Cancer Association of South Africa (CANSA)

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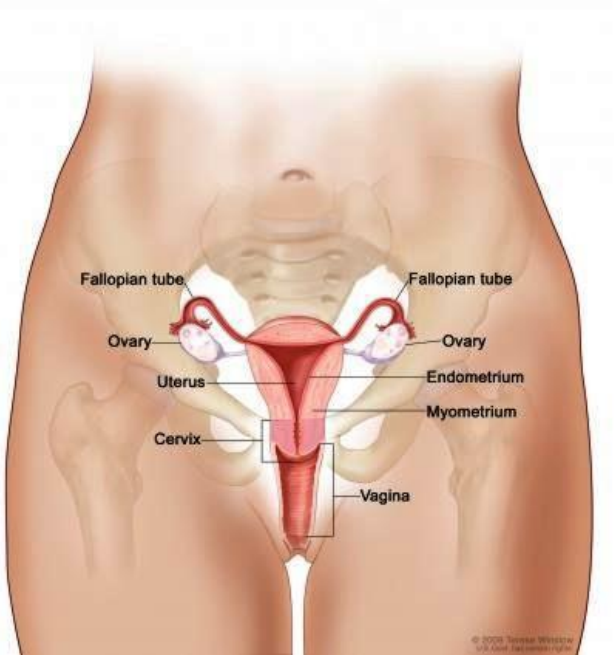
Fact Sheet
On
Ovarian Cancer

Introduction

The ovaries form part of the female reproductive organs that house the ova and are also responsible for the production of sex hormones. The ovaries are paired organs located on either side of the uterus within the broad ligament below the uterine (fallopian) tubes. Each ovary is within the ovarian fossa, a space that is bound by the external iliac vessels, obliterated umbilical artery, and the ureter. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. At birth, a female has approximately 1-2 million ova, but only about 300 of these eggs will ever become mature and be released for the purpose of fertilisation.



[Picture Credit – Ovarian Anatomy]

Ovarian Cancer

Ovarian cancer is cancer of the cells of one or both ovaries.

Incidence of Ovarian Cancer in South Africa

According to the National Cancer Registry (2012) the following number of ovarian cancer cases was histologically diagnosed in South Africa during 2012:

Group - Females 2012	No of Cases	Lifetime Risk	Percentage of All Cancer
All females	493	1:391	1,31%
Asian females	26	1:261	2,44%
Black females	202	1:702	1,22%
Coloured females	56	1:266	1,34%
White females	208	1:166	1,31%

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The frequency of histologically diagnosed cases of ovarian cancer in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Females 2012	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	8	14	29	54	116	133	98	35
Asian females	1	0	1	1	10	6	2	1
Black females	7	11	15	23	41	50	31	11
Coloured females	0	1	2	5	14	15	15	1
White females	0	0	8	19	47	59	46	18

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 Ovarian Cancer

It is not clear what causes ovarian cancer. In general, cancer begins when healthy cells acquire a genetic mutation that turns normal cells into abnormal cells. Healthy cells grow and multiply at a set rate, eventually dying at a set time. Cancer cells grow and multiply out of control, and they do not die. The accumulating abnormal cells form a mass (tumour). Cancer cells invade nearby tissues and can break off from an initial tumour to spread elsewhere in the body (metastasise).

Generally, it's not possible to say what causes ovarian cancer in an individual woman. However, some features are more common among women who have developed ovarian cancer. These features are called risk factors.

Having certain risk factors increases a woman's chance of developing ovarian cancer. Having one or more risk factors for ovarian cancer doesn't mean a woman will definitely develop ovarian cancer. In fact, many women with ovarian cancer have no obvious risk factors.
(Mayo Clinic).

