

**This fact sheet talks about when breast cancer is considered to be a hereditary or familial condition. This is known as an inherited susceptibility to cancer. A small number of families have an increased chance of developing cancer because they have inherited a non-working copy of a cancer gene.**



## IN SUMMARY

- Cancer is very common in the community and mostly occurs just by chance
- A small proportion of families have an inherited susceptibility to developing some cancers
- People with an inherited non-working copy of the *BRCA1*, *BRCA2* or *PALB2* gene (breast cancer protection genes) have an increased likelihood of developing breast and ovarian cancer.
- Being a woman
- Getting older. Most women who develop breast cancer are over the age of 50
- Having a strong / significant family history of breast and/or ovarian cancer
- Having Ashkenazi Jewish ancestry. Families with this background are more likely to carry a genetic change in the breast cancer protection genes such as *BRCA1* and *BRCA2*.

## WHAT IS CANCER?

Cancer occurs when cells in the body continue to divide uncontrollably. This can happen in any tissue or organ in the body. Cancerous cells have the potential to spread to other parts of the body. A breast cancer is a cancer starting in the breast.

**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. For this reason, it is not unusual to have a family member with breast cancer. It is, however, less common, to have a strong family history of breast cancer. Breast cancer can occur in men, but this is rare.

## WHAT CAUSES BREAST CANCER?

There are several risk factors which can influence someone's chance of developing breast cancer. The most important are:

- Being a woman
- Getting older. Most women who develop breast cancer are over the age of 50
- Having a strong / significant family history of breast and/or ovarian cancer
- Having Ashkenazi Jewish ancestry. Families with this background are more likely to carry a genetic change in the breast cancer protection genes such as *BRCA1* and *BRCA2*.

## WHAT IS MEANT BY A FAMILY HISTORY OF BREAST CANCER?

Not all women with a family history of breast cancer are at increased risk for developing breast cancer themselves. Many women will have blood relative(s) in their immediate or extended family with breast cancer, just because breast cancer is so common. Such women may still be at average or slightly above the average risk.

Some women, however, have a *stronger* family history. This is where a number of their close blood relatives have had breast and/or ovarian cancer and/or they were diagnosed at a young age. Depending on the pattern of cancers in the family, these women may be considered at moderate or potentially high risk of developing breast and/or ovarian cancer.

## CELLS, DNA AND GENES

Our bodies are made up of billions of cells. Each cell contains a complete copy of our genetic information or DNA. Our DNA contains the instructions for growth and development and is packaged into chromosomes that contain all our genes. Genes provide a code for the proteins our body needs to function.

We all have two copies of every gene, one that is inherited from the mother, and one from the father. As we age and grow, our cells are continually dividing to form new cells by the process of cell division. This means our DNA is copied over and over again.

**INHERITED SUSCEPTIBILITY TO BREAST CANCER**

Most breast cancer is not due to an inherited susceptibility. However a small number of cases (about 5% -10%) in Australia involve an inherited susceptibility to developing cancer (Figure 32.1). In these cases, a person has inherited a non-working copy of a 'breast cancer protection' gene. A spelling mistake in the gene that stops it working properly is called a **pathogenic variant** or **mutation**.

We all have many different genes that control the growth and division of our cells throughout life. These genes can be thought of as **cancer protection** genes.

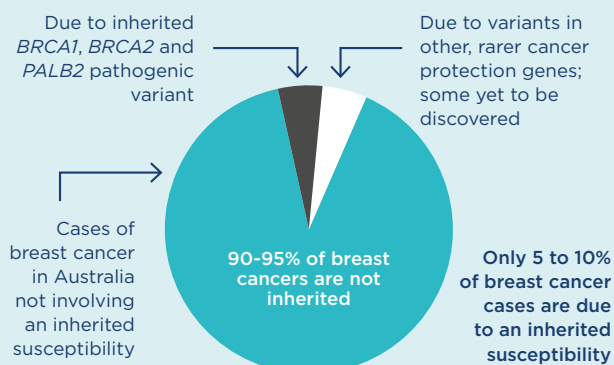
Pathogenic variants in these 'cancer protection' genes may cause cells to grow and divide in an uncontrolled way. For a cell to become cancerous, multiple variants have to occur in a number of different 'cancer protection' genes within the cell, over time.

It can take many years for a cancer to develop, and this is the reason why the risk of cancer increases with age and most cancers occur in older people.

