

## BreastScreen-based mammography screening in women with a personal history of breast cancer, Western Australian study

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**G**lobally, breast cancer accounts for 23% of all cancers occurring in women.<sup>1</sup> Due to the excellent prognosis and longer life expectancy in early-stage breast cancer, the number of women with a personal history of breast cancer (PHBC) — “breast cancer survivors” — is increasing. Women with PHBC have a long-term increased risk of developing a recurrent or new cancer in the previously affected breast (where treated with breast conservation) or a contralateral cancer.<sup>2-4</sup> Given that population mammography screening reduces breast cancer deaths,<sup>5</sup> and that observational data show potential benefit from early detection of second breast cancers in PHBC women,<sup>6-10</sup> international and Australian recommendations include mammography screening for these women.<sup>11-16</sup> Annual breast clinical examination is also advised for PHBC women.<sup>11,13-16</sup>

Evidence reviews have highlighted the lack of high-quality screening evaluations and the paucity of data from screening programs for PHBC women.<sup>17,18</sup> A recent report of outcomes from screening PHBC women who attended Breast Cancer Surveillance Consortium-affiliated mammography facilities in the United States<sup>2</sup> has provided international benchmarks for screening performance measures in PHBC women. Screening PHBC women is particularly relevant in Australia, where there is inconsistent policy on whether these women may access mammography through BreastScreen Australia services and where there is little evidence to inform practice.

Here, we report the first Australian study of mammography screening outcomes in women with PHBC who participated in population-based

### Abstract

**Objective:** To evaluate mammography screening outcomes in women with a personal history of breast cancer (PHBC), who have an increased risk of recurrent or new breast cancer, relative to women without PHBC.

**Design, setting and participants:** Retrospective study of 713 191 screening mammograms from two groups of women — those with versus those without PHBC — who participated in the BreastScreen WA program in Western Australia between 1997 and 2006.

**Main outcome measures:** Cancer detection rate (CDR), recall to assessment rate, recall positive predictive value (PPV) for cancer, and distribution of cancer characteristics within and between the two groups.

**Results:** Screening detected 4125 breast cancers: CDR per 10 000 screens was significantly higher in women with PHBC (95.5; 95% CI, 78.3–112.7) than in women without PHBC (57.2; 95% CI, 55.4–58.9). Recall to assessment rate per 10 000 screens was lower in women with PHBC (385.2; 95% CI, 350.6–419.8) than in women without PHBC (504.9; 95% CI, 499.7–510.2). Recall PPV was higher for women with PHBC (24.8%; 95% CI, 21.0%–28.9%) than those without PHBC (11.2%; 95% CI, 10.9%–11.6%). Cancer characteristics were consistent with early detection (most were smaller than 2 cm and node-negative) and were similarly distributed in both groups, except for tumour grade, with PHBC women having fewer low-grade cancers and slightly more high-grade cancers than women without PHBC.

**Conclusions:** The relative rate of cancer detection between women with PHBC and women without PHBC who attended an Australian population-based breast screening program was similar to estimates from international studies. Recall rates were within national standards. Screen-detected cancers had similar characteristics in both groups, except for tumour grade. These data support national integration of mammography screening for women with PHBC into BreastScreen, although evaluation of interval cancers will be necessary.

screening through the BreastScreen program. We aimed to examine rates of cancer detection and recall to assessment and to define the characteristics of screen-detected cancers in PHBC women, and to compare these outcome measures with those in concurrent screening participants who did not have PHBC.

### Methods

#### Study design and participants

This was a retrospective study of two groups of women who participated in screening through BreastScreen WA, the Western Australian component of BreastScreen Australia, between Jan-

uary 1997 and December 2006. BreastScreen WA provides free population-based mammography screening to all women aged 40 years or older,<sup>19</sup> actively targeting women aged 50–69 years according to BreastScreen Australia policy.<sup>20</sup> BreastScreen WA has granted PHBC women access to breast screening since its statewide implementation in 1995.

