ASK EVE

GENETIC TESTING IN OVARIAN CANCER

the eve appeal

Foreword

We all have thousands of genes. They are vital for life and hold the information our bodies use to grow and function properly. In some cases, genes play a role in protecting us from cancer.

If you, or someone close to you, has been diagnosed with ovarian cancer, you may well hear about certain genes and be asked to consider whether you would like to be tested to see if you have any alterations on them (sometimes called gene mutations).

Knowing if you have alterations on certain genes may be very important

Sometimes genes can become altered, meaning that they do not work in quite the way they should. Genetic testing checks to see if you have any of these altered genes. If we know this, we can tell if a person may be at a higher risk of developing some cancers. For those already diagnosed with a cancer (such as ovarian cancer), it also helps to assess

what the most appropriate treatment may be.

Over the past two decades, there has been significant progress in our understanding of genes and the role they play in some cancers if they become altered. Having this knowledge should therefore help you or your family to make any important decisions.

Ask Eve is always here to help

Genetic testing can be complicated, and it is not always easy to be sure of the best thing to do. To help you better understand your options, *The Eve Appeal* has developed this booklet using the latest clinical guidance developed by the *British Gynaecological Cancer Society* and the *British Association of Gynaecological Pathology*.

But of course, every person's situation is different. Whether you or someone close to you has been diagnosed, if you are uncertain about your options you can always contact *Ask Eve - The Eve Appeal's* nurse-led information service.

You can contact us by phone or email. We are here to listen and always happy to help.

Tracie Miles

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Contact

For more information, you can contact The *Eve Appeal's* nurse-led information line, *Ask Eve*. It is completely free and confidential.

nurse@eveappeal.org.uk

0808 802 0019

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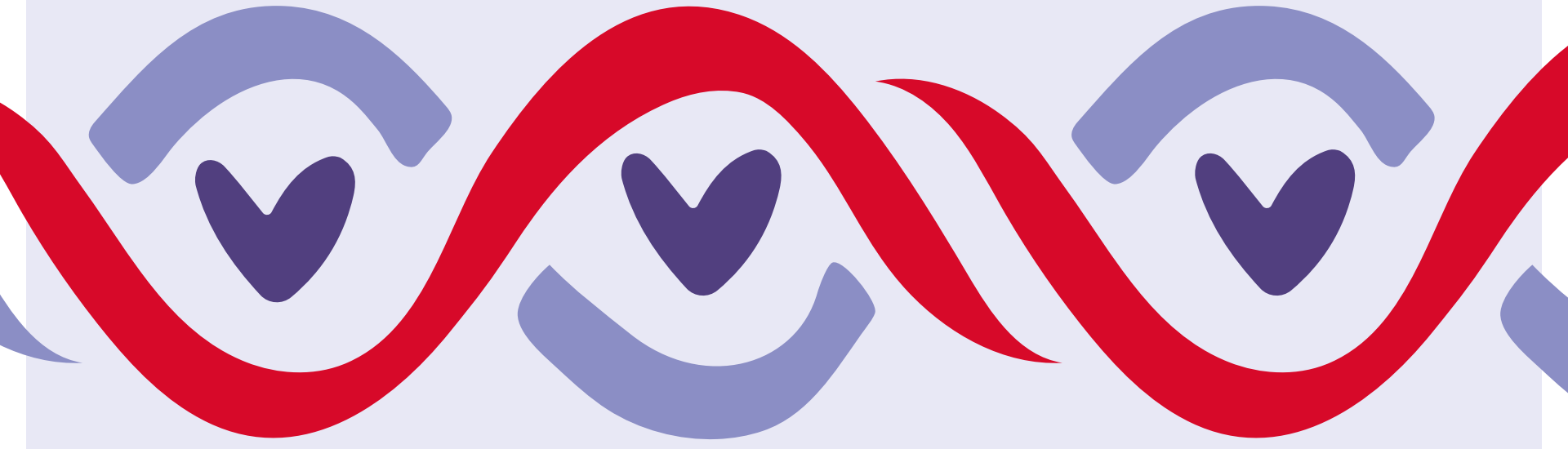
A BIT ABOUT GENES



What are genes?

Genes make up our DNA, which is found in almost every cell in our body.
They act like blueprints and contain the information that enables our bodies to grow and function correctly.

Are genes inherited?

Genes are inherited. You received half of yours from each parent, and any biological children you may have would have inherited half of their genes from you.

What are gene alterations / mutations?

Sometimes the information in a gene can become altered. You may hear this talked about as a gene alteration, gene mutation or as a 'pathogenic variant'. Generally, these all mean the same thing – that there is a slight change in a gene that means it is not working as it should.

How does a gene alteration happen?

