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ORIGINAL ARTICLE

Breast cancer screening—opportunistic use of registry and linked screening data for local evaluation

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Abstract

Rationale   Screening has been found to reduce breast cancer mortality at a population level in Australia, but these studies did not address local settings where numbers of deaths would generally have been too low for evaluation. Clinicians, administrators, and consumer groups are also interested in local service outcomes. We therefore use more common prognostic and treatment measures and survivals to gain evidence of screening effects among patients attending 4 local hospitals for treatment.

Aims and objectives   To compare prognostic, treatment, and survival measures by screening history to determine whether expected screening effects are occurring.

Methods   Employing routine clinical registry and linked screening data to investigate associations of screening history with these measures, using unadjusted and adjusted analyses.

Results   Screened women had a 10-year survival from breast cancer of 92%, compared with 78% for unscreened women; and 79% of screened surgical cases had breast conserving surgery compared with 64% in unscreened women. Unadjusted analyses indicated that recently screened cases had earlier tumor node metastasis stages, smaller diameters, less nodal involvement, better tumor differentiation, more oestrogen and progesterone receptor positive lesions, more hormone therapy, and less chemotherapy. Radiotherapy tended to be more common in screening participants. More frequent use of adjunctive radiotherapy applied when breast conserving surgery was used.

Conclusions   Results confirm the screening effects expected from the scientific literature and demonstrate the value of opportunistic use of available registry and linked screening data for indicating to local health administrations, practitioners, and consumers whether local screening services are having the effects expected.

KEYWORDS

evaluation, health care, public health

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1 | INTRODUCTION

Roll-out of population-based breast cancer screening commenced in Australia in 1991, directed principally at 50- to 69-year-old women until 2013-2014 when this age range was extended to 50-74 years.[1,2] Four separate evaluation studies indicated breast cancer mortality reductions in screening participants in the 34% to 52% range.[3–7] Estimates of overdiagnosis varied widely with jurisdiction and methodology.[8,9]

Less attention has been given in Australia to quantifying screening effects in local operational settings where numbers of deaths are often too small for evaluation purposes. Use of more prevalent prognostic characteristics, patterns of care, and post-diagnostic survivals may be more applicable as performance indicators of screening effect in these settings.

Lead-time effects of screening are well known and post-diagnostic survivals unadjusted for lead time should not be used to evaluate mortality effects of screening.[10,11] However, post-diagnostic survival data are of great interest and relevance to clinicians and patients when considering prognosis.[12] Also, if screening is working as intended, both lead-time effects and actual mortality reductions would be expected to increase measured post-diagnostic survivals,[10,11] which can therefore be used as an indicator of whether local screening services are working as intended.

Prognostic data for early invasive breast cancers reported by surgeons in the BreastSurgANZ QUALITY Audit indicated that BreastScreen referrals had smaller tumor diameters than symptomatic cases (54% ≤15 mm compared with 28%), fewer high-grade cancers (20% compared with 37%), fewer node positive cancers (28% compared with 44%), and a higher proportion of hormone receptor positive tumors (ie, 87% compared with 78% estrogen receptor positive; 73% compared with 66% progesterone receptor positive).[13] Audit data also indicated that the proportion having breast-conserving surgery was higher for BreastScreen referrals (74% compared with 56% for symptomatic referrals).[13] Surgeons reported a higher proportion of referrals of BreastScreen cases for first-round adjuvant treatments by radiotherapy (78% compared with 68%) and hormone treatment by

aromatase inhibitor (49% compared with 37%), but fewer referrals for chemotherapy (37% compared with 55%) and ovarian ablation (1% compared with 3%).

Other studies show similar associations between breast screening and smaller cancer size, negative nodal status, lower tumor grade, hormone receptor positive cancers (estrogen and/or progesterone receptors), non-ductal histology types, surgical treatment by breast conservation, and higher post-diagnostic survivals.[14–22] Opportunity therefore presents to use these characteristics as indicators of screening effect in individual operational settings.

In this study we compare the prognostic profiles, treatments, and post-diagnostic survival outcomes of 2039 invasive female breast cancers diagnosed in 50- to 69-year-olds in 1997-2010 who were treated at 4 major public hospitals in South Australia (1 of 8 Australian states/territories), according to whether cases had participated in BreastScreen and according to duration since last BreastScreen participation.[23,24] The purpose was to determine whether BreastScreen was delivering the outcomes expected in these local operational settings.

