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Outcomes of Multimodality Breast Screening for Women at Increased Risk of Familial Breast Cancer

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Abstract
Background While population-based breast screening for women over the age of 50 years is a generally accepted and proven health strategy, the role of breast screening specifically among women at high risk of familial breast cancer has remained controversial. Indeed, there are very few services specifically offering a breast-screening program for women at high risk of familial breast cancer.
Methods In 1999 a Familial Breast Cancer Screening Clinic (FBCSC) was established at the North Brisbane BreastScreen Queensland Service to provide a regular multimodality screening program utilizing clinical breast examination, breast ultrasound, and mammography for women at higher risk of hereditary breast cancer and with entry into the program commencing from the age of 30 years.
Results Since its inception, a total of 2440 women have participated in the FBCSC. A total 7051 breast-screening examinations have been performed on these participants, with 53 breast cancers being diagnosed, including 8 in situ ductal carcinomas, 38 invasive ductal carcinomas, and 7 invasive lobular carcinomas. The mean size of the cancers was 16 mm (range = 1–45 mm), and of the 45 invasive cancers, 60% were less than or equal to 15 mm in size. The overall axillary node positive rate was 24.5% (13/53). The invasive cancer detection rate for first-round screening was 8.3 cancers per 1000 women screened, with 5.2 cancers per 1000 women detected on subsequent round screening.
Conclusions The results from this service demonstrate that multimodality screening for women at high risk of familial breast cancer and including women of younger age is effective and appropriate, with very acceptable cancer detection rates and pathological cancer characteristics being observed consistent with early-stage detection. The colocated siting of this service within a BreastScreen Queensland facility has proven to be efficient and cost effective.

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Abbreviations

FBCSC Familial Breast Cancer Screening Clinic
NBOCC National Breast & Ovarian Cancer Centre

Introduction

The ideal paradigm for the management of women at increased risk of familial breast cancer remains to be elucidated, but current options for high-risk women include breast surveillance, chemoprevention, prophylactic mastectomy, and/or oophorectomy [1, 2]. Over the past 15 years our understanding of hereditary breast cancer has greatly increased, particularly with the recognition of a number of predisposition genes, including the highly penetrant *BRCA1* and *BRCA2* genes, as well as a number of less penetrant or less frequently occurring gene mutations such as *ATM*, *P53*, *PTEN*, and *CDH1* [2–5]. Estimates of breast cancer risk by the age of 80 years are approximately 60–80% for carriers of *BRCA1* and *BRCA2* mutations, and the corresponding risks for ovarian cancer are 30–45% and 10–20% for each of these gene mutations, respectively [6]. However, as genetic testing is not currently universally and readily available at reasonable cost, the identification of women at high risk of breast cancer can alternatively be gauged by using various clinical assessment tools and decision-making paradigms, including the Gail [7], Claus [8], and Tyrer-Cusick [9] models, and the BRCAPRO [10] and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) [11], which estimate breast cancer risk based on family history and sometimes in combination with other risk factors such as reproductive history or prior breast biopsies. In Australia, the National Breast & Ovarian Cancer Centre (NBOCC) has also developed a familial breast cancer risk classification system (Table 1) [12], providing a clinical tool for the classification of women into three risk categories on the basis of family pedigree, with category 1 representing general population risk, category 2 including women of moderately increased risk (4% of the female population), and category 3 representing women at highest risk and including less than 1% of the female population.

