Introduction
Cancer begins when normal cells change and grow uncontrollably, forming a mass called a tumour. A tumour can be benign (noncancerous) or malignant (cancerous, meaning it can spread to other parts of the body). Neuroblastoma is a solid cancerous tumour that begins in the nerve cells of infants and young children. It can start in the nerve tissue near the spine in the neck, chest, abdomen, or pelvis, but it most often begins in the adrenal glands. The adrenal glands are located on top of both kidneys and make hormones that help control body functions, such as heart rate and blood pressure.

Neuroblasts are immature nerve cells found in unborn babies. Normal neuroblasts mature into nerve cells or adrenal medulla cells (cells found in the centre of the adrenal gland). A neuroblast that does not mature properly can continue to grow, leading to neuroblastoma. However, babies are sometimes born with small clusters of neuroblasts that eventually mature into nerve cells and do not become cancer.

Neuroblastoma develops most often in infants and children younger than five. It can form before the baby is born and can sometimes be found during a prenatal (before birth) ultrasound. Most often, however, neuroblastoma is found after the cancer has spread to other parts of the body, such as the lymph nodes (tiny, bean-shaped organs that help fight infection), liver, lungs, bones, and bone marrow (the spongy, red tissue in the inner part of large bones).

BACKGROUND: Males have worse survival for childhood cancer, but whether this disparity exists among all childhood cancer types is undescribed.
METHODS: We estimated sex differences in survival for 18 cancers among children (0–19 years) in Surveillance, Epidemiology, and End Results 18 (2000-2014). We used Kaplan-Meier survival curves (log-rank P values) to characterize sex differences in survival and Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between sex and death for each cancer type. We used an inverse odds weighting method to determine whether the association between sex and death was mediated by stage of disease for solid tumors.
RESULTS: Males had worse overall survival and a higher risk of death for acute lymphoblastic leukemia (HR = 1.24, 95% CI = 1.12 to 1.37), ependymoma (HR = 1.36, 95% CI = 1.05 to
1.77), neuroblastoma (HR = 1.28, 95% CI = 1.09 to 1.51), osteosarcoma (HR = 1.29, 95% CI = 1.08 to 1.53), thyroid carcinoma (HR = 3.25, 95% CI = 1.45 to 7.33), and malignant melanoma (HR = 1.97, 95% CI = 1.33 to 2.92) (all log-rank $P$ values < .02). The association between sex and death was mediated by stage of disease for neuroblastoma (indirect HR = 1.12, 95% CI = 1.05 to 1.19), thyroid carcinoma (indirect HR = 1.24, 95% CI = 1.03 to 1.48), and malignant melanoma (indirect HR = 1.28, 95% CI = 1.10 to 1.49). For these six tumors, if male survival had been as good as female survival, 21% of male deaths and 13% of total deaths after these cancer diagnoses could have been avoided.

**CONCLUSIONS:** Consideration of molecular tumor and clinical data may help identify mechanisms underlying the male excess in death after childhood cancer for the aforementioned cancers.

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**Incidence of Childhood Neuroblastoma in South Africa**

The National Cancer Register (2014) does not provide any information on the incidence of neuroblastoma.

**Causes of Childhood Neuroblastoma**

The causes of most neuroblastomas are not known. But researchers have found important differences between neuroblastoma cells and the normal neuroblasts (early forms of nerve cells) from which they develop. They have also found differences between neuroblastomas that are likely to respond to treatment and those that have a poor prognosis (outlook). These differences (known as prognostic markers) are sometimes helpful in choosing the best treatment.

Both nerve cells and cells of the medulla (centre) of the adrenal gland develop from neuroblasts in the fetus. Neuroblastomas develop when normal foetal neuroblasts fail to become mature nerve cells or adrenal medulla cells. Instead, they continue to grow and divide.

Neuroblasts may not have matured completely in babies by the time they are born. In fact, studies have shown that there are small clusters of neuroblasts in the adrenal glands of some infants less than 3 months old. Most of these eventually mature into nerve cells or simply die off and do not form neuroblastomas. Sometimes, neuroblasts remaining in very young infants continue to grow and then form tumours. Some can even spread to other parts of the body. But many of these tumours will still eventually mature into nerve tissue or go away on their own.

