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ORIGINAL ARTICLE

Female breast cancer treatment and survival in South Australia: Results from linked health data

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Abstract

Objective: We investigated treatment and survival by clinical and sociodemographic characteristics for service evaluation using linked data.

Method: Data on invasive female breast cancers (n = 13,494) from the South Australian Cancer Registry (2000–2014 diagnoses) were linked to hospital inpatient, radiotherapy and universal health insurance data. Treatments ≤12 months from diagnosis and survival were analysed, using adjusted odds ratios (aORs) from logistic regression, and adjusted sub-hazard ratios (aSHRs) from competing risk regression.

Results and conclusion: Five-year disease-specific survival increased to 91% for 2010–2014. Most women had breast surgery (90%), systemic therapy (72%) and radiotherapy (60%). Less treatment applied for ages 80+ vs <50 years (aOR 0.10, 95% CI 0.05–0.20) and TNM stage IV vs stage I (aOR 0.13, 95% CI 0.08–0.22). Surgical treatment increased during the study period and strongly predicted higher survival. Compared with no surgery, aSHRs were 0.31 (95% CI 0.26–0.36) for women having breast-conserving surgery, 0.49 (95% CI 0.41–0.57) for mastectomy and 0.42 (95% CI 0.33–0.52) when both surgery types were received. Patients aged 80+ years had

lower survival and less treatment. More trial evidence is needed to optimise trade-offs between benefits and harms in these older women. Survival differences were not found by residential remoteness and were marginal by socioeconomic status.

KEYWORDS
breast cancer, differences, South Australia, survival, treatment

1 | INTRODUCTION

Breast cancer is the most common cancer recorded in Australian females by population-based registries (Australian Institute of Health and Welfare, 2019). A decrease in age-standardised mortality from female breast cancer of approximately 38% has been reported between 1982 and 2019, along with an increase in breast cancer survival, attributed mostly to treatment advances and earlier detection from population screening (Australia Government and Department of Health, 2014; Australian Institute of Health and Welfare, 2019;).

Australian and international studies show females with early-stage breast cancer to have the highest survival (Li, Roder, et al., 2020; Walters et al., 2013). Increasing early detection through screening of more women at high risk likely would increase survival further (Li, Warner-Smith, et al., 2020).

Breast cancer treatment has changed in recent decades in line with better understanding of disease biology, pharmacological discoveries and advances in clinical practice (Hortobagyi, 2020; Waks & Winer, 2019). Treatment generally includes surgery, and, where appropriate, adjuvant radiotherapy and systemic therapy (Cancer Australia, 2000, 2001). Breast-conserving surgery is now more common than mastectomy, and systemic therapies have broadened beyond chemotherapy to include hormone and targeted therapies and immunotherapy (Cancer Australia, 2000, 2001).

Apart from clinical factors, such as cancer stage, histology, differentiation, hormone receptor status and general health status, treatment and outcomes can vary with age at diagnosis, cultural background, socioeconomic status and residential remoteness. Breast cancer treatment and survival have been investigated in South Australia using registry data from several public hospitals (Roder et al., 2017), but corresponding population-wide investigations have not been possible with registry data alone due to gaps in treatment data.

Health services seek data to assess trends in treatment and survival, and to evaluate effects of changes in policy, practice and resource allocation. This is so in South Australia, one of eight states and territories of Australia, which has a population of 1.76 million covering a vast area of 984,482 km^2 of whom 76% live in the state capital.

The present study investigates population-wide differences and trends in breast cancer care and outcomes using linked cancer registry, hospital inpatient, radiotherapy and universal medical and pharmaceutical health insurance data for breast cancers diagnosed in South Australia in 2000–2014.

2 | METHODS

2.1 | Data sources and linkage

Invasive female breast cancer data (ICD-O-3, C50) from the South Australian Cancer Registry (SACR) comprised the main linkage spine. SACR uses international registry standards with legally mandated reporting from pathology laboratories and hospitals (Esteban et al., 1995; South Australian Cancer Registry: Epidemiology Branch, 2000). The SACR is population-based, recording primary cancer site, histology, diagnosis date, and person's age, country of birth, postcode-derived relative socioeconomic disadvantage and geographic remoteness, plus radiotherapy notifications (South Australian Cancer Registry: Epidemiology Branch, 2000). The Registry of Births, Deaths and Marriages and Australia-wide National Death Index is used to obtain death dates and causes, classified by cancer type or as non-cancer (South Australian Cancer Registry: Epidemiology Branch, 2000).

Treatment data mostly were extracted from hospital inpatient databases, radiotherapy centres and universal health insurance claims (i.e. claims under the Medical Benefits Schedule [MBS] and Pharmaceutical Benefits Scheme [PBS]). Hospital inpatient data included dates of admission and clinical procedure codes, whereas radiotherapy centre data included dates of all treatments.

Collectively, data from these sources covered most treatment. MBS and PBS subsidise privately funded hospital and community treatments and costs of drugs (Australian Government, Department of Health, 2020a, 2020b).

Linkage of SACR and hospital data was undertaken by SANT Data Link, with 97% deterministic matching to a Master linkage file derived from 60 data sources, and with subsequent probabilistic matching (using name, sex, date of birth and address) and clerical review of uncertain matches (Australian Government, National Statistical Service, 2017). This followed the principle of separating patient identifiers from clinical content data to protect privacy (Australian Government, National Statistical Service, 2017). Data linkage between these data and MBS and PBS benefits claims was undertaken through the AIHW, also using the principle of separation to protect privacy.

2.2 | Cancer treatment

Treatment in the first 12 months from diagnosis was investigated according to whether any was recorded, that is any surgery

(mastectomy, breast-conserving surgery or both), radiotherapy or systemic therapy. Systemic therapies comprised chemotherapy, hormonal drugs, targeted and immunotherapies. Data for a subset of systemic therapies reimbursed through the PBS were also available to identify hormonal treatments. Data sources included: for surgery—inpatient databases; for radiotherapy—inpatient +radiotherapy + SACR + MBS; and for systemic therapy—inpatient + PBS + MBS. Codes used for treatment types were those included in the 10th Revision of the Australian Classification of Health Interventions and MBS and PBS coding systems (Australian Government, Department of Health, 2020a, 2020b; National Centre for Classification in Health, 2010).