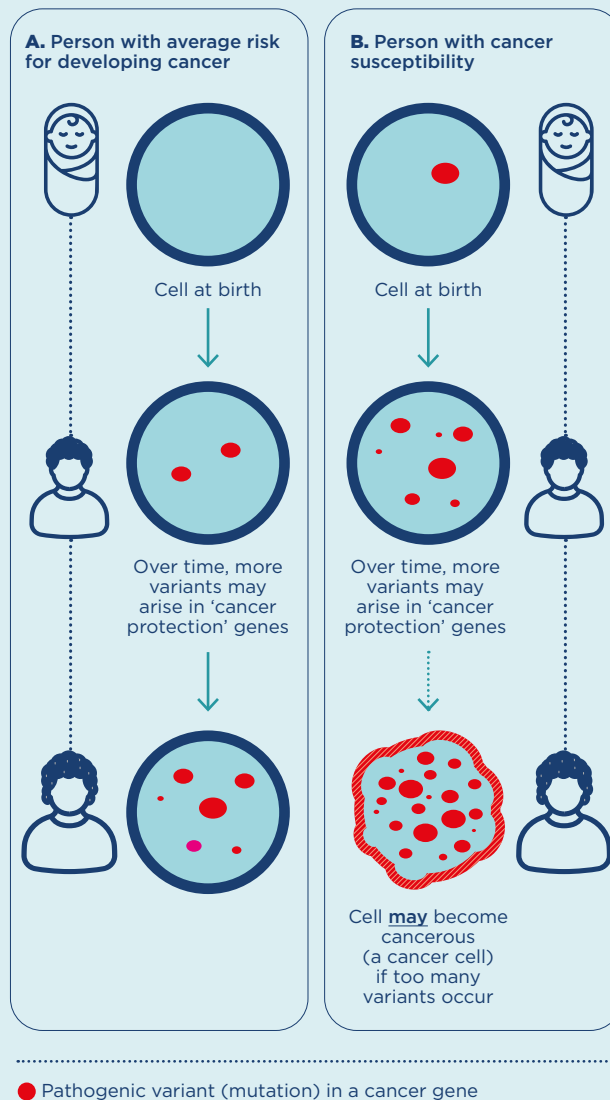
The reason why these variants occur is thought to be a combination of genetic factors, environmental factors and the process of ageing.

Figure 32.2 shows a stylised image of a cell from a person with average risk of developing cancer (left hand side) and the cell of someone with an inherited *BRCA1*, *BRCA2* or *PALB2* pathogenic variant at birth (right hand side).

**Figure 32.1:** Proportion of cases of breast cancers that involve an inherited susceptibility.



**Figure 32.2:** Increased chance of cancer cell development in those born with a cancer susceptibility compared with the average person



Over time, as we age, we accumulate variants in genes that may increase the 'burden' or risk for developing cancer. If enough of these variants arise over time, the cell becomes cancerous (a 'cancer cell'). The person with the inherited pathogenic variant is more likely to have a cancer develop in their lifetime, because their cells started with a pathogenic variant already present at birth. This means that fewer variations need to happen to the cells' protective genes for a cancer to develop.

### WHAT IS A 'STRONGER' FAMILY HISTORY THAT SUGGESTS AN INHERITED SUSCEPTIBILITY?

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

Characteristics of a family that may suggest an inherited pathogenic variant include:

- Many relatives with breast or ovarian cancer on the same side of the family.
- A family member diagnosed with breast cancer at a younger age, usually before the age of 40
- Relatives who have both breast and ovarian cancer
- A person with breast cancer in both breasts
- Breast cancer in a male relative
- A breast cancer which is said to be 'triple negative'. This refers to the specific testing of cells in tissues (pathology)
- An ovarian cancer diagnosed before the age of 70 years
- Ashkenazi Jewish ancestry as variants in the *BRCA1* and *BRCA2* breast cancer protection genes are more common in this population.

In some instances where someone has had breast or ovarian cancer, genetic testing may be covered by Medicare and arranged by one of their medical specialists. People with a strong family history can be referred by their doctor to a family cancer service.

### WHAT ARE THE CANCER PROTECTION GENES THAT CAUSE AN INCREASED RISK OF BREAST CANCER WHEN NOT WORKING?

There are several 'cancer protection' genes which, if not working, can increase the risk of breast and/or ovarian cancer developing.

