



Advice about familial aspects of breast cancer and epithelial ovarian cancer

a guide for health professionals DECEMBER 2010

This guide has 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 guide has been developed to cover familial aspects of both breast and epithelial ovarian cancer.*

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

The information on page two can be used to determine an unaffected 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.

To estimate the risk of a woman developing breast or ovarian cancer, based on family history, with additional family history scenarios not covered in this guide, visit the Familial Risk Assessment – Breast and Ovarian Cancer (FRA-BOC) on-line at www.nbooc.org.au/fraboc

In some families genetic testing can be used to assess risk. The availability, limitations, potential benefits and possible consequences of genetic testing can be discussed at a family cancer clinic.

** Note: Many of these cancers may originate in the fallopian tubes but they are managed as epithelial ovarian cancer.*

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 (male or female) or ovarian cancer
- young 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

Consider relatives on each side of the family separately.

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.*

Breast cancer

One in 9 Australian women develops breast cancer before the age of 85. In 2006 breast cancer was second most common cause of cancer death in Australian women.

Ovarian cancer

One in 78 Australian women develops epithelial ovarian cancer before the age of 85. Ovarian cancer is the leading cause of death from gynaecological malignancy.

NB: The average life expectancy of Australian women is 84 years.

For key statistics about breast and ovarian cancer see www.nbocc.org.au

Table 1: Approximate risk of developing breast or ovarian cancer in the next 10 years (NBOCC 2005).

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 known 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

Family cancer clinics provide a service for people with a family history of cancer and their health professionals. The service is offered to any family members, whether or not they have been diagnosed with cancer. After assessing detailed information about a woman's family history of cancer, these clinics provide genetic counselling including:

- information about a person's risk of developing cancer based on family history and other relevant factors

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 ^d	Other possible sites with up to 10% lifetime risk
BRCA1	~1/1000 ^a	Breast Ovary	40% - 80% 10% - 60%	Prostate
BRCA2	~1/1000 ^a	Breast Ovary	40% - 80% 10% - 40%	Male breast, prostate, pancreas
Tp53 ^b	~1/10,000	Breast Bone or Soft tissue	>50% 10% - 50%	Brain, lung, adrenal gland, haematological and other
Mismatch repair genes (MMR) ^c	~1/1000	Large bowel Uterus	50% - 80% 40%	Ovary, other gastro-intestinal, renal tract

^a ~1/100 for individuals of Jewish descent

^b This syndrome is commonly referred to as the Li-Fraumeni syndrome

Risk factors for breast and ovarian cancer

The main risk factors for breast and ovarian cancer are

- being female
- increasing age
- family history.

Family history does not necessarily imply an inherited genetic cause. However, at least 1% to 5% of breast cancers and up to 15% of all cases of invasive ovarian cancer 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.

- advice about strategies that reduce the risk of cancer
- information about early detection of cancer
- an estimate of the likelihood of carrying an inherited mutation in a cancer-predisposing gene
- if appropriate, the offer of genetic testing.

Genetic testing

It is possible to detect mutations in some cancer-predisposing genes. Some mutations may not be detected using current technology. Testing involves first searching for a gene mutation, usually in a blood sample from 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.

For a list of family cancer clinics see www.nbocc.org.au/fraboc

^c This syndrome is commonly referred to as hereditary non-polyposis colorectal cancer (HNPCC) or Lynch Syndrome

^d There is a wide range of risk associated with mutations in these genes

CATEGORIES OF RISK

MANAGEMENT

1. At or slightly above average risk

Covers more than 95% of the female population

As a group, risk of breast cancer up to age 75 is between 1 in 11 and 1 in 8. This risk is no more than 1.5 times the population average.

- 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).

- **Clarify** risk. See www.nbocc.org.au/fraboc
- **Advise** risk is similar to that of the general population
- **Reassure** that 9 out of 10 women in this group will not develop breast cancer
- **Inform** that breast cancer risk increases with age (see Table 1)
- BreastScreen Australia provides free screening mammograms every two years from age 40. **Call 13 20 50 for an appointment**
- **Discuss** modifiable risk factors for breast cancer (See www.nbocc.org.au/risk/index.html)
- **Encourage** all women to be aware of the normal look and feel of their breasts and promptly report persistent or unusual changes to their GP
- **Investigate** women with symptoms using the Triple Test. (See *The investigation of a new breast symptom*, National Breast Cancer Centre (NBCC),* 2006).

2. Moderately increased risk

Covers less than 4% of the female population

As a group, risk of breast cancer up to age 75 is between 1 in 8 and 1 in 4. This risk is 1.5 to 3 times the population average.

- One 1° relative diagnosed with breast cancer before the age of 50 (*without the additional features of the potentially high-risk group – see category 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 category 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 category 3*).

- **Clarify** risk. See www.nbocc.org.au/fraboc
- **Advise** that there is a moderately increased risk of developing breast cancer
- **Reassure** that most of the women in this group will not develop breast cancer
- **Advise** the woman to attend BreastScreen for regular screening mammograms
- **Advise** that a more precise risk assessment and management plan is available from a family cancer clinic or specialist cancer clinic.

Additional surveillance

- Annual mammograms from age 40 may be recommended if the woman has a first degree relative < 50 years diagnosed with breast cancer
Referral to a family cancer clinic may be appropriate
- Annual mammograms are not recommended for women with a single relative diagnosed > 50 years, as there is no clear evidence of benefit
- In women over 35 years of age, consider the use of medication, such as tamoxifen or raloxifene, to reduce risk of developing breast cancer
This requires careful assessment of risk and benefits in the individual case by an experienced medical professional
- **Discuss** possible participation in a relevant clinical trial for risk reduction/prevention of breast cancer
See www.australiancancertrials.gov.au, www.anzctr.org.au, www.anzbctg.org.au
- **Discuss** modifiable risk factors for breast cancer. (See www.nbocc.org.au/risk/index.html)
- **Encourage** all women to be aware of the normal look and feel of their breasts and promptly report persistent or unusual changes to their GP
- **Investigate** women with symptoms using the Triple Test.