However, as children get older, it becomes less likely that these cells will mature and more likely that they will grow into a cancer. By the time neuroblastomas are large enough to be felt or cause symptoms, most can no longer mature on their own and will grow and spread unless treated.

The failure of some neuroblasts to mature and to stop growing is due to abnormal DNA inside the cells. DNA is the chemical in each of our cells that makes up our genes – the instructions for how our cells function. The DNA inside our cells is in long string-like structures called chromosomes.

Some genes contain instructions for controlling when our cells grow, divide into new cells, and die. Certain genes that help cells grow, divide, or stay alive are called oncogenes. Others that slow down cell division or cause cells to die at the right time are called tumour suppressor genes. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumour suppressor genes. These gene changes can be inherited from a parent (as is sometimes the case with childhood cancers), or they may happen during a person’s lifetime as cells in the body divide to make new cells.
In most cases, neuroblastoma cells have chromosome changes (such as having too many or too few chromosomes or missing part of a chromosome) that are likely to affect certain genes. Scientists are still trying to determine which genes are affected by these chromosome changes, as well as how these changes affect the growth of neuroblastoma cells.

In rare cases, neuroblastoma seems to occur because of gene changes inherited from a parent. Inherited changes in the ALK oncogene seem to account for most cases of hereditary neuroblastoma. A small number of inherited neuroblastomas are caused by changes in PHOX2B, a gene that normally helps nerve cells mature.

Still, most neuroblastomas are not caused by inherited DNA changes. They are the result of gene changes that happen early in the child’s development, often before birth. These changes are found only in the child’s cancer cells, so they will not be passed on to his or her children. For example, about 10% to 15% of sporadic (non-inherited) neuroblastomas have changes in the ALK gene. But in many neuroblastomas the exact genes affected are not known.

Some gene changes seem to affect how quickly a neuroblastoma is likely to grow. For example, neuroblastoma cells sometimes have extra copies of an oncogene called MYCN, which is often a sign that the tumour will grow quickly and be harder to treat. On the other hand, the NTRK1 gene (which makes the TrkA protein) is often overactive in the cells of neuroblastomas that have a better outlook. Researchers recently found that neuroblastoma cells in older children are more likely to have changes in the ATRX tumour suppressor gene. Tumours with this gene change tend to grow more slowly, but they are also harder to cure. This may help explain why younger children with neuroblastoma tend to do better long term than children who are older when they are diagnosed. Researchers have found some of the gene changes that may lead to neuroblastoma, but it is still not clear what causes these changes. Some gene changes may be inherited. Some might have unknown outside causes, but others may just be random events that sometimes happen inside a cell, without having an outside cause. There are no known lifestyle-related or environmental causes of neuroblastomas at this time, so it is important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Geurten, C., Geurten, M., Hoyoux, C. & Lebrethon, M.C. 2019. “Background Neuroblastoma (NBL) is a child neoplasia affecting extracranial tissue of neuroectodermal origin. It accounts for 10% of solid malignancies in children and is characterized by a survival rate approaching 70%, confronting physicians with the emergence of an adult survivor population who have been previously exposed to surgery, cytotoxic drugs, radiation therapy or metaiodobenzylguanidine (MIBG) therapy. All these treatments potentially affect the endocrine system. Our study consists in a retrospective review of late endocrine effects arising in survivors treated for NBL during childhood. Methods The medical files of 47 patients (M/F = 26/21) treated for NBL were reviewed. Collected data consisted of age, height, weight and biological hormonal values at diagnosis and at the last follow-up consultation. The incidence of late effects in our sample was compared to the data from the literature. Results Patients were between 0 and 15.8 years of age at diagnosis (median: 1.16 years) and between 1 and 25 years of age at last follow-up (median: 16 years). Twenty-six patients were treated with chemotherapy (CT), 11 underwent CT and radiation therapy and five were treated with CT and MIBG therapy. Ten percent of the patients died before reaching the end of therapy. Late effects occurred in 54% of the patients. Thirty-six percent of patients had non-endocrine complications (musculoskeletal, neurological, hematological or hepatic chronic conditions). Endocrine complications (28%) affected mainly patients treated with CT and consisted of gonadal

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dysfunction (up to 42% patients of over 12 years of age at follow-up) and hypothyroidism (21%). Our analysis revealed that CT had a significant impact on final height \((p < 0.05)\). Conclusions Treatment for childhood malignancies exposes children to late effects affecting the endocrine system. In children treated for NBL, hypothyroidism, gonadal failure and impaired growth appear to be the main endocrine complications. Close follow-up of survivors is thus appropriate.”