Data from these hospitals are not population-based but covered about half the South Australian female breast cancers diagnosed in the principal screening age range of 50-69 years during the study period. The study period of 1997-2010 followed initial roll-out of the BreastScreen program that reached a plateau in population coverage during the mid-1990s. The study therefore investigates effects of a fully developed screening program. Although not population-based, the characteristics of patients at these major hospitals and their screening outcomes are of direct interest to clinicians and patients at these hospitals.[23,24] In addition, the data can be used as performance indicators by health administrations to interpret screening and other local health-system effects.[12,23,24]

We hypothesized, based on BreastSurgANZ Quality Audit data and the international evidence,[13–22] that screen-detected and other recently screened cases in this study would have: (1) higher post-diagnostic survivals; (2) earlier stage characteristics (smaller diameters, less nodal involvement, and lower tumor

node metastasis [TNM] stage), less high-grade histology, and more estrogen and progesterone receptor positive lesions; and (3) more conservative breast surgery, more radiotherapy, and more hormone therapy, but less chemotherapy. If this pattern were found, we decided a priori that these data, alongside the previously reported breast cancer mortality reductions,[3–6] would indicate that breast screening was delivering the outcomes expected in these local operational settings.

Because source data came primarily from hospitals, adjuvant therapies commencing post-discharge would often have been excluded.[24] Emphasis has therefore been placed on assessing comparative rather than absolute exposures to adjuvant treatments according to BreastScreen participation.[24]

2 | METHODS

Operations of the South Australian Clinical Cancer Registry (SACCR) have been described previously in SA Cancer Registry reports.[25] Ethical approval for the study was provided by the South Australian Human Research Ethics Committee. The SACCR is authorized under Section 64D of the South Australian Health Care Act (2008) to support quality assurance of service activity.[26] Patient consent is not legally required to use the data for quality assurance or research, so long as reported data are non-identifiable.[26]

Data linkage of extracted SACCR and BreastScreen South Australia data was used to identify histories of BreastScreen participation among women aged 50-69 years at invasive breast cancer diagnosis.[24] This was classified as no participation or participation last occurring <6 months, 6-24 months, or 25+ months prior to breast cancer diagnosis. Probabilistic data linkage was used based on full names and dates of birth as linking variables, with additional guidance from residential address, with a false positive rate of about 3 per 1000.[24]

Postcode of residence was used to indicate socioeconomic quartile, using the SEIFA Index of Relative Socioeconomic Disadvantage; geographic remoteness (classified as metropolitan, regional, and remote); and locality by Local Health Network (central, southern, northern, and country) and former Medicare Local of residence (northern, central, southern, country south, and country north).[27,28] The term "country" referred to areas outside the metropolitan capital of South Australia, which have poorer access to tertiary services and which were subclassified by Medicare Local area (as south or north) according to official government boundaries.[28] These variables were chosen to investigate and adjust for the sociodemographic impact of screening.

Person characteristics were analyzed, depending on their distribution, as age at diagnosis (four 5-year ordinal categories); SEIFA socioeconomic disadvantage (4 ordinal categories), geographic remoteness (3 ordinal categories), Local Health Network (4 nominal categories), and Medicare Local (5 nominal categories). Tumor characteristics, including histology, TNM (UICC 7th

Revision) stage, diameter, nodal status, differentiation, and estrogen and progesterone receptor status were classified as shown in Table 1.[24,25]

Primary site was coded according to the International Classification of Disease (version 3) (ICD-O-3), or corresponding ICD-9 codes for earlier years, and histology type using ICD-O-3 or Systematized Nomenclature of Medicine II codes for earlier years.[24,25] Tumor diameters, nodal status, and hormone receptor status were extracted from pathology reports.[24,25] First-round treatments were recorded as including surgery—specifying type as mastectomy or breast-conserving surgery—and according to whether radiotherapy and/or systemic therapies were provided.

Death data were extracted from the South Australian population-based cancer registry, which used official death files, and for deaths occurring outside of South Australia, the National Death Index at the Australian Institute of Health and Welfare as data sources, although correcting underlying causes-of-death when clinical data available to the registry indicated this to be appropriate.[24,25] The extent of loss to follow-up of deaths has been checked through active tracing and found to be minimal and to have little effect on calculated survivals.[25,29]

Disease-specific survivals were calculated using Kaplan-Meier product limit estimates, with censoring of live cases on December 31, 2012.[30,31] This method was preferred to relative survival because risks of deaths from competing causes could not be assumed to be equivalent to population norms (an underlying assumption for relative survival) because of the referral of high-risk cases (including those with high levels of comorbidity) to the referral centers covered by the SACCR.[25]

