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Celebrities and breast cancer groups praised Angelina Jolie for her decision to undergo a preventive double mastectomy and share her story.

How to manage *BRCA1* and *BRCA2*

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Introduction

BREAST cancer is common. About 14,000 women are newly diagnosed each year in Australia, with a lifetime risk approaching 1:8. From a population of 23 million (half being female), it is important to remember, however, that most women do not develop breast cancer, the incidence being about 114 per 100,000 women with an average age of 60.

Those women with a very high risk due to a genetic predisposition, such as *BRCA1* or *BRCA2*, comprise fewer than 5% of women presenting with a newly diagnosed breast cancer. Increasingly, however, there are well women like Angelina Jolie, who have not yet developed breast or ovarian cancer, but are at very high risk due to a proven predisposition breast cancer gene.

Celebrities and breast cancer groups praised Jolie for her "courageous" decision to undergo a preventive double mastectomy and share her story, saying her openness could save lives by leading to a surge in women being tested for the cancer gene. A clinic in North America reported twice as many women presented for BRCA testing after Jolie's pronouncement that she had undergone bilateral prophylactic mastectomies following discovery of her positive BRCA status. Similar phenomena were reported in Australia.[1,2]

The greatest risk factors for developing breast cancer is being a woman and getting older, with family history the next most important risk factor.

Australia has one of the highest incidences worldwide. For the average woman with any family history, a first-degree relative with breast cancer roughly doubles her risk, hence a recommendation for annual screening, rather than the biennial screening recommended for a woman with no family history.

BRCA carriers pose quite a different risk problem and it is important to identify these potentially higher risk individuals.

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Aetiology

Inherited gene mutations

CANCER is a genetic disease associated with mutations in genes that normally act to control cell growth, proliferation and DNA repair. Up to 95% of all cancers are caused by these somatic mutations in cancer-associated genes.

As these faults occur in somatic cells (such as the cells lining breast ducts), they cannot be inherited. However, some individuals come from families who have an inherited mutation in one of these same genes (for example, BRCA), and consequently start life with a defective copy of a particular tumour suppressor gene (the 'first hit') present in every cell of the body.

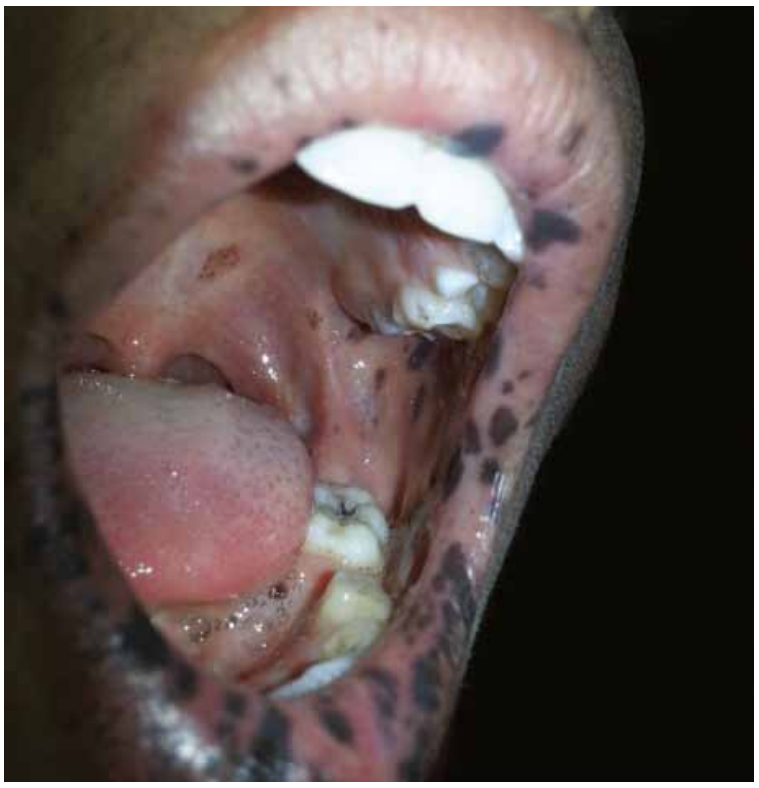
In a person with a rare genetic susceptibility, the 'first hit' has already been inherited either in the egg or the sperm (germline mutation).

People who inherit a germline mutation in a cancer-associated gene are therefore at increased risk of developing cancer and in addition, can pass a germline mutation on to the next generation. For each of their offspring (male or female), there is a 50% chance they will inherit the mutated copy of the gene.