**Signs and Symptoms of Childhood Neuroblastoma**

The effects of neuroblastoma can vary widely depending on where the disease first started and how much it has spread to other parts of the body. The first symptoms are often vague and may include irritability, fatigue, loss of appetite, and fever. But because these early warning signs can develop gradually and mimic those of other common childhood illnesses, neuroblastoma can be difficult to diagnose.

In young children, neuroblastoma often is discovered when a parent or doctor feels an unusual lump or mass somewhere in the child’s body — most often in the abdomen, though tumors also can appear in the neck, chest, and elsewhere.

The most common signs of neuroblastoma are caused by the tumor pressing on nearby tissues as it grows or by the cancer spreading to other areas. These signs vary depending on how much the cancer has grown and where it has spread.

For example, a child may have:

- a swollen stomach, abdominal pain, and decreased appetite (if the tumor is in the abdomen)
- bone pain or soreness, black eyes, bruises, and pale skin (if the cancer has spread to the bones)
- weakness, numbness, inability to move a body part, or difficulty walking (if the cancer presses on the spinal cord)
- drooping eyelid, unequal pupils, sweating, and red skin, which are signs of nerve damage in the neck known as Horner’s syndrome (if the tumor is in the neck)
- difficulty breathing (if the cancer is in the chest)

**Diagnosis of Childhood Neuroblastoma**

The following tests and procedures may be used in the diagnosis of Childhood Neuroblastoma:

- Physical examination and history - an examination of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient’s health habits and past illnesses and treatments will also be taken.

- Twenty-four-hour urine test - a test in which urine is collected for 24 hours to measure the amounts of certain substances. An unusual (higher or lower than normal) amount of a substance can be a sign of disease in the organ or tissue that makes it. A higher than normal amount of the substances homovanillic acid (HMA) and vanillyl mandelic acid (VMA) may be a sign of neuroblastoma.
• Blood chemistry studies - a procedure in which a blood sample is checked to measure the amounts of certain substances released into the blood by organs and tissues in the body. An unusual (higher or lower than normal) amount of a substance can be a sign of disease in the organ or tissue that makes it. A higher than normal amount of the hormones dopamine and norepinephrine may be a sign of neuroblastoma.

• Cytogenetic analysis - a test in which cells in a sample of blood or bone marrow are viewed under a microscope to look for certain changes in the chromosomes.

• Bone marrow aspiration and biopsy - the removal of a small piece of bone, bone marrow, and blood by inserting a needle into the hipbone or breastbone. A pathologist views both the bone and the bone marrow samples under a microscope to look for signs of cancer. Biopsy: The removal of cells or tissues so they can be viewed under a microscope by a pathologist to check for signs of cancer.

• X-ray - an X-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.

• 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, computerized tomography, or computerized axial tomography.

• Neurological examination - a series of questions and tests to check the brain, spinal cord, and nerve function. The exam checks a person’s mental status, coordination, and ability to walk normally, and how well the muscles, senses, and reflexes work. This may also be called a neuro examination or a neurologic examination.

• Ultrasound examination - a procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram.

• Immunohistochemistry study - a procedure in which dyes or enzymes are added to a blood or bone marrow sample to test for certain antigens (proteins that stimulate the body’s immune response).