Population-based data show disease-specific survival, based on South Australian registry coding, to be a good proxy for relative survival for female breast cancer. For example, a 1977-2003 study gave cohort relative survivals of 80% at 5 years and 69% at 10 years following diagnosis that were virtually identical to corresponding disease-specific survivals of 80% and 70%, respectively.[32] This validation is important as cause-specific survivals are known to be vulnerable to variations in cause-of-death coding.[33]

Cox proportional hazards regression analyses were used to examine differences in disease-specific survival by BreastScreen participation, and person and tumor characteristic. This was undertaken both for single predictors and in multivariable analyses, using the same follow-up period and censoring rules as for the Kaplan-Meier analyses.[30,31] Two sets of multivariable analyses were performed, the first incorporating TNM stage and the second, tumor diameter and nodal status instead of TNM stage. As results were very similar, only outputs from models using TNM stage are presented in this report.

Assumptions underlying the Cox regression analyses, including proportionality and lack of colinearity, were tested and found to be met. When competing risk regression was substituted for disease-specific Cox proportional hazards regression, similar results applied (data not shown).[30,31]

First-round treatments were analyzed by BreastScreen exposure, person, and tumor characteristic using the Pearson chi-square

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TABLE 1 Female breast cancer characteristics by duration from last breast screen to time of diagnosis, 1997-2010—recorded by major public hospitals in South Australia[a]

Characteristic	No Past Screen (%) (n = 635)	Duration <6 mo (%) (n = 977)	Duration 6-24 mo (%) (n = 255)	Duration 25+ mo (%) (n = 172)	P Value
Histology:					
Ductal	81.7 (n = 519)	76.3 (n = 745)	74.1 (n = 189)	78.5 (n = 135)	X^2
Lobular	8.7 (n = 55)	11.8 (n = 115)	14.1 (n = 36)	14.0 (n = 24)	(df = 6)
Other	9.6 (n = 61)	12.0 (n = 117)	11.8 (n = 30)	7.6 (n = 13)	P = .044
Total	100 (n = 635)	100 (n = 977)	100 (n = 255)	100 (n = 172)	
TNM stage:[b]					
I	31.3 (n = 190)	62.2 (n = 599)	32.9 (n = 82)	32.1 (n = 54)	KWp < 0.001
IIA	28.8 (n = 175)	24.5 (n = 236)	33.7 (n = 84)	25.6% (n = 43)	
IIB/IIUK	20.1 (n = 122)	8.9 (n = 86)	18.5 (n = 46)	24.4 (n = 41)	
IIIA	5.3 (n = 32)	2.2 (n = 21)	7.6 (n = 19)	6.0 (n = 10)	
IIIB/IIIUK	3.1 (n = 19)	0.4 (n = 4)	2.4 (n = 6)	1.8 (n = 3)	
IV	11.4 (n = 69)	1.8 (n = 17)	4.8 (n = 12)	10.1 (n = 17)	
Total	100 (n = 607)	100 (n = 963)	100 (n = 249)	100 (n = 168)	
Diameter (mm):[b]					
<10	11.6 (n = 67)	26.1 (n = 246)	16.4 (n = 39)	11.5 (n = 18)	KWp < 0.001
10-14	14.8 (n = 86)	28.2 (n = 266)	13.0 (n = 31)	12.8 (n = 20)	
15-19	16.4 (n = 95)	18.1 (n = 171)	16.0 (n = 38)	13.5 (n = 21)	
20-29	22.6 (n = 131)	16.8 (n = 158)	30.7 (n = 73)	35.3 (n = 55)	
30-39	15.2 (n = 88)	5.5 (n = 52)	10.1 (n = 24)	11.5 (n = 18)	
40+	19.5 (n = 113)	5.3 (n = 50)	13.9 (n = 33)	15.4 (n = 24)	
Total	100 (n = 580)	100 (n = 943)	100 (n = 238)	100 (n = 156)	
Nodal status:[b]					
Negative	46.4 (n = 286)	71.0 (n = 685)	44.6 (n = 112)	45.6 (n = 77)	X^2
Positive	53.6 (n = 330)	29.0 (n = 280)	55.4 (n = 139	54.4 (n = 92)	(df = 3)
Total	100 (n = 616)	100 (n = 965)	100 (n = 251)	100 (n = 169)	P < .001
Differentiation:[b]					
Well	21.6 (n = 125)	40.8 (n = 376)	20.5 (n = 49)	22.5 (n = 36)	KWp = 0.001
Moderate	40.0 (n = 231)	42.4 (n = 391)	39.7 (n = 95)	41.3 (n = 66)	
Poor/undifferentiated	38.4 (n = 222)	16.8 (n = 155)	39.7 (n = 95)	36.3 (n = 58)	
Total	100 (n = 578)	100 (n = 922)	100 (n = 239)	100 (n = 160)	
Estrogen receptor:					
Negative	24.9 (n = 158)	14.1 (n = 138)	27.8 (n = 71)	20.3 (n = 35)	X^2
Positive	75.1 (n = 477)	85.9 (n = 839)	72.2 (n = 184)	79.7 (n = 137)	(df = 3)
Total	100 (n = 635)	100 (n = 977)	100 (n = 255)	100 (n = 172)	P < .001
Progesterone receptor:					
Negative	27.2 (n = 173)	18.3 (n = 179)	30.6 (n = 78)	23.3 (n = 40)	X^2
Positive	72.8 (n = 462)	81.7 (n = 798)	69.4 (n = 177)	76.7 (n = 132)	(df = 3)
Total	100 (n = 635)	100 (n = 977)	100 (n = 255)	100 (n = 172)	P < .001