Risk Factors for Ovarian Cancer

The risk for developing ovarian cancer appears to be affected by several factors:

- The more children a woman has and the earlier in life she gives birth, the lower her risk for ovarian cancer
- Certain genes defects (BRCA1 and BRCA2) are responsible for a small number of ovarian cancer cases. Women with a personal history of breast cancer or a family history of breast or ovarian cancer have an increased risk for ovarian cancer
- Women who take oestrogen replacement only (not with progesterone) for 5 years or more seem to have a higher risk of ovarian cancer
- Birth control pills decrease the risk of ovarian cancer.
- Being infertile or having fertility treatment
- Using a coil (intra-uterine device (IUD)

- Older women are at highest risk for developing ovarian cancer. Most deaths from ovarian cancer occur in women age 55 and older
- Research suggests that the risk of ovarian cancer is slightly higher for women who:

    - have medical conditions such as endometriosis
    - smoke tobacco products
    - are obese
    - are tall

(Cancer Research UK; Australian Government, Cancer Australia; PubMed Health)

Ovarian Cancer and Use of Talc

There have been several successful lawsuits in the United States of America against the manufacturer of a popular brand of baby powder which contains talc. Retrospective research was conducted by Cramer, et al. (2016). They concluded that multiple studies of ovarian cancer and genital talc use have led only to consensus about possible carcinogenicity. Risks for epithelial ovarian cancer from genital talc use vary by histologic subtype, menopausal status at diagnosis, hormone therapy use, weight, and smoking. These observations suggest that oestrogen and/or prolactin may play a role via macrophage activity and inflammatory response to talc.

Protective Factors for Ovarian Cancer

There's currently nothing that can be done to prevent ovarian cancer. However, there are some things that are thought to protect against ovarian cancer. These are called protective factors. Women with protective factors may still develop ovarian cancer.

You may be able to reduce your risk of developing ovarian cancer by making changes to your lifestyle, such as stopping smoking and eating a healthy, balanced diet.
(BUPA, UK).

Getting enough vitamin D may reduce your risk of developing a number of cancers, including ovarian cancer – although more research needs to be done to be certain (*ibid*).

Research has shown that the following are associated with a reduced risk of certain types of ovarian cancer:

- removal of the uterus (womb)
- removal of the ovaries
- having the fallopian tubes tied
- having the fallopian tubes removed
- having been pregnant
- using oral contraceptives

(Australian Government, Cancer Australia).

Prophylactic Oophorectomy

Prophylactic oophorectomy significantly reduces one's odds of developing breast cancer and ovarian cancer if one is at high risk. Weigh the pros and cons of this cancer-prevention option in collaboration with an oncology geneticist and a medical practitioner.

Women with BRCA1 or BRCA2 gene mutations have a significantly increased risk of developing breast cancer and ovarian cancer. Several options are available for reducing the risk of cancer in these women.

One option is preventive (prophylactic) bilateral oophorectomy - the surgical removal of the ovaries. Although removing one's ovaries is usually performed to reduce the risk of ovarian cancer, oophorectomy can also reduce the risk of breast cancer.

What is an oophorectomy?

In an oophorectomy, a surgeon removes both the ovaries — the almond-shaped organs on each side of the uterus. The ovaries contain eggs and secrete the hormones that control one's reproductive cycle.

Removing the ovaries greatly reduces the amount of the hormones oestrogen and progesterone circulating in the body. This surgery can halt or slow breast cancers that need these hormones to grow.

Women with BRCA gene mutations usually also have their fallopian tubes removed at the same time (salpingo-oophorectomy) since they have an increased risk of fallopian tube cancer as well.

Who can consider prophylactic oophorectomy?

Prophylactic oophorectomy is usually reserved for women with a significantly increased risk of breast cancer and ovarian cancer due to an inherited mutation in the BRCA1 or BRCA2 gene - two genes linked to breast cancer, ovarian cancer and other cancers. Women who have inherited mutations and have completed childbearing are the best candidates for this surgery.

Prophylactic oophorectomy may also be recommended if one has a strong family history of breast cancer and ovarian cancer but no known genetic alteration. It might also be recommended if one has a strong likelihood of carrying the gene mutation based on one's family history but choose not to proceed with genetic testing.

Women who are at risk, could consider this procedure as follows:

- Having a BRCA1 gene mutation: age 35 to 40
- Having a BRCA2 gene mutation: age 45 and older

How much can oophorectomy reduce the risk of cancer?

