



Genetic testing and hereditary ovarian cancer

A guide for women with ovarian cancer
and their families

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Introduction

If you have a diagnosis of ovarian cancer, it is a common reaction to wonder what caused it or worry that other family members may be at risk. This guide talks through what a family history of ovarian cancer means. It explains whether your family members are at risk of developing cancer as well. It also explains whether you and your family could have a genetic test, and what it might mean for you and your family if you do have hereditary ovarian cancer (cancer that can run in the family).

This guide has been written with the help of health professionals and experts in ovarian cancer and genetics. We have also included thoughts from women who either have hereditary ovarian cancer themselves or are at risk and have been through many of the experiences you are facing.

We hope it provides you with enough information to make an informed decision about having a genetic test, and supports you and your family in dealing with what the results of the test might mean for you if you choose to go ahead.

We understand how isolating it can feel to have a diagnosis of ovarian cancer. That's why we offer a full programme of support and information across the UK including opportunities to meet others going through similar experiences. If you would like to know more, or if you have any questions or concerns about any of the information you read in this guide, please get in touch with us.

With warmest wishes,
From all of us at Target Ovarian Cancer

What is a cell?

Cells are the building blocks that our bodies are made of. We have lots of different types of cells that do different things.

What is DNA?

DNA stands for deoxyribonucleic acid. It is a chemical in our cells that tells the cells how to work and behave.

What is a gene?

Genes are made up of short sections of DNA. Our genes carry information about us like the colour of our eyes.

Why do genes have names?

Genes have names so that we can tell them apart. This helps us to talk about any problems or changes in specific genes.

There are different types of ovarian cancer. To be able to fully understand what your treatment options are it is helpful to have specific information from your medical team about your diagnosis, including the type of ovarian cancer, stage and grade.

You can use the space below to record this information if you wish.

(You can find out more about the different types of ovarian cancer, stages and grades at targetovariancancer.org.uk/types)





Is my ovarian cancer hereditary?

Cancer is a common illness so it is not unusual to have more than one family member with the same type of cancer and/or different types of cancer within one family. However, some families may have a greater chance than normal of developing ovarian cancer.

Up to 20 per cent of cases of ovarian cancer occur because of a genetic cause - a mutation (alteration or change) in one or more genes known to increase the risk of ovarian cancer, which has been passed on from your mother or father. Some types of ovarian cancer (such as serous epithelial ovarian cancer) are more likely to be caused by a mutation in a gene than others (such as mucinous or germ cell ovarian cancer).

How do mutations in genes cause cancer?

Genes are instructions made from our DNA which tell the cells in our bodies how to work. Every cell in our body contains genes that decide and control our body's functions, growth and appearance. Each person has two copies of most genes, one inherited from their mother and one from their father.

In general, our genes enable our cells (the building blocks that make up our body) to function normally. However, sometimes the genes that we have inherited have small changes, known as alterations or mutations. If one of our genes is altered or mutated, this can sometimes result in an increased risk of developing different illnesses compared to people who don't have the genetic change.

A person with a gene mutation usually has a 50 per cent (one in two) chance of passing it on to their children.

Mutation? Alteration? Fault?

When a change occurs in an inherited gene it is called a mutation. You might hear it called a faulty gene or an altered gene elsewhere, but in this guide it is referred to as a 'mutation' or 'mutated gene'.

What is meant by hereditary or familial ovarian cancer?

'Hereditary' means the passing on of specific characteristics in your DNA (genetic makeup) from one generation to another – in this case, passing on a mutation in a gene. The term 'familial' means something that occurs or tends to occur in families.

'Familial cancer' or 'hereditary cancer' is a cancer which has developed as a result of carrying a mutation in a gene. Throughout this guide, we refer to it as hereditary ovarian cancer.

How do I know if I have hereditary ovarian cancer?

Women diagnosed with non-mucinous epithelial ovarian cancers including high-grade serous ovarian cancer (the most common form of epithelial ovarian cancer) are often offered access to genetic testing for mutations in their BRCA1 and BRCA2 genes, even if they have no family history of ovarian cancer. Over 90 per cent of ovarian cancers diagnosed are non-mucinous which means that the majority of women diagnosed with ovarian cancer fit the criteria for genetic testing. This means that genetic testing could be available even if you don't know your family history. >



Some women may not be eligible for genetic testing due to the specific type of cancer they have (for example germ cell or sex cord stromal tumours) but it is important that all women discuss genetic testing with their clinician, oncologist (a doctor who specialises in cancer treatment) or genetic counsellor (a professional who is trained to talk to you about the risks and benefits of genetic testing) to find out if testing is appropriate.

Mutations in genes such as BRCA1 and BRCA2 can occur in both women and men in any family so a gene mutation can be inherited from either your mother or your father. They are more common in some communities than others. For example, members of the Ashkenazi Jewish population are approximately 10 times more likely to have a mutated BRCA1 or BRCA2 gene, and so are more at more risk of developing hereditary ovarian and/or breast cancer than people from the general population.

"I had no previous family history of cancer, on either side of my family, other than an uncle who died of bowel cancer. I didn't even know about possible familial risk until I attended a Target Ovarian Cancer Being Together day, after a question was asked to the expert panel."

Shani

What should I consider if I have hereditary ovarian cancer?

There are a number of things to think about if you find out you have hereditary ovarian cancer. Firstly, there's the impact on you – it may have some implications for the treatment of your ovarian cancer. Over the last few years new drugs have been developed that target ovarian cancers specifically in women with a mutated BRCA1 or BRCA2 gene and you may be eligible for treatment with these drugs. Please speak to your oncologist about this. Some hereditary ovarian cancer genes also increase your risk

of developing other cancers, including breast cancer, and so you would need to consider ways to manage this increased risk. Your medical team will support you with this.

Secondly, there could be an impact on family members who may also have inherited the gene mutation which could put them at increased risk of ovarian and breast cancer. This guide talks through these considerations and gives more information on each.

