

Cancer Association of South Africa (CANSA)

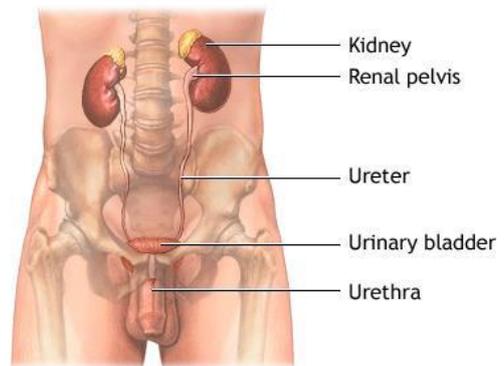


Fact Sheet on Bladder Cancer

Introduction

The urinary bladder is the organ that collects urine excreted by the kidneys before disposal by means of urination. It is a hollow muscular, and distensible (elastic) organ. The bladder is situated on the pelvic floor. Urine enters the bladder via the ureters and exits via the urethra.

[Picture Credit: Male Urinary Tract]

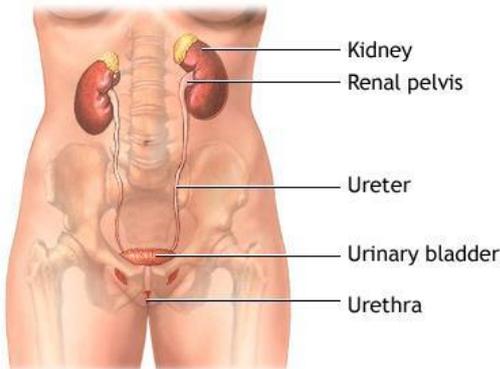


ADAM.

In males, the base of the bladder lies between the rectum and the pubic symphysis. It is superior (above) to the prostate, and separated from the rectum by the rectovesical excavation.

In females, the bladder is situated inferior (below) to the uterus (womb) and anterior (in front) to the vagina. Its maximum capacity is lower than in males. It is separated from the uterus by the vesico-uterine excavation. In infants and young children, the urinary bladder is in the abdomen even when empty.

[Picture Credit: Female Urinary Tract]



ADAM.

When the bladder is empty it is situated entirely within the pelvis. As it fills with urine its superior (upper) surface gradually rises into the abdominal cavity carrying with it its peritoneal covering. The bladder is lined by layers of muscle tissue that stretch to accommodate urine. The normal capacity of the bladder is 400 to 600 ml.

During urination, the bladder muscles contract, and two sphincters (valves) open to allow urine to flow out. Urine exits the bladder into the urethra, which carries urine out of the body. Because it passes through the penis, the urethra is longer in men (20cm) than in women (5cm) - (WebMD).

Bladder Cancer

Bladder cancer is cancer that forms in tissues of the bladder (the organ that stores urine). Most bladder cancers are transitional cell carcinomas (cancer that begins in cells that normally make up the inner lining of the bladder). Other types include squamous cell carcinoma (cancer that begins in thin, flat cells) and adenocarcinoma (cancer that begins in cells that make and release mucus and other fluids). The cells that form squamous cell carcinoma and adenocarcinoma develop in the inner lining of the bladder as a result of chronic irritation and inflammation (National Cancer Institute).

Incidence of Bladder Cancer in South Africa

According to the National Cancer Registry (2013) the following number of bladder 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	952	1:147	2,65%
Asian males	44	1:148	5,33%
Black males	135	1:653	1,25%
Coloured males	150	1:85	3,58%
White males	623	1:54	3,09%

Group - Females 2013	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	307	1:709	0,84%
Asian females	16	1:340	1,54%
Black females	98	1:1 651	0,63%
Coloured females	44	1:385	1,07%
White females	150	1:275	1,94%

The frequency of histologically diagnosed cases of bladder 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	2	5	11	51	178	274	290	136
Asian males	0	0	0	2	11	11	9	5
Black males	2	3	4	17	33	34	29	8
Coloured males	0	1	3	9	34	51	32	15
White males	0	1	2	23	94	167	213	104

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	1	4	14	20	59	78	91	37
Asian females	0	1	1	0	4	5	3	1
Black females	0	2	8	14	22	19	17	7
Coloured females	1	0	3	2	6	10	16	3
White females	0	1	2	2	22	37	52	25

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.

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Risk Factors for Bladder Cancer

The following are risk factors for bladder cancer:

Use of tobacco products - smoking cigarettes, cigars or pipe tobacco may increase the risk of bladder cancer by causing harmful chemicals to accumulate in the urine. When smoking, the body processes the chemicals in the smoke and excretes some of it in the urine. These harmful chemicals may damage the lining of the bladder, which can increase the risk for cancer

Obesity - Compared with normal-weight individuals (body mass index [BMI] 18.50–24.99 kg/m²), pre-obese and obese individuals (BMI 25.00–29.99 and 30 or greater, respectively) had a 7% and 10% increased risk of bladder cancer, respectively, the researchers reported in *PLOS One*.

Increasing age - the risk for bladder cancer increases with age. Bladder cancer can occur at any age, but it is rarely found in people younger than 40.

