Cancer Association of South Africa (CANSA)

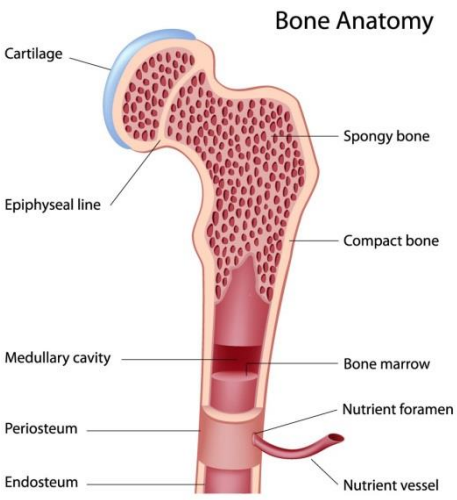
Research • Educate • Support

Fact Sheet
on
Bone Cancer

Introduction

Bones are rigid organs that constitute part of the endoskeleton of vertebrates. Bone tissue is a type of dense connective tissue. Bones come in a variety of shapes and have a complex internal and external structure, are lightweight yet strong and hard, and serve multiple functions. One of the types of tissue that makes up bone is the mineralised osseous tissue, also called bone tissue, that gives it rigidity and a coral-like three-dimensional internal structure. Other types of tissue found in bones include marrow, endosteum, periosteum, nerves, blood vessels and cartilage.

[Picture Credit: Skeleton]



At birth, there are over 270 bones in an infant human's body, but many of these fuse together as the child grows, leaving a total of 206 separate bones in an adult. The largest bone in the human body is the femur and the smallest bones are auditory ossicles (found in the human ear).

[Picture Credit: Bone Structure]

Bones form an important component of the skeletal system. They perform a wide range of important functions that can be classified into three categories:

Mechanical Functions of bones:

- Protection - at numerous places inside the body, bones serve to protect important and delicate organs. The best examples to be

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quoted here are those of brain (which is protected by the skull) and heart (which is protected by the ribcage)

- Shape - because of their rigid nature, bones provide a framework around which the body is built. Bones are responsible for the shape and form of human body

- Movement - working with skeletal muscles, tendons, ligaments and joints, the bones form the moving machinery of the human body. The major role of bones in movement is that they act as levers, which make use of the forces generated by skeletal muscles in a beneficial way

Synthetic Functions of Bones:

- Synthesis of blood cells - the major synthetic role of bones is to produce blood cells. The bones themselves are not capable of doing this. Instead, it houses the bone marrow, which contains *Haematopoietic* stem cells, capable of producing blood cells. In infants, bone marrow of all long bones is capable of this synthesis, however, as a person gets older, the red marrow turns into yellow fatty marrow, which is no more capable of haematopoiesis. The red marrow in adults and older individuals is restricted to vertebrae and the heads of the tibia and femur

Metabolic Functions of Bones:

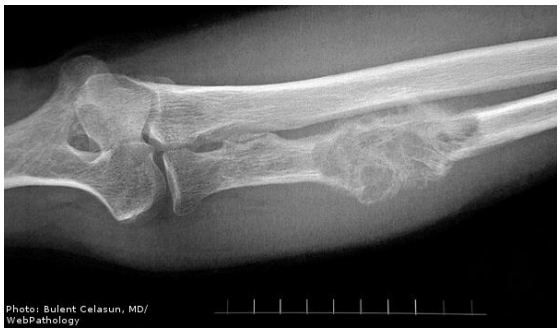
- Mineral Storage - bones serve as an important store house of minerals such as calcium and phosphorus
- Fat storage - the yellow bone marrow of long bones act as a storage of fats
- Role in acid-base balance - bone buffers the blood against excessive pH changes by absorbing or releasing alkaline salts

(Wikipedia; Mananatomy).

Bone Cancer

Bone cancer is the uncontrolled growth of bone cells.

A *primary* bone tumour starts in the bone itself. True (or primary) bone cancers are called *sarcomas*. Sarcomas are cancers that start in bone, muscle, fibrous tissue, blood vessels, fat tissue, as well as some other tissues. They can develop anywhere in the body.



[Picture Credit: Bone Cancer]

There are several different types of bone tumours. Their names are based on the area of bone or surrounding tissue that is affected and the kind of cells forming the tumour. Some primary bone tumours are *benign* (not cancerous), and others are *malignant* (cancerous). Most bone cancers are sarcomas.
(American Cancer Society).

Types of Bone Tumours
Bone tumours comprise of:

Osteosarcoma: osteosarcoma (also called *osteogenic sarcoma*) is the most common primary bone cancer. This cancer starts in the bone cells. It most often occurs in young people between the ages of 10 and 30, but about 10% of osteosarcoma cases develop in people in their 60s and 70s. It is rare in middle aged people, and is more common in males than females. These tumours develop most often in bones of the arms, legs, or pelvis.

Chondrosarcoma: chondrosarcoma is a cancer of cartilage cells. It is the second most common primary bone cancer. This cancer is rare in people younger than 20. After age 20, the risk of getting a chondrosarcoma goes up until about age 75. Women get this cancer as often as men.

Chondrosarcomas can develop anywhere there is cartilage. Most develop in bones such as the pelvis, leg bone or arm bone. Occasionally, chondrosarcoma will develop in the trachea, larynx, and chest wall. Other sites are the scapula (shoulder blade), ribs, or skull.

