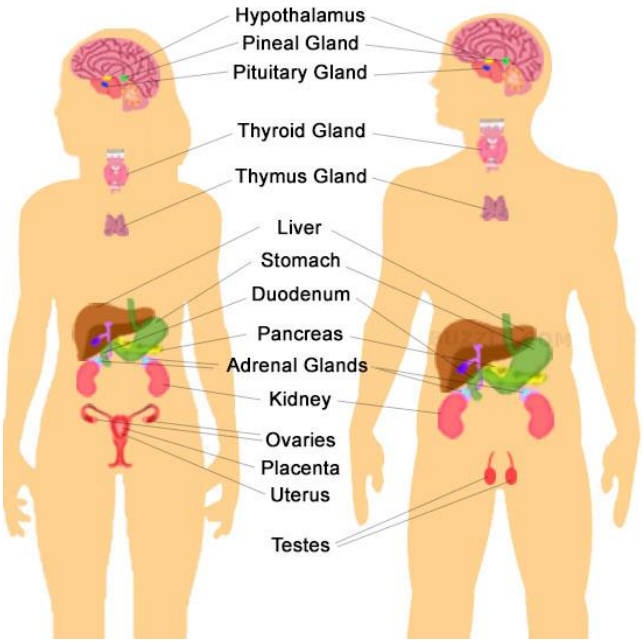
# Cancer Association of South Africa (CANSA)

Research • Educate • Support

## Fact Sheet
## on
## Parathyroid Gland Cancer

**Introduction**

The endocrine system is a network of endocrine glands and nerves throughout the body. Endocrine glands produce and release hormones, which circulate around the body in the blood. Hormones keep an even balance of chemicals and fluid within the body, and help the body respond to changes in the environment. Normally, the hormones released by endocrine glands are carefully balanced to meet the body's needs. There are many more organs in the body capable of secreting hormones than is popularly believed.




[Picture Credit: Major Endocrine Organs]

Endocrine organs (those organs that secrete hormones) include:

- Hypothalamus
- Pineal body
- Pituitary gland (anterior lobe)
- Pituitary gland (posterior lobe)
- Thyroid
- Alimentary system
  - Stomach
  - Duodenum
  - Liver
  - Pancreas
- Kidney
- Adrenal cortex
- Adrenal medulla
- Reproductive system
  - Testes
  - Ovaries
  - Placenta (during pregnancy)

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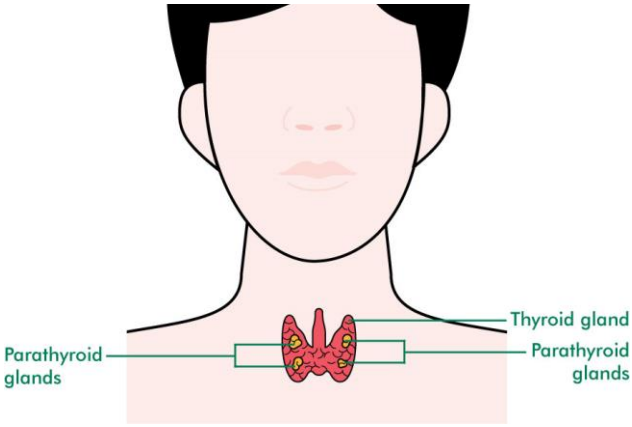
- Uterus (during pregnancy)
  - Parathyroid
  - Skin

(MacMillan Cancer Support; KidsHealth; MedLine Plus; Emedicinehealth; Wikipedia).

**Parathyroid Gland Cancer**

Parathyroid gland cancer occurs when the cells of the parathyroid gland multiplies uncontrollably. Parathyroid disease is caused by a single defective parathyroid gland (a benign parathyroid tumour) about 80% of the time. Parathyroid cancer is extremely rare, to the extent that most doctors have never seen it.
(Parathyroid.com).

[Picture Credit: Parathyroid Glands]




There are four parathyroid glands, which are attached to the thyroid gland in the front of the neck. The parathyroid glands are small, but their function is very important. They maintain the correct levels of calcium in the body. Calcium plays an essential role in controlling muscle and nerve function. A tumour of the parathyroid gland may cause overproduction of the hormone that controls the level of calcium in the body. This hormone is called parathyroid hormone (PTH) or parathormone.
(MacMillan Cancer Support).

