ovarian cancer action

I have ovarian cancer

Everything you need to know about BRCA1/2 gene mutations

(Scotland only)

An introduction to BRCA1/2 gene mutations

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 cancer in her lifetime and a 35-60% chance of developing ovarian cancer in her lifetime.

For men, a BRCA2 mutation increases the risk of developing prostate cancer and the BRCA1/2 gene mutations have also been linked to pancreatic cancer and melanoma in both 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.

Should I get tested?

Knowing your BRCA status can affect your treatment pathway. Testing for a BRCA1/2 gene mutation also provides a significant opportunity for preventing future cases of cancer, for both you and your family members, through options including risk-reducing surgery and increased surveillance.

Such options could reduce the number of cases of ovarian cancer by around 17%. That amounts to a potential 1,000 cases per year.

BRCA1/2 gene mutations are genetic, so if you are a carrier then there is a chance that other members of your family are too. If you test positive for a BRCA1/2 gene mutation you can tell other members of your family that they may be at risk, giving them the option to get tested themselves if they wish. Those with a BRCA1/2 gene mutation have a 50% chance of passing the mutation on to their children.

Everyone has the right to choose whether or not to be tested and it's not a decision to be taken lightly. Genetic counselling can be provided if you're thought to be at risk, to help you make this decision.

How do I get tested?

If you have a **high-grade serous epithelial carcinoma** you are automatically eligible for BRCA1/2 genetic testing. This is because a high-grade serous epithelial carcinoma diagnosis automatically puts you over the significant risk threshold.

The Scottish Intercollegiate Guidelines Network (SIGN) guidance states the following women should be offered BRCA1 and 2 testing:

- Women with non-mucinous ovarian or fallopian tube cancer
- Women who's family history suggests there is a 10% or greater risk of a mutation being present

Women with ovarian cancer who have a family history of breast, ovarian or colon cancer should have a genetic risk assessment.

It is now normal in Scotland for women who meet the criteria to be offered a referral for testing when their ovarian cancer is diagnosed. If this has not happened, you can ask your cancer team about testing.

Together you will decide whether you are to be referred to a Regional Genetics Unit for a BRCA1/2 genetic test.

In some hospitals, such as in Edinburgh, the oncologist may discuss testing with you and, if you decide to go ahead, take a blood sample. If you test positive, you will then be referred for further genetics counselling.

If you are to be BRCA1/2 genetic tested, you should have 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 have BRCA1/2 gene testing.

Interpreting your test results: What's next?

What if my 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 gene 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 variants of uncertain significance some might be re-classified as being 'clinically significant' and hence associated with an increased risk of developing cancer.

There is currently no system in place to systematically review VUS, so patients are encouraged to get back in contact with their local genetic centre if they wish for their VUS to be reviewed.

A positive test result

If you have tested positive for a BRCA1 mutation you will also have a 40-60% lifetime risk of developing breast cancer.

Estimated Cancer Risk by Age 70			
Type of Cancer	**Normal risk**	**BRCA1 Risk**	**BRCA2 Risk**
Ovarian cancer	**2%**	**40-60%**	**10-20%**
Breast cancer in women	**11%**	**60-85%**	**45-60%**
Breast Cancer in men	**0.1%**	**Up to 3%**	**Up to 12%**
Pancreatic cancer	**1.3%**	**3-4%**	**7%**

How your BRCA1/2 status affects your treatment

It's useful for your oncology team to know if you have a BRCA1/2 gene mutation so they can take it into account when considering options for your treatment and/or clinical trials.

Currently women with a BRCA1/2 gene mutation are given the same chemotherapy treatment as women without a genetic predisposition and, in some cases, this treatment can be more beneficial to carriers of a BRCA1/2 gene mutation.

For example, BRCA1/2 gene mutation carriers with ovarian cancer receiving standard platinum treatments have higher response rates and longer times to relapse than women with non-hereditary ovarian cancer.

Studies are currently researching how BRCA1/2 gene mutation related tumours respond to both standard treatments and to new agents, which are designed specifically to target the BRCA1/2-mutated cancer cells.

In 2016, a drug called Olaparib was approved for women with a BRCA1/2 gene mutation facing a second recurrence of ovarian cancer. This new class of drug, known as a PARP inhibitor, can delay the progression of the disease by up to two years.

Clinical trials

Once standard treatments have been tried it's possible that your oncologist will recommend you for a clinical trial. It is also possible that there may be a clinical trial available which is specifically tailored to women with a BRCA1/2 gene mutation.

It is important to note that availability of these trials is patchy so you will need to discuss options with your oncologist.

You can also look online for current trials at:
www.cancerhelp.org.uk/trials
www.cancer.gov/clinicaltrials

Telling your family

Telling your family that you have a BRCA1/2 gene mutation may seem daunting. Just remember that you have options, and support is available.

Telling your children

1. You can delay telling your children until you feel they are old enough. The benefit of this is that it doesn't cause them any distress at an age when you may feel it is too much for them to handle or understand.

2. You can tell them at a young age. The benefit of this is that they have time to come to terms with their possible risk and you can start having discussions early on about some of the difficult decisions they may have to make.

Telling your extended family

Your genetics team will help you identify which of your extended family may also have inherited the mutation. This will depend on what side of the family – your father's or mother's – the gene was passed down from.

Once this is established, your brothers, sisters, aunts, uncles and cousins on that side of the family will be known to be at risk of having inherited the mutation. While it is recommended that they are informed,

There is no right or wrong time to tell your children. You'll want to discuss this with someone close to you, and with your genetics team, to help you to decide which would be the best option for your family.

Given that the cancers attributed to the BRCA1/2 gene mutations don't usually arise until people are in their 20s or 30s (or later), the testing of young children is not usually available, as action can't be taken until they are over 18. It is also generally better if children can be involved in discussions about their own genetic testing, and this is not possible for very young children. Teenagers may benefit from a discussion with a genetics team, even if testing is not carried out until they are 18.

there are currently no official procedures to assist with this and the responsibility and decision to tell them lies with you.

If you don't feel comfortable having this discussion with your family members, your genetics clinic can help with this. For example, they may be able to give you information to pass on. This will explain that a family member has an inherited genetic mutation and will describe what this might mean to them and how they can obtain a referral to their nearest genetics clinic for genetic counselling and testing.

The real impact of BRCA1/2 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."

References & resources

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

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

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

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