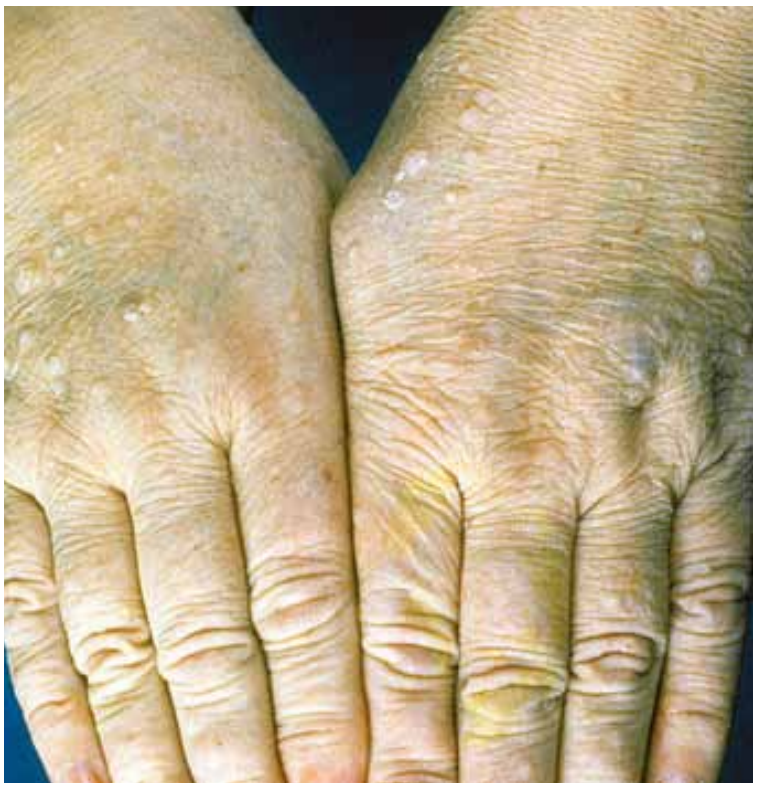
What is BRCA?

BRCA is a tumour suppressor gene and produces a protein that assists in DNA repair. Germline mutations are therefore associated with a higher risk specifically for breast and epithelial ovarian cancer.

The first gene to be discovered was *BRCA1* on chromosome 17. Since then, *BRCA2* and other cancer susceptibility genes have been identified. People who have an inherited fault in these genes are gene mutation carriers, with an increased risk of developing cancer. Inherited faults in *BRCA1* and *BRCA2* are more common in individuals of Ashkenazi Jewish heritage.



Peutz-Jeghers syndrome.
Source: Abdullah Sarhan http://bit.ly/1GF50Rd



Cowden disease.
Source: Thomas Habif http://bit.ly/1HN1zGS

Examples of hereditary breast cancers

- *BRCA1* and *BRCA2* — most common
- Li–Fraumeni syndrome — p53 mutation (also known as sarcoma, breast, leukaemia and adrenal gland (SBLA))
- Cowden syndrome phosphatase and tensin homolog (PTEN)
- Familiar type gastric cancer and lobular breast cancer
- Peutz–Jeghers syndrome

Risk of breast or ovarian cancer

Lifetime risk breast cancer
• 50-80% *BRCA1* & *BRCA2*
Lifetime risk ovarian cancer
• 20-40% *BRCA1*
• 10-20% *BRCA2*
Familial cancer tends to occur at a younger age
Increased risk is life-long

Diagnosis and investigations

Who should be tested?

REMEMBERING that the majority of women affected with breast cancer do not have a high-risk gene and those at high risk represent a small portion of the population, women should be very selectively screened. Overestimating risk may lead to unnecessary fear, anxiety and even overtreatment.

Genetic testing should be accompanied with pre- and post-test counselling, and performed in a setting where the test can be adequately interpreted. The results of testing may aid in diagnosis or influence the medical or surgical management of the patient or family members at hereditary risk of cancer. This should include discussion of the possible risks and benefits of early detection of cancer and prevention strategies.

Maternal and paternal family history is equally important, even though breast and ovarian cancer are predominantly female malignancies.

Importance of a thorough family history

Ask about all relatives affected by cancer, over three generations. Document all cancers on both sides of the family and age at diagnosis. Maternal and paternal family history is equally important, even though breast and ovarian cancer are predominantly female malignancies. Inquire about ethnic background, especially whether there is an Ashkenazi Jewish origin. This population has a high prevalence of BRCA mutations.

The National Breast and Ovarian Cancer Centre (NBOCC) has developed three categories of risk based on family history. The first category is slightly above average risk, the second, moderate, and the third, potentially high risk.

The category gives a guide to screening recommendations based on level of risk and the appropri-

ateness of referral for consideration of genetic testing.[3]

BRCA women and relatives may fall into a high-risk category, as outlined below.

The NBOCC also has produced the online tool The Familial Risk Assessment — Breast and Ovarian Cancer (FRA-BOC) (see Online resources). This is a useful tool for practitioners and assists in assessing within which category of risk their patient falls.[4]

Testing

The initial step in genetic testing is usually to take blood from one of the family members affected by breast or ovarian cancer. This first phase, the 'mutation search', must be done with full informed consent. The laboratory then searches the large *BRCA1* and *BRCA2* genes to determine whether a causative gene mutation can be found. This may take many months.

If found, unaffected relatives — male or female — can easily be tested to find out whether they harbour the gene, namely whether they are at very high risk or at the normal population risk. This is known as 'predictive' testing and is a relatively quick process.

A causative gene mutation cannot be found in every family tested, as mutations may be missed or may be present in other genes not yet identified (non-BRCA genes). Even for BRCA carriers, about 10% may not be identified with current testing methods. Therefore, if the family history is strong and the genetic test (mutation search) fails to identify a gene mutation in an affected family member, that test result should be considered 'inconclusive' and all relatives remain at potentially high risk.[5]

A multidisciplinary approach

Management options for affected and unaffected women at genetic risk are complex, and may require the interaction of specialists in cancer genetics, breast and reconstructive surgery, gynaecological oncology, medical oncology, endocrinology, psychology and the patient's GP.