We included all screening mammograms for women who reported a PHBC. As a comparison group, we included screens for women who had screening during the same time frame and who did not report a PHBC. We used self-reported history of breast cancer (from information routinely collected at each screen) to classify the

**1 Breast cancer detection rates in women with and without a personal history of breast cancer (PHBC) participating in the BreastScreen WA program, 1997–2006**

Age group	Women with PHBC			Women without PHBC		
	No. of screening mammograms	No. of cancers	Cancer detection rate per 10 000 screens (95% CI)	No. of screening mammograms	No. of cancers	Cancer detection rate per 10 000 screens (95% CI)
Initial screening examinations (prevalent screening)						
40–49 years	161	0	—	57 978	219	37.8 (32.8–42.8)
50–69 years	767	11	143.4 (58.6–228.2)	71 920	590	82.0 (75.4–88.7)
≥ 70 years	263	4	152.1 (42.0–385.0)	5 174	102	197.1 (158.9–235.4)
All age groups	1191	15	125.9 (62.2–158.5)	135 072	911	67.4 (63.1–71.8)
Repeat screening examinations (incident screening)						
40–49 years	423	6	141.8 (52.0–306.0)	68 874	183	26.6 (22.7–30.4)
50–69 years	8 634	79	91.5 (71.3–111.7)	462 646	2585	55.9 (53.7–58.0)
≥ 70 years	2 110	18	85.3 (45.9–124.7)	34 241	328	95.8 (85.4–106.2)
All age groups	11 167	103	92.2 (74.4–110.0)	565 761	3096	54.7 (52.8–56.7)
<b>All screening examinations</b>						
40–49 years	584	6	102.7 (38.0–222.0)	126 852	402	31.7 (28.6–34.8)
50–69 years	9 401	90	95.7 (76.0–115.5)	534 566	3175	59.4 (57.3–61.5)
≥ 70 years	2 373	22	92.7 (54.0–131.5)	39 415	430	109.1 (98.8–119.4)
All age groups	12 358	118	95.5 (78.3–112.7)	700 833	4007	57.2 (55.4–58.9)

group of women with PHBC, because this has been shown to be highly accurate.<sup>21</sup> Self-reported history of breast surgery (including site/side of scars) is routinely verified by the technologist at time of screening.

### The screening process

BreastScreen WA participants receive two-view mammography of each breast, and all screens are read by two radiologists. Women who have a possible abnormality on mammography are recalled to assessment (this may include further imaging or needle biopsy); disagreement about recall to assessment is resolved by arbitration from a third reader. Most women recalled to assessment will be reassured that they do not have breast cancer after further testing.

Data are routinely collected from each woman who attends screening with BreastScreen WA. Participants are asked to complete a standard questionnaire (collecting demographic and breast history data), and to provide written consent for de-identified data about each screening episode to be used for program evaluation and research publication. Ethics approval was therefore not required for this study. Information from pathology and radiology or clinical reports for each screening episode is linked to client identification to ascertain outcomes in all screened women, including those

referred for surgery, and to classify cancer characteristics in screening participants. These data are securely stored in dedicated BreastScreen WA databases and are routinely used to monitor quality as part of BreastScreen national accreditation processes.

### Outcome measures and statistical analysis

The number of screens (initial or repeat) and the number of breast cancers detected were calculated for each group: overall, and by three age groups conventionally reported in screening participants (40–49, 50–69 and ≥ 70 years). We also compared 5-year age-group distributions between the two groups. We calculated cancer detection rate (CDR) per 10 000 screens (overall and by age group) for initial screens (ie, the first recorded screen in the program), repeat screens, and all screens, assuming independence of observations. Recall (to assessment) rates, positive predictive value (PPV) for recall, and the proportion of screens (of those that detected cancer) that required multiple reads were calculated. Exact 95% confidence intervals were calculated for rates and proportions.<sup>22</sup> The distribution of cancer characteristics (histological type, size, grade and node status) was compared for the two groups using contingency tables and the  $\chi^2$  statistic.