There is an emerging perspective that for women at high risk of familial breast cancer, moderately intensive breast screening and surveillance with the anticipation of early detection represents a reasonable alternative and often preferred mode of management as opposed to the more interventional strategy of prophylactic surgery [13]. However, while large screening trials have demonstrated the effectiveness of population-based mammographic screening for women over the age of 50 years, and have been shown to be associated with at least a 22% reduction in breast cancer mortality in meta-analyses [14] and even greater reductions in mortality of 30–40% in some individual series [15–17], the issue of screening women at high risk for breast cancer, including women of a younger age, has continued to remain contentious. While there have been no randomized controlled trials of screening women under the age of 50 years with a family history of breast cancer, there have been some recent observational studies that have reported varying success rates in screening high-risk women utilizing predominantly mammography-based screening programs [18–27]. All of these studies have reported cancer detection rates at least equal to or greater than the cancer detection rates seen in screened populations at normal risk and of an older age. In addition, in recent years there have also been a number of prospective screening studies [28–33] that used MRI screening, with some of these reports also comparing mammography and ultrasound. These studies have also

Table 1 Australian NHMRC National Breast & Ovarian Cancer Centre risk classification for familial breast cancer

1. At or slightly above average risk
Covers over 95% of the female population
No confirmed family history of breast cancer
One 1° or 2° relatives 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.
One 2° relative diagnosed with breast cancer at any age
Lifetime risk: 1 in 14 to 1 in 8
2. Moderately increased risk
Covers less than 4% of the female population
One or two 1° relatives diagnosed with breast cancer before the age of 50 (without potentially high-risk features)
Two 1° or 2° relatives on the same side of the family diagnosed with breast or ovarian cancer (without potentially high-risk features)
Lifetime risk: 1 in 8 to 1 in 4
3. Potentially high risk
Covers less than 1% of the female population
Three or more 1° or 2° relatives on the same side of the family diagnosed with breast or ovarian cancer
Two or more 1° or 2° relatives on the same side of the family diagnosed with breast or ovarian cancer, including any of the following high-risk features: bilaterality, diagnosed at age 40 or younger, breast and ovarian cancer in one individual, or breast cancer in a male
One 1° or 2° relative diagnosed with breast cancer at age 45 or younger plus another 1 or 2 relatives 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
Lifetime risk: 1 in 4 to 1 in 2 or higher is shown to have a high-risk breast cancer gene mutation

shown very satisfactory cancer detection rates, with MRI being reported to have a sensitivity as high as 91%.

However, considerable debate still continues over many specific issues regarding the screening of women with a family history of breast cancer, including which screening modalities should be utilized and at what age surveillance should commence. The role of mammographic screening in this group has been questioned in view of the known reduced sensitivity in mammography in younger women with increased breast parenchymal density, and because the theoretical potential carcinogenic effects of radiation in this younger group of women with high-risk predisposition genes also remains unclear [1, 2, 34, 35]. On the other hand, in a multicentre case-control study, Narod et al. [36] found no excess risk of breast cancers among female *BRCA1* and *BRCA2* mutation carriers who underwent regular mammographic screening.

The purpose of this report is to present in a descriptive fashion the results of a multimodality screening program that has utilized clinical breast examination, screening breast ultrasound, and screening mammography in a familial breast cancer screening clinic, specifically designed to provide a service for women at high risk of hereditary breast cancer. In 1999 the Familial Breast Cancer Screening Clinic (FBCSC) was established at the BreastScreen Queensland North Brisbane Service as a pilot project with the intention of providing a regular multimodality screening program for women at increased risk of familial breast cancer. This evaluation of the performance of the clinic was undertaken to assess breast-screening cancer detection rates, interval cancer rates, and pathology findings and to review the method of operation of the clinic in providing a screening service for high-risk women.

Methodology

The FBCSC was established in 1999 as a dedicated high-risk screening clinic colocated with the BreastScreen Queensland North Brisbane Service. Women at a high risk of familial breast cancer were invited to attend the clinic either through the mechanism of referral from their general practitioner or, in the latter years of the clinic's function, by the selection of high-risk women attending the regular North Brisbane BreastScreen Queensland program identified by means of a questionnaire, given to all screening attendees, that asked specific questions in regard to their family history.

