Family history and hereditary breast cancer
Background Paper

This background paper serves as a backdrop to Breast Cancer Network Australia’s (BCNA) position statement on family history and hereditary breast cancer. This paper provides an overview of:

- family history, genetic risk and breast cancer
- current guidelines for risk management
- developments in risk management
- issues in genetic testing.

Family history, genetic risk and breast cancer

An extensive family history of breast cancer is a known predictive risk factor for the disease. A strong family history can indicate an inherited predisposition through the presence of a germline mutation in genes associated with breast cancer. A germline mutation is a mutation that occurs in the genetic material of the egg or sperm, and can be passed on at conception. Scientists estimate that inherited gene mutations account for 5% to 10% of all breast cancer.¹

The search for breast cancer genes susceptible to inherited abnormalities has largely progressed through studies on families with multiple affected members. These studies led to the identification in the 1990s of BRCA1 and BRCA2. Some research suggests that BRCA1 and BRCA2 are tumour suppressor genes; that is, genes whose loss of function can lead to neoplastic growth. Other research points to the role of BRCA1 and BRCA2 in DNA repair, where the loss of repair function may lead to additional mutations and ultimately cancer.

The estimated frequency of BRCA1 or BRCA2 gene mutation carriers in the general population is one per 1,000 people.² The frequency in specific population groups has also been estimated: for those of Ashkenazi (Eastern European) Jewish descent, the rate of BRCA1 or BRCA2 gene mutation carriers is one per 50 to 100 people.³

Women with inherited mutations in genes such as BRCA1 and BRCA2 have a potentially high risk for developing breast cancer, and for developing the disease at an earlier age. Those carrying mutations are also at increased risk of cancers of the ovary and fallopian tube (and perhaps other cancers).

It is important to note that the risk for developing breast cancer never reaches 100%, which means that those with inherited gene mutations have a genetic predisposition to the disease but are not certain to develop it.

Other genes associated with an inherited predisposition to breast cancer include Tp53 (Li-Fraumeni syndrome), a rare gene which is estimated to attribute for less than 1 per cent of all breast cancer.⁴ There are likely to be unidentified genes as well. At this stage BRCA1 and BRCA2 are considered the most important in terms of breast cancer risk. Germline mutations in BRCA1 and BRCA2 are estimated to cause about 5% of all breast cancer.⁵
Current guidelines for risk management

Whilst most breast cancers (around 90%) are ‘sporadic’, those whose family history suggests a predisposition through inherited gene mutations are an important group in terms of the management of their risk and the challenges they face.

Testing for inherited gene mutations occurs in the context of risk management. Cancer Australia (formerly The National Breast and Ovarian Cancer Centre - NBOCC) has produced guidelines for health care professionals that cover familial aspects of both breast and epithelial ovarian cancers and how to manage risk. Risk management always begins with an assessment of family history to determine the level of risk. Women concerned about family history can talk to their health care professional. Those whose family history suggest a potentially high risk for developing breast cancer can be referred (or can self-refer) to a Family Cancer Clinic or specialist cancer genetic service for a more detailed assessment of family history.

After thoroughly assessing the details of family history, specialists can then:
• provide information about the risk of the individual developing breast cancer
• estimate the likelihood of having inherited a mutation in a breast cancer susceptibility gene
• provide counselling and support (information and advice)
• discuss the medical check-ups (and their frequency) that may be appropriate such as breast awareness, mammography (with or without other imaging techniques), clinical breast examinations and ovarian screening
• discuss the potential benefits, limitations and possible consequences of undergoing genetic testing, which should always be offered with pre- and post-test counselling
• discuss strategies that can reduce risk, such as bilateral mastectomy and/or salpingo-oophorectomy and participation in clinical trials involving chemoprevention agents.

Genetic testing is not listed on the Medicare Benefits Schedule but is provided to consumers through publicly funded Family Cancer Clinics. Family Cancer Clinics are generally co-located within hospitals, some of which contribute to meeting the costs of genetic testing services. Consumers can also elect to pay for testing through private laboratories; however, it is understood that most tests are provided at no cost to the consumer through the 23 Family Cancer Clinics across the country.

The testing process involves two stages. Tissue samples are first taken from a living family member who has been diagnosed with breast cancer to search for a causative gene. If a gene mutation is found, then the inquirer, and any other adult family members, can undergo predictive testing for the same mutation.

Developments in risk management

In February 2009, the Australian Government introduced a Medicare rebate for MRI screening for women aged under 50 who are at high risk of developing breast cancer. Information on the rebate, including eligibility criteria, can be found here.

This decision came on the back of a growing movement – and a pilot program in Western Australia – to incorporate MRI with mammography and ultrasound as best practice management for young women at high risk of developing breast cancer.

