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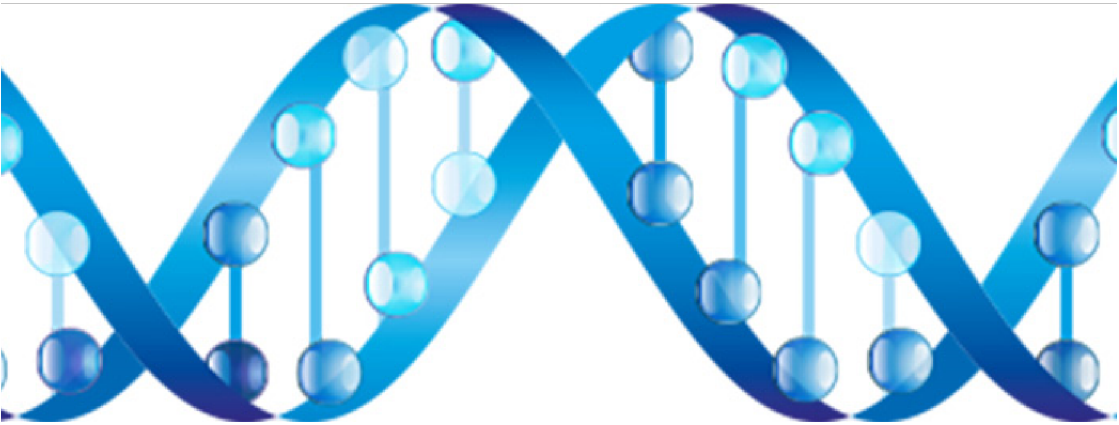
GENETIC TESTING FOR INHERITED BREAST AND OVARIAN CANCER



PREDICTIVE GENETIC TESTING

PREDICTIVE GENETIC TESTING FOR INHERITED BREAST AND OVARIAN CANCER

This booklet has been written for those who are considering having predictive testing for a gene change associated with cancer that has been identified in a relative. It has been written for use with a genetic medicine appointment, and may help to 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) change in a high-risk cancer gene. In the UK, around 1 in 7 females* will be diagnosed with breast cancer in their lifetime, whilst around 1 in 50 will receive an ovarian cancer diagnosis. Around 5-10% of these cases are thought to be linked to an inherited faulty gene, whilst the other 90-95% are thought to be caused by a combination of age, lifestyle, environmental exposures, and low risk genetic factors.

* refers to biological sex assigned at birth

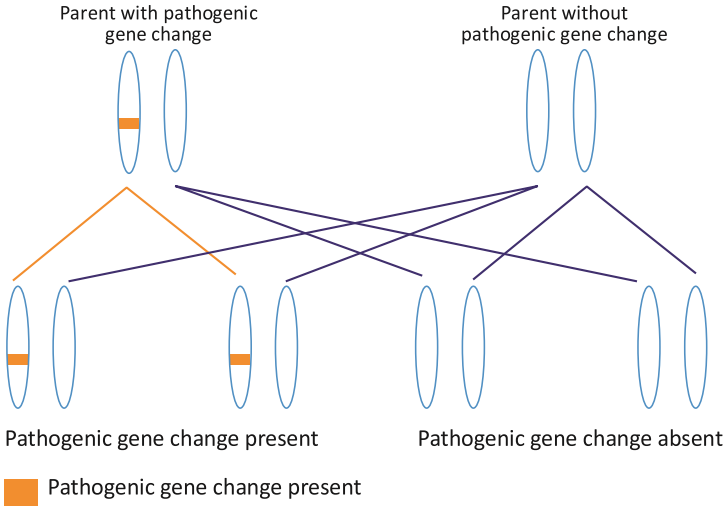
WHAT ARE CANCER PREDISPOSITION GENES?

We each have several genes which normally help to protect us from developing cancer. These are known as **cancer predisposition genes**. The most well-known are BRCA1 and BRCA2, but we now know of, and can test many others. Some individuals inherit a change within one of their two copies of a certain cancer predisposition gene that can prevent it from working properly. This can therefore increase their risks of developing certain cancers compared to the risks of the general population. The associated risks vary depending on which cancer predisposition gene is affected. Cancers caused by hereditary gene changes are also more likely to occur at a younger age than cancers in the general population.

HOW ARE THESE GENES INHERITED?

All of our genes come in pairs; we inherit one of each pair from our mother and the other from our father. When we have children, we randomly pass on one of each gene pair. If an individual has a pathogenic change in one copy of a cancer predisposition gene, each of their children (male or female) has a 50% (1 in 2) chance of inheriting it. If they do not inherit the copy with the pathogenic change, they cannot pass it on to their own children. For most cancer predisposition genes, having a pathogenic change in one of the two copies is associated with increased cancer risks. This is known as '**autosomal dominant inheritance**'.