Being white - whites have a greater risk for bladder cancer than do people of other races.

Being a male - men are more likely to develop bladder cancer than women.

Exposure to certain chemicals - the kidneys play a key role in filtering harmful chemicals from the bloodstream and moving them to the bladder. Because of this, it is thought that being around certain chemicals may increase the risk for bladder cancer. Chemicals linked to bladder cancer risk include arsenic and chemicals used in the manufacture of dyes, rubber, leather, textiles and paint products. Industries carrying the highest risks include the makers of rubber, leather, textiles, and paint products as well as printing companies. Other workers with an increased risk for developing bladder cancer include painters, machinists, printers, hairdressers (likely because of heavy exposure to hair dyes) and truck drivers (likely because of exposure to diesel fumes).

Previous cancer treatment - treatment with the anti-cancer drug cyclophosphamide (Cytoxan) increases the risk for bladder cancer. People who received radiation treatments aimed at the pelvis for a previous cancer may also have an elevated risk for developing bladder cancer.

Chronic bladder inflammation - chronic or repeated urinary infections or inflammations (cystitis), such as what happens with long-term use of a urinary catheter, may increase the risk for a squamous cell bladder cancer. In some areas of the world including South Africa, squamous cell carcinoma is linked to chronic



bladder inflammation caused by the parasitic infection known as schistosomiasis.

[Picture Credit: Schistosoma haematobium]

Schistosomiasis (Bilharzia) is a parasitic infection that occurs throughout Africa and the Middle East. One form of the parasite, *schistosoma haematobium* is linked to bladder cancer and it was estimated to have caused around 10 600 cases of the disease worldwide in 2002.

Personal or family history of cancer – a history of previously having had bladder cancer, makes one more likely to get it again. If one or more immediate relatives have a history of bladder cancer, there is also an increased risk for the disease, although it is rare for bladder cancer to run in families. A family history of hereditary non-polyposis colorectal cancer, also called Lynch syndrome can increase the risk for cancer of the urinary system, as well as the colon, uterus, ovaries and other organs.

Bladder birth defects - before birth, there is a connection between the belly button and the bladder. This connection, called the *urachus*, normally goes away before birth. If part of this connection remains after birth, it could become cancerous. Cancers that start in the *urachus* are usually *adenocarcinomas*, which are made up of malignant gland cells. About one third of the adenocarcinomas of the bladder start here. However, this is still rare, accounting for less than a half of 1% of all bladder cancers.

Another rare birth defect called *exstrophy* greatly increases a person's risk for developing bladder cancer. In bladder exstrophy, both the bladder and the abdominal wall in front of the bladder fail to close completely during development and are fused together. This leaves the inner lining of the bladder exposed outside the body. Surgery soon after birth can close the bladder and abdominal wall (and repair other related defects), but patients who have this are still at increased risk for urinary infections and bladder cancer.

Inherited gene mutations - a small number of people inherit a gene syndrome that increases their risk for bladder cancer. For example:

- A mutation of the retinoblastoma (*RB1*) gene can cause cancer of the eye in infants, and also increases the risk of bladder cancer
- Cowden disease, caused by mutations in a gene called *PTEN*, is linked mainly to cancers of the breast and thyroid. People with this disease also have a higher risk of bladder cancer
- Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC) is mainly linked to colon and endometrial cancer. People with this syndrome also have an increased risk of bladder cancer, as well as cancer of the ureters.

Researchers have studied the effects of mutations in several genes, including *FGFR3*, *RB1*, *HRAS*, *TP53*, and *TSC1*, on the formation and growth of bladder tumours. Each of these genes plays a critical role in regulating cell division by preventing cells from dividing too rapidly or in an uncontrolled way. Alterations in these genes may help explain why some bladder cancers grow and spread more rapidly than others.

Deletions of part or all of chromosome 9 are common events in bladder tumours. Researchers believe that several genes that control cell growth and division are probably located on chromosome 9. They are working to determine whether a loss of these genes plays a role in the development and progression of bladder cancer.

Most of the genetic changes associated with bladder cancer develop in bladder tissue during a person's lifetime, rather than being inherited from a parent. Some people, however, appear to inherit a reduced ability to break down certain chemicals, which makes them more sensitive to the cancer-causing effects of tobacco smoke and industrial chemicals.

Low fluid consumption - not drinking enough fluids may increase the risk for bladder cancer. People who drink a lot of fluids each day have a lower rate of bladder cancer. This is thought to be because they empty their bladders often. By doing this, they keep chemicals from lingering in the urinary bladder.

Hormonal factors - two cohort studies show a 60% increase in the risk for bladder cancer in women undergoing menopause before the age of 42-45 compared to 48 or later. Women who have had a bilateral oophorectomy also have a 60% increased risk for bladder cancer

Foods and drinks - two Chinese cohort studies have reported a significant increase in risk with higher consumption of soya foods. This association is not clearly understood: one theory is that the chemical reaction of chlorine in water with humic substances in beans during fermentation may act as a bladder carcinogen. (Mayo Clinic; American Cancer Society; Cancer Research UK; Cancer.Net; Genetics Reference; Cancer Treatment Centers of America; Renal & Urology News).