Benign (non-cancerous) tumours of cartilage are more common than malignant ones. These are called *enchondromas*. Another type of benign tumour that has cartilage is a bony projection capped by cartilage called an *osteochondroma*. These benign tumours rarely turn into cancer. There is a slightly higher chance of cancer developing in people who have many of these tumours, but this is still not common.

Chondrosarcomas are classified by grade, which measures how fast they grow. The grade is assigned by the pathologist (a doctor specially trained to examine and diagnose tissue samples under a microscope) after looking at the tumour under the microscope. The lower the grade, the slower the cancer grows. When a cancer is slow growing, the chance that it will spread is lower and so the outlook is better. Most chondrosarcomas are either low grade (grade I) or intermediate grade (grade II). High grade (grade III) chondrosarcomas, which are the most likely to spread, are less common.

Some chondrosarcomas have distinctive features under a microscope. These variants of chondrosarcoma can have a different prognosis (outlook) than usual chondrosarcomas.

- *Dedifferentiated chondrosarcomas* start out as typical chondrosarcomas but then some parts of the tumour change into cells like those of a high grade sarcoma (such as high grade forms of malignant fibrous histiocytoma, osteosarcoma, or fibrosarcoma). This variant of chondrosarcoma tends to occur in older patients and is more aggressive than usual chondrosarcomas.
- *Clear cell chondrosarcoma* is a rare variant that grows slowly. It rarely spreads to other parts of the body unless it has already come back several times in the original location.
- *Mesenchymal chondrosarcomas* can grow rapidly, but like Ewing tumour, are sensitive to treatment with radiation and chemotherapy.

Ewing's tumour: Ewing's tumour is the third most common primary bone cancer, and the second most common in children, adolescents, and young adults. This cancer (also called *Ewing sarcoma*) is named after the doctor who first described it in 1921, Dr. James Ewing. Most Ewing's tumours develop in bones, but they can start in other tissues and organs. The most common sites for this cancer are the pelvis, the chest wall (such as the ribs or shoulder

blades), and the long bones of the legs or arms. This cancer is most common in children and teenagers and is rare in adults older than 30. Ewing's tumours occur most often in white people and are very rare among African Americans and Asian Americans. More detailed information about this cancer can be found in our document called *Ewing Family of Tumours.*

Malignant fibrous histiocytoma: Malignant fibrous histiocytoma (MFH) more often starts in soft tissue (connective tissues such as ligaments, tendons, fat, and muscle) than in bones. This cancer is also known as *pleomorphic undifferentiated sarcoma*, especially when it starts in soft tissues. When MFH occurs in bones, it usually affects the legs (often around the knees) or arms. This cancer most often occurs in elderly and middle-aged adults and is rare among children. MFH mostly tends to grow locally, but it can spread to distant sites, like the lungs.

Fibrosarcoma: This is another type of cancer that develops more often in 'soft tissues' than it does from bones. Fibrosarcoma usually occurs in elderly and middle-aged adults - leg, arm, and jaw bones are the ones most often affected.

Giant cell tumour of bone: This type of primary bone tumour has benign and malignant forms. The benign (non-cancerous) form is most common. Giant cell bone tumours typically affect the leg (usually near the knees) or arm bones of young and middle-aged adults. They do not often spread to distant sites, but tend to come back where they started after surgery (this is called *local recurrence*). This can happen several times. With each recurrence, the tumour becomes more likely to spread to other parts of the body. Rarely, a giant cell bone tumour spreads to other parts of the body without first recurring locally. This happens in the malignant (cancer) form of the tumour.

Chordoma: This primary tumour of bone usually occurs in the base of the skull and bones of the spine. It develops most often in adults older than 30, and is about twice as common in men than in women. Chordomas tend to grow slowly and often do not spread to other parts of the body, but they often come back in the same area if they are not removed completely. When they do spread, lymph nodes, the lungs, and the liver are the most common areas for secondary tumours.
(American Cancer Society).

Incidence of Bone Cancer in South Africa
According to the National Cancer Registry (2013) the following number of cases of bone cancer was histologically diagnosed in South Africa during 2013:

Group - Males 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	81	1:4 115	0,23%
Asian males	0	-	-
Black males	47	1:6 744	0,44%
Coloured males	7	1:3 806	0,17%
White males	27	1:1 197	0,13%

Group - Females 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	75	1:4 379	0,20%
Asian females	0	-	-
Black females	42	1:7 654	0,27%
Coloured females	12	1:2 461	0,29%
White females	21	1:1 493	0,13%

The frequency of histologically diagnosed cases of bone cancer in South Africa for 2013 was as follows (National Cancer Registry, 2013):

Group - Males 2013	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	36	15	6	7	8	5	4	0
Asian males	0	0	0	0	0	0	0	0
Black males	23	10	3	6	1	2	1	0
Coloured males	3	1	1	0	1	1	0	0
White males	3	5	1	2	9	3	1	0

Group - Females 2013	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	31	8	7	5	8	8	5	2
Asian females	0	0	0	0	0	0	0	0
Black females	21	3	5	4	3	0	1	1
Coloured females	4	3	0	0	0	3	0	1
White females	4	2	1	0	4	5	3	0

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Signs and Symptoms of Bone Cancer in Adults

Bone cancer is a rare cancer that occurs in the bone and destroys normal bone tissue. Although it may afflict any bone in the body, bone cancer typically affects long bones such as those found in the arms and legs.