TNM, tumor node metastasis.

[a]Data from South Australian Clinical Cancer Registry (see text).

[b]Missing values—all cases: TNM (n = 52), diameter (n = 122), nodal status (n = 38), differentiation (n = 140).

- No past screen: TNM (n = 28), diameter (n = 55), nodal status (n = 19), differentiation (n = 57).

- Duration <6 mo: TNM (n = 14), diameter (n = 34), nodal status (n = 12), differentiation (n = 55).

- Duration 6 to 24 mo: TNM (n = 6), diameter (n = 17), nodal status (n = 4), differentiation (n = 16).

- Duration 25+ mo: TNM (n = 4), diameter (n = 16), nodal status (n = 3), differentiation (n = 12).

or Kruskal-Wallis analysis of variance, depending on whether variables were distributed on binary, nominal, or ordinal scales.[30,31] Univariate and multiple logistic regression analyses were also used.[30,31] Multivariable analyses were undertaken to check for confounding, effect modification, and clustering by treatment center, but did not show statistically significant effects, and so the data presented here are from conventional analyses unadjusted for such effects.[30]

3 | RESULTS

3.1 | Descriptive characteristics

Residential remoteness, socioeconomic status, Local Health Network, and Medicare Local did not differ by BreastScreen participation in bivariable analyses (P values ≥ .077). Age did vary (P < .001), with BreastScreen participants more likely to be aged 60+ years (56.5% vs 45.2%). The proportion aged 60+ years was also higher among BreastScreen participants with the shortest duration since last screen (ie, 58.3% for <6 months vs 52.2% for 6+ months) (P = .033).

Table 1 shows differences by BreastScreen participation/duration since last screen, according to: (1) histology type (P = .044)—participants having more lobular and other non-ductal cancers; (2) TNM stage (P < .001)—participants having earlier stages; (3) diameters (P < .001)—participants having smaller cancers; (4) nodal status (P < .001)—fewer participants having positive nodes; (5) differentiation (P = .001)—participants having better differentiated lesions; and (6) estrogen receptor status (P < .001) and progesterone receptor status (P < .001)—participants more likely to have a positive estrogen and progesterone receptor status. Apart from histology type (P = .334), BreastScreen participants last screened within 6 months were more likely to show these features than participants screened less recently (P < .001 for each characteristic).

3.2 | Survivals

Five-year survivals were highest at 95.7% for BreastScreen participants last screened within 6 months of diagnosis and lowest at 84.3% for those without a BreastScreen history (Table 2). Ten-year survivals showed a similar pattern (Table 2). Similarly, unadjusted hazards ratios (HRs) were lowest for those last screened within 6 months (HR 0.30, 95% confidence limits: 0.22, 0.41) when compared with the never screened. A reduced unadjusted HR also applied for those last screened within 6-24 months of diagnosis (HR 0.67 (0.46, 0.97)), but there was little evidence of a reduction for those screened 25 or more months before diagnosis (Table 2). Overall, BreastScreen participants had a reduced unadjusted HR of 0.43 (0.34, 0.55).

Unadjusted HRs were higher for more advanced TNM stages (P < .001) (and larger cancers [P < .001] and node positive cases [P < .001]), more poorly differentiated tumors (P < .001), and estrogen receptor negative (P < .001) and progesterone receptor negative (P < .001) tumors. Outcomes also varied by histology type (P = .005), with lower HRs suggested for non-ductal cancers. By comparison, little evidence of survival differences presented by age at diagnosis or residential location classified by socioeconomic status, remoteness, or local health service administration (Local Health Network/Medicare Local), or diagnostic period.

