

Office of Population Health Genomics

Policy:
Protocol for the management
of female BRCA mutation
carriers in Western Australia

Purpose: Best Practice guidelines for the management of female BRCA mutation carriers in Western Australia based on current evidence. This document replaces the July 05 protocol.

June 2007

Protocols developed by the Familial Breast and Ovarian Cancer Sub-Committee of the Western Australian Genetics Council



Location: S:\COMMITTEE - Familial Cancer\COMMITTEE - Familial Breast Ovarian Cancer\BRCA Management Protocols\2007 BRCA Management Protocol

Protocol for the Management of Female BRCA Mutation Carriers in Western Australia

BACKGROUND

Genetic testing for the familial breast and ovarian cancer genes (BRCA1/2) can provide information on an individual's specific risk of developing breast and ovarian cancer [1, 2]. BRCA mutations contribute to only a small proportion of all cases of breast and ovarian cancer, but it is estimated that as many as 75% of all familial cases occur in carriers of these mutations [2]. Carriers of a BRCA1 mutation have a 50 to 85% lifetime risk of developing breast cancer and a 20 to 40% lifetime risk of ovarian cancer. Women with a mutation in BRCA2 appear to have a similar risk of breast cancer and a 10 to 20% risk of ovarian cancer [2, 3]. Individuals identified as non-carriers have been shown to have a sustained reduction in cancer related anxiety [4].

The development of precise protocols for the management of BRCA mutation carriers may be considered controversial given the paucity of longer term data [5, 6]. Further, management for men with BRCA mutations has not received adequate evaluation in the literature and therefore available data regarding surveillance for this group is also limited.⁶ Nevertheless, the following recommendations are considered best practice for the management of female BRCA mutation carriers in Western Australia based on current evidence.

The Familial Breast and Ovarian Cancer Sub-Committee of the Western Australian Genetics Council have developed these recommendations based on national and international best practice

RECOMMENDATIONS FOR MANAGEMENT (summarised in Table 1)

Breast

Mammographic screening

The value of mammographic screening is that it offers the opportunity to improve outcome through detection of the disease at an earlier phase [6]. Whilst the effectiveness of mammographic screening has been debated internationally, screening programs and cancer societies remain strongly in support of mammography as the most effective tool available for early detection of breast cancer and reduction in mortality [7].

In Australia, mammographic screening accounts for just over 30% of detected breast cancers [8] and has been used to detect early stage cancers in BRCA mutation carriers [5].

Recommendation: Annual screening from 40 years of age or 5 years younger than the youngest affected family member, whichever is earlier.

Clinical examination

NHMRC guidelines recommend that clinical breast examination may be an important addition to a screening strategy for breast cancer in young, high-risk women. This is primarily due to doubt about the sensitivity of mammography given the density of breast tissue for this group [9] It is also effective in detecting cancer which appears between regular mammographic screening. Approximately 10% of breast cancers may be detected by clinical examination alone [10] .

Recommendation: At least one to two times per year [6] beginning at age 18 years. Post mastectomy, every six months.

Self-examination

A significant proportion of breast cancers are found by women themselves [8, 11]. There are anecdotal reports of mammography being insufficient to detect breast cancers for BRCA mutation carriers, and therefore monthly breast self-examination may take on greater value in high risk women provided they have had previous instruction on how to undertake self-examination [12]. In contrast, there is no demonstrable benefit from BSE in the general population.

Recommendation: Monthly beginning at age 18 years.

Prophylactic mastectomy

Prophylactic mastectomy has been viewed by some as a controversial method of reducing personal risk of developing breast cancer for three reasons: concern about the personal effects of such drastic surgery, the fact that breast cancer does not develop in all carriers of these mutations, and that cancer detected in the early stages can often be treated effectively [2].

Prophylactic bilateral mastectomy substantially reduces the incidence of breast cancer among women with a BRCA1 or BRCA2 mutation [5, 13, 14]. However surgery does not eliminate the risk of breast cancer or replace the need for ongoing surveillance [13].

According to statistical models, for 30 year old women who carry BRCA1 or BRCA2 mutations, they may gain three to five years of life expectancy from prophylactic mastectomy [1]. Gains in life expectancy decline with age.

Recommendation: Discussed as an option [6].

Chemoprevention (Tamoxifen)

Tamoxifen has been found to be a useful addition to other management strategies for breast cancer [5, 15]. Grann et al (2000) found that a 30 year old woman may prolong her survival by approximately 1.8 years with the use of tamoxifen. In Australia, tamoxifen is not available on the PBS for prevention of breast cancer. There are several ongoing trials that are evaluating the role of aromatase inhibitors in high-risk women but as yet no published evidence is available.

Recommendation: Tamoxifen is currently not registered for use as a chemopreventative agent.
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Prophylactic oophorectomy

Prophylactic oophorectomy may decrease breast cancer incidence by as much as 50% among cancer-free women with BRCA1 mutations irrespective of hormone replacement therapy usage [16-18].

Magnetic Resonance Imaging (MRI)

Breast MRI may be able to identify breast cancers earlier in high-risk women when compared with mammography, and thus potentially improve disease outcome. The recent paper by Kriege et al (2004) [19] showed that in a group of women with >15% lifetime risk of developing breast cancer, breast MRI had greater sensitivity than clinical breast examination and mammography in detecting invasive breast cancers. However, the specificity of MRI for malignant lesions was low and as a result women with MRI abnormalities in which it was not clear if they were certainly benign (56 cases), 43% underwent biopsies that ultimately were shown to be benign. In total 4169 MRI's were performed with an overall biopsy rate of 1.6%.

