Cancer Association of South Africa (CANSA)

Research • Educate • Support

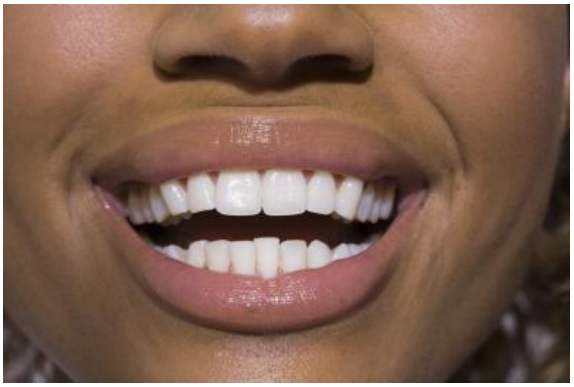
Fact Sheet on Cancer of the Lips

Introduction

Lips are a visible body part at the mouth of humans and many animals. Lips are soft, movable, and serve as the opening for food intake and in the articulation of sound and speech. Human lips are a tactile sensory organ, and can be erogenous when used in kissing and other acts of intimacy.

[Picture Credit: Lips]

The upper and lower lips are referred to as the 'Labium superius oris' and 'Labium inferius oris', respectively. The juncture where the lips meet the surrounding skin of the mouth area is the vermilion border, and the typically reddish area within the borders is called the vermilion zone. The vermilion border of the upper lip is known as the cupid's bow. The fleshy protuberance located in the center of the upper lip is a tubercle known by various terms including the procheilon (also spelled *prochilon*), the 'tuberculum labii superioris', and the 'labial tubercle'. The vertical groove extending from the procheilon to the nasal septum is called the philtrum



[Picture Credit: Lips 2]

The skin of the lip, with three to five cellular layers, is very thin compared to typical face skin, which has up to 16 layers. With light skin colour, the lip skin contains fewer melanocytes (cells which produce melanin pigment, which give skin its colour). Because of this, the blood vessels appear through the skin of the lips, which leads to their notable red colouring. With darker skin colour this effect is less prominent, as in this case the skin of the lips contains more melanin and thus is visually darker. The skin of the lip forms the border between the exterior skin of the face, and the interior mucous membrane of the inside of the mouth.

The lip skin is not hairy and does not have sweat glands. Therefore it does not have the usual protection layer of sweat and body oils which keep the skin smooth, inhibit pathogens,

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

and regulate warmth. For these reasons, the lips dry out faster and become chapped more easily.

Cancer of the Lips

Lip cancer is cancer that develops in the tissue of the lips. It is the most common form of oral cancer, and mostly affects men. There are two types of lip cancer: squamous cell and basal cell. The most common type of lip cancer begins in the squamous cells, the thin, flat cells that line the lips and mouth.

Incidence of Cancer of the Lips in South Africa

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

Group - Males 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	60	1:2 683	0,17%
Asian males	0	-	-
Black males	13	1:8 677	0,12%
Coloured males	6	1:2 681	0,14%
White males	41	1:750	0,20%

Group - Females 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	22	1:8 180	0,06%
Asian females	1	1 : 3 921	0,10%
Black females	5	1:25 668	0,03%
Coloured females	3	1:6 053	0,08%
White females	13	1:2 494	0,08%

The frequency of histologically diagnosed cases of cancer of the lips 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	0	0	7	11	16	11	9	3
Asian males	0	0	0	0	0	0	0	0
Black males	0	0	3	2	3	1	1	0
Coloured males	0	0	0	3	2	0	1	0
White males	0	0	4	6	11	10	7	3

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	0	1	0	3	3	7	5	3
Asian females	0	0	0	0	0	1	0	0
Black females	0	0	0	1	1	1	1	1
Coloured females	0	1	0	1	0	1	0	0
White females	0	0	0	1	2	4	3	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.

