This fact sheet describes when breast and ovarian cancer is considered to be a hereditary or familial condition. A small number of families have an increased chance of developing cancer because of an inherited faulty gene in the family. This is known as an inherited predisposition to cancer.

**In summary**

- Cancer is very common in the community and mostly occurs just by chance
- Some rare families have an inherited faulty gene that can increase the likelihood of some individuals developing cancer
- People with an inherited faulty BRCA1 or BRCA2 gene have an increased likelihood of developing breast and ovarian cancer.

**WHAT ARE BREAST CANCER AND OVARIAN CANCER?**

Breast cancer is a common disease in the community. About 1 in 8 women (12%) will develop breast cancer by the age of 85 years. It is the most common cause of cancer deaths in women. It also occurs in men, but it is rare.

Ovarian cancer refers to having a tumour in one or both ovaries. Ovarian cancer affects about 1 in 100 women (1%) in the community by the age of 75 years and is the leading cause of death from gynaecological cancers.

**WHAT CAUSES BREAST AND OVARIAN CANCER?**

There is no single cause for these types of cancers. There are a number of risk factors which can influence an individual's chance of developing breast and/or ovarian cancer. The most important are:

- Being a woman
- Getting older. Most women who develop breast and/or ovarian cancer are over the age of 50
- Having a family history of breast and/or ovarian cancer
- Having Ashkenazi Jewish ancestry. Families with this background are more likely to carry specific types of faulty genes causing breast and/or ovarian cancer.

**WHAT IS MEANT BY A FAMILY HISTORY OF BREAST AND/OR OVARIAN CANCER?**

A family history of breast and/or ovarian cancer means having one or more close blood relatives who have, or have had, breast or ovarian cancer.

Relatives could be on either the father's or the mother's side of the family, but not added together.

The closest blood relatives (not relatives by marriage) are parents, siblings and children and are called first-degree relatives. Aunts, uncles, nephews and nieces are second-degree relatives.

A family history of cancer can be due to:

- Chance, because cancer is common
- Common environmental and lifestyle influences among family members
- Having a faulty ‘cancer protection’ gene in the family.

**Figure 32.1:** Proportion of cases of breast and ovarian cancers that do and do not involve an inherited predisposition (susceptibility).
Many women have a few relatives who have or had breast cancer just because breast cancer is common in women. Such women may be only slightly above the average risk.

Some women have a ‘stronger’ family history where a number of their close blood relatives have or had breast and/or ovarian cancer.

Most of these women will have a moderately increased chance of developing breast cancer.

A small number will have a potentially high chance of developing breast and/or ovarian cancer because their family has an inherited predisposition to this cancer.

**INHERITED PREDISPOSITION TO BREAST AND/OR OVARIAN CANCER**

Most breast and ovarian cancer cases are not due to an inherited predisposition. However a small number of cases (about 5%-10%) in Australia involve an inherited predisposition to develop the cancer (*Figure 32.1*). In these cases, a person has inherited a faulty copy of a breast and/or ovarian ‘cancer protection’ gene.

Cancer occurs when cells in the body continue to divide uncontrollably. This can happen in any tissue or organ in the body. A group of cells that has resulted from uncontrolled cell division and growth is called a tumour.
We all have two copies of a number of different genes that normally control orderly growth and division of our cells throughout life. These genes can therefore be thought of normally acting as ‘cancer protection’ genes.

Variations to the information in one of these ‘cancer protection’ genes such as a breast or bowel cell may cause the process of cell division to be less well controlled and cells may grow and divide abnormally. A variation that makes the gene faulty is called a mutation or a pathogenic variant.

The cycle of cell division and growth continues throughout the lifespan and mutations can build up over this time. Mutations have to occur in a number of different ‘cancer protection’ genes in a cell, building up over time, before that cell becomes cancerous.

This is why the development of breast and/or ovarian cancer can take many, many years and is often seen in older people.

The reason why these mutations occur is thought to be a combination of genetic factors, environmental factors and the process of ageing.