Table 1: Potentially high risk for developing breast cancer — 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 three times the population average. Individual risk may be higher or lower if genetic test results are known.

- Two 1-degree or 2-degree 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-degree or 2-degree relative diagnosed with breast cancer at age 45 or younger plus another 1-degree or 2-degree 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.

Source: NBOCC. *Advice about familial aspects of breast cancer and epithelial ovarian cancer — A guide for health professionals*, December 2010.

Cost of *BRCA1* and *BRCA2* mutation testing

The cost of *BRCA1* and *BRCA2* mutation testing is covered by the genetic service requesting the test.

There is no Medicare rebate for *BRCA1/2* tests requested by doctors outside of genetics services.

Individuals who have had breast or ovarian cancer will be tested where there is at least a 10% chance of a mutation being identified, based on personal and family history and tumour pathology.

Unaffected individuals who have not had a relevant cancer diagnosis will only be tested where they have at least a 20% chance of having a mutation.

Individuals not meeting these criteria can elect to fund the test privately. The average cost for *BRCA1* and 2 testing is currently about $1000.

If a mutation has already been identified in a family, the cost of testing relatives for the mutation is covered by the referring genetics service.

For further information, see www.eviq.org.au (registration and log on required) and search for Genetic Testing for Heritable Mutations in the *BRCA1* and *BRCA2* genes.

Source: Dr Lesley Andrews, conjoint senior lecturer at the University of NSW, Hereditary Cancer Clinic, Prince of Wales Hospital, Randwick NSW.

Table 2: Family cancer clinics*

NSW	
Contact the Centre for Genetics Education NSW on 02 9926 7324 for details of genetic counselling services in other areas of NSW which may provide cancer genetics services.	
Royal Prince Alfred Hospital CAMPERDOWN	02 9515 5080
St George Hospital KOGARAH	02 9350 3815
Nepean Hospital PENRITH	02 4734 3362
Hunter Genetics WARATAH	02 4985 3132
Prince of Wales Hospital RANDWICK	02 9382 2551
St Vincent's Hospital DARLINGHURST	02 8382 3395
Westmead Hospital WESTMEAD	02 9845 6947
Royal North Shore Hospital ST LEONARDS	02 9926 5665
Wollongong Hospital WOLLONGONG	02 4222 5576
SA	
Various locations. Contact the Familial Cancer Unit at Women's and Children's Hospital NORTH ADELAIDE Phone: 08 8161 6995 Email:cywhs.famcancer@cywhs.sa.gov.au	
Women's and Children's Hospital NORTH ADELAIDE	08 8204 7375
Victoria	
Monash Medical Centre CLAYTON	03 9594 2026
Peter MacCallum Cancer Centre EAST MELBOURNE	03 9656 1199
Royal Children's Hospital PARKVILLE	03 8341 6201
Royal Melbourne Hospital PARKVILLE	03 9342 7151
Austin Repatriation Hospital WEST HEIDELBERG	03 9496 5000 and ask for pager #3494
ACT	
The Canberra Hospital GARREN	02 6244 4042
NT	
Women's and Children's Hospital NORTH ADELAIDE SA	08 8204 7375
Queensland	
QBRCA clinic, Royal Brisbane and Women's Hospital	07 3636 1686
Brisbane North Breast Cancer Family CHERMSIDE	07 3350 7411
Tasmania	
Clinics held regularly at Burnie, Launceston and Hobart	
Royal Hobart Hospital HOBART	03 6222 8296 0408 127 363 0438 213 145
WA	
Genetic Services of Western Australia SUBIACO Mount Hospital PERTH	08 9340 1603 08 9483 2824
Royal Perth Hospital PERTH	089224 2723

*Sourced from http://bit.ly/1JtW6Z1

Management

Managing high-risk individuals

Breast surveillance

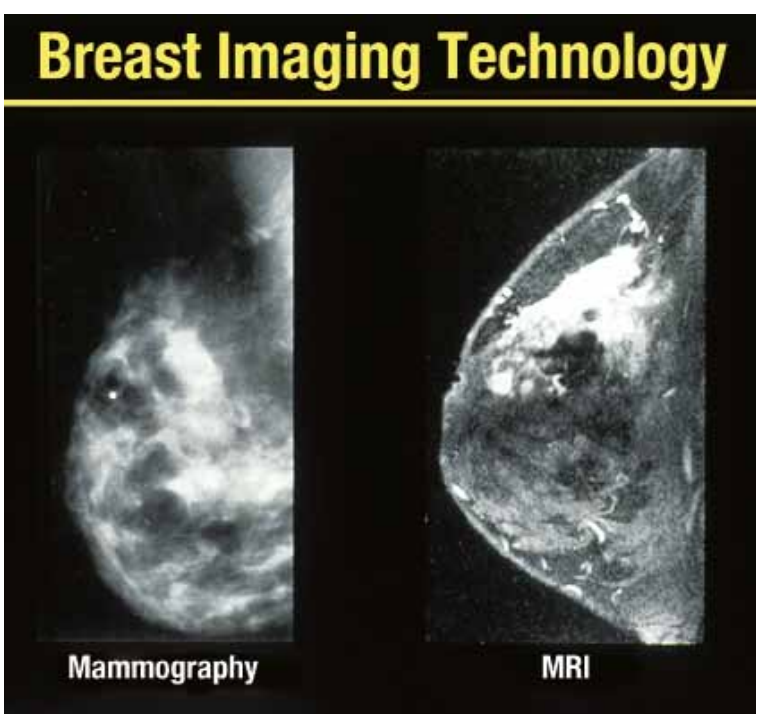
ANNUAL mammography and ultrasound are still the mainstay for high-risk women aged over 35, but breast density should always be considered when determining the best surveillance method, as there may be variation among individuals.

