



# BMJ Open Monitoring TNM stage of female breast cancer and survival across the South Australian population, with national and international TNM benchmarking: A population-based cohort study

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## ABSTRACT

**Objective** Using linked cancer registry and administrative data to monitor, tumour, node and metastases (TNM) stage and survival from female breast cancer in Australia.

**Method** Analysis of 2000–2014 diagnoses with linked population-based data to investigate: (1) sociodemographic predictors of advanced stage (stages III and IV), using unadjusted and adjusted logistic regression; and (2) sociodemographic factors and stage as predictors of breast cancer survival using competing risk regression.

**Design** Population-based registry cohort.

**Setting and participants** 14 759 South Australian women diagnosed in 2000–2014.

**Primary and secondary outcome measures** Stage and survival.

**Results** At diagnosis, 46% of women were classified as stage I, 39% as stage II, 12% as stage III and 4% as stage IV. After adjusting for sociodemographic factors, advanced stage was more common: (1) for ages <50 years; and although not statistically significant, for ages 80+ years; and (2) in women from socioeconomically disadvantaged areas. Compared with 2000–2004 diagnoses, stage and sociodemographic adjusted risks (sub-HRs (SHRs)) of breast cancer death were lower in 2005–2009 (SHR 0.75, 95% CI 0.67 to 0.83) and 2010–2015 (SHR 0.57, 95% CI 0.48 to 0.67). Compared with stage I, the SHR was 3.87 (95% CI 3.32 to 4.53) for stage II, 10.87 (95% CI 9.22 to 12.81) for stage III, and 41.97 (95% CI 34.78 to 50.65) for stage IV. Women aged 70+ years at diagnosis and those living in the most socioeconomically disadvantaged areas were at elevated risk of breast cancer death, independent of stage and sociodemographic factors.

**Conclusions** Stage varied by age, diagnostic period and socioeconomic status, and was a stronger predictor of survival than other statistically significant sociodemographic predictors. Achieving earlier diagnosis outside the original BreastScreen target of 50–69 years (as applying <2014) and in residents of socioeconomically disadvantaged areas likely would increase cancer survival at a population level.

## Strengths and limitations of this study

- Shows the utility of readily available registry and administrative data for population-based monitoring of tumour, node and metastases (TNM) stage.
- Shows the face validity of these TNM stage distributions through comparisons with data from special studies and international benchmarks.
- Shows plausible predictive effects of stage on survival.
- Study limited to broad TNM categories due to limited detail available.
- Use of American Joint Committee on Cancer seventh revision with further adaptation required for the eighth revision.

## INTRODUCTION

Breast cancer is the most common cancer recorded in Australian women by population registries.<sup>1</sup> The 5-year relative survival from female breast cancer increased markedly from 72% in 1984–1988 to 91% in 2011–2015.<sup>1</sup> This was attributed mostly to treatment advances and earlier cancer detection through the national population screening programme established in 1991.<sup>1,2</sup> The screening programme offered 2-yearly screening mammograms to women in the target age of 50–69 years, extending to 74 years from 2014.<sup>1,2</sup> Approximately 54% of women in the target age range participate during a 2-year period. Women aged 40–49 years, particularly women with a strong family history and those older than the screening target, are eligible for screening but not actively invited.<sup>1,2</sup>

Anatomic stage of cancer is a key predictor of cancer survival.<sup>3,4</sup> The tumour, node and

metastases (TNM) staging system is a gold standard for staging most solid cancers in clinical practice and can be used, with minor modification, to monitor stage at a population level through cancer registries.<sup>5</sup> TNM stage was recorded by population registries for 95% of female breast cancers diagnosed in Australia in a one-off study in 2011.<sup>5</sup> This followed an earlier pathfinder study for methodological development.<sup>6</sup> Staging data are useful to service planners as indicators of need, to assess alignment of care with recommendations, to evaluate survival, to design interventions to address disparities and to evaluate population impact of new therapies by stage.

We use linked registry and administrative data for 14759 South Australian women diagnosed with invasive breast cancer in 2000–2014 to investigate: (1) sociodemographic predictors of advanced TNM stage; and (2) TNM stage as a predictor of breast cancer survival.

## METHODS

### Study design

Two historic cohort designs were used. The predictor variables for stage as the outcome in the first analysis were sociodemographic characteristics (ie, age at diagnosis, country of birth, residential area socioeconomic disadvantage and remoteness, and diagnostic period), and for survival as the outcome in the second analysis, TNM stage and these sociodemographic variables.