Signs and Symptoms of Bladder Cancer

People with bladder cancer may experience the following symptoms or signs. Sometimes, people with bladder cancer do not show any of these symptoms. Or, these symptoms may be caused by a medical condition that is not cancer. Bladder cancer usually does not cause symptoms that specifically indicate cancer:

- blood in urine (haematuria) — urine may appear dark yellow, bright red or cola coloured.

or

urine may appear normal, but blood may be detected in a microscopic examination of the urine

- frequent urination
- bladder spasm
- painful urination (dysuria)
- urgent need to urinate
- inability to urinate
- reduced bladder capacity
- back pain

- pelvic pain

Symptoms of advanced bladder cancer may include:

- pain
- unexplained appetite loss
- weight loss

Sometimes when the first symptoms of bladder cancer appear, the cancer has already spread to another part of the body. The symptoms depend on where the cancer has spread to. For example, cancer that has spread to the lungs may cause a cough or shortness of breath, cancer that has spread to the liver may cause abdominal pain or jaundice (yellowing of the skin and whites of the eyes) and cancer that has spread to the bone may cause bone pain or a bone break.

(Mayo Clinic; Cancer.Net; Canadian Cancer Society).

Diagnosis of Bladder Cancer

Bladder cancers are usually found when a person goes to the doctor because of signs or symptoms they are having. If bladder cancer is suspected, tests will be needed to confirm the diagnosis.

- blood in the urine
- changes in bladder habits or irritating symptoms such as:
 - frequency: having to urinate more often than usual
 - dysuria: feeling pain or burning during urination
 - urgency: feeling as if you need to go right away, even when the bladder is not full
- medical history and physical exam
- cystoscopy - If bladder cancer is suspected the doctor will recommend a cystoscopy. For this exam, a urologist places a cystoscope – a slender tube with a light and a lens or a small video camera on the end – through the opening of the urethra and advances it into the bladder. Sterile salt water is then injected through the scope to expand the bladder and allow the doctor to look at the bladder lining.
- laboratory tests
 - urine cytology - for this test, a sample of urine is looked at under a microscope to see if it contains any cancer or pre-cancer cells. Cytology is also done on any bladder washings taken when the cystoscopy was done. Cytology can help find some cancers, but this test is not perfect. Not finding cancer on this test does not always mean that the patient is cancer free.
 - urine culture
 - urine tumour marker test – a number of different urine tests look for specific substances released by bladder cancer cells.

- biopsy - a biopsy is the removal of a sample of tissue to see if it is cancer. The tissue that is removed is sent to the laboratory where it is looked at by a pathologist, a doctor who specialises in diagnosing diseases by examining tissues with a microscope. If bladder cancer is suspected a biopsy is needed to confirm the diagnosis.
 - bladder biopsies - Bladder biopsy samples are most often obtained during cystoscopy. A biopsy can show whether cancer is present and what type of bladder cancer it is. If bladder cancer is found, two important features are its invasiveness and grade.
 - biopsies to look for cancer spread - if imaging tests suggest the cancer may have spread outside of the bladder, a biopsy is the only way to be sure. In some cases, biopsy samples of suspicious areas are obtained during the surgery to remove the bladder cancer.
 - another way to get a biopsy sample is to use a thin, hollow needle to take a small piece of tissue from the abnormal area. This is known as a needle biopsy, and it can allow the doctor to take samples without an operation. Needle biopsies are sometimes done using a CT scan or ultrasound to help guide the biopsy needle into the abnormal area.
- imaging tests - imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body
 - intravenous pyelogram - an intravenous pyelogram (IVP), also called an *intravenous urogram* (IVU) is an x-ray of the urinary system taken after injecting a special dye into a vein. This dye is removed from the bloodstream by the kidneys and then passes into the ureters and bladder. The dye outlines these organs on x-rays and helps find urinary tract tumours. Some people may have allergic reactions to the dye, so it's important to tell your doctor if you have any allergies or have ever had any reactions to x-ray dyes
 - retrograde pyelogram - for this test, a catheter (thin tube) is placed through the urethra and up into the bladder or into a ureter. Then a dye is injected through the catheter to make the lining of the bladder, ureters, and kidneys easier to see on x-rays
 - computed tomography (CT) scan - The CT scan is an x-ray test that produces detailed cross-sectional images of your body. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body
 - magnetic resonance imaging (MRI) scan - Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays
 - ultrasound - Ultrasound (ultrasonography) uses sound waves to create pictures of internal organs. It can be useful in determining the size of a bladder cancer and whether it has spread beyond the bladder to nearby organs or tissues. It can also be used to look at the kidneys.
 - chest x-ray - A chest x-ray may be done to look for spread of bladder cancer to the lungs. This test is not needed if a CT scan of the chest has been done.
 - bone scan - A bone scan can help look for cancer that has spread to bones. Doctors don't usually order this test unless you have symptoms such as bone pain, or if blood tests show the cancer might have spread to your bones. For this test, a small amount of low-level radioactive material is injected into a

vein (intravenously, or IV). The substance settles in areas of damaged bone throughout the entire skeleton over the course of a couple of hours. You then lie on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. The picture is not detailed like an MRI or CT scan, but it shows possible areas of cancer spread to all of the bones in the body at once. Areas of active bone changes appear as “hot spots” on the skeleton – that is, they attract the radioactivity. These areas may suggest the presence of cancer, but other bone diseases can also cause the same pattern. To distinguish among these conditions, other imaging tests such as plain x-rays, MRI scans, or even a bone biopsy might be needed. (American Cancer Society; Mayo Clinic; MacMillan Cancer Support; Memorial Sloan-Kettering Cancer Center).