2.3 | Other descriptors

Age at diagnosis was classified as: <50, 50–59, 60–69, 70–79 or 80+ years. To compare outcomes by cultural background, country of birth was classified as Australia, other mainly English-speaking or non-English-speaking country, as described previously (Australian Bureau of Statistics, 2008). Socioeconomic status was derived from residential postcode at diagnosis using the Socioeconomic Index for Areas Index of Relative Socio-economic Disadvantage expressed in quintiles (Australian Bureau of Statistics, 2019). Residential area was classified as a major city area, inner regional, outer regional, remote or very remote area, using the Australian Standard Geographical Classification Remoteness index (Australian Bureau of Statistics, 2006).

Cancer descriptors included stage, histology, differentiation, and for subsets, oestrogen receptor status and human epidermal growth factor receptor 2 (HER2) status. Stage was derived from pathology laboratory, hospital and clinical reporting and broadly classified for study purposes as TNM stage I, II, III or IV (Walters et al., 2013). Cancer differentiation was categorised as low, intermediate or high, histology as ductal, lobular or other (not ductal or lobular), and oestrogen receptor status as negative or positive. Charlson Comorbidity Index scores were derived from inpatient data for the 2000–2014 study period, classified as 0 to 3+ (Quan et al., 2005). Comorbidities included disease groups which appeared unlikely to have been treatment side effects arising during or soon after treatment, that is diabetes mellitus ± complications, dementia, pulmonary diseases, acute myocardial infarction, congestive heart failure, connective tissue diseases, peptic ulcer, liver diseases, paraplegia, renal diseases, other cancers, severe liver disease and HIV (Quan et al., 2005).

2.4 | Statistical analysis

Breast cancer treatment was compared by sociodemographic and cancer characteristic using the conventional chi-square or non-parametric ranked test depending on variable distribution. Logistic regression was used to model treatment after adjusting for differences in sociodemographic variables, year of diagnosis, TNM stage, differentiation, histology and comorbidity status (Stata 14; StataCorp).

Deaths were coded as due to breast cancer, another cancer or another cause, and predictors of survival from breast cancer were analysed for follow-up periods to death or 31 December 2014, whichever came first. Cancer-specific survival at 1, 5 and 10 years from diagnosis was estimated using the Kaplan–Meier product-limit estimator.

Predictors of breast cancer death were investigated using multivariate competing risk regression (Stata module 'stcrreg'), adjusting for sociodemographic characteristics, TNM stage, cancer histology, differentiation and cancer diagnosis year. Deaths from causes other than cancer were regarded as the competing risk. Proportionality assumptions were tested by plotting the log-cumulative hazard against log-time and found to be met.

All analyses were conducted using Stata 14 (StataCorp), with the statistical significance level set as $p < 0.05$. Analyses were based on complete case data. Diagnostic period was treated as an adjustment variable rather than a primary variable for radiotherapy and systemic therapy, due to changes in funding arrangements which altered methods of data collection.

3 | RESULTS

3.1 | Patient profile

Overall, 21% of patients were aged <50 years and 10% were 80+ years at diagnosis; 70% were born in Australia and 13% in mainly non-English-speaking countries; and 74% lived in a major city area and 17% in the most disadvantaged and 23% in the least disadvantaged area quintiles (Table 1).

3.2 | Cancer profile

Excluding missing values, 79% of cancers were ductal and 10% lobular; 33% had low differentiation (high grade) and 23% high differentiation; and the TNM stage distribution was 45% Stage I, 40% stage II, 11% stage III and 4% stage IV. Seven per cent had a Charlson Comorbidity Index score ≥1 (Table 1). Among a subset of 1750 patients in the PBS subset, 83% were positive for oestrogen receptor status, and of 1727, 15% were positive for the HER2 receptor.

3.3 | Breast cancer treatment

3.3.1 | Any treatment

Almost all patients (98%) had some form of treatment (surgery, radiotherapy or systemic therapy) (Table 1). Compared with diagnostic ages <50 years, the odds ratio for treatment was lower for ages 70+ years (aOR 0.18, 95% CI 0.09–0.36 for 70–79 years and

TABLE 1 Patient and clinical factors for breast cancers with treatment within 12 months following diagnosis[a] during 2000–2014 (*N* = 13,494).

