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BRCA GENES AND INHERITED BREAST AND OVARIAN CANCER

DIAGNOSTIC GENETIC TESTING for BRCA1 and BRCA2

BRCA GENES AND INHERITED BREAST AND OVARIAN CANCER

This booklet has been written for people who have a personal or family history of breast or ovarian cancer that might be explained by an inherited factor and who are considering having genetic testing. It has been written for use with a genetic medicine appointment and may answer some of your questions.

ARE BREAST AND OVARIAN CANCERS INHERITED?

It is uncommon for breast and ovarian cancer to be caused by an inherited pathogenic (disease causing) variant in a very high-risk cancer gene. Breast cancer occurs in many women with around one in ten women in the UK developing the disease during their lifetime. Ovarian cancer develops in around one in sixty four women in their lifetime. In about 5%-10% of these cases a specific pathogenic variant plays a part. Currently, we can offer testing in our clinics for two genes known as BRCA1 and BRCA2.

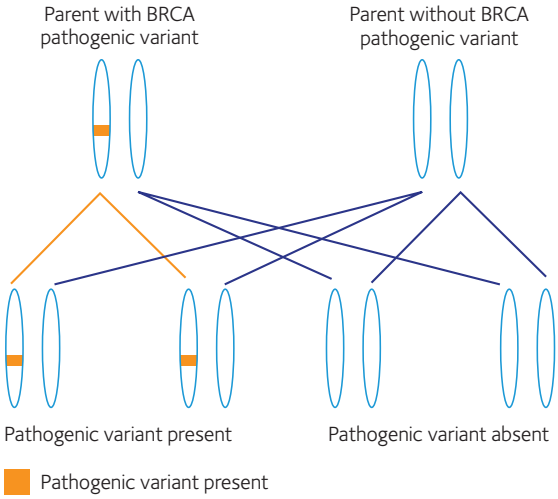
WHAT ARE BRCA1 AND BRCA2?

Everyone has BRCA1 and BRCA2 genes and normally they help to protect us from developing cancer. Some individuals have a pathogenic variant within one of these genes which can affect the function of the gene and this can increase the chance of developing breast, ovarian or prostate cancer. Hereditary or genetic cancers are also more likely to occur at a younger age than cancers in the general population.

HOW ARE THE BRCA1 AND BRCA2 GENES INHERITED?

All our genes come in pairs; we inherit one of the pair from our mother and the other from our father. When we have children we randomly pass on one of each pair. If a person has a pathogenic variant in one copy of a BRCA1 or BRCA2 gene, each of his or her children (male or female) has a 50% (1 in 2) chance of inheriting it. If a person has not inherited a BRCA1 or BRCA2 pathogenic variant, they cannot pass it on to their children.

AUTOSOMAL DOMINANT INHERITANCE



CAN I HAVE A TEST TO SEE IF THE CANCERS IN MY FAMILY ARE DUE TO A PATHOGENIC VARIANT IN EITHER BRCA1 OR BRCA2?

Possibly. A person's genes can be examined from a blood sample. However, only a small proportion of people with these cancers will have a BRCA1or BRCA2 pathogenic variant, and because the test can be difficult to interpret at present, it is usually only offered to certain individuals. This would include families with a strong history of breast, ovarian or prostate cancer or individuals with specific forms of breast or ovarian cancer.

We usually start by obtaining a sample of blood from a family member who has had a BRCA related cancer. The sample is then tested to see if any pathogenic variants are present in the BRCA1 and BRCA2 genes. Finding a pathogenic variant in a relative who has had cancer is the key to developing a genetic test for other family members. Testing for other family members is then known as predictive testing.

We know that at present we cannot find all the causes of inherited cancer. Our techniques are constantly improving and in years to come testing will be more straightforward. At present some families are likely to have a genetic predisposition to developing cancer but the laboratory may not yet be able to find it.

I'VE HEARD OF GENETIC VARIANTS OF UNKNOWN SIGNIFICANCE, WHAT ARE THESE?

Sometimes we find a change in the genetic code and we are not sure of its significance. This is called a variant of uncertain significance (VUS). If we are uncertain whether the gene change found is the cause of the cancers in your family, we will not be able to offer a genetic test that helps relatives predict the chance of developing cancer. We may however ask for extra samples from you or other family members to try and gather more information and these extra tests may help to decide whether the VUS is the explanation for your family history of cancer.

WHAT IF A RELATIVE WITH CANCER IS NOT AVAILABLE, CAN I BE TESTED EVEN IF I HAVE NEVER HAD CANCER?