## Results

During the study period, there were 713 191 screens: 12 358 in PHBC women and 700 833 in women without PHBC (Box 1). More than three-quarters of all screens were in women aged 50–69 years (the program's target age group). However, 5-year age-group distributions differed between the two groups ( $P < 0.001$ ; Box 2). There were relatively fewer screens in the 40–49-years age group for women with PHBC (5%) than those without (18%), and conversely more screens in the ≥ 70-years age group for PHBC women relative to those without PHBC.

Among all screening participants, 4125 breast cancers were detected. Screening detected 118 breast cancers

**2 Five-year age-group distribution\* for screening examinations in women with and without a personal history of breast cancer (PHBC)**

Age group	Women with PHBC	Women without PHBC
40–44 years	0.90%	5.85%
45–49 years	3.98%	12.33%
50–54 years	13.42%	24.38%
55–59 years	20.41%	21.30%
60–64 years	22.04%	17.12%
65–69 years	22.81%	13.81%
70–74 years	10.65%	3.71%
≥ 75 years	5.79%	1.50%

\*  $\chi^2$  statistic for comparison of 5-year age-group distributions between the two groups,  $P < 0.001$ . ◆

**3 Rates of recall to assessment in women with and without a personal history of breast cancer (PHBC) participating in the BreastScreen WA program, 1997–2006**

Age group	Women with PHBC		Women without PHBC	
	No.	Rate per 10 000 screens (95% CI)	No.	Rate per 10 000 screens (95% CI)
<b>Initial screening examinations (prevalent screening)</b>				
40–49 years	9	559.0 (259.0–1035.0)	6 384	1101.1 (1074.1–1128.1)
50–69 years	51	664.9 (482.4–847.4)	7 182	998.6 (975.5–1021.7)
≥ 70 years	20	760.5 (427.2–1093.7)	481	929.6 (846.4–997.3)
All age groups	80	671.7 (524.5–818.9)	14 047	1040.0 (1022.8–1054.0)
<b>Repeat screening examinations (incident screening)</b>				
40–49 years	24	567.4 (340.4–794.4)	3 508	509.3 (492.5–526.2)
50–69 years	303	350.9 (268.9–390.5)	16 600	358.8 (353.4–364.3)
≥ 70 years	69	327.0 (249.9–404.2)	1 232	359.8 (339.7–379.9)
All age groups	396	354.6 (319.7–389.5)	21 340	377.2 (372.1–382.2)
<b>All screening examinations</b>				
40–49 years	33	565.1 (372.3–757.9)	9 892	779.8 (764.4–795.2)
50–69 years	354	376.6 (337.3–415.8)	23 782	444.9 (439.2–450.5)
≥ 70 years	89	375.1 (297.1–453.0)	1 713	434.6 (414.0–455.2)
All age groups	476	385.2 (350.6–419.8)	35 387	504.9 (499.7–510.2)

in PHBC women, with a CDR of 95.5/10 000 screens (95% CI, 78.3–112.7); this was significantly higher than the

CDR of 57.2/10 000 screens (95% CI, 55.4–58.9) for women without PHBC, in whom 4007 cancers were detected. A relatively higher CDR in PHBC women was evident in the 40–49-years and 50–69-years age groups, but not in women aged ≥ 70 years (Box 1).

Box 3 shows recall rates for each group: these were generally lower in PHBC women than women without PHBC (or similar in both groups) across all age groups and screening rounds. Overall, recall rates were significantly lower in PHBC women (385.2/10 000 screens; 95% CI, 350.6–419.8) than in women without PHBC (504.9/10 000 screens; 95% CI, 499.7–510.2).

PPV for recall was significantly higher for PHBC women (24.8%; 95% CI, 21.0%–28.9%) than for women without PHBC (11.2%; 95% CI, 10.9%–11.6%). In screening examinations that detected cancer, the rate of screens requiring three or more reads was 36.4/10 000 screens (95% CI, 25.8–47.1) in the PHBC group, higher than the 15.5/10 000 screens (95% CI, 14.6–16.4) in women without PHBC.