	No treatment (*n* = 210)	Having treatment (*n* = 13,284)	*p* value[b]	Adjusted OR[a] (95% CIs)
Age at diagnosis (years)			<0.001	
<50 (*n* = 2819)	10 (4.8%)	2809 (21.2%)		1.00
50–59 (*n* = 3466)	14 (6.7%)	3452 (26.0%)		0.89 (0.39–2.03)
60–69 (*n* = 3584)	26 (12.4%)	3558 (26.8%)		0.55 (0.26–1.16)
70–79 (*n* = 2244)	58 (27.6%)	2186 (16.5%)		0.18 (0.09–0.36)
80+ (*n* = 1381)	102 (48.6%)	1279 (9.6%)		0.10 (0.05–0.20)
Country of birth			0.004	
Australia (*n* = 9281)	118 (60.2%)	9163 (70.2%)		1.00
Other mainly English-speaking countries (*n* = 2235)	49 (25.0%)	2186 (16.7%)		0.63 (0.43–0.92)
Mainly non-English-speaking countries (*n* = 1737)	29 (14.8%)	1708 (13.1%)		0.87 (0.56–1.36)
Unknown (*n* = 241)	14	227		0.48 (0.25–0.94)
SEIFA quintile			0.315	
Most disadvantage (*n* = 2322)	38 (18.1%)	2284 (17.2%)		1.00
2 (*n* = 2661)	46 (21.9%)	2615 (19.7%)		0.75 (0.47–1.21)
3 (*n* = 2735)	50 (23.8%)	2685 (20.2%)		0.70 (0.47–1.21)
4 (*n* = 2680)	39 (18.6%)	2641 (19.9%)		0.87 (0.52–1.43)
Least disadvantage (*n* = 3095)	37 (17.6%)	3058 (23.0%)		1.20 (0.72–2.00)
Remoteness			0.068	
Major city (*n* = 9985)	170 (81.0%)	9815 (73.9%)		1.00
Inner regional (*n* = 1529)	17 (8.1%)	1512 (11.4%)		1.42 (0.83–2.43)
Outer and remote (*n* = 1980)	23 (11.0%)	1957 (14.7%)		1.46 (0.88–2.42)
Histology			0.298	
Ductal (*n* = 10,454)	129 (77.7%)	10,325 (79.0%)		1.00
Lobular (*n* = 1387)	14 (8.4%)	1373 (10.5%)		1.41 (0.78–2.55)
Other (*n* = 1399)	23 (13.9%)	1376 (10.5%)		1.24 (0.75–2.03)
Unknown (*n* = 254)	44	210		0.62 (0.39–1.01)
Differentiation			0.679	
Low (*n* = 4127)	34 (31.8%)	4093 (32.6%)		1.00
Intermediate (*n* = 5689)	52 (48.6%)	5637 (44.8%)		0.92 (0.59−−1.44)
High (*n* = 2865)	21 (19.6%)	2844 (22.6%)		1.01 (0.57–1.80)
Unknown (*n* = 813)	103	710		0.21 (0.13–0.34)
TNM staging			<0.001	
I (*n* = 5462)	32 (23.5%)	5430 (45.4%)		1.00
II (*n* = 4799)	43 (31.6%)	4756 (39.7%)		0.68 (0.42–1.09)
III (*n* = 1389)	5 (3.7%)	1384 (11.6%)		1.88 (0.72–4.93)
IV (*n* = 458)	56 (41.2%)	402 (3.4%)		0.13 (0.08–0.22)
Unknown (*n* = 1386)	74	1312		0.24 (0.15–0.38)
Charlson Index			<0.001	
0 (*n* = 12,535)	169 (80.5%)	12,366 (93.1%)		1.00
1–2 (*n* = 907)	32 (15.2%)	875 (6.6%)		0.90 (0.58–1.39)
3+ (*n* = 52)	9 (4.3%)	43 (0.3%)		0.52 (0.21–1.25)

Abbreviation: SEIFA, Socioeconomic Index for Areas.

[a]Adjusted ORs adjusted for other variables in the Table, plus diagnostic period.; [b]Unknown values excluded from p values and percentages, dates of diagnosis: 2000–2014.

0.10, 95% CI 0.05–0.20 for 80+ years). Patients born in another mainly English-speaking country had lower odds of any treatment than the Australian-born (aOR 0.63, 95% CI 0.43–0.92). Those with stage IV cancers had lower odds than for stage I to have any treatment (aOR 0.13, 95% CI 0.08–0.22). No difference was found in treatment status by socioeconomic disadvantage, remoteness, histology type, differentiation, diagnostic period or comorbidity status (Table 1).

3.3.2 | Surgical treatment

A total of 12,204 patients in the cohort had surgery (56% breast-conserving, 26% a mastectomy and 9% both procedures) (Table 2; Table S1). Overall, 67% (5828) of patients having breast-conserving surgery had adjuvant radiotherapy, and 10% (348) of patients having a mastectomy had immediate breast reconstruction.

Compared with patients aged <50 years, those aged 80+ years were less likely to have each surgery type (Table 2), whereas those aged 60–69 years were more likely to have breast-conserving surgery (aOR 1.56, 95% CI 1.24–1.97) and less likely to have both breast-conserving surgery and mastectomy (aOR 0.68, 95% CI 0.52–0.90). The aORs for having both breast-conserving surgery and mastectomy declined with increasing age (Table 2).

Compared with residents of the most disadvantaged areas (quintile 1), those from least disadvantaged areas were less likely to have both surgery types (aOR 0.70, 95% CI 0.52–0.94 for quintile 4 and aOR 0.73, 95% CI 0.54–0.98 for quintile 5). An increased odds ratio for having surgery was evident for patients diagnosed in 2010–2014 than 2000–2004 (aOR 1.27, 95% CI 1.04–1.53 for breast-conserving surgery, 1.66, 95% CI 1.36–2.03 for mastectomy, and 1.40, 95% CI 1.11–1.76 for women having both surgery types).

Compared with stage I, women with TNM stage IV disease were less likely to have surgery of any type (Table 2), while those with TNM stage II or III disease were less likely to have breast-conserving surgery (aOR 0.46, 95% CI 0.38–0.57 and 0.16, 95% CI 0.12–0.21 respectively), and both treatment types (aOR 0.77, 95% CI 0.61–0.97 and 0.51, 95% CI 0.37–0.70 respectively), but more likely to have mastectomy (aOR 1.35, 95% CI 1.09–1.67 and 1.70 95% CI 1.30–2.23 respectively).

Higher differentiation was associated with increased odd of breast-conserving surgery, whereas increased comorbidity was associated with decreased odd of breast-conserving surgery and mastectomy (Table 2).

3.3.3 | Systemic therapy

Almost three-quarters of women (72%, 9691) had systemic therapy (Table 3; Table S2). The odds ratio for systemic therapy: reduced with age from <50 years to an aOR 0.37 (95% CI 0.32–0.43) for 80+ years; was higher at 1.24 (95% CI 1.10–1.40) for patients born in other mainly non-English-speaking countries compared with the Australian-born; was lowest in residents from the most disadvantaged area; and by comparison, was highest at 1.43 (95% CI 1.26–1.63) in those from least disadvantaged areas (Table 3).