Types of Bladder Cancer

- Transitional cell bladder cancer - sometimes called urothelial cancer. It is a cancer that develops from the cells of the bladder lining (urothelium). The cells are called transitional cells. When the bladder is empty, they are all bunched together. When the bladder is full, they are stretched out into a single layer. Because they line the bladder, these cells come into contact with waste products in the urine that may cause cancer, such as chemicals in cigarette smoke
- Non muscle invasive (superficial) bladder cancer - superficial bladder cancers are early stage transitional cell bladder cancer. The cancer is only in the lining of the bladder and hasn't grown into the deeper layers of the bladder wall. It usually appears as small growths, shaped like mushrooms, growing out of the bladder lining. This is called papillary bladder cancer. Your surgeon can remove these growths and they may never come back
- Invasive bladder cancer - Transitional cell bladder cancer can become invasive. This means it has grown into the muscle layer of the bladder, or beyond. Some people have invasive bladder cancer when they are first diagnosed. Invasive bladder cancer needs more intensive treatment than superficial bladder cancer. This is because there is a risk that it could spread to other parts of the body. Invasive bladder cancers are divided into T2, T3 or T4. This is part of the staging of bladder cancer. There is more about the stages of bladder cancer in the section about treating bladder cancer
- Squamous cell bladder cancer - Squamous cells are flat cells that make up the moist, skin like, tissues lining the body organs. Up to 8 out of every 100 (8%) bladder cancers in the UK are squamous cell cancers. They are more common in developing countries where a worm infection called bilharzia or schistosomiasis is widespread.
- Adenocarcinoma of the bladder - This is a very rare type of bladder cancer. Between 1 and 2 out of every 100 people diagnosed with bladder cancer have this type (1 to 2%). It is a cancer that develops from the cells in the lining of the bladder that produce mucus. All the moist, skin like, tissues lining the body have some gland cells that produce mucus.
- Rare types of bladder cancer - It is possible to get a cancer of the bladder muscle or other structural tissues, rather than the bladder lining. Cancers that start in the bladder lining are called sarcomas and are very rare. If you are looking for information about sarcoma of the bladder, you need to go to the section on soft tissue sarcoma
- Small cell cancer of the bladder - it is very rare
- Cancer that has spread to the bladder - Sometimes, a cancer that has started elsewhere in the body can spread to the bladder. For example:

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- prostate cancer
- cancer of the back passage (rectum)
- cancer of the ovary
- womb cancer (cancer of the uterus)
- cancer of the cervix

These cancers are called secondary cancer. This section is only about primary bladder cancer. Secondary cancer cells are the same type as the primary cancer. So the treatment will be the same as for the primary cancer. If you have a cancer that has spread to the bladder, you need to look at the section for your type of primary cancer to get the right information.

(Cancer Research UK; Weill Cornell Medical College; MD Anderson Cancer Center).

Reducing the Risk for Bladder Cancer

Bladder cancer cannot be prevented altogether, but one can reduce the risk for getting it.

- stop smoking - smokers are much more likely to get bladder cancer than non-smokers.
- avoiding exposure to industrial chemicals, such as benzene substances and arylamines. Occupational exposure from working with dyes, rubbers, textiles, paints, leathers, and chemicals raises one's risk for bladder cancer
- drinking water throughout the day - in theory, drinking liquids, especially water, may dilute toxic substances that may be concentrated in one's urine and flush them out of one's bladder more quickly. Studies have been inconclusive as to whether drinking water will decrease the risk of bladder cancer
- choose a variety of fruits and vegetables - choose a diet rich in a variety of colourful fruits (in season) and vegetables. The antioxidants in fruits and vegetables may help reduce one's risk of cancer. Take at least five portions of vegetables and fresh fruit (in season) each day
- limit the intake of smoked or cured meats
- limit the intake of other processed foods
- research suggests that people with adequate vitamin B₆, beta-carotene, and selenium in their diets have a reduced risk of developing bladder cancer.
- work safely around carcinogenic chemicals - follow safety guidelines to avoid exposure

(WebMD; Life is Beautiful; Mayo Clinic; MD Anderson Cancer Center).

Staging of Bladder Cancer

The following staging is used for bladder cancer:

Knowing the stage helps the doctor to decide what kind of treatment is best. It can also help predict a patient's prognosis (chance of recovery). There are different stage descriptions for different types of cancer.

