ovarian cancer action

I'm worried about my family history of cancer

Everything you need to know about BRCA1/2 gene mutations

(NHS England only)

Facts about BRCA

BRCA1 and BRCA2 are genes that repair damage in cells and prevent them from growing and dividing too rapidly. All of us have two copies of these genes. Mutations in these genes can cause cells to become abnormal and grow in an uncontrolled way.

Having a mutation in one of these genes can increase a woman's risk of both breast and ovarian cancer. This can mean that a woman has an 80% chance of developing breast and a 35-60% chance of developing ovarian cancer in her lifetime. There's an increased risk of melanoma too but as yet, the percentage of this increased risk is unknown.

For men, a BRCA2 gene mutation increases the risk of developing prostate cancer and BRCA1/2 gene mutations have also been linked to pancreatic cancer and melanoma in men and women. Those from Ashkenazi Jewish, Dutch, Icelandic, Norwegian, Pakistani, Polish and Swedish populations are more likely to have a BRCA1/2 gene mutation than some other populations.

How many people do BRCA1/2 gene mutations effect?

It is thought that, in the general population, around 1 in every 1000 people carry a BRCA1/2 gene mutation. This figure is, however, significantly higher in certain backgrounds. For example, it rises to 1 in 40 for people from an Ashkenazi Jewish background.

Why is BRCA1/2 testing important?

There can be benefits to genetic testing, regardless of whether a person receives a positive or a negative result.

The potential benefits of a *true negative result,* which is where the test results show that you do not carry a mutation, include a sense of relief regarding the future risk of cancer, learning that one's children are not at risk of inheriting the family's cancer susceptibility, and the possibility that special check-ups, tests, or preventive surgeries may not be needed.

A *positive* test result may bring relief by resolving uncertainty regarding future cancer risk and may allow people to make informed decisions about their future, including taking steps to reduce their cancer risk. In addition, people who have a positive test result may choose to participate in medical research that could, in the long run, help reduce deaths from hereditary breast and ovarian cancer.

Sometimes genetic testing will not give a clear positive or negative result. Some BRCA1/2 gene mutations are yet to be linked with an increased risk of breast and ovarian cancer, these are known as 'variants of uncertain significance' (VUS). Read more about VUS in Section 5 of this guide, entitled 'After the test: What's next?'

How do I know if I have a BRCA1/2 gene mutation?

If you have just one relative with ovarian or breast cancer this is likely to have happened by chance and not due to an inherited genetic mutation. This will not significantly increase your risk of ovarian cancer.

A significant risk is defined as having a 10% chance of carrying a BRCA1/2 gene mutation and is usually worked out using a method known as the Manchester Scoring System. This takes into account personal and family history of breast and ovarian cancer and is often referred to as your carrier probability.

You may be at a higher risk of developing ovarian cancer if:

- Two or more of your relatives who are related by blood have had ovarian cancer
- There have been multiple cases of breast and/or ovarian cancer in your family
- There have been multiple cases of bowel, womb or ovarian cancer in your family
- If any of these cancers presented at a young age (typically before the age of 50), it is more likely that there may be an inherited genetic mutation in your family.

What to do if you are concerned about your family history

Ovarian Cancer Action has developed a BRCA risk tool which will help you explore your family history. You can find the tool at www.ovarian.org.uk/brcarisktool

If you do appear to have a strong family medical history of cancer, you should discuss it with your GP. Before speaking to your doctor make a note of all the cases of cancer in your family and at what age they were diagnosed.

This will help you to have an informed discussion with your GP so that s/he can understand your family medical history and recommend whether it is appropriate to explore it further. The more documented evidence you have, the easier this process will be.

If your GP thinks that you have a significant family history s/he will refer you to your nearest genetics clinic for genetic counselling. If you have serious concerns about familial cancer ask your GP to refer you.

In England genetics services are commissioned through the NHS, so anyone can be referred to a genetic service and your GP does not have to pay for this out of their own budget. Note that access to services across the UK can be patchy so it's important to be persistent if you feel you're not getting access to the services you're entitled to.

How do I get tested?