Research is currently being undertaken to more fully understand the cause of specific gene mutations.
For the small number of people that have inherited a mutation in a ‘cancer protection’ gene the division and growth of breast and ovarian cells is not as tightly controlled as in other women in the population.

One way of representing this process is to think of the path to cancer as a staircase where the bottom of the staircase represents a normal cell and the top a cancerous cell (Figure 32.4)

The steps of the staircase represent a progression of changes to the information that may occur in one or both copies of a number of different ‘cancer protection’ genes in a cell. Some of these changes will be mutations.

So for a normal cell to become cancerous, both copies of a number of different ‘cancer protection’ genes in the cell of a tissue or organ must become faulty over time.

If a person is born with a mutation in one of the ‘cancer protection’ genes, they are already on the first step of the staircase (see Figure 32.4).

Their chance of developing breast and/or ovarian cancer is higher than average but unless further mutations occur over time in a number of other ‘cancer protection’ genes, those cells will never become cancerous.

It is thought that not just one but many gene changes are associated with the development of breast and ovarian cancer.

WHAT ARE THE INHERITED FAULTY ‘CANCER PROTECTION’ GENES THAT CAUSE BREAST AND OVARIAN CANCER?

It is important to remember that the breast and/or ovarian cancer itself is not inherited, although cancer caused by an inherited faulty ‘cancer protection’ gene is sometimes called hereditary cancer.

There are a number of ‘cancer protection’ genes in which inherited mutations can contribute to the development of breast and/or ovarian cancer. Two genes that have been identified are:

- Breast Cancer 1 gene (BRCA1)
- Breast Cancer 2 gene (BRCA2)

The BRCA1 and BRCA2 ‘cancer protection’ genes are known as tumour suppressor genes and their role is to act as the ‘brakes’ on uncontrolled cell growth.
There are also a number of families where it is clear from the family history that members are at potentially high risk for having an inherited predisposition to breast and ovarian cancer, but where mutations in these two genes are not identified.

It is likely that there are a number of as yet unidentified genes in which mutations predispose to breast and ovarian cancer. Research is continuing to try to identify these genes and their function.

**WHAT IS THE PATTERN OF INHERITANCE IN FAMILIES WITH A FAULTY BRCA1 OR BRCA2 GENE?**

BRCA1 or BRCA2 gene mutations are inherited in an autosomal dominant pattern (*Figure 32.5*). This is because:

1. The BRCA1 and BRCA2 genes are located on the autosomes (numbered chromosomes) called chromosome 17 and 13.
2. The effects of the mutations in the BRCA1 and BRCA2 genes are **dominant** over the information in the working copy of the genes.

Where one of the parents has a BRCA1 or BRCA2 gene mutation, in every pregnancy each of their children has a:

- 1 chance in 2 (50% chance) of inheriting the gene mutation
- 1 chance in 2 (50% chance) of **not** inheriting the gene mutation and inheriting a working copy of the gene from both parents.

A BRCA1 or BRCA2 gene mutation can be inherited from either the mother or the father and passed on to either a son or a daughter.

Women who have not inherited a faulty gene are not at increased risk of developing breast and/or ovarian cancer over their lifetime and cannot pass the faulty gene on to their own children. However, they still have the same risk for developing breast and/or ovarian cancer as the average woman in the Australian population.

**WHAT ARE THE CLUES IN A FAMILY HISTORY OF BREAST AND/OR OVARIAN CANCER?**

Documenting the health history of family members over several generations helps determine if a person has a strong family history. It is important to record how the individual is related, the type of cancer they have or had and the age of the individual when cancer was first diagnosed.

A strong family history of breast and ovarian cancer may mean an inherited gene mutation is present in the family. This usually includes one or more of the following:

- Many relatives with breast or ovarian cancer
- A family member diagnosed with breast or ovarian cancer at a younger age, usually before the age of 40
- Relatives who have both breast and ovarian cancer
- An individual with breast cancer in both breasts
- Breast cancer in a male relative
- Ashkenazi Jewish ancestry as BRCA gene mutations are more common in this population.
People with a strong family history can be referred by their doctor to a specialist family cancer service or their local genetic counselling service.