Bone cancers are classified into three main types, based on the type of cell the cancer first affects. Although symptoms of bone cancer may vary between individuals, pain is typically the most common symptom.

Symptoms of bone cancer include:

- Bone fracture (especially as a result of a minimal injury)
- Bone pain
- Fatigue
- Swelling in the affected area
- Weight loss
- The presence of a mass or lump in the affected area

(Symptomfind).

Signs and Symptoms of Bone Cancer in Children
Symptoms of bone cancer in children include:

- Fever
- Chills
- Night sweats
- Bone fracture (especially as a result of a minimal injury)
- Bone pain
- Fatigue
- Swelling in the affected area
- Weight loss
- The presence of a mass or lump in the affected area

(Medicine.Net).

Signs and Symptoms of Bone Cancer in Adults
The Signs and symptoms include:

- Bone pain
- Swelling and tenderness near the affected area
- Broken bone
- Fatigue
- Unintended weight loss

(Mayo Clinic).

Diagnosis of Bone Cancer
The following is used to diagnose bone cancer:

X-Rays - bone x-rays may help to show whether the cancer has started in the bone (primary bone cancer), or has spread into the bone from a cancer elsewhere in the body (secondary bone cancer). Sometimes, how the bone looks on an x-ray can help the doctor diagnose which type of bone cancer it is. This is often the case for osteosarcoma. However, other tests will still be needed before the doctor can definitely say whether it is a primary or secondary bone cancer and what type of cancer it is.

Bone scan - This test looks at all the bones in the body. It shows up any signs of cancer in any other bones away from the main tumour.

A small amount of a radioactive substance is injected into a vein in the hand or arm. Abnormal bone absorbs more radioactivity than normal bone, so these areas are highlighted and picked up by the scanner as ‘hot spots’. The level of radioactivity used in the scan is very small and does not cause any harm to the body.

A person will need to wait for 2-3 hours between having the injection and the scan.

If ‘hot spots’ do show up on a bone scan, it is not always clear whether they are caused by cancer or by other conditions, such as arthritis. Sometimes a CT scan or MRI scan may help the doctors decide whether the changes seen on a bone scan are caused by bone cancer or by another condition.

Magnetic Resonance Imaging - An MRI scan is used to assess the extent of the primary tumour so that the doctors can plan the best treatment. Some centres may do an MRI scan of the whole skeleton instead of a bone scan. This is to check for signs of cancer in any other bones away from the main tumour.

An MRI scan uses magnetism to build up a detailed picture of areas of the body. The scanner is a powerful magnet so one may be asked to complete and sign a checklist to make sure it is safe. The checklist asks about any metal implants one may have (for example a pacemaker, surgical clips or bone pins).

Before the scan, patients are asked to remove any metal belongings including jewelry. Some people are given an injection of dye into a vein in their arm, which doesn't usually cause discomfort. This is called a contrast medium and can help the images from the scan to show up more clearly.

During the test the person lies very still on a couch inside a long cylinder (tube) for about 30 minutes. It is painless but can be slightly uncomfortable, and some people feel a bit claustrophobic. It is also noisy, but the person will be given earplugs or headphones. During the scan the person be able to hear and speak to the person operating the scanner.

Bone biopsy - A sample of bone is needed to diagnose bone cancer. This is because x-rays and bone scans cannot always show whether a tumour is non-cancerous or cancerous and, if it is cancerous, the exact type of bone cancer it is.

There are two ways of taking a bone biopsy:

Core needle biopsy:
In a core needle biopsy, the doctor uses a special needle to take a sample from the bone. Before the biopsy, the doctor will give the patient an injection of local anaesthetic around the bone to numb it. He/she will then put the biopsy needle into the bone to take the sample. Several samples may be taken.

If the doctor cannot feel the bone lump or it is deep within the body, the doctor may use an ultrasound or CT scanner to help guide the needle into the right place.

The patient is usually awake during a core needle biopsy, although he/she may be given a sedative to make them feel more relaxed and drowsy. Sometimes, particularly in children, the biopsy is done under a general anaesthetic.

For most people, a core needle biopsy will show whether the lump is a cancer. However, sometimes it does not provide enough cells to give a clear diagnosis. In this situation a surgical biopsy is needed.

Surgical biopsy:
This type of biopsy is done less often than a core needle biopsy. The surgeon uses a surgical knife (scalpel) to open the area and remove a sample from the lump in the bone. If the lump is small enough, all of it may be removed. A surgical biopsy may be done under a local or a general anaesthetic. This depends on the age, the size of the tumour and how deep it is within the body.

Once taken, the bone sample or samples are sent to a specialist doctor (pathologist). The pathologist can tell whether the tumour is a cancer or not by examining the cells from the bone samples under a microscope. If it is a cancer, the doctor may arrange for further tests on the sample to find out which type of bone cancer it is.
(MacMillan Cancer Support).