For bladder cancer, the stage is determined based on the results of the sample removed during a TURBT and whether the cancer has spread to other parts of the body, which is determined by imaging tests, a physical examination, and laboratory tests. A TURBT is a

procedure in which bladder tumours can be removed from the bladder wall. This is a procedure performed completely with a scope that is inserted through the urethra into the bladder. It is generally performed in the hospital setting as an outpatient with the patient anaesthetised.

One tool doctors use to describe the stage is the **TNM** system. This system judges three factors: the tumour itself, the lymph nodes around the tumour, and if the tumour has spread to other parts of the body. The results are combined to determine the stage of cancer for each person. There are five stages of bladder cancer: stage 0 (zero) and stages I through IV (one through four). The stage provides a common way of describing the cancer, so doctors can work together to plan the best treatments.

TNM is an abbreviation for tumour (**T**), node (**N**), and metastasis (**M**). Doctors look at these three factors to determine the stage of cancer:

- How large is the primary tumour and how deeply has it invaded the tissue? (**Tumour, T**)
- Has the tumour spread to the lymph nodes? (**Node, N**)
- Has the cancer metastasized to other parts of the body? (**Metastasis, M**)

Tumour. Using the TNM system, the 'T' plus a letter and/or number (0 to 4) is used to describe the size and location of the tumour. Some stages are also divided into smaller groups that help describe the tumour in even more detail. If there is more than one tumour, the lowercase letter 'm' (multiple) is added to the 'T' stage category. Specific tumour stage information is listed below:

- TX:** the primary tumour cannot be evaluated
- T0:** there is no evidence of a primary tumour in the bladder
- Ta:** this refers to non-invasive papillary carcinoma. This kind of growth often is found on a small section of tissue that easily can be removed with TURBT and tends to be recurrent
- Tis:** this stage is carcinoma (cancer) in situ, or 'flat tumour'. This means that the cancer is only found in cells within the lining of the bladder. The doctor may also call it non-muscle-invasive/superficial bladder cancer or noninvasive flat carcinoma (the cancer is on or near the surface of the bladder). This type of bladder cancer often comes back after treatment, usually as another noninvasive cancer in the bladder
- T1:** the tumour has spread to the sub-epithelial connective tissue (the tissue below the inside lining of the bladder)
- T2:** the tumour has spread to the muscle of the bladder wall
- T2a:** the tumour has spread to the inner half of the muscle of the bladder wall (which may be called the superficial muscle.)
- T2b:** the tumour has spread to the deep muscle of the bladder (the outer half of the muscle)
- T3:** the tumour has grown into the *peri-vesical* tissue (the fatty tissue that surrounds the bladder)
- T3a:** the tumour has grown into the peri-vesical tissue, as seen through a microscope
- T3b:** the tumour has grown into the peri-vesical tissue macroscopically, meaning that the tumour(s) is large enough to be seen during imaging tests or to be seen or felt by the doctor

- T4:** the tumour has spread to any of the following: the abdominal wall, the pelvic wall, a man's prostate or seminal vesicle (the tube(s) that carry semen), or a woman's uterus or vagina
- T4a:** the tumour has spread to the prostate, uterus, or vagina
- T4b:** the tumour has spread to the pelvic wall or the abdominal wall

Node. The 'N' in the TNM staging system stands for lymph nodes, the tiny, bean-shaped organs that help fight infection. Lymph nodes near where the cancer started, within the true pelvis (called hypogastric, obturator, iliac, perivesical, pelvic, sacral, and presacral lymph nodes), are called regional lymph nodes. Lymph nodes in other parts of the body are called distant lymph nodes.

- NX:** the regional lymph nodes cannot be evaluated
- N0:** the cancer has not spread to the regional lymph nodes
- N1:** the cancer has spread to a single regional lymph node in the pelvis
- N2:** the cancer has spread to more than one regional lymph node in the pelvis
- N3:** the cancer has spread to the common iliac lymph nodes, which are located behind the major arteries in the pelvis, above the bladder

Distant metastasis. The 'M' in the TNM system indicates whether the cancer has spread to other parts of the body.

- M0:** the disease has not metastasized
- M1:** there is distant metastasis

Cancer stage grouping

Doctors assign the stage of the bladder cancer by combining the T, N, and M classifications.

Stage 0a:

This is an early cancer that is only found on the surface of the inner lining of the bladder. Cancer cells are grouped together and can often be easily removed. The cancer has not invaded the muscle or connective tissue of the bladder wall. This type of bladder cancer is also called non-invasive papillary urothelial carcinoma (Ta, N0, M0).

Stage 0is:

This stage of cancer, also known as flat or carcinoma in situ, is found only on the inner lining of the bladder. It has not grown in toward the hollow part of the bladder, and it has not spread to the thick layer of muscle or connective tissue of the bladder (Tis, N0, M0). This is always a high-grade cancer (see Grading, below).

Stage I:

The cancer has grown through the inner lining of the bladder to the lamina propria. It has not spread to the thick layer of muscle in the bladder wall or to lymph nodes or other organs (T1, N0, M0).

Stage II:

The cancer has spread into the thick muscle wall of the bladder (also called invasive cancer or muscle-invasive cancer). It has not reached the fatty tissue surrounding the bladder and has not spread to the lymph nodes or other organs (T2, N0, M0).

