



**OvarianGene**

GeneHealth  UK





## What is hereditary ovarian cancer?

Ovarian cancer is the fifth most common cancer in women. In the general population women have a 1.5% risk of ovarian cancer, with 75% being diagnosed after the age of 55. When ovarian cancer is diagnosed at an early stage more than 90% of women survive more than 5 years, however, sadly this drops to only 5% in those diagnosed at a later stage.

Most ovarian cancers occur by chance, however up to 20% is hereditary and in some families it may be possible to find the genetic change (mutation) which is responsible for the cancer. This allows appropriate cancer screening and risk-reducing options.

## What are genes?

Genes are the body's instructions and determine how the body develops and is maintained. Some genes prevent cancer developing: if there is a mutation in one of these cancer genes, then the gene doesn't work correctly and causes an increased risk of cancer.

Mutations in at least 9 genes can cause an increased risk of ovarian cancer and other cancers. However, we know that there are other genes which are also associated with ovarian cancer and researchers are attempting to understand these other genes.

## How do I know if I am at risk?

Families with hereditary ovarian cancer generally show one or more of the following clues:

- Relative(s) with high grade serious ovarian cancer
- Breast cancer diagnosed before the age of 50/bilateral breast cancer/male breast cancer
- Jewish ancestry and a history of breast/ovarian/prostate cancer
- Bowel/womb cancer diagnosed at a young age (before the age of 50)
- Multiple generations with cancer

It is important to be aware that hereditary ovarian cancer can be present on either the maternal (mother's) or paternal (father's) side of the family.

## How can genetic testing help?

Genetic testing can help determine the risk of cancer within a family and guide appropriate cancer screening. Depending on the specific genetic risk different screening tests can be arranged and risk-reducing strategies can be considered.

## What is OvarianGene?

OvarianGene looks at 10 genes which cause an increased risk of ovarian cancer. The following genes are tested:

Gene	Condition	Risk of Ovarian cancer by age 70
BRCA1	HBOC	< 60%
BRCA2	HBOC	< 30%
EPCAM	Lynch syndrome	~ 10%
MLH1	Lynch syndrome	~ 10%
MSH2	Lynch syndrome	~ 10%
MSH6	Lynch syndrome	~ 10%
PMS2	Lynch syndrome	~ 10%
RAD51C	Inherited Ovarian Cancer	~ 10%
RAD51D	Inherited Ovarian Cancer	~ 10%
BRIP1	Inherited Ovarian cancer	10 - 20%

## Hereditary Breast and Ovarian Cancer (HBOC)

Mutations in BRCA1 & BRCA 2 cause hereditary breast and ovarian cancer. In the general population 0.4% of non-Jewish people and 2% of the Ashkenazi Jewish people will have a BRCA mutation.

The estimated cancer risk associated with BRCA mutations vary, however, BRCA1 mutations are estimated to have up to an 85% risk of breast cancer and a 40-60% risk of ovarian cancer, while men with BRCA1 mutations have a slightly increased risk of male breast cancer and prostate cancer.

Women with BRCA2 mutations have up to a 90% risk of breast cancer and up to a 26% risk of ovarian cancer. Men with BRCA2 mutations have a 7% lifetime risk of developing breast cancer, and an increased risk of prostate cancer (2-5 times the general population risk). Individuals with BRCA2 mutations also have an increased risk of pancreatic cancer and possibly other cancers.

Women with BRCA gene mutations should have annual breast screening from the age of 30 onwards, including mammograms and breast MRI. Ovarian screening has not been shown to be beneficial and therefore some women may consider risk-reducing surgery. Men may benefit from prostate cancer screening.

Occasionally, a baby will inherit two BRCA2 mutations and will therefore have the congenital condition known as Fanconi Anemia.

## Lynch syndrome (LS)

LS is the most common hereditary bowel cancer syndrome and is the cause of approximately 1–3% of all bowel cancer. LS causes an increased risk of bowel (25-70%), ovarian (~10%), stomach (5%), womb (30-70%) , prostate (18-30%) and other cancers. It has been estimated that in Europe approximately one million people have LS.

If someone has LS, regular bowel screening with colonoscopy is vital and other risk-reducing strategies will be considered. These strategies include detecting and treating an infection called Helicobacter Pylori as well as taking aspirin, and, in women, consideration of risk-reducing surgery.

## RAD51C / RAD51D

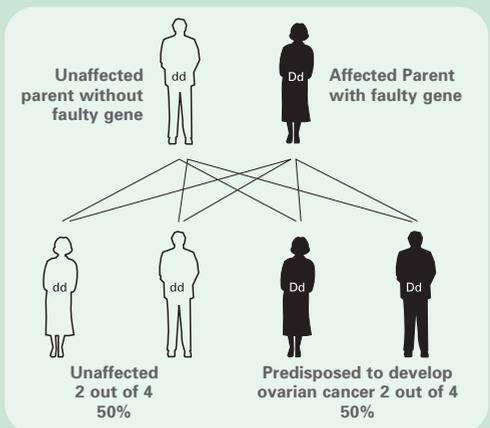
RAD51C inherited ovarian cancer and RAD51D are known to cause an increased risk of ovarian cancer and possibly breast cancer. The risk of ovarian cancer has been estimated to be 6-8 times higher than the general population risk which is the equivalent of approximately 9% lifetime risk. Women with RAD51 mutations may wish to have risk reducing removal of the ovaries to lower their risk. Additional breast cancer screening may be helpful.