Risk Factors for Bone Cancer
The following risk factors have been identified:

Genetic disorders
A very small number of bone cancers (especially osteosarcomas) appear to be hereditary and are caused by defects (mutations) in certain genes.
Osteosarcomas - Children with certain rare inherited syndromes have an increased risk of developing osteosarcoma.

- The Li-Fraumeni syndrome makes people much more likely to develop several types of cancer, including breast cancer, brain cancer, osteosarcoma, and other types of sarcoma. Most of those cases are caused by a mutation of the *p53* tumour suppressor gene, but some are caused by mutations in the gene *CHEK2*.
- Another syndrome that includes bone cancer is the Rothmund-Thomson syndrome. Children with this syndrome are short, have skeletal problems, and rashes. They also are more likely to develop osteosarcoma. This syndrome is caused by abnormal changes in the gene *REQL4*.
- Retinoblastoma is a rare eye cancer of children that can be hereditary. The inherited form of retinoblastoma is caused by a mutation (abnormal copy) of the *RB1* gene. Those with this mutation also have an increased risk of developing bone or soft tissue sarcomas. Also, if radiation therapy is used to treat the retinoblastoma, the risk of osteosarcoma in the bones around the eye is even higher.

There are families with several members who have developed osteosarcoma without inherited changes in any of the known genes. The gene defects that may cause cancers in these families haven't been discovered yet.

Chondrosarcomas - Multiple exostoses (sometimes called *multiple osteochondromas*) syndrome is an inherited condition that causes many bumps on a person's bones. These bumps are made mostly of cartilage. They can be painful and cause bones to deform and/or fracture. This disorder is caused by a mutation in any one of the 3 genes *EXT1*, *EXT2*, or *EXT3.* Patients with this condition have an increased risk of chondrosarcoma. An enchondroma is a benign cartilage tumour that grows into the bone. People who get many of these tumours have a condition called *multiple enchondromatosis*. They have an increased risk of developing chondrosarcomas.

Chordomas - Chordomas seem to run in some families. The genes responsible have not yet been found, but familial chordoma has been linked to changes on chromosome 7.

Patients with the inherited syndrome *tuberous sclerosis*, which can be caused by defects (mutations) in either of the genes *TSC1* and *TSC2*, seem to have a high risk of chordomas during childhood.

Paget disease

Paget disease is a benign (non-cancerous) but pre-cancerous condition that affects one or more bones. It results in formation of abnormal bone tissue and is mostly a disease of people older than 50. Affected bones are heavy, thick, and brittle. They are weaker than normal bones and more likely to fracture (break). Most of the time Paget disease is not life threatening. Bone cancer (usually osteosarcoma) develops in about 1% of those with Paget disease, usually when many bones are affected.

Radiation

Bone exposure to ionizing radiation may also increase the risk of developing bone cancer. A typical x-ray of a bone is not dangerous, but exposure to large doses of radiation does pose a risk. For example, radiation therapy to treat cancer can cause a new cancer to develop in one of the bones in the treatment area. Being treated at a younger age and/or being treated with higher doses of radiation (usually over 60 Gy) increases the risk of developing bone cancer.

Exposure to radioactive materials such as radium and strontium can also cause bone cancer because these minerals build up in bones.

Non-ionizing radiation, like microwaves, electromagnetic fields from power lines, cellular phones, and household appliances, does not increase bone cancer risk.

Bone marrow transplantation

Osteosarcoma has been reported in a few patients who have undergone bone marrow (stem cell) transplantation.

Injuries

People have wondered whether injury to a bone can cause cancer, but this has never been proven. Many people with bone cancer remember having hurt that part of their bone. Most doctors believe that this did not cause the cancer, but rather that the cancer caused them to remember the incident or that the injury drew their attention to that bone and caused them to notice a problem that had already been present for some time.
(American Cancer Society).

Grading of Bone Cancer

Grading describes the appearance of the cancer cells under a microscope. The grade gives an idea of how quickly the cancer may develop. The most common grading system for bone cancer uses two grades: low-grade and high-grade.

Low-grade means that the cancer cells look very similar to normal bone cells. They are usually slow-growing and are less likely to spread.

In high-grade tumours the cells look very abnormal. They're likely to grow more quickly and are more likely to spread. All Ewing's sarcomas are high-grade.
(MacMillan Cancer Support).

Staging of Bone Cancer
The stage of a cancer describes its size and whether it has spread. The stages of bone cancer are also based on the grade of the cancer.

There are two different staging systems used for bone cancer. This is the Enneking staging system, which is commonly used to stage bone cancers:

Stage 1
The cancer is low-grade and has not spread beyond the bone. Stage 1 is further divided into:

- Stage 1A The cancer is low-grade and is still completely inside the bone it started in. The cancer may be pressing on the bone wall and causing a swelling, but it has not grown through it.
- Stage 1B The cancer is low-grade and has grown through the bone wall.

Stage 2
The cancer is high-grade and hasn't spread beyond the bone. Stage 2 is further divided into:

- Stage 2A The cancer is high-grade and is still completely inside the bone it started in.
- Stage 2B The cancer is high-grade and has grown through the bone wall.

Stage 3
The bone cancer may be any grade and has spread to other parts of the body, such as the lungs.
(MacMillan Cancer Support).