"I think it is very important to find out your BRCA status as not only can it affect you... but also – more importantly – you can protect your family too. Keeping my daughter 'safe' has helped to keep me driven throughout my treatments. It broke all of our hearts when we had it confirmed that she too was a BRCA1 carrier. I was diagnosed simultaneously with both breast and ovarian cancer in July 2014 and then found out I had inherited a BRCA mutation from my father. I am also Ashkenazi Jewish which I know now meant I was at a much higher risk. I didn't know before my diagnosis that you could inherit ovarian or breast cancer from a man. It is hard enough being told you have cancer but knowing that it was a BRCA mutation that had caused both my cancers made me angry in that it could have and should have been prevented. Knowledge is power."

Berni



Tumour profile testing

All tumours have genetic mutations that arise as the tumour develops. These are called 'somatic' mutations and are not present in the normal healthy cells of a person who has cancer. Somatic mutations cannot be inherited.

The inherited genetic mutations referred to in the rest of this guide which may increase the risk of developing cancer are known as 'germline' mutations. This is because they occur in the body's germ cells – cells that develop into eggs in women and sperm in men. Germline mutations can be passed on from parent to child when a sperm and egg come together.

When a tumour is removed during a biopsy or surgery, the tissue will be sent to a pathologist (a professional who studies the changes in the body's cells caused by disease) who will study the tissue under a microscope and may arrange additional tests on the tissue to profile it. This tumour profiling test gives information about the somatic mutations, and can help the medical team identify which treatments the tumour is most likely to respond to, and in some cases whether the woman is eligible for treatments or certain clinical trials.



Which genes are most likely to have a mutation which increases the risk of ovarian cancer?

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Hereditary ovarian cancer is most commonly caused by a mutation in either the BRCA1 or BRCA2 gene. Some mutations in other genes such as RAD51C, RAD51D and BRIP1 are also known to be associated with an increased risk of ovarian cancer, but scientists have not yet found all of the genes associated with an increased risk.



What are the BRCA1 and BRCA2 genes?

The BRCA1 and BRCA2 genes (Breast Cancer genes) were discovered in the mid-1990s in families that had a lot of cases of breast cancer. BRCA1 and BRCA2 genes are normally protective against cancer because they help repair breaks in DNA that can lead to cancer. But mutations can occur in these genes which increase the risk of developing breast cancer and increase the risk of developing ovarian cancer from two per cent (among women generally) to 30-50 per cent for BRCA1 and 10-25 per cent for BRCA2 gene mutations.

Mutations in the BRCA1 or BRCA2 genes account for the majority of hereditary ovarian cancers. About 15 per cent of women who develop ovarian cancer have a mutation in either their BRCA1 or BRCA2 gene.

It is important to note that not everyone who inherits a mutation in their BRCA1 or BRCA2 gene will develop cancer but it does substantially increase the risk.

Which other gene mutations put me at risk?

Mutations in the BRCA1 and BRCA2 genes account for the majority of hereditary ovarian cancer cases. However, mutations in other genes can also increase the risk of ovarian cancer:

- Lynch Syndrome (also known as Hereditary Non-Polyposis Colorectal Cancer or HNPCC) is a type of bowel cancer predisposition which is linked to mutations in one of the genes **MLH1, MSH2, MSH6 and PMS2**. A woman with a mutation in the **MLH1, MSH2 or MSH6** gene has an estimated 10 to 17 per cent chance of developing ovarian cancer at some point during her lifetime. There is a much lower or possibly no increased risk for **PMS2**. The chance of developing other cancers including endometrial, small bowel, urinary tract, stomach, gall bladder and pancreas can also be increased by a mutation in one of the Lynch Syndrome genes.
- Mutations in the **RAD51C, RAD51D and BRIP1** genes can increase a woman's risk of ovarian cancer. However these mutations are very rare. Women carrying mutations in these genes have about a five to 10 per cent risk of developing ovarian cancer by the time they reach the age of 80.

- Mutations in the **STK11** gene may also increase the risk of developing ovarian sex cord-stromal tumours – a different type of ovarian cancer. Mutations in this gene cause Peutz-Jeghers syndrome, which is an extremely rare condition estimated to affect one in 100,000 people. People with Peutz-Jeghers syndrome have an 18 per cent risk of developing gynaecological cancers by age 70.
- Through ongoing research, newer genes such as **FANCM** are being identified which may slightly increase susceptibility to high grade serous ovarian cancer.

Mutations in different genes carry different increases in risk. A clinical geneticist (a doctor who specialises in genetics) or a genetic counsellor (a professional who is trained to talk to you about the benefits and risks of genetic testing) will be able to give you a more accurate and personalised risk assessment.

This guide focuses on information about the BRCA1 and BRCA2 gene mutations as this is what is most commonly tested for at the moment. Testing is currently in development for a number of other genes. For the most up-to-date information about genetic testing, please contact Target Ovarian Cancer's Support Line on **020 7923 5475**



Getting tested for a BRCA1 or BRCA2 gene mutation

What should I do if I think I have hereditary ovarian cancer?

Your oncologist (or another member of your medical team) may have already talked to you about genetic testing. Some hospitals offer genetic testing in the same place that you are having/had your treatment (the oncology clinic). This is called mainstreaming. Others may refer people to a genetics centre (a specialist clinic that looks at everything to do with medical genetics including genetic testing) for a more in-depth conversation about genetic testing.

If you have been diagnosed with ovarian cancer and not offered genetic testing, arrange to talk with your oncologist and discuss whether you may be eligible. There may be reasons why genetic testing might not be appropriate for you and your team can discuss this with you. If you haven't been offered a test and you are still wondering whether genetic testing might be right for you, you may still be able to ask for a referral to a genetics centre via your GP or oncologist. You can find your nearest centre at www.bsgm.org.uk/information-education/genetics-centres

You may then be offered the chance to speak with a genetic counsellor (a professional who is trained to talk to you about the risks and benefits of genetic testing) to help you make a decision about whether or not to have the test, and what the effects would be for you and your family members based on your choice.



