

RESEARCH INTO OVARIAN CANCER

Scientists all over the world are carrying out research studies into the prevention, screening, diagnosing and treatment of ovarian cancer and its side effects.

This information sheet discusses research into:

- **risk factors**
- **prevention**
- **screening (early detection)**
- **new treatments**
- **treating side effects of cancer therapy.**

It is important to remember that many ovarian cancer trials are in the very early stages. Some trials may not be available to you in your state or territory, at your treatment hospital or even here in Australia. However, we feel it is important to give an overview of worldwide research.

At the end of this fact sheet we provide links to Australian trials for women with ovarian cancer. **We encourage you to discuss any national or international clinical trials you may be interested in with your doctor.**

For detailed information about ovarian cancer and its treatment, call Ovarian Cancer Australia on 1300 660 334 and ask for a copy of our *Resilience Kit*.

RISK FACTORS

Hereditary ovarian cancer

We don't know all the causes of ovarian cancer, but one known risk, and an area of research interest, is hereditary ovarian cancer.

Ovarian cancer caused by inheriting a faulty gene is called 'hereditary cancer'. Having a personal or family history of ovarian, breast, colon or endometrial cancer may mean you have inherited an increased risk of developing ovarian cancer.

Hereditary cancer accounts for about 20% of all ovarian cancers. In most cases, the woman has inherited a faulty BRCA1 or BRCA2 gene. (These gene faults are named for their connection to breast cancer (BReastCAnceR genes 1 and 2) but are also associated with inherited

ovarian cancer, fallopian tube cancer and other types of cancer).

Several other genes are also linked to an increased risk of ovarian cancer. For example, two genetic faults that can increase the risk of ovarian cancer risk are:

- Lynch syndrome (also called hereditary non-polyposis colorectal cancer or HNPCC)
- RAD51D gene (which is normally involved in the repair of damaged DNA).

Scientists are looking for ways to disrupt genes that can lead to cancer. It is hoped the research will lead to new drugs to help prevent and treat hereditary cancer.

Note: Most cancers happen by chance or due to cell damage throughout our lives and not because of an inherited faulty gene.

Other risks

Scientists are also looking into lifestyle factors, such as smoking tobacco, being overweight or eating a high-fat diet, which may increase the risk of developing ovarian cancer.

PREVENTION

Surgical removal of ovaries and fallopian tubes

Women with a faulty gene, and therefore an increased risk for the development of ovarian cancer, may choose to have their ovaries and fallopian tubes removed.

Many ovarian cancers start in the fallopian tubes and spread into the ovaries. To prevent ovarian cancer, both the fallopian tubes and ovaries need to be taken out.

Because of the possible side effects, this can be a difficult and complex decision for a woman to make, especially if she wants to have children or wants to avoid early menopause. Removing the ovaries before menopause means a woman will go through an early menopause. This leads to a sudden drop in the normal oestrogen and progesterone levels in the body, which



causes symptoms such as hot flushes and sleep disturbance. It may also increase the risk of bone density (strength) loss and heart disease.

Researchers have come up with mathematical models allowing a woman with BRCA gene faults and a strong family history of ovarian cancer to estimate the possible years of life she may gain by having this surgery (These statistics provide a general idea of risk – doctors cannot calculate individual outcomes.)

This research is ongoing as there are still many unanswered questions. For example, some researchers are looking into first removing the fallopian tubes and later the ovaries. This approach would mean women could continue to produce oestrogen and delay challenging menopausal symptoms and other side effects caused by removing the ovaries.

These studies are still in the early stages, with no confirmation this will lead to a reduction in risk of ovarian cancer.

New drugs

Clinical trials are also looking into new drugs to reduce the risk of developing ovarian cancer.

SCREENING (EARLY DETECTION)

A screening test is a test that can be done when there is a known risk but no signs of anything wrong. It enables a doctor to pick up a cancer at its earliest stages, when there is the best possible chance of cure.

At present, there is no reliable screening test for early ovarian cancer. Research is underway to try and develop a screening test to detect ovarian cancer at earlier stages to improve women's outcomes.

The following tests **have not** been shown to be effective in detecting early ovarian cancer or pre-cancer changes:

- CA125 blood test
- transvaginal ultrasound.