Mammography is likely to be less useful for younger women with greater breast density, and ultrasound will be needed for screening and diagnosis. MRI is recommended for younger women or women aged over 35 with dense breast tissue.

A Medicare rebate is available only for identified high-risk individuals aged under 50.

The screening interval may need to be six-monthly for younger, at-risk woman (aged under 35) with very dense breast tissue.

A useful strategy is to alternate MRI and ultrasound with six-monthly reviews. Likewise, ultrasound may be omitted in older woman with minimal breast density if mammography is deemed to provide very good surveillance. This would usually be for older woman significantly beyond 50 years.



Mammogram vs MRI. A mammogram on left and MRI on right. Note MRI's enhancement ability to confirm diagnosis. MRI is an important adjunct for the high-risk young woman with dense breasts.
Source: Mitchell D Schnall, MD, PhD. University Of Pennsylvania http://bit.ly/1HNhwwL

Ovarian surveillance

CA125 and endovaginal ultrasound are considered unreliable for ovarian screening. At an appropriate time, oophorectomy is a better option.[6]

Bilateral mastectomy will reduce the risk of developing breast cancer to 1-2%, but does not reduce the risk to zero.

Prevention

Endocrine therapy

The use of tamoxifen and aromatase inhibitors as a chemo-preventive measure may have a role for some women not wanting prophylactic surgery. There may be up to a 30-50% lowering of risk, but the overall risk still remains high for mutation carriers, and the pros and cons of this strategy require informed discussion.

Prophylactic surgical procedures

Mastectomy — Bilateral mastectomy will reduce the risk of developing breast cancer to 1-2%, but does not reduce the risk to zero.[7]

Significant preoperative counselling is essential. The option of breast reconstruction should be discussed. Unlike women with newly diagnosed breast cancer, women considering risk-reducing mastectomy can be encouraged to take their time in making decisions and spend as much time as they

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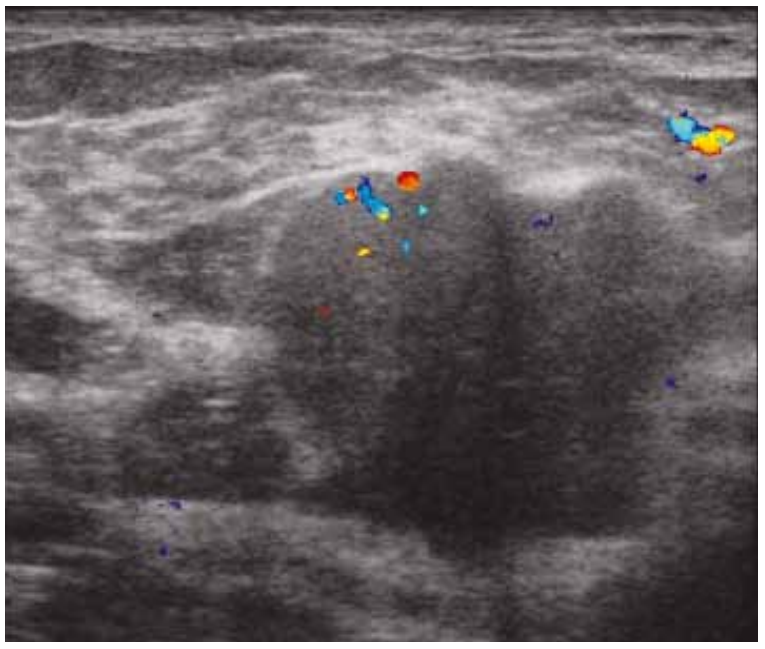
feel is necessary to understand the surgery and its implications.

Many younger women choose to complete their families before considering prophylactic surgery. Most women with partners wish to include them in their decision-making. Most women want to at least discuss immediate breast reconstruction, and treatment teams need to offer the full range of options.

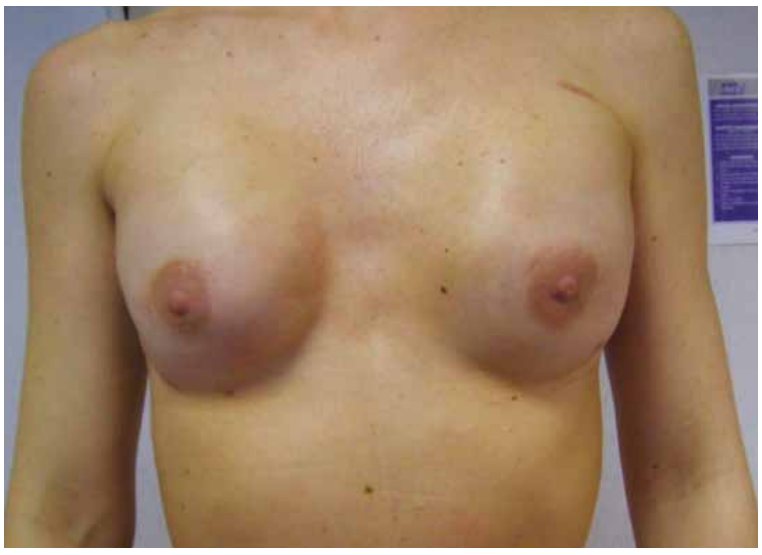
Reconstruction — It is important to manage expectations realistically. While surgical reconstructive options are many, no procedure can 'restore' a normal breast. Only the best results tend to be posted on the internet and individual examples viewed from such a large resource may not be applicable to their own situation.