What should I consider before having a genetic test?

There are some important things to think about before going ahead with genetic testing. In particular you should think about the impact of the testing on yourself and on those who are close to you. It's important that you have a chance to discuss all your concerns and uncertainties about genetic testing before you decide whether or not to have the test.

In many places genetic testing is done by the same team and in the same place as your ovarian cancer treatment (the oncology clinic) so you won't be referred to a genetics centre. This is called mainstreaming and it means that genetic testing can happen faster than if you had to go elsewhere. Your medical team should give you written information about genetic testing and you should have the chance to ask them any questions that you might have. It's important to tell your team if you still have unanswered

questions or if there is anything you are not sure about after your discussion with them. In this situation it might be helpful for you to be referred to a genetics centre so that you can speak to a genetics counsellor before deciding whether to have genetic testing.

Considerations for me

Some women find it helpful to have an explanation for why they developed ovarian cancer. But there will be other implications for you if you find out you have a hereditary cancer risk as you will have an increased risk of developing other cancers. In the case of the BRCA1 or BRCA2 genes you will have a higher risk of developing breast cancer (in comparison to the general population). Your options for managing this risk will depend on your current cancer diagnosis and treatment. There is more information about this in Chapter 7 of this guide.

The results of genetic testing may also have implications for your ovarian cancer treatment. There is more information about this in Chapter 7 of this guide.

Considerations for my family

A second consideration is the impact on your family. Other members of your family may also have the gene mutation if you do, including your mother or father, siblings, aunts, uncles and cousins, depending on which side of the family the mutation is passed down. The children of someone with a BRCA1 or BRCA2 gene mutation have a 50 per cent (one in two) chance of having inherited it and therefore being at increased risk. They also have a 50 per cent (one in two) chance of having inherited a normal copy of the gene from the parent with the gene mutation. In that case, they would not have an increased risk of cancer due to a gene mutation.

Women with a BRCA1 or BRCA2 gene mutation have a high risk of developing breast and ovarian cancer and men may have an increased risk of developing prostate cancer and male breast cancer. There may also be a small increased risk of pancreatic cancer for men and women who carry BRCA2 gene mutations.

There is information in Chapter 6 of this guide about discussing your genetic test result with your wider family.

Due to the potential implications, it can be very helpful to discuss genetic testing with your relatives at an early stage. If you have contact with your local genetics centre prior to deciding about genetic testing, they will talk about these issues with you in more detail.

When should I have genetic testing?

If you are eligible for a genetic test, it is important to ask yourself, "When is the right time for me to have genetic testing?" There is evidence that having genetic testing soon after a cancer diagnosis can be distressing. But having genetic testing early also means that people with a gene mutation can receive treatment such as PARP inhibitors (a group of drugs which work by stopping cancer cells repairing themselves) at an earlier stage. There is more information about PARP inhibitors in Chapter 7 of this guide. If you feel that now is not the right time to have genetic testing, you may choose to think about it again at a later stage. Some women have DNA stored (from a blood sample) so that it is available for genetic testing in the future.

"I felt that I was on a hamster wheel of cancer after being diagnosed. It's hard to keep your head in gear while being practical the whole time."

Berni



What is a genetic test and what are the possible results?

There are a few stages to having a genetic test.

- **Deciding if the test is right for you.**

In many places genetic testing is done by the same team and in the same place as your ovarian cancer treatment (the oncology clinic). This means that someone in your medical team will speak to you about genetic testing during one of your oncology appointments. You may be asked to complete a form about your family history. You may find it helpful to talk to your family members to gather as much information as possible. Don't worry if you can't answer any/all of these questions. Lots of women don't know about their family history and it's important to remember that not knowing does not affect your test.

During the appointment you will be given information about what a genetic test involves and what the results might mean for you and your family. You will also be able to ask questions. It's

important that you take your time to think about whether you want to have the test. Some centres will want you to wait until your next appointment to decide. If you are struggling with the decision you should be given the chance to talk to someone about your feelings. This person may be called a genetic counsellor (a professional who is trained to talk to you about the benefits and risks of genetic testing).

If your treatment centre does not offer genetic testing then your oncologist can refer you to the local genetics centre for the test. You will be asked to make an appointment to visit the genetics centre where a clinical geneticist (a doctor who specialised in genetics) or a genetic counsellor will discuss with you what is involved in a test and what the implications might be for you and your family.

- **Having the genetic test (blood test).**

After this, if you choose to go ahead with the test, you will have some blood taken to be tested. In lots of oncology clinics this will happen during your next routine blood test (for example a blood test before having chemotherapy). In other oncology clinics you may have the choice to go back to the clinic at a different time (because your appointment is too soon or not soon enough).

Your blood sample will be sent to a genetics laboratory to be tested. In many places, you will be given a choice of how you'd like to receive the results of the test – whether by phone or in writing, or sometimes face to face.

- **Receiving the results.**

The time it takes for your blood test to be analysed and the results to be available varies slightly between the genetics centres and you will be told how long it will take for yours. It is usually between four and ten weeks.

When you're told about your test result, you will be given some more information about what the result means and what the next steps are. You will also be able to speak with your treatment team in the oncology clinic (or the genetics team at the genetics centre) who will talk you through your result and the next steps in as much detail as you need.

"At the first meeting, they talked about the likelihood of it being genetic, and completing the family history forms. Because an aunt on my dad's side had died of ovarian cancer, and another of breast cancer, the counsellor said this indicated a strong familial link."

Berni



What are the possible results of a genetic test?

There are three possible results for testing for a BRCA1 or BRCA2 gene mutation:

- 1 Mutation present – sometimes called a positive test result:** Testing identifies a mutation that causes a significant change to the gene and is therefore very likely to be the cause of your cancer.
- 2 Variant of unknown significance (VUS) – sometimes called an inconclusive test result:** Testing may identify a mutation or an alteration in the gene where it is uncertain whether or not this would cause an increased cancer risk. This is known as a variant of unknown/uncertain clinical significance because it is not clear if it causes significant changes to the gene.
- 3 Mutation not present – sometimes called a negative test result:** Testing has not identified any gene mutations.