Treatment of Bone Cancer
As with many cancers, the treatment options are surgery, chemotherapy and radiotherapy. Surgery and chemotherapy are the most common treatments for primary bone cancer. Radiotherapy is an important part of treatment for Ewing's sarcoma. The doctor will plan the treatment taking into account the following:

- The type of bone cancer
- How far the cancer has grown or spread (the stage)
- The patient's general health
- The patient's age and level of fitness

Treatment for different types of bone cancer
As with many types of cancer, the earlier the cancer is diagnosed, the easier it is to get it under control and possibly cure it. Some bone cancers are treated with a combination of surgery and chemotherapy. These include:

- Osteosarcoma
- Ewing's sarcoma
- Spindle cell sarcoma (fibrosarcoma and malignant fibrous histiocytoma)

For these types of bone cancer, doctors often give chemotherapy before surgery to help shrink the tumour and make it easier to remove.

Children and young adults who have a high grade osteosarcoma may have a biological therapy called mifamurtide (Mepact) alongside chemotherapy after surgery.

Ewing's sarcoma responds well to radiotherapy and this may be used:

- To shrink a tumour after chemotherapy
- Before or after surgery to help lower the risk of the cancer coming back

A patient may have radiotherapy as the main treatment instead of surgery if the tumour is difficult to remove surgically. For example, Ewing's sarcoma sometimes develops in the pelvis and it may then be very difficult to remove.

Doctors most often treat chondrosarcomas with surgery. Doctors do not routinely use chemotherapy or radiotherapy to treat this type of bone cancer as its treatments do not work very well. In some situations, a doctor may suggest radiotherapy, either after surgery or to help relieve symptoms.

Chordoma is usually treated with surgery followed by radiotherapy.

Surgery

The type of surgery a person has will depend on the size of the cancer, where it is in the body and whether it has grown into the tissues surrounding the bone. The surgeon may suggest:

- Removing the bone affected by the cancer
- Limb sparing surgery
- Removal of an arm or leg (amputation)
- Surgery to remove cancer that has spread

Removing the bone affected by the cancer

The surgeon removes part or all of the bone affected by the cancer. This is called resection. The person may have this type of surgery for cancer in bones such as a rib or fibula (calf bone). The bone is removed along with a surrounding area of healthy tissue. If the cancer is in a bone in an arm or leg this type of surgery is called limb salvage surgery.

Limb sparing surgery

This means surgery to an arm or leg to take out the bit of the bone where the cancer is growing. It is also sometimes called limb salvage surgery. The surgeon replaces the piece of bone containing the cancer with a piece of metal (a prosthesis) or with a bone graft. A graft is a piece of healthy bone from somewhere else in the body. Bone can also be taken from another person. Using bone from another person is called a bone allograft. This type of surgery is very skilled and complicated. It has to be done by specialist surgeons working in specialist centres. A patient may have to travel to a major treatment centre, rather than going to a local hospital.

Removal of an arm or leg (amputation)

It can be devastating news to be told one must lose an arm or leg. But such a person may need the operation to try to cure the cancer. Amputation may be needed if the bone tumour has spread into the tissues surrounding the bone. It may be that if the surgeon only removes the tumour, there may be a very high risk of the cancer coming back or the tumour may be in a place where the function of the limb would not be very good after limb sparing surgery.

After the surgery, a specialist in false limbs (prosthetic limbs) will usually fit the patient with a prosthesis made especially for him/her. The limb specialist and the specialist physiotherapists will make sure the patient has all the help needed to learn to cope with the prosthesis.

Surgery to remove cancer that has spread
Primary bone cancer that has spread can sometimes be removed with surgery. This is called metastatectomy and is most often done with lung secondaries. It can also be used for bone secondaries. This type of surgery is not always possible. It depends on how many secondary cancers there are and its size and shape. Successful removal of lung cancer secondaries is more common after osteosarcoma than other types of primary bone cancer.

Chemotherapy
Chemotherapy works very well for some types of bone cancers, particularly Ewing's sarcomas and osteosarcomas, but not for all patients. Unfortunately one cannot tell how the cancer will respond until treatment has been tried.

Chemotherapy can help cure bone cancer. It can be very intensive treatment. Chemotherapy is usually used with surgery to treat bone cancer. For Ewing's sarcoma, osteosarcoma and spindle cell sarcomas, one usually has the treatment before and after surgery. The treatment before surgery helps to shrink the cancer and make it easier to remove. It may sometimes make it possible to do limb sparing surgery instead of an amputation. After chemotherapy one will have to wait for the blood count to come back to normal before undergoing surgery.

The chemotherapy after surgery is to try to kill off any cancer cells that escaped before the tumour was removed. This lowers the risk of the cancer coming back in the future.

Radiotherapy
Radiotherapy can be an important part of treatment for Ewing's sarcoma. It can shrink a tumour and make it easier to remove. After surgery, the patient usually has radiotherapy to try to kill off any cancer cells that may have been left behind. This lowers the risk of the Ewing's sarcoma coming back in the future. If surgery to remove the tumour would be too difficult, radiotherapy and chemotherapy treatment may be used instead.

Radiotherapy is sometimes used after surgery for chordomas. Doctors occasionally use radiotherapy after surgery for osteosarcomas if there is a risk of cancer cells remaining in the area after the surgery, but it is not a routine treatment.

