In the wake of Angelina – managing a family history of breast cancer

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Background
Accurate risk assessment by general practitioners (GPs) of breast and ovarian cancer for unaffected women with a family history is important to ensure appropriate referral. Family cancer clinics can provide significant benefits for those at high risk, but genetic testing is unlikely to benefit those who are unaffected, or have little or no family history. The overwhelming increase in referrals following celebrity Angelina Jolie’s decision to have a risk-reducing mastectomy because she carries a gene mutation has put pressure on services.

Objective
To provide information for GPs about managing women with concerns about their family history of breast cancer and highlight the resources available.

Discussion
GPs are well placed to assess risk of breast and ovarian cancer and are encouraged to use the available resources to assist them in appropriate risk assessment and referral.

Keywords
genetics; risk management; women’s health

Perhaps we should thank Angelina Jolie for raising an important issue for some Australian women and their families. Her announcement in a very well written New York Times article of her decision to have a risk-reducing mastectomy because she has a BRCA1 gene mutation was reported widely in the media, drawing attention to breast cancer risk for women with a strong family history of breast and/or ovarian cancer. Helplines and general practitioners (GPs) reported a surge in calls – an enviable public health response. So how best should GPs manage those with concerns about family history, particularly following the rush of enquiries, and what tools and services are available?

What the GP can do
GPs are well placed to assess the risk of breast and ovarian cancer for unaffected women with a family history. A systematic family history can be used to estimate risk and determine appropriate referral to family cancer clinics. Generally, a strong family history is characterised by multiple relatives affected by breast or ovarian cancer, younger age at diagnosis, a relative affected by breast and ovarian cancer, bilateral breast cancer and Ashkenazi Jewish ancestry (as BRCA gene mutations are more common in the Jewish population). These factors may indicate a heritable BRCA1 or BRCA2 mutation.

There are many resources available to assist risk assessment. Cancer Australia’s Familial Risk Assessment – breast and ovarian cancer (FRA–BOC) is an online tool designed for use by health professionals specifically for this task and is easy to access. EviQ, the national online cancer protocols resource hosted by the New South Wales Cancer Institute provides referral guidelines and patient information relating to cancer genetics, including breast, ovarian and bowel cancer (Table 1).

General practice to family cancer clinics
Family cancer clinics have provided risk assessment, genetic testing if required, and risk management for families with a strong family history of cancer over many years. Following the Angelina Jolie story, there was an overwhelming increase in referrals of concerned women to family cancer clinics from GPs nationally. In New South Wales, for example, the Hereditary Cancer Clinic at the Prince of Wales Hospital in Randwick and the Familial Cancer Service in Westmead reported a 300–400% increase across the board for the 6 weeks following the story; this remains elevated at a 200% increase, compared with the same time last year. This has placed considerable pressure on services. Given that hereditary breast cancer is uncommon (about 5% of breast cancers are due to a BRCA1 or BRCA2 gene mutation), many of these women may have been well managed initially at the GP level.
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Unfortunately, stories of celebrities having a genetic test to clarify their risk may promote the idea that every woman might benefit from such a test. Community knowledge is limited, so many women think that there is a simple blood test that will either detect breast cancer or provide an accurate level of risk but genetic testing is not that simple.

Genetic testing process for cancer predisposition

In family cancer clinics, tools are used to calculate the mutation detection rate. If there is at least a 10% chance of finding a causative gene mutation, genetic testing costs are covered by state health departments if ordered by a genetic specialist (they are not available under Medicare). The usual process for genetic testing for cancer predisposition involves:

- a mutation search – a blood test in an affected family member to determine if a mutation in \( BRCA1 \) or \( BRCA2 \) is present
- a predictive test, which is available to family members only when a mutation has been found, to determine whether they have the family mutation
- founder mutation testing may be offered to individuals with a high population frequency of \( BRCA \) mutations and any family history of breast or ovarian cancer.

As the Jewish community has a 2.5% carrier frequency of two \( BRCA1 \) mutations and one \( BRCA2 \) mutation, testing an individual with Jewish ancestry and any family history of breast or ovarian cancer for those three specific mutations is relatively cheap.\(^4\) The mutation detection rate is dependent on the strength of the family history.

At present, even in families with a strong family history of breast cancer, the mutation detection rate for \( BRCA1 \) and \( BRCA2 \) in the absence of ovarian cancer is 10–15%,\(^5\) and if ovarian cancer is present it is about 50–55%.\(^6\) Such testing is often uninformative in that it has not detected a genetic cause for the family, and yet there is still a genetic risk. These family histories may eventually be attributed to a combination of mutations. Recent data suggest multiple genes of minor and moderate effect interact to cause familial cancer.\(^7\)

Australia is fortunate to have the Kathleen Cuningham Foundation Consortium for research into familial breast cancer (kConFab), one of the world’s best resources for research into familial breast cancer, enabling on-going research in this area (Table 1). For the unaffected woman with little or no family history, publicly funded genetic testing is not available because such a test is unlikely to find a \( BRCA \) gene mutation and her risk would be better assessed using her family history.

