

# Advice about familial aspects of breast cancer and epithelial ovarian cancer

a guide for health professionals FEBRUARY 2006

**These guidelines contain three parts:**

1. Information for health professionals
2. Tables which describe risk based on family history and current suggested management
3. Information for consumers that may be photocopied for distribution.

The guidelines have been developed to cover familial aspects of both breast and epithelial ovarian cancer. In some families genetic testing can be used to assess risk. This testing is available through family cancer clinics.

The information on page two can be used to determine a woman's risk of developing breast cancer, based on her family history. The information on page three can similarly be used to determine her risk of developing ovarian cancer.

These guidelines are a general guide for appropriate practice to be followed subject to the health professional's judgement of each case. They are designed to provide information to assist decisions made by health professionals and their patients. They are based on the best available evidence or consensus opinion of experts where evidence does not exist at the date of publication.

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# INFORMATION FOR WOMEN ABOUT FAMILY HISTORY OF BREAST CANCER OR OVARIAN CANCER

## What is cancer?

Cancer occurs when cells in the body become abnormal and grow out of control.

## Why does breast or ovarian cancer occur?

Cell growth is controlled by a cell's genes. Genes contain the information that determines how our cells grow and work throughout our lifetime. This information can be passed from one generation to the next (i.e. inherited). Sometimes, genes in breast or ovarian cells develop a fault. This causes the cells to grow out of control, leading to cancer. These genetic faults, which occur throughout life, are not inherited.

This occurs more often in older women. The reasons for this are not yet fully understood.

## What is a woman's chance of developing breast or ovarian cancer?

All women have a chance of developing breast or ovarian cancer at some time during their life. The risk of developing either cancer increases with age.

- About 1 in 11 women will develop breast cancer at some time during their life
- About 1 in 100 women will develop ovarian cancer at some time during their life

## What are the "risk factors" for breast and ovarian cancer?

There are many things, called risk factors, which can increase a woman's chance of developing breast or ovarian cancer.

Being female, increasing age and family history are the main risk factors.

*Most women who develop breast or ovarian cancer are over the age of 50.*

## What is meant by a family history of breast or ovarian cancer?

A family history of breast or ovarian cancer means having one or more blood relatives who have, or have had, breast or ovarian cancer. These relatives could be on either the father's or the mother's side of the family. Because breast cancer is common, some women will have a family history by chance.

However, some women with a family history may have inherited a faulty gene which increases the risk of cancer. The women most likely to have inherited a faulty gene are those with the strongest family history of breast or ovarian cancer.

Understanding your family history of breast or ovarian cancer can provide an indication of your chance of developing either disease:

- most women have close to the average chance for the Australian population
- some women have a moderately increased chance
- a few women have a high chance

## How does your family history affect your chance of developing breast or ovarian cancer?

A woman could be at potentially high risk of developing either breast or ovarian cancer if she has:

1. Three or more close blood relatives on the same side of the family with breast or ovarian cancer

**OR**

2. Two or more close blood relatives on the same side of the family (mother's or father's) with breast or ovarian cancer, plus one or more of the following features on the same side of the family:

- additional relative(s) with breast or ovarian cancer
- breast and ovarian cancer in the same person
- breast cancer before the age of 40
- breast cancer in both breasts
- breast cancer in a male relative
- Ashkenazi Jewish ancestry

**OR**

3. Three or more close relatives on the same side of the family with colorectal cancer, cancer of the uterus, gastric cancer and others involving the renal tract (possibly hereditary non-polyposis colorectal cancer)

**OR**

4. A family member who has had a genetic test that has shown that she has an inherited fault in a gene associated with breast or ovarian cancer.