Georgantzi, K., Sköldenberg, E., Janson, E.T., Jakobson, A. & Christofferson, R. 2019. BACKGROUND: Neuroblastoma (NB) is the most common extracranial solid tumor of childhood and accounts for 15% of deaths in pediatric oncology. Apart from the clinical stage at diagnosis, molecular factors are important for the characterization of the tumor and for decision on adequate treatment. Pretreatment diagnosis and molecular profiling are based on analysis of a tumor sample, obtained either by fine needle aspiration cytology (FNAC), cutting needle biopsy or open surgical biopsy. The method used depends on local tradition and routines. Ultrasound-guided cutting needle biopsy (UCNB) has been used at the Uppsala University Hospital since 1988 for diagnosis of pediatric solid tumors.
PROCEDURES: Medical records of 29 patients with NB who underwent pretreatment, diagnostic, ultrasound-guided needle biopsy were reviewed. Information extracted from the patients’ records included: age at diagnosis, gender, tumor site, clinical stage, molecular profiling made on biopsies (e.g. MYCN status, ploidy and chromosomal aberrations), and UCNB complications (i.e. bleeding, pain, or anesthesiologic complications).

RESULTS: A total of 34 UCNBs were performed in the 29 patients. Repeated biopsies were done in three patients. UCNB was diagnostic in 90% (26/29). A complete molecular profiling was obtained in all UCNBs after 2008. Two patients (7%) developed a significant bleeding and two (7%) needed analgesics following UCNB. Neither infection nor tumor growth in the needle tract was observed. There were no anesthesiologic complications.

CONCLUSIONS: UCNB is reasonably safe in patients with NB and usually gives a sufficient amount of tumor tissue for a histological diagnosis, molecular profiling, and biobank storage.

Staging of Childhood Neuroblastoma
Staging is a way of describing where the cancer is located, if or where it has spread, and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the cancer’s stage, so staging may not be complete until all of the tests are finished. Knowing the stage helps the doctor to decide what kind of treatment is best and can help predict a patient’s prognosis.

There are different stage descriptions for different types of cancer. Once a diagnosis of neuroblastoma is confirmed, how much the tumour has grown and spread is evaluated or staged. The tumour’s stage helps your child’s doctor plan treatment.

There are two staging systems for neuroblastoma: INSS and INRGSS. Each is described below, followed by an explanation of risk groupings.

International Neuroblastoma Staging System Committee (INSS) system
The following is a brief summary of each INSS stage:

Stage 1:
The tumour can be removed completely during surgery. Lymph nodes removed during surgery may or may not contain cancer, but other lymph nodes near the tumour do not.

Stage 2A:
The tumour is located only in the area it started and cannot be completely removed during surgery. Nearby lymph nodes do not contain cancer.
Stage 2B:
The tumour is located only in the area where it started and may or may not be completely removed during surgery. Nearby lymph nodes contain cancer.

Stage 3:
The tumour cannot be removed with surgery. It has spread to regional lymph nodes (lymph nodes near the tumour) or other areas near the tumour, but not to other parts of the body.

Stage 4:
The original tumour has spread to distant lymph nodes (lymph nodes in other parts of the body), bones, bone marrow, liver, skin, and/or other organs (except for those listed in stage 4S, below).

Stage 4S:
The original tumour is located only where it started (as in stage 1, 2A, or 2B), and it has spread only to the skin, liver, and/or bone marrow (in infants younger than one). The spread to the bone marrow is minimal (usually less than 10% of cells examined show cancer).

The International Neuroblastoma Risk Group Staging System (INRGSS)
The INRGSS was recently designed specifically for the newly developed International Neuroblastoma Risk Group (INRG) pre-treatment classification system (see Risk groups, below). Unlike the INSS explained above, the INRGSS only uses the results of imaging tests taken before surgery and does not include surgical results or spread to lymph nodes to determine the stage.

Stage L1:
The tumour is located only in the area where it started; no risk factors found on imaging scans, such as CT or MRI.

Stage L2:
The tumour has not spread beyond the area where it started and the nearby tissue; risk factors are found on imaging scans, such as CT or MRI.

Stage M:
The tumour has spread to other parts of the body (except stage MS, see below).

Stage MS:
The tumour only has spread to the skin, liver, and/or bone marrow.

Treatment of Childhood Neuroblastoma
The treatment of neuroblastoma depends on the age of the child, the size and position of the tumour, the tumour biology (including the MYCN status) and whether the neuroblastoma has spread.