High risk was defined as those women who were noted to have an increased lifetime risk of developing breast cancer of 15% or greater. This included all women who fell into categories 2 and 3 in the NBOCC familial breast cancer classification schedule (Table 1) [12], as well as women who were proven to have a predisposition genetic mutation (including *BRCA1*, *BRCA2*, *ATM*). Screening was initially offered to women from the age of 30 years and above, but in the last 2 years of the clinic's operation, the upper age limit has been capped at 65.

Table 2 North Brisbane Familial Breast Cancer Clinic: screening protocol

NBOCC category 2
Age 30–40 years: 2 yearly CBE, mammography ± US (∼density)[a]
Age >40–65 years: annual CBE, mammography
NBOCC category 3 and mutation carriers
Age 30–40 years: annual CBE, mammography ± US (∼density)[a]
Age >40–65 years: annual CBE, mammography ± US (∼density)[a]

[a] Ultrasound examination performed selectively in those women with significant parenchymal density on mammography as determined by the attending radiologist

The screening methods utilized in the clinic include clinical breast examination (CBE) by a nurse or medical officer, breast ultrasound, and film screen mammography. The screening mode and frequency is based on a schedule that takes into account the risk categorisation of the woman, her age, and the density of her breast parenchyma; this protocol is outlined in Table 2. NBOCC category 2 women aged 30–39 years are offered screening on a 2-year basis, utilizing clinical breast examination and mammography, with ultrasound screening also used if a dense parenchymal pattern was noted on mammography. NBOCC category 2 women aged 40–65 years are rescreened on an annual basis using CBE and mammography. Category 3 women aged 30–65 years are offered an annual screening examination. Once again the methods of screening are clinical breast examination, mammography and breast ultrasound if a dense parenchymal pattern is noted. In both category 2 and category 3 women 30–39 years old, the initial mammographic examination is conducted with two views, with subsequent mammographic examinations with a single oblique view only until the age of 40 years to reduce the amount of radiation exposure. While it might have been preferable to use ultrasound more extensively, the constraints of manpower issues necessitated that ultrasound screening be applied in the selective manner as outlined.

In accordance with the usual protocols followed by BreastScreen Queensland [37], patients who were noted to have an abnormality on any of these screening modalities were recalled to an assessment clinic where further workup was done; this may have included fine-needle aspiration biopsy (FNAB) or core biopsy.

All women who attend the FBCSC are initially counselled in a formal interview process to discuss their risk based on their family pedigree. This counselling is conducted by a specialist surgeon, a medical officer, or a nurse counsellor. The patient's lifetime risk of breast cancer is discussed based on her familial risk categorization or any

gene-testing results that might be available. Management options are discussed with the patient, including an outline of the screening protocol offered by this service. In addition, however, other options are discussed with the patient, including prophylactic surgery (both mastectomy and oophorectomy), drug prevention trials, and lifestyle and dietary issues.

Women who fall into NBOCC category 3 or who are considered to have a lifetime risk of breast cancer greater than or equal to 25% are offered referral to the Queensland Clinical Genetics Service for consideration of the performance of genetic testing. From its beginning, the FBCSC has had a very close working relationship with the Queensland Clinical Genetics Service and both services have initiated and received referrals from each other, an arrangement that has been mutually complementary. The FBCSC was the first of its kind in Australia to provide such a formalised screening service for high-risk women in this context, and the clinic is also unique in that it functions as an ancillary service to the regular BreastScreen Australia program. Logistically, this coexistence of two services has functioned well and has provided a very efficient model for the provision of a familial breast cancer screening service, with the obvious advantage of the ability to share resources, including both equipment and skilled personnel.

Data for the analysis provided in this report was extracted from the database collected prospectively by the FBCSC and from the BreastScreen Queensland Registry database operated by Queensland Health. Cancer detection rates and interval cancer rates have been analysed and reported, and although the authors appreciate that the screening data from this unique group of women is not strictly comparable to that of general population screening data, the rates have been contrasted against the baseline figures of the National Accreditation Standards (NAS) [37] for BreastScreen Australia simply because there is little other data against which to make a comparison in regard to standards of screening performance.