Two big studies, one in the United Kingdom and one in the United States, used the CA125 blood test and transvaginal ultrasound to detect ovarian cancer. Although more cancers were found in the women who were screened, the overall outcomes were not better – women who were screened did not live longer than those who were not.

If we could find more accurate ways to detect ovarian cancer early, it would significantly help the cure rate. Research is looking at new ways to screen for ovarian cancer using blood and tissue samples from women with ovarian cancer. Samples have come from the large screening studies in the United Kingdom and

United States and from women who took part in the Australian Ovarian Cancer Study (AOCS). The AOCS is a collaborative research program between clinicians, scientists, patients and advocacy groups, aimed at improving the prevention, diagnosis and treatment of ovarian cancer. Ovarian Cancer Australia contributes funding to this important work. For more information contact Ovarian Cancer Australia (OCA) on 1300 660 334.

More about CA125 and transvaginal ultrasound

Although the CA125 test cannot be used to screen for ovarian cancer, it is a useful test to help with diagnosis. Read Ovarian Cancer Australia's fact sheet on the [CA125 test](http://www.ovariancancer.net.au) www.ovariancancer.net.au.

Transvaginal ultrasound is done by inserting the ultrasound probe into the vagina. It is not completely accurate in diagnosing ovarian cancer as it is not always easy to tell the difference between a harmless cyst and a malignant tumour. In addition, research suggests many ovarian cancers start their growth in the fallopian tube, and a transvaginal ultrasound would not detect these cancers until they had spread to the ovary.



FRANCINE, SCIENTIST.
DIAGNOSED WITH OVARIAN CANCER 2015.

NEW TREATMENTS

Treatment for ovarian cancer is constantly being improved. The main way improvement happens is through clinical trials.

Clinical trials

In clinical trials, new treatments can be developed, evaluated and compared with current treatments.

The main aim of clinical trials is to find out if a new treatment or procedure:

- is safe and has any side effects
- works better at treating ovarian cancer than the current standard treatment.

Participating in a clinical trial may provide you with a better outcome, as well as benefiting other women who may eventually receive the treatment being trialled.

If you consent to participate in a clinical trial, you can withdraw from the trial and return to regular treatment at any time. This will not affect the care you receive.

Clinical trials into ovarian cancer are looking at:

- chemotherapy
- biological therapy (immunotherapy)
- hormone therapy

Chemotherapy

Clinical trials are looking into new chemotherapy drugs as well as the best combinations and doses of drugs and when is the best time to give them (e.g. before or after surgery).

Trials are also underway looking into alternative ways to administer the drugs and prevent problems with existing drugs.

New drugs

Two new chemotherapy drugs are being tested:

- trabectedin (Yondelis®)
- belotecan.

These drugs have shown potential in possibly treating some ovarian cancer.

Addressing platinum resistance

Two chemotherapy drugs routinely used to treat ovarian cancer are cisplatin and carboplatin (known as platinum chemotherapy). Women with ovarian cancer can take these drugs for some time with benefits. However, there comes a time when these drugs may stop working, as the cancer becomes 'platinum resistant'. Researchers are looking into ways to try and prevent this resistance.

Intraperitoneal chemotherapy

Most chemotherapy drugs are injected directly into a vein into the bloodstream (intravenously). Another way

of giving chemotherapy is to inject the drugs directly into the abdominal cavity through a small tube. This is called 'intraperitoneal chemotherapy' (IP chemo). Having chemotherapy in this way means you will get a more concentrated dose of the drug directly into the cancer cells.

Cisplatin is sometimes given this way to help treat ovarian cancer, as it is less toxic than carboplatin. The drug is also absorbed into the bloodstream, meaning it can get to cancer cells that have spread outside the abdominal cavity. IP chemo works well but the side effects of the drugs can be more severe than if they are given intravenously.

Studies are now looking at also using IP carboplatin to help treat ovarian cancer.

Some clinical trials are looking into giving IP chemo during surgery, using drugs that have been heated up. This is known as heated (hyperthermic) intraperitoneal chemotherapy or HIPEC. Early studies have shown this could be very successful; however, the side effects are harsh. More research is needed before we will know for sure if HIPEC works better than standard IP chemo.

