Hereditary Breast and Ovarian Cancer

(HBOC)

Information for individuals and families

Ospidéal San Séamas
Seirbhís Dé agus A Phobail

ST. JAMES'S HOSPITAL

What is Hereditary Breast and Ovarian Cancer (HBOC)?

Hereditary Breast and Ovarian Cancer is a genetic condition which causes women to have an increased risk of developing breast and ovarian cancer. In some families there may also be an increased susceptibility to other cancers, such as male breast cancer, prostate cancer, malignant melanoma and pancreatic cancer.

How do I know if the cancers in my family are due to HBOC?

HBOC is uncommon. Fewer than 1 in 20 women who develop breast cancer have HBOC. In most families, cancer is not inherited or passed down through the generations. In Ireland, breast cancer affects approximately 1 in 10 women during their lifetime. The majority of women are diagnosed over the age of 50. Ovarian cancer is less common, affecting approximately 2% of women in their lifetime. Most of these women will have already been menopause. Prostate cancer affects about 1 in 8 men (12.5%), the majority of affected men are over the age of 70. The risk of male breast cancer is very small, about 1 in 1000 (0.10%).

HBOC may be more likely in a family where at least three relatives on the same side of the family have developed breast or ovarian cancer, particularly if at a young age. In rare cases HBOC might also be diagnosed in an individual with cancer regardless of their family history. Your family history may be due to HBOC if:

- Several relatives have developed breast cancer and/or ovarian cancer
- A relative was diagnosed at a much younger age than is usual
- A relative developed breast cancer more than once, or had breast and ovarian cancer
- A male relative developed breast cancer as well as female relatives
- Multiple generations on one side of the family were affected by breast, ovarian or prostate cancer

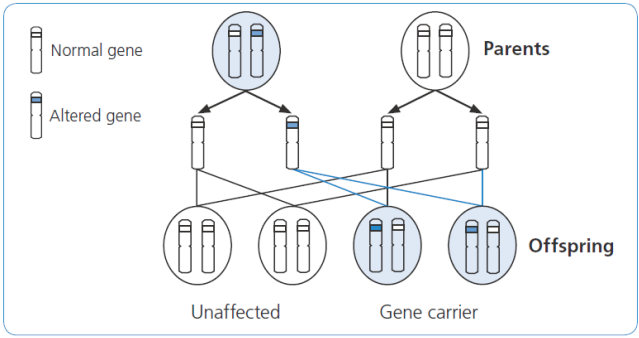
Which genes cause HBOC?

The two main genes associated with HBOC are called BRCA1 and BRCA2. Genes are instructions which control how the body works. We each have approximately 20,000 genes. Most of our genes come in matching pairs. We inherit one copy of a gene from our mother, and one copy from our father. Each gene has a specific job in the body.

BRCA1 and BRCA2 are involved in repairing damage in our cells. By doing this job, the genes help to protect us from getting cancer. If a gene contains an alteration (similar to a spelling mistake in the gene's instruction), the gene can no longer do its job properly. There may be other important genes involved in HBOC. In some populations certain alterations in either BRCA1 or BRCA2 are more frequent than normal. For example this may include Ashkenazi Jewish or Eastern European populations.

How does HBOC run in families?

We have two copies of each BRCA gene. People who have a BRCA alteration have one altered copy and one working (normal) copy of the gene. Each time they have a child; there is a 1 in 2 (50%) chance that they will pass on the working copy and a 1 in 2 (50%) chance that they will pass on the altered copy. This is called dominant inheritance and is shown in the diagram below.



Women AND men can carry an altered copy of a BRCA gene, so HBOC can be inherited from either parent. Therefore, the father's family history of cancer is also important.

What is the risk of developing breast and ovarian cancer?

A woman who has an altered BRCA1 or BRCA2 gene will not always develop cancer, but the likelihood of developing breast or ovarian cancer during her lifetime is greatly increased.

For women with a proven alteration in either BRCA1 or BRCA2, the risk of developing breast cancer may be as high as 85% across their lifetime. The risk of ovarian cancer is lower and is different for the two genes. The lifetime risk of ovarian cancer associated with BRCA1 is approximately 40-60%, and with BRCA2 is approximately 15-30%.

What about men in HBOC families?

Men who carry a BRCA1 gene alteration, may have a slightly higher risk of male breast cancer. About 1% or 1 in 100 men who carry BRCA1 develop breast cancer. Recent evidence suggests an increased risk of prostate cancer in the region of 15-20%. Men who carry a BRCA2 gene alteration, have a higher lifetime risk of developing prostate cancer. It is estimated that 20-25% of men who carry a BRCA2 alteration develop prostate cancer. Most of these prostate cancers occur over the age of 45. Men who carry a BRCA2 alteration also have a higher chance of developing breast cancer across their lifetime, which is estimated at 6-8%. Further information is available in our leaflet 'BRCA1 and BRCA2 for men'.

Genetic testing

Where there is a significant chance that the cancers in a family may be due to HBOC we may offer a genetic test to look for alterations in the BRCA1 and BRCA2 genes. The most useful way of carrying out genetic testing is to start with someone who had a diagnosis of breast or ovarian cancer. This is called a diagnostic genetic test and involves a blood test.