There are a number of reasons for a gene becoming altered. This can be simply through chance, or because of environmental factors, such as exposure to certain substances, or lifestyle factors, such as obesity or smoking.

It is not always clear what the cause is, and it may be a combination of factors.

Are all gene alterations passed on to children?

If a person has a gene alteration, it does not always mean that it will be passed onto their children. A test is needed to

check whether the alteration has passed down or not.

If a gene is hereditary and can therefore be passed to children, there is a **50% chance** that a child may inherit it, whether they are female or male.

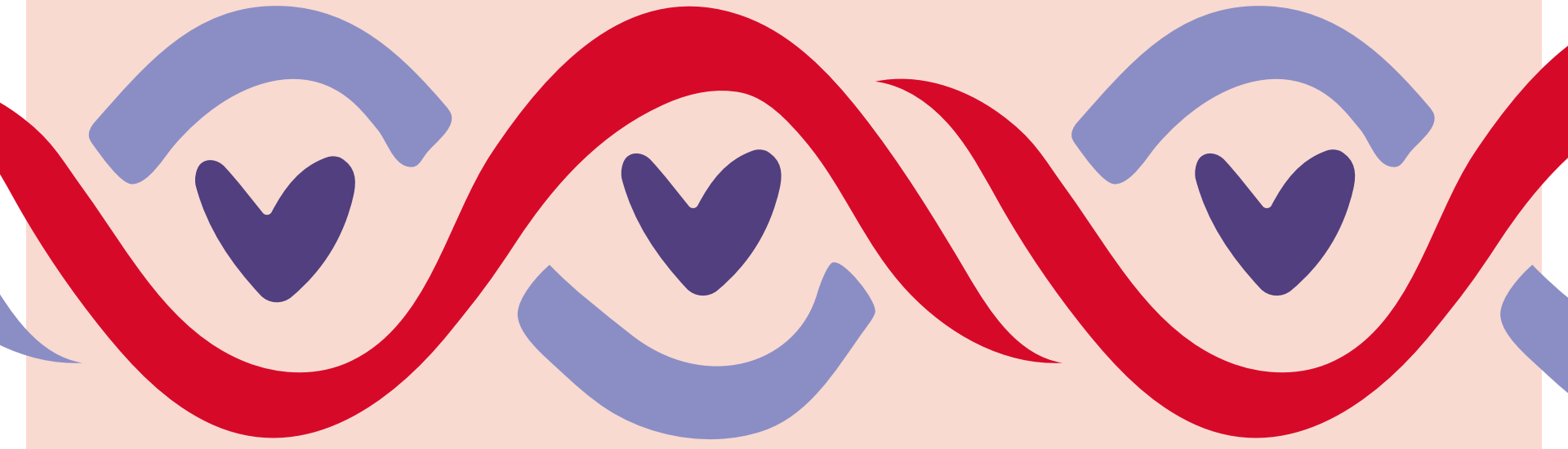
It is important to note that, even if a person has inherited a gene alteration that may increase their risk of cancer, it does not mean they will always develop cancer.

Does having a gene alteration mean you need to look out for cancer symptoms?

If you have been tested and told that you have a gene alteration that puts you at an increased risk of cancer, it may mean that you need to be more vigilant of symptoms.

It could also mean that you may be able to access some forms of cancer prevention on the NHS, such as screening or risk-reduction surgery.

BRCA GENES



What are BRCA genes?

Two genes that are commonly talked about in ovarian cancer are **BRCA1** and **BRCA2**.

Alterations in these genes increase the chance of ovarian cancer developing and may influence whether certain types of treatment are given.

BRCA1 and BRCA2 are also commonly linked to breast and prostate cancer, so they can affect both women and men. They are not the only genes that are linked to cancer so you may hear of others.

What do BRCA genes do?

Everyone has BRCA1 and BRCA2 genes. They are known as *tumour suppressor genes* as they play a role in protecting us from cancer.

They do this by helping to prevent the cells in our bodies from growing and dividing out of control.

What happens when a BRCA gene has an alteration?

If there is a significant alteration in either of the BRCA1 or BRCA2 genes, they may lose the ability to protect us from a cancer developing.

Does having a BRCA gene alteration impact treatment in ovarian cancer?

Some treatment options for advanced ovarian cancer are influenced by BRCA status so knowing this can help guide your clinical team.

How common are BRCA gene alterations?

Around 1 in every **200-300** people in the general population will have a BRCA gene alteration.[1]

In some populations, they are more frequent. People of Ashkenazi Jewish descent, for example, have around a **1 in 40** chance of carrying a BRCA gene alteration.[2]

How common is it to find a BRCA gene alteration in ovarian cancer?

Overall, around **10-20%** of ovarian cancers are linked to a BRCA gene alteration. However, they are found in some types of ovarian cancer more than others.