What is the impact of the different results for me and my family?

What is the impact of 'mutation not present'?

Some people can feel relief and reassurance if they are not found to have a genetic cause for their cancer.

If you have this result, and do not have a family history of ovarian and/or breast cancer (two or more close relatives with either ovarian or breast cancer), it is most likely that your ovarian cancer was a one-off in your family ('sporadic'). It means your risk, and the risk of your children, of developing breast cancer and other cancers associated with the BRCA1 and BRCA2 genes is probably similar to the general population.

If you have this result, but have a strong family history of ovarian and/or breast cancer, the result can be less helpful. Scientists still do not know all the mutations in different genes that may increase a woman's risk of ovarian cancer, so it is possible that you have a mutation in a different gene not found by this test. This means there is still a level of uncertainty even after genetic testing.

The results of genetic testing may also have implications for the treatment you are offered for ovarian cancer. There is more information about this in Chapter 7 of this guide.

Can my family members still receive a genetic test if my result is ‘mutation not present’?

Predictive genetic testing would not be available for the rest of your family as this result makes it less likely that there is a significantly increased risk of developing cancer in your family. If you have a family history of ovarian and/or breast cancer, close relatives may still be able to access additional screening or discuss risk reduction, which your genetics specialist could help assess.

What is the impact of ‘variant of unknown significance’ (VUS)?

If you have been told the result showed a genetic variant of unknown significance (or VUS), this means that the test has found a gene alteration in the BRCA1 or BRCA2 gene but it is not known if it causes an increased risk of ovarian cancer or not. The majority of VUS results are harmless differences in a person’s genes, but if it has not been seen many times before, then it is included in the test report as being of unknown significance. The proportion of women who are given a VUS result is decreasing as scientists learn more and more about the different alterations that increase the risk of ovarian cancer. It may also mean that your VUS is reclassified over time. As more is discovered about genes, there is likely to be further information about the VUS in the future and you may like to contact your Clinical Genetics Service to discuss this in a few years’ time.

Can my family members still receive a genetic test if my result is ‘variant of unknown significance’ (VUS)?

If you have a VUS, you will not be offered predictive genetic testing for the rest of your family. However, if you have a family history of

ovarian and/or breast cancer, close relatives could receive risk reducing advice.

If a VUS is found, your family may feel more uncertain than before. You may find the uncertainty very difficult to understand or deal with emotionally, as it is less clear whether you and other family members have an increased risk. So it’s important that you ask your doctor or genetic counsellor for support and advice about the options available to you.

What is the impact of ‘mutation present’?

If you’ve been told there is a mutation present, you will be told whether the mutation is in your BRCA1 or BRCA2 gene. The result will have an impact on your risk of developing other cancers, the risk of your family members developing cancer, and it may also have an impact on your treatment for ovarian cancer. You will receive more counselling to explain the impact of this result.

“The genetic counsellors were brilliant and very sensitive in the way they approached it. They offered further support and counselling.”

Berni



“My test came back negative which was good but also left a lot of questions unanswered for me and my relatives. I still have a strong family history which leaves us wondering why and what the unknown possible risks are.”

Sue

“I was very stunned. After I’d completed the family history form I’d been told I was at a very low risk of having the gene mutation so didn’t have any counselling about what the impact of a positive test would be.”

Shani

How might I feel?

"It adds another dimension to the journey, just when you think you're through it and can get off the wheel; finding out about BRCA throws you off kilter. It's the hardest part to deal with because you know cancer is not going away."

Berni

Naturally people can have very different feelings and reactions when they find out they have a gene mutation that explains their cancer diagnosis. At first many women feel shock, anger or anxiety. Some people expect to have a gene mutation and are glad to have an explanation for the cancers in their family.

"I felt like I'd been diagnosed all over again, which sounds dramatic, but I was really shocked. I got over this shock by reassuring myself that at least my children would know about their risk."

Shani

"If I'm honest, knowing I have a faulty gene has given me a sense of relief because it helped explain why I was unlucky to get cancer twice. But then I realised the implications for my family."

Adele

With time, most women adjust to this new information. Many are pleased that although it does not change their own diagnosis, there is important information available for other family members.

"My sister pointed out that now she can be monitored and will not have to go through the same as me."

Berni

It is important for you and your loved ones to remember that you can't control the genes you inherit from your parents or the ones you pass on to your children.

"I felt a bit guilty that I could have passed this on to my children, but you can't choose what genes you pass on."

Shani

You will have the option of a follow up appointment with your local Clinical Genetics Service to further discuss how you are feeling and the impact the result can have on you and your family. They will be able to provide you with further information and tell you where you can access further support.



"When I was diagnosed 15 years ago as having a BRCA1 gene mutation following my ovarian cancer diagnosis, I wasn't offered information about preventative surgery as less was known about it then. I did unfortunately go on to be diagnosed with breast cancer 10 years later, and now get regular follow ups. The clinicians are always approachable and I have their phone numbers if I'm ever worried about anything. I had a recent scare and called them, and was seen by the clinician the same day."

Diane

What is the impact on my treatment and my risk of other cancers?

For women with ovarian cancer who have a mutation in the BRCA1 or BRCA2 genes, the risk of developing breast cancer is also increased. For a woman in the general population the lifetime risk of developing breast cancer is about 12 per cent (one in eight). If she has a BRCA1 or BRCA2 mutation, the risk is around 65 to 80 per cent. Remember, an increased risk does not mean you definitely will develop breast cancer. There are a number of risk management options which we talk more about in Chapter 7 of this guide.

There is ongoing research into new treatment options for women with ovarian cancer who carry known mutations in the BRCA1 or BRCA2 gene. You can find out more about this research at targetovariancancer.org.uk/clinicaltrials. Studies indicate that the prognosis (prediction of how your ovarian cancer might change in the future) for BRCA1 or BRCA2 carriers may be better than for those with no gene mutation because carriers can have an increased response to specific therapies. We talk more about the impact of having a BRCA1 or BRCA2 gene mutation on your treatment in Chapter 7 of this guide.