Consumer resources for individuals concerned about having a family history of cancer are listed in Table 1.

Predictive testing can be done when a cancer-predisposing gene mutation has been found in the family. It is available to all adult relatives, funded again by the public system, provided appropriate pre- and post-test counselling are available, which should cover all of the medical management and psychosocial aspects of such testing. There are pros and cons associated with genetic testing of patients, which include how to manage unexpected findings, findings of variants of unknown significance, the potential for family conflict and challenging decisions around risk management. For all cancer-related genetic tests this process should result in fully informed and documented consent outlined in the Human Genetics Society of Australasia (HGSA) guidelines and there are a number of decision aids available for individuals regarding genetic testing (Table 1).

Risk management

For the right person, genetic testing and risk management can have significant benefits. A woman with a \( BRCA1 \) gene mutation, such as Angelina Jolie, has a very high risk of breast and ovarian cancer. Removal of the ovaries and fallopian tubes at about the age of 40 years (after child-bearing) almost completely removes the risk of ovarian cancer and will halve the risk of breast cancer (even when hormone replacement is given up to age 50 years).\(^8,9\) Risk-reducing salpingo-oophorectomy (RRSO) is the single most important

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**Table 1. Health professional and consumer resources**

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<tr>
<th>Health professional resources</th>
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<tr>
<td>EviQ – national online cancer genetics protocols</td>
<td><a href="https://www.eviq.org.au/">https://www.eviq.org.au/</a></td>
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<tr>
<td>Kathleen Cuningham Foundation Consortium for research into Familial Breast Cancer</td>
<td><a href="http://www.kconfab.org/Index.shtml">http://www.kconfab.org/Index.shtml</a></td>
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<table>
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<th>Consumer resources</th>
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<tr>
<td>Victoria: Cancer in the family</td>
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<tr>
<td>Information and Decision Aids for patients and families with a strong family history</td>
<td><a href="http://www.genetics.edu.au/Publications-and-Resources/PublicationsBrochuresandPamphlets/individualsandfamiliescancerresources">http://www.genetics.edu.au/Publications-and-Resources/PublicationsBrochuresandPamphlets/individualsandfamiliescancerresources</a></td>
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risk-reduction strategy for women at high genetic risk. For that same woman bilateral risk-reducing mastectomy (RRM) reduces breast cancer risk by at least 90%. Using modelling, the chance of being alive at the age of 70 years increases from 53% to 77% with RRSO and RRM (compared with 84% in the general population). In 2006, 11% of Australian women positive for BRCA1 and BRCA2 mutations underwent RRM, mostly with reconstruction, and anecdotally this incidence is now about 20%. These are difficult decisions, often involving many hours of advice and counselling from members of the genetics team, including nurses and the clinical psychologist. Most women, after surgery, are satisfied with the decisions they have made and levels of breast cancer anxiety are certainly reduced. For women who do not choose risk-reducing surgery, surveillance is strongly recommended although there is no evidence to date that early detection of breast cancer is associated with a better survival in carriers of BRCA1 and BRCA2 mutations. Risk-reducing medications have been shown to reduce the risk of breast cancer in women at increased risk. Tamoxifen is an option for women who are pre- or post-menopausal, and raloxifene for post-menopausal women only. The decision to use tamoxifen or raloxifene should be guided by an assessment of each woman’s individual needs and existing comorbidities, including osteoporosis.

Breast cancer in men is uncommon (<1% lifetime risk); however, men who have a BRCA1 or BRCA2 mutation do have an increased risk of developing breast cancer (1% lifetime risk in BRCA1 and 6–8% lifetime risk in BRCA2 carriers). The risk of developing prostate cancer is also increased by about 8% and 15% consecutively (compared with 5.9% population risk). There is preliminary evidence for value of surveillance of men with BRCA mutations.

**Summary**

Comprehensive risk assessment and appropriate referral to family cancer clinics is the key to good management. GPs are encouraged to use the resources available to them. The spotlight on risk-reducing strategies for women at very high risk of breast cancer has been helpful – Angelina’s story can be used to assist understanding and is a good starting point for discussion of family history.

For the right person, genetic testing and risk management can have significant benefits, but for most women, genetic testing is not a tool that can provide accurate estimation of the risk of breast cancer. In this situation, women will benefit from the support of informed GPs.

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**References**