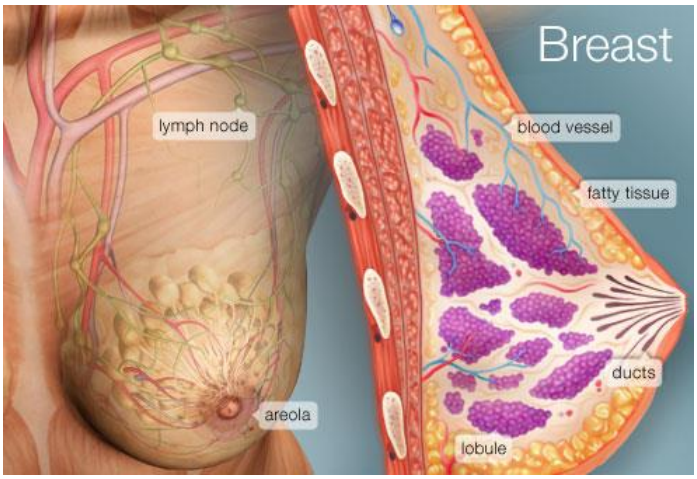
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet on Breast Cancer in Women

Introduction

The breast is the tissue overlying the chest (pectoral) muscles. Women's breasts are made of specialised tissue that produces milk (glandular tissue) as well as fatty tissue. The amount of fat determines the size of the breast.



[Picture Credit: Female Breast]

The milk-producing part of the breast is organised into 15 to 20 sections, called lobes. Within each lobe are smaller structures, called lobules, where milk is produced. The milk travels through a network of tiny tubes called ducts. The ducts connect and come together into larger ducts, which eventually exit the skin in the nipple. The dark area of skin surrounding the nipple is called the areola.

Connective tissue and ligaments provide support to the breast and give it its shape. Nerves provide sensation to the breast. The breast also contains blood vessels, lymph vessels, and lymph nodes.
(WebMD).

Although both men and women have breasts, it is in the female that the breast becomes prominent and a vital component of her persona. In the male, the breast is rudimentary.

The female breast is a symbol of womanhood and femininity but, at the same time, it has an important function. It is an organ that, with appropriate stimulation, will produce milk. Breast milk comes from tiny glands within the breast that resemble bunches of grapes. Breast milk is essential for the sustenance and growth of the new born baby. The breast is, in fact, a modified sweat gland. But, while a sweat gland secretes sweat (perspiration), the breast / mammary gland secretes milk.

Structure of the Female Breast - **t**he anatomy of the breast is quite simple. It is made up of about eighteen lobules of glandular tissue. These lobules resemble bunches of grapes and

each grape represents the secreting unit, called alveolus (pleural: alveoli). The alveolus consists of cells, which line the unit and produce the milk.

Blood supply to the breast - the main blood supply comes from the internal mammary artery that comes off the subclavian artery, which supplies the arm. This is one of the main branches of the arch of the aorta. Additional supplies come from branches of the axillary artery and from the intercostal arteries of the pectoralis major muscle overlying the breast. The venous drainage corresponds with the arterial supply.

Function of the female breast - the physiology of the breast is directly dependent on parts of the body's endocrine system. This system is essential in controlling the function of the human body. This is done by the production of hormones by these endocrine glands. These hormones are chemical messengers that circulate in the blood stream and act on organs remote from their organ of primary secretion.

Gland Hormone Physiology - with regard to breast function, at birth the breast is just a little nipple bud with essentially no function. At puberty, the breasts begin to enlarge, under the influence of the hormones oestrogen and progesterone. The hormonal flux associated with the menstrual cycle is dependent on oestrogen and progesterone levels.

During pregnancy - the pituitary gland secretes the hormone prolactin (luteotrophic hormone) which initiates and stimulates milk production (lactogenesis). This prolactin hormone is stimulated by oestrogen and inhibited by progesterone.

Post Pregnancy - with the disappearance of the corpus luteum of pregnancy and the expulsion of the placenta, the levels of progesterone drop precipitously. Thus the unopposed action of oestrogen stimulates prolactin production, which in turn stimulates the formation of milk. The feeding baby, by its sucking action on the nipple, expresses milk from the breast ducts, but it cannot get at the milk lying deep within the alveoli. Here again another hormone, called oxytocin, comes into action. Stimulation of the nipples by sucking sends nerve impulses to the brain (hypothalamus). The brain in turn activates the pituitary gland to produce oxytocin, which reaches the breast via the blood stream. The woman's monthly ‘periods’ are again harmoniously controlled. The breasts also enlarge pre-menstrually and occasionally become painful. This is called cyclical mastalgia. This pain disappears with the onset of menstruation, as the breast contracts.

Shape and form - the shape and form of the breast is basically determined by the genes and is thus inherited. The factors that determine the appearance of the breasts are:

The amount of fat in the breast. The glandular tissue is similar in small and large breasts. It is mainly the fat that determines size. Thus losing weight by diet and exercise will probably decrease the size of the breasts to a certain extent. The shape of the breast is strongly influenced by the triangle of skin, which extends from the chin to fan out over the breast. This triangle of skin is supported by the fan shaped platysma muscle. This skin triangle, together with its supporting fan shaped platysma muscle, is sometimes referred to as the ‘natural bra’. By exposing her lower teeth, the women contracts the platysma muscle, and this will lift the breast upwards (the natural bra effect).

Coopers ligaments also contribute to breast firmness. Thus by looking after the skin with a good skin oil or cream, and by doing the correct exercises (push ups and swimming are excellent breast toners), and finally by eating a healthy diet, the condition of the breasts can be maintained to a certain extent.
(Breast Health Foundation).

Statistic of Breast Cancer Incidence in South Africa
According to the National Cancer Registry (2013) the following number of breast cancer cases in women was histologically diagnosed during 2013:

Group 2013	Actual Number of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	8 132	1 : 28	22,22%
Asian females	363	1 : 19	35,03%
Black females	3 341	1 : 51	21,37%
Coloured females	1 098	1 : 20	22,07%
White females	3 331	1 : 11	20,98%

Frequency of Histologically Diagnosed Cases of Breast Cancer
According to the National Cancer Registry (2013), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follow:

Group 2013	0 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	80 + Years
All females	2	115	777	1 722	1 900	1 783	1 162	325
Asian females	0	5	27	68	89	78	53	22
Black females	2	71	418	790	779	588	351	176
Coloured females	0	13	88	230	277	240	144	72
White females	0	23	217	825	717	824	585	278

Risk Factors for Breast Cancer in Women
The following are known risk factors for breast cancer in women:

Sex - just being a woman is the biggest risk factor for developing breast cancer.

Age - as with many other diseases, one's risk of breast cancer goes up as one gets older. About two out of three invasive breast cancers are found in women 55 or older.

Family history - women with close relatives who have been diagnosed with breast cancer have a higher risk of developing the disease. If one has had one first-degree female relative (sister, mother, daughter) diagnosed with breast cancer, one's risk is doubled.

Genetics - about 5% to 10% of breast cancers are thought to be hereditary, caused by abnormal genes passed from parent to child. Certain gene mutations that increase the risk of breast cancer can be passed from parents to children. The most common gene mutations are referred to as BRCA1 and BRCA2. These genes can greatly increase one's risk of breast cancer and other cancers, but they do not make cancer inevitable.

BRCA1:

- Mutations are more common in families with both breast and ovarian cancer (approximately 81% of such families)

- Women with *BRCA1* mutations appear to have a lifetime breast cancer risk similar to that of women with *BRCA2* mutations, although the age of onset for both breast and ovarian cancer may be somewhat younger in *BRCA1* families
- Cumulative risk for breast cancer by age: 30 years (3.2%); 40 years (19%); 50 years (51%); 60 years (54%); 70 years (85%)
- Histology: see excess of breast cancers with medullary features, basaloid phenotype, and more frequently negative for oestrogen and progesterone receptors, *ERBB*2 (formerly *HER2* or *HER2/neu*)/c-erb-2 and cyclin-D
- Higher lifetime risk (20%-60%) and earlier age of onset of ovarian cancer than for women in the general population (1.5%), requires referral to gynaecologic oncologist to discuss option of prophylactic salpingo-oophorectomy
- Some *BRCA1* families also have male breast cancer although this is more commonly seen in *BRCA2* families
- Families also have a higher incidence of prostate cancer with male carriers having a 3-fold risk over the general population

BRCA2:

- Mutations seen less frequently in families with both breast and ovarian cancer (approximately 14% of such families)
- Women with *BRCA2* mutations appear to have a lifetime breast cancer risk similar to that of women with *BRCA1* mutations, although the age of onset for both breast and ovarian cancer may be somewhat older in *BRCA2* families
- Cumulative risk for breast cancer by age: 30 years (4.6%); 40 years (12%); 50 years (46%); 60 years (61%); 70 years (85%)
- Breast tumours in *BRCA2* carriers tend to be similar in histology to their nonhereditary counterparts
- Lower lifetime risk of ovarian cancer (10%-27%) than *BRCA1* families but still significant over general population risk of 1.5%. Also earlier age of onset requires referral to gynaecologic oncologist to discuss option of prophylactic salpingo-oophorectomy

Recent research (June, 2017) showed that for BRCA 1 and BRCA2, the risk increased if there was a strong family history of breast cancer. The same research also showed that Breast Cancer risk peaks around the 40s for BRCA1 mutation carriers and around the 50s for BRCA2 carriers.
(Antoniou, 2017).

