- Eat more fruits and vegetables. Add a variety of colourful fruits and vegetables to the diet. Try and eat at least five portions of vegetables and fresh fruit (in season) every day

- Maintain a healthy weight. If overweight or obese, talk to a doctor about strategies to help lose weight
- Individuals with Barrett's Oesophagus should go for screening every year

(Life is Beautiful; Mayo Clinic).

Staging of Oesophageal Cancer

The stage of a cancer is the most significant factor when devising a treatment plan. For oesophageal cancer, the system usually used to stage the disease is the TNM system (also known as the American Joint Committee on Cancer, or AJCC, system).This system is based on three main variables: 'T', which refers to the size of the tumour; 'N', which describes how far the cancer has spread to nearby lymph nodes; and 'M', which indicates whether the cancer has spread to distant organs in the body or to lymph nodes not located near the oesophagus.

The TNM system is used to categorise the cancer in stages 0 through IV (0–4).The higher the stage number, the more the cancer has spread. Some doctors also divide the stages into letters (for example, IIA or IIB) to further clarify the extent of the cancer.

There are 4 stages of tumour size in oesophageal cancer. They are:

- T1 means the tumour has grown no further than the layer of supportive tissue
- T2 means the tumour has grown into the muscle layer of the wall of the oesophagus
- T3 means the tumour has grown into the membrane covering the outside of the oesophagus
- T4 means the tumour has grown into other organs or body structures next to the food pipe. It is divided into T4a and T4b. T4a means that the cancer has grown into the tissue covering the lungs (pleura), the outer covering of the heart (pericardium), or the muscle at the bottom of the rib cage (diaphragm). T4b means that the cancer has spread into other nearby structures such as the windpipe (trachea), a spinal bone (vertebra) or a major blood vessel (the aorta).

In cancer of the oesophagus, the N stages refer to lymph nodes that surround the food pipe (the regional lymph nodes). There are 4 possible stages:

- N0 means there are no lymph nodes containing cancer cells
- N1 means there are cancer cells in 1 or 2 nearby lymph nodes
- N2 means there are cancer cells in 3 to 6 nearby lymph nodes
- N3 means there are cancer cells in 7 or more nearby lymph nodes

There are two stages of metastasis

- M0 means there is no cancer spread to other organs
- M1 means the cancer has spread to other parts of the body

(National Foundation for Cancer Research; Cancer Research UK)

Prognosis (Outlook)

The likelihood of being cured of cancer depends in large part on the stage of the cancer at the time it is diagnosed. From 80% to 90% of patients with the earliest stage of oesophageal cancer can expect to be alive and cancer free 5 years after treatment. However, since the

typical oesophageal cancer is discovered at a relatively advanced stage, the overall success rate in curing oesophageal cancer is disappointing (The society of Thoracic Surgeons).

Survival rates are slowly improving as oesophageal cancers are being detected earlier and more effective treatments are developed, but even so they remain poor. Overall, about 40 per cent of people are still alive one year after diagnosis, but currently only about 1 in 8 survive to 5 years. Survival rates are, of course, better for those with early stage disease (MacNair).

Treatment of Oesophageal Cancer

As with most cancers, if a case of oesophageal cancer is found, the first step is to work out what type of cancer it is and how far it has spread. This is called staging, and it helps to predict how the cancer is likely to progress and which treatments are most appropriate

Treatments that may be offered include:

Surgery - what exactly is done will depend on where the tumour is, the stage of the cancer and the person's general level of fitness. In early stage cancer the lining of the oesophagus may simply be removed, but more often part (or all) of the oesophagus is taken away. Often nearby lymph nodes and other tissues must be removed too. The oesophagus is then repaired so the patient can swallow food. Sometimes a section of the lower intestine may be used to replace the removed part of the oesophagus or to bypass a whole area if the tumour is too large.

During the operation, the surgeon will examine the oesophagus and surrounding area. Some of the lymph nodes will be removed from around the oesophagus. The doctor will send the lymph nodes to the laboratory to check to see if they contain cancer cells. This helps the doctor to know the stage of the cancer.

Endoscopic mucosal resection (EMR) - if the patient has high grade Barrett's oesophagus, or a very early stage cancer which is only on the lining of the oesophagus (the mucosal layer), it may be possible to remove it using endoscopic mucosal resection (EMR). High grade Barrett's oesophagus means that some of the cells are very abnormal. If left untreated, these cells may develop into an invasive cancer. For this procedure, the doctor puts a tube called an endoscope down the patient’s throat. The endoscope contains a camera so the doctor can see inside the body. The endoscope can be used to inject fluid into the layer of cells below the cancer or abnormal area, which makes it stand out from the rest of the tissue. Then a thin wire (snare) is used to remove the area.