Causes of Cancer of the Lips

The exact cause of cancers is unknown, but certain risk factors are associated with specific types of cancer. The risk factors for lip cancer are synonymous to the risk factors of oral cancer. These include:

[Picture Credit: Cigarette Smoke]

Smoking and tobacco - has been the most often associated factor for lip and oral cancers. Cigarettes contain various carcinogens including tar. The chemical substances found in cigarettes damages the lining of the lip, which causes abnormal cells to proliferate. Almost all patients who suffered from lip cancer are smokers.

The Vast Chemicals of Cigarettes Cause Lip Cancer.

The intake of alcohol - leads to the penetration of DNA-damaging substances in the cells of the lip and mouth. When alcohol is paired by smoking, there is higher risk for the development of lip cancer.

Exposure to the harmful ultraviolet radiation from the sun - in prolonged periods can cause skin cancers, including lip cancer.

Warts caused by HPV - can contribute to the development of lip cancer. HPV commonly affects the vagina, penis and cervix. The practice of certain sexual practices contributes to the spread of the virus in the lips and oral cavity.

Chronic irritations on the lip - caused by poor fitting dentures and other dental appliances may cause changes on the cells on the mouth and lips.

Lack of fresh vegetables and fruits in the diet - these foods have antioxidant properties and it is thought that a lack of these in the diet may predispose someone to have lip cancer.

Males - have higher percentage of smokers and alcoholic drinkers, which predisposes the male population to oral cancers.

Immunosuppression - mmunosuppressed populations in particular must remain extremely vigilant about lip cancer. Kidney transplant patients have a 30-fold increased risk due to use of immunosuppressive anti-rejection drugs. People receiving higher doses of immunosuppressants tend to develop more non-melanoma skin cancers (NMSCs) than those on lower doses, and patients with HIV also demonstrate higher skin cancer risk. Immunocompromised patients, especially those with chronic sun exposure (which further suppresses the immune system), must be monitored closely.

Adults - who have reached the age of 40 have higher risk because of more exposure to carcinogens and ultraviolet rays.
(Cancerwall.com; Skin Cancer Foundation).

Lowering the Risk of Cancer of the Lips
Regular use of photoprotective lip blocks (lip products that contain sunscreen) reduce the risk of lip cancer. However, many people remain unaware how important consistent lip protection is. In a study of 299 beachgoers, 94 percent demonstrated a high awareness of the risks of UV damage to the skin in general, but only 69 percent demonstrated a high awareness of risk factors specifically for lip cancer. Seventy percent of beachgoers used no lip protection whatsoever, and even among those who otherwise properly applied sunscreen, only 37% used any lip protection.

Furthermore, while photoprotective lip blocks can be effective in reducing UV exposure, most people do not apply them properly. From a practical standpoint, the actual Sun Protection Factors (SPFs, which measure protection against the sun's UVB rays) provided by lip blocks are almost always lower than the number on the package because the blocks are not applied thickly or frequently enough. Additionally, many commercially available photoprotective lip blocks may be poorly absorbed and can be broken down quickly by UV light, losing their effectiveness — two compelling reasons for frequent reapplication.

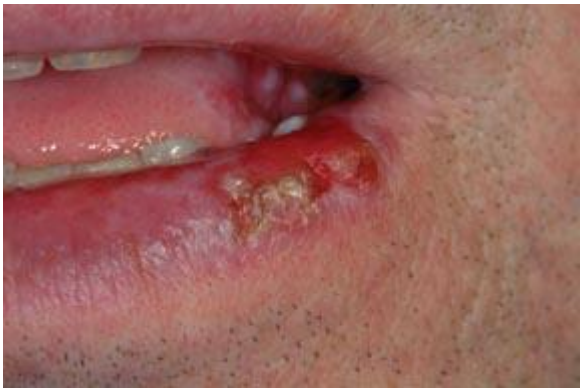
Despite being exposed to large amounts of UV light, the lips are often overlooked as a potential site for skin cancers. It is critical to exercise careful sun protection through a combination of sun avoidance and shade-seeking; frequent application of a high-SPF lip block; and careful monitoring of skin changes. Any changes to the lip that concern you should be brought to the attention of your physician immediately.
(Skin Cancer Foundation).