**Incidence of Parathyroid Gland Cancer in South Africa**

The National Cancer Registry (2013 does not provide any information on the incidence of parathyroid cancer. The Registry combines all the endocrine cancers together.

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

| Group - Males 2013 | Actual No of Cases | Estimated Lifetime Risk | Percentage of All Cancers |
|---|---|---|---|
| All males | 17 | 1:18 374 | 0,05% |
| Asian males | 0 | - | - |
| Black males | 7 | 1:55 226 | 0,07% |
| Coloured males | 2 | 1:8 700 | 0,05% |
| White males | 7 | 1:3 759 | 0,04% |

| Group - Females 2013 | Actual No of Cases | Estimated Lifetime Risk | Percentage of All Cancers |
|---|---|---|---|
| All females | 25 | 1:15 192 | 0,07% |
| Asian females | 0 | - | - |
| Black females | 11 | 1:31 642 | 0,07% |
| Coloured females | 1 | 1:7 317 | 0,04% |
| White females | 13 | 1:2 911 | 0,08% |

The frequency of histologically diagnosed cases of endocrine 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 | 12 | 0 | 1 | 1 | 1 | 2 | 0 | 0 |
| Asian males | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Black males | 6 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Coloured males | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |
| White males | 5 | 0 | 0 | 0 | 1 | 1 | 0 | 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 | 11 | 4 | 1 | 2 | 4 | 0 | 1 | 2 |
| Asian females | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Black females | 8 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |
| Coloured females | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| White females | 3 | 2 | 1 | 1 | 3 | 0 | 0 | 2 |

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.

## Symptoms of Parathyroid Gland Cancer

Symptoms of parathyroid cancer are mainly caused by high levels of calcium in the blood (hypercalcemia) and may affect different parts of the body.

They include:

- Bone pain
- Constipation
- Fatigue
- Fractures
- Frequent thirst
- Frequent urination
- Kidney stones
- Muscle weakness
- Nausea
- Poor appetite
- Vomiting

(MedlinePlus).

## Causes of Parathyroid Gland Cancer

Parathyroid cancer is an extremely rare type of cancer. Men and women are equally affected. It usually occurs in people older than 30.

The cause of parathyroid cancer is unknown. People with a genetic condition called multiple endocrine neoplasia type I have an increased risk for this disease. People who had head or neck radiation may also be at increased risk. Such radiation exposure, however, is more likely to cause thyroid cancer.
(MedlinePlus).

**Diagnosis of Parathyroid Gland Cancer**
The facts about parathyroid cancer:

- Parathyroid cancer is very rare: about one case in every 1 000 patients with parathyroid disease, or possibly even rarer
- Parathyroid cancer is often mild and not very aggressive
- Parathyroid cancer is often hard for the pathologist to diagnose under the microscope. Thus the diagnosis often depends on the clinical picture (very high parathyroid hormone levels, and very high serum calcium levels)
- Parathyroid cancer is *almost always* associated with extremely high parathyroid hormone (PTH) levels (typically in the thousands)
- If the patient's parathyroid hormone level is not in the thousands, and the calcium is not consistently over 14mg/dL, the patient does not have parathyroid cancer (a generalisation, but a good one)
- Most people with calcium levels above 14mg/dL still do not necessarily have parathyroid cancer
- Parathyroid cancer is occasionally associated with a genetic defect, therefore, parathyroid cancer may be found in families

(EndocrineWeb.com).

**Staging of Parathyroid Gland Cancer**
There is no standard staging process for parathyroid cancer.

Parathyroid cancer is described as either localized or metastatic:

- Localised parathyroid cancer is found in a parathyroid gland and may have spread to nearby tissues
- Metastatic parathyroid cancer has spread to other parts of the body, such as the lungs, liver, bone, sac around the heart, pancreas, or lymph nodes

The process used to determine if cancer has spread to other parts of the body is called staging. The following imaging tests may be used to determine if cancer has spread to other parts of the body such as the lungs, liver, bone, heart, pancreas, or lymph nodes:

- CT scan (CAT scan): A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerised tomography, or computerised axial tomography.
- MRI (magnetic resonance imaging): A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).