Stage III:

The cancer has spread throughout the muscle wall to the fatty layer of tissue surrounding the bladder. It may also have spread to the prostate in a man or the uterus and vagina in a woman. It has not spread to the lymph nodes or other organs (T3 or T4a, N0, M0).

Stage IV:

Any of these conditions:

- the tumour has spread to the pelvic wall or the abdominal wall but not to the lymph nodes or other parts of the body (T4b, N0, M0)
- the tumour has spread to one or more regional lymph nodes but not to other parts of the body (any T, N1-3, M0)
- the tumour may or may not have spread to the lymph nodes but has spread to other parts of the body (any T, any N, M1)

Recurrent Bladder Cancer: Recurrent cancer is cancer that comes back after treatment. If there is a recurrence, the cancer may need to be staged again (called re-staging) using the system above. Lymph nodes, bones, lung, liver, and peritoneum are the most common sites of metastasis from bladder cancer. Tumours in a more advanced T category and those with atypical histologic features metastasize earlier. Tumours with atypical histologic features also have a higher frequency of peritoneal metastasis (Shinagare, *et al*).

Grading

Tumour grade.

In addition to the TNM system, the cancer may also be evaluated and assigned a grade (G). Doctors use the term 'grade' to describe how much the tumour tissue looks like normal bladder tissue under a microscope. Many urologic surgeons classify grading based on the chance that the cancer will recur (come back after treatment) or progress (grow and spread), and plan their treatment based on the grade, using the following categories:

Papilloma.

This is also called benign papillary urothelial neoplasm of low malignant potential (PUNLMP). These types of cancer may recur but have a low risk of progressing.

Low grade.

These types of cancer are more likely to recur and progress compared with PUNLMP.

High grade.

These types of cancer are the most likely to recur and progress.

More recently, the World Health Organization (WHO) has recommended changing bladder cancer grading to only two categories:

- 1) well-differentiated or low grade, and
- 2) poorly differentiated or high grade.

This is the system that is used in the latest version of the American Joint Committee on Cancer (AJCC) Staging System.

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(Cancer.Net).

Prognosis (Outlook)

Medical professionals advise that early detection and prompt treatments are the key a positive bladder-cancer prognosis. The outlook for people with bladder cancer varies dramatically depending on the stage of the cancer at the time of diagnosis.

- Nearly 90% of people treated for superficial bladder cancer (Ta, T1, CIS) survive for at least five years after treatment
- Only about 5% of people with metastatic bladder cancer survive for at least two years after diagnosis
- Recurrent cancer indicates a more aggressive type and a poor outlook for long-term survival for patients with high-stage or high-grade bladder cancer. Recurrent low-grade superficial bladder cancer is rarely life threatening

(Actos Bladder Cancer Association; eMedicineHealth).

Where Bladder Cancer Spreads to

Should bladder cancer spread to other parts of the body, it would most probably spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Bone, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

(National Cancer Institute).

Treatment of Bladder Cancer

The following comprises standard treatment for bladder cancer:

Surgery - one of the following types of surgery may be done:

- Transurethral resection (TUR) with fulguration - surgery in which a cystoscope (a thin lighted tube) is inserted into the bladder through the urethra. A tool with a small wire loop on the end is then used to remove the cancer or to burn the tumour away with high-energy electricity. This is known as fulguration
- Radical cystectomy - surgery to remove the bladder and any lymph nodes and nearby organs that contain cancer. This surgery may be done when the bladder

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cancer invades the muscle wall, or when superficial cancer involves a large part of the bladder. In men, the nearby organs that are removed are the prostate and the seminal vesicles. In women, the uterus, the ovaries, and part of the vagina are removed. Sometimes, when the cancer has spread outside the bladder and cannot be completely removed, surgery to remove only the bladder may be done to reduce urinary symptoms caused by the cancer. When the bladder must be removed, the surgeon creates another way for urine to leave the body

- Segmental cystectomy - surgery to remove part of the bladder. This surgery may be done for patients who have a low-grade tumour that has invaded the wall of the bladder but is limited to one area of the bladder. Because only a part of the bladder is removed, patients are able to urinate normally after recovering from this surgery
- Urinary diversion - surgery to make a new way for the body to store and pass urine.

Radiation therapy - radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep 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 cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy). Bladder cancer may be treated with intravesical (into the bladder through a tube inserted into the urethra) chemotherapy. The way the chemotherapy is given depends on the type and stage of the cancer being treated.