If one has a BRCA mutation, a prophylactic oophorectomy can reduce the:

- Breast cancer risk by up to 50 percent in premenopausal women. As an example, if a woman with a high risk of breast cancer had a 60 percent chance of being diagnosed with breast cancer at some point in her lifetime, bilateral oophorectomy could reduce her risk to 30 percent.

Put another way, for every 100 women just like her, 60 could be expected to be diagnosed with breast cancer without oophorectomy. And 30 would be expected to be diagnosed with breast cancer after oophorectomy.

- Ovarian cancer risk by 80 to 90 percent. As an example, if a woman with a high risk of ovarian cancer had a 30 percent chance of being diagnosed with ovarian cancer at some point in her lifetime, oophorectomy could reduce her risk to 6 percent, assuming an 80 percent risk reduction.

  Put another way, for every 100 women just like her, 30 could be expected to be diagnosed with ovarian cancer without oophorectomy. And six would be expected to be diagnosed with ovarian cancer after oophorectomy.

(Mayo Clinic; Medscape).

Types of Ovarian Cancer

The type of cell where the cancer begins determines the type of ovarian cancer you have. Ovarian cancer types include:

- Cancer that begins in the cells on the outside of the ovaries. Called epithelial tumours, these cancers begin in the thin layer of tissue that covers the outside of the ovaries. Most ovarian cancers are epithelial tumours

- Cancer that begins in the egg-producing cells. Called germ cell tumours, these ovarian cancers tend to occur in younger women

- Cancer that begins in the hormone-producing cells. These cancers, called stromal tumours, begin in the ovarian tissue that produces the hormones oestrogen, progesterone and testosterone
- The type of ovarian cancer you have helps determine your prognosis and treatment options

(Mayo Clinic).

Symptoms of Ovarian Cancer

Many ovarian cancer symptoms mimic those of less life-threatening conditions such as irritable bowel syndrome. These symptoms include:

- Bloating
- Pelvic or abdominal pain
- Urinary urgency or frequency
- Difficulty eating or feeling full quickly

(Ovarian Cancer National Alliance).

Further Late Stage Symptoms of Ovarian Cancer

- Spread of the cancer to other organs
- Loss of organ function
- Fluid in the abdomen (ascites)

- Blockage of the intestines

Early Detection of Ovarian Cancer
Early detection of ovarian cancer saves women's lives. No screening test exists that can test all women for ovarian cancer. The Pap test does not test for ovarian cancer; it screens for cervical cancer.

Not only do researchers need to develop an early detection test for ovarian cancer, like mammograms for breast cancer and Pap tests for cervical cancer, but also women and medical professionals need to become more aware of ovarian cancer symptoms.

While no early detection tool exists for all women, several tests exist for women who are at a high risk. If a woman has ovarian cancer symptoms, a strong family history, or a genetic predisposition such as a BRCA mutation, doctors may monitor her with one of the following tests or a combination of them:

The protein CA-125 Blood Test – The protein CA-125 exists in greater concentration in cancerous cells. Though a high count of this protein may help doctors identify ovarian cancer, premenopausal women may have an elevated CA-125 due to benign conditions unrelated to ovarian cancer. Uterine fibroids, liver disease, inflammation of the fallopian tubes and other types of cancer can raise a woman's CA-125 level, often causing a false positive test for ovarian cancer.

Although the CA-125 blood test is more accurate in postmenopausal women, it is not a reliable early detection test for ovarian cancer. In about 20 percent of advanced stage ovarian cancer cases and 50 percent of early stage cases, the CA-125 is not elevated even though ovarian cancer is present. As a result, doctors generally use the CA-125 blood test in combination with a trans-vaginal ultrasound.

The CA-125 blood test can be an important tool for evaluating the disease's progress and tumours' response to treatment. Additionally, this test can monitor a woman's CA-125 level for evidence of recurrence.

The CA125+HE4 Blood Test - has been approved by the Food and Drug Administration (FDA) for risk stratification. A woman who presents with a known tumour may have this test to determine if her surgery should be done by a gynaecologist or a gynaecologic oncologist – doctors who are specially trained to treat women with gynaecologic cancers. Ovarian cancer is not the silent killer it was once thought to be. Studies have shown that there are symptoms that appear in the early stages of the disease. Recognition of these symptoms in the early stages is critical.