## BRIP1

BRIP1 has shown to cause an increased risk of ovarian cancer. The risk is estimated to be about 11 times higher than the general population with the majority (over 90%) occurring over the age of 50. Women with a BRIP1 mutation may wish to consider having their ovaries removed once they have been through the menopause. Breast screening may also be helpful.

## How are these conditions inherited?

Genes come in pairs; we get one copy from our mother and one copy from our father. At present most cancer syndromes are inherited in a dominant pattern. This means that if someone has a mutation in one copy of a gene then there is a 50% chance that they will pass this onto their children. The risk of ovarian cancer can be inherited from either side of the family. The diagram illustrates this.





### **How does the test work?**

OvarianGene is performed on a blood sample and it takes 8-12 weeks to obtain the results. OvarianGene uses state of the art technology known as nextgeneration sequencing to examine the code for each of the 10 genes in detail.

OvarianGene is a comprehensive way to assess a person's risk for hereditary ovarian and associated cancers. However, no test is 100% and it is possible that someone could have an undetectable genetic mutation in one of these genes or in a different gene which is not tested.

It is most accurate to perform genetic testing on someone who has had ovarian cancer so that a possible genetic cause can be found in the family. If this is not possible, genetic testing can be performed on someone who has not had cancer, although if the results are normal this will not be as informative.

### **What will the test show?**

There are 3 possible results:

1. A mutation is found in one of the genes which is known to increase the risk of ovarian cancer. Increased screening and/or risk-reducing techniques will be recommended.
2. A genetic variation is found, but whether or not this is the definite cause of cancer is unknown. Screening will be recommended based on the family history.

3. No mutation is found. It is possible that there may be an undetectable mutation or a mutation in a different gene. Cancer screening may still be beneficial.

### **What does it mean if I have a mutation?**

If you have a mutation this means that you have an increased risk of ovarian cancer and possibly other cancers. Your exact risks will depend on which gene mutation has been found. Extra screening and/or risk-reducing strategies will be discussed. It will also be possible to offer predictive testing to other people in your family to see if they also have the mutation.

### **Screening**

Unfortunately, screening for ovarian cancer (with the blood test CA125 and vaginal ultrasounds) is not thought to increase survival and therefore risk reducing surgery is often most appropriate. Women over the age of 40 may choose to have bilateral salpingo-oophorectomy.

Screening for other cancers may also be needed and will be discussed if necessary.

## Ovarian awareness

It is helpful for women to be aware of the signs of ovarian cancer which are:

- Increased abdominal size/significant bloating that doesn't come and go
- Difficulty eating/feeling very full after a small meal
- Abdominal/pelvic pain
- Needing to pass urine more urgently or more frequently.

Most of the time people with these signs will not have cancer but it is always important to get them checked out.

## Other risk factors

Diabetes, endometriosis, and ovarian cysts may increase the risk of ovarian cancer. Exposure to asbestos also increases the risk of ovarian cancer.

Child birth, pregnancy and breast feeding lower the risk of ovarian cancer.

Tubal ligation (female sterilisation) lowers the risk of ovarian cancer by 35%. In addition, oral contraceptives lower the risk of ovarian cancer by up to 50% when taken for 5 or more years.

## Lifestyle Factors

It is known that a healthy diet can promote good general health and lower the risk of cancer. In particular, consuming a diet high on fruit and vegetables and low in dietary fat as well as maintaining a normal body weight will lower the risk of ovarian cancer.

## Financial issues

Some individuals may be concerned about difficulties obtaining insurance coverage following genetic testing. Currently, this is not a problem as there is a moratorium ensuring that individuals do not need to disclose predictive genetic test results unless a very large policy is being taken out. This moratorium is valid until 2017. More information about insurance can be found at: <http://www.abi.org.uk>

## Further information and support can be found at:-

<http://ovarian.org.uk/>

<http://www.ovacome.org.uk/>

<http://brcaumbrella.ning.com/>

<http://www.facingourrisk.org/>

<http://www.targetovariancancer.org.uk/>

<http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Ovary/Ovariancancer.aspx>

<http://www.eveappeal.org.uk>

Our knowledge of cancer genetics is rapidly growing, and the information given summarises this to date. Please keep us informed of any significant changes in your family in the future as this may alter our advice to you.

Please do not hesitate to contact us if you have any questions or concerns.



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### **Clinics - Locations**

Please visit our website [www.GeneHealthUK.com/Clinics](http://www.GeneHealthUK.com/Clinics) for an up-to-date list of clinic locations and directions. Please be aware that most genetic counselling sessions are undertaken by phone so a clinic may not be needed.

*GeneHealth UK is the leading provider of genetic tests and offers national and international counselling and testing services. We have designed our services to be comprehensive and to detect all of the clinically relevant mutations, however no genetic test will pick up all genetic mutations. If your results are abnormal you may be eligible for referral to an NHS clinic via your GP, or to a consultant in one of our private clinics throughout the UK. This may be funded by either self-pay or private medical insurance.*

Please visit [www.GeneHealthUK.com](http://www.GeneHealthUK.com) for more information and advice.

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