Biological therapy (immunotherapy)

Biological therapies, also known as immunotherapies, are treatments that help to slow down or stop the growth of cancer cells. They work by changing the way the cells in our body work. They can help in three ways:

1. boosting the immune system to kill the cancer cells
2. changing how cancer cells signal to each other to grow
3. stopping the growth of the cancer's blood supply.

Examples of biological therapies being researched for ovarian cancer include:

- growth and blood supply blockers
- immunotherapy
- monoclonal antibodies.

Growth factor blockers

These drugs attach to the surface of cancer cells and 'tell' the cells to stop dividing (and therefore multiplying and spreading). Most growth factor blockers work by blocking the signals that would normally encourage the cancer cells to divide.

Because cancer cells can be very sensitive to growth factors, researchers are developing different inhibitors for different growth factors. Examples of growth factor blockers being used in clinical trials include nintedanib (BIBF 11200) and trametinib.

One example of a small molecule treatment being tested in clinical trials is vintafolide (EC145). This drug targets the folic acid receptor that is on the surface

of the cancer cells in some types of ovarian cancer. It has shown some promise. But further trials are needed before we will know the full benefit of this drug in helping to treat women with ovarian cancer.

Blood supply blockers (anti-angiogenic drugs)

The growth of new blood vessels is called 'angiogenesis'. This must happen in our body to maintain healing and new growth. Cancers may also develop their own blood supplies, which helps them to grow and spread.

A blood supply blocker (also known as an 'angiogenesis inhibitor') is a substance preventing new blood vessels growing. Blood supply blockers can stop a cancer developing its own blood vessels. This means the cancer cannot keep growing.

Blood supply blocker drugs being used in clinical trial for ovarian cancer include:

- bevacizumab (Avastin®)
- cediranib (Recentin®)
- pazopanib (Votrient®)
- fosbretabulin (also known as CA4P or combretastatin).

Please note: Avastin is also available as standard treatment for some women. Speak with your specialist about whether this might be beneficial in the treatment of your ovarian cancer.

Monoclonal antibodies

Monoclonal antibodies are a type of protein made in the laboratory that can attach to substances in the body, including cancer cells. Several monoclonal antibodies are being trialled, such as nivolumab and ipilimumab. They are being researched as single treatments, and in combination with chemotherapy and biological therapies.

Ovarian cancer can cause a build-up of fluid in the abdomen known as 'ascites'. This causes bloating, swelling and discomfort. It can be painful and make you short of breath.

Scientists are studying a monoclonal antibody called 'catumaxomab' to help treat ascites. Catumaxomab attaches to a protein present in some immune system and cancer cells. If given directly into the abdominal cavity when a cancer is present, it can help to stop ascites.

PARP-1 inhibitors

PARP is a protein in our body that helps damaged cells to mend themselves. Cancer cells with altered BRCA genes depend on PARP to keep their DNA functioning. PARP-1 inhibitors are drugs that stop PARP from mending the DNA cell damage, which means cancer cells don't survive.

Rucaparib, olaparib (Lynparza®) and Niraparib are PARP drugs being used in clinical trials to see which women will benefit most from them.

Olaparib is for women who have a change in a BRCA gene. It is currently only for women who have had a recurrence of their cancer and whose cancer is still responsive to platinum chemotherapy (carboplatin or cisplatin). There is good evidence olaparib maintenance can lengthen the remission in these women, and research continues in the area. Olaparib is now listed on the [Pharmaceutical Benefits Scheme www.pbs.gov.au/pbs](http://www.pbs.gov.au/pbs) (PBS) for BRCA mutations. It is also being trialled in women with non-BRCA mutations.

Note: Olaparib is a new treatment and only available to some women.

Vaccines

Vaccines are a type of biological therapy. They stimulate the body's immune system to fight cancer. A vaccine can allow our normal immune system to recognise a cancer cell as abnormal and create an immune reaction to destroy the cancer cells.

Cancer vaccines have been very successful in some cancers, such as melanoma.

Research is looking into how a vaccine called TroVax® may help slow the growth of ovarian cancer and delay the start of chemotherapy.

Hormone therapy

Research is trying to find out whether lowering the levels of oestrogen in the body will help fight gynaecological cancers such as ovarian and breast cancer. The treatment may help some women who have a hormone receptor-positive cancer (meaning the cancer needs the female hormones oestrogen and/or progesterone to grow and reproduce). One drug being studied is anastrozole (Arimidex®).