Implants are a straightforward option and provide good symmetry especially if performed bilaterally. If the woman is large-breasted or very ptotic then size match may not be possible using an implant.

Autologous reconstruction with a latissimus dorsi or rectus abdominis myocutaneous flap is a more complex reconstruction, but provides natural tissue replacement.



Ultrasound images of breast cancer.
Source: Nevit Dilmen http://bit.ly/1FExIzB



Bilateral nipple-sparing mastectomy and implant reconstruction. In selected cases, nipple sparing may be possible. It may not be possible for a large, ptotic breast.
Source: Sara Reefy, Neill Patani, Anne Anderson, Gwyne Burgoyne, Hisham Osman, Kefah Mokbel http://bit.ly/1LLuoov

Salpingo-oophorectomy — Risk-reducing bilateral salpingo-oophorectomy (BSO) is a procedure sometimes more easily accepted than mastectomy by the high-risk woman, particularly if she is post-menopausal. It is important to also remove the salpinx, as tubal malignancies may also occur, as well as peritoneal carcinomas. Hence, BSO can reduce the risk of epithelial ovarian carcinoma by 96%, but cannot reduce the risk to zero.[8]

BSO is recommended in the mid-30s-40s, but individual consideration might be given to women with a family history of younger women affected with ovarian cancer. BSO with hormone replacement is an option at any age for a high-risk premenopausal woman, once she is certain she no longer needs to preserve her fertility.

In the post-menopausal woman, oophorectomy can of course be performed without physiological consequences.

The symptoms of menopause can be quite severe, especially when occurring abruptly following ovarian surgery in the premenopausal woman. For most women, BSO is relatively straightforward and can be performed laparoscopically.

Oophorectomy also confers up to a 50% reduction in breast cancer risk for the premenopausal woman who has not already undergone prophylactic mastectomy. If there are uterine abnormalities or the woman wishes to take tamoxifen, then hysterectomy should be considered.

The prophylactic dilemma

FOR the individual with the BRCA mutation, the risk of breast cancer becomes significant at a younger age (20s) and ovarian cancer risk somewhat later (40s). There will of course be exceptions, for example, the family with a history of ovarian cancer occurring in younger family members.

Psychologically and emotionally, oophorectomy may seem more palatable than mastectomy, particularly for younger women, who may not have a steady and supportive partner when the implications of their BRCA status is being considered.

Outward appearances and body image are unchanged after an oophorectomy but significantly changed after a mastectomy. Physiologically and physically however, oophorectomy may be devastating for the premenopausal woman who may not have completed her family, and would be thrust into sudden and complete menopause at a young age.

The long-term effects of being devoid of oestrogen may be far worse. A young woman undergoing prophylactic oophorectomy should therefore be placed on hormone replacement to avert the complications of oestrogen depletion. Recent evidence suggests that hormone replacement does not negate the breast cancer risk, reducing the benefits of a premenopausal oophorectomy.[9]

Fertility preservation and breastfeeding for some women may be paramount in their decision-making. Conversely, some of my patients have stated a reluctance to have children, given the chance of passing on their BRCA gene.

In my view, the ovaries are more problematic than the breast. Surveillance is unreliable and the consequences of a likely late diagnosis devastating. Modalities for breast surveillance, however, have considerably improved, so this is a viable option for women not prepared to undergo risk-reducing mastectomy.

Women should be encouraged towards bilateral salpingo-oophorectomy at an appropriate time. Ideally, this should follow mastectomy (should the woman be accepting), which would remove at-risk breast tissue and any concerns over hormone replacement.

Table 3: Uptake of risk-reducing interventions among 325 women who were aware they carried a *BRCA1* or *BRCA2* mutation

		Age at intervention (yrs)	
Risk-reducing intervention	**Number**	**Median**	**Range**
RRM (Risk-reducing mastectomy)	69/325 (21%) Seven before cohort entry	40	26–67
RRBSO (Risk-reducing bilateral salpingo-oophorectomy)	125/325 (38%) Eight before cohort entry	44	30–77
By age 40 *Restricted to 62 women who were followed to at least the age of 40 years and knew their genetic result before the age of 40 years*	16/62		
BRCA1	12/35		
BRCA2	4/27		
By age 50 Restricted to 44 women who were followed to at least the age of 50 years and knew their genetic result before the age of 50 years	29/44		
BRCA1	17/27		
BRCA2	12/17		
Both RRM and RRBSO	38/325 (12%)	—	—
Risk-reducing medication or placebo (on trial)	9/325 (3%)	36	35–56
Risk-reducing medication (off trial)	1/325 (< 1%)	—	—
Tubal ligation	71/325 (22%) 60 before cohort entry	32	20–54

Collins IM, et al. Preventing breast and ovarian cancers in high-risk BRCA1 and BRCA2 mutation carriers. *Medical Journal of Australia* 2013; 199(10):680-83. © Copyright 2013 The Medical Journal of Australia — adapted with permission. The Medical Journal of Australia accepts no responsibility for any errors in adaptation.