Results

From its inception to August 2007, a total of 2440 women have participated in the FBCSC. Of these 1865 women (76%) were classified as NBOCC risk category 2 and 575 women (24%) were classified as NBOCC category 3 or having a gene mutation, including 15 women with a proven *BRCA1* gene mutation and 6 women with a proven *BRCA2* gene mutation. This proportional division of the total into the two groups is approximately as expected, as category 2 and category 3 women make up 4 and 1% of the population, respectively. A total of 7051 breast-screening examinations have been performed on these 2440 participants: 5303 screens in category 2 women and 1748 screens in category 3 women (including 73 screens performed on the 21 *BRCA1/2* gene mutation carriers). As a result of these screening events, 187 FNABs and 84 core biopsies were performed. A total of 64 open surgical biopsies were performed but this included surgery that was part of treatment.

A total of 53 cancers occurring in 52 women are included in this series. Of these, 49 breast cancers were detected by screening in 49 women; these included 8 in situ ductal carcinomas (DCIS), 36 invasive ductal cancers (IDC), and 5 invasive lobular cancers. An additional three women presented with interval cancers within the 12-month screening interval, one of whom was found to have bilateral disease, making four additional cancers in this interval group and a total of 53 cancers in the overall series (Table 3). Of the 53 cancers in this series, 36 occurred in NBOCC risk category 2 women and 17 in NBOCC risk category 3 women, including 1 breast cancer diagnosed in a known *BRCA2* gene mutation carrier. The average age of the women diagnosed with breast cancer was 51 years (range = 34–62 years). The majority of the 45 invasive cancers were high grade, with 35 either grade 2 or 3 (77.8%). Six of the eight DCIS (75%) cancers were of high nuclear grade, one was of intermediate grade, one was of low grade. The mean size of the cancers detected was 16 mm (range = 1–45 mm). Of the 45 patients with invasive cancer, 60% were 15 mm or smaller, and of the 41 screening-detected invasive cancers, 61% were 15 mm or smaller. Of the 45 patients with invasive cancer, 13 (28.9%) had axillary lymph node metastases; however, the overall axillary nodal involvement rate for this series of cancers was 24.5% (13/53). In 30 instances (57% overall), breast-conserving treatment was able to be done in lieu of mastectomy.

Table 4 shows the distribution of cancers by age decade. It indicates that most cancers (84%) were detected between the ages of 40 and 59 years, with the mean tumour size in the younger patients only slightly larger than in their older counterparts. In the younger groups, there was a higher proportion of high-risk women (category 3) among those diagnosed with cancer.

There were 14 malignancies detected on first or prevalent round screening and 35 cancers were detected on subsequent screening episodes. Over the same time period in which these 49 cancers were detected at planned screening episodes, there were 3 women who developed interval cancers, one of whom had bilateral disease, and who have been excluded from the following analyses of the cancer detection rates. Overall, in this series the 49 screening-detected cancers were diagnosed as a result of 7051 screening episodes. This represents an overall global

Table 3 Details and characteristics of 53 breast malignancies: 49 screen detected; 4 interval

Age of patients		
Mean age = 51 years (range = 34–62 years)		
NBCC risk categories		
36 NBOCC 2		
17 NBOCC 3 (including 1 *BRCA2* carrier)		
Cancer type		
Screen detected		Interval
DCIS only	8	0
IDC	36	2
ILC	5	2
Grade of invasive cancers		
Grade 1	10	
Grade 2	23	
Grade 3	12	
Tumour size		
Mean = 16 mm (1–45 mm)		
Of total 45 invasive cancers, 27 (60%) $\leq$ 15 mm		
Of 41 screen-detected invasive cancers, 25 (61%) $\leq$ 15 mm		
Axillary lymph node involvement		
Positive	13	
Negative	28	
Not performed	12	
First- or subsequent-round screen detection:		
First round	14	
Subsequent round	35	
Interval	4 (3 women)	
Treatment		
Lumpectomy only	9	
Lumpectomy + AD	21	
Mastectomy	5	
Mastectomy + AD	18	