The most common side effects are bleeding and a narrowing of the oesophagus, which can happen some time after the procedure. There is a very small risk of tearing the oesophageal wall. The patient may also have photodynamic therapy or radiofrequency ablation after EMR, to try to destroy any abnormal areas or cancer cells that may be left.

Chemotherapy - relieves symptoms and may slow cancer growth. Giving chemotherapy before surgery is called neo adjuvant chemotherapy. This is commonly used for treating oesophageal cancer. The chemotherapy can shrink the cancer, making it easier to remove. It also helps reduce the chances of the cancer coming back.

If there is cancer of the lower oesophagus or where the oesophagus meets the stomach (gastro-oesophageal junction) chemotherapy may be ordered after surgery, as well as before. This also helps to lower the chances of the cancer coming back.

If the oesophageal cancer has spread to other parts of the body (advanced oesophageal cancer) the patient may be given chemotherapy on its own. This may help to control or shrink the cancer and reduce symptoms.

Radiotherapy - may be used to shrink a tumour before surgery. It may be given on its own, in combination with chemotherapy or after surgery to try to prevent recurrence. A patient may be given radiotherapy alongside chemotherapy (chemoradiation) before, or instead of, surgery. Or in some cases, the patient may have radiotherapy on its own if he/she is unable to have chemotherapy or surgery. In the case of advanced oesophageal cancer, the patient is most likely to have radiotherapy on its own to help control the cancer and relieve symptoms.

Radiotherapy is painless to have, although it may make the throat sore as the course of treatment goes on. It is usual to have this treatment as an outpatient. The length of the course of radiotherapy treatment will depend on the size and type of oesophageal cancer the patient has. Usual treatment is for a few minutes every day, over a few weeks.

Sometimes radiotherapy is given from inside the body. This is known as internal radiotherapy or brachytherapy. For oesophageal cancer, this means having a radioactive source put down your throat and into the food pipe. The doctor may use a flexible tube known as an endoscope to get the radioactive source in the right place. A patient is most likely to have this treatment if he/she has an advanced cancer that is making it difficult to swallow.

Combined chemotherapy and radiotherapy - In some cases, a patient may have chemotherapy and radiotherapy together. This is called chemoradiation. A patient may have it before surgery to help shrink the cancer, making it easier to remove. If a patient is unable to have surgery, or do not want it, he/she may have chemoradiation on its own. Particularly if they have squamous cell cancer near the top of the oesophagus. Some studies have shown that chemoradiation can be as good as surgery for this type of cancer. Chemoradiation is quite an intensive treatment and there are side effects. The doctor will consider the patient's general health before deciding if this treatment is an option.

Laser treatment - if the cancer is blocking the oesophagus and making it difficult to swallow, the patient may need treatment to clear the blockage. Sometimes laser treatment is used to burn away the tumour. This may help to reduce the size of the tumour and relieve symptoms but is not curative. Laser treatment may be combined with the use of a light-sensitive drug (known as photo-dynamic therapy or PDT).

Insertion of a stent - a rigid tube is placed in the oesophagus to help keep it open and allow food to pass through to the stomach. It can help deal with symptoms but does not treat the cancer itself

Biological (Immuno-) therapies - made from chemicals that occur naturally in the body such as antibodies, or substances that counteract the effect of the protein signalling molecules which naturally stimulate growth of the cells (known as growth factor blockers). Another type of biological therapy is a vaccine, which can stimulate the immune system to identify cancerous cells and destroy them. Biological therapy is not often used, however, if the tumour is in the area where the oesophagus joins the stomach (oesophagogastric junction), doctors sometimes use a biological therapy drug called trastuzumab (Herceptin).

Two main types of cancer affect the oesophagus, a muscular tube through which food passes from the mouth to the stomach: squamous cell carcinoma (cancer that begins in flat cells lining the oesophagus) and adenocarcinoma (cancer that begins in cells that make and release mucus, which are usually associated with ectopic gastric mucosa). Oesophageal cancer is more common in men than in women.

The 5-year relative survival rate for patients with oesophageal cancer is 40% for patients with localised disease; 22% for regional disease; and 4% for metastatic disease.

Surgery remains the most common treatment for oesophageal cancer, though chemotherapy, radiation, and immunotherapy may also be used. The two immunotherapies approved for oesophageal cancer are trastuzumab and ramucirumab. Several approaches to immunotherapy for oesophageal cancer have shown promise in early clinical trials. These treatments can be broken into 5 main categories: checkpoint inhibitors/immune modulators, adoptive cell transfer, monoclonal antibodies, therapeutic vaccines, and cytokines.

Are you a patient or caregiver interested in learning more about cancer immunotherapy treatment and clinical trials?

Immunotherapy has the potential to improve the outlook for patients and families affected by the disease and bring us ever closer to effective, lasting cures for oesophageal cancer. That's why CRI supports scientific research being done to advance the potential of immunotherapies for oesophageal cancers.