A new biomarker, HE4, has shown an increased sensitivity and specificity for detection of ovarian cancer over that of CA125 alone. HE4 was also found to increase the sensitivity of CA125 for the detection of ovarian cancer in patients presenting with a pelvic mass.

The new CA125 + HE4 risk stratification tool is a new differential diagnostic for women presenting with pelvic mass to help determine the most appropriate course of care. It is designed to measure levels of the CA125 and HE4 proteins in the blood to aid in the risk

stratification of women who present with pelvic mass. It may help determine the best course of care for women presenting with a pelvic mass (HE4.com).

The OVA1 Blood Test - The FDA approved a new ovarian cancer blood test, called OVA1, that can help detect ovarian cancer in a pelvic mass that is already known to require surgery.

In a news release, the FDA says the test helps patients and health care professionals decide what type of surgery should be done and by whom - but not to screen for ovarian cancer and not for a definitive diagnosis of ovarian cancer.

"The OVA1 test identifies some women who will benefit from referral to a gynaecological oncologist for their surgery, despite negative results from other clinical and radiological tests for ovarian cancer. If other test results suggest cancer, referral to an oncologist is appropriate even with a negative OVA1 result," the FDA states.

The FDA says the OVA1 test should be used by primary care physicians or gynaecologists to complement, but not replace, other diagnostic and clinical procedures.

OVA1 uses a blood sample to test for levels of five proteins that change because of ovarian cancer. The test combines the five separate results into a single numerical score between 0 and 10 to indicate the likelihood that the pelvic mass is benign or malignant.

OVA1 is only intended for women aged 18 and older who are already selected for surgery because of their pelvic mass. Interpreting test results requires knowing whether the woman has gone through menopause (WebMD).

Trans-vaginal Ultrasound - A trans-vaginal ultrasound is a test used to examine a woman's reproductive organs and bladder. To administer the test, the doctor inserts a probe into the woman's vagina. The probe sends off sound waves which reflect off body structures. The waves are then received by a computer that turns them into a picture.
(Ovarian Cancer National Alliance)

Diagnosis of Ovarian Cancer
In someone showing the symptoms mentioned above, the doctor may order one or more of the following tests:

Ultrasound - Ultrasound (ultrasonography) is the use of sound waves to create an image on a video screen. Sound waves are released from a small probe placed in the woman's vagina or on the surface of her abdomen. The sound waves create echoes as they enter the ovaries and other organs. The same probe detects the echoes that bounce back, and a computer translates the pattern of echoes into a picture.

This is often the first test done to if a problem with the ovaries is suspected. Ultrasound can be useful to find an ovarian tumour and see if it is a solid mass (tumour) or a fluid-filled cyst. It can also be used to look better at the ovary to see how big it is and how it looks inside (the internal appearance or complexity). These factors help the doctor decide which masses or cysts are more worrisome.

Computed Tomography - The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional 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. The machine will take pictures of multiple slices of the part of your body that is being studied.

CT scans do not show small ovarian tumours well, but they can see larger tumours, and may be able to see if the tumour is growing into nearby structures. A CT scan may also find enlarged lymph nodes, signs of cancer spread to liver or other organs, or signs that an ovarian tumour is affecting your kidneys or bladder.

You may be asked to drink 1 to 2 litres of a liquid before the CT scan called "oral contrast." This helps outline the intestine so that certain areas are not mistaken for tumours. You may also receive an IV (intravenous) line through which a different kind of contrast dye is injected. This helps better outline structures in your body.

The injection can cause some flushing (redness and warm feeling that may last hours to days). A few people are allergic to the dye and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. Medicine can be given to prevent and treat allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for imaging tests.

CT scans are not usually used to biopsy (see biopsy in the section ‘Other tests’) an ovarian tumour, but they can be used to biopsy a suspected metastasis. For this procedure, called a *CT-guided needle biopsy*, the patient stays on the CT scanning table, while a radiologist moves a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about 1½cm long and less than 3mm in diameter) is removed and examined under a microscope.

