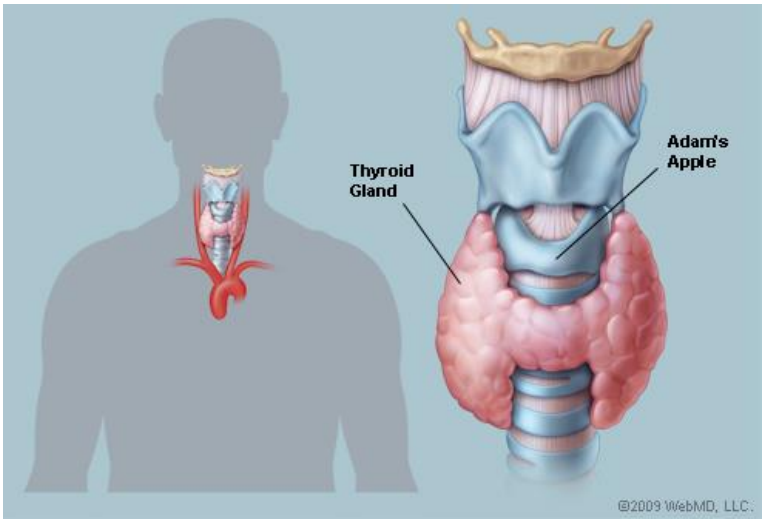
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Cancer of the Thyroid

Introduction

The thyroid is a butterfly-shaped gland that sits low on the front of the neck. The thyroid lies below the Adam's apple, along the front of the windpipe. It has two side lobes, connected by a bridge (isthmus) in the middle. When the thyroid is its normal size, it cannot be felt.



[Picture Credit: Thyroid Gland]

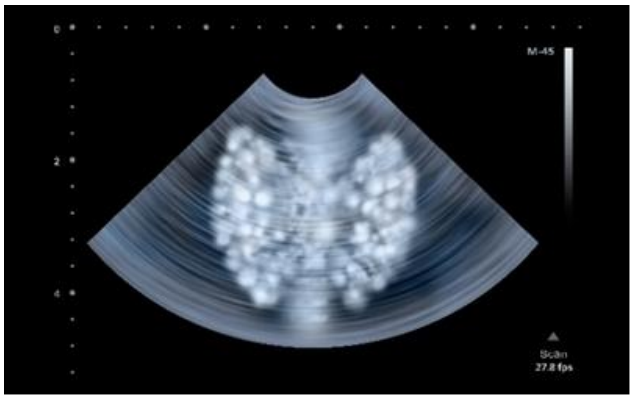
Brownish-red in colour, the thyroid is rich with blood vessels. Nerves important for voice quality also pass through the thyroid.
The thyroid secretes several hormones, collectively called thyroid hormones. The main hormone is thyroxine, also called T4. Thyroid hormones act throughout the body, influencing metabolism, growth and development, and body temperature. During infancy and childhood, adequate thyroid hormone is crucial for brain development.

The C cells in the thyroid make calcitonin. This hormone plays a small role in keeping a healthy level of calcium in the body. Four or more tiny parathyroid glands are on the back of the thyroid. These glands make parathyroid hormone. This hormone plays a big role in helping the body maintain a healthy level of calcium.
(WebMD; MedicineNet.com).

Thyroid Cancer

Thyroid cancer is when cancer develops in the cells of the thyroid. Cancer begins in cells, the building blocks that make up tissues. Tissues make up the thyroid and other organs of the body. Normal thyroid cells grow and divide to form new cells as the body needs them. When normal cells grow old or get damaged, they die, and new cells take their place.

Sometimes, this process goes wrong. New cells form when the body does not need them, and old or damaged cells do not die as they should. The build up of extra cells often forms a mass of tissue called a nodule. It may also be called a growth or tumour. Most thyroid nodules are benign. Benign nodules are not cancer (malignant).



[Picture Credit: Thyroid]

Thyroid cancer cells can spread by breaking away from the thyroid tumour. They can travel through lymph vessels to nearby lymph nodes. They can also spread through blood vessels to the lungs, liver, or bones. After spreading, cancer cells may attach to other tissues and grow to form new tumours that may damage those tissues (MedicineNet.com).

Incidence of Thyroid Cancer in South Africa

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

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	126	1:1 344	0,34%
Asian males	6	1:1 274	0,75%
Black males	22	1:5 274	0,19%
Coloured males	19	1:944	0,44%
White males	79	1:380	0,39%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	407	1:556	1,08%
Asian females	26	1:308	2,43%
Black females	126	1:1 305	0,76%
Coloured females	48	1:423	1,16%
White females	206	1:158	1,30%

The frequency of histologically diagnosed cases of cancer of the thyroid gland 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	1	6	17	19	36	28	11	6
Asian males	0	0	1	3	1	1	0	0
Black males	0	1	3	0	7	7	0	1
Coloured males	0	0	2	5	8	2	1	0
White males	0	4	11	10	19	17	10	4

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	3	34	65	101	82	65	41	13
Asian females	0	4	9	2	3	4	1	1
Black females	1	6	20	31	26	16	8	5
Coloured females	1	1	9	9	10	7	5	2
White females	1	18	23	53	37	30	22	3

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.

