

This fact sheet describes when prostate 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

- Prostate cancer is common in the community and mostly occurs by chance
- Some rare families have an inherited faulty gene that can increase the likelihood of some individuals developing cancer
- Men with an inherited faulty *BRCA2* gene have an increased likelihood of developing prostate cancer and a slightly increased risk of breast cancer.

### WHAT IS PROSTATE CANCER?

Prostate cancer is a common disease in the community. About 1 in 5 Australian men will develop prostate cancer before the age of 85. Prostate cancer is the most common cancer for men over 55 years of age, but rarely occurs before the age of 50.

The prostate, a small gland found only in men, is located at the base of the bladder. As men grow older, especially over the age of 50, the prostate normally gets bigger. This enlargement can block the passage of urine, causing problems. While this is commonly due to a non-cancerous enlargement, prostate cancer may also cause these problems.

### WHAT CAUSES PROSTATE CANCER?

There is no single cause.

There are a number of risk factors which can influence a man's chance of developing prostate cancer. The most important are:

- Getting older. More than two-thirds (70%) of men newly diagnosed with prostate cancer are over the age of 65
- Having a family history of prostate cancer, particularly having a father or a brother with prostate cancer. The greater the number of relatives with prostate cancer, the greater the risk.

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

A family history of prostate cancer means having one or more close blood relatives who have, or have had, prostate cancer.

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

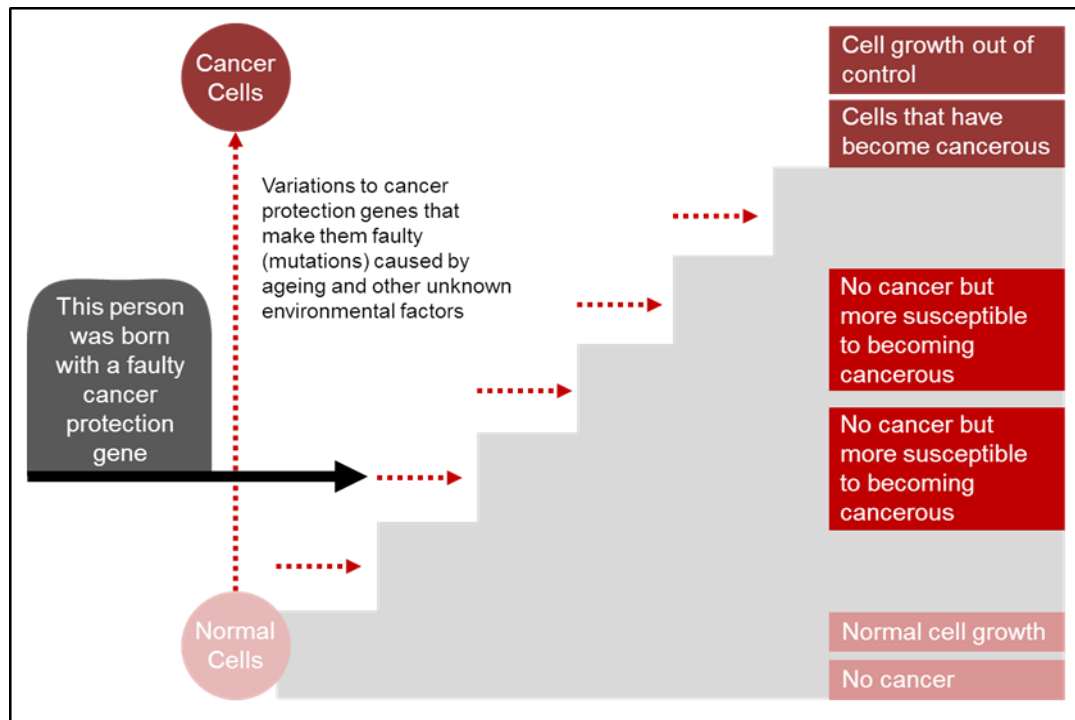
The closest male blood relatives (not relatives by marriage) are fathers, brothers and sons and are called first-degree relatives. Uncles, nephews and grandfathers are second-degree relatives.