## Inheriting a breast or ovarian cancer gene fault

Breast or ovarian cancer caused by inheriting a faulty gene is called hereditary cancer. We all inherit a set of genes from each of our parents. Sometimes there is a fault in one copy of a gene which stops that gene working properly. This fault is called a mutation. There are several genes for which inherited faults may be involved in the development of breast or ovarian cancer. These are genes which normally prevent a woman developing breast or ovarian cancer. Some of these are genes that you may have heard of called BRCA1 and BRCA2.

Their names come from the abbreviation of "breast cancer one" and "breast cancer two". If a woman has inherited a fault in one of these genes, she has a high chance of developing breast or ovarian cancer, although it does not mean that she is certain to develop cancer.

**Around 5% of all breast and ovarian cancers can be explained by an inherited gene fault in BRCA1 or BRCA2**

## Early detection - what you can do

The earlier that cancer is found the more successful the outcome is likely to be. Therefore, it is recommended that:

### Breast Cancer

- women of all ages, regardless of whether they attend for mammographic screening, are aware of how their breasts normally look and feel and promptly report any new or unusual changes to their general practitioner.
- women 50-69 years attend the BreastScreen Australia program for free screening mammograms every two years. Women aged 40-49 years are also eligible for this Program, but mammographic screening is not recommended for women younger than 40 years. (For a BreastScreen appointment ring 13 20 50 from anywhere in Australia)

### Ovarian Cancer

- women consult their GP if they have persistent symptoms that are unusual for them such as abdominal or pelvic pain, bloating, unexplained weight gain or loss, or fatigue.

### In addition, for women with a family history:

Women concerned about their family history can talk to their general practitioner. It may be appropriate for some women with a strong family history to be referred to a family cancer clinic. After assessing detailed information about a woman's family history of cancer, these clinics can:

- provide information about a person's risk of developing cancer
- give an estimate of the likelihood of carrying an inherited mutation in a cancer-predisposing gene
- provide advice about possible strategies that might help reduce the risk of cancer
- provide counselling and support
- discuss what medical check-ups may be appropriate
- if appropriate, discuss the limitations, potential benefits, and possible consequences of genetic testing.

**You can find out more about breast and ovarian cancer by visiting the NBCC website at [www.nbcc.org.au](http://www.nbcc.org.au)**

# ADVICE ABOUT FAMILIAL ASPECTS OF BREAST CANCER AND OVARIAN CANCER

## Assessing family history

Family history of breast or ovarian cancer can be used to estimate:

- a woman's risk of developing these cancers
- the probability of having an inherited mutation in a known cancer predisposing gene

Key factors associated with increased risk include:

- Multiple relatives affected by breast cancer (male or female) or ovarian cancer
- Younger age at cancer diagnosis in relatives
- Relatives affected by both breast and ovarian cancer
- Relatives affected with bilateral breast cancer
- Ashkenazi Jewish ancestry

## Taking a family history

An accurate family history should include:

- asking the woman about any primary cancer in all 1° (parents, siblings, children) and 2° (aunts, uncles, nieces, nephews, grandparents) relatives on **both sides of the family**
- establishing the site and age at diagnosis of the cancer(s)
- confirming, if possible, reports of cancer in relatives – *a person's knowledge of their family history may be inaccurate*
- updating the family history regularly – it may change with time

Consider relatives on each side of the family separately.

## Breast cancer

About 1 in 11 Australian women develop breast cancer before the age of 75.<sup>1</sup> It is the most common cause of cancer death in Australian women.

## Ovarian cancer

About 1 in 100 Australian women develop epithelial ovarian cancer before the age of 75.<sup>1</sup> Ovarian cancer, although not the most common gynaecological malignancy, is the leading cause of death from such malignancies.

## Risk factors for breast and ovarian cancer

The main risk factors for breast and ovarian cancer are being female, increasing age and family history.

Family history does not necessarily imply an inherited genetic cause. However, at least 1% to 5% of breast cancers, and 5% to 10% of ovarian cancers, involve the inheritance of a mutated gene.

The vast majority of affected women do not carry an inherited mutation in a known breast or ovarian cancer predisposing gene.