The three ways that cancer spreads in the body are:

- Through tissue - cancer invades the surrounding normal tissue
- Through the lymph system - cancer invades the lymph system and travels through the lymph vessels to other places in the body
- Through the blood - cancer invades the veins and capillaries and travels through the blood to other places in the body

When cancer cells break away from the primary (original) tumour and travel through the lymph or blood to other places in the body, another (secondary) tumour may form. This process is called metastasis. The secondary (metastatic) tumour is the same type of cancer as the primary tumour. For example, if breast cancer spreads to the bones, the cancer cells in the bones are actually breast cancer cells. The disease is metastatic breast cancer, not bone cancer.

Recurrent Parathyroid Cancer - recurrent parathyroid cancer is cancer that has recurred (come back) after it has been treated. More than half of patients have a recurrence. The parathyroid cancer usually recurs between 2 and 5 years after the first surgery, but can recur up to 20 years later. It usually comes back in the tissues or lymph nodes of the neck. High blood calcium levels that appear after treatment may be the first sign of recurrence.
(National Cancer Institute).

**Treatment of Parathyroid Gland Cancer**
Different types of treatment are available for patients with parathyroid cancer. Some treatments are standard (the currently used treatment) while some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Patients may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment.

Treatment includes control of hypercalcaemia (high levels of calcium in the blood) in patients who have an overactive parathyroid gland.

In order to reduce the amount of parathyroid hormone that is being made and control the level of calcium in the blood, as much as possible of the tumour is removed in surgery. For patients who cannot have surgery, medication may be used.

Four types of standard treatment are used:

Surgery - surgery (removing the cancer in an operation) is the most common treatment for parathyroid cancer that is in the parathyroid glands or has spread to other parts of the body. Because parathyroid cancer grows very slowly, cancer that has spread to other parts of the body may be removed by surgery in order to cure the patient or control the effects of the disease for a long time. Before surgery, treatment is given to control hypercalcaemia.
The following surgical procedures may be used:

- *En bloc* resection: Surgery to remove the entire parathyroid gland and the capsule around it. Sometimes lymph nodes, half of the thyroid gland on the same side of the body as the cancer as well as muscles, tissues and a nerve in the neck are also removed
- Tumour debulking: Surgery to remove as much of the tumour as possible. Sometimes, not all of the tumour can be removed
- Metastasectomy: Surgery to remove any cancer that has spread to distant organs such as the lung

Surgery for parathyroid cancer sometimes damages nerves of the vocal cords. There are treatments to help with speech problems caused by this nerve damage.

No effective medical therapy for parathyroid carcinoma is known. Trials of chemotherapeutic agents have been generally disappointing with only anecdotal reports of success. This tumour is sufficiently rare that controlled trials are impossible.

Medical therapy is primarily geared toward management of the hypercalcaemia that is often quite severe. Treatment is similar to hypercalcaemia due to other causes. At initial presentation and for rapid treatment of severe hypercalcaemia volume loading and diuresis with a calcium-wasting loop diuretic is the treatment of choice. The next line of therapy, used for chronic treatment, is the bisphosphonates.

Hypercalcaemia due to parathyroid cancer is often resistant to long-term medical management and is usually the cause of death in patients with metastatic disease.

Radiation therapy - radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or stop them from growing. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.

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 spinal column, 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.

Supportive care - supportive care is given to lessen the problems caused by the disease or its treatment. Supportive care for hypercalcaemia caused by parathyroid cancer may include the following:

- Intravenous (IV) fluids.
- Drugs that increase how much urine the body makes.
- Drugs that stop the body from absorbing calcium from the food we eat.
- Drugs that stop the parathyroid gland from making parathyroid hormone.

(Medscape).

**About Clinical Trials**

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the

development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials

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

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

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

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

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

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

Where Clinical Trials are Conducted

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

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

Research Team

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

Clinical Trial Protocol

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

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

National and International Regulations

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

Informed Consent

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

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

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

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

Phases of a Clinical Trial

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

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

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

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

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure

that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

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

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.
In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

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

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

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

Use of Placebos

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

Possible benefits of taking part in a clinical trial

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

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

Potential harms associated with taking part in a clinical trial
The potential harms of participating in a clinical trial include the following:

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

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

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

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

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

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