Signs and Symptoms of Cancer of the Lips
The lips are a not uncommon, but often overlooked site for non-melanoma skin cancers (NMSC), including the two most common skin cancers, basal and squamous cell carcinoma (BCC and SCC). Most frequently occurring in fair-skinned males over the age of 50, cancer of the lip comprises approximately 0.6 percent of all cancers in the US. Studies have shown that males are 3-13 times more likely to develop lip cancers, likely due to occupation-related sun exposure combined with greater tobacco and alcohol use.

The lower lip is approximately 12 times more likely to be affected, owing to its greater exposure to sunlight. A recent 25-year retrospective study of 2,152 patients with lip cancer revealed that 81 percent occurred on the lower lip, with males predominating by 3 to 1. Large epidemiological studies have shown that up to 95 percent of NMSCs on the lower lip are SCCs.

Given their highly visible location, the majority of lip cancers are easily detectable and treatable at an early stage. The most commonly employed treatments include surgery, radiation, and cryotherapy (freezing with liquid nitrogen), with cure rates for early lesions nearing 100 percent. Although cancers of the lip have relatively low rates of spread to nearby lymph nodes and distant sites, the relapse rate after treatment can range from 5-35 percent, and the mortality associated with large or recurrent SCC of the lip is as high as 15

percent in some studies. Once these cancers spread to local lymph nodes, five-year survival rates decrease to approximately 50 percent (Skin Cancer Foundation).



[Picture Credit: Lip Cancer]

Lip cancer symptoms are very similar to those of other types of oral cancer. It can often be mistaken for a cold that won't go away, or a persistent toothache. Other symptoms and signs include:

- a sore in the mouth or on the lips that does not heal
- persistent pain around the lips
- a lump or thickening in the cheek or near the lips
- a white or red patch on or near the lips

(Cancer Treatment Centers of America).

Diagnosis of Cancer of the Lips

Tests and procedures used to diagnose mouth cancer include:

- physical exam - the doctor or dentist will examine the lips and mouth to look for abnormalities - areas of irritation, such as sores and white patches (leukoplakia)

- biopsy - removal of tissue for testing. If a suspicious area is found, the doctor or dentist may remove a sample of cells for laboratory testing in a procedure called a biopsy. Unusual cells can be scraped away with a brush or cut away using a scalpel. In the laboratory, the cells are analysed for cancer or precancerous changes that indicate a risk of cancer

(Mayo Clinic).

Staging of Cancer of the Lips

Cancer staging is the process used to determine how much a cancer has spread.

Oral cancer stages are based on the results of physical exams, endoscopies, biopsies, and any imaging tests (CT scan, MRI, chest X-ray, and/or PET scans).

The American Joint Committee on Cancer (AJCC) developed the TNM cancer staging system to evaluate three primary factors when it comes to treating cancer: T, N and M:

T refers to the size of the primary tumour and to which, if any, tissues in the oral cavity and oropharynx the cancer has spread.

N described the involvement of lymph nodes near the primary tumour. Lymph nodes are small, bean-shaped clusters of immune system cells that are key to fighting infections and are usually one of the first sites in the body to which cancer spreads.

M indicates whether the cancer has spread (metastasised) to other areas of the body. With oral cancer, the most common site of metastases is the lungs, followed by the liver and bones.

The doctor will assign T, N and M values to the disease based upon its microscopic appearance. The care team will thoroughly review the medical history, family history and other factors to develop an individualised treatment plan for each patient.

T Categories

These measurements refer to the primary cancer tumour

TX primary tumour cannot be assessed – information not known

T0 no evidence of primary tumour

Tis carcinoma in situ – this means that the disease is still localised or contained within the top layers of cells lining the oral cavity and oropharynx. Cancer cells have not invaded the deeper layers of oral or oropharyngeal tissue.