What is the impact on my family members?

What is predictive testing?

- If your test shows that you have a BRCA1 or BRCA2 gene mutation ('mutation present'), it is possible that your relatives will also have a BRCA1 or BRCA2 mutation. So adult members of your family can choose to have a genetic test to find out if they have inherited the same mutated gene.

- This is called 'predictive testing' because a positive result ('mutation present') for them means they have an increased risk of developing cancer. It doesn't mean they have cancer or are definitely going to develop it.

- The mutation in your BRCA1 or BRCA2 gene will have been inherited from your mother or father. If they are unaware of their BRCA1 or BRCA2 status, they can access advice about testing, as can their siblings, nieces and nephews (your aunts, uncles and cousins).

- It's important to note that both men and women who inherit a BRCA1 or BRCA2 mutation, whether or not they develop cancer themselves, may pass the mutation on to their sons and daughters.

- Remember, not all individuals with a BRCA1 or BRCA2 mutation will develop cancer.

What does this mean for my siblings?

- Your siblings will have a 50 per cent chance of also carrying the BRCA1 or BRCA2 gene mutation, and will be able to access predictive testing.

What does this mean for my children?

- Your children will also have a 50 per cent chance of inheriting the BRCA1 or BRCA2 gene mutation. Testing is only available to adults over the age of 18 because the risk management options are either not available or not yet necessary for those under 18 and it is important that they make their own informed choice about whether or not to be tested.

"My mum had never had cancer, and wasn't aware of BRCA until I got ovarian cancer and was tested. She subsequently also tested positive and at the age of 75 was diagnosed with breast cancer - caught and treated very early because she was put on a screening programme because of her BRCA status."

Sharon

How do I tell them and how might they feel?

If your relatives are aware that you are having genetic testing, a conversation about the results may arise naturally. Depending on how you are feeling (physically and emotionally) it can feel like a difficult discussion to have. It can be particularly challenging if there are young family members you want to share the information with: we know that some women struggle with the thought of potentially passing on a gene mutation to their children. All of these feelings are completely normal so please remember you are not alone. Some women find that confiding in their partner or a friend can be beneficial. Your local Clinical Genetics Service is also available to provide support.

In many cases women find that their relatives are wondering whether they may have an increased cancer risk and are very accepting of the news about a gene mutation. It means they are able to have a predictive genetic test that can allow them to take action if they are at increased risk.

Many people choose to have predictive genetic testing because they would rather be aware of any increased risk of cancer and take up the chance to have regular tests or even surgery (a risk-reducing operation) to manage this risk. However, knowing about a possible increased cancer risk may cause

anxiety for relatives. Some people are concerned about the possible impact on their work or insurance. There is more information about this in Chapter 8 of this guide. Some people are worried about the impact a possible increased cancer risk might have on future relationships and having children of their own. There is no right or wrong way to feel and there is help and support available, including from your local Clinical Genetics Service.

"I was really worried for my children, but relieved to know they can be tested and be alert for the signs. I was open with my family the whole way through about what it might mean for them."

Shani

"When I was first diagnosed as a BRCA gene carrier, I wanted my daughter tested straight away, but was counselled against it as she was only 13. They said she should be at least 18 and should be fully aware of the implications of the possible results."

Adele

Some women find they have relatives who are resistant to genetic testing and who prefer not to receive the information. Some have relatives they are not in contact with. These situations are challenging and may be distressing. Your local Clinical Genetics Service will be able to discuss this with you. If you think it will be helpful, they can provide an 'open letter' that you can send to relatives that explains about the gene mutation and the genetic testing available to them.

"I was given a letter by my genetics service to share with my brothers and children explaining the gene and about being tested."

Shani

Ultimately, whether and when your relatives decide to have predictive genetic testing is up to them. People are all different and some adjust to the news quicker than others. You will have given them an option that may not otherwise have been available to them.

"All my family are aware, and some have already been tested. My three daughters have had very different reactions. One is finding it difficult to cope with cancer deaths in the family and then my subsequent diagnosis, but says she will get round to getting tested. One does not want to be tested, and did not even want to know the result of my test, but I felt it was important she had all the information. One has been tested and also carries the BRCA1 mutation, and says her team have been fantastic. She's been offered counselling and will be talking to them about preventative measures soon."

Berni

There is a section in Chapter 8 of this guide on implications for a family member who is also found to have a BRCA1 or BRCA2 mutation.





I have a BRCA1 or BRCA2 gene mutation – what now?

How can I manage my increased risk of breast cancer?

Your genetic counsellor will discuss with you the different ways of reducing your risk of developing breast cancer. There are three options to consider - **screening, risk reducing surgery and drug treatment**. The choice will take into account your current health and predictions of whether your ovarian cancer might grow or change. You may also be referred to a family history breast cancer clinic where specialists in this area will take over your care.

Screening

The NHS runs a breast screening programme for women throughout the UK. Women between the ages of 50-70 are typically invited for breast screening every three years, but women at high risk can access screening tests before the age of 50 and any woman can request screening to continue after the age of 70. Women with a BRCA1 or BRCA2 gene mutation will be considered for yearly MRI scans and mammograms from the ages of 30-40 onwards. Ask your genetic counsellor for further information. Screening aims to detect tumours that are too small to be felt by you or your doctor. Breast screening will not stop women from developing breast cancer, but it will help detect tumours at an early stage, when they are easier to treat.



Risk-reducing surgery – bilateral mastectomy (removal of both breasts)

For some women with a BRCA gene mutation, having surgery to remove both breasts may be an option to greatly reduce the risk of developing breast cancer. Your medical team may recommend that you don't have this surgery until after you have recovered from your ovarian cancer treatment. Risk-reducing breast surgery cannot guarantee that you will not develop breast cancer, but the risk afterwards is small enough that breast screening is not needed. Most women are offered the option of having reconstructive surgery to rebuild both breasts using implants and/or tissue from another part of your body. This may be carried out at the same time as the natural breast tissue is removed or it may be done at another time as a separate surgery.