Almost half of people older than 40 years have a thyroid nodule. Most are benign and present little risk; only 7% to 15% are malignant. [2] In 2016, an estimated 64,300 cases of thyroid cancer were diagnosed, which is approximately double the number of cases diagnosed in 2002. Despite the rising incidence of thyroid cancer, mortality rates have remained relatively stable, and epidemiology experts say this points to overdiagnosis of subclinical disease.

Recent studies have shown that most excess cases of thyroid cancer involved small indolent tumours that would likely have never been detected were it not for advances in imaging technologies and fine-needle aspiration (FNA). Many people received aggressive, risky, and costly treatments for these harmless tumours, previously known as encapsulated follicular variant of papillary thyroid carcinomas (EFVPTCs).

In 2016, an Endocrine Pathology Society working group proposed revising the nomenclature for EFVPTC to noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Also in 2016, the American Thyroid Association (ATA) published updated evidence-based guidelines for diagnosing and managing adults with thyroid nodules and differentiated thyroid cancer (DTC). These changes should help clinicians and pathologists understand the variants of thyroid cancer better and improve their ability to communicate with one another and with patients about prognosis and treatment needs.
(Endocdrinology Advisor).

Signs and Symptoms of Thyroid Cancer
Thyroid cancer doesn't always have symptoms, so it can be hard to detect and diagnose. In fact, some of the possible symptoms aren't actually caused by thyroid cancer itself. Instead, these symptoms can be caused by a thyroid nodule—and thyroid nodules aren't necessarily cancerous.

People may visit a doctor because they notice one or more of the following symptoms and signs:

Lump in the Neck - Not all thyroid nodules are big enough to cause a noticeable lump. Some people, though, may notice a lump in the front of their neck. Other people may notice a lump in someone's neck when they swallow. The most common way that a thyroid lump (and potential thyroid cancer) is detected, however, is when a doctor performs a thyroid examination and feels the thyroid.

[Picture Credit: Lump in Neck]

Swollen Lymph Node - Swollen lymph nodes in the neck are another symptom of thyroid cancer (a symptom not related to thyroid nodules). Thyroid cancer can spread to the lymph nodes, which are scattered throughout your body to help you fight infection. The lymph nodes in your neck (you can feel them under your jaw) become swollen when you have a cold or sore throat, for example. When the infection is gone, they should return to their normal size, so if the lymph nodes in your neck stay enlarged for an extended period—and you aren't sick—you should talk to your doctor.

Hoarse Voice - The thyroid gland sits just below the larynx (more commonly known as the voice box or Adam's apple). A thyroid nodule (which may be thyroid cancer) may be pressing on the voice box, causing hoarseness or voice changes. This is an uncommon way that thyroid cancer is detected.

Difficulty Swallowing or Breathing - The thyroid is on top of the trachea or windpipe. A developing thyroid cancer may put pressure on the trachea, making breathing more difficult. The esophagus is below the trachea, so again, a developing thyroid cancer can cause trouble swallowing. This is also an uncommon way that thyroid cancer is detected.

Neck Pain **-** Pain is usually a clue that something in the anatomy is not working quite as it should. If experiencing neck pain that lasts longer than a few weeks, one should make an appointment with a doctor. Thyroid cancer is a rare cause of neck pain.

Throat Pain - Similar to neck pain, throat pain that will not go away should be reported to a doctor as it is a possible symptom of thyroid cancer.
Swollen lymph nodes in the neck.

The above symptoms are associated with thyroid nodules of all types, not just cancerous nodules. Since most thyroid cancers develop in thyroid nodules, it is essential to be aware of these symptoms and signs that may point to thyroid cancer. The symptoms of thyroid cancer are hard to detect - and usually the noticeable symptoms are caused not by the cancer itself but by the thyroid nodule where the thyroid cancer is developing.
(Endocrineweb; Mayo Clinic).

Risk Factors for Thyroid Cancer
The following risk factors for thyroid cancer have been identified:

Gender and age - for unclear reasons thyroid cancers (like almost all diseases of the thyroid) occur about 3 times more often in women than in men. Thyroid cancer can occur at any age, but the risk peaks earlier for women (who are most often in their 40s or 50s when diagnosed) than for men (who are usually in their 60s or 70s).
A diet low in iodine

Diet low in iodine - follicular thyroid cancers are more common in areas of the world where people's diets are low in iodine. In the United States, most people get enough iodine in their diet because it is added to table salt and other foods. A diet low in iodine may also increase the risk of papillary cancer if the person also is exposed to radioactivity.

Radiation - exposure to radiation is a proven risk factor for thyroid cancer. Sources of such radiation include certain medical treatments and radiation fallout from power plant accidents or nuclear weapons.