Recent developments include the analysation of NY-ESO-1 cancer-testis (CT) antigen expression in oesophageal cancer, seeking to correlate this expression with disease stage and clinical outcome in a trial of 123 oesophageal cancer specimens with a 33% expression rate. The high expression frequency of NY-ESO-1 indicates this as a feasible vaccine target in oesophageal cancer. Additionally, clinical investigators and colleagues in Japan have reported that a vaccine composed of the NY-ESO-1f long peptide administered with the immune stimulants could elicit integrated immune responses including antibodies, CD4+ helper T cells, and CD8+ killer T cells in nine out of the ten patients enrolled in a phase I clinical trial, stabilizing the disease for three patients, including one with oesophageal cancer. The strong results of this study suggest that oesophageal vaccines using immunotherapy-treated long peptides are a promising therapy option for oesophageal cancer.
(Cancer Research Institute).

Photodynamic Therapy (PDT) - this treatment involves the use of low powered lasers combined with a light sensitive drug to destroy cancer cells. PDT is a relatively new treatment, and you may need to have it repeated a number of times. A patient may be given this:

- as a treatment to try to prevent high grade Barrett's oesophagus developing into cancer, if you are unable to have an endoscopic mucosal resection (EMR) or surgery

- after EMR for high grade Barrett's or very early oesophageal cancer, to treat any abnormal or cancerous cells left behind
- to destroy part of a tumour and improve swallowing when advanced oesophageal cancer is making this difficult

Radiofrequency ablation (RFA) – If a patient has high grade Barrett's oesophagus, he/she may have RFA either on its own or after an endoscopic mucosal resection (EMR). RFA uses heat made by radio waves to destroy the abnormal cells. Radiofrequency is a type of electrical energy. And ablation means 'destroying completely'. A tube with a camera (endoscope) is passed down the throat into the oesophagus. A small balloon or probe is then guided to the area of abnormal cells. A few quick 'pulses' of electrical energy is given to destroy the abnormal cells on the inside of the oesophagus. RFA may also be used after EMR for a very early stage oesophageal cancer.

Argon plasma coagulation (APC) - APC is sometimes recommended after EMR or as a treatment if swallowing remains difficult. Using an endoscope, a probe is placed close to the area to be treated. Using a combination of argon gas and electricity, the doctor can destroy the cancer.
(MacNair; Cancer Research UK; MacMillan Cancer Support; Mayo Clinic).

Changing of Lifestyle Following Oesophageal Cancer Diagnosis
Lifestyle changes following an oesophageal cancer diagnosis can be helpful in a variety of important ways:

- Strengthening the body so that one can withstand some of the rigors of treatment
- Optimising the function of the immune system to aid in the fight against cancer
- Improving one's emotional outlook, so one can enjoy life to the fullest, even during treatment for oesophageal cancer
- Making healthful choices that will help to avoid other medical problems that could complicate health

General Guidelines
Stop smoking - Smoking is a known risk factor for many cancers. It is never too late to stop smoking. Join CANSA's e-KickButt Programme or ask a doctor about programmes to help stop smoking.

Reduce the risk of infection - To decrease the risk of infection, avoid exposure to bacteria and viruses:
- Try to avoid crowds, especially during cold and flu season
- Ask a doctor about immunisation against the flu and pneumonia
- Wash hands thoroughly and often. Hand washing is the most effective method of decreasing the chance of catching colds and flu. You may wish to carry hand sanitizer with you for occasions when washing is not convenient.

Follow a Nutritious Diet - Eating a healthful diet may help avoid other medical conditions linked to poor nutrition. Because cancer itself and some cancer treatment may have a dulling effect on one's appetite, it's important that one makes the most of the calories taken in.

Strongly consider consulting a registered dietician (RD) to help learn more about the best kinds of foods to eat and how to eat other less healthful foods in moderation.

Rest when tired - The treatments for cancer can add to the fatigue patients may experience. Fatigue is the most frequently experienced symptom of cancer and cancer treatments. The fatigue can range from 'just feeling tired' to complete and utter exhaustion. It is important to allow the body time to rest. This will help the body have the strength to heal itself. Studies have shown a relationship between fatigue and an increased morbidity of cancer and cancer treatments as a result of fatigue's adverse effect on appetite, diminished quality of life, and loss of hope.

Seek support - The diagnosis of cancer is a life-defining event that is difficult to handle for anyone. Facing the uncertainty of a serious disease, feeling anxious about how one will feel during treatment, and worrying about the impact of both the diagnosis and treatment can take a devastating toll that no one should have to tackle on their own. Try to have access to the following:

- Family
- Friends
- Religious community
- Empathetic support groups for people with your type of cancer
- Professional support (social workers, psychologists, and/or psychiatrists who are trained to help support cancer patients and their families)

People who allow themselves to seek help while they are recovering from cancer can often maintain better emotional equilibrium, which will help them face the challenges of cancer and its treatment (Winchester Hospital).

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).

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