After adjusting for these variables, reductions in HRs for BreastScreen participants were no longer statistically significant (P ≥ .116) (Table 2).

3.3 | Treatments

Surgery—Breast surgery treatment was recorded for 93.5% of breast cancers and surgery type for 90.5% of these cases. The percentage having breast-conserving surgery (as opposed to a mastectomy) was

TABLE 2 Disease-specific survivals from female breast cancer, diagnosed in 1997-2010, by duration from last breast screen to time of diagnosis—major public hospitals in South Australia[a]

Duration From Last Breast Screen	Survival % 1-year	Survival % 2-year	Survival % 5-year	Survival % 10-year	Hazards Ratio (Unadjusted)	Hazards Ratio (Adjusted[b])
No past screen (n = 635)	95.8	92.1	84.3	78.0	1.00	1.00
Duration <6 m (n = 977)	99.6	98.7	95.7	92.1	0.30 (0.22, 0.41)	0.77 (0.56, 1.07)
Duration 6-24 m (n = 255)	98.4	95.3	89.2	84.6	0.67 (0.46, 0.97)	0.82 (0.55, 1.21)
Duration 25+ m (n = 172)	95.4	92.4	86.3	81.5	0.87 (0.58, 1.31)	0.90 (0.59, 1.37)
Any duration (n = 1404)	98.9	97.3	93.4	89.5	0.43 (0.34, 0.55)	0.81 (0.63, 1.05)

[a]Kaplan-Meier disease-specific survival; Cox proportional hazards ratios (95% confidence limits); date of censoring of live cases—December 31, 2012.

[b]Adjusted for histology type, grade, TNM stage, estrogen receptor status, progesterone receptor status, diagnostic year, age at diagnosis, and residential socioeconomic status, remoteness, Local Health Network, and Medicare Local (see text).

TABLE 3 Percentage of female breast cancer surgical cases diagnosed in 1997-2010 who were treated by BCS rather than mastectomy, by duration from last breast screen to time of diagnosis—recorded by major public hospitals in South Australia[a]

Duration From Last Breast Screen	% Having BCS	Odds Ratio—BCS vs Mastectomy (Unadjusted)	Odds Ratio—BCS vs Mastectomy (Adjusted[b])
No past screen (n = 573)	64.2	1.00	1.00
Duration <6 mo (n = 888)	78.6	2.05 (1.62, 2.59)	1.47 (1.13, 1.91)
Duration 6-24 mo (n = 228)	71.1	1.37 (0.98, 1.91)	1.54 (1.07, 2.21)
Duration 25+ mo (n = 157)	67.5	1.16 (0.80, 1.68)	1.21 (0.81, 1.82)
Any duration screen (n = 1273)	75.9	1.76 (1.48, 2.08)	1.44 (1.13, 1.82)

BCS, breast-conserving surgery.

[a]Logistic regression (see text); odds ratios (95% confidence limits).

[b]Multiple logistic regression, adjusted for histology type, grade, TNM stage, estrogen receptor status, progesterone receptor status, diagnostic year, age at diagnosis, and residential socioeconomic status, remoteness, Local Health Network, and Medicare Local (see text).

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TABLE 4 Percentage of female breast cancer cases diagnosed in 1997-2010 who were treated by radiotherapy and/or systemic therapies as part of first-round care, by duration from last breast screen to time of diagnosis—recorded by major public hospitals in South Australia[a]

Duration From Last Breast Screen	% Having Radio and/or Systemic Therapy	Odds Ratio— Radio and/or Systemic Therapy Yes vs No (Unadjusted)	Odds Ratio— Radio and/or Systemic Therapy Yes vs No (Adjusted[b])	% Having Radiotherapy	Odds Ratio— Radiotherapy Yes vs No (Unadjusted)	Odds Ratio— Radiotherapy Yes vs No (Adjusted[b])
No past screen (n = 622)	89.2	1.00	1.00	70.7	1.00	1.00
Duration <6 mo (n = 964)	87.7	0.86 (0.62, 1.20)	1.13 (0.81, 1.59)	73.8	1.16 (0.92, 1.46)	1.16 (0.91, 1.48)
Duration 6-24 mo (n = 249)	82.7	0.58 (0.37, 0.89)	1.50 (0.89, 2.53)	79.1	1.56 (1.08, 2.24)	1.54 (1.08, 2.21)
Duration 25+ mo (n = 168)	91.1	1.24 (0.67, 2.33)	1.09 (0.62, 1.93)	72.0	1.07 (0.72, 1.59)	1.04 (0.71, 1.53)
Any duration (n = 1381)	87.2	0.82 (0.60, 1.12)	1.19 (0.87, 1.62)	74.5	1.21 (0.97, 1.50)	1.21 (0.97, 1.51)