Perioperative Chemotherapy (Neoadjuvant or Adjuvant)

Regimen:	Dosing:
Dose-dense methotrexate +vinblastine + doxorubicin + cisplatin (DDMVAC) with growth factor support	Day 1: Methotrexate 30mg/m ² IV Day 2: Vinblastine 3mg/m ² IV, plus doxorubicin 30mg/m ² IV, plus cisplatin 70mg/m ² IV Day 4: Granulocyte colony-stimulating factor (G-CSF) 240µg/m ² SQ for 7 consecutive days (day 4 through 10). May be extended for up to a total of 14 consecutive days. Repeat every 2 weeks for 3-4 cycles
Gemcitabine + cisplatin	Day 1, 8 and 15: Gemcitabine 1 000mg/m ² IV over 30-60 minutes Day 2: Cisplatin 70mg/m ² Repeat every 2 weeks for 3-4 cycles
Cisplatin + methotrexate + vinblastine (CMV)	Day 1: Methotrexate 30mg/m ² IV bolus plus vinblastine 4mg/m ² IV bolus Day 2: Cisplatin 100mg/m ² IV infusion; followed by hydration; followed by leucovorin 15mg PO of IV every 6 hours for 4 doses (commencing 24 hours after methotrexate on day 1) Day 8: Methotrexate 30mg/m ² IV bolus plus vinblastine 4mg/m ² IV bolus

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	Day 9: Leucovorin 15mg PO every 6 hours for 4 doses after methotrexate on day 8 Repeat every 3 weeks for 3 cycles
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(Cancer Therapy Advisor)

First-Line Chemotherapy for Metastatic Disease

Regimen:	Dosing:
Gemcitabine + cisplatin (Category 1)	Days 1, 8 and 15: Gemcitabine 1,000mg/m ² IV over 30–60 minutes Day 2: Cisplatin 70mg/m ² . Repeat every 4 weeks for a maximum of 6 cycles.
DDMVAC with growth factor support (Category 1)	Day 1: Methotrexate 30mg/m ² IV Day 2: Vinblastine 3mg/m ² IV, plus doxorubicin 30mg/m ² IV, plus cisplatin 70mg/m ² IV Day 4: G-CSF 240µg/m ² SQ for 7 consecutive days (days 4 through 10). May be extended for up to a total of 14 consecutive days. Repeat every 2 weeks for 3–4 cycles. OR Day 1: Methotrexate 30mg/m ² IV Day 2: Vinblastine 3mg/m ² IV, plus doxorubicin 30mg/m ² IV, plus cisplatin 70mg/m ² IV Day 3: G-CSF SQ for 5 consecutive days (days 3 through 7). Repeat cycle every 15 days.

(Cancer Therapy Advisor)

Second-Line (Palliative) Chemotherapy for Metastatic Disease

Preferred Treatment: Single-agent taxane or gemcitabine
Additional Single-Agent Treatment Options: Cisplatin Carboplatin Doxorubicin 5-fluorouracil (5-FU) Ifosfamide Pemetrexed Methotrexate Vinblastine

(Cancer Therapy Advisor)

First-Line Radiosensitising Chemotherapy Regimens

Regimen:	Dosing:
Cisplatin	Cisplatin 100mg/m ² IV every 2 weeks for 3 cycles
Cisplatin _ 5-FU	Days 1, 2, 3, 15, 16, and 17: IV hydration at a rate of 500mL/hour; followed by 5-FU 400mg/m ² IV push; followed by cisplatin 15mg/m ² IV over 1 hour as induction and consolidation therapy
5-FU + mitomycin C	Day 1 of radiotherapy: Mitomycin 12mg/m ² IV bolus, plus Week 1 (fractions 1–5) and Week 4 (fractions 16–20) of radiotherapy: 5-FU 500mg/m ² continuous IV infusion (10 days total)
Cisplatin + paclitaxel (Category 2B)	Days 1, 8 and 15: Paclitaxel 50mg/m ² Days 1–3, 8–10, 15–17: Cisplatin 15mg/m ² ; followed by twice-daily radiotherapy for 8 days
Low-dose gemcitabine (Category 2B)	Gemcitabine 75mg/m ² IV weekly given concurrently with radiotherapy

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Radiosensitising Chemotherapy with Conventionally Fractionated Radiation

- Cisplatin
- Docetaxel or paclitaxel (Category 2B)
- 5-FU (Category 2B)
- 5-FU and mitomycin C (Category 2B)
- Capecitabine (Category 3)
- Low-dose gemcitabine (Category 2B)

(Cancer Therapy Advisor)

Biologic therapy - biologic therapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defences against cancer. This type of cancer treatment is also called biotherapy or immunotherapy.

Chemoprevention - chemoprevention is the use of drugs, vitamins, or other substances to reduce the risk of developing cancer or to reduce the risk that cancer will recur (come back).

Photodynamic therapy - photodynamic therapy (PDT) is a cancer treatment that uses a drug and a certain type of laser light to kill cancer cells. A drug that is not active until it is exposed to light is injected into a vein. The drug collects more in cancer cells than in normal cells. Fibre-optic tubes are then used to carry the laser light to the cancer cells, where the drug becomes active and kills the cells. Photodynamic therapy causes little damage to healthy tissue.

Immunotherapy - bladder cancer affects men more likely than women—with an estimated 77,000 new cases predicted to be diagnosed in 2016, and approximately 16,000 deaths expected. Because of the recurrent nature of bladder cancer, patients with bladder cancer must monitor their health closely for an extended period of time.

Immunotherapy has seen and continues to deliver promising results in the treatment of bladder cancer - the first diagnosis for which immunotherapy the Food and Drug Administration (FDA) granted approval in 1990. Since last year, two checkpoint inhibitors - atezolizumab and nivolumab - were also approved for bladder cancer, and there are numerous additional immune-based treatments for bladder cancer currently in development, with immunotherapy clinical trials for bladder cancer patients on the rise.