The adjusted odds ratio for systemic therapy was not different by histology or presence of comorbidity, but was higher for TNM stages >stage I and lower for higher differentiation (Table 3).

3.3.4 | Radiotherapy

Of the study cohort, 60% (8095) had radiotherapy (Table 3; Table S3). Compared with patients aged <50 years at diagnosis, the odds of radiotherapy reduced with age to aOR 0.40 (95% CI 0.36–0.45) for 70–79 years and 0.14 (95% CI 0.12–0.17) for 80+ years (Table 3). Patients born in mainly non-English-speaking countries had an elevated odd ratio for radiotherapy at aOR 1.13 (95% CI 1.01–1.26) compared with the Australian-born. A lower aOR 0.88 (95% CI 0.78–0.99) for radiotherapy applied to residents of outer regional and remote areas compared with major city areas.

Differences in use of radiotherapy presented by differentiation and TNM stage but did not show a consistent pattern (Table 3; Table S3). Associations with radiotherapy use were not seen by socioeconomic disadvantage of residential area, tumour histology or comorbidity status.

A difference presented by surgery type where women having breast-conserving surgery were more likely than those having a mastectomy to receive radiotherapy at aOR 5.68 (95% CI 5.11–6.30). This difference applied to stage I at OR 14.49 (95% CI 11.80–17.80), and less so to stage II at OR 5.04 (95% CI 4.38–5.81), but not for stage III at OR 1.03 (95% CI 0.73–1.45), or stage IV at OR 0.83 (95% CI 0.31–2.21).

3.3.5 | Hormone therapy

For the subset of cases of known hormone treatment status, use of hormone agents applied to 85% (92% when oestrogen receptor status was positive). Use of hormone therapy was higher in women aged 70+ years (Table 3; Table S4). Compared with patients aged <50 years, the odds ratio for hormone use was aOR 1.58 (95% CI 1.15–2.16) for ages 70–79 years and aOR 1.55 (95% CI 1.07–2.25) for ages 80+ years. A greater use of these treatments was also evident with higher differentiation from the elevated aORs for intermediate and highly differentiated tumours (Table 3).

Although a variation was seen by TNM stage, a consistent gradient did not apply (Table 3). A marginal difference was apparent by country of birth with a lower aOR 0.79 (95% CI 0.62–1.00) applying to women born in mainly non-English-speaking countries compared with the Australian-born. Use of hormone therapies was not different by level of residential area disadvantage or remoteness or presence of comorbidity (Table 3).

TABLE 2 Adjusted odds ratios[a] (95% CIs) for having surgery within 12 months following breast cancer diagnosis[b] (*n* = 12,204).

	Conservative (*n* = 7498)	Mastectomy (*n* = 3491)	Conservative and mastectomy (*n* = 1215)
Age at diagnosis (years)			
<50 (*n* = 2819)	1.00		
50–59 (*n* = 3466)	1.48 (1.17–1.86)	1.14 (0.91–1.45)	0.86 (0.66–1.12)
60–69 (*n* = 3584)	1.56 (1.24–1.97)	1.11 (0.87–1.41)	0.68 (0.52–0.90)
70–79 (*n* = 2244)	1.20 (0.94–1.53)	1.11 (0.86–1.43)	0.53 (0.39–0.72)
80+ (*n* = 1381)	0.45 (0.36–0.58)	0.35 (0.28–0.46)	0.14 (0.10–0.20)
Country of birth			
Australia (*n* = 9281)	1.00		
Other mainly English-speaking countries (*n* = 2235)	1.05 (0.85–1.29)	1.08 (0.86–1.33)	1.07 (0.84–1.38)
Mainly non-English-speaking countries (*n* = 1737)	1.10 (0.88–1.39)	1.19 (0.94–1.51)	1.11 (0.84–1.47)
Unknown (*n* = 241)	0.22 (0.15–0.32)	0.20 (0.13–0.32)	0.13 (0.06–0.26)
SEIFA quintile			
1 most disadvantage (*n* = 2322)	1.00		
2 (*n* = 2661)	1.12 (0.88–1.43)	0.99 (0.77–1.27)	0.92 (0.69–1.23)
3 (*n* = 2735)	1.07 (0.84–1.36)	0.99 (0.77–1.27)	0.87 (0.65–1.16)
4 (*n* = 2680)	0.95 (0.74–1.21)	0.77 (0.59–0.99)	0.70 (0.52–0.94)
5 least disadvantage (*n* = 3095)	0.99 (0.77–1.26)	0.88 (0.68–1.13)	0.73 (0.54–0.98)
Remoteness			
Major city (*n* = 9985)	1.00		
Inner regional (*n* = 1529)	1.22 (0.95–1.56)	1.12 (0.86–1.45)	1.18 (0.88–1.59)
Outer and remote (*n* = 1980)	0.87 (0.69–1.08)	1.03 (0.82–1.30)	0.91 (0.69–1.19)
Diagnosis year			
2000–2004 (*n* = 4047)	1.00		
2005–2009 (*n* = 4410)	1.07 (0.88–1.28)	1.34 (1.10–1.63)	1.20 (0.95–1.50)
2010–2014 (*n* = 5037)	1.27 (1.04–1.53)	1.66 (1.36–2.03)	1.40 (1.11–1.76)
Histology			
Ductal (*n* = 10,454)	1.00		
Lobular (*n* = 1387)	0.85 (0.65–1.09)	1.10 (0.85–1.43)	1.09 (0.88–1.36)
Other (*n* = 1399)	1.03 (0.80–1.32)	0.80 (0.61–1.04)	1.28 (0.95–1.72)
Unknown (*n* = 254)	0.23 (0.15–0.35)	0.18 (0.11–0.31)	0.29 (0.20–0.41)
Differentiation			
Low (*n* = 4127)	1.00		
Intermediate (*n* = 5689)	1.32 (1.10–1.58)	1.03 (0.86–1.25)	1.09 (0.88–1.36)
High (*n* = 2865)	2.06 (1.60–2.64)	1.00 (0.77–1.31)	1.28 (0.95–1.72)
Unknown (*n* = 813)	0.19 (0.15–0.25)	0.19 (0.14–0.25)	0.29 (0.20–0.41)
TNM staging			
I (*n* = 5462)	1.00		
II (*n* = 4799)	0.46 (0.38–0.57)	1.35 (1.09–1.67)	0.77 (0.61–0.97)
III (*n* = 1389)	0.16 (0.12–0.21)	1.70 (1.30–2.23)	0.51 (0.37–0.70)
IV (*n* = 458)	0.009 (0.006–0.01)	0.05 (0.03–0.07)	0.005 (0.002–0.02)
Unknown (*n* = 1386)	0.16 (0.12–0.19)	0.38 (0.29–0.48)	0.24 (0.18–0.32)
Charlson Index			
0 (*n* = 12,535)	1.00		
1–2 (*n* = 907)	0.68 (0.52–0.88)	0.81 (0.62–1.06)	0.72 (0.51–1.02)
3+ (*n* = 52)	0.19 (0.07–0.48)	0.26 (0.10–0.67)	0.15 (0.02–1.16)