Table 3 shows the uptake of risk-reducing measures in a population of women aware of their BRCA status.

Participants were female members of families in which there were multiple cases of breast cancer who were also enrolled in the Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer. This consortium is a resource of stored biospecimens, epidemiological and clinical data.

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Summary

- A thorough family history, both maternal and paternal, is important.
- Genetic testing should be accompanied by pre- and post-test counselling.
- Management of high-risk individuals and family members is multidisciplinary.
- It is preferable to test an affected relative before other family members.
- Breast surveillance will depend on a woman's age but may also need to be individualised.
- Ovarian surveillance is unreliable.
- Breast and ovarian prophylactic surgery if effective.

Recent evidence suggests that hormone replacement does not negate the breast cancer risk, reducing the benefits of a premenopausal oophorectomy.

Case studies

Case study one

JENNY is a 35-year-old woman whose mother had breast cancer at the age of 52. Jenny presents seeking advice about screening. She is asymptomatic, apart from mild cyclical breast pain, but is unaware of any specific lumps.

Her maternal grandmother also had breast cancer diagnosed when she was 60. There are no other relatives who have had breast cancer and there is no family history of ovarian cancer. Jenny's mother has an unaffected sister and a brother. Her affected grandmother had three sisters and none of them had breast cancer.

Advice

Jenny has a first- and a second-degree relative on the same side of the family with breast cancer, and both were over 50 years of age when diagnosed. Jenny has a moderately increased risk of developing breast cancer in her lifetime, between 1 in 8 and 1 in 4, and 1.5 -3 times the population average.

Emphasise to Jenny that there is still a 75-90% chance of not developing breast cancer.

She should have baseline investigations, and if these are clear, recommend annual screening from age 40. She does not require gene testing, but may of course discuss matters further with a clinical geneticist if she wishes.

Case study two

Daisy, aged 26, has discovered a right breast lump. A focused ultrasound scan revealed a 2cm lesion with well-defined borders and an overall benign appearance. A core biopsy confirms a fibroadenoma.

Daisy is extremely anxious about her lump and requests its removal. Her mother was diagnosed with breast cancer at the age of 26 and died with recurrence of her cancer in her mid-30s.

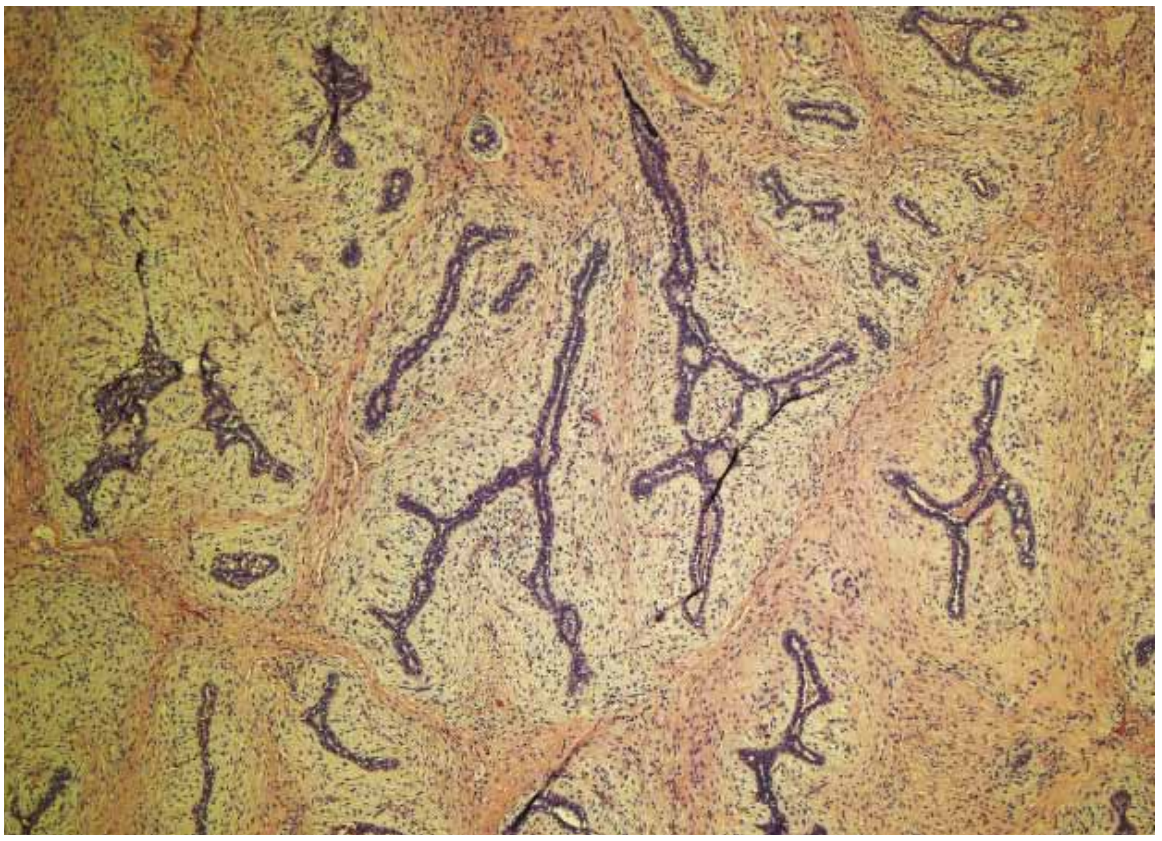
Her maternal aunt (mother's sister) was diagnosed with breast cancer at the age of 45 and her daughter (Daisy's first cousin) has just been diagnosed with breast cancer at the age of 28.