Bladder cancer immunotherapy has significantly reduced the risk of recurrence for bladder cancer, while also increasing the percentage of patients who see a complete response post-surgery. Investigational bladder cancer immunotherapies - those that "train" the body's immune system to recognize bladder cancer cells - have the potential to further improve the general outcomes for patients with this disease.

Thanks to groundbreaking advancements in immunology research and clinical trials, immunotherapy has become one of the most promising bladder cancer treatments of our time.

Currently, the overall 5-year survival rate for bladder cancer is 77% - a rate which has not changed significantly over the last 10 years. Additionally, no new drugs for bladder cancer were approved by the FDA during this time.

New and developing bladder cancer immunotherapies have the potential to reduce recurrence rates and improve survival rates for patients with bladder cancer. Join us as we work to change the future of bladder cancer treatment - forever.

(National Cancer Institute; Mayo Clinic; Cancer Council Victoria; Cancer Research Institute).

Changing of Lifestyle Following Bladder Cancer Diagnosis

Stop smoking - Smoking is a known risk factor for many cancers. It is never too late to stop smoking. Join CANSA's e-KickButt Programme or ask a doctor about programmes to help stop smoking.

Follow a nutritious diet - Eating a healthful diet may help avoid other medical conditions linked to poor nutrition. Because cancer itself and some cancer treatment may have a dulling effect on one's appetite, it's important that one makes the most of the calories taken in. Strongly consider consulting a registered dietitian (RD) to help learn more about the best kinds of foods to eat and how to eat other less healthful foods in moderation. Eat five portions of vegetables and fresh fruit (in season) every day.

Rest when tired - The treatments for cancer can add to the fatigue patients may experience. Fatigue is the most frequently experienced symptom of cancer and cancer treatments. The fatigue can range from 'just feeling tired' to complete and utter exhaustion. It is important to allow the body time to rest. This will help the body have the strength to heal itself. Studies have shown a relationship between fatigue and an increased morbidity of cancer and cancer treatments as a result of fatigue's adverse effect on appetite, diminished quality of life, and loss of hope.

Seek support - The diagnosis of cancer is a life-defining event that is difficult to handle for anyone. Facing the uncertainty of a serious disease, feeling anxious about how one will feel during treatment, and worrying about the impact of both the diagnosis and treatment can take a devastating toll that no one should have to tackle on their own. Try to have access to the following:

- family
- friends
- religious community
- empathetic support groups for people with your type of cancer
- professional support (social workers, psychologists, and/or psychiatrists who are trained to help support cancer patients and their families)

People who allow themselves to seek help while they are recovering from cancer can often maintain better emotional equilibrium, which will help them face the challenges of cancer and its treatment (Winchester Hospital; Life is Beautiful).

About Clinical Trials

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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.

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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.

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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

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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.

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- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

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

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

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

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

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

When a clinical trial is over

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

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

Medical Disclaimer

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

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MD Anderson Cancer Center

<http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/bladder-cancer/index.html>

<http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/bladder-cancer/prevention/index.html>

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National Cancer Institute

<http://www.cancer.gov/cancertopics/types/bladder>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page12>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page11>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page10>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page9>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page8>
<http://www.cancer.gov/cancertopics/pdq/treatment/bladder/HealthProfessional/page7>
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http://www.renalandurologynews.com/bladder-cancer-obesity-link-confirmed/article/405908/?DCMP=EMC-RENALUROLOGY_TODAYSUPDATE&cpn=&hmSubId=&hmEmail=OdsiBxRYPdkldpZ00Ap-a5dX4uYlpfYu0&spMailingID=11028228&spUserID=MzMyODk3NTcxNTcS1&spJobID=520047546&spReportId=NTlwMDQ3NTQ2S0

Schistosoma haematobium

https://www.google.co.za/search?q=schistosoma+haematobium&source=lnms&tbm=isch&sa=X&ei=kVCLUr-LMo2shQfcylCAAg&sqi=2&ved=0CAcQ_AUoAQ&biw=1366&bih=642#facrc=_&imgdii=_&imgrc=0tbwqQZ9obCEsM%3A%3B10m6DmY1pcavtM%3Bhttp%253A%252F%252Fwikom.pl%252Fparafree%252Fpictures%252Fs.haematobium_str13.jpg%3Bhttp%253A%252F%252Fwww.wikom.pl%252Fparafree%252Fstrona13.htm%3B400%3B298

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TNM Classification Help

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<http://www.webmd.com/urinary-incontinence-oab/picture-of-the-bladder>
<http://www.webmd.com/cancer/bladder-cancer/bladder-cancer-prevention>
<http://www.webmd.com/cancer/bladder-cancer/understanding-bladder-cancer-prevention>
<http://www.webmd.com/cancer/bladder-cancer/tc/bladder-cancer-treatment-patient-information-nci-pdq-stages-of-bladder-cancer?page=2>

Weill Cornell Medical College

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Winchester Hospital

<http://www.winchesterhospital.org/health-library/article?id=32653>