If there is a very significant family history of breast, ovarian or prostate cancer but no living relatives who have been affected by these cancers then we may be able to offer a genetic test to unaffected family members in very limited circumstances. Please discuss this with your genetic health professional.

DOES EVERYONE WHO HAS A PATHOGENIC VARIANT IN BRCA1 OR BRCA2 DEVELOP CANCER?

Not everyone with a pathogenic variant in a BRCA1 or BRCA2 gene will develop cancer. We do not yet understand why some people develop cancer and others do not. We do know that lifestyle and other genetic factors will play a role. It is important that all women should be breast aware and check their breasts regularly. In addition, people may make medical choices which reduce their risks of certain cancers.

ARE BRCA1 AND BRCA2 THE ONLY GENES THAT CAN CAUSE HEREDITARY BREAST CANCER?

No, but they are two of the major breast cancer genes. There are other genes that increase the chance of developing breast cancer. In some families further testing for other genes may be considered either now or in the future. Research is continually updating our knowledge in this area.

WHAT ARE THE CANCER RISKS ASSOCIATED WITH PATHOGENIC VARIANTS IN BRCA1 OR BRCA2?

The figures below show the increased risk of cancer over a lifetime for a person who carries a BRCA1 gene pathogenic variant

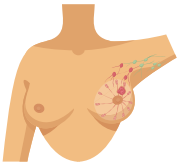
	BRCA1 Carriers (Female)	BRCA1 Carriers (Male)	General Population
Breast Cancer	60-90%	1%	10% (female) <1% (male)
Ovarian Cancer	40-60%	N/A	1-2% (female)
Prostate Cancer	N/A	Minimal Increased Risk	11% (male)

The figures below show the increased risk of cancer over a lifetime for a person who carries a BRCA2 gene pathogenic variant

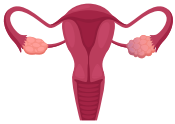
	BRCA2 Carriers (Female)	BRCA2 Carriers (Male)	General Population
Breast Cancer	45-85%	5-10%	10% (female) <1% (male)
Ovarian Cancer	10-30%	N/A	1-2% (female)
Prostate Cancer	N/A	25%	11% (male)

For someone who has already had cancer once, there is also an increased chance of developing a completely new cancer. This is different to cancer that recurs or spreads from a first (original) cancer. Please discuss this with your clinician.

IF I HAVE A PATHOGENIC VARIANT IN BRCA1 OR BRCA2 WHAT ARE MY OPTIONS?



Breast Cancer



Ovarian Cancer

Prostate Cancer

	Screening Options	Surgical Options
Breast Cancer	Annual breast MRI scans (between 30-49 years) Annual mammograms (between 40-69 years) Action cancer offers 2 yearly mammograms to women 70+	Risk reducing mastectomy (removal of breast tissue with or without reconstruction)
Ovarian Cancer	Screening has not proven to be effective	Bilateral salpingo-oophorectomy (removal of ovaries and fallopian tubes)
Prostate Cancer	Men with a pathogenic variant in BRCA2 can be offered annual prostate specific antigen (PSA) blood tests from 40 years. These can be arranged by your GP.	N/A

I HAVE CANCER, COULD THE RESULTS OF GENETIC TESTING AFFECT MY TREATMENT?

If you have breast and ovarian cancer the results of genetic testing may affect your treatment options. Knowing whether or not you have a pathogenic variant in BRCA1 or BRCA2 can help decisions about the treatments the cancer team recommend for you, for example which chemotherapy drugs or surgery would be most suitable. It will also give better information about your risk of developing cancer in the future.

WHAT ARE THE IMPLICATIONS OF GENETIC TESTING?

Some people experience a range of emotions when they are told they have a pathogenic variant that increases their chance of cancer. They may feel angry, empowered, shocked, anxious, or guilty about possibly passing the pathogenic variant on to children.

Genetic testing in a family can affect other family members, they may need to be told that they may have an increased risk of cancer. You may decide not to have genetic testing. Whether or not you have genetic testing, you should talk to your clinician about screening options appropriate for you.

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ARE THERE ANY SUPPORT GROUPS FOR PEOPLE WITH PATHOGENIC VARIANTS IN THE BRCA GENES?

There are several UK based support groups for individuals with pathogenic variants in the BRCA genes. These groups can provide information and peer support. Some useful websites are www.brcani.co.uk and www.breastcancergenetics.co.uk

The health professionals involved in your care are:

Genetic Counsellor: _____

T: _____

Consultant: _____

T: _____

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