ovacome..
ovarian cancer

Ovarian cancer and genetics

Ovacome is a national charity providing support and information to anyone affected by ovarian cancer.

We run a free telephone and email support line and work to raise awareness and give a voice to all those affected by ovarian cancer.

This booklet is part of a series giving clinical information about ovarian cancer.

It is one of three booklets discussing genetics, genetic testing and reducing genetic risk.

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Ovarian cancer and genetics

Every year around 7,500 people in the UK are diagnosed with ovarian cancer.

We don't know what causes all of these, but around 15 per cent (15 in 100) are likely to be due to changes in certain genes *(1)*.

In the UK the risk of developing ovarian cancer is about two per cent (2 in 100). If you have inherited a changed gene, then your risk may be more than this *(2)*.

Gene changes that are known to affect the risk of ovarian cancer are found in genes BRCA1 and BRCA2. They also affect breast and prostate cancer risk. Changes in other genes can cause Lynch syndrome. This is a condition that increases the risk of ovarian cancer and other cancers such as colorectal (bowel) and endometrial (womb).

What is a gene change?

Our bodies are made up of millions of tiny cells. These are the smallest, basic units in our bodies. They carry out all the processes we need to live.

Inside each cell is a series of genes, that carry the information we need for our bodies to function. Genes control how the cells work. They tell the cells how to grow and develop. Your height, features and sometimes your health, depend on the messages sent out by your genes.

We each have about 20,000 genes. Your entire gene sequence is called your genome.

A gene may develop a change in its structure which affects the way it works. This is rather like a spelling mistake in a very long word. It means the gene may not be able to carry out its tasks properly. A result of this might be an increase in the risk of disease, such as cancer, including ovarian cancer.

We inherit our genes from both our parents. This means we have two copies of each gene. If your father or mother carries a gene with a change, then you have a 50 per cent (50 in 100) chance of inheriting it. If you have a changed gene, your children will have a 50 per cent chance of inheriting it from you.

Family characteristics are passed down the generations by inheriting genes. Your genes can show where your ancestors came from, and sometimes the health problems you are more likely to have.

Which genes affect ovarian cancer risk?

The best-known genes that can carry changes that can increase the risk of ovarian cancer are the two BRCA genes, BRCA1 and BRCA2. BRCA stands for breast cancer, but these genes, if they have changes, can increase the risk of ovarian cancer, prostate cancer, some pancreatic cancers and male breast cancer.

BRCA1 was identified in 1990, so the risks posed by changes to it have been known for a long time.

BRCA genes control cell growth in our bodies. They are tumour suppressor genes, so they can prevent cancer from developing. If they

develop changes and faults that stop them working properly this can allow cells to grow abnormally and sometimes form cancers.

Around one person in 400 in the UK carries a changed BRCA gene. The figure is higher in some groups, such as Ashkenazi Jewish, Sephardic Jewish and Greenlander communities *(3)*.

In the UK the risk of developing ovarian cancer is around two per cent (2 in 100).

Having a change in the BRCA1 gene is estimated to increase the risk of getting ovarian cancer to 40 to 60 per cent (40 to 60 in 100) from the age of 40.

A change in the BRCA2 gene is estimated to increase the risk to 10 to 30 per cent (10 to 30 in 100) from the mid-40s *(4)*.

BRCA and breast cancer

BRCA gene changes can increase the risk of breast cancer too. In the UK the lifetime risk of breast cancer is 15 per cent (15 in 100) *(4)*.

A changed BRCA1 gene increases this risk to 60 to 90 per cent (60 to 90 in 100) up to age 80.

A changed BRCA2 gene increases risk to 45 to 85 per cent (45 to 85 in 100) up to age 80 *(5)*.

Learn more about BRCA gene changes and breast cancer here:

https://breastcancernow.org/information-support/have-i-got-breast-cancer/family-history/genetic-testing-altered-breast-cancer-genes

Lynch syndrome

Lynch syndrome is also inherited from your parents and can be passed on to your children.

It is caused by a group of genes which can develop changes that can increase the risk of colorectal (bowel), endometrial (womb) and ovarian cancers, particularly clear cell, and endometrioid type ovarian cancers.

It can raise the risk of ovarian cancer from the UK population risk of two per cent (2 in 100) to 17 per cent (17 in 100) by age 70 *(6)*.

Lynch syndrome can also raise the risk of stomach, pancreatic, ureter, kidney and skin cancers.

About 175,000 people in the UK are thought to have Lynch syndrome. But most of them are not aware of this *(7)*.

You may also hear it called HNPCC which stands for hereditary nonpolyposis colorectal cancer.

These are the genes which, after changes, can cause Lynch syndrome and increase the risk of ovarian cancer:

- MSH2, which raises ovarian cancer risk to 17 per cent (17 in 100).
- MLH1, which raises the risk of ovarian cancer to 11 per cent (11 in 100).
- MSH6, which raises ovarian cancer risk to 11 per cent (11 in 100) *(8)*.

Lynch syndrome and female cancer risks up to age 75

Colorectal cancer, risk increases of up to 48 per cent (48 in 100).

Endometrial (womb), risk increases of up to 37 per cent (37 in 100).

Upper gastrointestinal, risk increases of up to 11 per cent (11 in 100) *(9)*.

Other gene changes that can affect your risk

Changes in genes BRIP1, RAD51D, RAD51C or PALB2 can also increase the risk of ovarian cancer.

- BRIP1, changes can increase the risk of ovarian cancer to 10 per cent (10 in 100).
- RAD51D, changes can increase the risk of ovarian cancer to about 10 per cent (10 in 100).
- RAD51C, changes can increase the risk of ovarian cancer by age 70 to 5.2 per cent (just over 5 in 100).
- PALB2, changes to this gene mostly affect breast cancer risk, but it can increase ovarian cancer risk by a small amount.