Having had head or neck radiation treatments in childhood is a risk factor for thyroid cancer. Risk depends on how much radiation is given and the age of the child. In general, the risk increases with larger doses and with younger age at treatment. Before the 1960s, children were sometimes treated with low doses of radiation for things we wouldn't use radiation for now, like acne, fungus infections of the scalp (ringworm), or enlarged tonsils or adenoids. Years later, the people who had these treatments were found to have a higher risk of thyroid cancer. Radiation therapy in childhood for some cancers such as lymphoma, Wilms tumour, and neuroblastoma also increases risk. Thyroid cancers that develop after radiation therapy are not more serious than other thyroid cancers.

Imaging tests such as x-rays and CT scans also expose children to radiation, but at much lower doses, so it's not clear how much they might raise the risk of thyroid cancer (or other cancers). If there is an increased risk it is likely to be small, but to be safe, children should not have these tests unless they are absolutely needed. When they are needed, they should be done using the lowest dose of radiation that still provides a clear picture.

Several studies have pointed to an increased risk of thyroid cancer in children because of radioactive fallout from nuclear weapons or power plant accidents. For instance, thyroid cancer was many times more common than normal in children who lived near Chernobyl, the site of a 1986 nuclear plant accident that exposed millions of people to radioactivity. Adults involved with the cleanup after the accident and those who lived near the plant have also had higher rates of thyroid cancer. Children who had more iodine in their diet appeared to have a lower risk.

Some radioactive fallout occurred over certain regions of the United States after nuclear weapons were tested in western states during the 1950s. This exposure was much, much lower than that around Chernobyl. A higher risk of thyroid cancer has not been proven at these low exposure levels. If you are concerned about possible exposure to radioactive fallout, discuss this with your doctor.

Being exposed to radiation as an adult carries much less risk of thyroid cancer.

A question that is often asked is whether radiation exposure during a mammogram may be a cause of thyroid cancer and whether it is advisable to rather make use of a thyroid guard during mammography. The answer is that there is little chance that a breast X-ray (mammogram) will cause thyroid cancer. In addition, a thyroid guard could interfere with the accuracy of the mammogram.

A thyroid guard or thyroid shield is a lead collar that wraps around one's neck to block the radiation that is generated in making X-ray images.

During an X-ray, the majority of radiation needed to create the images goes exactly where it's aimed. In the case of a mammogram, most radiation exposure occurs in the breast. But the rest of the body is often exposed to small amounts of what is called scatter radiation. Scatter radiation during a mammogram is often a fraction of the natural radiation one would receive in one day (Mayo Clinic).

Hereditary conditions and family history - several inherited conditions have been linked to different types of thyroid cancer, as has family history. Still, most people who develop thyroid cancer do not have an inherited condition or a family history of the disease.

- Medullary thyroid cancer

About 1 out of 3 medullary thyroid carcinomas (MTCs) result from inheriting an abnormal gene. These cases are known as *familial medullary thyroid carcinoma* (FMTC). FMTC can occur alone, or it can be seen along with other tumours.

The combination of FMTC and tumours of other endocrine glands is called *multiple endocrine neoplasia type 2* (MEN 2). There are 2 subtypes, MEN 2a and MEN 2b, both of which are caused by mutations (defects) in a gene called *RET*.

- in MEN 2a, MTC occurs along with pheochromocytomas (tumours that make adrenaline) and with parathyroid gland tumours
- in MEN 2b, MTC is associated with pheochromocytomas and with benign growths of nerve tissue on the tongue and elsewhere called *neuromas*. This subtype is much less common than MEN 2a

In these inherited forms of MTC, the cancers often develop during childhood or early adulthood and can spread early. MTC is most aggressive in the MEN 2b syndrome. If MEN 2a, MEN 2b, or isolated FMTC runs in your family, you may be at very high risk of developing MTC. Ask your doctor about having regular blood tests or ultrasound exams to look for problems and the possibility of genetic testing.

- Other thyroid cancers
  People with certain inherited medical conditions have a higher risk of more common forms of thyroid cancer. Higher rates of thyroid cancer occur among people with uncommon genetic conditions such as:

  - familial adenomatous polyposis (FAP): People with this syndrome develop many colon polyps and have a very high risk of colon cancer. They also have an increased risk of some other cancers, including papillary thyroid cancer. *Gardner syndrome* is a subtype of FAP in which patients also get certain benign tumours. Both Gardner syndrome and FAP are caused by defects in the gene *APC*.
  - Cowden disease: People with this syndrome have an increased risk of thyroid, endometrial (uterine), and breast cancers. The thyroid cancers tend to be either the papillary or follicular type. This syndrome is caused by defects in the gene *PTEN*.
  - Carney complex, type I: People with this syndrome may develop a number of benign tumours and hormone problems. They also have an increased risk of papillary and follicular thyroid cancers. This syndrome is caused by defects in the gene *PRKAR1A*.

If one suspects that one might have a familial condition, talk to a doctor, who might recommend genetic counseling if the medical history warrants it.

Papillary and follicular thyroid cancers do seem to run in some families. Having a first-degree relative (parent, brother, sister, or child) with thyroid cancer, even without a known inherited syndrome in the family, increases one's risk for thyroid cancer. The genetic basis for these cancers is not totally clear.
(American Cancer Society; Mayo Clinic).