In Ashkenazi Jewish women, around **30-40%** of ovarian cancers are caused by BRCA gene alterations.[2]

WHY GENETIC TESTING IS IMPORTANT

What is genetic testing?

In ovarian cancer, genetic testing involves taking a sample of blood, tumour or saliva and then analysing it to see if the DNA inside the cells contains any alterations.

Is everyone with ovarian cancer able to get a genetic test?

Genetic testing is an option for many people diagnosed with ovarian cancer, so it is important to ask your clinical team early on about whether it may be suitable for you.

In some cases, testing may not be suitable, or you may not feel ready. If this is the case, do not worry and be sure to discuss what options are open to you with your nurse, oncologist, or you can *Ask Eve*.

What are the benefits?

The presence of certain gene alterations, such as on the BRCA1 and BRCA2 genes, can have several implications:

- If you have ovarian cancer, it may help guide your treatment choices
- It can determine your risk of developing other types of cancer (such as breast cancer) and help you decide if you would like to take measures to help prevent these
- It can provide important information for your family, as some gene alterations can be passed on to children

If you have a hereditary gene alteration, your family members may be eligible for genetic testing on the NHS. They can then make informed decisions about if they should be tested or consider options to help prevent cancer from occurring.

What gene alterations are being tested for?

If you have been diagnosed with ovarian cancer, you will most commonly be offered testing to look at your BRCA genes (BRCA1 and BRCA2).

Other gene alterations play a role in ovarian cancer (and other cancers), so you may also undergo testing looking at genes such as **RAD51C**, **RAD51D** and **BRIP1**.

Is genetic testing the same across all parts of the UK?

Across the UK, there is variation as to when, or if, a genetic test is offered after a diagnosis of ovarian cancer.

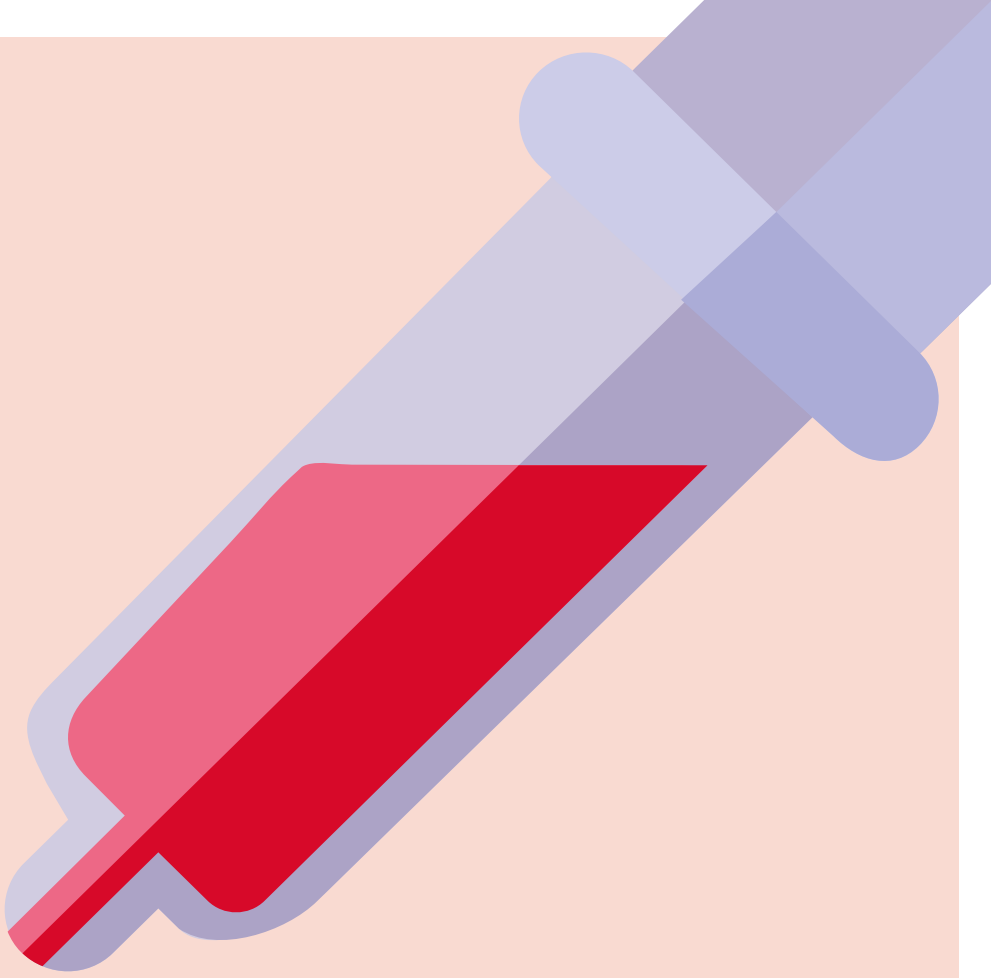
In England, a National Genomic Test Directory specifies which genomic tests the NHS should offer and who would be eligible.