(Continues)

highest at 78.6% for those screened within 6 months of diagnosis and lowest at 64.2% for those never screened (Table 3). Compared with those never screened, logistic regression gave the highest unadjusted odds ratio (OR with 95% confidence limits) for breast-conserving surgery of 2.05 (1.62, 2.59) for those screened within 6 months and 1.76 (1.48, 2.08) for those ever screened (irrespective of duration between screening and diagnosis).

Unadjusted ORs for breast-conserving surgery were lower for higher stages (P < .001) (including larger tumors [P < .001] and node positive cases [P < .001]), poorer differentiated cancers (P < .001), and lobular histology (P < .001), and higher for more recent diagnostic years (P = .019). Variations also applied by residential Local Health Network (P = .001) and Medicare Local (P = .008), with lower odds of breast-conserving surgery tending to apply in central localities. Little variation in surgery type was suggested by age at diagnosis, estrogen and progesterone receptor status, and residential location classified by socioeconomic status or remoteness.

After adjusting for these tumor and demographic variables, ORs for breast-conserving surgery were still elevated at 1.47 (1.13, 1.91) for those screened within 6 months and 1.44 (1.13, 1.82) for those ever screened (Table 3). An elevated adjusted OR of 1.54 (1.07, 2.21) also was suggested for cases who had been screened within 6-24 months of diagnosis compared with those never screened.

Radiotherapy and/or systemic therapy—Details of these therapies were recorded for 98.2% of breast cases, with 87.8% of them recording 1 or more therapies. Little variation was suggested by BreastScreen exposure and duration since last screen in unadjusted analysis, except that use of ≥1 of these therapies tended to be lower in cases last screened within 6-24 months of diagnosis when compared with those without a past screen (OR of 0.58 (0.37, 0.89)) (Table 4). Similarly, little variation was suggested in adjusted analyses (Table 4)—even though unadjusted ORs for 1 or more of these therapies were elevated for more advanced TNM (P < .001) (including for larger cancers [P < .001] and node positive cases [P < .001]) and poorer differentiation (P = .036). The odds of radiotherapy and/or systemic therapy were lower, but not significantly so, in unadjusted analyses of cases who had obtained breast-conserving surgery rather than a mastectomy—an OR of 0.78 (0.57, 1.07).

Radiotherapy—Of cases with radiotherapy details available, 73.3% received this treatment. The percentage was highest at 79.1% for those last screened within 6-24 months of diagnosis and lowest at 70.7% for those never screened. Compared with those never screened, the unadjusted OR for radiotherapy was 1.56 (1.08, 2.24) for those screened within 6-24 months of diagnosis (Table 4).

Unadjusted ORs logistic regression indicated a difference in radiotherapy by age (P = .048), with a relatively low radiotherapy exposure for 65- to 69-year-olds. Little difference was evident by other demographic and cancer characteristics or diagnostic epoch.

After adjusting for tumor and demographic variables, the OR for radiotherapy among those screened within 6-24 months remained elevated at 1.54 (1.08, 2.21) when compared with the never screened (Table 4). In a separate unadjusted analysis, the odds of radiotherapy were higher among cases who obtained breast-conserving surgery than among mastectomy cases—an OR of 2.86 (2.29, 3.58).

Chemotherapy—Of cases with chemotherapy details available, 32.7% received this treatment. The percentage was lowest at 19.4% for those last screened within 6 months of diagnosis and highest at 53.0% for those last screened 6-24 months earlier (Table 4). Compared with those never screened, unadjusted OR for chemotherapy was lowest at 0.32 (0.26, 0.40) for those last screened within 6 months. This compared with 1.45 (1.08, 1.94) for those last screened within 6-24 months, and 0.51 (0.42, 0.62) for those ever screened, irrespective of duration before diagnosis.

Unadjusted ORs for chemotherapy were lower for older groups (P < .001), less advanced TNM stage (P < .001) (including smaller cancers [P < .001] and node negative tumors [P < .001]), better differentiation (P < .001), non-ductal cancers (P < .001), and estrogen receptor positive (P < .001) and progesterone positive (P = .003) tumors. Higher odds of chemotherapy were suggested for residents of the Central Local Health Network (P = .023) and Central Medicare Local (P = .032). Chemotherapy was more likely in the 2004-2010 than 1997-2003 diagnostic epoch (P = .046). Little variation applied by residential socioeconomic status and remoteness.