**GENETIC COUNSELLING AND TESTING**
The genetic counselling team may be able to:

- Clarify the chance of developing breast and/or ovarian cancer based on a person’s family history
- Answer any questions about the family history of cancer
- Discuss the limitations, potential benefits, disadvantages and appropriateness of genetic testing
- Discuss cancer screening and risk reducing strategies.

Genetic testing for mutations in the **BRCA1** and **BRCA2** genes is complex and involves

- First, identifying the gene mutation via a blood sample in a family member who has or had breast and/or ovarian cancer (a **mutation search**). This may take considerable time
- Second, and only if a mutation is found, testing other family members to determine if they have inherited the mutation (**predictive genetic testing**).

### WHAT IS THE CHANCE OF DEVELOPING BREAST AND OVARIAN CANCER AND OTHER CANCERS?
People with a **BRCA1** or **BRCA2** gene mutation have an increased chance of developing breast and ovarian cancer and some other cancers (Table 32.1).

### MANAGING AN INCREASED RISK OF DEVELOPING BREAST AND OVARIAN CANCER DUE TO A **BRCA1** OR **BRCA2** GENE MUTATION

**Discuss your family health history with your doctor**
Many cancers can be cured if picked up at the earliest stage. Discuss your personal and family history of cancer with your GP.

**Genetic counselling and risk management**
It is recommended that people with a **BRCA1** or **BRCA2** gene mutation and their relatives, seek management advice from a genetic service, a family cancer clinic or medical specialist.

Surgery to reduce the risk of breast cancer developing should be discussed with a specialist doctor and may be considered for some women.

Regular breast screening is important to detect cancer early and usually starts at a younger age than for most women.

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**Table 32.1: Chance of developing breast and ovarian or other cancers for people with a BRCA1 or BRCA2 gene mutation.**

<table>
<thead>
<tr>
<th>Gene mutation</th>
<th>Chance (risk) for women developing breast or ovarian cancer up until age 70 years</th>
<th>Chance (risk) for men developing breast cancer up until age 70 years</th>
<th>Chance (risks) over a lifetime of developing other cancers in men and women</th>
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<tbody>
<tr>
<td><strong>BRCA1</strong></td>
<td>About 60% for breast cancer (between 40% and 80%)</td>
<td>Very slight increased risk for breast cancer</td>
<td>Very slight increased risk for prostate cancer for men</td>
</tr>
<tr>
<td></td>
<td>About 40% for ovarian cancer (between 10% and 50%)</td>
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<tr>
<td><strong>BRCA2</strong></td>
<td>About 50% for breast cancer (between 40% and 60%)</td>
<td>Slight increased risk for breast cancer</td>
<td>Slight increased risk for prostate cancer. Risk may be very slightly increased for pancreatic cancer and melanoma</td>
</tr>
<tr>
<td></td>
<td>About 20% for ovarian cancer (between 10% and 30%)</td>
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</table>
Risk-reducing surgery should also be discussed to reduce the risk of ovarian cancer for which there is no screening test available.

Medication has been shown to reduce the risk of breast and ovarian cancer in some women with inherited cancer susceptibility, however, careful assessment of risks and benefits for each individual by an experienced medical professional is recommended.

Research is continuing to investigate cancer prevention with drug therapy.

**Screening is important for all women**
The earlier a cancer is found, the more successful the outcome of treatment is likely to be. Therefore, all women should be aware of changes in their breasts and visit their doctor promptly with any unusual changes. Having a mammogram every two years from the age of 50 is recommended.

These are conducted free of charge at Breastscreen. For an appointment ring 13 20 50 from anywhere in Australia.

**Lifestyle may help**
The progression to breast or ovarian cancer requires mutations to build up in a number of the ‘cancer protection’ genes in the cells over time.

The reason why these mutations occur is thought to be a combination of genetic factors, environmental factors and the process of ageing.

Research is currently being undertaken to more fully understand the cause of specific gene mutations however researchers do believe a balanced diet high in fibre and low in fat, no smoking and living a healthy lifestyle will reduce the chance of developing cancer.