### Deriving stage

TNM stage was recorded for 96% of women with breast cancers diagnosed in 2000–2014, using pathology and hospital reporting. The stage distribution was checked with aggregated statistical profiles from the Breast Quality Audit of Breast Surgeons of Australia and New Zealand.<sup>7</sup> For consistency, staging processes followed national guidelines developed for population-based registries and used in a 2011 national study.<sup>5,6</sup>

Breast tumour diameters and nodal status were obtained for assessing stage through the South Australian Cancer Registry (SACR) and distant metastases were indicated by inpatient diagnosis codes. SA Clinical Cancer Registry data for major public hospitals were used for validity checking and to fill gaps. Receptor status and other biomarkers were not addressed as they were not routinely recorded by registries throughout the study period and not included in the national TNM staging protocol developed for population-wide monitoring.<sup>5</sup>

Stage was broadly classified as stage I, II, III or IV, according to criteria of the American Joint Committee on Cancer (AJCC, seventh revision), to reduce inconsistencies from changes in AJCC revisions.<sup>8</sup>

### Data sources

Population-based invasive breast cancer data (International Classification of Diseases (ICD)-O-3 C50) were obtained from the SACR. Operations of the SACR have been described previously.<sup>9</sup> All invasive breast cancers

diagnosed in South Australia were included and coded using international registry standards.<sup>9,10</sup> Reporting by pathology laboratories and hospitals is a legal requirement.<sup>9</sup>

For each cancer, SACR records the primary site, morphology, diagnosis date and the woman's country of birth, death date and cause, and postcode-derived relative socioeconomic disadvantage and geographical remoteness.<sup>9</sup> The Registry of Births, Deaths and Marriages and National Death Index are used as sources of death data, with causes coded to cancer type or non-cancer.<sup>9</sup>

Linkage of SACR and hospital inpatient data was predominantly through South Australia Northern Territory DataLink using name, sex, date of birth and address for matching.<sup>11,12</sup> Patient identifiers were separated from clinical content to protect privacy.<sup>12</sup> The process comprised: (1) after record deduplication, deterministic matching to a Master Linkage File built from extracts of over 60 data sources, achieving 97% deterministic matching of inpatient and SACR data; (2) non-exact matches then linked through probabilistic means; (3) uncertain matches clerically reviewed for final determination.

### Other variables

Age at diagnosis was classified as: <50, 50–59, 60–69, 70–79 or 80+ years; and country of birth as Australia, other predominantly English-speaking country or predominantly non-English speaking country, as previously.<sup>13,14</sup> Socioeconomic status was derived from residential postcode at diagnosis using the Socioeconomic Index for Areas (SEIFA) Index of Relative Socioeconomic Disadvantage expressed in quintiles.<sup>15</sup> Residential area was classified as a major city, inner regional, outer regional, remote or very remote area, using the Australian Standard Geographical Classification Remoteness Index.<sup>16</sup> Diagnostic period was categorised as 2000–2004, 2005–2009 and 2010–2014.

### Statistical analysis

TNM stage was analysed by population characteristic using analysis of variance for age and conventional  $\chi^2$  or ranked tests depending on variable distributions.<sup>17,18</sup> Advanced stage (III or IV) as opposed to early stage (I or II) was analysed by sociodemographic descriptors using unadjusted and adjusted logistic regression.<sup>17,18</sup>

Deaths were classified as due to breast cancer, as compared with another cause, and predictors of survival from breast cancer were analysed for period from diagnosis to death or until 31 December 2014, whichever came first. Predictors of breast cancer death were investigated using competing risk regression models (Stata module 'stcrreg'),<sup>18,19</sup> regarding deaths from causes other than breast cancer as the competing risk. Predictors were adjusted for stage and sociodemographic characteristics.

Stata V.14 (StataCorp) was used, with statistical significance set at  $p < 0.05$ . All survival analyses used complete case data.

## Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

## RESULTS

### Population description

The mean age of the 14759 staged cases was 61 years, with 53% aged 50–69 years (table 1). For women of known

**Table 1** Patient characteristics by tumour, node and metastases cancer stage; invasive breast cancers diagnosed in South Australia, 2000–2014\*