Diagnosis of Thyroid Cancer
Diagnosis of thyroid cancer typically involves a number of procedures and tests.

Physical Exam - the doctor should conduct a thorough physical exam, including palpation of the thyroid to feel for enlargement and lumps, as well as the gland's size and firmness. The doctor will also look for any enlarged lymph nodes in the neck.

Biopsy - doctors often will do a biopsy of suspicious thyroid nodules, to evaluate for potential cancer. Typically thyroid nodules are biopsied using a needle, in a procedure known as 'fine needle aspiration biopsy' -- sometimes abbreviated FNA. Some patients have a surgical biopsy, where the nodule, or the thyroid gland itself, is removed surgically.

A new test available since 2011, called the Veracyte Afirma Thyroid Analysis (VATA), eliminates indeterminate or inconclusive thyroid nodule biopsy results.

Imaging Tests - A variety of imaging scans are used to evaluate thyroid nodules for possible thyroid cancer. These include:

- Nuclear scan, also known as radioactive iodine uptake (RAI-U) scan. Nodules that absorb more radioactive iodine, and therefore are more visible, are known as "hot nodules" and are more likely to be benign.
- CT scan, known as computed tomography or a "cat scan," is a specialized type of x-ray that is sometimes used to evaluate the thyroid. A CT scan can't detect smaller nodules, but may help detect and diagnose a goiter, or larger thyroid nodules.
- Magnetic resonance imaging (MRI), can help detect enlargement in the thyroid, as well as tumours, tumour size, and may be able to detect tumour spread.
- Thyroid ultrasound, can tell whether a nodule is a fluid-filled cyst, or a mass of solid tissue, but it cannot determine if a nodule or lump is malignant.

Blood Tests - blood tests cannot diagnose thyroid cancer itself, or detect a cancerous thyroid nodule. Thyroid stimulating hormone (TSH) blood tests, however, may be used to evaluate the thyroid's activity and test for hypothyroidism or hyperthyroidism.

Other Tests - when medullary thyroid cancer is suspected, doctors will typically test for high levels of calcium, as this can be an indicator. They may also do genetic testing to identify the abnormal gene associated with some cases of medullary thyroid cancer.
(About.com Thyroid Disease).

Staging of Thyroid Cancer

Thyroid cancer staging describes how large a cancer is, and the degree to which the disease has spread. Once cancer of the thyroid is found (diagnosed), more tests ware done to find out if cancer cells have spread to other parts of the body. This is called staging. A doctor needs to know the stage of the disease to better plan treatment. There are different types of staging used in thyroid cancer. The following stages are used:

Papillary and Follicular Thyroid Cancer in Patients Younger than 45 Years of Age

Stage I Papillary and Follicular Thyroid Cancer – in Stage I papillary and follicular thyroid cancer, the tumour is any size, may be in the thyroid, or may have spread to nearby tissues and lymph nodes. Cancer has not spread to other parts of the body.

Stage II Papillary and Follicular Thyroid Cancer – in Stage II papillary and follicular thyroid cancer, the tumour is any size and cancer has spread from the thyroid to other parts of the body, such as the lungs or bone, and may have spread to lymph nodes.

Papillary and Follicular Thyroid Cancer in Patients Older than 45 Years of Age

Stage I papillary and Follicular Thyroid Cancer – in Stage I papillary and follicular thyroid cancer, cancer is found only in the thyroid and the tumour is 2 centimetres or smaller.

Stage II Papillary and Follicular Thyroid Cancer – in Stage II papillary and follicular thyroid cancer, cancer is only in the thyroid and the tumour is larger than 2 centimetres but not larger than 4 centimetres.

Stage III Papillary and Follicular Thyroid Cancer – in Stage III papillary and follicular thyroid cancer, either of the following is found:

- The tumour is larger than 4 centimetres and only in the thyroid or the tumour is any size and cancer has spread to tissues just outside the thyroid, but not to lymph nodes; or

- The tumour is any size and cancer may have spread to tissues just outside the thyroid and has spread to lymph nodes near the trachea (windpipe) or larynx (voice box).

Stage IV Papillary and Follicular Thyroid Cancer – Stage IV papillary and follicular thyroid cancer is divided into stages IVA, IVB, and IVC

- In Stage IVA, either of the following is found:
  - The tumour is any size and cancer has spread outside the thyroid to tissues under the skin, the trachea (wind pipe), the oesophagus (food pipe), the larynx (voice box), and/or the recurrent laryngeal nerve (a nerve with two branches that go to the larynx); cancer may have spread to nearby lymph nodes; or

  - The tumour is any size and caner may have spread to tissues just outside the thyroid. Cancer has spread to lymph nodes on one or both sides of the neck or between the lungs.

- In Stage IVB, cancer has spread to tissue in front of the spinal column or has surrounded the carotid artery or the blood vessels in the area between the lungs; cancer may have spread to lymph nodes.

- In Stage IVC, the tumour is any size and cancer has spread to other parts of the body, such as the lungs and bones, and may have spread to lymph nodes.

