Female Breast Cancer Treatment and Survival in South Australia: Results from Linked Health Data

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Abstract

Background: We investigated treatment and survival by clinical and sociodemographic characteristics in South Australia for service evaluation using linked data.

Method: Data on invasive female breast cancers (n=13494) 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: Five-year disease-specific survival increased to 91% for 2010-2014. Survival was lower for: ages 70+ years, and lowest for 80+ years (aSHR 2.04, 95%CI 1.69-2.47), compared with ages <50 years; and in the presence of comorbidity (aSHR 2.00, 95%CI 1.06-3.78), higher TNM stage and higher grade. Differences in aSHRs were not found by birth country or residential remoteness, but survival was higher in the least disadvantaged areas (aSHR 0.77, 95%CI 0.65-0.92). Most women had breast surgery (90%) (breast conserving surgery (56%), mastectomy (26%), and both surgery types (9%)), 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. More women from least disadvantaged areas had systemic therapy (aOR 1.43, 95%CI 1.26-1.63). Radiotherapy was less common in outer regional/remote residents compared with major city residents (aOR 0.88, 95%CI 0.78-0.99).

Conclusions:

High survival from breast cancer in South Australia was comparable to the Australia-wide rate and did not differ by residential remoteness and country of birth. Surgical treatment within 12 months after cancer diagnosis increased during the study period and strongly predicted higher survival. Patients aged 70+ years had lower survival and less treatment, and more trial evidence is needed to optimize trade-offs between benefits and harms in this older age range. Systemic therapy was less for residents from most disadvantaged areas, while radiotherapy was less for residents of outer regional and remote areas.

Background

Breast cancer is the most common cancer recorded in Australian females by population-based registries [1]. An increase in breast cancer survival has occurred, attributed mostly to treatment advances and earlier detection from population screening [1, 2]. Australian and international studies show females with early-stage breast cancer to have the highest survival [3, 4]. Increasing early detection through screening of more women at high risk likely would increase survival further [5].

Breast cancer treatment has changed in recent decades in line with better understanding of disease biology, pharmacological discoveries, and advances in clinical practice [6, 7]. Treatment generally includes surgery, and, where appropriate, adjuvant radiotherapy and systemic therapy [8, 9]. Breast conserving surgery is now more common than mastectomy and systemic therapies have broadened beyond chemotherapy to include hormone and targeted therapies, and immunotherapy [8, 9].

Apart from clinical factors, such as cancer stage, histology, grade (differentiation), hormone receptor status and general health status, treatment and outcomes can vary with age at diagnosis, cultural background, socioeconomic status, and residential remoteness. The breast cancer treatment and survival had been attempted in South Australia using inpatient data from several public hospitals [10]. Due to limited treatment data available from population-based registries, it is not possible with registry data to: (1) investigate treatment by clinical and sociodemographic characteristics; and (2) examine differences in survival by treatment pathway.

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 8 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 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.

Methods

Data sources and linkage

Invasive female breast cancer data (ICD-O-3, C50) were obtained from the South Australian Cancer Registry (SACR), which comprised the main linkage spine. SACR operations follow international registry standards with legally mandated reporting from pathology laboratories and hospitals [11, 12]. 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 [11]. The Registry of Births, Deaths and Marriages and National Death Index (NDI) are used to obtain death dates and causes, classified by cancer type or as non-cancer [11].

Treatment data are mostly retrieved from hospital inpatient statistics, radiotherapy centres, and claims data from universal health insurance, i.e., the Medical Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS). Hospital inpatient data include dates of admission and clinical procedure codes, whereas radiotherapy centre data include dates of all treatments.

Collectively these sources cover most treatments. MBS is a universal health insurance scheme that covers hospital and community provision of treatments funded privately [13], whereas the PBS subsidises costs of drugs provided for most medical conditions [14].

Linkages of SACR, hospital and radiotherapy data were undertaken by SANT Data Link using probabilistic matching of identifiers (name, sex, date of birth and address) [15, 16]. This followed the principle of separating patient identifiers from clinical content data to protect privacy [16]. Data linkage between these data and MBS and PBS benefits claims was undertaken through the Australian Institute of Health and Welfare (AIHW) data linkage unit, also using the principle of separation to protect privacy.

Cancer treatment

Treatment in the first 12 months from diagnosis was investigated according to whether any was recorded, i.e., any surgery (mastectomy, breast-conserving surgery, or both), radiotherapy or systemic therapy. Systemic therapies comprised chemotherapy, hormonal drugs, targeted and immunotherapies. A sub-set of systemic therapies reimbursed through the PBS was also available to identify hormonal treatments. Data sources included: for surgery – inpatient statistics; for radiotherapy - inpatient + radiotherapy + SACR + MBS; and for systemic therapy - inpatient + PBS + MBS. Codes used to specify treatment types were those included in the 10th Revision of the Australian Classification of Health Interventions (ACHI) and the MBS and PBS coding systems [13, 14, 17].