Issues in genetic testing

Psychological issues
Genetic testing can open a floodgate of mixed emotions for the women concerned.
A positive predictive test result can relieve uncertainty and allow inquirers to clarify their risk management plan. Literature suggests that positive results can trigger anxiety and depression, and produce feelings of guilt regarding the risk status of their children. Positive test results can also impact on sense of self and body image. For younger women, the implications for future reproductive choices can further affect their emotional wellbeing.

A negative predictive test result can produce a sense of relief and may eliminate the need for risk management for the inquirer. But not finding a causative gene in an affected relative can leave inquirers feeling even more uncertain about their next steps. Failure to identify a causative gene does not necessarily imply the absence of inherited gene mutations in the family since existing tests look only for the more common mutations in BRCA1 and BRCA2 (and there may be other mutations and genes involved). The test itself is also not 100% effective.

It is therefore important to acknowledge that women undergoing genetic testing will have different responses to the process and that their responses will shape different actions. The range of psychological issues associated with genetic testing highlights the importance of pre- and post-test counselling as a key component of the process.

**Family relationships**

The genetic testing process can mean negotiating complex family relationships and pose difficult questions around privacy.

The genetic testing process involves the inquirer as well as other family members. Some women find that they have no living family members with breast cancer to commence the first part of the genetic testing process. Others realise that they are not in a position to request the participation of living family members who may be able to provide samples, or that requested family members decline to be involved. It is important that women with expectations of progressing to a predictive test and who encounter such barriers are given adequate counselling to manage any disappointment or frustration.

Test results are similarly unusual in that they reveal information about the inquirer and her blood relatives. Results can present further challenges to family relationships. What should be done with the information? Who needs to know? Who wants to know? The answers to these questions may strengthen or weaken relationships, or pose obligations that never before existed. Deciding on what to do with the information may be a source of anxiety for some women, particularly if they need to decide between preserving personal privacy and a sense of 'duty' to family/relatives.

Note that in Australia, individuals can refuse to have genetic information disclosed without breach of law. The *Privacy Act 1998* (Commonwealth) exists to protect the privacy of personal information and gives individuals control over how information is to be collected, used and disclosed.

The genetic material obtained through the testing process includes tissue and blood specimens. Since this material may be of value to future generations, women undergoing testing need to consider the extent to which their specimens can be accessed by others in the future. This raises the complex issue of just who 'owns' the genetic material: such material is 'uniquely personal' and yet shared. Again, women may experience conflict between an obligation to future generations and their own desire for privacy.

**Confidentiality and informed consent**

Confidentiality is a key part of the informed consent process. Women undertaking genetic testing are required to make important decisions about how they would like their genetic
information to be released – and have these decisions clearly recorded. Some women are happy to provide the information to family members themselves. Some may wish to share information but retain their anonymity. Some may not have strong feelings about being identified, but prefer the information to be delivered by someone else (eg a family member or specialist counsellor). All need to think about what is to happen with the genetic information in the event of their death.

Testing laboratories are legally obliged not to use the genetic information for any purpose other than that specified by inquirers. Whilst this is an integral component of the medical code of ethics and must be understood by inquirers prior to testing, women may nonetheless experience anxiety around confidentiality – both now and beyond.

Information in the form of medical records and test results is the basis for risk management plans and therefore needs to be available to those involved in the provision of health care. It is critical that health professionals and testing laboratories use information storage systems that provide adequate access to providers whilst protecting privacy and confidentiality. One emerging issue is the multidisciplinary nature of health service delivery and developments in information technology – both of which increase the scope for information to be shared and potentially misused.

Women undergoing genetic testing can be included in familial breast cancer research by allowing the use of their blood or tissue specimens. Great care is needed when preparing consent forms and counselling inquirers. Researchers must clearly explain the purpose of the research, methods, storage and use of genetic material, and all related foreseeable eventualities related to the process of the research and its outcomes. It is critical that complex concepts and documents are comprehended so that consent is truly informed.

Both confidentiality and informed consent remain highly critical issues for those undertaking genetic testing and/or agreeing to the use of their genetic material for research purposes.

**Genetic discrimination**

Genetic discrimination refers to differential treatment by a third party – such as an insurer or employer – on the basis of a person’s actual or presumed genetic status. The person is asymptomatic and may never go on to develop the disease to which they are predisposed, but is treated differently nonetheless.

Third parties are entitled to request the disclosure of genetic information in the same way as they would other medical information. Whilst there is no legislation to prevent the request of a genetic test to obtain such information, industry sector policy – in the insurance setting at least – stipulates that applicants cannot be asked to take a genetic test or be influenced or coerced into taking one. To our knowledge, there are no insurance companies in Australia that routinely require genetic tests as a pre-requisite to insurance.