In Scotland, Wales and Northern Ireland the process is likely to be similar, but may differ from place to place.

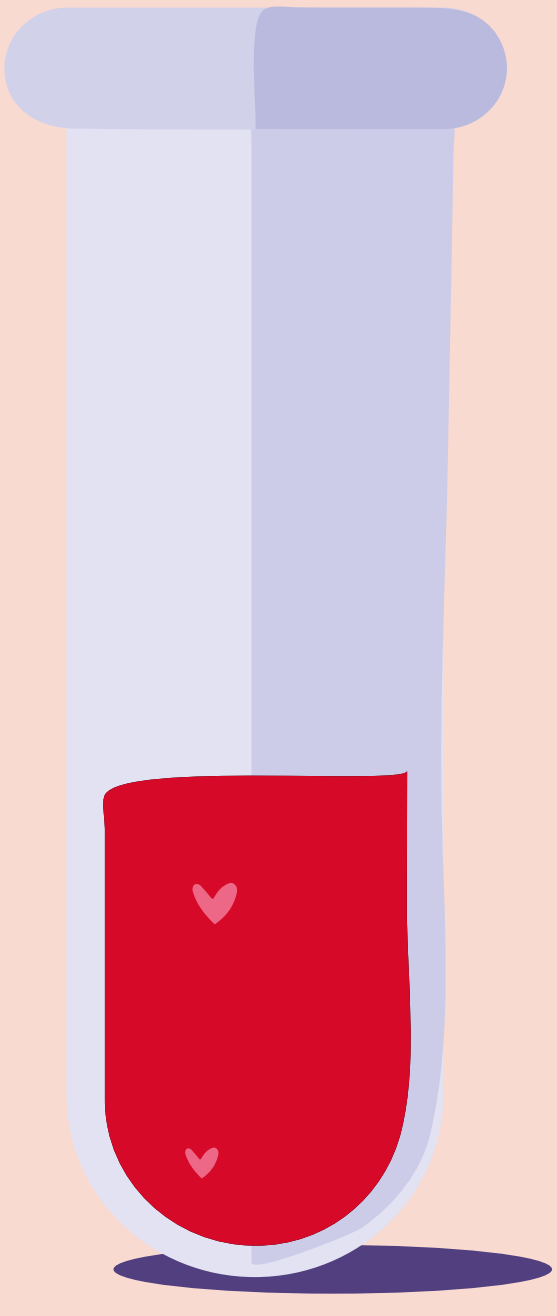
Ask about genetic testing

We would encourage you to bring up the topic of genetic testing with your clinical team as early as possible.

If you feel that you would like to have testing but are unsure if you can (or should), you can always contact *Ask Eve* for advice.



WHAT TESTING INVOLVES



If you have been diagnosed with ovarian cancer, when is testing usually done?

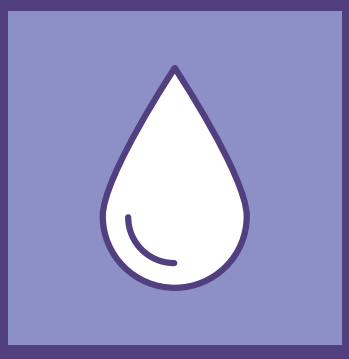
If testing is appropriate, it is usually offered early on, during the initial stages of treatment. However, your clinical team will also consider the timing of your ongoing (or planned) therapy and any support that may be needed.

Some examples of times when genetic testing may be discussed with you include:

- At initial consultation, when ovarian cancer is suspected or diagnosed.
- At a consultation before surgery.
- At a consultation after surgery.
- During a consultation for chemotherapy.

Types of tests you may have

Your clinical team will decide on the most appropriate test for you based on your specific circumstances. There are three main tests used in ovarian cancer:

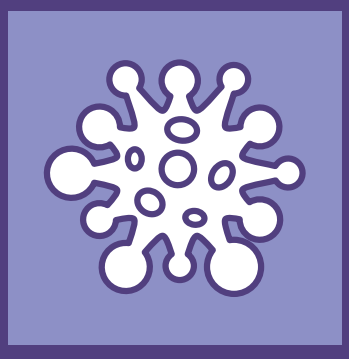


Taking a blood sample

This looks for inherited gene alterations (known as germline). The results may have implications for family members as well as for the person being tested.

Taking a sample of saliva

While not common on the NHS, this also looks for inherited (germline) alterations. It simply involves giving a sample of saliva. In some cases, this can be provided as a kit to do at home.