Medullary Thyroid Cancer

Stage 0 Medullary Thyroid Cancer – Stage 0 medullary thyroid cancer is found only with a special screening test. No tumour can be found in the thyroid.

Stage I Medullary Thyroid Cancer – Stage I medullary thyroid cancer is found only in the thyroid and is 2 centimetres or smaller.

Stage II Medullary Thyroid Cancer – In Stage II medullary thyroid cancer, either of the following is found:

- The tumour is larger than 2 centimetres and only in the thyroid; or
- The tumour is any size and has spread to tissues just outside the thyroid, but not to lymph nodes.

Stage III Medullary Thyroid Cancer – in Stage III medullary thyroid cancer, the tumour is any size, has spread to lymph nodes near the trachea (wind pipe) and the larynx (voice box), and may have spread to tissues just outside the thyroid.

Stage IV Medullary Thyroid Cancer – Stage IV medullary thyroid cancer is divided into stages IVA, IVB, and IVC.

- In Stage IVA, either of the following is found

  - The tumour is any size and cancer has spread outside the thyroid to tissues under the skin, the trachea (wind pipe), the oesophagus (food pipe), the larynx (voice box), and/or the recurrent laryngeal nerve (a nerve with 2 branches that go to the larynx); cancer may have spread to lymph nodes near the trachea (wind pipe) or the larynx (voice box); or

  - The tumour is any size and cancer may have spread to tissues just outside the thyroid. Cancer has spread to lymph nodes on one or both sides of the neck or between the lungs.

- In Stage IVB, cancer has spread to tissue in front of the spinal column or has surrounded the carotid artery or the blood vessels in the area between the lungs. Cancer may have spread to lymph nodes.

- In Stage IVC, the tumour is any size and cancer has spread to other parts of the body, such as the lungs and bones, and may have spread to lymph nodes.

<u>Anaplastic Thyroid Cancer</u>

Anaplastic thyroid cancer grows quickly and has usually spread within the neck when it is found. Stage IV anaplastic thyroid cancer is divided into stages IVA, IVB, and IVC.

- In Stage IVA, cancer is found in the thyroid and may have spread to lymph nodes.

- In Stage IVB, cancer has spread to tissue just outside the thyroid and may have spread to lymph nodes.

- In Stage IVC, cancer has spread to other parts of the body, such as the lungs and bones, and may have spread to lymph nodes.

(Thy.Ca).

The staging guidelines developed by the American Joint Committee on Cancer (AJCC) are often used to stage thyroid cancers. The stages are based on three categories:

T - Describes the primary tumour size.
N – Indicates whether the thyroid cancer cells have spread to regional lymph nodes.
M – Refers to whether the cancer has metastasized (spread to distant areas of the body).

Primary Tumour **(T)**

TX primary tumour cannot be assessed
T0 no evidence of primary tumour
T1 tumour ≤2cm in greatest dimension limited to they thyroid
T1a tumour ≤1cm, limited to the thyroid
T1b tumour >1cm but ≤ 2cm in greatest dimension, limited to the thyroid
T2 tumour > 2cm but ≤ 4cm in greatest dimension, limited to the thyroid
T3 tumour > 4cm in greatest dimension limited to the thyroid or any tumour with minimal extrathyroid extension (e.g. extension to sternothyroid muscle or perithyroid soft tissues)
T4a moderately advanced disease
Tumour of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, oesophagus or recurrent laryngeal nerve
T4b very advanced disease
Tumour invades prevertebral fascia or encases carotid artery or mediastinal vessels
T4a intrathyroidal anaplastic carcinoma
T4b anaplastic carcinoma with gross extrathyroid extension

Regional Lymph Nodes **(N)**

NX regional lymph nodes cannot be assessed
N0 no regional lymph node metastasis
N1 regional lymph node metastasis
N1a metastases to Level VI (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes)
N1b metastses to unilateral, bilateral or contralateral cervical or retropharyngeal or superior mediastinal lymph nodes

Distant Metastasis **(M)**[a]

M0 no distant metastasis
M1 distant metastasis

(National Cancer Institute).

<u>Thyroid Cancer Stage Groupings</u>

Once the individual TNM components are scored, they are combined to determine the overall stage group. The thyroid cancer stage classification is unique and different from most other tumour types because it incorporates not just the TNM information, but also the patient's age and tumour subtype.

How Thyroid Cancer Can Spread
Should Cancer of the thyroid spread to organs in the body, it may spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

(National Cancer Institute).

Papillary or follicular (differentiated) thyroid cancer in patients younger than 45
The prognosis of a patient under the age of 45 with a differentiated (papillary or follicular) thyroid cancer is very good, and there is a very low chance of dying. The thyroid cancer staging system takes this information into account, and classifies these cancers simply into two groups based on whether or not they have spread to distant organs:

Stage I: The primary tumour can be any size and the cancer may or may not have spread to lymph nodes. Distant sites in the body are not affected.

Stage II: The primary tumour can be any size and the cancer may or may not have spread to lymph nodes, but cancer cells have spread to distant areas of the body.