Personal history of breast cancer - if one has been diagnosed with breast cancer, one has a 3 to 4 times increased risk to develop a new cancer in the other breast or a different part of the same breast. This risk is different from the risk of the original cancer coming back (called risk of recurrence).

Radiation to chest or face before age 30 - if one has had radiation to the chest to treat another cancer (not breast cancer), such as Hodgkin's lymphoma or non-Hodgkin's lymphoma, one has a higher-than-average risk of breast cancer. If one has had radiation to the face as an adolescent to treat acne (something that is no longer done), one is at higher risk of developing breast cancer later in life.

Certain breast changes - if one has been diagnosed with certain benign (non-cancer) breast conditions, one may have a higher risk of breast cancer. There are several types of benign breast conditions that affect breast cancer risk.

Race or ethnicity – It is said that white women are slightly more likely to develop breast cancer than African American, Hispanic, and Asian women. But African American women are more likely to develop more aggressive, more advanced-stage breast cancer that is diagnosed at a young age. There is insufficient evidence to categorically make this statement for South African women.

Being overweight - overweight and obese women have a higher risk of being diagnosed with breast cancer compared to women who maintain a healthy weight, especially after menopause. Being overweight also can increase the risk of the breast cancer coming back (recurrence) in women who have had the disease.

Pregnancy history - women who haven't had a full-term pregnancy or had their first child after age 30 have a higher risk of breast cancer compared to women who gave birth before age 30.

Breastfeeding history - breastfeeding can lower breast cancer risk, especially if a woman breastfeeds for longer than 1 year.

Menstrual history - women who started menstruating (having periods) younger than age 12 have a higher risk of breast cancer later in life. The same is true for women who go through menopause when they are older than 55.

Using HRT (Hormone Replacement Therapy) - current or recent past users of HRT have a higher risk of being diagnosed with breast cancer. Since 2002 when research linked HRT and risk, the number of women taking HRT has dropped dramatically.

Drinking alcohol - research consistently shows that drinking alcoholic beverages - beer, wine, and spirits - increases a woman's risk of hormone-receptor-positive breast cancer.

Having dense breasts - research has shown that dense breasts can be 6 times more likely to develop cancer and can make it harder for mammograms to detect breast cancer.

Lack of exercise - research shows a link between exercising regularly at a moderate or intense level for 4 to 7 hours per week and a lower risk of breast cancer.

Smoking - smoking causes a number of diseases and is linked to a higher risk of breast cancer in younger, premenopausal women. Research also has shown that there may be a link between very heavy second-hand smoke exposure and breast cancer risk in postmenopausal women.

The following emerging risks have been identified:

Low Vitamin D levels - research suggests that women with low levels of vitamin D have a higher risk of breast cancer. Vitamin D may play a role in controlling normal breast cell growth and may be able to stop breast cancer cells from growing.

Light exposure at night - the results of several studies suggest that women who work at night - factory workers, doctors, nurses, and police officers, for example - have a higher risk of breast cancer compared to women who work during the day. Other research suggests that women who live in areas with high levels of external light at night (street lights, for example) have a higher risk of breast cancer.

DES (Diethylstilbestrol) exposure - some pregnant women were given DES from the 1940s through the 1960s to prevent miscarriage. Women who took DES themselves have a slightly higher risk of breast cancer. Women who were exposed to DES while their mothers were pregnant with them also may have slightly higher risk of breast cancer later in life.

Eating unhealthy food - diet is thought to be at least partly responsible for about 30% to 40% of all cancers. No food or diet can prevent one from getting breast cancer. But some foods can make one's body the healthiest it can be. It is important to boost one's immune system, and help keep one's risk for breast cancer as low as possible.

Exposure to chemicals in cosmetics and other personal care products - research strongly suggests that at certain exposure levels, some of the chemicals in cosmetics and other personal care products may contribute to the development of cancer in people.

Exposure to chemicals in food – there is a real concern that pesticides, antibiotics, and hormones used on crops and livestock may cause health problems in people, including an increase in breast cancer risk. There are also concerns about mercury in seafood and industrial chemicals in food and food packaging.

Exposure to chemicals from lawns and gardens - research strongly suggests that at certain exposure levels, some of the chemicals in lawn and garden products may cause cancer in people. But because the products are diverse combinations of chemicals, it is difficult to show a definite cause and effect for any specific chemical.

Exposure to chemicals in plastics - research strongly suggests that at certain exposure levels, some of the chemicals in plastic products, such as Bisphenol A (BPA), may cause cancer in people.

Exposure to chemicals in sunscreens - while chemicals can protect us from the sun's harmful ultraviolet rays, research strongly suggests that at certain exposure levels, some of the chemicals in some sunscreen products may cause cancer in people.

Exposure to chemicals in water - research has shown that drinking water - whether it is from one's home supply or bottled water from a store - may not always be as safe as it could be. Everyone has a role in protecting the water supply. There are steps one can take to ensure one's water is as safe as it can be. In general, filtered tap (municipal) water is as safe as or safer than bottled water from the store, because bottled water is less regulated.

Exposure to chemicals when food is grilled or prepared - research has shown that women who ate a lot of grilled, barbecued, and smoked meats and very few fruits and vegetables had a higher risk of breast cancer compared to women who did not eat a lot of grilled meats. (Breastcancer.org; Mayo Clinic; Cancer Research UK; Clinical Key \Elsevier).

The World Health Organization and Breast Health

The World Health Organization (WHO) states the following about breast health:

Early diagnosis - early diagnosis remains an important early detection strategy, particularly in low- and middle-income countries where the diseases is diagnosed in late stages and resources are very limited. There is some evidence that this strategy can produce "down staging" (increasing in proportion of breast cancers detected at an early stage) of the disease to stages that are more amenable to curative treatment.

Mammography screening - mammography screening is the only screening method that has proven to be effective. Although there is evidence that organised population-based mammography screening programmes can reduce breast cancer mortality by around 20% in the screened group versus the unscreened group across all age groups, in general there appears to be a narrow balance of benefits compared with harms, particularly in younger and older women. There is uncertainty about the magnitude of the harms – particularly overdiagnosis and overtreatment. Mammography screening is very complex and resource intensive and no research of its effectiveness has been conducted in low resource settings.

Breast Self-examination (BSE) - there is no evidence on the effect of screening through breast self-examination (BSE). However, the practice of BSE has been seen to empower women, taking responsibility for their own health. Therefore, BSE is recommended for raising awareness among women at risk rather than as a screening method.

Clinical Breast Examination (CBE) - research is underway to evaluate CBE as a low-cost approach to breast cancer screening that can work in less affluent countries. Promising preliminary results show that the age-standardised incidence rate for advanced-stage breast cancer is lower in the screened group compared to the unscreened group.
(World Health Organization).

Breast Self-Examination

Research has shown that regular breast self-examination (BSE) may play an important role in finding breast cancer compared with finding a breast lump by chance. Some women feel very comfortable doing BSE regularly (usually monthly after their period) which involves a

systematic step-by-step approach to examining the look and feel of their breasts. Other women are more comfortable simply looking and feeling their breasts in a less systematic approach, such as while showering or getting dressed or doing an occasional thorough exam. Sometimes, women are so concerned about 'doing it right' that they become stressed over the technique. Doing BSE regularly is one way for women to know how their breasts normally look and feel and to notice any changes. The goal, with or without BSE, is to report any breast changes to a doctor or nurse right away (American Cancer Society).