Discrimination on the grounds of genetic status – such as unfavourable underwriting decisions or unfair dismissals – potentially falls under the *Disability Discrimination Act 1992* (Commonwealth). The concept of genetic predisposition does not fit easily within existing terminology on disability. While a Productivity Commission inquiry into the *Disability Discrimination Act 1992* (DDA) in 2004 found that “the current definition of disability in the DDA is broad enough to include genetic disorders and conditions”, it went on to state that the definition of ‘disability’ should be amended so that “there is no doubt that it includes the presence of genetic predispositions to disabilities, and conditions that have medically recognised symptoms but have not necessarily been diagnosed”. This change in the terminology may help to further protect carriers of genetic mutations, such as the BRCA1 and BRCA2 genes, from discrimination.
In the end, the real issues for consumers may not lie in the legal definitions of disability and discrimination but elsewhere. In both the insurance and employment context, exemptions exist to excuse conduct that would otherwise amount to discrimination on the grounds of disability. To acknowledge conduct as discriminatory therefore does not always mean it is unlawful since the conduct in question may be exempt from the legislation and part of differentiating between individuals to make insurance or employment decisions. But the conduct could nonetheless be perceived as discriminatory from a lay perspective.

Case studies and anecdotal evidence indicate that this perception of discrimination has far-reaching consequences. These include deterring individuals from undergoing genetic testing or attending Family Cancer Clinics for counselling, which in turn affect the degree of care they could receive. The ‘fear factor’ is therefore a significant issue and provides a compelling reason for a concerted policy response, irrespective of the actual incidence of genetic discrimination in the strictly legal sense.

**Equity and access**
Ensuring access to the laboratory aspects of genetic testing is relatively straightforward since blood and tissue samples can be transported to central laboratories from distant sites across the country. Currently, all public and private pathology laboratories are able to carry out testing for the BRCA1 and BRCA2 gene mutations if they so choose.

There was concern in 2008, however, that testing for the BRCA1 and BRCA2 genes would be restricted to one Australian laboratory, that of Genetic Technologies Ltd., the company that holds the exclusive Australian licence for the tests. When the tests were introduced in Australia in 2003, Genetic Technologies decided not to enforce its licence, thereby allowing all Australian laboratories to conduct BRCA1 and BRCA2 tests. In 2008, the company wrote to laboratories advising that it would be enforcing its licence and that from 6 November 2008 they would no longer be able to carry out the tests.

This decision was deeply worrying, with real concerns that women’s access to genetic testing would be significantly compromised. After considerable public pressure, Genetic Technologies reversed its decision and returned to its original position. There is no mechanism that we are aware of, however, that would prevent the company from enforcing its licence in this way in the future.

Access to specialist pre- and post-test counselling services is an issue of concern for some groups of women, particularly women in rural and remote areas. Most Family Cancer Clinics are located in major cities, so women in country Australia can have difficulty accessing specialised counselling services in their local area.

Another important equity issue relates to women for whom English is not their preferred language. It is important that these women have access to qualified interpreters if necessary (rather than family members) to help support them in their decision making.

**Gene Patents**
Partly in response to the Genetic Technologies episode, in November 2008 the Australian Senate established a public inquiry into ‘the impact of the granting of patents in Australia over human and microbial genes and non-coding sequences, proteins, and their derivatives, including those materials in an isolated form’.

BCNA provided a submission to the inquiry and, in August 2009, four BCNA representatives appeared before The Senate Standing Committee on Community Affairs to present our views. BCNA believes that the Patents Act 1990 should be amended to expressly prohibit
the granting of patent monopolies over such materials. A copy of BCNA's submission can be viewed here.

The Committee will release its report in March 2010.

Socio-political considerations

The decision to proceed with genetic testing or not is an intensely personal one, and women must be supported as much as possible by counsellors to make choices that are ultimately their own. Some social scientists are beginning to question the extent to which truly autonomous choices can be made. Genetic testing involves women and their families, and some women may overlook their own desire not to know their inherited genetic risk in favour of their sense of duty to family members. The specifically gendered way in which women experience their family obligations is currently an under-researched area but one that would complete the picture of genetic testing in contemporary society.

Other social scientists point to role of genetic testing in the ‘geneticisation’ of health and illness (also known as ‘genetic determinism’). The geneticisation of health can lead to the unintended consequence of blaming individuals (read: their genes) for their health status and shifting attention away from environmental or socio-political determinants.

Last updated May 2013

1 National Breast and Ovarian Cancer Centre: Breast Cancer Risk Factors – a review of the evidence, July 2009