Papillary or follicular (differentiated) thyroid cancer in patients 45 years of age or older AND medullary thyroid cancer (any age)
The thyroid cancer staging classification system is very similar for older patients with differentiated tumours and for those with medullary thyroid cancer. Age is not a consideration when classifying medullary cancers.

Stage I: In this stage of thyroid cancer, the tumour is 2 cm or smaller (less than an inch wide), and has not grown outside the thyroid. It has not spread to nearby lymph nodes or distant sites.

Stage II: Cancers at this stage meet one of the following criteria:
The diameter of the primary tumour ranges from 2 to 4 cm. There are no cancer cells in regional lymph nodes or distant sites in the body.
The primary tumour is larger than four cm in diameter or has started to grow outside of the thyroid gland. No cancer was found in the lymph nodes or other parts of the body (medullary thyroid cancer only).

Stage III: Cancers at this stage meet one of the following criteria:

The primary tumour is larger than 4 cm, or has grown outside the thyroid, but has not spread to nearby lymph nodes or beyond (differentiated cancers only).
The tumour can be any size or be growing outside the thyroid, and has spread to lymph nodes in the neck but no farther.

Stage IV: The most advanced stage of thyroid cancer is further subdivided depending on where the cancer has spread:

Stage IVA: Cancers at this stage have grown beyond the thyroid gland and may have spread into nearby tissue, or they may have spread to lymph nodes in the neck and upper chest, but not to distant sites.

Stage IVB: The primary tumour has grown into the spine or into nearby large blood vessels. In this thyroid cancer stage, the disease may or may not have spread to lymph nodes, but has not reached distant sites.

Stage IVC: The thyroid cancer cells have metastasized, or spread to distant sites.

Anaplastic (undifferentiated) thyroid cancer

Anaplastic/undifferentiated thyroid cancers are much more aggressive than the other subtypes and are all considered stage IV:

Stage IVA The primary tumour is contained within the thyroid gland, although it may or may not have spread to nearby lymph nodes. It has not spread to distant organs.

Stage IVB The tumour has spread outside of the thyroid gland, and cancer cells may or may not have been found in regional lymph nodes, but have not reached distant sites.

Stage IVC The cancer cells have spread beyond the thyroid gland to more distant parts of the body (Cancer Treatment Centers of America).

What is New in Thyroid Cancer Research and Treatment?

Important research into thyroid cancer is being done right now in many university hospitals, medical centres, and other institutions around the country. Each year, scientists find out more about what causes the disease, how to prevent it, and how to improve treatment. In past years, for example, evidence has grown showing the benefits of combining surgery with radioactive iodine therapy (RAI) and thyroid hormone therapy. The results include higher cure rates, lower recurrence rates, and longer survival.

Genetics - the discovery of the genetic causes of familial (inherited) medullary thyroid cancer now makes it possible to identify family members carrying the abnormal *RET* gene and to remove the thyroid to prevent cancer from developing there.

Understanding the abnormal genes that cause sporadic (not inherited) thyroid cancer has led to better treatments as well. In fact, treatments that target some of these gene changes are already being used, and more are being developed

Treatment - most thyroid cancers can be treated successfully. But advanced cancers can be hard to treat, especially if they do not respond to radioactive iodine (RAI) therapy. Doctors and researchers are looking for new ways to treat thyroid cancer that are more effective and lead to fewer side effects.
(American Cancer Research).

Treatment of Thyroid Cancer
Thyroid cancer treatment options depend on the type and stage of the thyroid cancer, the overall health of the patient and his/her preferences.
Most cases of thyroid cancer can be cured with treatment.

Surgery
Most people with thyroid cancer undergo surgery to remove all or most of the thyroid. Operations used to treat thyroid cancer include:

Removing all or most of the thyroid (thyroidectomy) - Surgery to remove the entire thyroid is the most common treatment for thyroid cancer. In most cases, the surgeon leaves small rims of thyroid tissue around the parathyroid glands to reduce the risk of parathyroid damage. Sometimes surgeons refer to this as a near-total thyroidectomy.

Removing lymph nodes in the neck - When removing your thyroid, the surgeon may also remove enlarged lymph nodes from the neck and test them for cancer cells.

Thyroid surgery is performed by making an incision in the skin at the base of the neck. Thyroid surgery carries a risk of bleeding and infection. Damage can also occur to the parathyroid glands during surgery, later leading to low calcium levels in the body. There is also a risk of accidental damage to the nerves connected to the vocal cords, which can cause vocal cord paralysis, hoarseness, soft voice or difficulty breathing.

Thyroid hormone therapy
After thyroid cancer surgery, patients are given thyroid hormone medication levothyroxine (Levothroid, Synthroi or, others) for life. These pills have two benefits: It supplies the missing hormone the thyroid would normally produce, and it suppresses the production of thyroid-stimulating hormone (TSH) from the pituitary gland. High TSH levels could conceivably stimulate any remaining cancer cells to grow.

Patients are likely have blood tests to check their thyroid hormone levels every few months until the doctor finds the proper dosage for them.