After adjusting for tumor and demographic variables, and compared with those never screened, the OR for chemotherapy among those last screened within 6-24 months remained elevated at 1.78 (1.21, 2.61)

TABLE 4 (continued)

Duration From Last Breast Screen	% Having Chemotherapy	Odds Ratio—Chemotherapy Yes vs No (Unadjusted)	Odds Ratio—Chemotherapy Yes vs No (Adjusted[b])	% Having Hormone Therapy	Odds Ratio—Hormone Therapy Yes vs No (Unadjusted)	Odds Ratio—Hormone Therapy Yes vs No (Adjusted[b])
No past screen (n = 622)	43.4	1.00	1.00	49.2	1.00	1.00
Duration <6 mo (n = 964)	19.4	0.32 (0.26, 0.40)	0.81 (0.60, 1.09)	54.5	1.24 (1.02, 1.53)	1.09 (0.87, 1.38)
Duration 6-24 mo (n = 249)	53.0	1.45 (1.08, 1.94)	1.78 (1.21, 2.61)	42.6	0.76 (0.57, 1.03)	0.79 (0.57, 1.09)
Duration 25+ mo (n = 168)	38.7	0.82 (0.58, 1.16)	0.73 (0.46, 1.15)	49.4	1.00 (0.72, 1.40)	0.90 (0.62, 1.30)
Any duration (n = 1381)	27.8	0.51 (0.42, 0.62)	0.97 (0.75, 1.26)	51.7	1.11 (0.92, 1.34)	0.99 (0.80, 1.23)

[a]Logistic regression (see text); odds ratios (95% confidence limits).

[b]Multiple logistic regression, adjusted for histology type, grade, TNM stage, estrogen receptor status, progesterone receptor status, diagnostic year, age at diagnosis, and residential socioeconomic status, remoteness, Local Health Network, and Medicare Local (see text).

(Table 4). In an unadjusted analysis, chemotherapy was found to be less common among cases treated by breast conservative surgery than mastectomy irrespective of screening history—an OR of 0.39 (0.32, 0.49). *Hormone therapy*—Of women with hormone therapy data available, 50.9% were recorded to have received this treatment. The percentage was highest at 54.5% when screening was undertaken within 6 months of diagnosis (Table 4). Compared with those never screened, the unadjusted OR for hormone therapy was 1.24 (1.02, 1.53) for these recently screened women.

Unadjusted logistic ORs for hormone therapy varied by age (P = .038) (tending to be higher for 65- to 69-year-olds) and were higher for lobular lesions (P = .005), better differentiated lesions (P < .001), and estrogen receptor positive (P < .001) and progesterone receptor positive lesions (P < .001). There was also a variation by residential Local Health Network (P < .001) and Medicare Local (P < .001), with higher ORs tending to apply for central than other localities. Little variation in ORs was evident by residential socioeconomic status, remoteness or tumor stage, size, nodal status, or diagnostic epoch.

After adjusting for tumor and demographic variables, little variation in ORs of hormone therapy was observed by screening history (Table 4). An unadjusted analysis indicated that hormone therapy was less common among cases treated by breast conservative surgery than mastectomy, irrespective of screening history—an OR of 0.65 (0.52, 0.80).

4 | DISCUSSION

We have been opportunistic in using readily available clinical registry and linked screening data to evaluate local screening effects. Results confirm a priori hypotheses, in that women screened within 6 months of diagnosis had a 10-year survival from breast cancer of 92% compared with 78% for unscreened women.[10] Of surgical cases diagnosed within 6 months of screening, 79% had breast-conserving surgery, which was significantly higher than the 64% having breast-conserving surgery among unscreened women.

Our unadjusted results are consistent with previous study results, indicating that recently screened cases had higher post-diagnostic survivals, earlier TNM stage, smaller diameters, less nodal involvement, better tumor differentiation, more estrogen and progesterone receptor positive lesions, more breast-conserving surgery, and more hormone therapy, but less chemotherapy.[13-23]

It is likely that adjusted analyses did not show the differences in survivals, chemotherapy, and hormone therapy seen in unadjusted analyses, largely because of adjustment for the means whereby screening was having an effect (eg, through achieving earlier stages, smaller tumors, and fewer node positive tumors). By comparison, the retention in adjusted analyses of evidence for greater use of adjuvant radiotherapy among screened cases, particularly those last screened within 6-24 months of last diagnosis, may reflect greater use of breast-conserving surgery in these cases and recommendations that adjuvant radiotherapy be given for cases so treated.[34]

The higher odds of chemotherapy 6-24 months post screen were unexpected and warrant further investigation. Although alternative explanations may apply, potentially it could reflect the timing of interval cancers with aggressive characteristics or the progression of some cases diagnosed earlier through screening who did not respond to early care.