Other descriptors

Age at diagnosis was classified as: <50, 50–59, 60–69, 70–79 or 80 + years. To compare outcomes by cultural background, we classified country of birth as Australia, other mainly English-speaking country or mainly non-English speaking country, as described previously [18]. Socio-economic status was derived from residential postcode at diagnosis using the Socioeconomic Index for Areas (SEIFA) Index of Relative Socio-economic Disadvantage (IRSD) expressed in quintiles [19]. Residential area was also classified as a major city area, inner regional, outer regional, remote or very remote area, using the Australian Standard Geographical Classification (ASGC) Remoteness index [20]. Diagnostic period was categorized as 2000–2004, 2005–2009, and 2010–2014.

Cancer descriptors included stage, histology, grade (differentiation), and, for a sub-set, oestrogen receptor and human epidermal growth factor receptor 2 (HER2) status [11]. Stage was derived from pathology laboratory, hospital and clinical reporting and broadly classified for study purposes as TNM stage I, II, III, or IV [3]. Cancer grade was categorised as high, intermediate or low grade [11], cancer histology as ductal, lobular or other (not ductal or lobular), and oestrogen receptor status as negative or positive [11]. Charlson Comorbidity Index scores were derived from inpatient data for the 2000–2014 study period, classified as 0 to 3+ [21]. Comorbidities included disease groups which appeared unlikely to have been treatment side effects arising during or soon after treatment, i.e., diabetes mellitus ± complications, peripheral vascular diseases, cerebrovascular accident, 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 [21].

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 [11]. Logistic regression was used to model treatment after adjusting for differences in age, country of birth, SEIFA Index of Relative Socioeconomic Disadvantage residential area, geographic remoteness, year of diagnosis, TNM stage, cancer grade (differentiation), histology, and comorbidity status [11].

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 December 31st, 2014, whichever came first. Cancer-specific survival at 1, 5, and 10 years from diagnosis was estimated using the Kaplan-Meier product-limit estimator [11].

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 [11]. 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, College Station, Texas, USA), 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 for radiotherapy and systemic therapy data collection.

Results

Patient profile

Overall, 21% of patients were aged < 50 years and 10% 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).

Cancer profile

Excluding missing values, 79% of cancers were ductal and 10% lobular; 33% were high grade (low differentiation) and 23% low grade (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. 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.

Table 1
Patient and clinical factors for breast cancers with treatment within 12 months following diagnosis*

	No treatment (n = 210)	Having treatment (n = 13284)	P value*	Adjusted OR** (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 English-speaking countries (n = 2235)	49 (25.0%)	2186 (16.7%)		0.63 (0.43–0.92)
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 = 10454)	129 (77.7%)	10325 (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)

*Unknown values excluded from p values and percentages, dates of diagnosis: 2000–2014.

**Adjusted ORs adjusted for other variables in the Table, plus diagnostic period.

	No treatment (n = 210)	Having treatment (n = 13284)	P value*	Adjusted OR** (95% CIs)
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 = 12535)	169 (80.5%)	12366 (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)
*Unknown values excluded from p values and percentages, dates of diagnosis: 2000–2014.				
**Adjusted ORs adjusted for other variables in the Table, plus diagnostic period.				

Breast cancer treatment

Any treatment:

Almost all patients (98%) had some form of treatment (surgery, radiotherapy or systemic therapy) (Table 1). Compared with diagnostic ages < 50 years, likelihood of treatment was lower for ages 70 + years (aOR 0.18, 95%CI 0.09–0.36 for 70–79 years and 0.10, 95%CI 0.05–0.20 for 80 + years). Patients born in another mainly English-speaking country were less likely to have any treatment than the Australian-born (aOR 0.63, 95%CI 0.43–0.92). Those with stage IV cancers were less likely 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).

Surgical treatment:

A total of 13494 patients (90%) had surgery, 56% had breast conserving surgery, 26% had mastectomy, and 9% had both breast conserving surgery and mastectomy (Table 2/Supplement Table 1). Overall, 67% (5828) of patients having breast-conserving surgery had adjuvant radiotherapy, and 10% (348) of patients having a mastectomy had an 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 the 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 likelihood of 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). Likelihood of individual treatment types did not vary by country of birth or residential remoteness.

Compared with stage I, women with TNM stage IV disease were less likely to have surgical treatment 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).

Lower grade (higher differentiation) was associated with increased likelihood of breast conserving surgery, whereas increased comorbidity was associated with a decreased likelihood of breast conserving surgery and mastectomy (Table 2). Treatment types did not vary by histology type.