Taking a sample of the tumour itself

Known as tumour testing, this involves extracting DNA from the ovarian tumour itself (via a biopsy). If this test is positive (for example, showing a BRCA gene alteration), then a blood or saliva test will be required to confirm if there is a risk of it being hereditary.

Parallel testing

You may be offered blood and tumour testing at the same time. This is known as parallel testing.

If the results show the presence (or possible presence) of alterations in the BRCA1 or BRCA2 genes, you may be referred to a genetics service for follow up.

BLOOD TEST

- Looks for inherited gene alterations
- May have implications for family members and the person being tested

TUMOUR TEST

- Takes DNA from the tumour
- If a gene alteration is found another test will be needed to confirm if hereditary

Access to a genetic counsellor

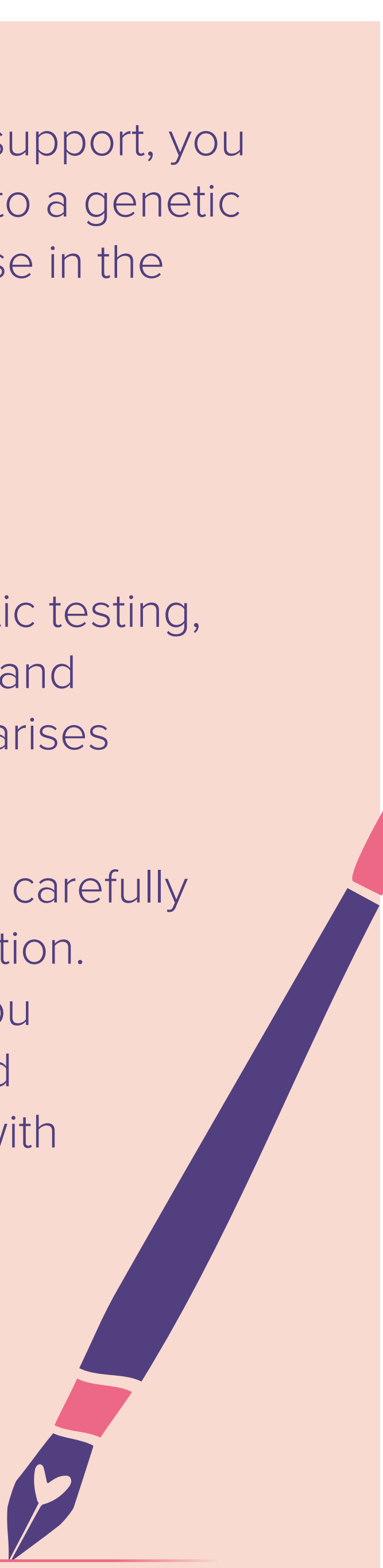
It is completely understandable to feel anxious about genetic testing. Your cancer team will be able to take you through the process and discuss what the implications may be for you and your family.

If you would like additional support, you can also ask to be referred to a genetic counsellor who will specialise in the issues you may be facing.

Giving your consent

If you choose to have genetic testing, you will be asked to review and complete a form that summarises your discussion.

You should be given time to carefully review any forms or information. If anything is unclear, or if you need any wording explained or translated, bring this up with your cancer team as soon as possible.



GETTING YOUR RESULTS

Results will usually be delivered by the health professional who took the original test sample(s), either over the phone or face to face.

What could my test results look like?

Results can include a lot of unfamiliar language and should always be given to you by a trained professional. You should also feel free to ask any questions you may have.

Some of the common terms you may see or hear include:

Pathogenic

Sometimes referred to as ‘positive’, this means the test shows you have a gene alteration that is very likely to be cancer-causing.

Likely Pathogenic

The test shows an alteration that is likely to be cancer-causing.

Variant of Uncertain Significance

The test shows an alteration that is known; however, there is uncertainty of its behaviour. It is not currently known to be cancer-causing and should not affect your care. It may be that, in the future, more becomes known about this alteration.

Likely Not Pathogenic

Sometimes referred to as ‘negative’, the test shows a gene alteration that is unlikely to be cancer-causing.

Not Pathogenic

The test shows an alteration that is understood not to be cancer-causing.

What happens after I get my results?

What happens after you receive your results will depend partly on the test or tests that you have had.

1 You had both a blood and a tumour test (parallel testing)

If you were given both a blood test and a tumour test at the same time, your clinical team will be able to make a fully-informed decision about your treatment and talk through any implications for you and your family.

2 You had a blood test (germline testing)

If you were given just a blood test initially, and this comes back negative for a BRCA gene alteration, your team may still advise that you have a tumour test to check for non-inherited (somatic) gene alterations, as these may influence your treatment choices.

There can be several reasons for this, but it will likely be because your clinical team suspects the presence of a BRCA gene alteration based on your symptoms.

3

You had a tumour test

If you were given a tumour test initially, and this shows you do not have a BRCA gene alteration, you may still be advised to have a blood test to check for possible hereditary gene alterations.