Surgery will have a very big impact on you both physically and emotionally, especially following an ovarian cancer diagnosis. It is important that you take your time and discuss all the advantages and disadvantages with a counsellor and your medical team before making a decision.

"As I'm still dealing with the aftermath of cancer treatment, the counsellors and clinical team have agreed to discuss preventative surgery in a few more months as I feel I need to take a breath. I think I will have it, but haven't decided about reconstructive surgery – I have an appointment with the plastic surgeon to help me decide."

Berni

Drug treatment and lifestyle choices

In some cases, 'chemoprevention' may be considered to reduce the risk of breast cancer. Chemoprevention is the use of drugs, vitamins, or other agents to try to reduce the risk of, or delay the recurrence of, cancer. This includes treatment with drugs such as tamoxifen, anastrozole and raloxifene. Tamoxifen and anastrozole are usually used as treatments for breast cancer, and raloxifene is used to treat or prevent osteoporosis (bone thinning) after the menopause. In this situation they are given to reduce the chance of you developing breast cancer. Your genetics doctor, genetic counsellor or breast cancer specialist can discuss this with you and give you written information on the absolute risks and

benefits of chemoprevention, including the side effects of the drugs and how much they might reduce the risk, before you make a decision.

Women with ovarian cancer who are carriers of a BRCA1 or BRCA2 gene mutation should be offered advice about other factors which may affect their risk of breast cancer. These include:

- The use of the oral contraceptive pill which has long term protective effects for the risk of ovarian cancer but can increase the risk of breast cancer. (If a woman stops taking the pill, this increased risk of breast cancer drops down again.)
- The use of hormone replacement therapy (HRT) which, depending on your clinical circumstances, may increase your risk of developing breast cancer. Your clinician should discuss with you whether the increased risk outweighs the benefit, and what alternatives there are.
- Reducing how much alcohol you drink, stopping smoking, and maintaining a healthy weight through healthy eating and exercise to reduce your risk.

What are the implications for my treatment for ovarian cancer?

There are a number of drugs in use and in development that are targeted at cancers in women with a mutation in their BRCA1 or BRCA2 gene so it is important to ask your clinician if your genetic test result has an impact on your ability to access different treatments or clinical trials.

"My counsellor explained about the increased risk of breast cancer and that I should be screened every year."

Shani

PARP inhibitors

PARP inhibitors are a group of drugs which work by stopping cancer cells repairing themselves. There are currently a number of PARP inhibitors at different stages of development and research.

The PARP inhibitor called olaparib (also known as Lynparza®) has been licensed to treat ovarian, fallopian tube, and primary peritoneal cancer in women who carry mutations in the BRCA1 or BRCA2 genes and whose cancer has come back. However, access to olaparib is different across the UK, and it depends on the number of recurrences of ovarian cancer you have had so you will need to have a detailed discussion with your clinician about your eligibility for this and other PARP inhibitors.

"I knew I would have the mastectomy as soon as I found out I was a carrier. I felt my breasts were ticking time bombs. It is emotionally tough when you get your results back but I had wonderful support and encouragement from other young carriers who had already had the surgery. I had my first preventative surgery two years ago, when I was 26. I was very relieved to get this done as I know I've reduced my risk of breast cancer right down. Now I have to think about the ovarian cancer side. I get my CA125 checked every four months and I know what symptoms to look out for, but I know I will have my ovaries removed when I'm 35 - 40, which will put me into premature menopause. You can change your destiny by having preventative surgery. How wonderful is that."

Gaby

As a maintenance treatment following your first course of platinum-based chemotherapy

If you have a BRCA1 or BRCA2 mutation and are diagnosed with ovarian cancer at Stage III or IV (sometimes called advanced ovarian cancer) your treatment will usually involve a combination of chemotherapy and surgery. This treatment can be very effective but unfortunately some women will need to have more treatment in the future because their cancer will start growing again. A maintenance treatment tries to give women as much time as possible before this happens.

A clinical trial called SOLO1 looked at whether a PARP inhibitor called olaparib (also known as Lynparza®) could be used as a maintenance treatment for women with a BRCA1 or BRCA2 mutation who have been diagnosed with ovarian cancer at Stage III or IV. The researchers measured whether taking olaparib tablets after chemotherapy and surgery would keep ovarian cancer under control for longer than not taking the tablets after chemotherapy and surgery. The first results of this trial were published in 2018 and suggest that using a PARP inhibitor in this situation can help keep ovarian cancer under control for longer than standard treatment.

At the time of writing, this data is very new and this treatment is not currently available on the NHS. Other PARP inhibitors are also being investigated in this setting and we hope the results of these studies will be available in the near future.

As a maintenance treatment following your second (or more) course of platinum-based chemotherapy

If your ovarian cancer returns (recurs) six months or more after you have had treatment with platinum-based chemotherapy (carboplatin or cisplatin) your medical team will usually talk to you about having treatment with platinum-based chemotherapy again. There have been several studies which have shown that taking a PARP inhibitor (as a maintenance treatment)

after chemotherapy in this setting can keep ovarian cancer under control for longer than chemotherapy alone. The PARP inhibitors that have been shown to help in this setting are olaparib (Lynparza®), niraparib (Zejula®) and rucaparib (Rubraca®).

At the moment if you have recurrent ovarian cancer (cancer that has come back more than six months after your last treatment with platinum-based chemotherapy) and a BRCA1 or BRCA2 mutation you are eligible for (allowed to have) a PARP inhibitor as a maintenance treatment after chemotherapy. The exact PARP inhibitor you get will depend on where you live in the UK and your individual situation.

As a solo treatment

There is some evidence that PARP inhibitors can be effective as a treatment on their own instead of intravenous chemotherapy (chemotherapy that is given through a drip in your veins) but there is less research about this than using PARP inhibitors as a maintenance treatment. Your medical team will be able to talk with you about the best treatments for your individual situation.