For osteosarcoma, Ewing’s sarcoma and chordoma radiotherapy may be used to relieve symptoms or treat advanced bone cancers. It can be very good at shrinking cancers in the bones and so relieving pain and other symptoms caused by pressure from the cancer.

Radiotherapy is rarely used to treat chondrosarcoma because it does not usually work very well for this type of bone tumour.
(Cancer Research UK).

Bone Cancer Treatment Regimens

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly.

Chordoma - All recommendations are category 2A unless otherwise indicated.

Regimen:	**Dosing:**
Imatinib	Imatinib 800mg orally once daily
Imatinib + cisplatin	Imatinib 400mg orally once daily + cisplatin 25mg/m2 weekly
Imatinib + sirolimus	Imatinib 400mg orally once daily + sirolimus 2mg orally once daily
Erlotinib	Erlotinib 150mg orally once daily
Sunitinib	Sunitinib 37.5mg orally once daily
Lapatinib for epidermal growth factor receptor (EGFR)-positive chordomas (Category 2B)	Lapatinib 1,500mg orally once daily

(Cancer Therapy Advisor)

Ewing's Sarcoma and Mesenchymal Chondrosarcoma - First-line Therapy (Primary/Neoadjuvant/Adjuvant)

Regimen:	**Dosing:**
VAC/IE (vincristine + doxorubicin† + cyclophosphamide alternating with ifosfamide + etoposide)	Alternating VAC and IE cycles *VAC cycles* **Day 1**: Vincristine 2mg/m^2 (max 2mg) IV + doxorubicin 75mg/m^2 IVP + cyclophosphamide 1,200mg/m^2 IV. Dactinomycin 1.25mg/m^2 IV can be substituted for doxorubicin when a total doxorubicin dose of 375mg/m^2 is reached. *IE cycles* **Days 1–5**: Ifosfamide 1,800mg/m^2 IV + mesna + etoposide 100mg/m^2 IV. Repeat each cycle every 3 weeks for 17 cycles
VAIA (vincristine + dactinomycin [actinomycin D] + ifosfamide + doxorubicin)	**Day 1**: Vincristine 1.5mg/m^2 IV **Days 1-3**: Ifosfamide 2,000mg/m^2 IV + mesna **Days 1, 3, and 5**: Dactinomycin 0.5mg/m^2 IV **Days 2 and 4**: Doxorubicin 30mg/m^2 IV. Repeat cycle every 21 days for 4 cycles, then proceed to local therapy. After local therapy, high-risk patients should receive 10 additional cycles of VAIA; standard-risk patients should receive 10 additional cycles of VAIA of 10 cycles of VACA; **Day 1**: Vincristine 1.5mg/m^2 IV + cyclophosphamide 1,200mg/m^2 IV + mesna **Days 1, 3, and 5**: Dactinomycin 0.5mg/m^2 IV **Days 2 and 4**: Doxorubicin 30mg/m^2 IV. Repeat cycle every 21 days for 10 cycles. **OR** **Days 1, 8, 15, and 22**: Vincristine 1.5mg/m^2 IV **Days 1, 2, 22, 23, 43, and 44** : Ifosfamide 3,000mg/m^2 IV + mesna **Days 1, 2, 43, and 44** : Doxorubicin 30mg/m^2 IV **Days 22, 23, and 24**: Dactinomycin 0.5mg/m2 IV After completion of one 9-week cycle, proceed to local therapy. High-risk patients should then receive 3 additional cycles
VIDE (vincristine + ifosfamide + doxorubicin + etoposide)	**Day 1**: Vincristine 1.5mg/m^2 (max 2mg) IV push **Days 1–3**: Doxorubicin 20mg/m^2 IV + ifosfamide 3g/m^2

	IV + mesna continuous IV infusion + etoposide 150mg/m^2 IV. Repeat cycle every 3 weeks for up to 6 cycles

(Cancer Therapy Advisor)

Ewing's Sarcoma and Mesenchymal Chondrosarcoma1 (continued)
Primary Therapy for Metastatic Disease at Initial Presentation

