# Hereditary breast and ovarian cancer

## Key facts

- Breast cancer is the most commonly diagnosed cancer in the UK, affecting approximately 1 in 8 women during their lifetime. Breast cancer in men is less common, affecting approximately 1 in 870 men during their lifetime.
- The majority of cases of breast cancer are not due to an inherited condition, but it is important to recognise the 5-10% of breast cancer cases that occur due to an inherited predisposition to develop cancer. Although this is often referred to as inherited cancer, the altered gene is inherited, not the cancer itself.
- Two major genes associated with familial breast cancer are the *BRCA1* and *BRCA2* genes.
- Women with a variant in the *BRCA1* or *BRCA2* genes have a significantly increased chance of developing breast and ovarian cancer during their lifetime, and may be offered additional screening and/or risk-reducing surgery.
- Men with a variant in the *BRCA1* or *BRCA2* (more commonly *BRCA2*) genes have an increased probability of developing prostate and male breast cancer, and may be offered additional screening.

## Clinical features

Clinical indications that may suggest an inherited predisposition to breast and associated cancers include:

- several women who have had breast cancer and/or ovarian cancer on one side of the family;
- breast cancer being diagnosed at a younger age than is usual;
- a breast cancer diagnosed with grade 3 triple negative histology (tests negative for oestrogen, progesterone and HER2 receptors), especially at a young age;
- an individual who has had primary breast cancer more than once, or has had early breast cancer and ovarian cancer; and
- a male with breast cancer in a family where female relatives have also had breast cancer.

## Diagnosis

- Individuals may seek information, either because they have been affected with breast cancer themselves or because they have a family history of breast cancer.
- A family history will first be taken by the breast cancer team or GP. If the family history is considered to be significant, then a referral should be made to the local genetics department or family history clinic. Most regional genetic centres publish guidelines on their website for referrals based on information from a family history.
- A detailed risk assessment will then be carried out. This will estimate an individual's lifetime probability of developing breast cancer and also the chance of developing breast cancer over the next 10 years. An assessment can also be done to calculate the chance that there is a *BRCA1* or *BRCA2* gene alteration in the family.
- At this stage, recommendations about additional screening or genetic testing may be offered.

- In some areas, genetic testing for *BRCA1* and *BRCA2* is beginning to be offered in oncology and surgical clinics at the point of diagnosis, particularly for primary serous ovarian cancer.

## Genetic basis and genetic testing

- The two main genes associated with familial breast cancer are known as *BRCA1* and *BRCA2*. There are other genes known to be associated with predisposition to breast cancer, but *BRCA1* and *BRCA2* are those most commonly involved.
- *BRCA1* and *BRCA2* are known as tumour suppressor genes. Tumour suppressor genes regulate cell division and programmed cell death, and repair DNA mistakes.
- Variants in these genes can cause cells to grow out of control, which can lead to cancer.
- An individual who inherits a *BRCA1* or *BRCA2* gene variant will not always develop cancer, but the chance of developing breast (and ovarian/prostate) cancer will be significantly increased.
- For women with a *BRCA1* or *BRCA2* variant, the chance of developing breast cancer before the age of 80 is around 80%. The lifetime probability of developing ovarian cancer is between 10% and 60%.
- For men with a *BRCA1* variant, the cancer risk does not significantly increase. For men with a *BRCA2* variant, the chance of developing male breast cancer over their lifetime is slightly higher than the general population. The lifetime risk for developing prostate cancer is 20-25%.
- *BRCA1* and *BRCA2* variants are inherited in an autosomal dominant manner. This means that an individual with an inherited predisposition to breast cancer has one copy of the gene with a variant and one without a variant. The variant copy was most likely inherited from one parent.
- An individual with a gene variant has a 50% (one-in-two) chance of passing on the usual gene and a 50% (one-in-two) chance of passing on the variant gene to each of their children, male or female. As mentioned above, if a child inherits a copy of the variant gene, it is likely but not certain that breast or associated cancer will develop in adulthood.
- NICE guidelines state that genetic testing for *BRCA1* and *BRCA2* gene variants should be available to individuals where there is a 10% or greater chance of carrying a gene variant.
- Genetic testing is most useful if carried out in an affected member of the family first to establish the specific variant for that family. If a gene variant is identified in an affected family member, other relatives can also be tested to see whether they carry the same gene variant. This is known as predictive genetic testing.
- If there are no affected relatives available to test (for example, if everyone who has had breast cancer is deceased), genetic testing may still be possible for unaffected individuals in the family if there is a strong family history of breast and/or ovarian cancer.

## Clinical management

There are several options available to women and men at an increased probability of developing breast and associated cancers:

- **Breast screening:** The National Breast Screening Programme offers all women between the ages of 50 and 70 a mammogram every three years. Depending on the level of risk, breast screening may be offered from an earlier age, and on a more frequent basis. Sometimes other types of examinations (such as an MRI scan) may also be offered to women at high risk. NICE guidelines for women with an alteration in the *BRCA1* or *BRCA2* gene suggest annual screening by MRI scan between the ages of 30 and 50, and then by annual mammogram between the ages of 50 and 69, although this may not be available in every area.

- **Risk-reducing surgery:** Some women who have a high chance of developing breast cancer may be offered surgery to reduce their risk. Double mastectomy with reconstruction can reduce the chance of developing breast cancer by up to 90%. Bilateral salpingo-oophorectomy (BSO), the surgical removal of the ovaries and the fallopian tubes, may also be offered, usually between the ages of 35 and 40. It is important to note that these are both major surgeries with potential complications and possible psychological implications.
- **Breast awareness:** Most breast cancers will present as a painless breast lump. It is important that all women and men (due to the small risk of male breast cancer) know how to check their breasts and which symptoms to be aware of.
- **Prostate screening:** Men with a *BRCA1* or *BRCA2* alteration may be offered prostate screening using PSA blood tests annually from the age of 40 to 69.

There is a small chance of the development of some other cancers, for which screening is not usually considered to be useful.

## Further reading and patient groups

- For more information about inherited cancer genes and increased cancer risk, visit Cancer Research UK or the National Institute for Health and Care Excellence (NICE).
- For more information on male breast cancer, visit Cancer Research UK or the NHS website.
- Patient support:
  - Breast Cancer Now Tel: 0808 800 6000
  - Macmillan Cancer Support Tel: 0808 808 00 00
  - National Hereditary Breast Cancer Helpline: 01629 813000
  - Target Ovarian Cancer Tel: 020 7923 5475
  - Prostate Cancer UK Tel: 0800 074 8383
  - Cancer Research UK Facebook group
- Local support group information can be provided via local genetics services.

*This information is intended for educational use and was current in May 2020. For clinical management, it is recommended that local guidelines and protocols are used.*

*Produced in collaboration with Birmingham Women's NHS Foundation Trust's Clinical Genetics department and Royal Cornwall Hospital NHS Trust's Clinical Genetics department.*