Advice

Daisy is at potentially high risk for developing breast cancer. She has three relatives on the same side of the family, including a first-degree relative (mother), who have developed breast cancer at a young age. If a breast cancer gene exists in the family, her chance of inheriting such a mutation is 50%.

She should be referred for genetic counselling. A mutation search (gene testing) would be recommended. Ideally, this should be done first for one of her affected living relatives (aunt or cousin) if they are willing.

Once the gene mutation is identified, Daisy and other family members can have predictive testing. Daisy should be reassured that her right breast lump is benign and does not require removal for clinical reasons. Fibroadenomas do not evolve to breast cancer. If she remains anxious about her benign lump, however, removal is not unreasonable.



Cellular fibroadenoma.
Source: Difu Wu http://bit.ly/1dz3GnL

While awaiting advice from the clinical geneticist, bilateral breast surveillance with ultrasound and MRI should be arranged. A mammogram may be less helpful in a young woman who is likely to have more breast density.

Case study three

Val is a 34-year-old woman who has just discovered a lump in her left breast. Further imaging investigations and a core biopsy confirm that she has an early breast cancer. The tumour measures 1.5cm in diameter and she is clinically node-negative. She would be suitable for breast conservation surgery.

Val has two young children and has completed her family. She has two brothers. Neither Val's mother nor any of her mother's relatives has had breast cancer. Her father's family all live abroad, but she recalls that her paternal grandmother had breast cancer in her 50s. Her father has three sisters.

After exploring her family history further, it is revealed that one of her paternal aunts had bilateral breast cancer first diagnosed when she was in her 30s, then the second time in her early 40s. This aunt also has a daughter recently diagnosed with breast cancer at the age of 45. The other paternal aunt had ovarian cancer at the age of 41. The third paternal aunt remains unaffected.

Interpretation

Even without gene testing individuals, it is clear that the paternal side of Val's family likely has a *BRCA1* or *2* mutation. The men in the family are unlikely to manifest the disease, although the incidence of male breast cancer is higher in a male BRCA carrier.

Given Val's young age at diagnosis, it is likely she has a BRCA mutation inherited from her father. If other affected family members have already had BRCA status confirmed, then other family members, including Val, could undergo predictive testing and this would provide a quick answer. If this has not been already done, then a mutation search for her would have to be done. At best, an answer might be obtained in a few weeks or the result for BRCA testing could be inconclusive (~10% of cases).

There are other high-risk mutations, as yet undiscovered, that some families may possess. Therefore, even if one of the known mutations (eg, BRCA) isn't found for Val, an underlying high-risk gene may still exist if the family history is strongly suggestive.

Advice

The options for management of her left breast cancer is conservation surgery (lumpectomy and breast radiotherapy) or mastectomy. Either is equally effective in terms of breast cancer survival and the axilla should have sentinel

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Online resources

National Cancer Institute Breast Cancer Treatment — for health professionals
1.usa.gov/1eji4Ro

Cancer Australia — Risk calculator
bit.ly/1Bjpj61

Cancer Australia — Ovarian cancer
bit.ly/1GXSFJv

Cancer Institute Decision Tool for Women with BRCA Mutations
brcatool.stanford.edu

NSW Health. What is Family Cancer?
bit.ly/1FYJYZM

Cancer Council Victoria
www.cancervic.org.au/how-we-can-help/family-cancer

Cancer Council Genetics directory
bit.ly/1Tpj8TO

American Cancer Society
www.cancer.org

Cancer Research UK
www.cancerresearchuk.org

NBOCC. The Familial Risk Assessment — Breast and Ovarian Cancer online tool
bit.ly/1241QmH

Cancer Institute NSW. Genetic Testing for Heritable Mutations in the BRCA1 and BRCA2 Genes
bit.ly/1dHmwst (registration and logon required)

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node-based management. The discussion is necessarily complex.

If Val is considering a prophylactic mastectomy for her unaffected contralateral breast, then bilateral mastectomy with or without reconstruction would be her best option. If ongoing surveillance of her unaffected breast is her preference, then conservation would probably be a better option for her.

It is important to explain at this time, however, that radiation therapy is a routine component of breast conservation and will cause some permanent changes to the treated breast. This would have implications for future breast reconstructive considerations should she later decide on this.

At some time there will need to be a discussion about ovarian management. If her tumour has oestrogen (ER) and progesterone (PR) receptors, then oophorectomy may be a therapeutic option and may be considered sooner.

Otherwise, a discussion about prophylaxis can be had later. There are no reliable surveillance options and given the likelihood of a BRCA mutation, removal of her ovaries at some time should be considered.

Oophorectomy would lead to an abrupt menopause and a prolonged period of oestrogen deprivation. It is unavoidable for an ER/PR positive breast tumour where oestrogen blockade is necessary. If the breast tumour is ER/PR negative, hormone replacement following prophylactic oophorectomy would be appropriate.

Conclusion

WITH appropriate support and counselling, BRCA carriers can be helped towards an individualised solution. There is so much more to managing the woman with a predisposition gene than simply performing a mastectomy. Prevention is still better than early detection but for the breast, good surveillance methods are available for the woman not wishing to undergo surgical prophylaxis. Ovarian surveillance is unreliable and high-risk women should consider oophorectomy.