AUTOSOMAL DOMINANT INHERITANCE



A RELATIVE HAD GENETIC TESTING AND A PATHOGENIC CHANGE WAS FOUND IN A CANCER PREDISPOSITION GENE- SHOULD I BE TESTED?

This is an entirely personal decision, and it is important to make the best decision for you. Finding a pathogenic gene change in an individual who has had cancer is the key to developing a genetic test for their family members. This allows relatives to have a blood test to determine whether they have inherited the same gene change. We usually start by testing first-degree relatives (siblings, children, parents) and if any have inherited it, the offer of predictive testing would then be extended out to their own first-degree relatives.

WHAT HAPPENS IF I HAVE NOT INHERITED THE GENE CHANGE?

If you have not inherited the gene change present in your family, you are not at an increased risk associated with this gene change. In this case, we would not recommend any additional screening for you beyond that offered to the general population. There would also be no risk of passing this gene change to subsequent generations. Cancer is however a very common condition, and this result would not guarantee that you will never develop cancer. It is important that all women are breast health aware, and check their breasts regularly. We strongly encourage participation in the NHS breast screening programme from the age of 50. The NI-based charity 'Action Cancer' offer earlier access to screening for those aged 40-49. Maintaining an active and healthy lifestyle is also encouraged, as this is known to reduce an individual's risk of developing cancer.

IF I HAVE INHERITED THE FAMILIAL GENE CHANGE, WILL I DEFINITELY DEVELOP CANCER?

No, not everyone with a pathogenic gene change in a cancer predisposition gene will develop cancer. We do not yet understand why some people develop cancer and others do not. However, we know that lifestyle and other genetic factors will play a role. There are continuous efforts being made to better understand the genetics of inherited cancers.

WHAT ARE THE CANCER RISKS ASSOCIATED WITH PATHOGENIC CHANGES IN CANCER PREDISPOSITION GENES?

This depends on which gene the pathogenic change has been found in. For some breast and ovarian cancer predisposition genes, the associated risks vary significantly when family history is considered. Your genetic health professional may give an individualised risk figure which takes into account your family history and individual circumstances (such as age).

The table below shows the approximate lifetime cancer risks for individuals with a pathogenic change in their BRCA1 gene *

	BRCA1 Carriers (Female)	BRCA1 Carriers (Male)	General Population
Breast Cancer	72%	0.4%	14% (female) Rare (male)
Ovarian Cancer	44%	-	2% (female)
Prostate Cancer	-	12-17%	12% (male)

The table below shows the increased risk of cancer over a lifetime for an individual who carries a pathogenic change in their BRCA2 gene *

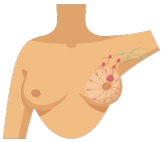
	BRCA2 Carriers (Female)	BRCA2 Carriers (Male)	General Population
Breast Cancer	69%	4%	14% (female) Rare (male)
Ovarian Cancer	17%	-	2% (female)
Prostate Cancer	-	27-41%	12% (male)

* It is important to note that the figures quoted refer to the risk over an individual's lifetime, to age 80-85. Risks of developing the associated cancers increase with age. (Risk figures from '**UK Cancer Genetics Group**' *https://www.ukcgg.org* July 2023)

However, many other less common cancer predisposition genes are now known (such as PALB2, ATM, BRIP1, CHEK2, PTEN, RAD51C, RAD51D, TP53, STK11, PMS2). For some of the breast and ovarian cancer predisposition genes, not enough is known about the associated cancer risks to provide accurate risk estimations. Researchers are continuously working on better characterising these, and your genetic health professional will give you the most up-to-date, tailored information available at that time.

IF I HAVE INHERITED THE FAMILIAL PATHOGENIC GENE CHANGE, WHAT ARE MY OPTIONS?

These will vary greatly depending on which gene the pathogenic change is in. Your genetic health professional will discuss the options that are available to you based on your individualised risks. The following options are relevant to those where a pathogenic change is found in BRCA1 or BRCA2.