Like the BRCA gene, changed forms of these genes can be inherited and passed on through families.

Homologous recombination deficiency (HRD)

Some of the genes listed above, along with BRCA genes, work to repair damage in the genetic make-up of ovarian cells.

This process is called homologous recombination repair (HRR). If the genes doing this work develop changes, this can mean the cell repair process no longer works properly. This is called homologous recombination deficiency (HRD).

Cells with HRD become abnormal over time and may become cancerous.

HRD is found in about half of high-grade serous tumours. This is the most common type of ovarian cancer.

The changed genes that cause HRD may have inherited their changes, or the changes may have occurred spontaneously by chance. The condition of HRD itself cannot be inherited or passed on.

Tumour testing for HRD is called somatic testing. It is done by taking a sample of the tumour during surgery. Being HRD positive can affect treatment choices for ovarian cancer.

Rarer ovarian cancer types

If you have been diagnosed with a less common form of ovarian cancer such as low grade serous, borderline, clear cell or mucinous, your cancer could involve one or more of these genes: KRAS, BRAF, PTEN, PIK3CA, CTNNB1, ARID1A, PPP2R1A.

These genes are likely to have developed changes spontaneously, called somatic changes, rather than changes that can be inherited.

You may be offered a genetic test on a tumour sample to check for these, as it may affect decisions about your treatment. Testing for inherited gene changes may not be needed.

Current NICE guidelines (NG241) recommend genetic testing for all epithelial ovarian cancers, including subtypes. So, people diagnosed with mucinous, clear cell, endometrioid, high and low grade serous and some rarer forms are now eligible *(3)*.

What patients say

Linda: "For me, genetic testing was being used to widen the options of other treatments. When you have a rare cancer, you are possibly more likely to grab at any opportunity to widen treatment options and to get access to drugs.

"I would welcome a wider base of genetic testing for all rare cancers, so as to give better options to patients and perhaps learn if certain mutations are more common within the cancer types."

Should I get tested?

If you are worried about inherited risk

You may recognise a history of cancers occurring in your own family.

If you think you may carry a BRCA gene change or be affected by Lynch syndrome or another genetic condition that increases your cancer risk, you can ask your GP to refer you to your nearest genetic centre for an assessment.

You should be able to speak to a genetic counsellor who can give expert guidance before any genetic test, so that you fully understand the results and how these might affect you and your family.

Being found to be BRCA positive or to be affected by Lynch syndrome or other genetic conditions may mean telling other members of your family and suggesting they get tested too. This may be upsetting news for them.

Ruth* says: *"I was not offered genetic testing but sought it by a referral from my GP because of the concerns I had about my family history. My maternal grandmother had breast cancer at an early age and my maternal grandfather died of bowel cancer in his 40s. I wanted it done particularly for my sister and my children. I was also concerned that if I carried one of the Lynch syndrome mutations, whether I needed regular bowel screening."

If you have ovarian cancer

All patients diagnosed with epithelial ovarian cancer, including people with rarer subtypes, should be offered genetic testing to check for inherited BRCA gene changes, Lynch syndrome or other changed genes. This will usually be a blood test.

This is germline testing. It looks for gene changes that have been inherited from your parents and that can be passed on to your children.

A sample taken from your ovarian cancer tumour during surgery can be tested for HRD and other gene changes. This is called somatic testing.

Being found to be BRCA positive and/or HRD positive can widen access to drug treatments called targeted therapies, such as bevacizumab (Avastin) or olaparib and niraparib (which is also available to people without BRCA changes or HRD). This widens your treatment options.

Learn more about targeted therapies here:
https://www.ovacome.org.uk/targeted-therapies-booklet

Being BRCA positive or having Lynch syndrome or other inherited gene changes means you have to decide how to use this information with family members who could be at increased risk of ovarian and other cancers. You can find out more in the two further Ovacome booklets about genetic testing and reducing and managing genetic risk.

References

1. Clinical commissioning policy – Genetic testing for BRCA1 and BRCA2 NHS England Feb 2018
2. Lifetime risk of ovarian cancer CRUK Life experiences and population projections ONS 2016
3. NICE Ovarian cancer: identifying and managing familial and genetic risk (NG241) March 2024
4. Predictive genetic tests for cancer risk genes NHS July 2021
5. A beginner's guide to BRCA1 and BRCA2 The Royal Marsden Hospital
6. A beginner's guide to Lynch syndrome The Royal Marsden Hospital
7. Bowel Cancer UK
8. Prevalence of Lynch syndrome in women with mismatch repair-deficient ovarian cancer Dec 2020 Rachel Hodan, Kerry Kingham et al

Useful links

Ovarian Cancer Action https://www.ovarian.org.uk/ovarian-cancer/brca
Breast cancer now https://breastcancernow.org
Lynch syndrome UK https://www.lynch-syndrome-uk.org
NICE guidance https://www.nice.org.uk/guidance/ng241/chapter/Recommendations#criteria-for-genetic-counselling-and-genetic-testing-in-genetics-services-or-in-gynaecology

We welcome your feedback on this booklet, email ovacome@ovacome.org.uk or call us on 0800 008 7054. Calls are free. If you would like to discuss anything about ovarian cancer, please phone our free support line on 0800 008 7054 Monday to Friday between 10am and 5pm.

You can also visit our website at www.ovacome.org.uk

Reviewed by Charlotte Hitchcock, Associate Director of Genomic Nursing and Midwifery, Central and South Genomic Medicine Service Alliance

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Support line: 0800 008 7054
Office phone: 0207 299 6654
Website: www.ovacome.org.uk
Email: ovacome@ovacome.org.uk

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