TREATING SIDE EFFECTS OF CANCER THERAPY

Palm oil supplements for side effects of pelvic radiation

Radiotherapy can be an effective treatment for ovarian cancer symptoms such as vaginal bleeding. However, radiotherapy can cause side effects such as diarrhoea, abdominal pain and bleeding from the bowel. It can also cause scar tissue to form in the bowel (radiation fibrosis). These side effects can be very difficult for women to cope with and decrease their quality of life.

Researchers are using a combination of a palm oil supplement with a drug called 'pentoxifylline' to try to relieve the side effects of pelvic radiation.

Exercise to help cancer-related fatigue

'Fatigue' means feeling very tired and having no energy. People with cancer often describe their fatigue as 'overwhelming' and 'debilitating'.

Cancer-related fatigue is one of the most common problems during and after cancer treatment. It affects your ability to do day-to-day activities such as going to work, cooking, dressing and washing. Many say it is not relieved by sleep and can affect your self-esteem and relationships.

Fatigue may be caused by chemotherapy, radiotherapy or other medicines. The cancer itself may also cause fatigue, which may be related to low red blood cells (anaemia) or a tumour pressing on vital organs such as the lungs.

Exercise has been proven to enhance mood, improve sleep, control weight gain, protect against heart disease and maintain bone health. It may help counteract some of the side effects of cancer treatment.

Research is looking into how combinations of aerobic exercise, resistance training and mindfulness (e.g. yoga and Tai Chi) exercise can be effective in helping people with cancer cope with their disease, its treatment and its side effects. It is also finding out how exercise can help people improve their life after cancer.

Not every cancer treatment centre offers trials using exercise programs. Ask your doctor how exercise may help you during and after your treatment.

For general information about fatigue and cancer, call Ovarian Cancer Australia on 1300 660 334.

Note: Talk to your specialist doctor before starting any exercise program. We strongly recommend that exercise testing for people with cancer and survivors be done by qualified exercise professionals.

Cold caps to prevent hair loss from chemotherapy

Preventing hair loss from chemotherapy is not always possible. But you may be able to reduce the amount of hair you lose by using cold caps.

Cold caps decrease the scalp temperature. This reduces the blood flow to the scalp and lowers the amount of chemotherapy getting to your hair follicles. If less chemotherapy gets to the hair follicles, it can stop some of the hair dying and falling out.

There is no guarantee cold caps will work, and you will not know until you try it. Some women who use cold caps still have hair thinning or lose their hair completely.

There are several trials using various types/brands of cold caps to see which best helps prevent hair loss.

Note: Cold caps are not suitable for everyone having chemotherapy. Please discuss this option or possible trials with your specialist doctor.

A note on cannabis use

It is thought cannabis and cannabinoids (the active compounds in the cannabis plant) may help relieve symptoms such as pain and nausea in cancer patients. This has been an important topic of debate in recent years. Many cancer trials are using cannabis and cannabinoids in people with cancer.

Ovarian Cancer Australia follows the same guidelines as Cancer Council Australia on the use of cannabis in people with cancer. You may find it helpful to read their statement and information on cannabis and cancer www.cancer.org.au/policy-and-advocacy/supportive-care-policy/cannabis-for-medical-purposes.html

ADDITIONAL INFORMATION

For further information on clinical trials, download a free copy of Understanding clinical trials and research from the Cancer Council <http://trials.cancervic.org.au/downloads/resources/Clinical-Trials-Booklet.pdf>. It explains what clinical trials are, the different clinical trial phases, benefits and risks, eligibility, questions to ask your doctor and how to find out about current trials.

MORE LINKS

To review the range of current clinical trials for women in Australia with ovarian cancer, visit:

- Australian Cancer Trials www.australiancancertrials.gov.au/
- The Australian New Zealand Clinical Trials Registry www.anzctr.org.au/default.aspx
- The Australia New Zealand Gynaecological Oncology Group (ANZGOG) www.anzgog.org.au

WANT TO KNOW MORE

CALL 1300 660 334 | EMAIL support@ovariancancer.net.au | VISIT www.ovariancancer.net.au