Abbreviation: SEIFA, Socioeconomic Index for Areas.

[a]Adjusted odd ratios from logistic regression analyses, including all variables in the Table.; [b]No surgery as reference, all cases diagnosed between 2000–2014.

TABLE 3 Adjusted odds ratios[a] (95% CIs) for systemic therapy, radiotherapy and hormone therapy for breast cancer within 12 months following diagnosis during 2000–2014.

	Systemic therapy (vs. no systemic treatment) n = 13,494	Radiotherapy (vs. no radiotherapy) *n* = 13,494	Hormone therapy (vs. no hormone therapy)[b] *n* = 4262
Age group			
<50 (*n* = 2819)	1.00		
50–59 (*n* = 3466)	0.80 (0.70–0.90)	1.08 (0.96–1.20)	1.03 (0.82–1.30)
60–69 (*n* = 3584)	0.52 (0.46–0.59)	0.91 (0.82–1.02)	1.19 (0.92–1.52)
70–79 (*n* = 2244)	0.39 (0.34–0.45)	0.40 (0.36–0.45)	1.58 (1.15–2.16)
80+ (*n* = 1381)	0.37 (0.32–0.43)	0.14 (0.12–0.17)	1.55 (1.07–2.25)
Country of birth			
Australia (*n* = 9281)	1.00		
Other mainly English-speaking countries (*n* = 2235)	1.10 (0.99–1.23)	1.02 (0.93–1.14)	0.91 (0.72–1.14)
Mainly non-English-speaking countries (*n* = 1737)	1.24 (1.10–1.40)	1.13 (1.01–1.26)	0.79 (0.62–1.00)
Unknown (*n* = 241)	1.64 (1.18–2.27)	1.21 (0.91–1.62)	1.80 (0.63–5.14)
SEIFA quintile			
1 most disadvantage (*n* = 2322)	1.00		
2 (*n* = 2661)	1.24 (1.10–1.41)	0.95 (0.84–1.08)	0.93 (0.70–1.23)
3 (*n* = 2735)	1.15 (1.02–1.31)	0.91 (0.81–1.03)	1.04 (0.78–1.39)
4 (*n* = 2680)	1.26 (1.11–1.44)	0.98 (0.88–1.13)	1.14 (0.84–1.54)
5 Least disadvantage (*n* = 3095)	1.43 (1.26–1.63)	0.92 (0.81–1.04)	0.99 (0.74–1.31)
Remoteness			
Major city (*n* = 9985)	1.00		
Inner regional (*n* = 1529)	0.98 (0.87–1.11)	0.93 (0.82–1.05)	1.09 (0.82–1.46)
Outer and remote (*n* = 1980)	1.04 (0.92–1.17)	0.88 (0.78–0.99)	1.08 (0.82–1.43)
Histology			
Ductal (*n* = 10,454)	1.00		
Lobular (*n* = 1387)	1.05 (0.93–1.20)	1.00 (0.88–1.13)	1.15 (0.82–1.62)
Other (*n* = 1399)	0.96 (0.84–1.08)	0.96 (0.85–1.09)	0.92 (0.67–1.25)
Unknown (*n* = 254)	0.98 (0.73–1.32)	0.68 (0.50–0.93)	3.04 (0.92–10.05)
Differentiation			
Low (*n* = 4127)	1.00		
Intermediate (*n* = 5689)	0.70 (0.64–0.78)	0.85 (0.77–0.93)	2.70 (2.20–3.30)
High (*n* = 2865)	0.59 (0.53–0.67)	0.95 (0.85–1.06)	3.64 (2.67–4.94)
Unknown (*n* = 813)	0.62 (0.51–0.74)	0.60 (0.50–0.72)	2.25 (1.41–3.62)
TNM staging			
I (*n* = 5462)	1.00		
II (*n* = 4799)	1.52 (1.38–1.66)	0.98 (0.90–1.07)	0.92 (0.74–1.14)
III (*n* = 1389)	1.89 (1.63–2.20)	2.96 (2.54–3.45)	0.61 (0.46–0.80)
IV (*n* = 458)	1.75 (1.38–2.22)	1.01 (0.81–1.26)	0.86 (0.51–1.46)
Unknown (*n* = 1386)	1.27 (1.11–1.46)	0.67 (0.59–0.77)	0.76 (0.55–1.04)
Charlson Index			
0 (*n* = 12,535)	1.00		
1–2 (*n* = 907)	0.92 (0.79–1.07)	0.76 (0.66–0.89)	0.87 (0.59–1.29)
3+ (*n* = 52)	0.91 (0.50–1.67)	0.28 (0.13–0.60)	2.40 (0.30–19.30)

Abbreviation: SEIFA, Socioeconomic Index for Areas.