Before a genetic test is carried out it is helpful to have a discussion with a specialist genetics team. Following your genetic test result the specialist genetic team will plan and discuss the

options for screening and for reducing your risk. If a BRCA1/2 alteration is found in the family, it may be possible to offer genetic testing to other family members including those unaffected by cancer, to check if they share this gene alteration. This is called a predictive test. As there would be implications for cancer screening, it would be important for relatives considering genetic testing to attend for genetic counselling to discuss the possible benefits and disadvantages of having a genetic test before going ahead with the test. Some people worry that genetic testing can affect their ability to obtain life insurance. The Oireachtas passed an Act in 2005 to prevent such discrimination. Further information about this can be found at: http://www.insuranceireland.eu/.

Not all suspected HBOC families have gene alterations that can be found. If no genetic alteration is found in your family we would not be able to offer genetic testing to other relatives. However, we would still be able to provide advice about cancer screening or risk-reducing options, based on the family history.

What can you do if you are at increased risk?

If you are at increased risk of breast and ovarian cancer you have several options. Depending on your age and personal choices you might want to manage your risk differently to other family members. The options available include increased breast surveillance (screening) and risk reducing surgery.

Breast screening

Most women will be offered regular mammograms (X-rays of the breast) and a breast examination by a clinician. Sometimes the clinician will decide to use other types of examination including ultrasound scans, or MRI of the breast because breast screening is difficult in younger women who tend to have denser breast tissue. Depending on your personal risk, breast screening might be offered earlier than usual. Women who are confirmed as having a BRCA1 or BRCA2 gene alteration are typically offered breast screening from the age of 30 involving MRI scans.

Mammograms will sometimes detect changes in the breast which are harmless but might require further investigations. It is also important to know that not all cancers will be picked up by screening. You should be 'breast aware' and report any unusual symptoms to your doctor as soon as possible. Breast screening does not prevent the development of cancer, nor does screening guarantee early detection or better outcome. It is given in the hope of picking up cancer at an early stage where treatment is more likely to succeed. However, it might still involve surgery and possibly chemotherapy and radiotherapy too.

Risk-reducing surgery of the breast

You may wish to discuss the various types of risk reducing surgery available with a surgeon, and we will be able to arrange a referral for you. Counselling may also be beneficial as part of this process.

Ovarian screening

If you have an increased risk of ovarian cancer we will suggest referring you to a Gynaecologist with expertise in oncology. They will discuss various options with you, such as screening for cancer or risk-reducing surgery. Unfortunately there is no convincing evidence to show screening for early signs of ovarian cancer is effective. You may be offered an internal (transvaginal) ultrasound scan every year and a blood test called CA125. This is the only method available at present, but these procedures are not proven to be reliable in picking up early cancers. Many Gynaecologists have now stopped offering this type of screening. If offered, ovarian cancer screening for women who carry an alteration in the BRCA1 or BRCA2 gene usually starts from the age of 35. It is important to remember that ovarian screening is not the same as cervical screening (smear tests) which is done at your GP surgery.

Risk-reducing surgery of the ovaries (Oophorectomy)

It is advisable for women who carry a BRCA1/2 gene alteration to consider the preferable option of having their ovaries and fallopian tubes removed at an appropriate age once they have completed their families. We suggest a referral to Gynaecology from the age of 35 to discuss this further.

Removal of the ovaries and fallopian tubes reduces the risk of ovarian cancer by more than 90%. In pre-menopausal BRCA2 carriers it may also reduce the risk of breast cancer. If performed in pre-menopausal women, oophorectomy causes an immediate menopause. This may require Hormone Replacement Therapy (HRT) for a period of time until the age of natural menopause (around 50 years of age). HRT given in this way will not increase the risk of breast cancer significantly. The suitability of HRT would be determined by your Gynaecologist in conjunction with your breast care team.

It has not been proven that the risk of womb cancer and cervical cancer is increased in BRCA1 and BRCA2 carriers. Therefore, a full hysterectomy is not required unless you have other unrelated gynaecological problems. You might be offered keyhole surgery to remove your ovaries and tubes. You can get further advice about this from your Gynaecologist.

Screening for men

For men who have a BRCA gene alteration, there are screening tests available for prostate cancer and recent evidence suggests that prostate cancer screening may be of benefit to men with BRCA1/2 gene alterations. Prostate screening involves a blood test to measure the level of a marker called PSA (prostate specific antigen). The doctor may also examine the prostate by inserting a finger into the back passage to check that the prostate is not enlarged. PSA levels may be raised in prostate cancer, but these tests will not detect all cases of prostate cancer. PSA levels can also be raised in men who do not have cancer. Often, a man with a raised PSA level does not have prostate cancer but this can cause unnecessary investigations and anxiety. If a man has a raised PSA, he may need another PSA test, an examination or a biopsy.

If you carry a BRCA gene alteration you could discuss the benefits and limitations of prostate screening with your GP from the age of 40. There is no proven useful screening for male breast cancer. It remains important to remain chest aware and to report any concerns to your GP, you may also wish to consider discussing clinical examinations of the chest with your GP when you attend for your prostate screening.

This leaflet is based, with permission, on a leaflet produced by:

The West Midlands Regional Genetics Service

Birmingham Women's and Children's NHS Foundation Trust

Developed by:
C.Giffney Registered Genetic Counsellor MMUH, E Berkeley Cancer Genetics Nurse Specialist SJH and Prof. D Gallagher Consultant Medical Oncologist and Geneticist

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