This is because not all alterations are always detected from tumour testing and the results from a blood test may have important implications for your family.

A variant of uncertain significance (VUS)

If your results show a variant of uncertain significance, your clinical team will likely treat this as a negative result. However, they will note the findings in your patient record.

Although unlikely, should the gene alteration found become reclassified by the testing laboratory as disease-causing at a later date, you would be contacted and the implications discussed with you.

Passing hereditary gene alterations on to children

Hereditary genes alterations have a 50% chance of being passed on to children (of either gender).

INFORMING FAMILY MEMBERS

Is there support to communicate with family members?

If you are worried about how to talk about your test results with family members, you should be able to discuss this with a genetic counsellor.

It may also be possible to ask your GP or cancer team for a letter that explains your results to family members, and any steps they may need to consider.

Can they access screening or preventative care?

Whether they are female or male, if a member of your family is at risk of having inherited a gene alteration that is known to be cancer-causing they should discuss their options with a GP or specialist.

They will be able to refer them on for genetic testing to see if they carry the same gene alteration.

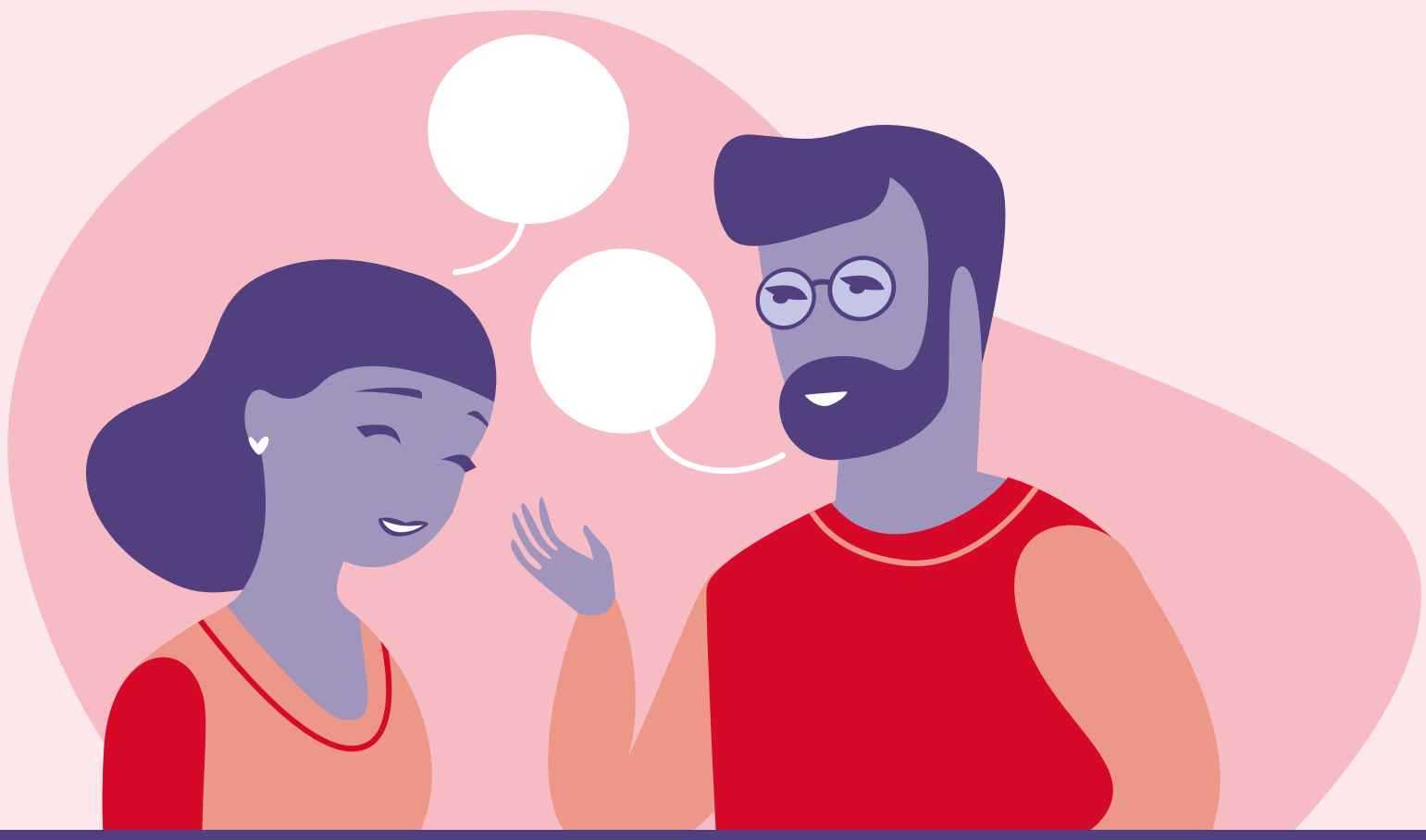
If they are shown to have a gene alteration, they may have the option of:

Screening or regular checks aimed at spotting a cancer as early as possible

Preventative care, such as surgery to help prevent ovarian or breast cancer

Is it possible to minimise risk through lifestyle choices?