[a]Adjusted odd ratios from 3 separate logistic regressions including all the variables in the Table plus diagnostic year, with systemic therapy, or radiotherapy, or hormone therapy as the dependent variable, 95% confidence intervals.; [b]Hormone therapy (a subset of Systemic therapy).

3.4 | Cancer survival

The percentage survival from breast cancer at 1, 5 and 10 years from diagnosis was 98%, 89% and 84% respectively (Table 4). Five-year survival increased from 88% in 2000–2004 to 90% for 2005–2009 and 91% for 2010–2014 ($p < 0.001$).

Adjusted SHRs suggested similar outcomes by age <70 years, but an elevated SHR applied to older age groups compared with women aged <50 years at aSHR 1.54 (95% CI 1.31–1.82) for 70–79 years and aSHR 2.04 (95% CI 1.69–2.47) for ages 80+ years. Compared with 2000–2004, lower SHRs applied for more recent diagnoses with aSHRs of 0.82 (95% CI 0.72–0.92) for 2005–2009 and 0.72 (95% CI 0.62–0.85) for 2010–2014 (Table 4).

Residents of the least disadvantaged areas (quintile 5) also had a lower aSHR 0.77 (95% CI 0.65–0.92) compared with the most disadvantaged. Other differences included higher aSHRs for more advanced TNM stage and in the presence of comorbidity, but lower aSHRs for higher differentiation, other histology (i.e. not ductal or lobular), and with treatment (Table 4). Differences in aSHRs were not evident by country of birth or residential remoteness.

Surgery was a key predictor of survival. Compared with no surgery, aSHRs were 0.31 (95% CI 0.26–0.36) for women having breast-conserving surgery, 0.49 (95% CI 0.41–0.57) for mastectomy and 0.42 (95% CI 0.33–0.52) when both surgery types applied (Table 5).

4 | DISCUSSION

Results indicate a continuing increase in 5-year cancer survival from 88% for 2000–2004 to 91% for 2010–2014 diagnoses. This equates with the 91% 5-year relative survival estimated for Australia overall for 2011–2015 (Australian Government, Cancer Australia, 2019), which is at the high end of the international scale (Allemani et al., 2018). We regard this as a positive finding despite uncertainties around potential influences from differences in registry practices, lead time, overdiagnosis and related effects (Allemani et al., 2018). These results complement the age-standardised reduction in breast cancer mortality recorded at a population level for Australia between 1982 and 2019 (Australian Institute of Health and Welfare, 2019).

Survival was equivalent by residential remoteness and country of birth, which is reassuring from an equity perspective as it was anticipated that some women from mainly non-English-speaking countries may have lower survival due to language and cultural barriers. Although the difference was small, residents of the least disadvantaged areas had a higher survival than the most disadvantaged, as reported Australia-wide (Australian Institute of Health and Welfare, 2012). Further study is warranted to investigate the underlying causes.

The lower cancer survival for ages 70+ years confirms earlier results (Allemani et al., 2018; Li, Roder, et al., 2020), which are in line with the lower uptake of cancer treatment confirmed by the present study. As proportions of older people with breast cancer increase with ageing, requirements for service adaptations at a population level to meet their needs will escalate. Increased attention to older people is already occurring through extension of the target age range for breast screening from an upper limit of 69 to 74 years (Australian Bureau of Statistics, 2019; Australian Government, Department of Health, 2016). There is a need for trials and other research to inform decisions on clinical options for older people, and to develop better instruments for predicting the disease prognosis in the short term, such that complex trade-off decisions can be facilitated (Li et al., 2018).

Surgical treatment was strongly associated with higher survival. While we regard this association to be predominantly causal, it could have been influenced by residual confounding from risk factors like comorbidity and frailty which are unlikely to have been measured with enough accuracy for complete adjustment (Mayo Clinic, 2020). Better measures of these characteristics are needed to quantify their effects at a population level.

Of the study cohort, 98% had some treatment for their cancer, that is either surgery, radiotherapy, systemic or combination therapy, whereas 90% had surgery. Treatment by surgery, irrespective of whether by breast-conserving or mastectomy, increased over the study period. Approximately 60% had breast-conserving surgery rather than a mastectomy, which accords with findings from other Australian studies (Roder et al., 2013; South Australian Cancer Registry: Epidemiology Branch, 2000). Breast-conserving surgery rather than mastectomy was more common at ages 50–69 years, which may reflect a common screening-treatment pathway and potentially: (1) less aggressive cancers than in younger women; and (2) reluctance of less mobile older women to have radiotherapy, therefore opting for mastectomy.

Breast surgery was less common for women aged 80+ years, as previously reported (South Australian Cancer Registry: Epidemiology Branch, 2000), probably due to increased frailty and comorbidity, and less common in circumstances where comorbidity was recorded. A different pattern applied by stage with breast-conserving surgery becoming less common with more advanced TNM stage, but mastectomy more likely for stages II and III, which may reflect attempts to clear regional disease.

Irrespective of surgery type, surgery was least likely for stage IV disease where the potential to clear the disease through excision would generally have been lowest. Tumour differentiation was also predictive of surgery type with highly differentiated tumours more likely than poorly differentiated to be treated by breast-conserving therapy. Little difference in exposure to surgery was evident by residential remoteness and socioeconomic status, which we interpret as positive in equity terms.

About 70% of cohort members had systemic therapy in the 12 months following diagnosis. A reducing exposure with advancing age is consistent with previous study results (South Australian Cancer Registry: Epidemiology Branch, 2000; Tesarova, 2013), probably reflecting concerns whether patient resilience was enough to cope with treatment toxicity and also the potential, due to lower additional life expectancy, for reduced intermediate and long-term

TABLE 4 Percentage case survival: female breast cancers diagnosed 2000–2014[a] (*n* = 13,494).