3. Potentially high risk

Covers less than 1% of the female population

As a group, risk of breast cancer up to age 75 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.

- Women who are at potentially high risk of ovarian cancer (See page 3)
- Two 1° or 2° relatives on one side of the family diagnosed with breast or ovarian cancer **plus** one or more of the following 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
 - Jewish ancestry
 - 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.

- **Clarify** risk. See www.nbocc.org.au/fraboc
- **Advise** that although there is a high or potentially high risk of developing breast cancer, and perhaps other cancers, many women in this group will not develop breast cancer
- **Advise** referral to a family cancer clinic for risk assessment, possible genetic testing and management plan.

Discuss risk reduction strategies which may include:

- Risk-reducing surgery
- Consideration of the use of medication, such as tamoxifen or raloxifene, to reduce risk of developing breast cancer.

Ongoing surveillance strategies which may include:

- Regular clinical breast examination
- Annual breast imaging with mammography, MRI or ultrasound
- Consideration of ovarian cancer risk (see page 3).
- **Discuss** possible participation in a relevant clinical trial for risk reduction/prevention of breast cancer
For available trials see www.australiancancertrials.gov.au, www.anzctr.org.au, www.anzbctg.org.au
- **Discuss** modifiable risk factors for breast cancer. (See www.nbocc.org.au/risk/index.htm)
- **Encourage** all women to be aware of the normal look and feel of their breasts and promptly report persistent or unusual changes to their GP
- **Investigate** women with symptoms using the Triple Test.

CATEGORIES OF RISK

MANAGEMENT

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

Covers more than 99% of the female population

As a group, risk of ovarian cancer up to age 75 is between 1 in 100 and 1 in 30. This risk is no more than 3 times than the population average.

- 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 ancestry¹ 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).

¹High-risk ovarian and breast gene mutations are more common in people of Ashkenazi Jewish ancestry.

- **Advise** that risk is similar to the rest of the population
- **Reassure** that more than 9 out of 10 women in this group will not develop ovarian cancer
- **Inform** that evidence does not support screening women in this group with ultrasound or CA125

Note: If a woman reports a family history of epithelial ovarian cancer between the ages of 35 and 50, consider referral to a family cancer clinic for risk assessment, possible genetic testing and management plan.

3. Potentially high risk

Covers less than 1% of the female population

As a group, risk of ovarian cancer up to age 75 is between 1 in 30 and 1 in 2. This risk is more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.

- Women who are at high risk of breast cancer due to a gene fault
- One 1° or 2° relative diagnosed with epithelial ovarian cancer in a family of Ashkenazi Jewish ancestry¹
- One 1° or 2° relative 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 a family history suggestive of Lynch Syndrome (or HNPCC) e.g. colorectal cancer (particularly if diagnosed before the age of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the renal tract
- Member of a family in which the presence of a high-risk ovarian cancer gene mutation has been established.

- **Advise** there is a high /potentially high risk of developing ovarian cancer, and perhaps other cancers such as breast, bowel or endometrial cancer
- **Advise** referral to a family cancer clinic for risk assessment, possible genetic testing and management plan
- **Discuss** risk management strategies
 - **Risk-reducing surgery.** The **most effective** risk-reducing strategy for ovarian cancer is bilateral salpingo-oophorectomy (BSO). (NB: BSO also reduces breast cancer risk when done before age 40)
 - **Chemoprevention** (Use of medication to prevent ovarian cancer). Use of the oral contraceptive pill (OCP) may be an option for pre-menopausal women who choose not to have risk-reducing surgery. The impact on breast cancer risk for mutation carriers is unclear.
- **Ovarian cancer surveillance is not recommended for women at high or potentially high risk.** Evidence shows that ultrasound or CA125, singly or in combination, is not effective at detecting early ovarian cancer
- **Discuss** 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 Lynch Syndrome)
- **Discuss** possible participation in a relevant clinical trial. For information about possible trials see www.australiancancertrials.gov.au, www.anzgog.org.au

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INFORMATION FOR WOMEN ABOUT FAMILY HISTORY OF BREAST CANCER AND OVARIAN CANCER

Why does breast or ovarian cancer occur?

Sometimes some genes, which normally protect against cancer, 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 before the age of 75
- About 1 in 120 women will develop ovarian cancer before the age of 75
- Most women who develop breast or ovarian cancer are over the age of 50

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.

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 mother's side of the family.

Because breast cancer is common, many 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

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
 - 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 cancers involving the renal tract (possible hereditary non-polyposis colorectal cancer or Lynch Syndrome)

OR

4. A family member who has had a genetic test that has shown that he or 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 are 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 cancers and up to 15% of invasive ovarian cancers can be explained by an inherited gene fault in BRCA1 or BRCA2.

A woman who has had a gene fault in BRCA1 or BRCA2 found through genetic testing is at high risk of developing breast or ovarian cancer. Men can also carry these gene faults.

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 population mammographic screening is not recommended for women younger than 40 years. (For a BreastScreen appointment ring 13 20 50 from anywhere in Australia)
- Women at high risk of breast cancer may be advised to begin screening at a younger age, and at more frequent intervals, than those at population risk

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. 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 NBOCC website at www.nbocc.org.au

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