While it is not certain what causes ovarian cancer, there is good evidence to suggest that maintaining a healthy weight and not smoking reduces risk.



Frequently asked questions

Can I get a test privately if not on the NHS?

It is possible to get some genetic testing done privately.

We would always advise that you speak to your clinical team or a trained counsellor before deciding to have testing done if it is not provided by the NHS.

Do I need a genetic test to access treatment?

A genetic test may be used to see what the best treatment option(s) would be.

An example of this is in ovarian cancer, where you may need a test before being given certain medicines.

I am nervous about the results, what if I could have passed a higher risk of cancer to my children or grandchildren?

It is natural to be concerned about the risk of passing certain gene alterations

onto children or grandchildren. However, this knowledge can be very important for them to have and may help protect them or mean that they are better able to spot any cancer early.

If you feel like you need to discuss this in detail, you may be able to with a genetic counsellor through the NHS.

Do I have to tell a relative if I have a gene alteration they could have inherited?

You are under no obligation to disclose your results. However, the findings could carry important implications for others in your family.

If you would like to discuss your options, or you need help in how you might tell family members, this support should be available to you.

It may be possible that your genetics team can contact members of your family on your behalf by letter if needed.

I feel guilty about passing on a cancer-causing alteration – what should I do?

There is a lot of debate about what causes gene alterations. What is important to remember is that it is never a person's fault.

It is natural to be worried about the implications for you and family members. If you need support on this issue, please speak to your clinical team or contact *Ask Eve* using the details in this booklet.

How long does it take to get results?

Once the sample has been taken it can take a few weeks to get the results. A typical wait would be between 2 to 8 weeks.

Will having a BRCA gene alteration affect my insurance?

While a diagnosis of ovarian cancer may affect your ability to get insurance, having a test for a gene alteration such as BRCA will not impact this or influence existing insurance premiums. This is because there is broad agreement that having a test should not affect insurance.

Can results be uncertain / inconclusive?

While unlikely, it is possible that a test could need to be redone or that the results will come back as inconclusive.

In these cases your cancer team would explain any impact on your care and what they recommend as a next step.

Glossary

Biopsy

This is a medical procedure that involves taking a small sample of body tissue so it can be examined under a microscope. In ovarian cancer this usually refers to taking a small sample of the tumour.

DNA

This stands for deoxyribonucleic acid. Present in nearly every cell in the body, DNA contains lots of genes, which carry the genetic information that acts as the instructions the body needs to grow and function properly.

Germline testing

In genetic testing, germline refers to alterations in genes that can be passed down through generations (are hereditary/inherited).

Germline gene alterations will be present in all cells and will therefore show up in blood or saliva tests, as well as most tumour tests.

High-grade serous ovarian cancer

This is the most common form of epithelial ovarian cancer.

Ovarian cancer

Ovarian cancer is commonly used as an umbrella term for ovarian, Fallopian Tube and primary peritoneal cancer.