Box 4 summarises the characteristics of the 4125 breast cancers detected in all screening participants, by group. The distributions of tumour characteristics were not significantly different between the two groups, except for tumour grade where there was evidence ( $P=0.02$ ) of different

distributions (PHBC women had fewer low-grade cancers and more intermediate or high-grade cancers) after excluding data for reports with unknown grade.

**Discussion**

We found that mammography screening through the BreastScreen WA program was associated with a higher detection rate of breast cancer for women with PHBC than for women without PHBC (95.5 v 57.2/10 000 screens). Screening recall rates were within national standards, with ≤ 5% of all screening examinations resulting in recall to assessment for each group.<sup>20</sup> This is the first Australian evaluation of screening outcomes in PHBC women from a population screening program, and the second study ever to have also integrated a comparison group of women without PHBC who underwent mammography in the same screening services and time frame. The strength of our study design is that it provides an understanding of the *relative* screening outcomes in the two groups of women, and allows interpretation of our findings in the context of national standards for population screening.<sup>20</sup>

CDR and characteristics of detected cancers are routinely used to monitor screening outcomes and as surrogate measures of potential screening efficacy.<sup>15,20</sup> A relatively

**4 Characteristics of 4125 breast cancers detected in women with and without a personal history of breast cancer (PHBC) participating in the BreastScreen WA program, 1997–2006**

Breast cancer characteristic	Women with PHBC	Women without PHBC	<i>P</i> *
<b>Histological type</b>	<i>n</i> = 118	<i>n</i> = 4007	0.74
Ductal carcinoma-in-situ	31 (26.3%)	928 (23.2%)	
Invasive ductal carcinoma	67 (56.8%)	2369 (59.1%)	
Other invasive carcinoma	20 (16.9%)	700 (17.5%)	
Not specified	0	10 (0.2%)	
<b>Pathological tumour size</b>			0.93
< 1cm	34 (28.8%)	1080 (27.0%)	
1 cm to < 2 cm	51 (43.2%)	1681 (41.9%)	
2 cm to < 5 cm	27 (22.9%)	1011 (25.2%)	
≥ 5cm	6 (5.1%)	192 (4.8%)	
Not reported	0	43 (1.1%)	
<b>Pathological node status</b>			0.16
Lymph node metastases	2 (1.7%)	176 (4.4%)	
No lymph node metastases	116 (98.3%)	3831 (95.6%)	
<b>Tumour grade</b>			0.07 (0.02 <sup>†</sup> )
1 (low)	19 (16.1%)	1121 (28.0%)	
2 (intermediate)	53 (44.9%)	1590 (39.7%)	
3 (high)	29 (24.6%)	816 (20.3%)	
Not specified	17 (14.4%)	469 (11.7%)	
Data missing	0	11 (0.3%)	

\* *P* for Pearson  $\chi^2$  statistic for comparison of distributions. † *P* for  $\chi^2$  statistic excluding data for not specified and missing grades. ◆

higher CDR in PHBC women would be expected, as PHBC women have increased underlying risk for breast cancer,<sup>2-4,14</sup> and also because they are likely to have had more frequent screening (mostly annual) than women without PHBC (generally biennial). The age distribution (the PHBC group had relatively more screens from older women) may have also contributed to the observed higher CDR in PHBC women, although the majority of screens in both groups were in 50–69-year-olds, the program's target age group. To interpret our findings, given the absence of standards for screening outcomes in PHBC women, we can compare our estimates with those recently benchmarked by the Breast Cancer Surveillance Consortium (BCSC), which also compared two groups by PHBC status.<sup>2</sup> Although detection rates for each group in our study were generally higher than those reported by the BCSC, the relative detection between groups was similar in both studies, with a 1.7-fold higher rate of cancers detected in PHBC women relative to those without PHBC in our study, and a 1.6-fold higher rate reported from the BCSC.<sup>2</sup> Our CDRs for the group without PHBC (Box 1) demonstrate that cancer detection measures were well within BreastScreen national standards (counting in-situ and invasive cancer, CDR standards are  $\geq 62/10\,000$  for prevalent screens and  $\geq 42/10\,000$  for incident screens).<sup>20</sup>