T1 tumour is 2cm across or smaller

T2 tumour is larger than 2cm across but smaller than 4cm

T3 tumour is larger than 4cm across

T4 is divided into two subgroups:

T4a the tumour is growing into nearby structures. At this stage the oral cancer is called a moderately advanced local disease. The areas to which cells have spread vary according to the type of cancer – the tumour is growing into nearby bone, the inferior alveolar nerve (the nerve to the jawbone), the floor of the mouth or the skin of the chin or nose

T4b the tumour has grown through nearby structures and into deeper areas or tissues. At this stage, the cancer is called very advanced local disease and may include any of the following conditions:

The tumour is growing into other bones such as the pterygoid plates (in the skull) and/or the skull base – this type of spreading can occur with any oropharyngeal or oral cancer

The tumour is growing into an area called the masticator space (the area that contains the masticator muscles that attach to the ramus of the mandible. It is bounded by the superficial layer of deep cervical fascia)

N Categories

NX nearby lymph nodes cannot be assessed – information not known

N0 the oral cancer has not spread to any nearby lymph nodes

N1 the cancer has spread to one lymph node on the same side of the head or neck as the primary tumour – this lymph node is smaller than 3cm across

N2 is divided into three subgroups:

N2a the oral cancer has spread to one lymph node on the same side as the primary tumour and the lymph node measures 3-6cm across

N2b the cancer has spread to 2 or more lymph nodes on the same side as the primary tumour – no lymph nodes are larger than 6cm across

N2c the oral cancer has spread to one or more lymph nodes on both sides of the neck or on the side opposite the primary tumour – no lymph nodes are larger than 6cm across

N3 the cancer has spread to a lymph node that measures more than 6cm across

M Categories

M0 no distal spread

M1 the oral cancer has spread to distant sites outside the head and neck region (for example to the lungs, liver or bones).

Cancer Stage Groupings

Oral cancer is classified as stage 0, 1, 2, 3 or 4 according to the TNM measurements. Your doctor will assign a stage to the disease based upon this information, and will work with you to create a treatment plan.

Characteristics of each of the cancer stages include:

Stage 0:

Tis, N0, M0 Carcinoma in situ. The cancer is only growing in the epithelium, the outermost layer of tissue in the oral cavity or oropharynx. No cancer cells are present in deeper layers of tissue, nearby structures, lymph nodes, or distant sites.

Stage I:

T1, N0, M0 The primary oral cancer tumour is 2 cm across or smaller, and no cancer cells are present in nearby structures, lymph nodes, or distant sites.

Stage II:

T2, N0, M0 The tumour measures 2–4 cm across, and no cancer cells are present in nearby structures, lymph nodes, or distant sites.

Stage III:

One of the following applies –

T3, N0, M0: the tumour is larger than 4 cm across, and no cancer cells are present in nearby structures, lymph nodes, or distant sites.

or

T1–3, N1, M0: the tumour is any size but has not grown into nearby structures or distant sites. However, cancer cells are present in one lymph node, which is located on the same side of the head or neck as the primary tumour and is smaller than 3 cm across.

Stage IVA: One of the following applies –

T4a, N0 or N1, M0:

the oral cancer tumour is any size and is growing into nearby structures. Cancer cells may not be present in the lymph nodes, or they may have spread to one lymph node, which is located on the same size of the head or neck as the primary tumour and is smaller than 3 cm across. Cancer has not spread to distant sites.

or

T1–4a, N2, M0: the tumour is any size and may or may not have invaded nearby structures, it has not spread to distant sites, and one of the following is true:

- cancer cells are present in one lymph node, located on the same side of the head or neck as the primary tumour and measuring 3–6 cm across (N2a)
- cancer cells are present in one lymph node on the opposite side of the head or neck and measuring less than 6 cm across (N2b)
- cancer cells are present in 2 or more lymph nodes, all smaller than 6 cm across and located on either side of the head or neck (N2c)