Doing a Breast Self-Examination (BSE)

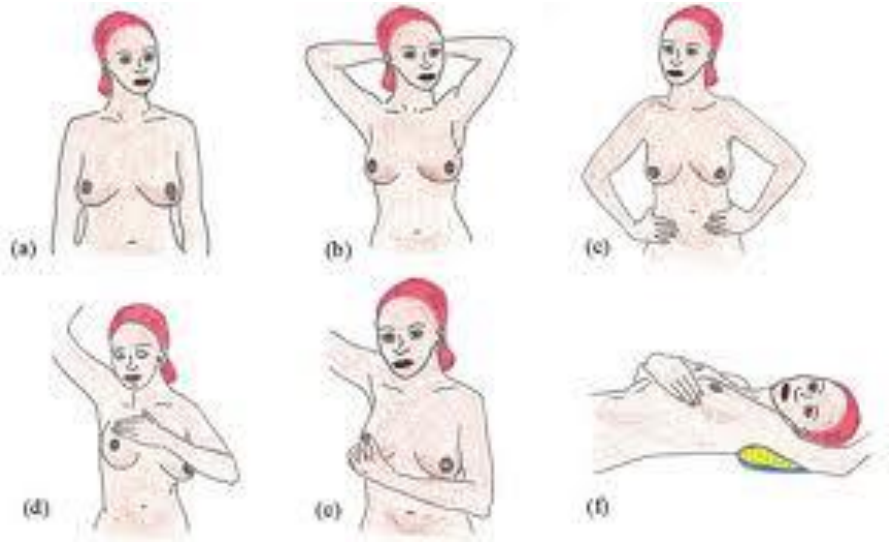
Breast self-examination (BSE) is to be performed each month in addition to any mammograms or a clinical breast examination. Knowing the cyclical changes, what is normal and what regular monthly changes in the breast feel like is the best way to keep an eye on breast health. Breast tissue extends from under the nipple and areola up towards the armpit.

Make a Regular Date for Doing a BSE - If pre-menopausal**:** Set a regular time to do the BSE a few days after the menstruation when hormone levels are relatively stable and the breasts are less tender.

If already menopausal (have not had a period for a year or more), pick a particular day of the month to do the BSE and then repeat the BSE on that day every month

Visual Examination of Breasts - Hands on Hips - In the privacy of the bathroom or bedroom, strip to the waist and stand in front of a mirror. Both breasts must be visible at the same time. Stand with the hands on hips and check the appearance of both breasts. Look at size, shape, colour, whether both nipples are at the same level and contour. Note any changes in the skin colour or texture. Look at the nipples and areolas, to see how healthy they look

Visual Examination - Arms Over the Head - Still standing in front of the mirror, raise both arms over the head and see if both breasts move in the same way, and make a note of any differences.



[Picture Credit: Breast Examination]

Look at the size, shape, and drape - checking for symmetry. Pay attention to both nipples and areolas, to see if there are any dimples, bumps, or retraction (indentation). Look up toward the armpits and note if there is any swelling in the lower armpit area

Manual Examination - Stand and Stroke - Raise the left arm overhead, and use the right-hand fingers to apply gentle pressure to the left breast. Stroke from the top to the bottom of the breast, moving across from the inside of the breast all the way into the armpit area. Make use of a circular motion, being sure to cover the entire breast area. Take note of any changes in texture, colour, or size. Switch sides and repeat the examination. This may be best done in the shower, as wet skin will have the least resistance to the friction of the fingers.

Manual Examination - Check Both Nipples - Still facing the mirror, lower both arms. With the index and middle fingers of the right hand, gently squeeze the left nipple and pull it forward. Does the nipple spring back into place? Does it pull back into the breast? Note whether or not any fluid leaks out. Reverse the hands and check the right nipple in the same manner.

Manual Examination - Recline and Stroke - This is best done in the bedroom, where one can lie down. Place a pillow on the bed so as to lie with both head and shoulders on the pillow. Lie down and put the left hand behind the head. Use the right hand to stroke the breast and underarm. Take note of any changes in texture, colour, or size. Switch sides and repeat the examination.

Guidelines For Doing a BSE:

- Mark the calendar as a reminder to do a BSE regularly.
- Stay relaxed and breathe normally while doing the BSE. Becoming tense may produce some knots that may be mistaken for something worrisome
- Report any changes or unusual pain to a doctor or nurse practitioner
- Keep a log of changes
- Remember to have an annual clinical breast examination and mammogram as described above

CANSA's Position on BSE

CANSA advocates that every woman should do regular (monthly) breast self-examinations (BSE) at the same time every month following her menstrual cycle from age 20 and to report any changes or concerns to a doctor or professional nurse practitioner without delay.

Regular monthly BSE should be seen as a method to raise awareness of breast cancer and taking responsibility for own health rather than as a screening method for breast cancer.

Symptoms and Signs of Breast Cancer in Women

Changes that could be due to a breast cancer include:

- A lump or thickening in an area of the breast
- A change in the shape of the nipple, particularly if it turns in, sinks into the breast, or has an irregular shape
- A blood stained discharge from the nipple
- A rash on a nipple or surrounding area
- A swelling or lump in the armpit
- Nipple tenderness or a lump or thickening in or near the breast or underarm area

- A change in the skin texture or an enlargement of pores in the skin of the breast (some describe this as similar to an orange peel's texture)
- Any unexplained change in the size or shape of the breast
- Dimpling anywhere on the breast
- Unexplained swelling of the breast (especially if on one side only)
- Unexplained shrinkage of the breast (especially if on one side only)
- Recent asymmetry of the breasts (Although it is common for women to have one breast that is slightly larger than the other, if the onset of asymmetry is recent, it should be checked.)
- Nipple that is turned slightly inward or inverted
- Skin of the breast, areola, or nipple that becomes scaly, red, or swollen or may have ridges or pitting resembling the skin of an orange

These signs do not necessarily mean cancer. Inverted nipples, blood stained nipple discharge or a rash can all be due to other medical conditions. In the event of any changes to what is normal, one should see a health professional. It is most likely to be a benign condition that can easily be treated. The health professional will refer to a breast health clinic or medical specialist where the staff can provide reassurance or provide any necessary treatment.

Seeing a doctor early also means that if it does turn out to be cancer, one has the best chance of successful treatment.
(Cancer Research UK; National Breast Cancer Foundation).

Diagnostic Tests for Early-Stage Breast Cancer
According to the South African National Cancer Registry (2011) 7 086 women and 149 men were diagnosed with breast cancer. If one is diagnosed with breast cancer, it is important that doctors get as much information as they can about the tumour so they can make the best recommendations to treat the cancer.

This section provides an overview of the general diagnostic tests that help doctors understand a patient's tumour type. It also describes newer tests that offer additional information for women with certain types of early-stage (stage I or II) breast cancer.

Understanding one's tumour type - tests performed on tumour samples give valuable information that helps guide treatment decisions for breast cancer. By examining tumour samples under a microscope, doctors can determine if the tumour is invasive or noninvasive (in situ).

The tumour sample will also help identify the tumour's grade -whether it is a fast-growing or slow-growing form of breast cancer - as well as the tumour's hormone receptor status and HER2 status. All of these tests will inform the oncologist about a recommended treatment plan.

Sentinel node mapping also helps doctors determine if breast cancer cells have spread to other parts of the body. If the sentinel (first) lymph node is cancer free, the nearby lymph nodes may also be unaffected and left intact. Removing a patient's lymph nodes can affect her/his quality of life because it increases her/his risk of lymphoedema, a painful swelling of the arm.

Determining hormone status - oestrogen and progesterone receptors are structures present on the surface of some cancer cells. These structures allow oestrogen and progesterone to enter the cells and encourage them to grow.

Tumours that test positive for these structures are called hormone receptor-positive and might be successfully treated with hormonal therapy (e.g., tamoxifen or aromatase inhibitors). These treatments prevent oestrogen from attaching to receptors on breast cancer cells.

As a result, oestrogen cannot get in the cells, and tumour growth is slowed. The treatments also reduce the amount of hormones circulating in the body that attach to oestrogen or progesterone receptors. By blocking hormones, the treatments deprive tumour cells of the substances they need to grow.

HER2-positive breast cancers are breast tumours that make too much of a substance called HER2/neu, which speeds the growth of cancer cells. About 20 percent of breast cancers are HER2-positive. Drugs that target HER2/neu slow the growth of the tumour.

Such drugs include trastuzumab (Herceptin) and lapatinib (Tykerb). The breast cancer will be tested to identify if it is HER2-positive to determine the best treatment options.

Triple-negative breast tumours do not depend on oestrogen, progesterone, or HER2 for their growth, and account for about 15 percent of all breast cancers. The standard treatments include surgery, radiation and chemotherapy.

Researchers are looking for new ways to combine chemotherapy and targeted drugs to offer the most benefit to those living with triple-negative breast cancer.

Personalising breast cancer treatment - some of the newest tools for women with breast cancer are tests that estimate the likelihood of deriving a benefit from chemotherapy. Currently, there are two tests approved for estimating a patient's risk of recurrence with early-stage breast cancer: Onco*type* DX and MammaPrint.