Radioactive iodine
Radioactive iodine treatment uses large doses of a form of iodine that is radioactive. Radioactive iodine treatment is often used after thyroidectomy to destroy any remaining healthy thyroid tissue, as well as microscopic areas of thyroid cancer that were not removed during surgery. Radioactive iodine treatment may also be used to treat thyroid cancer that recurs after treatment or that spreads to other areas of the body.

Radioactive iodine treatment comes as a capsule or liquid that one swallows. The radioactive iodine is taken up primarily by thyroid cells and thyroid cancer cells, so there is a low risk of harming other cells in the body.

Side effects may include:

- nausea
- dry mouth
- dry eyes
- altered sense of taste or smell
- pain where thyroid cancer cells have spread, such as the neck or chest

Most of the radioactive iodine leaves the body in the urine in the first few days after treatment. During that time the patient will be given instructions for precautions they need to take to protect other people from the radiation. For instance, the patient may be asked to temporarily avoid close contact with other people, especially children and pregnant women.

External radiation therapy

Radiation therapy can also be given externally using a machine that aims high-energy beams at precise points on the body. Called external beam radiation therapy, this treatment is typically administered a few minutes at a time, five days a week, for about six weeks. During treatment, the patient is requested to lie still on a table while a machine moves around him/her. External radiation therapy is generally used to treat thyroid cancer that has spread to the bones.

Chemotherapy

Chemotherapy is a drug treatment that uses chemicals to kill cancer cells. Chemotherapy is typically given as an infusion through a vein. The chemicals travel throughout your body, killing quickly growing cells, including cancer cells.

Chemotherapy is not commonly used in the treatment of thyroid cancer, but it may benefit some people who don't respond to other, more standard therapies.

Targeted therapy

In general, thyroid cancers do not respond well to chemotherapy. But exciting data are emerging about some newer targeted drugs. Unlike standard chemotherapy drugs, which work by attacking rapidly growing cells (including cancer cells), these drugs attack specific targets on cancer cells. Targeted drugs may work in some cases when standard chemotherapy drugs do not, and they often have different (and less severe) side effects.

Kinase inhibitors - a class of targeted drugs known as *kinase inhibitors* may help treat thyroid cancer cells with mutations in certain genes, such as *BRAF* and *RET/PTC*. Many of these drugs also affect tumour blood vessel growth (see below).

In many papillary thyroid cancers, the cells have changes in the *BRAF* gene, which helps them grow. Drugs that target cells with *BRAF* gene changes, such as vemurafenib (Zelboraf®), dabrafenib (Tafinlar®), and selumetinib, are now being studied in thyroid cancers with this gene change.

In one study, giving selumetinib to patients with thyroid cancers that had stopped responding to radioactive iodine (RAI) treatment helped make some patients' tumours respond to

treatment with RAI again. It helped patients not only with *BRAF* mutations, but also with mutations in a different gene called *NRAS*.

Other kinase inhibitors that have shown early promise against thyroid cancer in clinical trials include sorafenib (Nexavar®), sunitinib (Sutent®), pazopanib (Votrient®), motesanib (AMG 706), and axitinib (Inlyta®).

Some of these other drugs, such as sunitinib, sorafenib, and pazopanib, are already approved to treat other types of cancer, and might be useful against medullary thyroid cancer (MTC) and differentiated thyroid cancers if other treatments are no longer working.
Anti-angiogenesis drugs - as tumours grow, they need a larger blood supply to get enough nutrients. They get it by causing new blood vessels to form (a process called angiogenesis). Anti-angiogenesis drugs work by disrupting these new blood vessels. Some of the drugs listed above, such as axitinib, motesanib, sunitinib, and sorafenib, have anti-angiogenic properties.

Other anti-angiogenesis drugs being studied for use against thyroid cancer include bevacizumab (Avastin®) and lenalidomide (Revlimid®).

Other targeted drugs: A recent early study found the combination of the chemotherapy drug paclitaxel (Taxol) with the targeted drug efatutazone could be helpful in patients with anaplastic thyroid cancer. Efatutazone targets a receptor called PPAR-gamma.
(Mayo Clinic; American Cancer Society).

Increasing the Effectiveness of Radioactive Iodine Therapy
To increase the effectiveness of one's upcoming radioactive iodine therapy, one may be prescribed a low iodine diet. Iodine is used in the care and feeding of animals and as a stabiliser and/or safety element in food processing. Therefore, it may be found in varying amounts in all food and beverages. The highest sources (and those to be avoided) are iodized salt, grains and cereals, white bread, fish from the sea, shellfish, beef, poultry, pudding mixes, milk and milk products. Detailed recipes that follow a low iodine diet can be found on the following websites: www.checkyourneck.com (Light of Life Foundation) and www.thyca.org (ThyCa: Thyroid Cancer Survivors' Association).

Below are general guidelines to follow on this diet.