cancer detection rate of 6.5 cancers per 1000 women screened, with a cancer detection rate of 9.7 per 1000 women screened for first-round screening and 6.2 per 1000 women screened for subsequent-round screening (Table 5). There were 41 invasive cancers diagnosed in this screening-detected series and the corresponding cancer detection rates were as follows: first-round screening, 8.3 per 1000 screens; subsequent-round screening, 5.2 per 1000 screens; overall invasive detection rate, 5.5 per 1000 screened. For women over 50, these figures were 15.9 and 6.4, respectively, and for women under 50, they were 6.2 and 3.8, respectively. The cancer detection rate for invasive cancers among NBOCC category 3 women was higher (6.9 per 1000 screened) than that for category 2 women (5.5 per 1000 women screened).

There were three women who developed interval cancers over the period of this study, one of whom developed bilateral disease. Thus, of the 53 cancers in this series, there were 4 interval cancers (7.5%). Two of these women were high-risk category 3 and one was a *BRCA2* carrier. All of these cancers were mammographically occult, even on retrospective review, but were visible on subsequent interval ultrasound examinations. A 37-year-old category 3 woman was found to have a 9-mm high-grade IDC 6 months after her previous screen. The woman with bilateral cancer was 47 years old, in category 3, and was found to have small multifocal invasive lobular cancer 9 months after her first screen. The third woman, 54 years old and a *BRCA2* gene mutation carrier, attended the community North Brisbane BreastScreen program but refused to come under the umbrella of the family history clinic and thus did not receive additional screening with ultrasound and CBE; she was diagnosed at an interval of 8 months. These interval cancers have been excluded from the above cancer detection rate analyses. BreastScreen Australia [37] sets an acceptable upper-threshold-interval cancer rate of 7.5 per 10,000 screens up to 12 months after completion of a negative screening episode. Three interval cancer events of a total of 7051 screening episodes yields an interval cancer rate of 4.25 per 10,000 screens.

When the sensitivity of the various screening modalities was reviewed in relation to the 53 cancers in this series, it was found that clinical breast examination (CBE) detected an abnormality in 64.1% (34/53) of cases, mammography demonstrated 73.6% (39/53) of cancers, and ultrasound detected 79.2% (42/53) of breast cancers. However, the combined sensitivity of both mammography and ultrasound was 92.5%. Whereas mammography was utilized in all screening events, ultrasound was utilized in only category 3 women and category 2 women 30–40 years old who had mammographically dense breasts. While 11 cancers were not seen on ultrasound and were seen only on mammography, there were 14 cancers seen only on ultrasound and not detected on mammography, hence 26.4% (14/53) of cancers in this series were seen on ultrasound only and would has been missed if ultrasound had not been utilized as a screening, albeit in this selective fashion.

Discussion

The North Brisbane FBCSC is the first public clinic of its kind in Australia that offers both a familial cancer risk counselling service and a specific breast-screening surveillance program on the one site. The data documented in this report demonstrate that the clinic has been effective in providing surveillance for women at high risk for familial breast cancer, with the analyses showing very acceptable rates of breast cancer detection and a low interval cancer rate. The cancer detection rate for invasive cancers at the clinic was 8.3 cancers per 1000 women screened in the