Taking part in clinical trials about treatment

The best time to look into taking part in clinical trials is when you are first diagnosed with ovarian cancer or when your cancer has come back, before starting treatment. Some studies have restrictions on the number or the types of cancer treatments that you've had before. Talk to your medical team or visit Target Ovarian Cancer's Clinical Trials Information Centre – targetovariancancer.org.uk/clinicaltrials - for information about research on PARP inhibitors and other studies specifically designed for people with a BRCA1 or BRCA2 mutation or hereditary ovarian cancer.



"I was diagnosed with ovarian cancer in 2009, and subsequently tested positive for a BRCA1 mutation. Following surgery and chemotherapy, I had about 10 months of remission before the cancer returned. I then joined a clinical trial for a PARP inhibitor rather than have more chemotherapy. I was happy to be generally living a normal life with no nasty side effects; my cancer shrunk to 'non-measurable disease' and my CA125 tumour marker went from 204 to 10. I am very grateful for the trial that gave me a fantastic year without chemo. Although the drug stopped working for me after 10 months, it is still working for others, and I am hopeful that my involvement helps others."

Sharon



What are the implications for a family member with a BRCA1 or BRCA2 gene mutation?

Risk reducing options

If a family member has predictive testing and has been found to carry a gene mutation, they will have had genetic counselling to discuss the implications and risk management options. In all cases, they will be supported in all of their decisions by a team of professionals.

In the previous section we outlined the options for breast cancer. However, women may also want to consider risk reducing options for ovarian cancer.



“My sister was diagnosed with breast cancer about a month before getting her BRCA result. She took immediate action, with a bilateral mastectomy and reconstruction. A few months after completing treatment, she had her ovaries removed, minimising her risk of ovarian cancer. Six years later she remains cancer free.”

Adele

Removal of both ovaries and fallopian tubes – bilateral salpingo-oophrectomy

This operation will greatly reduce the risk of developing ovarian cancer and may, to a much lesser extent, reduce the risk of breast cancer, although the evidence for this is unclear. There is still a small remaining chance of developing ovarian cancer after the surgery because microscopic cancer cells may have started to grow in the abdomen or pelvis before the ovaries are removed, and these cells will not be removed during the operation.

Removal of both ovaries will mean the immediate start of the menopause. Your medical team will discuss the advantages, disadvantages and risks of taking hormone replacement therapy (HRT) to manage the side effects of early menopause.

In the future, it may be possible to have this surgery in two stages – firstly, removal of the fallopian tubes where the cancers are thought to arise, and secondly, removal of the ovaries. This can delay the onset of the menopause while still protecting against the development of ovarian cancer.

Surveillance

Risk-reducing surgery is the best way to manage the risk of developing ovarian cancer if you have a mutation in your BRCA1 or BRCA2 gene but many people choose not to have this operation straight away. Some people choose to wait because they want to have children, others may want to avoid early menopause and/or the symptoms related to menopause. Some people may not be well enough to have surgery and so want to wait until they are feeling well and the operation is less of a risk. There is currently a clinical trial taking place to look at how effective surveillance (monitoring) is in people at high risk of developing ovarian cancer. This involves using regular CA125 blood tests to work out the chances of someone developing ovarian cancer. This doesn't prevent ovarian cancer but it does detect the cancer at an earlier stage than if no surveillance is done, so it could be a reassuring option until you are ready for surgery. You can find out more about this trial at targetovariancancer.org.uk/clinicaltrials.

Contraceptive pill

Women who have ever used the oral contraceptive pill are less likely to develop ovarian cancer than women who have never used it. Using the contraceptive pill can reduce the risk of developing non-mucinous ovarian cancer (over 90 per cent of ovarian cancers diagnosed are non-mucinous) by as much as 50 per cent. Although the contraceptive pill has been shown to reduce the risk of ovarian cancer, it is not suitable for all women and it can slightly increase a woman's risk of developing breast cancer, although this risk is reversible within ten years of stopping the oral contraceptive pill.

A woman thinking of taking the oral contraceptive pill should first discuss her options with her GP/breast team and/or genetic counsellor.

“My niece plans to have surgery on completion of her family.”
Adele



Other implications

Family planning

The genetic counsellor will be able to provide more information to your family members about having children and the impact on the children they've had already.

The family planning options for men and women with a BRCA1/BRCA2 mutation are:

- To have children without any intervention - each child would have a 50 per cent chance of inheriting the mutation.
- To not to have children at all.
- Adoption.
- Egg or sperm donation.
- Pre-implantation genetic diagnosis (PGD) – some couples may choose this option to avoid passing the BRCA mutation to their children. PGD involves removing a woman's eggs to fertilize in a test tube (IVF). When the embryos start growing but are still tiny (at a few days old), a cell is removed and is tested for the hereditary condition. Once the genetic status is determined, the woman can have an embryo that does not have the condition put back to try to start a pregnancy.

- Prenatal testing - some couples may choose to get pregnant naturally and have a test during the pregnancy to see if the baby has inherited the BRCA1/BRCA2 mutation. The couple could then decide whether to continue with the pregnancy. This is not a common request from couples at risk of passing on a risk of cancer that develops in adults.

Your family members may want to discuss their options with their geneticist who can explain the implications and the funding options available, but it's important to note that there is no right or wrong answer.

Insurance

An open-ended agreement is in place which guarantees that anyone who has had a predictive genetic test (for breast and ovarian cancer) can take out life and critical illness insurance cover without disclosing the results of the test. This agreement, known as the Code on Genetic Testing and Insurance, has been in place since October 2018 and will be reviewed every three years.

However, you should check the Association of British Insurers (ABI) for the latest guidance at abi.org.uk or on

020 7600 3333.