Regimen:	**Dosing:**
VAC/IE (vincristine + doxorubicin† + cyclophosphamide alternating with ifosfamide + etoposide)	Alternating VAC and IE cycles *VAC cycles* **Day 1**: Vincristine 2mg/m^2 (max 2mg) IV + doxorubicin 75mg/m^2 IV bolus + cyclophosphamide 1,200mg/m^2 IV + mesna. Dactinomycin 1.25mg/m^2 IV can be substituted for doxorubicin when a total doxorubicin dose of 375mg/m^2 is reached. *IE cycles* **Days 1–5**: Ifosfamide 1,800mg/m^2 IV + mesna + etoposide 100mg/m^2 IV. Repeat each cycle every 3 weeks for 17 cycles
VAIA (vincristine + dactinomycin [actinomycin D] + ifosfamide + doxorubicin)	**Day 1**: Vincristine 1.5mg/m^2 IV **Days 1-3**: Ifosfamide 2,000mg/m^2 IV + mesna **Days 1, 3, and 5**: Dactinomycin 0.5mg/m^2 IV **Days 2 and 4**: Doxorubicin 30mg/m^2 IV. Repeat cycle every 21 days for 4 cycles, then proceed to local therapy. After local therapy, high-risk patients should receive 10 additional cycles of VAIA; standard-risk patients should receive 10 additional cycles of VAIA of 10 cycles of VACA; **Day 1**: Vincristine 1.5mg/m^2 IV + cyclophosphamide 1,200mg/m^2 IV + mesna **Days 1, 3, and 5**: Dactinomycin 0.5mg/m^2 IV **Days 2 and 4**: Doxorubicin 30mg/m^2 IV. Repeat cycle every 21 days for 10 cycles. **OR** **Days 1, 8, 15, and 22**: Vincristine 1.5mg/m^2 IV **Days 1, 2, 22, 23, 43, and 44** : Ifosfamide 3,000mg/m^2 IV + mesna **Days 1, 2, 43, and 44** : Doxorubicin 30mg/m^2 IV **Days 22, 23, and 24**: Dactinomycin 0.5mg/m^2 IV. After completion of one 9-week cycle, proceed to local therapy. High-risk patients should then receive 3 additional cycles
VIDE (vincristine + ifosfamide + doxorubicin + etoposide)	**Day 1**: Vincristine 1.5mg/m^2 (max 2mg) IV push **Days 1–3**: Doxorubicin 20mg/m^2 IV + ifosfamide 3g/m^2 IV + mesna continuous IV infusion + etoposide 150mg/m^2 IV. Repeat cycle every 3 weeks for up to 6 cycles
VAdriaC† (vincristine + doxorubicin + cyclophosphamide + dactinomycin)	**Day 1**: Vincristine 2mg/m^2 IV + cyclophosphamide 1,200mg/m^2 + doxorubicin 75mg/m^2 (the first 5 cycles) **OR** dactinomycin 1.25mg/m^2 IV (subsequent cycles). Repeat cycle every 3 weeks for 17 cycles

(Cancer Therapy Advisor)

Second-line Therapy (Relapsed/Refractory Disease or Metastatic Disease)

Regimen:	**Dosing:**
Cyclophosphamide + topotecan	**Days 1–5**: Cyclophosphamide 250mg/m^2/day IV + topotecan 0.75mg/m^2/day IV, each given as a 30-minute infusion once daily for 5 days.

	Repeat cycle every 3 weeks for 12–14 cycles
Irinotecan • } temozolomide	**Days 1–5**: Temozolomide 100mg/m^2/day orally, plus **Days 1–5 and 8–12**: Irinotecan 10–20mg/m^2/day IV at least 1 hour after temozolomide. Repeat cycle every 3 or 4 weeks
Ifosfamide (high dose) • } etoposide	**Days 1–5**: Ifosfamide 1,800mg/m^2/day IV + mesna **Days 1–5**: Etoposide 100mg/m^2/day IV. Repeat every 3 weeks for 12 cycles
Ifosfamide + carboplatin + etoposide	**Days 1 and 2**: Carboplatin 400mg/m^2/day IV, plus **Days 1–5**: Ifosfamide 1,800mg/m^2/day IV + mesna + etoposide 100mg/m^2/day IV. Repeat cycle every 3 weeks for up to 12 cycles (median 1 cycle)
Docetaxel + gemcitabine	**Days 1 and 8**: Gemcitabine 675mg/m^2 IV, plus **Day 8**: Docetaxel 75–100mg/m^2 IV. Repeat cycle every 3 weeks for up to 13 cycles (median 4 cycles)

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Giant Cell Tumour of Bone

Regimen:	**Dosing:**
Denosumab	Denosumab 120mg subcutaneously every 4 weeks with additional doses on **Days 8 and 15**
Interferon alfa	Interferon alpha-2 or beta (3,000,000 units/m2) 48 to 72 hours postoperatively **OR** increasing dosage from 4 x 106 units 3 times a week to 9 × 106 units 3 times a week
Peginterferon	Peginterferon alfa-2a 1.0µ/kg SQ injection weekly

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Osteosarcoma - First-line Therapy (Primary/Neoadjuvant/Adjuvant Therapy or Metastatic Disease)

Regimen:	**Dosing:**
Cisplatin + doxorubicin	**Days 1–3**: Doxorubicin 25mg/m^2/day IV, plus **Day 1**: Cisplatin 100mg/m^2 IV continuous IV infusion. Repeat cycle every 3 weeks for 6 cycles
MAP (high-dose methotrexate +cisplatin + doxorubicin)	Preoperative Chemotherapy **Days 1 and 28**: Methotrexate 8g/m^2 IV followed by citrovorum factor rescue **Days 7-9 and 34-36**: Cisplatin 120mg/m^2 by intra-arterial infusion for 72 hours **Days 9 and 36**: Doxorubicin 60mg/m^2 IV starting 8 hours after the beginning of cisplatin. Postoperative Chemotherapy (Necrosis ≥90%) **Days 1, 48, 96, and 144**: Doxorubicin 45mg/m^2/day for 2 consecutive days in a 4-hour IV infusion **Days 21, 69, and 117**: Methotrexate 8g/m^2 IV followed by citrovorum factor rescue **Days 27, 75, and 123**: Cisplatin 120mg/m^2 by intra-arterial infusion for 72 hours. Postoperative Chemotherapy (Necrosis <90%) **Days 1, 69, 138, and 207**: Doxorubicin 45mg/m^2/day for 2 consecutive days in a 4-hour IV infusion **Days 21, 90, and 159**: Ifosfamide 2g/m^2/day IV for 5 consecutive days in 90 minutes + mesna **Days 42, 111, and 180**: Methotrexate 8g/m^2 IV followed by citrovorum factor rescue **Days 48, 117, and 186**: Etoposide 120mg/m2/day in a 1-hour infusion for 3 days
Doxorubicin + cisplatin + ifosfamide + high-dose methotrexate	**Days 0, 6, 18, 27, and 36**: Methotrexate 12g/m^2 as a 4-hour infusion, increased by 2g/m^2 if the hour-4 level of serum methotrexate in the previous course was