The three main genes that have been identified are:

- Breast Cancer 1 gene (*BRCA1*)
- Breast Cancer 2 gene (*BRCA2*)
- *PALB2* gene

There are other known genes that can also cause a potentially high risk of breast cancer when not working, but these are usually seen in families with additional cancer types present. The *BRCA1*, *BRCA2* and *PALB2* 'cancer protection' genes are known more specifically as tumour suppressor genes because their role is to act as the 'brakes' on uncontrolled cell growth.

**Both men and women, have *BRCA1*, *BRCA2* and *PALB2* genes in their cells.**

Many families may have a strong history of breast cancer without a *BRCA1*, *BRCA2* or *PALB2* pathogenic variant being present. This indicates that there are other breast cancer susceptibility genes that have not yet been discovered. There have also been a number of genes found that are associated with a small or moderate increase in breast cancer risk. Research is continuing to study the effects of these genes and to identify new genes. Other genes linked with breast and other types of cancer are described further at the Cancer Institute NSW eviQ website.

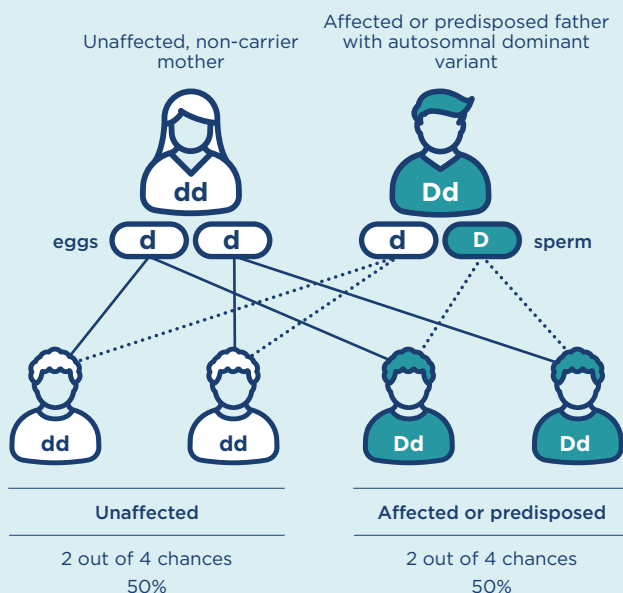
### HOW IS A BREAST CANCER PROTECTION GENE VARIANT INHERITED?

*BRCA1*, *BRCA2* and *PALB2* gene variants are inherited in an autosomal dominant pattern (*Figure 32.3*).

1. Every person carries two copies each of the *BRCA1*, *BRCA2* and *PALB2* genes, one inherited from their mother, one inherited from their father.
2. The effects of the pathogenic variant in the *BRCA1*, *BRCA2* and *PALB2* genes are **dominant** over the information in the working copy of the genes.

**Figure 32.3:**

Autosomal dominant inheritance when one parent has a non-working *BRCA1*, *BRCA2* or *PALB2* gene. The non-working gene is represented by 'D'; the working copy by 'd'.



Where one parent has a *BRCA1*, *BRCA2* or *PALB2* gene variant, in every pregnancy each of their children has a:

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

A *BRCA1*, *BRCA2* or *PALB2* gene variant can be inherited from either the mother or the father and passed on to either a son or a daughter.

People who have *not* inherited the pathogenic variant are *not* at increased risk of breast and ovarian cancer and cannot pass it on to their children. However, they still have the same risk for developing breast and ovarian cancer as the average person in the Australian population.

## GENETIC COUNSELLING AND TESTING

The genetic counselling team and in some instances other medical specialists such as oncologists may order testing covered by Medicare which may be able to:

- Work out the chance of developing breast and/or ovarian cancer based on a person's family history
- Work out whether genetic testing is likely to be helpful. Discuss the limitations, potential benefits and disadvantages of genetic testing
- Talk about cancer screening and ways to reduce risks for developing cancer.

Genetic testing for pathogenic variants in the *BRCA1* & 2 and *PALB2* genes is complex and involves:

- First identifying the gene variant via a blood sample in a family member who has or had breast and/or ovarian cancer (a **variant search**). A **variant search** is often performed on a group of selected genes (known as a panel). This group may include some different genes depending on the cancer types present in the family.