Breast MRI and the ability to biopsy abnormal lesions require special equipment and personnel with expertise in the interpretations of the results. Currently, there is no Medicare reimbursement for breast MRI and women considering this form of surveillance must be made aware of the potential cost incurred.

Given the uncertain utility of this form of breast imaging and other factors already mentioned, it is the recommendation of this committee and indeed the expert opinion across Australia, that high risk women considering breast MRI should have discussions regarding this form of surveillance within the confines of high risk / genetic assessment centres. Further, any breast MRI that is performed should only be undertaken in centres with established expertise. The results of breast MRI as part of breast cancer surveillance, need to be collected and evaluated as part of an ongoing program. Breast MRI should not be performed as the sole mechanism of surveillance in the high-risk group.

A Medicare rebate has been approved for Breast MRI and is underdevelopment.

Recommendation: Discussed at a high risk / genetic assessment centre.
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2. OVARIAN

Transvaginal Ultrasound

Ultrasound examination alone has neither sufficient specificity nor sufficient predictive value to justify its use in community screening [20], however despite its limitations it is the only screening imaging strategy available for high risk women.

Recommendation: Annual commencing from age 30 to 35 years or five years younger than the age of diagnosis of the youngest ovarian cancer case in the family, whichever is earlier [6].

This recommendation departs from the NHMRC guidelines with regard to the age at which to begin screening. Both the NHMRC recommendation and this recommendation are based on expert opinion in the absence of higher levels of evidence.

Serum CA-125 Measurement

Screening strategies using CA-125 level and ultrasound can detect ovarian cancer at an earlier stage. The usefulness of measuring the level of CA-125 as a screening test depends on the screening strategy, the cut-off value used and the population of women studied. It is of more benefit when used as part of a multimodal strategy [3].

CA-125 is not generally recommended as a surveillance test in pre-menopausal women in the general population [6, 21], however for those women with a BRCA mutation it may be appropriate for them to undergo this screening until further evidence is available. It should be noted that the use of CA 125 in pre-menopausal BRCA mutation carriers does present the risk of producing a high number of false positive results and women should be made aware of this.

Recommendation: Annually after menopause [6]

Prophylactic salpingo-oophorectomy

Prophylactic salpingo-oophorectomy is recommended as an effective means of reducing women's risk of developing ovarian cancer [22]. Induced early menopause and its consequences should be balanced against the benefits in terms of breast and ovarian cancer risk

Recommendation: Considered from age 30 to 35 years or at completion of childbearing [6].

Chemoprevention (oral contraceptive)

Cohort and cross-sectional studies have suggested that oral contraceptives are protective against ovarian cancer [6] and there is now some evidence from a case-

control study that use of the oral contraceptive pill may reduce the risk of ovarian cancer in women with a BRCA1 or BRCA2 gene mutation [15].

Recommendation: Balancing the risk between decreasing risk of ovarian cancer and the slight increased risk of breast cancer has to be made on an individual basis

Lifestyle risk factors

Modifiable risk factors for breast cancer include the following:

Hormone Replacement Therapy (HRT)

For women taking HRT for ten years or more there is a two fold associated increase in risk. NHMRC guidelines state that long term use of HRT should be avoided unless there are severe menopausal symptoms [6]. Risks and benefits of HRT should be considered [23].

Oral Contraceptive Pill (OCP)

The OCP has been shown to increase the risk of breast cancer for current and recent users (within 10 years) by 20% [6].

Alcohol

A meta-analysis of worldwide data on alcohol consumption and breast cancer indicated an increase in relative risk of 7.1% for each additional intake of 10g alcohol daily [23].

Physical activity

Within the general population there is a decrease in breast cancer risk with moderate physical exercise. Evidence suggests this decrease in risk to be between 20 and 40 per cent [23].

Weight

Within the general population a high BMI is associated with an increased breast cancer risk in postmenopausal women [23].

Recommendation: Lifestyle factors should be discussed.

Table 1. Breast and Ovarian Cancer Surveillance Recommendations for BRCA1 and BRCA2 Mutation Carriers

Modality	Frequency
BREAST	
Mammography	Annual screening from 40 years of age or 5 years younger than the youngest affected family member, whichever is earlier
Clinical breast examination	At least one to two times per year beginning at age 18 years Post mastectomy, every six months
Self breast examination	Monthly beginning at age 18 years
Prophylactic mastectomy	Discussed as an option
Chemoprevention (Tamoxifen)	Tamoxifen is currently not registered for use as a chemopreventative agent
Magnetic Resonance Imaging (MRI)	Discussed at a high risk / genetic assessment centre
OVARIAN	
Transvaginal ultrasound	Annual commencing from age 30 to 35 years or five years younger than the age of diagnosis of the youngest ovarian cancer case in the family, whichever is earlier
Serum CA-125	Annually after menopause
Prophylactic salpingo-oophorectomy	Considered from age 30 to 35 years or at completion of childbearing
Chemoprevention (oral contraceptives)	Balancing the risk between decreasing risk of ovarian cancer and the slight increased risk of breast cancer has to be made on an individual basis

Note: These guidelines are for mutation carriers within high risk clinics. Similar guidelines would be for high risk families where no mutation has been ascertained, however clinical recommendations would be made on an individual basis by the clinician responsible. Further, these recommendations are dynamic, and will be changed with the introduction of new information.

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