Table 1: Approximate risk of developing breast or ovarian cancer in the next 10 years<sup>2</sup>.

If the woman is now aged	Her risk in the next 10 years	
	Breast	Ovarian
20	1 in 2500	1 in 3000
30	1 in 250	1 in 2000
40	1 in 70	1 in 900
50	1 in 40	1 in 450
60	1 in 30	1 in 300
70	1 in 30	1 in 200

## Which genes are associated with a predisposition to breast or ovarian cancer?

Women born with a mutation in one of several genes (see Table 2) have an increased risk of breast and/or ovarian cancer. There may be other genes, as yet undiscovered, in which mutations are also associated with a risk of breast or ovarian cancer.

The women most likely to have inherited a mutation are those with the strongest family history of breast or ovarian cancer.

## Family cancer clinics<sup>3</sup>

Family cancer clinics provide a service for people with a family history of cancer and their health professionals. After assessing detailed information about a woman's family history of cancer, these clinics provide:

- information about a person's risk of developing cancer
- an estimate of the likelihood of carrying an inherited mutation in a cancer predisposing gene
- counselling and support
- advice about possible strategies that might help reduce the risk of cancer
- information about early detection of cancer
- if appropriate, the offer of genetic testing (see below)

## Genetic testing

It is possible to detect mutations in some cancer predisposing genes, but this is appropriate only for some families. Some mutations may not be detected using current technology. Testing involves first searching for a gene mutation, usually in an affected family member. Should a mutation be found, testing may then be offered to other adult relatives who may carry the same mutation. Genetic testing is offered only with pre- and post-test counselling to discuss the limitations, potential benefits and possible consequences.

Table 2. Genes for which mutations are known to be associated with an inherited predisposition to breast or ovarian cancer and possibly cancer at other sites

Gene	Mutation frequency	Major sites at risk	Risk to age 75 in mutation carriers <sup>d</sup>	Other possible sites with up to 10% lifetime risk
<b>BRCA1</b>	~1/1000 <sup>a</sup>	Breast Ovary	40% – 80% 10% – 60%	Prostate
<b>BRCA2</b>	~1/1000 <sup>a</sup>	Breast Ovary	40% – 80% 10% – 40%	Male breast, prostate, pancreas
<b>Tp53<sup>b</sup></b>	~1/10,000	Breast Bone or Soft tissue	>50% 10% – 50%	Brain, lung, adrenal gland
<b>Mismatch repair genes (MMR)<sup>c</sup></b>	~1/1000	Large bowel Uterus	50% – 80% 40%	Ovary, other gastro-intestinal, renal tract

<sup>a</sup> ~1/100 for individuals of Jewish descent

<sup>b</sup> This syndrome is commonly referred to as the Li-Fraumeni syndrome

<sup>c</sup> This syndrome is commonly referred to as hereditary non-polyposis colorectal cancer (HNPCC)

<sup>d</sup> There is a wide range of risk associated with mutations in these genes

# ADVICE ABOUT FAMILIAL ASPECTS OF BREAST CANCER

The following categorisation applies to women without breast or ovarian cancer:

## 1. At or slightly above average risk

### Covers more than 95% of the female population

- No confirmed family history of breast cancer
- One 1° relative diagnosed with breast cancer at age 50 or older
- One 2° relative diagnosed with breast cancer at any age
- Two 2° relatives on the same side of the family diagnosed with breast cancer at age 50 or older
- Two 1° or 2° relatives diagnosed with breast cancer, at age 50 or older, but on different sides of the family (i.e. one on each side of the family)

As a group, lifetime risk of breast cancer is between 1 in 11 and 1 in 8. This risk is no more than 1.5 times the population average.