CT scans take longer than regular x-rays and you need to lie still on a table while they are being done. But just like other computerized devices, they are getting faster and the most modern ones take only a short time.

Barium Enema X-ray - This is a test to see whether the cancer has invaded the colon (large intestine) or rectum (it is also used to look for colorectal cancer). After taking laxatives the day before, the radiology technician puts barium sulphate, a chalky substance, into the rectum and colon. Because barium is impermeable to x-rays (impossible for x-rays to go through), it outlines the colon and rectum on x-rays of the abdomen.

Magnetic Resonance Imaging - MRI scans use radio waves and strong magnets instead of X-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. Not only does this produce cross sectional slices of the body like a CT scanner, it can also produce slices that are parallel with the length of the body. A contrast material might be injected into a vein (same as with a CT scan). MRI scans are not used often to look for ovarian cancer.

MRI scans are particularly helpful to examine the brain and spinal cord. MRI scans take longer than CT scans, -- often up to 30 minutes or more. Also, you have to be placed inside a tube, which is confining and can upset people with claustrophobia (fear of enclosed

spaces). The machine also makes a thumping noise that you may find disturbing. Some places will provide headphones with music to block the sound.

Chest X-ray - This procedure may be done to determine whether ovarian cancer has spread (metastasized) to the lungs. This spread may cause one or more tumours in the lungs and more often causes fluid to collect around the lungs. This fluid, called a pleural effusion, can be seen with chest x-rays as well as other types of scans.

Positron Emission Tomography (PET scan) - In this test, radioactive glucose (sugar) is given to look for the cancer. Because cancers use glucose (sugar) at a higher rate than normal tissues, the radioactivity will tend to concentrate in the cancer. A scanner can spot the radioactive deposits. This test has can be helpful for spotting small collections of cancer cells. In some instances this test has proved useful in finding ovarian cancer that has spread. It is even more valuable when combined with a CT scan (PET/CT scan). PET scans can help find cancer when it has spread, but they are expensive and not all insurance companies will cover the cost when they are used to look for ovarian cancer.
(American Cancer Society).

Staging of Ovarian Cancer
Ovarian cancer is classified into the following categories (stages):

T-categories for ovarian cancer

Tx: No description of the tumour's extent is possible because of incomplete information

T1: The cancer is confined to the ovaries -- one or both

T1a: The cancer is only inside one ovary - it isn't on the outside of the ovary, it doesn't penetrate the tissue covering the ovary (called the capsule) and isn't in fluid taken from the pelvis

T1b: The cancer is inside both ovaries but doesn't penetrate to the outside and isn't in fluid taken from the pelvis (like T1a except the cancer is in both ovaries)

T1c: The cancer is in one or both ovaries and is either on the outside of an ovary, grown through the capsule of an ovary, or is in fluid taken from the pelvis

T2: The cancer is in one or both ovaries and is extending into pelvic tissues

T2a: The cancer has spread (metastasized) to the uterus and/or the fallopian tubes but isn't in fluid taken from the pelvis

T2b: The cancer has spread to pelvic tissues besides the uterus and fallopian tubes but it isn't in fluid taken from the pelvis

T2c: The cancer has spread to the uterus and/or fallopian tubes and/or other pelvic tissues (like T2a or T2b) and is also in fluid taken from the pelvis

T3: The cancer is in one or both ovaries and has spread to the abdominal lining outside the pelvis. This lining is called the *peritoneum*

T3a: The cancer metastases are so small that they cannot be seen except under a microscope

T3b: The cancer metastases can be seen but no tumour is bigger than 2 centimetres

T3c: The cancer metastases are larger than 2 centimetres)

T categories for fallopian tube cancer

Tx: No description of the tumour's extent is possible because of incomplete information

Tis: Cancer cells are only in the inner lining of the fallopian tube. They haven't grown into deeper layers. Also called carcinoma in situ

T1: The cancer is in the fallopian tube(s), but has not grown outside of them

T1a: The cancer is only inside one fallopian tube -- it has not grown through to the outside of the tube. It hasn't grown through the tissue covering the tumour (called the capsule) and isn't in fluid taken from the pelvis