Table 2
Adjusted odds ratios* (95% CIs) for having surgery within 12 months following diagnosis**

	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 English- speaking countries (n = 2235)	1.05 (0.85–1.29)	1.08 (0.86–1.33)	1.07 (0.84–1.38)
Other 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 = 10454)	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)

*Adjusted odd ratios from logistic regression analyses, including all variables in the Table

**no surgery as reference, all cases diagnosed between 2000–2014.

	Conservative (n = 7498)	Mastectomy (n = 3491)	Conservative and Mastectomy (n = 1215)
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 = 12535)	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)
*Adjusted odd ratios from logistic regression analyses, including all variables in the Table			
**no surgery as reference, all cases diagnosed between 2000–2014.			

Systemic therapy:

Almost three quarters of the study cohort (72%, 9691) had systemic therapy (Table 3/Supplement Table 2). 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, highest at 1.43, 95%CI 1.26–1.63 in those from the least disadvantaged areas (Table 3).

The adjusted odds ratio for systemic therapy was not observed to differ by histology or with presence of comorbidity, but it was higher for TNM stages > stage I and lower for lower grade (more differentiated) lesions (Table 3).

Table 3
Adjusted odds ratios* for systemic therapy, radiotherapy and hormone therapy within 12 months following diagnosis**

	Systemic therapy (vs no systemic treatment) n = 13493	Radiotherapy (vs no radiotherapy) n = 13493	Hormone therapy (vs no hormone therapy)** 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 English- speaking countries (n = 2235)	1.10 (0.99–1.23)	1.02 (0.93–1.14)	0.91 (0.72–1.14)
Other 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 = 10454)	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)

*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.

** Female breast cancers diagnosed 2000–2014

** Hormone therapy (a subset of Systemic therapy).

	Systemic therapy (vs no systemic treatment) n = 13493	Radiotherapy (vs no radiotherapy) n = 13493	Hormone therapy (vs no hormone therapy)** n = 4262
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 = 12535)	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)
*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.			
** Female breast cancers diagnosed 2000–2014			
** Hormone therapy (a subset of Systemic therapy).			

Radiotherapy:

Of the study cohort, 60% (8095) had radiotherapy (Table 3/Supplement Table 3). Compared with patients aged < 50 years at diagnosis, the likelihood of radiotherapy reduced with age with an 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 chance of 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 level of differentiation and TNM stage but did not show a consistent pattern (Table 3/Supplement Table 3). 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 conservative 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.

Hormone therapy:

For the sub-set of systemic therapy 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/Supplement 4). 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 lower grade from the elevated aORs for intermediate and low-grade 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. Differences in use of hormone therapies were not suggested by level of residential area disadvantage or remoteness or presence of comorbidity (Table 3).

Cancer survival

The percentage survival from breast cancer at 1, 5, and 10 years from diagnosis was 98%, 89%, and 84% respectively (Tale 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 compared with 2000–2004.

Table 4
Percentage case survival: female breast cancers diagnosed 2000–2014*

	1-year survival	5-year survival	10-year survival	P value**	Unadjusted SHR (95% CLs)**	Adjusted SHR (95% CI)***
All (n = 13494)	**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 English-speaking (n = 2235)	97.2	89.3	84.1		1.02 (0.89–1.17)	0.98 (0.84–1.14)
Non-English-speaking (n = 1737)	97.7	89.6	83.8		1.01 (0.87–1.18)	0.92 (0.78–1.08)
Unknow (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)**

* Kaplan-Meier product-limit disease-specific estimates; date of censoring of live cases - Dec 31, 2014.

** Derived from unadjusted competing risk analysis using death of other causes other than breast cancer as competing risk.

*** 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.

	1-year survival	5-year survival	10-year survival	P value**	Unadjusted SHR (95% CLs)**	Adjusted SHR (95% CI)***
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 = 10454)	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)**
Charlson Index						
0 (n = 12535)	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 = 13284)	97.9	89.6	84.5		**0.23 (0.17–0.29)**	**0.65 (0.47–0.91)**
* Kaplan-Meier product-limit disease-specific estimates; date of censoring of live cases - Dec 31, 2014.						
** Derived from unadjusted competing risk analysis using death of other causes other than breast cancer as competing risk.						
*** 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.						

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 lower grade (higher tumour 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 were received (Table 5).

Table 5
Percentage case survival from breast cancer by surgical treatment: female breast cancers diagnosed 2000–2014*

Surgical treatment	1-year survival	5-year survival	10-year survival	Unadjusted SHR (95% CLs)**	Adjusted SHR (95% CLs)***
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)**
* Kaplan-Meier product-limit disease-specific estimates; date of censoring of live cases - Dec 31, 2014.					
** Derived from unadjusted competing risk analysis using death of other causes other than breast cancer as competing risk.					
*** 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).					