## 2. Moderately increased risk

### Covers less than 4% of the female population

- One 1° relative diagnosed with breast cancer before the age of 50 (without the additional features of the potentially high-risk group – see section 3)
- Two 1° relatives, on the same side of the family, diagnosed with breast cancer (without the additional features of the potentially high-risk group - see section 3)
- Two 2° relatives, on the same side of the family, diagnosed with breast cancer, at least one before the age of 50, (without the additional features of the potentially high-risk group – see section 3)

As a group, lifetime risk of breast cancer is between 1 in 8 and 1 in 4. This risk is 1.5 to 3 times the population average.

## 3. Potentially high risk

### Covers much less than 1% of the female population

- Women who are at potentially high risk of ovarian cancer (See Category 3 below)
- Two 1° or 2° relatives on one side of the family diagnosed with breast or ovarian cancer **plus** one or more of the following features on the same side of the family:
  - additional relative(s) with breast or ovarian cancer
  - breast **and** ovarian cancer in the same woman
  - breast cancer diagnosed before the age of 40
  - Ashkenazi Jewish ancestry
  - bilateral breast cancer
  - breast cancer in a male relative
- One 1° or 2° relative diagnosed with breast cancer at age 45 or younger **plus** another 1° or 2° relative on the same side of the family with sarcoma (bone/soft tissue) at age 45 or younger
- Member of a family in which the presence of a high risk breast cancer gene mutation has been established

As a group, lifetime risk of breast cancer is between 1 in 4 and 1 in 2. Risk may be more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.

Contact a specialist cancer genetic service<sup>3</sup> if concerned about a woman's family history of cancer

1. Reassure the woman that her risk is the same as, or slightly above average for the general population and that **more than 90% of women in this group will not develop breast cancer**
2. It is recommended that women 50-69 years attend the BreastScreen Australia program for free screening mammograms every two years. Women aged 40-49 years are also eligible for this Program, but mammographic screening is not recommended for women younger than 40 years
3. A firm recommendation regarding clinical breast examination (CBE) is not possible as there is no evidence to either encourage or discourage the use of CBE as a screening method in women of any age.

1. Advise the woman that she has a moderately increased risk of developing breast cancer, but that **75% - 90% of women in this group will not develop breast cancer**. A more precise risk assessment and management plan may be available from a specialist cancer service or family cancer clinic.<sup>3</sup>
2. While evidence about optimal management strategies for this group does not exist, the following recommendations are based on expert consensus opinion: \*
  - advise the woman to at the very least attend for screening mammograms as recommended for Category 1
  - additional surveillance, such as mammography from a younger age, or more frequently, should be considered on an individual basis.
3. A firm recommendation regarding clinical breast examination (CBE) is not possible as there is no evidence to either encourage or discourage the use of CBE as a screening method in women of any age.
4. Discuss possible participation in a relevant approved clinical trial for the prevention of breast cancer

1. Advise the woman that she has a potentially high risk of developing breast cancer and perhaps other cancers, but that **50% – 75% of women in this group will not develop breast cancer**.
2. Referral to a family cancer clinic for risk assessment and management plan should be discussed, especially if the woman wishes to clarify her genetic risk or that of her family, or wishes to consider risk-reducing surgery.
3. It is recommended that an individual surveillance program be developed in consultation with a cancer specialist. While evidence about optimal strategies for this group does not exist, an appropriate surveillance program may include: \*
  - attending for regular clinical breast examination
  - annual mammography with or without other imaging techniques
  - surveillance for ovarian cancer
4. The age at which screening commences may be influenced by aspects of family history. Although this should be determined on an individual basis, it is generally accepted practice to begin screening at least five years prior to the age of diagnosis of the closest relative.
5. Discuss possible participation in a relevant approved clinical trial for the prevention of breast cancer.

\* Discussion should include information about the advantages and disadvantages of individual surveillance options

It is recommended that all women, regardless of whether they attend for mammographic screening, are aware of how their breasts normally look and feel and promptly report any new or unusual changes to their general practitioner.