BRCA1/2 genetic testing is usually carried out at a genetics clinic and, theoretically, anyone can be referred to a genetic service. You should also be offered genetics counselling before you decide whether to be tested. However the guidelines to accessing this service can often be confusing, and people are sometimes unclear about what they are entitled to, and where to access services. The table below has been designed to explain what your entitlement is and the steps to take if you want to be tested.

Circumstance	Entitlements	Next Steps
You have no personal history of breast or ovarian cancer, but you have a living relative who does and is available to be tested	The **NICE clinical guideline CG164 1.5.11** states that your affected relative should usually be offered genetic testing first before you, or any other relative. In order to access this **NHS England E01/P/b** says that genetics testing will be offered where your relative's carrier probability is more than 10%. If your relative tests positive **NHS England E01/P/b** says that genetics testing will be offered where your carrier probability is more than 10%.	Your relative should speak to their clinical oncology team about being referred for genetic testing. If they test positive you will be informed and invited to go to your local genetics centre. If they test positive and you do not get contacted then you can go and see your GP and ask for a referral via them by explaining the situation. You can take this leaflet with you to illustrate your entitlement. If your relative tests negative for BRCA1/2 gene mutations you will not require testing. It is always a good idea to find out about the cancer history in the other side of your family, and seek advice from your GP if you are concerned. BRCA1/2 gene mutations are not just carried on a mother's side, it is possible for a father to carry the mutation and pass it on to his children too.

Circumstance	Entitlements	Next Steps
You have no personal history of breast or ovarian cancer, you have a relative who does but they are unavailable for testing	The **NICE clinical guideline CG164 1.5.12** states that if your relative is unavailable you may still be able to access testing by speaking to your GP. **NHS England E01/P/b** says genetics testing will be offered where your carrier probability is more than 10%.	If the person is unavailable because they have died then you should go to your GP to discuss your family history and request referral for genetic testing. If there is a tumour sample available this would assist with the process, but it is not essential. If the person is unavailable because you have no contact with them then you should go to your GP to discuss the family history that you are aware of and explain the situation. They may then refer you to your local genetics centre for further discussion with a genetics counsellor. You can take this leaflet with you to illustrate your entitlement.
You have a family member who has already tested positive for a BRCA1/2 gene mutation	There are no specific NICE guidelines in this situation. **NHS England E01/P/b** says you will be offered genetics testing where carrier probability is more than 10%.	Your family member may have already advised you to contact your local genetics centre, or passed your details on to them to contact you directly. Do not worry if this hasn't happened, you should still be able to get tested. Go and see your GP and discuss your family history with them. They can refer you on to your local genetics centre for further discussions about your family history. You can take this leaflet with you to illustrate your entitlement.

Circumstance	Entitlements	Next Steps
You have not had breast or ovarian cancer, no known history of either disease and no known BRCA gene mutations in the family	In this situation it is unlikely that you would be eligible for testing under any of the current guidelines.	If you have concerns over breast or ovarian cancer then you should familiarise yourself with key information about the disease. If you have concerns about BRCA1/2 gene mutations you should try and find out about any family history of cancer. Make an appointment to see your GP and explain your concerns.

What about my children?

You can ask your GP about testing your children if they are under 18 but it is not usually available. If they are over 18, then the GP may prefer that your children go to see the GP themselves. The GP should be able to discuss this with you and, if appropriate, refer you to the genetics centre for a discussion about your carrier probability (how likely you are to have a BRCA1/2 gene mutation) and whether or not a BRCA1/2 genetic test is the right choice for you.

Getting tested: In practice

Genetic counselling

If you are considering being tested for a BRCA1/2 gene mutation, guidance recommends pre-test counselling with a genetics counsellor. This allows you the opportunity to discuss the potential risk and benefits of BRCA1/2 genetic testing, the chances of finding a mutation, the implications for you and your family, and the different types of test results. You should also have the chance to ask questions to help you make the decision about whether or not you wish to be tested for a BRCA1/2 gene mutation.

The appointment lasts around 40 minutes, and it will consist mainly of a discussion about your personal and family history of breast and ovarian cancer. There will also be a discussion about the pros and cons of getting tested, and what would happen next in the event of both a positive and negative outcome.