Surgery - for tumours that have not spread (localised tumours), the treatment is usually surgery. If the tumour is at an early stage and there’s no evidence that it has spread to the lymph nodes or any other parts of the body, an operation to remove the tumour, or as much of it as possible, will be done.
A cure is usually possible for children with localised tumours. However, if the tumour is classed as high-risk due to the tumour biology results, further treatment with chemotherapy and possibly radiotherapy will be needed. If the tumour is, at first, too large or in too difficult a position to remove safely, chemotherapy will be given to shrink it before surgery.

Chemotherapy - if the tumour has already spread by the time of diagnosis, or is indicated as being high-risk by the tumour biology result, intensive chemotherapy is needed. Chemotherapy is the use of anti-cancer (cytotoxic) drugs to destroy cancer cells. It's usually given as a drip or injection into a vein. Your child's specialist will discuss with you the type and amount of chemotherapy needed.

High-dose chemotherapy with stem cell support - if the neuroblastoma has spread to several parts of the body, or is high-risk with MYCN amplification, high-dose chemotherapy with stem cell support is used after the initial courses of chemotherapy.

High doses of chemotherapy wipe out any remaining neuroblastoma cells, but they also wipe out the body's bone marrow, where blood cells are made. To prevent the problems this causes, stem cells (blood cells at their earliest stages of development) are collected from your child through a drip before the chemotherapy is given. These stem cells are then frozen and stored.

After the chemotherapy, the stem cells are given back to your child through a drip. They make their way into the bone marrow, where they grow and develop into mature blood cells over a period of 14-21 days.

Monoclonal antibody treatment - monoclonal antibodies can destroy some types of cancer cells while causing little harm to normal cells. A new monoclonal antibody treatment called anti-GD2 is currently being tested in people with high-risk neuroblastoma. Children in the UK with high-risk neuroblastoma are being given anti-GD2 as part of a clinical trial. There is good evidence from a clinical trial carried out in America in 2009 that this may be a promising therapy when given alongside other standard treatment for neuroblastoma.

It is not yet a standard treatment for people with neuroblastoma because it has very unpleasant side effects. The benefits still need to be fully proven and the best way to administer it needs to be confirmed. Patients with high-risk neuroblastoma may be able to receive anti-GD2 in the UK if they are being treated within the European high-risk clinical trial.

Radiotherapy - external radiotherapy may be given if the neuroblastoma is high-risk, or has spread to several parts of the body. This uses high-energy rays to destroy the cancer cells, while doing as little harm as possible to normal cells. External radiotherapy is given from a machine outside the body.

Internal radiotherapy may sometimes be given using radioactive MIBG. Radioactive MIBG is similar to the MIBG used in an investigation to diagnose a neuroblastoma, but uses higher doses of radioactivity to kill the cancer cells.

Younger children - children under 18 months old with neuroblastoma often have low-risk tumours, and as long as there is no MYCN amplification, their outlook is good. Most children in this age group are cured.
Children with stage 4S disease almost always get better with very little treatment or none at all. These tumours either regress spontaneously or after chemotherapy, which is only given if the tumour is causing symptoms. They disappear completely or develop into a non-cancerous (benign) tumour, called a ganglioneuroma. Many of these children, after their initial diagnostic tests and staging investigations, will just need careful monitoring for some years.

Ganglioneuromas are usually harmless and will not cause any problems or need any treatment.

**Alexander, N., Vali, R., Ahmadzadehfar, H., Shammas, A. & Baruchel, S. 2018.**
**BACKGROUND:** Childhood neuroblastoma is a heterogeneous disease with varied clinical presentation and biology requiring different approaches to investigation and management. Metaiodobenzylguanidine (MIBG) is an essential component of metastatic staging for neuroblastoma and has been used as a treatment strategy for relapsed and refractory neuroblastoma. However, as 10% of children with neuroblastoma will have 123I-MIBG non-avid imaging and up to 60% with relapsed and refractory neuroblastoma will require further treatment with 131I-MIBG, alternative radioisotopes have been investigated for imaging and treatment. Neuroblastoma tumors express mostly somatostatin receptor-2 (SSTR2) that can be targeted by somatostatin analogues including DOTA-conjugated peptides e.g. DOTATATE, DOTATOC.

**OBJECTIVES:** This review summarizes the rationale, utility and experience of DOTA-conjugated peptides in imaging and treatment of childhood neuroblastoma.