Options for Breakfast

- Any fruit or fruit juices
- Egg Beaters
- Oatmeal with toppings – cinnamon, honey, applesauce, maple syrup, walnuts, fruit
- 1 slice toast with unsalted butter
- Black coffee or clear tea

Options for Lunch

- Vegetarian or chicken with rice soup (not canned)
- Unsalted Matzo crackers White or brown rice with vegetable plate (fresh or frozen)
- Salad – fruit or vegetable – oil and vinegar dressing

- Fruits – fresh, frozen or canned
- Black coffee or clear tea

Options for Dinner

- Small portion of Roast beef, lamb, veal, pork, or turkey
- Potato – baked or broiled with salt-free butter
- Vegetables (fresh or frozen)
- Salad – fruit or vegetable – oil and vinegar dressing Fruits
- Black coffee or clear tea

Options for Snacks

- Fresh fruit or juice
- Dried fruits such as raisens
- Fresh raw vegetables
- Applesauce
- Unsalted nuts
- Fruit juice
- Unsalted peanut butter (great with apple slices, carrot sticks, crackers or rice cakes)
- Matzoh and other unsalted crackers
- Home-made bread and muffins

[Picture Credit: Iodized Salt]

Summary Guide

- No iodized salt
- No dairy products or foods containing dairy products
- No foods from the sea
- No processed meats (i.e. ham, bacon, sausage, hot dogs, deli meats)
- No canned soups or broth
- Limited grain products (i.e. noodles, pasta, pastries) – 1 slice bread, ½ cup pasta daily
- Limited amounts of beef, chicken and turkey

Avoid the Following Foods

The following foods should be avoided:

- Iodized salt, sea salt, foods high in salt, baking soda and sodium
- Any vitamins or supplements that contain iodine, especially kelp and dulse (Palmaria palmata Kuntze, also called dulse, dillisk or dilsk, red dulse, sea lettuce flakes or creathnach, is a red alga previously referred to as Rhodymenia palmata Greville. It grows on the northern coasts of the Atlantic and Pacific oceans. Wikipedia)

[Picture Credit: Dulse]

- Milk or other dairy products including ice cream, cheese, yogurt and butter
- Seafood including fish, sushi, shellfish, kelp or seaweed
- Foods that contain the additive carrageen, agar-agar, alginate, or nori (nori is the Japanese name for edible seaweed species of the red algae genus Porphyra, including Purple Seaweed, *P. yezoensis* and *P. tenera*. Wikipedia)

- Cured and corned foods such as ham, lox (a fillet of brined salmon), corned beef, sauerkraut, cold cuts
- Commercially prepared bakery products that could be made with iodate dough conditioners
- FD&C red dye #3 – this appears in many foods or pills that are red or brown, including colas, and in maraschino cherries
- Egg yolks, whole eggs and foods containing whole eggs
- Dried fruits
- Canned vegetables (salt-free canned vegetables are fine)
- Most chocolate (due to milk content)
- Blackstrap Molasses (unsulfured molasses is fine)
- Soy products (soy sauce, soy milk, tofu)

[Picture Credit: Soy]

<u>Foods That Are In Order</u>

The following foods are safe to use:

- Non-iodized salt may be used as desired
- Egg whites
- Fresh non-cured meat from the butcher
- Homemade bread made with non-iodized salt and oil (***not soy!***) instead of butter or milk
- Most fresh fruits and vegetables (but not too much spinach & broccoli), washed well
- Frozen vegetables that do not have high-iodine ingredients (like regular salt) added
- Grain, cereal products and pasta without high iodine ingredients
- Canned peaches, pears and pineapples
- Natural unsalted nuts and nut butters (peanut, almond, etc)
- Clear sodas, beer, wine, lemonade, fruit juices
- Non-instant coffee or tea, preferably made with distilled water. But remember, only non-dairy creamer!
- Popcorn popped in vegetable oil or air popped, with non-iodized salt
- Black pepper, fresh or dried herbs and spices, all vegetable oils
- Sugar, jam, jelly, honey maple syrup
- Matzo crackers (unsalted)

[Picture Credit: Unsalted Matzo Crackers]

<u>Additional Guidelines</u>

The following additional guidelines may be of assistance:

- Avoid restaurant foods since there is no reasonable way to determine which restaurants use iodized salt.
- Consult the treating doctor before discontinuing any medication containing iodine (i.e., Amiodarone, expectorants, topical antiseptics).
- Avoid all herbal supplements (especially when one is not sure how much iodine they contain).

(American Thyroid Association).

Reducing the Risk for Thyroid Cancer

At present there are no generally accepted recommendations for reducing the risk for thyroid cancer.

Medullary thyroid cancer often is genetically inherited. If anyone in one's family has been diagnosed with medullary or other endocrine cancers or if someone in the family is known to carry a mutation (abnormal change) in the RET gene, one may wish to be tested to see if you have this mutation. Medullary thyroid cancers may be part of syndromes that involve other types of endocrine or other cancers, thus a careful family history for cancer is important.

If one carries the RET gene, one may be advised to have one's thyroid removed at a very early age to avoid the very high risk of developing medullary thyroid cancer.
(Cancer Care of Western New York).

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.

<u>Use of Placebos</u>
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 (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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