T1b: The cancer is growing in both fallopian tubes -- it has not grown through to the outside of the tube. It has not grown through the tissue covering the tumour (called the capsule) and isn't in fluid taken from the pelvis (like T1a but with tumour in both tubes)

T1c: The tumour is in one or both fallopian tubes and has either grown through the outer wall of the tube or cancer cells are found in fluid taken from the pelvis

T2: The tumour has grown from one or both fallopian tubes into the pelvis

T2a: The cancer is growing into the uterus and/or the ovaries

T2b: The cancer is growing into other parts of the pelvis

T2c: The cancer has spread from the fallopian tubes into other parts of the pelvis and cancer cells are found in fluid taken from the pelvis (either from ascites or from washings obtained at surgery

T3: The tumour has spread outside the pelvis to the lining of the abdomen

T3a: The areas of cancer spread outside the pelvis can only be found when the area is biopsied and looked at under the microscope

T3b: The areas of spread can be seen with the naked eye, but are 2 cm or less in size (less than an inch)

T3c: The areas of spread are greater than 2 cm in size

N categories

N categories indicate whether or not the cancer has spread to regional (nearby) lymph nodes

Nx: No description of lymph node involvement is possible because of incomplete information

N0: No lymph node involvement

N1: Cancer cells are found in the lymph nodes close to tumour

M categories

M categories indicate whether or not the cancer has spread to distant organs, such as the liver, lungs, or non-regional lymph nodes

M0: No distant spread

M1: Cancer has spread to the inside of the liver, to the lungs, or other organs

Stage Grouping

Once a patient's T, N, and M categories have been determined, this information is combined in a process called stage grouping to determine the stage, expressed in Roman numerals from stage I (the least advanced stage) to stage IV (the most advanced stage). The following table illustrates how TNM categories are grouped together into stages. This stage grouping also applies to fallopian tube carcinoma.

Stage	T	N	M
I	T1	N0	M0
IA	T1a	N0	M0
IB	T1b	N0	M0
IC	T1c	N0	M0
II	T2	N0	M0
IIA	T2a	N0	M0
IIB	T2b	N0	M0
IIC	T2c	N0	M0
III	T3	N0	M0
IIIA	T3a	N0	M0
IIIB	T3b	N0	M0
IIIC	T3c	N0	M0
	Any T	N1	M0
IV	Any T	Any N	M1

(American Cancer Society)

Where Ovarian Cancer May Spread to in the Body

Should ovarian cancer spread (metastasise) in 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	Boner, 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 Ovarian Cancer
Treatment for ovarian cancer usually involves a combination of surgery and chemotherapy. Less often, treatment may include radiotherapy. The type of treatment women receive depends on the type and stage of their ovarian cancer and their general health. Treatment is best managed by a gynaecological oncologist. A gynaecological oncologist specialises in treating cancers of the reproductive tract and has very specialised surgical skills.
(Ovarian Cancer Australia).

Surgery
Nearly all women who have ovarian cancer will require surgery. Sometimes, it is not possible to confirm the stage of the cancer until the surgery.

The doctor will discuss what will happen during the surgery. The surgery will probably involve removing:

- both ovaries and the fallopian tubes (called a bilateral salpingo-oophorectomy)
- the uterus (called a total abdominal hysterectomy)
- the omentum, a fatty layer of tissue within the abdomen (called an omenectomy)

The surgeon may also remove the lymph nodes from the pelvis and abdomen. They may also take samples of nearby tissue and send it to the laboratory to see if the cancer has spread.

If the cancer has spread, the surgeon will try to remove as much of it as possible. This is known as debulking surgery.

If the cancer is confined to one or both ovaries, only the ovary or ovaries may need to be removed, leaving your uterus (womb) intact. This means the woman may still be able to carry a pregnancy. For most women, however, pregnancy is not an issue and the normal procedure is to remove both ovaries and the uterus.