**RESULTS AND CONCLUSIONS:** Radiolabeled DOTA-peptides are used routinely in adults to image neuroendocrine tumors and have potential to be used to image and treat neuroblastoma. 68Ga-DOTATATE PET/CT has been shown to have better sensitivity, quicker clearance and administration times, reduced radiation exposure and limited toxicity compared to 123I-MIBG. Therapeutic studies of peptide receptor radionuclides e.g. 177Lu-DOTATATE in patients with relapsed neuroblastoma have used 68Ga-DOTATATE PET/CT to determine eligibility for therapy. Further studies would need to investigate appropriate indications, timings, scoring and clinical significance of radiolabeled DOTA-peptide conjugated PET/CT imaging in childhood neuroblastoma.

**Arumugam, S., Manning-Cork, N.J., Gains, J.E., Boterberg, T. & Gaze, M.N. 2019.**

**AIMS:** External beam radiotherapy is widely used in various ways in the management of neuroblastoma. Despite extensive clinical experience, the precise role of radiotherapy in neuroblastoma remains unclear. The purpose of this systematic review was to survey the published literature to identify, without bias, the evidence for the clinical effectiveness of external beam radiotherapy as part of the initial multimodality treatment of high-risk neuroblastoma. We considered four areas: treatment of the tumour bed and residual primary tumour, identification of any dose-response relationship, treatment of metastatic sites, identification of any technical advances that may be beneficial. We also aimed to define uncertainties, which may be clarified in future clinical trials.

**MATERIALS AND METHODS:** Bibliographic databases were searched for neuroblastoma and radiotherapy. Reviewers assessed 1283 papers for inclusion by title and abstract, with consensus achieved through discussion. Data extraction on 57 included papers was carried out by one reviewer and checked by another. Studies were assessed for their level of evidence and risk of bias, and a descriptive analysis of data was carried out.

**RESULTS:** Fifteen papers provided some evidence that radiotherapy to the tumour bed and residual tumour may possibly be of value. However, there is a significant risk of bias and no evidence that all subgroups will benefit. There is some suggestion from six papers that dose may be important, but no
hard evidence. It remains unclear whether irradiation of metastatic sites is helpful. Technical advances may be of value in radiotherapy of high-risk neuroblastoma.

**CONCLUSIONS:** There are data that show that radiotherapy is of some efficacy in the management of high-risk neuroblastoma, but there is no level one evidence that shows that it is being used in the best possible way. Prospective randomised trials are necessary to provide more evidence to guide development of optimal radiotherapy treatment schedules.

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**Side Effects of Neuroblastoma Treatment**

The prognosis for neuroblastoma depends upon the stage of the tumour and its biology.

The general side effects of chemotherapy include:

- **Bone marrow suppression (myelosuppression)** - chemotherapy drugs decrease the production of blood cells by the bone marrow for a variable period of time. This results in low red blood cells (anaemia), low white blood cells (neutropenia) and platelets (thrombocytopenia). Your child may need blood or platelet transfusions and will be at increased risk of infections. The doctors and nurses caring for your child will tell you more about these side effects.

- **Nausea and vomiting** - some of the chemotherapy drugs used may make your child feel sick or vomit. We will give anti-sickness drugs at the same time to stop nausea and vomiting. These are usually very effective.

- **Sore mouth (mucositis)** - some of the chemotherapy drugs make the lining of the mouth and throat very sore and ulcerated. We will give your child painkillers for this, and explain how to care for your child’s mouth during treatment.

- **Hair loss** - temporary hair loss is common.

Specific drugs - for details of the side effects of individual drugs please see Macmillan specific drug information leaflets.

- **Possible long-term effects of treatment** - a small number of children develop side effects many years later because of the treatment they have received. These may include growth problems, reduced fertility, hearing problems, impaired heart and kidney function and a small risk of developing a second cancer later in life.

About five years after treatment finishes we will transfer your child’s care to our long-term follow-up clinic. Your child will be seen at regular intervals in this clinic, indefinitely, so that we can help with any long-term effects of the treatment.

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**About Clinical Trials**

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:
• Trials to test effectiveness of new treatments
• Trials to test new ways of using current treatments
• Tests new interventions that may lower the risk of developing certain types of cancers
• Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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