Table 4 Screening-detected cancer distribution by the age decade

Age in decades	Cancer no. (%)	Mean size of cancer (mm)	Number of women in NBOCC = 3 at time of diagnosis
30–39	3 (6%)	17	3/3 (100%)
40–49	17 (35%)	18	4/17 (23%)
50–59	24 (49%)	14	6/24 (25%)
60–64	5 (10%)	16	1/5 (20%)

first-round screening, and 5.2 per 1000 women screened for subsequent-round screening. For women older than 50, these figures were 15.9 and 6.4, respectively, and for women under 50, the numbers were 6.2 and 3.8, respectively. For comparison, BreastScreen Australia sets National Accreditation Standards [37] for cancer detection for population screening of 5 or greater and 3.5 or greater for first- and subsequent-round screening, respectively. BreastScreen Australia also sets an acceptable upper-threshold interval cancer rate of 7.5 per 10,000 screens. Over the period of this study the interval cancer rate for the FBCSC was 4.25 per 10,000 screens. Whilst we appreciate the fact that BreastScreen Australia quality assurance standards are in fact directed at population-based screening programmes for women over 50, this comparison has been made simply to demonstrate that the efficiency of screening high-risk women across a broad range of ages is not inferior to general screening programmes. Indeed, there are presently no comparative reference guidelines for screening detection rates for high-risk/younger women, particularly for the 30-40-year age group, but it is still significant that the FBCSC results exceed these established benchmarks for population-based screening. Hence, the cancer detection figures presented in this report are very acceptable, particularly since the screening program at the FBCSC included younger women starting at 30 years of age in whom the incidence of breast cancer would usually be expected to be lower and the sensitivity of breast imaging modalities would be presumed to be reduced. As expected, the cancer detection rate for invasive cancers among NBOCC category 3 women was higher (6.9 per 1000 screened) than that for category 2 women (5.5 per 1000 women screened).

Other parameters reflecting an acceptable performance by the FBCSC include an overall small mean tumour size of 16 mm, 61% of screen-detected invasive cancers 15 mm or smaller, a significant proportion of in situ-only cancers being detected (15%, 8/53), and a low overall incidence of axillary lymph node involvement of 24.5% (13/53). The findings in our report with respect to tumour size are in keeping with Tabar's [38] recommendation that at least 50% of invasive cancers need to be 15 mm or less in diameter in order for there to be a mortality reduction. Interestingly, there was a very high proportion of high-grade malignancies observed in this series, with 35 of 45 invasive cancers (77.8%) either grade 2 or grade 3, and 6 of the 8 DCIS cancers of high nuclear grade (75%), a finding which is a well-documented pathological characteristic of hereditary breast cancers.

The issue of what is the most appropriate modality for screening high-risk women remains controversial in the current literature. At the FBCSC, a multimodality screening methodology has been used, offering CBE and mammography to all patients, with additional screening ultrasound for those women with dense breast parenchyma. The use of screening ultrasound in this context as an adjunct to mammography has proven to be highly successful, with 26.4% of cancers being detected on ultrasound but not seen on mammography. Indeed, in this series of cancers, ultrasound was noted to have the highest sensitivity at 79.2% compared to mammography at 73.6%. There is an increasing body of evidence that suggests that ultrasound may have a role as a breast-screening tool, particularly as an adjunct to mammography. As a diagnostic tool, studies suggest that ultrasound may have a sensitivity ranging from 72.6 to 92% [39–41]. In an independent study, investigators from Sydney Square found an 81.7% cancer detection rate with ultrasound following mammography; however, in women younger than 45, they found ultrasound's sensitivity of 13.2% was greater than that of mammography for detecting cancers [42]. Crystal et al. published results in 2003 [43] on of the use of ultrasound in screening women with mammographically dense breasts and demonstrated very satisfactory outcomes, detecting all cancers smaller than 15 mm in diameter and 67% of cancers smaller than 10 mm.