Stage IVB: One of the following applies –
T4b, any N, M0: the tumour has invaded deeper areas and/or tissues. It may or may not have spread to lymph nodes and has not spread to distant sites

or

Any T, N3, M0: the tumour is any size and may or may not have grown into other structures. It has spread to one or more lymph nodes larger than 6 cm across, but has not spread to distant sites

Stage IVC: Any T, Any N, M1
The oral cancer tumour is any size and may or may not have spread to lymph nodes. Cancer cells have spread to distant sites, most commonly the lungs

Recurrent Oral Cancer
Recurrent or relapsed disease means that the cancer has returned after treatment. Recurrent disease does not have a TNM classification or a staging system number. When oral cancer recurs in the mouth or throat, it is called a local recurrence. When it recurs in the lymph nodes, it is called a regional relapse. When other parts of the body, such as the lungs, are involved, it is called a distant recurrence.
Although early-stage oral cancer may be easier to treat than more advanced disease, treatment options are available for all patients. Your doctor will explain the options that may work for you, so that your treatment can be as effective as possible.
(Cancer8; Cancer Treatment Centers of America),

Treatment of Cancer of the Lips
Lip cancer is classified as oral cancer, or a cancer of the oral cavity, which also encompasses cancer of the throat, tongue, tonsils and salivary glands. It is estimated that there will be 29,000 new cases of oral cancer diagnosed this year, with approximately 10 to 15 percent of the cases being cancers found specifically on the lip. Risk factors for developing lip cancer include heavy tobacco and alcohol use, exposure to the sun and HPV infections.

Surgery
Surgery to remove the tumor is a common treatment for lip cancer. Depending on the size of the cancer on the lip, part of the tongue, jaw and palate also may be removed. This can affect the way many talk, swallow or chew, so reconstructive surgery is usually takes place to help rebuild these sections of the mouth that were removed.

Radiation Therapy
An option for very small tumours on the lip or people who cannot tolerate surgery, radiation therapy can be given internally or externally. It also is used prior to surgery to reduce the size of the tumour as well as after surgery to destroy any remaining cancer cells in the area.

Chemotherapy
Typically given at the same time as radiation therapy to treat lip cancer, the use of chemotherapy can result in infection and pain in the mouth and gum area. Commonly used chemotherapeutic drugs include 5-fluorouracil, bleomycin, carboplatin, cisplatin, docetaxel, ifosfamide, methotrexate and paclitaxel.

Targeted Therapy
A targeted anticancer therapy called Erbitux also can be used to treat lip cancer. It is usually is given in combination with radiation or chemotherapy. Designed to bind to a substance called epidermal growth factor receptor (EGFR) that is found on the surface of lip cancer cells, targeted therapies can cause less harsh side effects as compared to chemotherapy. (Cancer Treatment.net).

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).

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

Sources and References

Cancer Treatment Centres of America
http://www.cancercenter.com/oral-cancer/lip-cancer.cfm
http://www.cancercenter.com/oral-cancer/oral-cancer-staging.cfm

CancerTreatment.net
http://lip.cancertreatment.net/

Cancer8
http://www.cancer8.com/lip-cancer/stages.html

Cigarette Smoke
http://cancerwall.com/lip-cancer-photos-symptoms-pictures-signs-treatment/

Lips
http://www.bing.com/images/search?q=images+lips&view=detail&id=048A8457C382797BB2E23B589CB820E5ED10A005&first=179&FORM=IDFRIR

Lips 2
http://www.bing.com/images/search?q=images+lips+dark+skin&view=detail&id=6DAD24EFD02E3C15355AABCBCDC237B97F53BF7D&first=144&FORM=IDFRIR

Lip Cancer
http://www.bing.com/images/search?q=staging+lip+cancer&view=detail&id=489F278FE0485480967A92F746E8E7A5B572254B&first=75&FORM=IDFRIR

Mayo Clinic
http://www.mayoclinic.com/health/mouth-cancer/DS01089/DSECTION=tests-and-diagnosis

National Cancer Institute
http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials

Skin Cancer Foundation
http://www.skincancer.org/skin-cancer-information/lip-cancer-not-uncommon