Onco*type* DX and MammaPrint are appropriate for women with stage I or II breast cancer that is hormone receptor-positive and will be receiving hormonal therapy. For those who are “on the fence” about embarking on a course of chemotherapy, these tests may provide sufficient information to make the decision clearer and easier. Both tests work by analysing the genes in tumour tissue removed during surgery.

The tests look for patterns of abnormal genetic activity to predict how the tumour will behave. Oncotype DX examines the activity of 21 genes to determine chance of recurrence, and MammaPrint looks at 70 different genes.

The National Cancer Institute is using Onco*type* DX in a clinical trial called TAILORx to study recently diagnosed patients with hormone receptor-positive, HER2-negative breast cancer that has not spread to the lymph nodes.

The TAILORx study is just one example of how research is transforming the way that doctors treat breast cancer - that is, basing their treatment approach on the patient's tumour. If doctors know in advance that a treatment will not be of benefit, the patient could be spared unnecessary side effects from the treatment.
(Cancer Therapy Advisor)

Diagnosis of Breast Cancer in Women
The doctor will check both breasts during a clinical breast examination, feeling for any lumps or other abnormalities.

Doctors use many tests to diagnose cancer and find out if the cancer has spread or metastasised to other parts of the body beyond the breast and the lymph nodes under the arm. Some tests may also help the doctor decide which treatments may be the most effective.

For most types of cancer, a biopsy is the only way to make a definitive diagnosis of cancer. A biopsy is the removal of a small amount of tissue for examination under a microscope. If a biopsy is not possible, the doctor may suggest other tests that will help make a diagnosis. Imaging tests may be used to find out whether the cancer has spread. The doctor may consider the following factors when choosing a diagnostic test:

- Age and medical condition
- Type of cancer suspected
- Signs and symptoms
- Previous test results

(Cancer.Net).

Types of Breast Cancer in Women
The following types of breast cancer have been identified in women:

Ductal Carcinoma *in Situ*
Ductal Carcinoma in Situ (DCIS) is a non-invasive breast cancer where abnormal cells have been contained in the lining of the breast milk duct.

Ductal carcinoma *in situ* (DCIS) is a non-invasive cancer where abnormal cells have been found in the lining of the breast milk duct. The atypical cells have not spread outside of the ducts into the surrounding breast tissue. Ductal carcinoma *in situ* is very early cancer that is highly treatable, but if it is left untreated or undetected, it can spread into the surrounding breast tissue.

The earliest stages of cancers are called 'carcinoma *in situ'*. Carcinoma means 'cancer' and in situ means 'in the original place'.

Invasive Ductal Carcinoma
Invasive Ductal Carcinoma means that abnormal cells that originated in the lining of the breast milk duct have invaded surrounding tissue.

The abnormal cancer cells that began forming in the milk ducts have spread beyond the ducts into other parts of the breast tissue. Invasive cancer cells can also spread to other parts of the body. It is also sometimes called infiltrative ductal carcinoma.

- IDC is the most common type of breast cancer, making up nearly 70- 80% of all breast cancer diagnoses.
- IDC is also the type of breast cancer that can most commonly affects men.

DCIS means the cancer is still contained in the milk duct and has not invaded any other area. IDC is cancer that began growing in the duct and is invading the surrounding tissue. Cancer staging done by a physician, along with a physical examination and medical history can help identify the best treatment options.

Triple Negative Breast Cancer

Triple negative breast cancer means that the cells in the tumour are negative for progesterone, oestrogen, and HER2/neu receptors.

A diagnosis of triple negative breast cancer means that the three most common types of receptors known to fuel most breast cancer growth–oestrogen, progesterone, and the HER-2/neu gene– are not present in the cancer tumour. This means that the breast cancer cells have tested negative for hormone epidermal growth factor receptor 2 (HER-2), oestrogen receptors (ER), and progesterone receptors (PR). Since the tumour cells lack the necessary receptors, common treatments like hormone therapy and drugs that target oestrogen, progesterone, and HER-2 are ineffective. Using chemotherapy to treat triple negative breast cancer is still an effective option. In fact, triple negative breast cancer may respond even better to chemotherapy in the earlier stages than many other forms of cancer.

Triple negative breast cancer occurs in about 10-20% of diagnosed breast cancers and is more likely to affect younger people, African Americans, Hispanics, and/or those with a BRCA1 gene mutation.

Triple negative breast cancer can be more aggressive and difficult to treat. Also, the cancer is more likely to spread and recur. The stage of breast cancer and the grade of the tumour will influence the prognosis.

Inflammatory Breast Cancer

Inflammatory breast cancer is a less common form of breast cancer that may not develop a tumour and often affects the skin.

Inflammatory breast cancer is an aggressive and fast growing breast cancer in which cancer cells infiltrate the skin and lymph vessels of the breast. It often produces no distinct tumour or lump that can be felt and isolated within the breast. But when the lymph vessels become blocked by the breast cancer cells, symptoms begin to appear.

Early IBC symptoms may include persistent itching and the appearance of a rash or small irritation similar to an insect bite. The breast typically becomes red, swollen, and warm. The skin may appear pitted like an orange peel, and nipple changes such as inversion, flattening, or dimpling may occur.

A diagnosis of inflammatory breast cancer is classified as Stages of breast cancer and is diagnosed through the physician's clinical judgment and a biopsy. Typically, IBC grows rapidly and requires aggressive treatment. Most oncologists recommend both local treatment of the affected breast and systemic treatment (whole body treatment), which may include chemotherapy.

Surgery, radiation therapy, chemotherapy and hormone therapy may be included in the regimen. With aggressive treatment, the survival rate for inflammatory breast cancer patients has improved significantly in recent years.

Phyllodes Tumour of the Breast

Phyllodes tumours of the breast are rare, accounting for less than 1% of all breast tumours. The name "phyllodes," which is taken from the Greek language and means "leaflike," refers to that fact that the tumour cells grow in a leaflike pattern. Other names for these tumours are phyllodes tumour and cystosarcoma phyllodes. Phyllodes tumours tend to grow quickly, but they rarely spread outside the breast.

Although most phyllodes tumours are benign (not cancerous), some are malignant (cancerous) and some are borderline (in between noncancerous and cancerous). All three kinds of phyllodes tumours tend to grow quickly, and they require surgery to reduce the risk of a phyllodes tumour coming back in the breast (local recurrence).

Phyllodes tumours can occur at any age, but they tend to develop when a woman is in her 40s. Benign phyllodes tumours are usually diagnosed at a younger age than malignant phyllodes tumours. Phyllodes tumours are extremely rare in men.
(Breastcancer.Org).

Metastatic Breast Cancer

Metastatic breast cancer is cancer that has spread beyond the breast, sometimes into the lungs, bones, or brain.

Metastatic breast cancer is also classified as Stage 4 breast cancer. The cancer has spread to other parts of the body. This usually includes the lungs, liver, bones or brain.

The spread of cancer usually happens through one or more of the following steps:

- Cancer cells invade nearby healthy cells. When the healthy cell is taken over, it too can replicate more abnormal cells.
- Cancer cells penetrate into the circulatory or lymph system. Cancer cells travel through the walls of nearby lymph vessels or blood vessels.
- Migration through circulation. Cancer cells are carried by the lymph system and the bloodstream to other parts of the body.
- Cancer cells lodge in capillaries. Cancer cells stop moving as they are lodged in capillaries at a distant location and divide and migrate into the surrounding tissue.
- New small tumours grow. Cancer cells form small tumour at the new location (called micrometastases.)

The symptoms may vary, depending on how far your breast cancer has spread and what type of tissue the new cancer growth has invaded. All symptoms should be reported to your physician.

Here are some symptoms that vary by locations commonly associated with breast cancer metastasis.

Metastasis in the bone may cause:

- Severe, progressive pain
- Swelling
- Bones that are more easily fractured or broken

Metastasis to the brain may cause:

- Persistent, progressively worsening headache or pressure to the head
- Vision disturbances

- Seizures
- Vomiting or nausea
- Behavioural changes or personality changes

Metastasis to the liver may cause:
- Jaundice
- Itchy skin or rash
- Abnormally high enzymes in the liver
- Abdominal pain, appetite loss, nausea, and vomiting

Metastasis to the lungs may cause:
- Chronic cough or inability to get a full breath
- Abnormal chest X-ray
- Chest pain
- Other nonspecific systemic symptoms of metastatic breast cancer can include fatigue, weight loss, and poor appetite, but it's important to remember these can also be caused by medication or depression.

If these symptoms are noticed, be sure you talk with a physician. He/she could be important for getting the treatment one needs.