The patient will probably be ready to go home three to seven days after the operation, but it can take many weeks to fully recover. After the operation the patient will be encouraged to start moving about as soon as possible. This is very important. Even if it means having to stay in bed, it is important to keep doing regular leg movements to help the circulation and prevent blood clots. A physiotherapist will provide exercises to help prevent complications.

When going home, the patient will need to exercise gently to build up strength and fitness. Walking and swimming are good exercises that are suitable for most people after treatment for ovarian cancer. A discussion with a doctor or physiotherapist should be had about which types of exercise would be suitable.

Chemotherapy
Chemotherapy involves using anti-cancer (cytotoxic) drugs to kill cancer cells. It is often given after surgery for ovarian cancer. In some cases, it can be given before surgery as it may help to shrink the tumour and make it easier to remove. This is called neo-adjuvant chemotherapy.

Several different drugs can be used in chemotherapy. Often, a combination is given. The choice of drug and how and when it is given depends on the stage of the cancer and how much it has spread. The most common treatment for ovarian cancer is a platinum-containing drug (carboplatin), which is used alone or in combination with another drug, paclitaxel.

Chemotherapy is usually given as an injection into the vein, but is sometimes given as tablets. Some studies have looked at giving chemotherapy directly into the abdomen, called intra-peritoneal chemotherapy.

Most often, chemotherapy is given on an outpatient basis but sometimes a short stay in hospital may be required. It is usually given in cycles, with a period of treatment followed by a period of rest to allow the body to recover. Most women have six cycles of chemotherapy.

Radiotherapy

Radiotherapy uses high energy X-rays. Like chemotherapy, it works by targeting rapidly growing cancer cells. Radiotherapy is not often used to treat ovarian cancer. But occasionally, the multidisciplinary team may recommend it for ovarian cancer treatment under very specific circumstances, such as treating pain and bleeding from a localised tumour mass.

The Latest Guidelines for Treating Ovarian Cancer

The American Society of Clinical Oncology (ASCO) and the Society of Gynecologic Oncology (SGO) jointly issued new clinical practice guidelines for the treatment of patients with ovarian cancer.

Key recommendations of the new guideline include:

- All women with suspected stage IIIC or IV invasive epithelial ovarian cancer should be assessed by a gynaecologic oncologist before treatment initiation to determine whether they are candidates for primary cytoreductive surgery.
- Neoadjuvant chemotherapy should be given to women who have a high perioperative risk profile or a low likelihood of achieving cytoreduction to less than 1 cm (ideally to no visible disease).
- Women who are fit for primary cytoreductive surgery with potentially resectable disease may receive either primary cytoreductive surgery or neoadjuvant chemotherapy.

    - Primary cytoreductive surgery is preferred over neoadjuvant chemotherapy for women with a high likelihood of achieving cytoreduction to less than 1 cm (ideally to no visible disease).
    - Neoadjuvant chemotherapy is recommended for women who are fit for primary cytoreductive surgery but are deemed by a gynaecologic oncologist as unlikely to have cytoreduction to less than 1 cm (ideally to no visible disease).

For neoadjuvant chemotherapy, clinicians are advised to treat patients with a doublet regimen consisting of a platinum agent and a taxane, though alternate platinum-containing regimens may be selected for subjective reasons. The Expert Panel notes that it is unclear

how weekly dose-dense paclitaxel compares with every-3-week paclitaxel in the preoperative setting.

Prior to the delivery of chemotherapy, all patients should have histologic confirmation, preferentially by using core biopsy of an invasive ovarian, fallopian tube, or peritoneal cancer. When a core biopsy cannot be performed, cytologic evaluation with a serum CA-125 to carcinoembryonic antigen (CEA) ratio less than 25 can be used to confirm the primary diagnosis, and exclude a non-gynaecologic malignancy.
(Cancer Therapy Advisor).

Expectations (Prognosis) for Ovarian Cancer
Ovarian cancer is rarely diagnosed in its early stages. It is usually quite advanced by the time diagnosis is made

- About 3 out of 4 women with ovarian cancer survive 1 year after diagnosis
- Nearly half of women live longer than 5 years after diagnosis
- If diagnosis is made early in the disease and treatment is received before the cancer spreads outside the ovary, the 5-year survival rate is very high

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

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