Cancer type	Screening Options	Surgical Options
 Breast Cancer	Annual breast MRI scans offered from 25 years Annual mammograms from 40 years	Risk reducing mastectomy (removal of breast tissue with or without reconstruction)
 Ovarian Cancer	Screening has not proven to be effective	Removal of ovaries and fallopian tubes- when childbearing is complete and no earlier than 35-40 (BRCA1) and 40-45 (BRCA2). Your genetic professional may discuss participation in the PROTECTOR study (more information can be found at the link below)*
 Prostate Cancer	Men with a pathogenic gene change in **BRCA2** can be offered annual prostate specific antigen (PSA) blood tests from 40 years. These can be requested from your GP on an annual basis.	N/A

* http://protector.org.uk/information-for-participants/

For the other breast and ovarian cancer predisposition genes, screening and surgical options are determined on an individual basis according to current national guidance. Specific management options will be discussed with you in your results appointment. If you are found to carry the pathogenic gene change present in your family, your genetic health professional will refer you to the relevant healthcare specialists to discuss these options.

IF I DEVELOP CANCER IN THE FUTURE, COULD THE RESULTS OF GENETIC TESTING AFFECT MY TREATMENT?

If you develop breast and ovarian cancer and are known to carry a pathogenic change in a cancer predisposition gene, this may affect the treatments the cancer team recommends for you. For example, which chemotherapy drugs or surgery would be most suitable.

WHAT IS CHEMOPREVENTION?

Chemoprevention is the use of certain medicine to lower the risks of cancer in healthy individuals with an increased risk of developing cancer. This includes those with pathogenic changes in certain cancer predisposition genes such as BRCA1 and BRCA2. You may wish to discuss whether this option is available to you with your breast family history clinic as well as the risks and benefits.

WHAT ARE THE IMPLICATIONS OF GENETIC TESTING?

Some people may worry that genetic testing will affect their insurance prospects (e.g., health, life, disability). Insurance companies may consider an individual's personal medical history (including cancer), and family medical history. Detailed information about genetic testing and insurance can be found in the 'Code on Genetic Testing and Insurance' at:
https://www.abi.org.uk/globalassets/files/publications/public/genetics/code-on-genetic-testing-and-insurance-final.pdf

Some people experience a range of emotions when they are told they have a pathogenic gene change that increases their risk of developing cancer. They may feel angry, shocked, anxious, or guilty about possibly passing the pathogenic gene change on to their children. They may also feel guilty if they have not inherited the pathogenic gene change when other close family members have. Others feel empowered to make medical and health decisions to lower their cancer risks.

It is important to note that the results of genetic testing may provide information about your relatives' risk of developing cancer. If you are found to have a pathogenic gene change, there is a 1 in 2 chance that your children have also inherited this.

SHARING TEST RESULTS WITH RELATIVES

Whether your results are positive or negative, it is important to share them with relatives. If you are found to carry the familial gene change, sharing this information with relevant family members alerts them to their potential risk, and may encourage them to take appropriate action. It also gives them the option to have predictive genetic testing if they wish. Sharing negative test results is also helpful because then your children, grandchildren etc. will know that they do not need testing. Sharing genetic testing results with relatives can be difficult for many people. Your genetic counsellor can provide advice and support with this, along with written information on how people can seek a referral to our service. It is important to note that for the majority of cancer predisposition genes we do not offer predictive testing to children- those who wish to be tested between the ages of 18 and the minimum screening age will be assessed on an individual basis.

ARE THERE ANY RELEVANT SUPPORT GROUPS FOR PEOPLE WITH PATHOGENIC CHANGES IN CANCER PREDISPOSITION GENES?

Action cancer is a Northern Ireland-based charity provide free breast screening to women aged 40-49 and 70+ who fall outside the NHS screening age range, and health checks to men or women aged 16+
https://actioncancer.org

BRCA link NI is a Northern Ireland based organisation helping people with Hereditary Breast and Ovarian Cancer access information and support. They organise group meetings and formal events with guest speakers.
http://brcani.co.uk/about.html

National Hereditary Breast Cancer Helpline provide support and information to those concerned about their hereditary cancer risk through their website and phone helpline.
https://www.breastcancergenetics.co.uk

Together in Surgical Menopause is a UK-based patient-led resource for those experiencing surgical menopause, for example due to risk-reducing removal of the ovaries.
http://www.surgicalmenopause.co.uk/index.html

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Family reference number:

The health professionals involved in your care are:

Genetic Counsellor: _____

T: _____

Consultant: _____

T: _____

If you have any feedback or comments regarding the contents of this leaflet, we would be pleased to receive them at genetic.medicine@belfasttrust.hscni.net ; If your relatives are concerned about whether they have inherited the familial gene change and would like to discuss testing, they should ask their GP to be referred to their local genetics service or can self-refer to our service via our website (linked below). It is important when self-referring that they **provide details about the familial gene change and the relative that it was identified in-** those without this will be declined. Your genetic counsellor will discuss which of your relatives may be eligible for predictive testing.
https://belfasttrust.hscni.net/service/laboratory-services/clinical-genetics/how-to-make-a-referral-to-clinical-genetics/.

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