Cribriform Breast Cancer

Cribriform breast cancer is a rare form of breast cancer that is often combined with another form of breast cancer. It is typically a low-grade and slow-growing cancer with a better outlook than most other types of invasive breast cancer.

According to one study, an estimated 0,3 to 3,5% of people with breast cancer have cribriform breast cancer.

This type of breast cancer is characterised by breast cancer cells that feature a pattern of holes between the cancer cells. These holes closely resemble Swiss cheese.
As well as these cells, cribriform cancer can also include features from other types of breast cancers.

The higher the grade in Cribriform Breast Cancer, the faster the cancer cells usually grow. The grading of breast cancer is:

- **Grade 1**: The tumour cells are slow-growing and closely resemble those of normal breast cells.
- **Grade 2**: The tumour cells are moderately different from normal cells.
- **Grade 3**: The tumour cells are very abnormal and appear to be growing quickly.

Cribriform Breast Cancer type does not usually metastasise or spread to lymph nodes under the arm. As a result, the prognosis for cribriform breast cancer is often "favourable" or good.

This cancer type is often influenced by hormones, especially oestrogen and progesterone, but there are currently no standard treatment protocols specific to cribriform breast cancer. As a result, a doctor will consider the cancer's stage and discuss treatment options.

Examples of the treatments for cribriform breast cancer include:

- **Surgical removal:** A doctor may recommend a lumpectomy or mastectomy to remove some or all breast tissue and ensure all the cancerous cells are removed.
- **Chemotherapy**: Chemotherapy helps to kill fast-multiplying cancer cells.
- **Radiation**: Radiation involves exposing the tumour to high-energy radiation to kill cancerous cells.
- **Hormone therapy**: These drugs inhibit the action of hormones known to contribute to breast cancer, such as oestrogen and progesterone. A typical example is Tamoxifen, which keeps oestrogen from binding to cancer cells.

Each of these treatments has side effects that range from mild to severe. A person should discuss all treatment options with their doctor.

Breast Cancer During Pregnancy

Women who are diagnosed with breast cancer during pregnancy may face tremendous additional strain due to concern for the safety of the unborn child.

It is possible to be diagnosed with breast cancer during pregnancy, although it is rare and the breast cancer is not caused by the pregnancy. Women who are diagnosed with breast cancer during pregnancy have tremendous additional strain due to concern for the safety of the unborn child. It can be a traumatic and extremely difficult situation, but there is still hope for both mother and child, thanks to the many treatment options available.

If you are pregnant and have been diagnosed, be sure to communicate carefully with your obstetric care team as well as your oncology team, and it never hurts to verify that they have open communication with each other. Your medical team will take extra care in designing the treatment plan that best controls the breast cancer while protecting your unborn child.

The treatment plan will depend on the size of the tumour, its location, and the term of your pregnancy. As with women who are not pregnant, surgery is usually the first step for treating early-stage breast cancer. Surgery during pregnancy can be safely performed with little risk to your unborn child, so your medical team will most likely proceed by removing the lump with a lumpectomy or mastectomy, and possibly some lymph nodes from under the arm.

Chemotherapy may be a treatment option, depending on your cancer type and the stage of your pregnancy. The effects of hormone therapy on unborn foetuses are not entirely understood. Because of this, if hormone therapy is prescribed, it will most likely be used only after the baby is born.

Although the cancer itself cannot spread to and harm the unborn child, sometimes the best treatment plan for the mother may put the unborn child at risk. These decisions will require the expertise and consultation between your obstetrician, surgeon, medical oncologist, and radiation oncologist. You will also need the emotional support of family and friends and may benefit from the professional assistance of a skilled counsellor or psychologist.

Other Types of Breast Cancer

Less common types of breast cancer include Medullary Carcinoma, Tubular Carcinoma, and Mucinous Carcinoma. Although by far, the most common breast cancer type is ductal carcinoma in situ (DCIS), there are other types that are less commonly seen.

- Medullary carcinoma - medullary carcinoma accounts for 3-5% of all breast cancer types. The tumour usually shows up on a mammogram, but does not always feel like a lump. At times, it feels like a spongy change of breast tissue.

- Tubular Carcinoma - making up about 2% of all breast cancer diagnosis, tubular carcinoma cells have a distinctive tubular structure when viewed under a microscope. It is usually found through a mammogram and is a collection of cells that can feel like a spongy area of breast tissue rather than a lump. Typically this type of breast cancer is found in women aged 50 and above and usually responds well to hormone therapy.

- Mucinous Carcinoma (Colloid) - mucinous carcinoma represents approximately 1% to 2% of all breast cancers. The main differentiating features are mucus production and cells that are poorly defined. It also has a favourable prognosis in most cases.

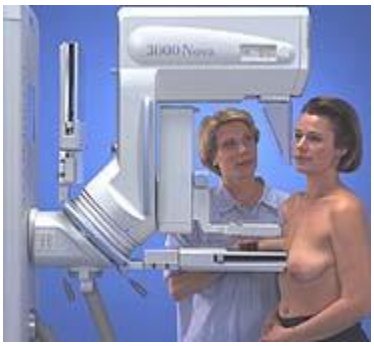
- Paget Disease of the Breast or Nipple - this condition (also known as mammary Paget disease) is a rare type of cancer affecting the skin of the nipple and often the areola, which is the darker circle of skin around the nipple. Most people with Paget disease evident on the nipple also have one or more tumours inside the same breast; generally either ductal carcinoma in situ or invasive breast cancer (1–3). Paget disease is frequently misdiagnosed at first because the first noticeable symptoms can easily be confused with more common skin conditions affecting the nipple. Like all breast cancers, the prognosis for Paget disease depends on a variety of factors, including the presence or absence of invasive cancer and whether or not it has spread to nearby lymph nodes.

(National Breast Cancer Foundation; Medical News Today).

Special Tests

The following tests or examinations may be done:

Mammogram - A mammogram is a low-dose x-ray of the breast. You'll need to take off your top and bra for the mammogram. The radiographer will position you so that your breast is against the x-ray machine and is gently but firmly compressed with a flat, clear, plastic plate. You'll have two mammograms of each breast taken from different angles.



[Picture Credit: Mammogram]

The breast tissue needs to be squashed to keep the breast still and to get a clear picture. Most women find this uncomfortable, and for some women it may be painful for a short time.

Mammograms are usually only used in women over the age of 35. In younger women, the breast tissue is more dense (has less fat), which makes it difficult to detect any changes on the mammogram.

CANSA's Position on Mammography:

CANSA is aware that in the developed world the starting age for regular breast screening by means of a mammogram has been raised to 45 years. This applies to First World countries where access to health care is freely available to everyone.

The South African situation is, however, somewhat different:

- The majority of South African women do not enjoy access to health care
- During 2012 a total of 1 409+ women between the ages 20 and 44 were diagnosed with breast cancer

CANSA, therefore, advocates a mammogram every year for all women from age 40 for purposes of non-symptomatic breast screening.

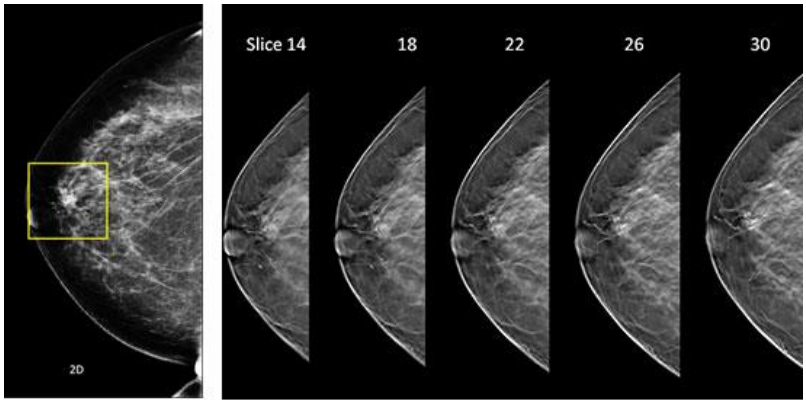
CANSA further advocates that:

- Women who are at risk and those that have had breast health problems in the past should consult their respective health professional to determine a schedule applicable to them
- Women aged 40 to 54 should have an annual mammogram
- Women 55 years and older should change to having a mammogram every 2 years – or have the choice to continue with an annual mammogram
- Screening should continue as long as a woman is in good health and is expected to live 10 years or longer
- Every woman should be informed of the known benefits, limitations, and potential harms linked to breast cancer screening by means of a mammogram

As women get older, the precision of breast cancer screening with mammography increases because the rate of false-positive results decreases and the detection of cancer increases significantly, according to new research presented here at the Radiological Society of North America 2016 Annual Meeting.