# ADVICE ABOUT FAMILIAL ASPECTS OF OVARIAN CANCER

The following categorisation applies to women **without** breast or ovarian cancer:

## 1. At average risk or 2. At moderately increased risk

### Covers more than 99% of the female population

- No confirmed family history of epithelial ovarian cancer.
- One 1° or 2° relative diagnosed with ovarian cancer at any age (provided the family is not of Ashkenazi Jewish ancestry\* and does not have any additional cases of breast cancer).
- Two 1° or 2° relatives diagnosed with ovarian cancer, but on different sides of the family (i.e. one on each side of the family).

*\*High-risk ovarian and breast gene mutations are more common in people of Ashkenazi Jewish ancestry.*

**As a group, lifetime risk of ovarian cancer is between 1 in 100 and 1 in 30. This risk is no more than 3 times than the population average.**

## 3. Potentially high risk

### Covers less than 1% of the female population

- Women who are at potentially high risk of breast cancer (see Category 3 above)
- One 1° relative diagnosed with epithelial ovarian cancer in a family of Ashkenazi Jewish ancestry\*.
- One woman with ovarian cancer at any age, and another with breast cancer before the age of 50, where the women are 1° or 2° relatives of each other
- Two 1° or 2° relatives on the same side of the family diagnosed with epithelial ovarian cancer, especially if one or more of the following features occurs on the same side of the family:
  - additional relative(s) with breast or ovarian cancer.
  - breast cancer diagnosed before the age of 40.
  - bilateral breast cancer.
  - breast and ovarian cancer in the same woman.
  - breast cancer in a male relative.

- Three or more 1° or 2° degree relatives on the same side of the family diagnosed with any cancers associated with hereditary non-polyposis colorectal cancer (HNPCC): colorectal cancer (particularly if diagnosed before the age of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the renal tract.
- A woman suspected to have HNPCC
- Member of a family in which the presence of a high-risk ovarian cancer gene mutation has been established.

**As a group, lifetime risk of ovarian cancer is between 1 in 30 and 1 in 3. This risk is more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.**

**Contact a specialist cancer genetic service<sup>1</sup> if concerned about a woman's family history of cancer**

1. Reassure the woman that her risk is at or at most moderately above the average for the general population and that **more than 97% of women in this group will not develop ovarian cancer.**
2. Advise the woman about current best practice for the early detection of cancers for the population.
3. Advise the woman to visit her general practitioner promptly with any health changes.

**Screening the general population for epithelial ovarian cancer cannot be justified on the basis of the low prevalence of ovarian cancer and the inadequate sensitivity of currently available tests.**

1. Advise the woman that she has a potentially high risk of developing ovarian cancer and perhaps other cancers, such as breast cancer, but that **the majority of women in this group will not develop ovarian cancer.**
2. If the woman wishes to clarify her genetic risk or that of her family, or wishes to consider risk-reducing surgery, discuss referral to a specialist family cancer clinic for advice, appropriate counselling and management.
3. Because bilateral salpingo-oophorectomy has been shown to reduce the risk of ovarian and breast cancer in women with a mutation in BRCA1 or BRCA2, advise the woman to see a gynaecological oncologist to discuss her options. Should a woman choose not to have risk-reducing surgery, an appropriate individualised surveillance program may include:
  - visiting her general practitioner promptly with any health changes.
  - transvaginal ultrasonography.\* (The age at which this commences may depend on the family cancer history and if a high-risk ovarian cancer gene mutation has been identified in the woman or her family).

- CA125 measurement (after the menopause)\*.
- surveillance relevant to other cancers (e.g. attending for clinical breast examination, mammography for breast cancer; or other surveillance if the family cancer history is consistent with HNPCC).
- 4. Discuss possible participation in a relevant approved clinical trial.

*\* There is no evidence that these tests reduce mortality from ovarian cancer but they may be considered for women who have not undergone risk-reducing salpingo-oophorectomy).*

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