	<1000 µmol/L **Days 1, 7, 19, 28, and 37**: Cisplatin 60mg/m^2/day as a 48-hour continuous IV infusion (total dose 120mg/m^2) **Days 1 and 7**: Doxorubicin (preoperative): 75mg/m^2 as a 24-hour continuous IV infusion **Day 12**: Surgery **Days 13, 22, and 31**: Doxorubicin (postoperative): 90mg/m^2 as a 24-hour continuous IV infusion Days 4, 10, 16, 25, and 34: Ifosfamide: 3 g/m2/day as a 120-hour (5-day) continuous IV infusion (total dose 15g/m^2)
Ifosfamide + cisplatin + epirubicin	**Day 1**: Epirubicin 90mg/m^2 IV + cisplatin 100mg/m^2 IV **Days 2–4**: Ifosfamide 2.0g/m^2 with an equivalent dose of mesna, repeated every 21 days. Six cycles of this combination regimen were administered (3 cycles preoperatively and 3 cycles postoperatively)

(Cancer Therapy Advisor)

Osteosarcoma - Second-line Therapy (Relapsed/Refractory or Metastatic Disease)

Regimen:	**Dosing:**
Carboplatin + ifosfamide + etoposide	**Days 1 and 2**: Carboplatin 400mg/m^2/day IV, plus **Days 1–5**: Ifosfamide 1,800mg/m^2/day IV + mesna + etoposide 100mg/m^2/day IV. Repeat cycle every 3 weeks for up to 12 cycles (median 1 cycles)
Gemcitabine + docetaxel	**Days 1 and 8**: Gemcitabine 675mg/m^2 IV, plus **Day 8**: Docetaxel 75–100mg/m^2 IV. Repeat cycle every 3 weeks for up to 13 cycles (median 4 cycles)
Cyclophosphamide + topotecan	**Days 1–5**: Cyclophosphamide 250mg/m2/day IV + topotecan 0.75mg/m^2/day IV, each given as a 30-minute infusion once daily for 5 days. Repeat cycle every 3 weeks for 12–14 cycles
Sorafenib	Sorafenib 400mg orally twice daily until progression or unacceptable toxicity
Ifosfamide (high dose) • } etoposide	Days 1–5: Ifosfamide 1,800mg/m^2/day IV + mesna, plus **Days 1–5**: Etoposide 100mg/m2/day IV. Repeat every 3 weeks for 12 cycles
Cyclophosphamide + etoposide	**Day 1**: Cyclophosphamide 4,000mg/m^2 3-hour IV infusion; all patients received mesna 1,400mg/m^2 before and after 4 hours and 8 hours from cyclophosphamide start **Days 2–4**: Etoposide 100mg/m^2 over 1 hour twice daily for 3 days on Days 2, 3, and 4 (total dose 600mg/m^2)
Gemcitabine	**Days 1 and 8**: Gemcitabine 1,200mg/m^2 IV. Repeat cycle every 21 days
High-dose methotrexate + etoposide + ifosfamide	**Weeks 1, 2, 3, 7, 8, 12, and 13**: High-dose methotrexate IV **Weeks 4 and 9**: Etoposide 75mg/m2/day IV + ifosfamide 3g/m^2/day + mesna 3.6mg/m^2/day continuous IV infusion for 4 days
Sorafenib + everolimus	Sorafenib 800mg orally + everolimus 5mg orally once daily until disease progression or unacceptable toxicity
^{153}Sm-EDTMP (for relapsed or refractory disease beyond second-line therapy)	Samarium-153 ethylene diamine tetramethylene phosphonate (153Sm-EDTMP) 1.0, 3.0, 4.5, 6.0, 12.0, 19.0, or 30.0mCi/kg can be considered; however, the 30mCi/kg dosage requires peripheral-blood progenitor cell grafts with more than 2 x 106 CD34(+)/kg to overcome the myeloablative effects of skeletal irradiation

^{223}RA	Three 75kBq/kg ^{223}RA infusion given in 4-week intervals (total administered dose of 14.44MBq or 0.390mCi); ^{223}RA doses of 50kBq/kg and 100Bq/kg are being investigated

(Cancer Therapy Advisor)

About Clinical Trials

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

Types of Clinical Trials

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

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

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

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

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

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

Where Clinical Trials are Conducted

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

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

Research Team

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

Clinical Trial Protocol

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

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

National and International Regulations

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

Informed Consent

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

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

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

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

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

Phases of a Clinical Trial

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

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

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

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

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

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

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

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

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

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

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

<u>Use of Placebos</u>

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

Possible benefits of taking part in a clinical trial

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

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

Potential harms associated with taking part in a clinical trial

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

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

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

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

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

When a clinical trial is over

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

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the

study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

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