This calls into question the recommendation of the US Preventive Services Task Force (USPSTF) that women undergo screening every 2 years only until age 74. Age 75 seems to be an arbitrary cut-off. The decision to stop mammography screening should be made on the basis of individual patient values, comorbidities, and health status — not some random cut-off age.

The Difference Between a 2D and a 3D Mammogram - in recent years, the US Food and Drug Administration (FDA) has approved advanced mammography devices that perform 3D digital breast tomosynthesis, a technology that creates cross-sectional (3D) images of the breast from X-rays taken from multiple angles. **3D** captures multiple slices of the breast, all at different angles. The images are brought together to create crystal clear **3D** reconstruction of the breast. These devices provide informative images of the breast tissue and are helpful in evaluating dense breast tissue. Dense breast tissue can make cancers more difficult to find on a mammogram.



2D image 3D image slices

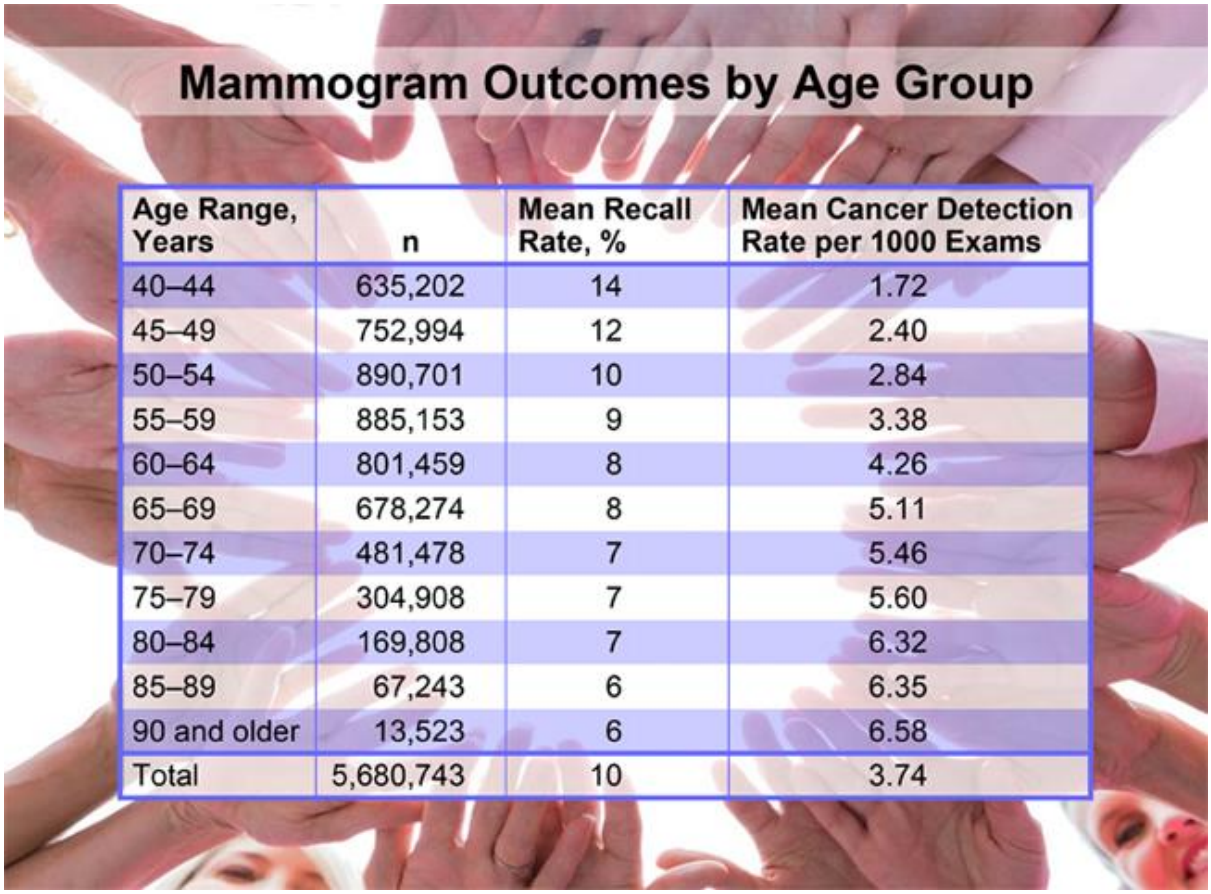
The radiologist can now look at the pictures of the breast one millimetre at a time.

[Picture Credit: 3D Mammogram]

The FDA's approval of 3D mammography devices was

based on a review of clinical studies involving multiple radiologists and hundreds of cases. The FDA also sought input on the safety and effectiveness of the devices from a panel of non-FDA clinical and technical experts.

The results from multiple studies show that the combination of 3D and 2D imaging can improve breast cancer screening for all women.
(US Food and Drug Administration).



Age Range, Years	n	Mean Recall Rate, %	Mean Cancer Detection Rate per 1000 Exams
40–44	635,202	14	1.72
45–49	752,994	12	2.40
50–54	890,701	10	2.84
55–59	885,153	9	3.38
60–64	801,459	8	4.26
65–69	678,274	8	5.11
70–74	481,478	7	5.46
75–79	304,908	7	5.60
80–84	169,808	7	6.32
85–89	67,243	6	6.35
90 and older	13,523	6	6.58
Total	5,680,743	10	3.74

(Medscape).

Breast ultrasound - An ultrasound uses sound waves to build up a picture of the breast. It can show if a lump is solid (made of cells) or is a fluid-filled cyst.

The woman will be asked to take off her top and bra, and lie down on a couch with the arm above the head. The person doing the scan puts a gel on to the breast and moves a small hand-held device around the area. A picture of the inside of the breast shows up on a screen. An ultrasound only takes a few minutes and is painless.

Ultrasound of lymph glands – the patient may also have an ultrasound of the lymph nodes in the armpit. If any of the nodes feel swollen or look abnormal on the ultrasound, the doctor will do a fine needle aspiration on the node or nodes.

Biopsy - This is when the doctor removes a small piece of tissue or cells from the lump or abnormal area. A pathologist (doctor who specialises in analysing cells) examines the tissue or cells under a microscope to look for cancer cells.
There are different ways of taking a biopsy. The doctor or nurse will explain the type of biopsy.

For a few days after the biopsy, the breast may feel sore and bruised. Taking painkillers will help with this and any bruising will go away in a couple of weeks.

- Needle (core) biopsy - this is the most common type of biopsy. It is a quick test where the doctor uses a needle to take small pieces of tissue from the lump or abnormal area. Before taking the biopsy, they inject some local anaesthetic into the area to numb it. One may feel a little pain or a sensation of pressure for a short time during the biopsy.

- Fine needle aspiration (FNA) - this is a quick, simple test. The doctor puts a very fine needle into the area and withdraws a sample of cells into a syringe.

- Vacuum-assisted biopsy (VAB) - this is a way of taking needle biopsies using a vacuum-assisted method. The doctor gives an injection of local anaesthetic into the skin to numb the area. They then make a small cut and insert a needle through it into the breast. A mammogram or ultrasound picture helps them guide the needle to the correct area. The doctor uses the vacuum to gently withdraw a piece of breast tissue into a small collecting chamber. They can take several biopsies without needing to remove the needle and put it in again.

- Excision biopsy - occasionally, the doctor makes a cut in the skin of the breast and removes the lump or abnormal area. This is done under a general or local anaesthetic, depending on the size of the lump. Usually, one will have stitches that dissolve and do not need to be removed.

- Wire localisation - sometimes, an X-ray or ultrasound is used to guide a fine wire into the breast to mark exactly where the surgeon should take the biopsy. This is usually when an abnormal area shows on a mammogram or a lump is too small for the doctor to feel. The surgeon removes the wire when the excision biopsy is done.
- Breast magnetic resonance imaging (MRI). An MRI machine uses a magnet and radio waves to create pictures of the interior of the breast. Before a breast MRI, the patient will be given an injection of dye.

(MacMillan Cancer Support; Mayo Clinic).

Grading and Staging of Breast Cancer in Women

Every patient that has been diagnosed with breast cancer must have other tests performed to determine whether the cancer has spread. This process is known as breast cancer staging. An appropriate treatment plan can be developed once the stage of the cancer is known. The following five (5) stages are used to stage breast cancer.

The stage of a cancer looks at how big the cancer is and whether it has spread. The tests and scans when diagnosing the cancer give some information about the stage. The stage is important because it helps the breast cancer specialist to decide on the best treatment. Specialists usually make decisions about treatment for breast cancer according to the TNM stage and the grade of the cancer.