While increased breast-conserving therapy would generally be regarded as a screening benefit for improved body image and psychological outcomes, any side effects from exposure to radiotherapy would need to be considered (eg, potential for cardio-toxicity from radiation to the left breast).[35] By comparison, mastectomy cases were more likely to receive chemotherapies and hormone therapies. To the extent that these systemic therapies can have adverse effects—fatigue, nausea, weight loss, mucositis, immunosuppression, and cardio-toxicities—the reduced need for these therapies in screened cases would be regarded as a positive screening effect.[36]

The present results are consistent with international and earlier Australian evidence of screening effects on prognosis, treatment, and post-diagnostic survivals rather than providing new scientific insights.[11-22,37] Their importance is demonstrating the feasibility of

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using local clinical registry and linked screening data to produce indicators of screening effects of local services along the diagnostic, treatment, and post-diagnostic pathway. This was so in this study despite inconsistencies in data completeness, as in the tendency for higher completeness of data for screened than unscreened cases (eg, completeness of 98.3% compared with 95.6% for TNM; 95.2% compared with 91.3% for diameter; and 98.7% compared 97.0% for nodal status).

These results also add value by complementing Australian evidence of mortality reductions from screening by indicating expected screening effects in local operational settings.[3–6] This is important evidence for local health service evaluation.

Other results also have policy implications, such as little or no evidence of benefit from screening less frequently than biennially, and evidence of differences in care patterns by screening history. These results could be used in cost-effectiveness research.

A broader network of clinical registries would be desirable to broaden the evidence base across other localities. The reach of the network could also be extended through linkage to population-based cancer registries that collect TNM stage and other prognostic markers (note: as facilitated by greater use of structured pathology reporting), and linkage to treatment data (note: as extracted from hospital inpatient files, radiotherapy records, and health insurance claims), and to BreastScreen data.[38] This would enable evaluation to be broadened from a health institution to population-based focus.

Uncertainties are commonly expressed about the quality of administrative data from hospitals and other service agencies for service evaluation.[38,39] Data quality audits are needed to ensure data are fit-for-purpose. Comparisons of findings from administrative data with overlapping data from clinical registries, clinical audits, and case-note reviews can be useful for this purpose. Even with limited attention to data quality improvement, it is noteworthy that hospital inpatient and other administrative data have shown high face-value validity in a number of studies.[39]

The roles of specialized clinical registries and linked administrative data should be complementary. Clinical registries can provide "drill-down" data of high quality that are designed to meet the clinical monitoring and research needs of their catchment institutions, whereas linked administrative data can provide system-wide data (albeit thinner) for gaining a broader population-wide perspective.[38,39]

Australia now has well-defined data linkage protocols for producing non-identifiable databases for service monitoring and research.[38–40] Most jurisdictions, including the Commonwealth, have access to data linkage facilities, and legal and ethically approved pathways exist for data linkage. With recent increases in data access, opportunities have increased to include health insurance claims data (Medical Benefits and Pharmaceutical Benefits data) in non-identifiable linked databases and for these data to be analyzed using remote access for increased privacy protection.[38] This will greatly increase the completeness and potential value of linked data sets for monitoring and assessing patterns of care across operational settings, while minimizing risk to privacy.

Cancer Australia is promoting the recording of TNM stage and other prognostic characteristics on population registries.[40] This would be greatly facilitated by increased use of structured pathology reporting developed through the Royal College of Pathologists of Australasia,[41] especially if parallel development of electronic transmission of these data as discrete data fields can occur, facilitating automated entry into cancer registry systems.

5 | CONCLUSIONS

- Clinical registry data indicate that breast screening in South Australia has delivered expected changes in prognosis, treatment patterns, and survival in patients attending 4 public hospitals. This complements the evidence of mortality effects at a broader population level.

- Greater use should be made of networks of clinical registries to evaluate whether screening programs are having expected effects in local settings. Complementary data from population-based registries that record stage, linked to population-wide administrative data on cancer detection and treatment, should also be used for this purpose.

- While lacking the clinical detail available in clinical registries, and requiring prior data quality checks to ensure "fitness for purpose," linked administrative data have the advantage of providing population-wide evidence of local service performance.

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