	1-year survival	5-year survival	10-year survival	*p* value[b,c]	Unadjusted SHR (95% CIs)[b,c]	Adjusted SHR (95% CIs)[d]
All (*n* = 13,494)	97.6	89.2	84.0			
Age at diagnosis (years)						
<50 (*n* = 2819)	98.9	90.7	85.5	<0.001	1.00	
50–59 (*n* = 3466)	98.9	91.0	86.7		0.89 (0.76–1.04)	1.06 (0.91–1.24)
60–69 (*n* = 3584)	98.4	92.5	88.0		0.80 (0.69–0.94)	1.06 (0.90–1.24)
70–79 (*n* = 2244)	96.8	86.6	81.4		1.28 (1.09–1.51)	1.54 (1.31–1.82)
80+ (*n* = 1381)	90.5	75.4	66.7		2.28 (1.94–2.68)	2.04 (1.69–2.47)
Country of birth						
Australia (*n* = 9281)	97.8	89.2	84.1	0.156	1.00	
Other mainly English-speaking (*n* = 2235)	97.2	89.3	84.1		1.02 (0.89–1.17)	0.98 (0.84–1.14)
Mainly non-English-speaking (*n* = 1737)	97.7	89.6	83.8		1.01 (0.87–1.18)	0.92 (0.78–1.08)
Unknown (*n* = 241)	90.7	82.9	78.9		1.46 (1.06–2.00)	1.24 (0.87–1.79)
Socioeconomic (SEIFA)						
Most disadvantage (*n* = 2322)	97.2	87.1	80.7	<0.001	1.00	
2 (*n* = 2661)	97.5	88.4	83.0		0.89 (0.76–1.04)	0.96 (0.81–1.13)
3 (*n* = 2735)	97.7	89.3	84.3		0.81 (0.70–0.95)	0.87 (0.73–1.02)
4 (*n* = 2680)	97.6	89.4	84.0		0.84 (0.72–0.98)	0.97 (0.82–1.15)
Least disadvantage (*n* = 3095)	97.9	91.0	87.0		0.68 (0.58–0.80)	0.77 (0.65–0.92)
Residential remoteness						
Major city (*n* = 9985)	97.5	89.4	84.3	0.799	1.00	
Moderate (*n* = 1529)	98.1	88.4	83.9		1.02 (0.87–1.20)	1.02 (0.87–1.21)
High (*n* = 1980)	97.7	88.6	82.9		1.05 (0.91–1.20)	0.96 (0.82–1.12)
Cancer stage:						
I (*n* = 5462)	99.8	97.7	95.7	<0.001	1.00	
II (*n* = 4799)	99.3	90.4	84.0		4.14 (3.46–4.95)	3.15 (2.62–3.77)
III (*n* = 1389)	96.7	76.4	63.1		10.66 (8.82–12.87)	7.75 (6.37–9.42)
IV (*n* = 458)	65.7	24.6	17.3		51.44 (41.88–63.19)	29.51 (23.53–36.99)
Unknown (*n* = 1386)	93.9	82.6	77.7		6.95 (5.59–8.65)	4.76 (3.78–5.99)
Differentiation						
Low (*n* = 4127)	96.8	81.0	74.7	<0.001	1.00	
Moderate (*n* = 5689)	99.1	93.5	87.5		0.40 (0.36–0.45)	0.38 (0.34–0.43)
High (*n* = 2865)	99.5	97.9	96.0		0.13 (0.11–0.17)	0.14 (0.11–0.17)
UK (*n* = 813)	84.4	64.1	55.2		2.08 (1.79–2.41)	1.39 (1.16–1.68)
Histology						
Ductal (*n* = 10,454)	97.9	89.0	83.8	<0.001	1.00	
Lobular (*n* = 1387)	98.8	91.6	85.2		0.85 (0.71–1.01)	1.15 (0.96–1.39)
Other (*n* = 1399)	97.9	94.8	93.6		0.47 (0.36–0.60)	0.63 (0.49–0.83)
Unknown (*n* = 254)	75.5	52.7	46.4		4.53 (3.62–5.65)	1.77 (1.34–2.33)
Diagnostic period (calendar year)						
2000–2004 (*n* = 4047)	97.2	87.8	82.5	<0.001	1.00	
2005–2009 (*n* = 4410)	97.5	89.6	—		0.81 (0.72–0.90)	0.82 (0.72–0.92)
2010–2014 (*n* = 5034)	98.0	90.8	—		0.71 (0.60–0.83)	0.72 (0.62–0.85)

(Continues)

TABLE 4 (Continued)

	1-year survival	5-year survival	10-year survival	*p* value[b,c]	Unadjusted SHR (95% CIs)[b,c]	Adjusted SHR (95% CIs)[d]
Charlson Index						
0 (*n* = 12,535)	98.0	89.7	84.5	<0.001	1.00	
1–2 (*n* = 907)	93.3	82.6	78.4		1.52 (1.27–1.81)	1.12 (0.92–1.35)
3+ (*n* = 52)	61.1	48.7	36.5		6.04 (3.58–10.12)	2.00 (1.06–3.78)
Treatment						
No (*n* = 210)	77.9	54.3	46.1	<0.001	1.00	
Yes (*n* = 13,284)	97.9	89.6	84.5		0.23 (0.17–0.29)	0.65 (0.47–0.91)

Abbreviation: SEIFA, Socioeconomic Index for Areas.

[a]Kaplan–Meier product-limit disease-specific estimates; date of censoring of live cases—December 31, 2014.; [d]Derived from competing risk regression analysis using death of other causes other than breast cancer as competing risk, adjusting for other variables in the Table.; b,cDerived from unadjusted competing risk analysis using death of other causes other than breast cancer as competing risk.

TABLE 5 Percentage case survival from breast cancer by surgical treatment: female breast cancers diagnosed 2000–2014[a].