TMN staging takes into account the size of the tumour (**T**), whether the cancer has spread to the lymph glands (lymph nodes) (**N**), and whether the tumour has spread anywhere else in the body (**M** – for metastases).
Doctors also sometimes use the number system of staging.

Below is a slightly simplified description of the TNM staging system for breast cancer.

The T stages (tumour)

TX means that the tumour size cannot be assessed
Tis means DCIS
T1 The tumour is 2 centimetres (cm) across or less
T1 is further divided into 4 groups
T1mi the tumour is 0.1cm across or less
T1a the tumour is more than 0.1 cm but not more than 0.5 cm
T1b the tumour is more than 0.5 cm but not more than 1 cm
T1c the tumour is more than 1 cm but not more than 2 cm

T2 The tumour is more than 2 centimetres, but no more than 5 centimetres across
T3 The tumour is bigger than 5 centimetres across
T4 **i**s divided into 4 groups
T4a The tumour has spread into the chest wall
T4b The tumour has spread into the skin and the breast may be swollen
T4c The tumour has spread to both the skin and the chest wall
T4d Inflammatory carcinoma – this is a cancer in which the overlying skin is red, swollen and painful to the touch

The N stages (nodes)

NX means that the lymph nodes cannot be assessed (for example, if they were previously removed)
N0 No cancer cells found in any nearby nodes
Isolated tumour cells (ITCs) are small clusters of cancer cells less than 0.2 mm across, or a single tumour cell, or a cluster of fewer than 200 cells in one area of a lymph node. Lymph nodes containing only isolated tumour cells are not counted as positive lymph nodes

N1 Cancer cells are in the upper levels of lymph nodes in the armpit but the nodes are not stuck to surrounding tissues are larger than 0.2mm **or** contain more than 200 cancer cells but are less than 2mm
N2 is divided into 2 groups
N2a there are cancer cells in the lymph nodes in the armpit, which are stuck to each other and to other structures
N2b there are cancer cells in the lymph nodes behind the breast bone (the internal mammary nodes), which have either been seen on a scan or felt by the doctor. There is no evidence of cancer in lymph nodes in the armpit

N3 is divided into 3 groups
N3a there are cancer cells in lymph nodes below the collarbone
N3b there are cancer cells in lymph nodes in the armpit and behind the breast bone
N3c there are cancer cells in lymph nodes above the collarbone

The M stages (metastases)

M0 means that there is no sign of cancer spread

cMo(i+) means there is no sign of the cancer on physical examination, scans or X-rays but cancer cells are present in blood, bone marrow, or lymph nodes far away from the breast cancer – the cells are found by laboratory tests

M1 means the cancer has spread to another part of the body

(Cancer Research UK).

Numeric Staging of Breast Cancer

Stage 0

In Stage 0 breast cancer, atypical cells have not spread outside of the ducts or lobules, the milk producing organs, into the surrounding breast tissue. It is referred to as carcinoma *in-situ*.

Stage I

In Stage I breast cancer, the cancer is not larger than two (2) centimetres and has not spread to surrounding lymph nodes or outside of the breast.

Stage II

Stage II breast cancer is divided into two (2) categories according to the size of the tumour and whether or not it has spread to the lymph nodes:

Stage IIA – the tumour is less than two (2) centimetres and has spread up to three auxiliary underarm lymph nodes.

or

the tumour has grown bigger than two (2) centimetres, but not larger than five (5) centimetres and has not spread to surrounding lymph nodes.

Stage IIB

the tumour has grown to between two (2) and five (5) centimetres and has spread to up to three auxiliary underarm lymph nodes.

or

the tumour is larger than five (5) centimetres, but has not spread to the surrounding lymph nodes.

Stage III

Stage III breast cancer is also divided into two (2) categories:

Stage IIIA

the tumour is larger than two (2) centimetres but smaller than five (5) centimetres and has spread to up to nine auxiliary underarm lymph nodes.

Stage IIIB

the cancer has spread to tissue near the breast including the skin, chest wall, ribs, muscles, or lymph nodes in the chest wall or above the collarbone.

Stage IV
In Stage IV breast cancer, the cancer has spread to other organs or tissues, such as the liver, lungs, brain, bones, or lymph nodes near the collarbone.
(National Breast Cancer Foundation).

Recurrent Breast Cancer
When breast cancer comes back, it may return in the same place. This is called a 'recurrence', because it is not a new cancer. But a recurrence can also appear in a place not directly related to the first breast cancer. This is called a 'metastasis', and if cancer is detected in several areas, these are called 'metastases'. When breast cancer comes back, it tends to show up in specific areas of the body:

- the breast or the area where the breast used to be
- the chest wall
- the lymph nodes
- the bones
- the lungs or around the lungs
- the liver
- the brain

(National Cancer Institute).

Treatment Options for Breast Cancer in Women
People with cancer should be cared for by a multidisciplinary team (MDT), a team of specialists who work together to provide the best treatment and care. The team often consists of a specialist cancer surgeon, an oncologist (a radiotherapy and chemotherapy specialist), a radiologist, a pathologist, a radiographer, a reconstructive surgeon and a specialist nurse. Other members may include a physiotherapist, a dietician and an occupational therapist, and you may have access to clinical psychology support.

When deciding what treatment is best, the doctors will consider:
- the stage and grade of your cancer (how big it is and how far it has spread)
- general health of the patient
- whether the patient has been through the menopause

The main treatments for breast cancer are:

Surgery - there are two types of surgery for breast cancer. These are surgery to remove just the cancerous lump (tumour), known as breast-conserving surgery, and surgery to remove the whole breast, which is called a mastectomy. In many cases, a mastectomy can be followed by reconstructive surgery to recreate the breast that was removed. Studies have shown that breast-conserving surgery followed by radiotherapy is as successful as total mastectomy at treating early-stage breast cancer.

Breast-conserving surgery - breast-conserving surgery ranges from a lumpectomy or wide local excision, in which just the tumour and a little surrounding breast tissue is removed, to a partial mastectomy or quadrantectomy, in which up to a quarter of the breast is removed.

If one has breast-conserving surgery, the amount of breast tissue that has been removed will depend on:

- the type of cancer
- the size of the tumour and where it is in the breast
- the amount of surrounding tissue that needs to be removed
- the size of the breasts

The surgeon will always remove an area of healthy breast tissue around the cancer, which will be tested for traces of cancer. If there is no cancer present in the healthy tissue, there is less chance that the cancer will recur. If cancer cells are found in the surrounding tissue, one may need to have more tissue removed from the breast.
After breast-conserving surgery, the patient will usually be offered radiotherapy to destroy any remaining cancer cells.

- Mastectomy - a mastectomy is the removal of all the breast tissue, including the nipple. If there are no obvious signs that the cancer has spread to the lymph nodes, the patient may have a mastectomy, in which the breast is removed, along with a sentinel lymph node biopsy (SLNB). If the cancer has spread to the lymph nodes, the patient will probably need more extensive removal (clearance) of lymph nodes from the axilla (under the arm).

- Reconstruction - breast reconstruction is surgery to make a new breast shape that looks as much as possible like the other breast. Reconstruction can be carried out at the same time as a mastectomy (immediate reconstruction) or it can be carried out later (delayed reconstruction). It can be done either by inserting a breast implant or by using tissue from another part of the body to create a new breast.

- Lymph node surgery - to find out if the cancer has spread, a procedure called a sentinel lymph node biopsy (SLNB) may be carried out. The sentinel lymph nodes are the first lymph nodes that the cancer cells reach if they spread. They are part of the lymph nodes under the arm (axillary lymph nodes). The position of the sentinel lymph nodes varies, so they are identified using a combination of a radioisotope and a blue dye.

The sentinel lymph nodes are examined in the laboratory to see if there are any cancer cells present. This provides a good indicator of whether the cancer has spread. If there are cancer cells in the sentinel nodes, you may need further surgery to remove more lymph nodes from under the arm.
(NHS Choices).

Radiotherapy - Radiation therapy is a form of cancer treatment that uses high levels of radiation to kill cancer cells or keep them from growing and dividing -- while minimising damage to healthy cells.

The doctor may recommend radiation treatments after a lumpectomy (a breast-sparing surgery to remove a tumour) or after a mastectomy to lower the odds of the cancer returning in that breast.

Radiation may also be used to treat some symptoms of advanced cancer.

Treatments generally start several weeks after surgery, so the body has some time to heal. If the doctor recommends chemotherapy, too, one may start chemo first.

The type of breast cancer radiotherapy that most people are familiar with is called external beam radiation. It's the type most commonly used in cases of breast cancer. External beam radiation works by focusing a beam of radiation from a machine to its target, the area of the body affected by cancer.