Table 5 Cancer detection rates: all screening-detected cancers ($n = 49$)

Screening episode	30–49 years	CI	50–64 years	CI	Total group	CI
First round	7.1	3.1–13.9	19.0	7.0–41.0	9.7	5.3–16.2
Subsequent round	4.6	2.4–8.0	7.7	4.9–11.5	6.2	4.4–8.7
All visits	5.3	3.3–8.2	8.8	5.9–12.6	6.5	4.8–8.6

Cancers detected per 1000 screen

CI confidence interval

There are a number of observational studies that have reported the results of screening high-risk younger women utilizing mammography as the dominant screening tool [18–27]. Most of these studies involved only small numbers of high-risk women and used varying criteria for defining risk and for inclusion in their study programs. All of these studies, however, have demonstrated cancer detection rates in this high-risk group of women to be at least equivalent to or, in most cases, greater than the cancer detection rates for screening women in the general population who are over 50.

There have been a number of recent reports that have been supportive of a role for MRI in screening high-risk women. Since the mid-1990s at least six substantial prospective nonrandomised studies [28–33] have been undertaken to determine the benefit of adding MRI to mammography for women at increased risk of breast cancer, and some of these studies have also included ultrasound and/or clinical breast examination. The four largest of these MRI trials, those of Kriege [28], Warner [29], Kuhl [30], and Leach [31], showed sensitivities for MRI ranging from 77 to 91% compared to sensitivities for mammography from 33 to 40%. These same MRI studies documented axillary lymph metastatic rates from 13 to 33% and interval cancer rates of from 4.5 to 8%. The MRI studies all demonstrated substantially better sensitivity for MRI over mammography in their studies; however, specificity was better for mammography. Interestingly the combined sensitivity of mammography and ultrasound for the FBCSC (92.5%) was in the same range as the sensitivities of MRI screening reported in the four MRI studies, and by way of comparison, the FBCSC lymph node positivity rate was 24.5% with an interval cancer rate of 7.5%. While it may be argued that these reports on MRI screening would suggest that MRI is the most effective screening modality for women at high risk of familial breast cancer and for *BRCA* mutation carriers, there remain a number of logistical and practical issues relating to the utilization of MRI as a breast-screening tool [44]. In particular, MRI equipment is very expensive and has significant spatial requirements. For this reason it is a radiological service that is often centred in metropolitan locations and tends not to be available in remote and rural centres. Interpretation of MRI breast images also requires a significant degree of expertise and experience which is not universally available among general radiologists. On the other hand, ultrasound and mammography are services that are more universally available and less expensive. The results from the FBCSC reported here suggest that the combination of these two radiological methods of screening can achieve very satisfactory outcomes. Ultrasound screening does have the drawback of needing greater manpower and time for radiographers/radiologists. However, in circumstances where access to MRI screening is not available, multimodality screening using CBE, ultrasound, and mammography would appear to be a not unreasonable alternative for screening high-risk women.

From a service point of view, the FBCSC has proven to be a huge success and has been strongly supported by regional general practitioners. An important functional advantage of the clinic has been its siting within the North Brisbane BreastScreen Queensland Service as a specialized ancillary clinic. This has resulted in substantial cost savings and overall efficiencies by enabling the sharing of expert radiological, medical, and nursing staff that have experience and skills in conducting breast screening, and of physical resources such as radiological equipment, biopsy equipment, and computer programs. In addition, there has been a crucial liaison between the FBCSC and the local Queensland Clinical Genetics Service which has proven to be a mutually beneficial relationship for both services in coordinating the care of these high-risk women.

In conclusion, the data provided in this report demonstrate that the multimodality screening programme offered by the FBCSC for women at high risk of familial breast cancer is effective and practical. While MRI screening may have slightly superior sensitivity based on recent reports, the information detailed in this review supports the view that in circumstances where MRI may not be readily available for screening purposes, multimodality screening of high-risk women using CBE, ultrasound, and mammography is in fact appropriate and worthwhile with excellent breast cancer detection rates able to be achieved. We propose that the extension of breast screening to women at higher risk of familial breast cancer should become a natural progression of the current population-based screening programs. However, it is important that such screening services for high-risk women involve a multidisciplinary team approach and utilize valid protocols that can be accountably subjected to ongoing evaluation.

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