Surgical treatment	1-year survival	5-year survival	10-year survival	Unadjusted SHR (95% CIs)[b]	Adjusted SHR (95% CIs)[c]
No (*n* = 1290)	80.4	54.4	45.3	1.00	1.00
Conservative (*n* = 7498)	99.6	95.3	92.1	0.10 (0.08–0.11)	0.31 (0.26–0.36)
Mastectomy (*n* = 3491)	98.8	86.7	78.1	0.27 (0.24–0.31)	0.49 (0.41–0.57)
Both surgery (*n* = 1215)	99.4	92.4	85.9	0.17 (0.14–0.20)	0.42 (0.33–0.52)

Abbreviations: PBS, Pharmaceutical Benefits Scheme; SHR, sub-hazard ratio.

[a]Kaplan–Meier product-limit disease-specific estimates; date of censoring of live cases—December 31, 2014.; [b]Derived from unadjusted competing risk analysis using death of other causes other than breast cancer as competing risk.; [c]Derived from 3 separate competing risk regression analyses with each using death of other causes other than breast cancer as competing risk, adjusting for age, country of birth, Indigenous status, residential socioeconomic disadvantage and remoteness, cancer stage, differentiation, histology, diagnosis time, and comorbidity status for systemic treatment, or radiotherapy, or hormone therapy (data source: PBS records).

benefits (Tesarova, 2013). This did not apply to hormone therapy which, as previously reported, was more common in the 70+ year age range (South Australian Cancer Registry: Epidemiology Branch, 2000).

Systemic therapy was least common in residents from the most disadvantaged areas and most common in the least disadvantaged areas, as shown previously (South Australian Cancer Registry: Epidemiology Branch, 2000). Women born in other mainly non-English-speaking countries were also more likely than the Australian-born to have systemic therapy. The reasons for these patterns are not clear and require further research. Similar patterns were not seen for hormone therapy which became more common over the study period.

Predictably, use of systemic therapies was greater for TNM stages that were more advanced than stage I and for less differentiated tumours (Edge & Compton, 2010). A similar pattern was not seen for hormone therapy which tended to be more common for more differentiated tumours.

Approximately 60% of the cohort had radiotherapy in the 12 months following diagnosis. The decreased use observed in older age has been reported previously (South Australian Cancer Registry: Epidemiology Branch, 2000). It may reflect perceptions of reduced benefit in older women, although reduced mobility and poorer access to radiotherapy in major metropolitan centres may have played a part. The reduced exposure seen in residents of outer regional and remote areas may reflect less ready access.

The greater use of radiotherapy by patients born in mainly non-English-speaking countries may have been influenced by cultural factors, but also better access, as these patients tended more to reside in major city areas where radiotherapy centres were located (Australia Bureau of Statistics, 2016, 2017). Better measures of ethnicity are needed to determine the role of this characteristic.

We were interested a priori in whether the non-Australian-born were disadvantaged in accessing treatment services compared with the Australian-born due to language or cultural barriers. The indication from this study that women born in another mainly English-speaking country were less likely to be treated either by surgery, radiotherapy or systemic therapy was confirmatory. Statistically significant differences were not found for separate treatment types, however, suggesting a tendency in this migrant group, when treated, to have multiple treatments. A similar difference did not apply for women born in mainly non-English-speaking countries.

We also observed a small sub-group of women (0.7%) who were long-term survivors without a history of recorded treatment in the initial 12 months from diagnosis. While this could be artefactual due to lack of access to treatment data outside South Australia, or because records did not link due to name changes or other reasons,

the tumours experienced by this sub-group may have included some with low potential to progress. Long-term survivors are a group where further research could provide useful insights.

This study investigates over a 15-year period, differences in breast cancer survival and treatments in South Australia, using linked data. Data sources including cancer registry and linked routinely collected data, with data linkage using a validated privacy-protecting methodology (Australian Government, National Statistical Service, 2017). Treatment types for breast cancer were assessed by sociodemographic characteristics and cancer characteristics such as TNM stage, histology and differentiation, as well as comorbidity status. Associations of treatment with survival were also adjusted for these factors. This study investigated broader population-wide treatment patterns, and associations with survival, than the earlier South Australian report (Roder et al., 2017).

Limitations should be noted. Firstly, radiotherapy and systemic therapy trends were susceptible to differences in recording over time, due to changes in funding mix and associated statistical collection, such that use of trend data was limited to statistical adjustment. In addition, treatment may be misclassified in the available administrative data. Secondly, disease-specific survival was used, due to limited access to lifetables, although prior validation studies have shown this to be an accurate proxy for relative survival in South Australia when subject to correction by cancer registry staff with access to broader clinical information (Roder et al., 2017). Thirdly, country of birth is far from ideal as a measure of ethnicity and further development of a more appropriate measure is needed for population studies. Fourthly, a more complete measure of comorbidity is needed, ideally incorporating data from primary care. Lastly, only limited data on hormonal therapies and targeted systemic therapies were available for the study period. They will need analysis in future studies, including those investigating anti-cancer treatments in older women.

This study examines treatment at a broad level only. More detailed study of treatment regimens would be desirable. Future analyses ideally would cover the entire screening and treatment pathway, including data on recurrence for determining recurrence rates and pre-and-post-recurrence treatment and survival.

In conclusion, the study illustrates the use of data linkage in Australia to describe treatment and survival at a population level for service evaluation. It indicates a high survival from breast cancer in South Australia by international standards. Women aged 70+ years had lower survival, and less treatment other than by hormone therapy. Surgical management increased and strongly predicted higher breast cancer survival.

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CONFLICT OF INTEREST

None to declare.

AUTHOR CONTRIBUTION

All authors qualify for the authorship according to the journal criteria of authorship.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval for the study was obtained from the South Australia Department for Health and Wellbeing Human Research Ethics Committee (HREC/17/SAH/38), the University of South Australia Human Research Ethics Committee (200021) and Australian Institute of Health and Welfare Human Research Ethics Committee (EO2017/3/361).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the South Australian Department for Health and Wellbeing (South Australian Cancer Registry & Integrated South Australian Activity Collection) and the Australian Institute of Health and Welfare (MBS, PBS and NDI) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the South Australian Department for Health and Wellbeing and the Australian Institute of Health and Welfare.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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