Results can be:

1. The pathogenic variant was found
  2. No pathogenic variant was found
  3. A variant of uncertain significance (VUS) was found. This is an unclear result. Further information to understand different types of results is available at [www.genetics.edu.au](http://www.genetics.edu.au)
- Then, and only if a pathogenic variant is found, testing other family members to determine if they have inherited the same variant (**predictive genetic testing**).

**Table 32.1:**

Chance of developing breast and ovarian or other cancers for people with a *BRCA1*, *BRCA2* or *PALB2* pathogenic variant. Information extracted from [eviQ Risk Management Guidelines](#).

Gene variant	Chance (risk) for women developing breast or ovarian cancer up until age 80 years	Chance (risk) for men developing breast or prostate cancer up until age 70 years	Chance (risks) over a lifetime of developing pancreatic cancer in men and women
<i>BRCA1</i>	About 70% for breast cancer About 45% for ovarian or fallopian tube cancer	About 1% risk for breast cancer About 9% for prostate cancer	Slightly increased risk for pancreatic cancer for men
<i>BRCA2</i>	About 70% for breast cancer About 15% for ovarian or fallopian tube cancer	About 7% for breast cancer About 15% for prostate cancer	Risk increased for pancreatic cancer for men (less than 5%) and women (unknown but increased)
<i>PALB2</i>	About 55% for breast cancer About 5% for ovarian or fallopian tube cancer	About 1% for breast cancer	About 2 or 3% risk for pancreatic cancer for men & women
Risk for the general population	About 12% for breast cancer About 1% for ovarian or fallopian tube cancer	Much less than 1% for breast cancer About 5% for prostate cancer	Less than 1% for men

### WHAT ARE THE CHANCES OF DEVELOPING CANCER FOR SOMEONE WHO CARRIES A PATHOGENIC VARIANT?

People with a pathogenic variant in *BRCA1* or *BRCA2* or *PALB2* have an increased chance of developing breast and ovarian cancer and some other cancers (*Table 32.1*).

### WHAT CAN BE DONE TO MANAGE AN INCREASED RISK OF BREAST AND OVARIAN CANCER DUE TO A *BRCA1*, *BRCA2* OR *PALB2* PATHOGENIC VARIANT?

#### Genetic counselling and risk management

It is recommended that people with a *BRCA1*, *BRCA2* or *PALB2* gene variant and their relatives seek management advice from a family cancer clinic or medical specialist. In some instances other medical specialists such as oncologists may order testing covered by Medicare. When meeting certain criteria for testing, genetic testing may be covered by Medicare or by the hospital. National guidelines for health care professionals exist at the Cancer Institute NSW eviQ website.

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

Options for surgery to reduce the risk of breast cancer developing should be discussed with a specialist doctor. This may be considered by some women.

Risk-reducing surgery should also be discussed to reduce the risk of ovarian cancer for which there is no screening test as yet available. In women who have a diagnosis of cancer, if they are found to have a variant in a gene that could explain their cancer, this may also inform a treatment approach for them.

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 and treatment.

#### Screening is important for all women

The earlier a cancer is found, the more successful the outcome of treatment is likely to be. All women are advised to 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 for the average woman.

These are conducted free of charge at BreastScreen. For an appointment, call 13 20 50 from anywhere in Australia.

### **Lifestyle may help**

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Most cancers occur due to a combination of genetic factors, environmental factors and the process of ageing.

Maintaining a balanced diet high in fibre and low in fat, not smoking and living a healthy lifestyle can reduce the risk of many cancers.

### **Planning a pregnancy**

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Testing may be available for inherited breast cancer during a pregnancy. [Genetic testing in a pregnancy](#) for genetic causes of breast cancer is optional and should be talked about in full with your doctor, midwife or [genetic counsellor](#). It may also be possible to have [pre-implantation genetic diagnosis \(PGD\)](#) to look for inherited causes in an embryo made using in vitro fertilisation (IVF). Some people also investigate egg, sperm or embryo donation. Others choose to have a natural pregnancy with no testing.

[Reproductive genetic carrier screening](#) for a range of genetic conditions that follow a recessive pattern of inheritance is also available for couples who are planning pregnancy, or are in early pregnancy.

When planning a family, options for testing are best talked about and considered before pregnancy.

More support and information is available for individuals and families through support organisations including the [Breast Cancer Network Australia](#), the [Cancer Council](#), [Pink Hope](#) and [Genetic Alliance Australia](#).