Recall rates allow monitoring of the burden (potential harm) of screening from unnecessary testing.<sup>5,20</sup> Our study reports the first international estimates of screening recall rates in PHBC women from a population-based mammography program. We found that recall rates were lower in PHBC women than in women without PHBC (385.2 v 504.9/10 000 screens), whereas recall PPV (for cancer detection) was relatively higher in PHBC women, due to both fewer recalls and a relatively higher CDR in PHBC women. Because there are no published recall data for PHBC women who participated in population-based screening, we cannot compare our recall estimates to other studies. The BCSC study did not estimate recall rates but reported that

PHBC women were relatively more likely to require additional imaging.<sup>2</sup> A possible explanation for the lower recall in our PHBC group may be the screen-reading strategy used in the program — although more screens in PHBC women required three or more reads, these reads effectively arbitrated such cases. It may also be (partly) due to having relatively more screens from older women in the PHBC group.

Our study has shown that mammography screening detected second breast cancers in PHBC women that were predominantly smaller than 2 cm and node-negative (Box 4). The characteristics of cancers detected in PHBC women were generally consistent with early-detected cancers, and, except for tumour grade, were similarly distributed to those of cancers detected in women without PHBC. Tumour grade distribution differed significantly between the two groups, with PHBC women having fewer low-grade cancers and slightly more high-grade cancers relative to women without PHBC. This may reflect underlying host factors in PHBC women, possibly genetic or biological determinants, or may be a manifestation of tumour biology "selection" in a group of women who are likely to have received systemic therapy for their first breast cancer.

Our findings are relevant and timely for breast screening practice in Australia, where there is inconsistent policy on screening PHBC women (partly due to paucity of data from screening programs), and given that an evaluation of BreastScreen has recommended consideration of national provision of screening for PHBC women through BreastScreen services.<sup>15</sup> Although our study represents the first Australian report of screening in PHBC women, our results should be considered with awareness of some study limitations. As we did not have data on interval cancers, we were unable to estimate screening sensitivity, and we therefore cannot make recommendations on the time frame (after first cancer diagnosis) at which PHBC women might be offered entry into BreastScreen. The BreastScreen evaluation has recommended annual screening for PHBC women from 5 years after

first cancer diagnosis,<sup>15</sup> and this seems reasonable based on the recent evidence.<sup>2</sup>

We were unable to examine screening outcomes according to the first cancer treatment received for PHBC women. Characterising this aspect of screening outcomes in PHBC women should be examined in future evaluations because the detection capability of mammography is modified by treatment received for the first cancer.<sup>2</sup> Although ours is one of the largest studies of breast screening in this context, we had modest numbers of second cancers for age-group and screening-round strata in the PHBC group, leading to some strata-specific wide confidence intervals. Therefore, we have focused on the precise estimates for all screens in defining our conclusions. Also, because some women had several screens, confidence intervals around our estimates may have been slightly wider if we had allowed for clustering in women with repeat screens. A further potential limitation is that screening outcomes for PHBC women in BreastScreen WA may not be generalisable to women undergoing screening in the private sector (where there are few available data on screening participants and outcomes).

Mammography screening in PHBC women who participated in BreastScreen WA was associated with a higher CDR and lower recall rates relative to women without PHBC. Cancer characteristics were predominantly consistent with early detection in PHBC women and were similar to characteristics of cancers detected in women without PHBC, with the exception of tumour grade. Our findings support the role of mammography screening for PHBC women, and support allowing these women (in target age groups for screening) to have nationally consistent access to mammography screening through BreastScreen. Future research into screening PHBC women requires both epidemiological and clinical (radiological) evaluation of interval cancers — this should be planned carefully and early, if implementation of a national policy allowing PHBC women access to BreastScreen is adopted.

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