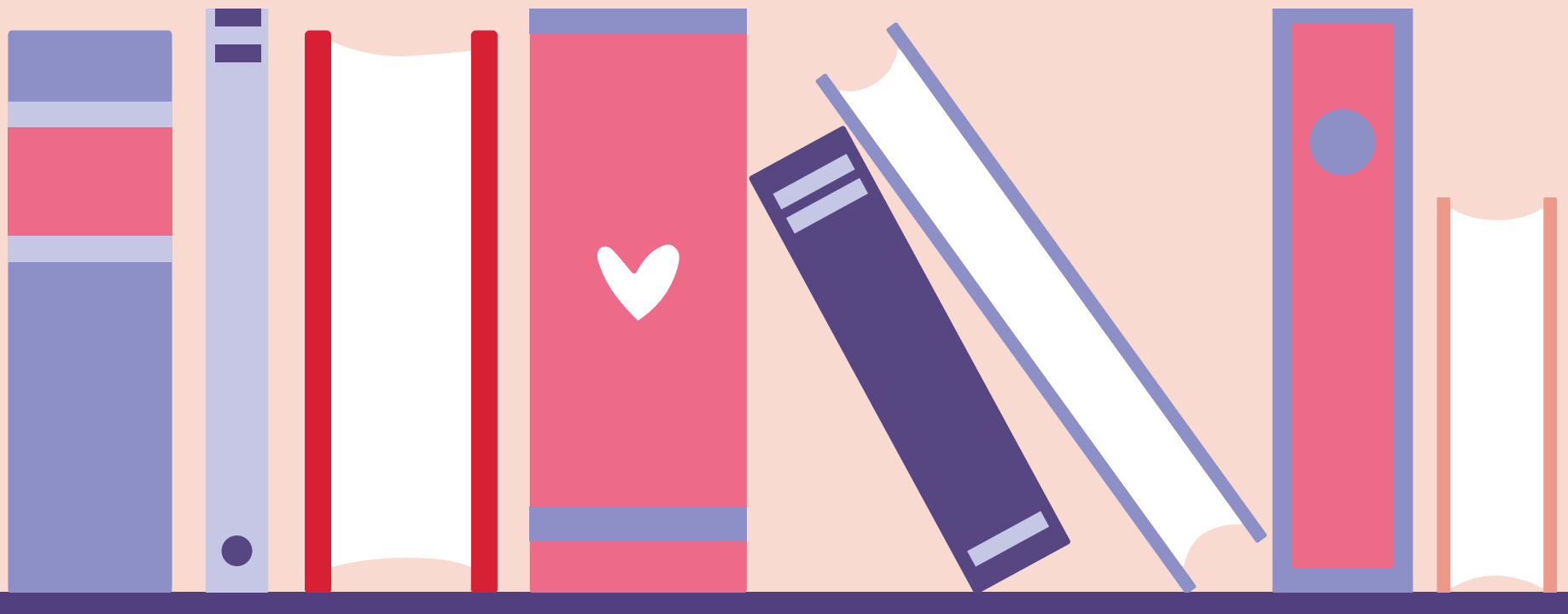
Pathogenic

A pathogenic gene alteration/mutation means that it is potentially cancer-causing.

Somatic alteration / mutation

A somatic alteration (or mutation) means a change to the gene which is present in the tumour alone and is not found throughout the rest of the body.

It is important to note that having a somatic gene alteration in the tumour tissue does not mean that you cannot also have a germline (hereditary) gene alteration.



THE PROCESS OF BRCA TESTING FOR PEOPLE WITH OVARIAN CANCER

Every person is different

While this diagram shows a typical process, every person is different. If you have questions, ask your cancer team or speak to *Ask Eve*, who can provide more information.

1

INITIAL DISCUSSION WITH YOUR CANCER TEAM

Genetic testing is likely to be brought up by your cancer team. This can take place any time after your diagnosis. If you are concerned about the implications, it may be possible to speak to a counsellor at this point.

2

GIVING YOUR CONSENT

Consent will usually be needed, and your cancer team will discuss this with you. You should be provided with information on the implications for yourself and your family as part of this process.

If you provide your consent verbally, this will be documented in your notes.

3

REFERRAL FOR A GENETIC TEST

The type of test(s) you are referred for will be based on national guidelines. You may be referred for a blood test, a tumour test or both (known as parallel testing).

4A

HAVING A TUMOUR TEST

Tumour testing involves taking a sample of the ovarian tumour (via a biopsy or during an operation).

Tumour testing results may have implications for family members, although this is not always the case.

4B

HAVING A BLOOD TEST (GERMLINE TESTING)

Blood tests look for germline gene alterations. These are ones that can be inherited and passed down through generations.

5

GETTING YOUR RESULTS

Your results can be delivered in person or over the phone. If possible, it is recommended that you ask for a face to face or video consultation.

Results should always be explained by a trained oncologist, gynaecologist, or other member of your cancer team, such as a nurse specialist.

If you feel anxious about your results, you should be given the option of counselling.

6A

YOU HAVE A GENE ALTERATION (BRCA1/BRCA2)

This means that your test has shown you have a gene alteration that is likely to be the cause of your cancer.

Depending on the type of test you have had, this may show an alteration that is only in the tumour, or one that is not only in the tumour and may be hereditary.

If you have had a tumour test, you may be offered a blood test as well.

6B

YOU DO NOT HAVE A GENE ALTERATION

This means that your test has shown you do not have a gene alteration.

YOU HAVE A VARIANT OF UNCERTAIN SIGNIFICANCE (VUS)

This means you do have a gene alteration, but it is not known to be cancer-causing and will not affect your care.

A small proportion of these may get re-classified as cancer-causing in the future as we learn more about these alterations. If you have a VUS it will be noted in your patient record.

Whether positive or negative, your results will help inform your treatment options so that you can receive the best care.

ASK EVE

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References: 1. NHS England. Clinical Commissioning Policy: Genetic Testing for BRCA1 and BRCA2 Mutations. July 2015. **2.** Manchanda et al 2020, Randomised trial of population-based BRCA testing in Ashkenazi Jews: long-term outcomes. BJOG 2020, 127, 364-375.