Summary

- A thorough family history, both maternal and paternal, is important.
- Genetic testing should be accompanied by pre- and post-test counselling.
- Management of high-risk individuals and family members is multidisciplinary.
- It is preferable to test an affected relative before other family members.
- Breast surveillance will depend on a woman's age but may also need to be individualised.
- Ovarian surveillance is unreliable.
- Breast and ovarian prophylactic surgery is effective.

How to Treat Quiz

How to manage *BRCA1* and *BRCA2* — 17 July 2015

INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points.
We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

GO ONLINE TO COMPLETE THE QUIZ

www.australiandoctor.com.au/education/how-to-treat

1. Which TWO statements regarding the background to breast cancer are correct?
a) Breast cancer is uncommon.
b) About 14,000 women are newly diagnosed each year in Australia with breast cancer.
c) The lifetime risk of developing breast cancer is approaching 1:8.
d) Those women with a very high risk due to a genetic predisposition, such as *BRCA1* or *BRCA2*, comprise 25% of women presenting with a newly diagnosed breast cancer.

2. Which THREE statements regarding the risk of developing breast cancer are correct?
a) The greatest risk factors for developing breast cancer is being a woman and getting older.
b) Family history is the next most important risk factor after being a woman and getting older.
c) Australia has one of the lowest incidences of breast cancer worldwide.
d) For the average woman with any family history, a first-degree relative with breast cancer roughly doubles her risk.

3. Which THREE statements regarding inherited gene mutations are correct?
a) Cancer is a genetic disease associated with mutations in genes that normally act to control cell growth, proliferation and DNA repair.
b) Female offspring have twice the chance of inheriting a germline mutation.
c) People who inherit a germline mutation in a cancer-associated gene are at increased risk of developing cancer.
d) Germline mutations can be inherited either in the egg or the sperm.

4. Which THREE are examples of hereditary breast cancers?
a) *BRCA1* and *BRCA2*.
b) Familiar type gastric cancer and lobular breast cancer.
c) Fanconi's anaemia.
d) Li–Fraumeni syndrome.

5. Which TWO statements regarding BRCA are correct?
a) The lifetime risk of breast cancer is 50-80% with *BRCA1* and *BRCA2*.
b) Gene mutation carriers do not have increased risk of developing cancer.
c) Germline mutations are associated with a higher risk specifically for breast and epithelial ovarian cancer.
d) Inherited faults in *BRCA1* and *BRCA2* are more common in individuals born in the Southern Hemisphere.

6. Which THREE statements regarding testing are correct?
a) The majority of women affected with breast cancer do not have a high-risk gene.
b) Overestimating risk may lead to unnecessary fear, anxiety and even overtreatment.
c) Genetic testing should be accompanied with pre- and post-test counselling and performed in a setting where the test can be adequately interpreted.
d) It is recommended all women concerned about a hereditary cancer are tested, as the risk of missing cancer is high.

7. Which TWO statements regarding testing are correct?
a) The 'mutation search' (searching the large *BRCA1* and *BRCA2* genes to determine whether a causative gene mutation can be found) is a quick process
b) If a causative mutation is not found in the 'mutation search', the patient and family can be reassured that it does not exist.
c) The initial step in genetic testing is usually to take blood from one of the family members affected by breast or ovarian cancer.
d) Predictive testing involves testing unaffected relatives to determine whether they harbour the gene.

8. Which TWO statements regarding breast cancer surveillance are correct?
a) Annual mammography and ultrasound are still the mainstay for surveillance for women aged over 35.
b) Mammography is likely to be more useful for younger women with greater breast density.
c) The screening interval may need to be 12-monthly for the younger at risk woman (aged under 35) with very dense breast tissue.
d) MRI is recommended for younger women or women aged over 35 with dense breast tissue.

9. Which TWO statements regarding bilateral mastectomy are correct?
a) Bilateral mastectomy will reduce the risk of developing breast cancer to zero.
b) Significant preoperative counselling is essential prior to bilateral mastectomy.
c) Surgical reconstruction can restore a normal breast.
d) Many younger women choose to complete their families before considering prophylactic surgery.

10. Which THREE statements regarding bilateral salpingo-oophorectomy (BSO) are correct?
a) Risk-reducing BSO is a procedure sometimes more easily accepted than mastectomy by the high-risk woman, particularly if she is postmenopausal.
b) It is important to also remove the salpinx, as tubal malignancies may also occur.
c) The symptoms of menopause can be quite severe, especially when occurring abruptly following ovarian surgery in the premenopausal woman.
d) BSO is recommended in the mid 40s-50s, but individual consideration might be given to women with a family history of younger women affected with ovarian cancer.

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2014-16 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

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NEXT WEEK

Next week's How to Treat offers clinical and imaging information to assist with distinguishing stroke from stroke. As the treatments and prognosis vary between strokes and mimics, it is essential to differentiate between them, and to manage as appropriate. The authors are **Dr Daniel Schweitzer**, staff neurologist, Nambour General Hospital, Nambour, Queensland; and **Dr Rohan Grimley**, geriatrician and stroke physician, and conjoint senior lecturer, University of Queensland and Sunshine Coast Hospital Health Service, Nambour General Hospital, Nambour, and chair, Queensland Statewide Stroke Clinical Network.