Discussion

Results indicate a continuing increase in 5-year survival from cancer 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 [22], which is at the high end of the international scale [23]. We regard this as a positive finding despite uncertainties around potential influences from differences in registry practices, lead time, overdiagnosis and related effects [23].

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 [24]. Further study is warranted to investigate the underlying causes.

The lower cancer survival for ages 70 + years confirms earlier results [4, 11, 23], which are in line with the lower uptake of cancer treatment confirmed by the present study. As numbers and 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 [25, 26]. There is a need for clinical trials and other research to inform decisions on the best clinical options for older people, and to develop better instruments for predicting the likelihood of death in the short term, such that complex trade-off decisions can be facilitated [27].

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 [28].

Of the study cohort, 98% were found from available data sources to have had some treatment for their cancer, i.e., 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 [11, 29]. Breast conserving surgery rather than mastectomy was more common in the 50-69-year age range, which may reflect a common screening-treatment pathway and potentially: (1) less aggressive cancers than in younger women; and (2) a 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 [11], 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 to be the treatment of choice 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 grade was also predictive of surgery type with highly differentiated tumours more likely than poorly

differentiated to be treated by breast conserving therapy. Notably, little difference in exposure to surgery, irrespective of type, was evident by residential remoteness and socioeconomic status, which we interpret as positive in equity terms.

About 70% of cohort members were observed to have systemic therapy in the 12 months following diagnosis. A reducing exposure with advancing age is consistent with previous study results [11, 30], 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 benefits [30]. This did not apply to hormone therapy which, as previously reported, was more common in the 70 + year age range [11].

Systemic therapy was least common in residents from the most disadvantaged areas and most common in the least disadvantaged areas, as shown in previous research [11]. 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 higher grade tumours [31]. A similar pattern was not seen for hormone therapy which tended to be more common for lower-grade tumours.

Approximately 60% of the cohort had radiotherapy in the 12 months following diagnosis. The decreased use observed with older age has been reported previously [11]. 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 for some women. 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 predominantly 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 [32].

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 artifactual 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, inpatient data, radiotherapy data, MBS and PBS data, with data linkage based on a validated privacy-protecting methodology [15, 16]. Treatment types for breast cancer were assessed by sociodemographic characteristics and cancer characteristics such as TNM stage, histology and grade, as well as comorbidity status. Associations of treatment with survival were adjusted for sociodemographic and specified cancer characteristics. This study included complete sources for treatment, investigated comprehensively the treatment pattern, and assessed rigorously the impact of treatment on survival, compared to the previous report in South Australia [10].

Limitations should be noted. Radiotherapy and systemic therapy trends were susceptible to differences in recording over time, due to changes in funding mix and associated statistical collection across the study period, such that use of trend data were limited to statistical adjustment. In addition, treatment may be misclassified due to incomplete or missing information in available administrative data. 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 [10].

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.

Conclusions

Results indicate:

- A high survival from breast cancer in South Australia by international standards, equating with high relative survival Australia-wide.
- Equivalent survival outcomes, irrespective of residential remoteness and country of birth, which is positive in equity terms.

- A higher survival in least disadvantaged areas, although the difference was small.
- A predictable association of breast cancer surgery with higher survival.
- Lower survival and less treatment for women aged 70+ years having. More trial evidence is needed to inform trade-off decisions between benefits and harms in this age range.
- A trend towards increased surgical management.
- A lower use of systemic therapy for residents from the most disadvantaged areas
- A lower use of radiotherapy for residents of outer regional and remote areas.

These findings highlight the value of linked registry and administrative data for evaluating health service delivery.

Abbreviations

aORs: adjusted odds ratios; aSHRs adjusted sub-hazard ratios; ICD: International Classification of Diseases; SACR: South Australian Cancer Registry; NDI: National Death Index; MBS: Medicare Benefits Schedule; PBS: Pharmaceutical Benefits Scheme; AIHW: Australian Institute of Health and Welfare; ACHI: Australian Classification of Health Interventions (10^{th} revision); SEIFA: Socioeconomic Index for Areas; IRSD: Index of Relative Socio-economic Disadvantage; ASGC: Australian Standard Geographical Classification; HER2: human epidermal growth factor receptor 2; TNM: tumour, node & metastases.

Declarations

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).

Consent for publication

Not applicable.

Availability of data and materials

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 & 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.

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

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Critical revisions: ML, DR, KDO, DW, GF, EB, CK, RJ, TP, AT, CM, DC, KP, DBT, IO

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