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.

Many men have a few relatives who have or had prostate cancer just because prostate cancer is common. Such men may be only slightly above the average risk. Some men have a 'stronger' family history where a number of their close male blood relatives have or had prostate cancer.

Most of these men will have a moderately increased chance of developing prostate cancer. A small number will have a potentially high chance of developing prostate cancer because their family has an inherited a predisposition to this cancer.



**Figure 35.1:** Changes build up in the different ‘cancer protection’ genes in the cells over time due to ageing and other environmental factors. Some of these changes make the ‘cancer protection’ genes faulty. Each step on the staircase to becoming cancerous cells represents a change in a copy of one of the many ‘cancer protection’ genes in the cells.

### INHERITED PREDISPOSITION TO DEVELOPING PROSTATE CANCER

Most prostate cancer cases are not due to an inherited predisposition to develop the condition. However, a very small number (around 5%-10%) of cases in Australia involve an inherited predisposition to develop the cancer. In these cases, the men have inherited a faulty copy of a prostate ‘**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 prostate 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 prostate cancer can take many, many years and is mostly seen in older men.

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 prostate cells is not as tightly controlled as in other men 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 35.1)

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 (*Figure 35.1*). Their chance of developing prostate 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 prostate cancer.

#### WHAT ARE THE INHERITED FAULTY 'CANCER PROTECTION' GENES THAT CAUSE PROSTATE CANCER?

It is important to remember that prostate cancer itself is not inherited, although cancer that arises from an inherited faulty 'cancer protection' gene is sometimes called hereditary cancer.

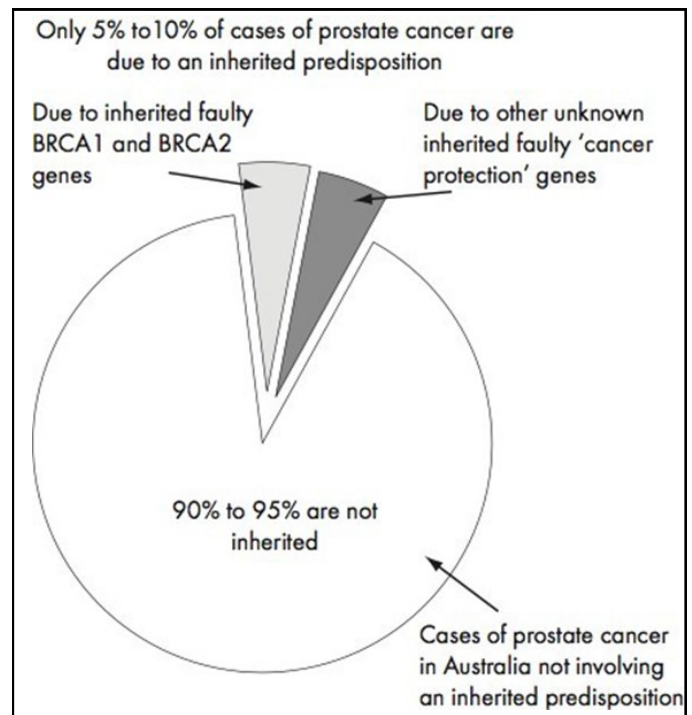
The inheritance of a predisposition to prostate cancer is not well understood and research is continuing. As yet there has been no single gene identified that is associated with most prostate cancers.

However, there are a number of 'cancer protection' genes in which inherited mutations have been found to contribute to the development of prostate cancer in men.

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. **Both men and women, have *BRCA1* and *BRCA2* genes in their cells.** Mutations in the *BRCA1* and *BRCA2* genes are also well known to be involved in increasing the risk of breast and ovarian cancer.