The other type of breast cancer radiation is called brachytherapy. This type delivers radiation to the cancer internally using an implant. In the case of breast cancer, radioactive seeds or pellets - as small as grains of rice - are placed inside the breast near the cancer.

Brachytherapy can be used alone or with external beam radiation. Tumour size, location, and other factors will determine if someone is a candidate for this type of radiation. Brachytherapy has side effects, including redness, bruising, breast pain, infection, weakness, and an increased risk of fractured ribs.

The therapist will escort the patient into the treatment room, help her onto the table, and help place the patient in the right position. He or she will leave the room and start the radiation treatment.

The patient will be under constant observation during the treatment. Cameras and an intercom allow the therapist to see and hear the patient. It is important that the patient holds still and stays relaxed during treatment.

The therapist will be in and out of the room to reposition the machine and the patient. The machine will not touch the patient, and she will feel nothing during the treatment.

The radiation therapist takes an X-ray called a ‘port film’ on the first day of treatment and every week thereafter. Port films verify that the patient is being accurately positioned during treatments.

Port films do not show how one’s cancer is responding.
Small marks that look like freckles are tattooed on the patient’s skin along the treatment area. They provide a permanent outline of the treatment area. Do not try to wash these marks off or retouch them if they fade. The therapist will re-mark the treatment area when needed (WebMD).

Chemotherapy - chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy). The way the chemotherapy is given depends on the type and stage of the cancer being treated.
(National Cancer Institute).

Hormone therapy - hormone therapy - perhaps more properly termed hormone-blocking therapy - is often used to treat breast cancers that are sensitive to hormones. Doctors sometimes refer to these cancers as oestrogen receptor positive (ER positive) and progesterone receptor positive (PR positive) cancers.

Hormone therapy can be used after surgery or other treatments to decrease the chance of your cancer returning. If the cancer has already spread, hormone therapy may shrink and control it.

Treatments that can be used in hormone therapy include:

- Medications that block hormones from attaching to cancer cells. Selective oestrogen receptor modulator (SERM) medications act by blocking oestrogen from attaching to the oestrogen receptor on the cancer cells, slowing the growth of tumours and killing tumour cells. SERMs, which can be used in both pre- and postmenopausal women, include tamoxifen, raloxifene (Evista) and toremifene (Fareston).

Possible side effects include hot flashes, night sweats and vaginal dryness. More significant risks include blood clots, stroke, uterine cancer and cataracts.

- Medications that stop the body from making oestrogen after menopause. Called aromatase inhibitors, these drugs block the action of an enzyme that converts androgens in the body into oestrogen. These drugs are effective only in postmenopausal women. Aromatase inhibitors include anastrozole (Arimidex), letrozole (Femara) and exemestane (Aromasin). Side effects include hot flashes, night sweats, vaginal dryness, joint and muscle pain, as well as an increased risk of bone thinning (osteoporosis).

- A drug that targets oestrogen receptors for destruction. The drug fulvestrant (Faslodex) blocks oestrogen receptors on cancer cells and signals to the cell to destroy the receptors. Fulvestrant is used in postmenopausal women. Side effects that may occur include nausea, hot flashes and joint pain.

- Surgery or medications to stop hormone production in the ovaries. In premenopausal women, surgery to remove the ovaries or medications to stop the ovaries from making oestrogen can be an effective hormonal treatment.

(Mayo Clinic).

<u>Biological therapy (targeted therapy)</u> - targeted therapies (sometimes called biological therapies) are new drugs that work differently from chemotherapy. The main targeted therapy used in breast cancer is trastuzumab (usually called Herceptin).

Trastuzumab reduces the risk of breast cancer coming back in women with HER2 positive breast cancer.

Trastuzumab attaches to the HER2 receptors on the surface of breast cancer cells and stops them from dividing and growing. You'll usually have trastuzumab every three weeks for a year.

It is given with chemotherapy, or on its own.

A patient may have one of these treatments or a combination. The type of treatment or the combination of treatments will depend on how the cancer was diagnosed and the stage it is at. Breast cancer diagnosed at screening may be at an early stage, but breast cancer diagnosed when one has symptoms may be at a later stage and require a different treatment. The healthcare team will discuss with the patient which treatments are most suitable.

The most commonly diagnosed cancer type among women around the world, breast cancer is also one of the main cancer types for which new immunotherapy treatments are currently being developed.

The need for effective, lasting breast cancer treatment is urgent, as breast cancer accounts for over 12 percent of all cancers diagnosed globally each year - making it the second most common cause of cancer-related death among women. There were approximately 1.7 million new diagnoses worldwide in 2012, and half a million deaths. The numbers are staggering, with approximately 1 in 8 U.S. women and about 1 in 1,000 men developing invasive breast cancer at some point in their lives.

Current methods for breast cancer treatment typically involve surgery if the disease is diagnosed early. Depending on the stage and molecular characteristics of the cancer when diagnosed, breast cancer surgery may be followed by additional chemo, radiation, or targeted therapies, including hormone therapy.

[Picture Credit: Cancer Research Institute]

Breast cancer has traditionally been regarded as immunologically silent, though several newer preclinical and clinical studies now suggest that immunotherapy treatment has the potential to improve outcomes for breast cancer patients, and displays numerous advantages over more conventional chemo-based treatments that directly target the tumour itself.

Three immunotherapies, have been been approved for breast cancer: the targeted antibodies pertuzumab and trastuzumab, as well as the antibody-drug conjugate trastuzumab emtansine. Several other breast cancer immunotherapies have shown promising results in recent clinical trials, including: therapeutic vaccines eliciting an immune response against tumour-related antigens; checkpoint inhibitors/immune modulators, treatments that enhances existing anti-cancer immune system responses; adoptive cell therapy (adoptive T cell transfer), in which T cells are genetically modified or treated to enhance their effect on the immune system's anti-cancer abilities. Additional breast cancer clinical trials involve oncolytic virus therapies, antibodies, adjuvant immunotherapies, and cytokines.

Our science-first organisation's commitment to breast cancer research and breast cancer immunotherapy goes back nearly four decades, when we first began to fund the New York Metropolitan Breast Cancer group - a coalition of physicians and surgeons from over 15 medical institutions working together to develop a coordinated breast cancer diagnosis and treatment program.

At the Cancer Research Institute, we're invested in the promise of effective breast cancer immunotherapy treatment and dedicated to developing lifesaving cures for all cancers. When you support CRI, you're supporting the best scientists in the field doing the best research, advancing breast cancer immunotherapy treatments and bringing more clinical trials to more patients around the world.
(MacMillan Cancer Support; Cancer Research Institute).

Follow-up Care and Treatment
Follow-up is recommended after treatment for breast cancer to check whether breast cancer has come back, to monitor side effects of treatment and to provide practical and emotional support.

Women who have been diagnosed and treated for early breast cancer have an increased risk of breast cancer coming back or developing in the other breast. Regular follow-up means that if breast cancer does come back or if a new breast cancer develops, it can be treated promptly. Follow-up also allows doctors to check for any side effects from treatment and to monitor any long-term treatments such as **hormonal therapies**. It also provides an opportunity for women to talk about how they're feeling.

Follow-up after treatment for breast cancer involves regular physical examinations and breast imaging tests (mammogram and/or ultrasound).

Appropriate follow-up does not involve chest X-rays, bone scans or blood tests unless the woman has symptoms which suggest that cancer has spread outside the breast or armpit area.

Some women assume that they should be having regular scans and blood tests. However, studies have shown that having more tests does not improve the length or quality of life for women who have been treated for breast cancer.

A woman's follow-up schedule will be planned based on her individual circumstances. Women who are involved in a clinical trial may have some tests in addition to those listed here.

Women who are receiving a hormonal therapy, such as tamoxifen or an aromatase inhibitor, will have follow-up tests while taking these therapies.

Some women find it reassuring to have regular follow-up tests. Others feel anxious around the time of their appointments. Both reactions are normal.

For most women, no changes are found during follow-up appointments. However, if breast imaging tests show an abnormal area, or if the doctor finds a lump during a physical examination, the woman will need to have further tests. This may include more imaging tests and a biopsy (Cancer Australia).

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.

<u>Types of Clinical Trials</u>
Cancer clinical trials differ according to their primary purpose. They include the following types:

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

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

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

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

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

Where Clinical Trials are Conducted

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

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

Research Team

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

Clinical Trial Protocol

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

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

National and International Regulations

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

Informed Consent

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

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

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

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

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is

processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

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

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

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

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

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

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

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

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.
Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

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

Use of Placebos

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

Possible benefits of taking part in a clinical trial

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

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

Potential harms associated with taking part in a clinical trial

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

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

Correlative research studies and how they are related to clinical trials

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

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

When a clinical trial is over

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

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

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (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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