The genetics counsellor will then work out whether you have a significant risk of carrying a BRCA1/2 gene mutation and, if you do, you will both make a final decision as to whether testing is right for you.

How is the test conducted?

BRCA1/2 genetic tests are usually conducted using blood samples. A sample of your blood will be taken and sent to a specialist lab where the test will be conducted. Usually you will have the results after around eight weeks. You can discuss with your genetics specialist how you would like to receive the results and s/he will be available to answer your questions to make sure you understand the implications of your test results.

The real impact of BRCA testing: The patient view

Angela Walker found out she had a BRCA1/2 gene mutation after her ovarian cancer diagnosis.
"Knowing I had the BRCA2 gene mutation helped me greatly because my children were little. It means we know what to look for in my daughter and she can be monitored in the future."

Annie Chillingworth says that knowing her BRCA1/2 status was useful for her whole family.
"My siblings and cousins are all taking measures to protect themselves. It puts them in a strog position of control. My daughter does not have the mutation so she's able to move on from the anxiety of not knowing."

Niki Orchard has a BRCA1/2 mutation and had preventative surgery after losing her mother to cancer.
"Knowledge is power and each individual person can choose what to do with that knowledge."

Caroline Presho is BRCA2 positive and has opted for risk reducing surgery.
"I felt vulnerable not knowing my BRCA status, given my family history of cancer, and I couldn't live with the worry and anxiety. After the surgery I felt happy and relieved that I have taken away another risk for breast and ovarian cancer."

After the test: What's next?

What if my BRCA test is inconclusive?

BRCA 1/2 genetic testing does not always give a clear yes/no answer. Many different mutations have been identified in BRCA1/2 genes but not all have been linked with an increased risk of cancer. These mutations are known as 'variants of uncertain significance' (VUS).

Identifying a VUS means that an abnormality has been found in your BRCA1/2 genetic test, but that based on available information, the specific mutation found has not been linked to an increased risk of developing cancer.

As we learn more about VUS, some might be re-classified as being 'clinically significant' and hence associated with an increased risk of developing cancer.

Should your test result show VUS, **NICE guideline CG164 1.5.9** says that you should be told of the result, and informed that you can request a review in the future. All VUS results are to be logged on a database in case of future changes that lead to them being found to be mutated (**NICE guideline CG164 1.5.10**).

What if I have tested positive for a BRCA1/2 gene mutation?

Please see our leaflet *I have a BRCA1/2 gene mutation: What now?*

What if I have tested negative for a BRCA1/2 gene mutation?

If your test results show that you do not carry a mutated BRCA gene you may feel a sense of relief regarding the future risk of cancer. This relief may also extend to knowing that if you have children they are not/will not be at risk of inheriting the family's cancer susceptibility, and the possibility that special check-ups, tests, or preventive surgeries may not be needed.

It is still always important to be aware of the symptoms of both ovarian and breast cancer, and to seek advice from you GP as early as possible if you feel that something is not right, or you are concerned.

References & resources

A Beginners Guide to BRCA1 and BRCA2, The Royal Marsden NHS Foundation Trust, 2013

Clinical Commissioning Policy: Genetic Testing for BRCA1 and BRCA2 Mutations, NHS England, 2015

Ovarian cancer: recognition and initial management, NICE, 2011

Familial breast cancer: classification, care and managing breast cancer related risks in people with a family history of breast cancer, NICE, 2013

UKGTN Testing criteria. www.ukgtn.nhs.uk/uploads/tx_ukgtn/UKGTN_breast_cancer_testing_criteria_Final_161014.pdf

Additional content supplied by Clinical Genetics department at Great Ormond Street Hospital. January 2016

Additional content gathered from Ovarian Cancer Action's acting on BRCA event. November 2015. http://ovarian.org.uk/news-and-campaigning/blog/brca-lecture-right-to-know-impact-on-family

Additional content supplied by Leela Barham, Independent Health Economist. October 2015.

For more information about ovarian cancer symptoms visit www.ovarian.org.uk

For more information about breast cancer symptoms visit www.breastcancernow.org.uk

For template letters to take to your GP, or further information about BRCA1/2 genetic testing and the other work undertaken by Ovarian Cancer Action, please contact Ross Little at:

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