"I was originally told about the possibility of using PGD to have children early on when talking to a genetic counsellor about having the BRCA mutation. The genetic counsellor also told me about the other options including having children naturally in the hope that they would be born without the gene mutation or conceiving naturally then having the embryo tested at 12 weeks. It was through her that I was referred onto a hospital that carries out PGD where I was further informed about PGD in detail. All parents want to protect their children from harm and although I am aware that PGD can't get rid of all the health risks to my unborn child, it does mean that my child won't have the genetic make-up that puts it at such a high risk of breast and ovarian cancer. I also don't want them to have to make the decisions I've had to make on whether to have risk reducing surgery or not, or for them to have to decide on how to have children or for them to worry about it. For me and my family using PGD means that the gene fault stops with me; future generations of my family will never have to worry about a gene that puts them at such high risk of cancer."

Carly





Further sources of support

More from Target Ovarian Cancer

This guide is for women who have been diagnosed with ovarian cancer and who would like to know more about hereditary ovarian cancer.

If you would like more information on dealing with practical and emotional needs after a diagnosis of ovarian cancer, we have a lot of information on our website and a range of information guides for women offering guidance and support.

- **What happens next?** – a guide for women with a recent diagnosis of ovarian cancer.
- **Back here again** – a guide for women with recurrent ovarian cancer.
- **My care, my future** – a guide for women living with incurable ovarian cancer.
- **A younger woman's guide to ovarian cancer** – information on treatment, relationships, fertility and facing an early menopause.

All of our guides can be downloaded from our website at targetovariancancer.org.uk/guides or posted to you as a printed guide through targetovariancancer.org.uk/orderguides.

Other sources of support and information

Genetic Alliance UK
geneticalliance.org.uk | 020 7704 3141

Macmillan Cancer Support
macmillan.org.uk | 0808 808 0000

Cancer Research UK
cancerresearchuk.org | 0808 800 40 40

Breast Cancer Care
breastcancercare.org.uk | 0808 800 6000

Breast Cancer Now
breastcancer.org
familyhistory.breastcancer.org

BRCA specific support

BRCA Kent: a support group and online support forum for BRCA carriers based in Kent
brcakent.org.uk

BRCA Umbrella Support and Social Network: an online support forum for BRCA carriers
brcaumbrella.ning.com

FORCE: a support group for BRCA carriers based in Essex and throughout America
facingourrisk.org
facingourrisk.org/essex

There are several BRCA peer support groups on Facebook with members based in the UK and overseas – facebook.com

Websites for further information:

Association of British Insurers (ABI)
abi.org.uk | 020 7600 3333

National Institute for Health and Care Excellence (NICE guidelines for familial breast cancer)
nice.org.uk/Guidance/CG164



About Target Ovarian Cancer

Target Ovarian Cancer is the UK's leading ovarian cancer charity. We work to:

- improve early diagnosis
- fund life-saving research
- provide much-needed support to women with ovarian cancer

We're the only charity fighting ovarian cancer on all three of these fronts, across all four nations of the UK. Ovarian cancer can be devastating. But there is hope – Target Ovarian Cancer. We work with women, family members and health professionals to ensure we target the areas that matter most for those living with ovarian cancer.

All of our information and publications are subject to an information production system that ensures quality and impartiality. All our publications are peer reviewed by experts in their field: health professionals and those affected by ovarian cancer.

We hope that you have found this publication useful, if you have any comments or suggestions please do let us know.

To access our list of references for this publication please contact us directly.

We make every effort to ensure that the information we provide is accurate. If you are concerned about your health, you should consult your doctor. Target Ovarian Cancer cannot accept liability for any loss or damage resulting from any inaccuracy in this information or third party information on websites to which we link.



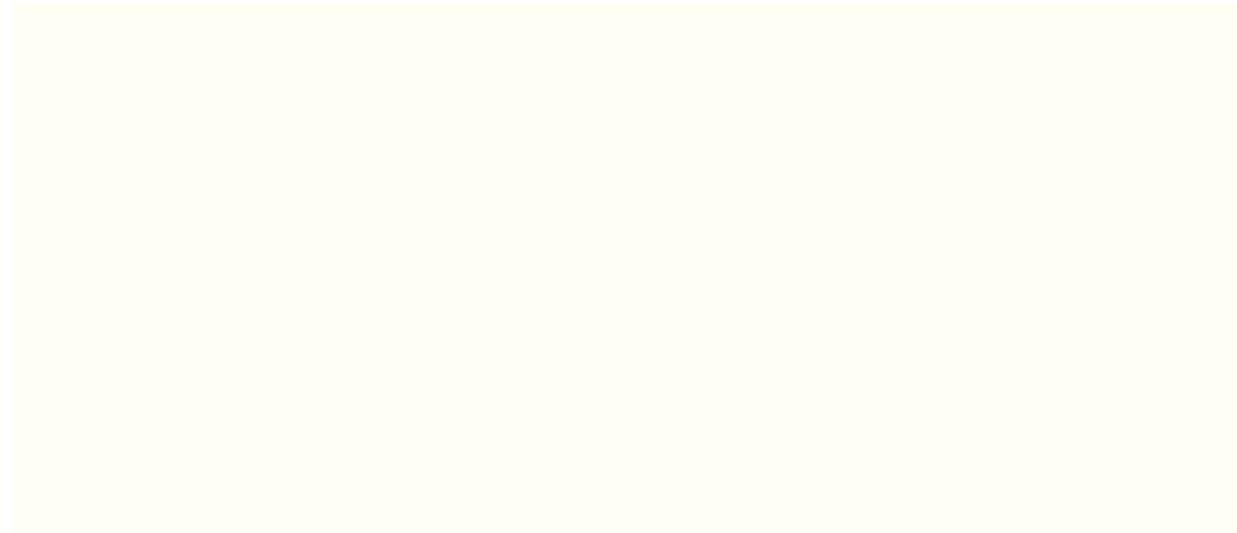
Notes



Useful contacts You can use this space to record useful contacts such as your nurse etc.



Questions I want to ask



My next steps





Target Ovarian Cancer
2 Angel Gate, London, EC1V 2PT



Support Line: 020 7923 5475



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