*Figure 35.2: Proportion of cases of prostate cancer that involve an inherited predisposition (susceptibility).*

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

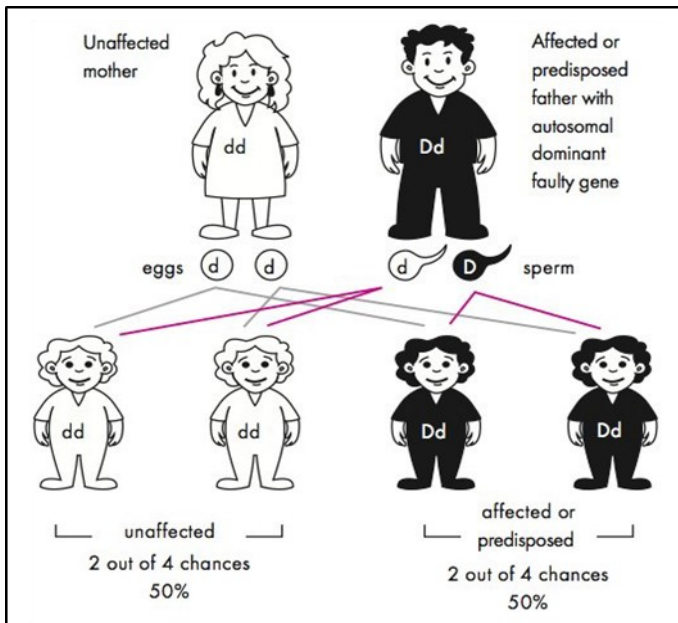
*BRCA1* or *BRCA2* gene mutations are inherited in an autosomal dominant pattern (*Figure 35.3*).

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.



**Figure 35.3:** Autosomal dominant inheritance when one parent has a faulty gene copy. The faulty gene is represented by 'D'; the working copy by 'd'.

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.

Men who have not inherited a faulty gene are not at significantly increased risk of developing prostate cancer over their lifetime and cannot pass the faulty gene on to their own children. However, they still have the same risk for developing prostate cancer as the average man in the Australian population.

**WHAT ARE THE CLUES IN A FAMILY HISTORY OF PROSTATE 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 prostate cancer may mean an inherited gene mutation is present in the family. This usually includes one or more of the following:

- a family member diagnosed with prostate cancer at a younger age usually before the age of 60
- two or more relatives on the same side of the family with prostate cancer, particularly a father and brother.

**GENETIC COUNSELLING AND TESTING**

People with a strong family history can be referred by their doctor to a specialist family cancer service or their local genetic counselling service.

The genetic counselling team may be able to:

- Clarify the chance of developing prostate 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 prostate 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**).

Gene mutation	Chance (risk) for a <b>man</b> developing prostate cancer up until age 65 years	Chance (risk) for a <b>man</b> developing other cancers
<i>BRCA 1</i>	Very slight increased risk for prostate cancer	Very slight increased risk for breast and pancreatic cancer
<i>BRCA2</i>	About 15% risk for prostate cancer	Slight increased risk for breast cancer. Very slight increased risk for pancreatic cancer.

**Table 35.1:** Chance of developing prostate cancer or other cancers for men with a *BRCA1* or *BRCA2* gene mutation

**WHAT IS THE CHANCE OF DEVELOPING PROSTATE CANCER AND OTHER CANCERS?**

Men with a **BRCA1** or **BRCA2** gene mutation have an increased chance of developing prostate cancer and some other cancers (*Table 35.1*).

**MANAGING AN INCREASED RISK OF DEVELOPING PROSTATE 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.

**Screening**

Screening men who are well with no symptoms of prostate cancer is a controversial issue as there is no test reliable enough to support screening all men for prostate cancer.

For men with a family history of prostate cancer, however, such as having a father or brother with prostate cancer diagnosed before 60, it is important to discuss the pros and cons of having prostate cancer screening with a doctor. Men are encouraged to increase awareness of their chest area and discuss regular chest palpation with their doctor.

**Lifestyle may help**

The progression to prostate 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 mutation. 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.