|                                  | I<br>(n=6718) | II<br>(n=5777) | III<br>(n=1708) | IV<br>(n=556) | Total<br>(n=14759) | P value |
|----------------------------------|---------------|----------------|-----------------|---------------|--------------------|---------|
| Mean age (year) (SD)             | 61.0 (12.2)   | 60.0 (13.9)    | 59.0 (14.3)     | 65.3 (15.2)   | 60.6 (13.3)        | <0.001  |
| Age group                        |               |                |                 |               |                    | <0.001  |
| <50                              | 1143 (17.0%)  | 1436 (24.9%)   | 486 (28.5%)     | 101 (18.2%)   | 3166 (21.5%)       |         |
| 50–59                            | 1877 (27.9%)  | 1493 (25.8%)   | 429 (25.1%)     | 103 (18.5%)   | 3902 (26.4%)       |         |
| 60–69                            | 2121 (31.6%)  | 1344 (23.3%)   | 363 (21.3%)     | 112 (20.1%)   | 3940 (26.7%)       |         |
| 70–79                            | 1072 (16.0%)  | 929 (16.1%)    | 267 (15.6%)     | 124 (22.3%)   | 2392 (16.2%)       |         |
| 80+                              | 505 (7.5%)    | 575 (10.0%)    | 163 (9.5%)      | 116 (20.9%)   | 1359 (9.2%)        |         |
| Country of birth                 |               |                |                 |               |                    | 0.002   |
| Australia                        | 4101 (61.0%)  | 3450 (59.7%)   | 1035 (60.6%)    | 332 (59.7%)   | 8918 (60.4%)       |         |
| Other English-speaking countries | 985 (14.7%)   | 858 (14.9%)    | 226 (13.2%)     | 75 (13.5%)    | 2144 (14.5%)       |         |
| Non-English-speaking countries   | 700 (10.4%)   | 715 (12.4%)    | 211 (12.4%)     | 69 (12.4%)    | 1695 (11.5%)       |         |
| Unknown                          | 932 (13.9%)   | 745 (13.1%)    | 236 (13.8%)     | 80 (14.4%)    | 2002 (13.6%)       |         |
| SEIFA IRSD quintile              |               |                |                 |               |                    | <0.001  |
| 1 (most disadvantaged)           | 1057 (15.7%)  | 1063 (18.4%)   | 319 (18.7%)     | 131 (23.6%)   | 2570 (17.4%)       |         |
| 2                                | 1404 (20.9%)  | 1126 (19.5%)   | 332 (19.4%)     | 125 (22.5%)   | 2987 (20.2%)       |         |
| 3                                | 1342 (20.0%)  | 1165 (20.2%)   | 355 (20.8%)     | 112 (20.1%)   | 2974 (20.2%)       |         |
| 4                                | 1342 (20.0%)  | 1168 (20.2%)   | 341 (20.0%)     | 88 (15.8%)    | 2939 (19.9%)       |         |
| 5 (least disadvantaged)          | 1572 (23.4%)  | 1254 (21.7%)   | 361 (21.1%)     | 100 (18.0%)   | 3287 (22.3%)       |         |
| Remoteness                       |               |                |                 |               |                    | 0.310   |
| Major city                       | 4978 (74.1%)  | 4293 (74.3%)   | 1290 (75.5%)    | 418 (75.2%)   | 10979 (74.4%)      |         |
| Inner regional                   | 760 (11.3%)   | 651 (11.3%)    | 186 (10.9%)     | 57 (10.3%)    | 1654 (11.2%)       |         |
| Outer regional                   | 783 (11.7%)   | 653 (11.3%)    | 193 (11.3%)     | 64 (11.5%)    | 1693 (11.5%)       |         |
| Remote                           | 162 (2.4%)    | 141 (2.4%)     | 32 (1.9%)       | 13 (2.3%)     | 348 (2.4%)         |         |
| Very remote                      | 34 (0.5%)     | 39 (0.7%)      | 7 (0.4%)        | 4 (0.7%)      | 84 (0.6%)          |         |
| Unknown                          | 1 (0.01%)     | 0              | 0               | 0             | 1 (0.01%)          |         |
| Diagnosis period                 |               |                |                 |               |                    | 0.346   |
| 2000–2004                        | 2022 (30.1%)  | 1889 (32.7%)   | 452 (26.5%)     | 197 (35.4%)   | 4560 (30.9%)       |         |
| 2005–2009                        | 2368 (35.3%)  | 1881 (32.6%)   | 630 (36.9%)     | 223 (40.1%)   | 5102 (34.6%)       |         |
| 2010–2014                        | 2328 (34.7%)  | 2007 (34.7%)   | 626 (36.7%)     | 136 (24.5%)   | 5097 (34.5%)       |         |
| Vital status                     |               |                |                 |               |                    | <0.001  |
| Died                             | 720 (10.7%)   | 1186 (20.5%)   | 582 (34.1%)     | 436 (78.4%)   | 2924 (19.8%)       |         |
| Alive                            | 5998 (89.3%)  | 4591 (79.4%)   | 1126 (65.9%)    | 120 (21.6%)   | 11835 (80.2%)      |         |
| Cause of death                   |               |                |                 |               |                    | <0.001  |
| Breast cancer                    | 209 (29.0%)   | 680 (57.3%)    | 460 (79.0%)     | 391 (89.7%)   | 1740 (59.5%)       |         |
| Other cancers                    | 170 (23.6%)   | 136 (11.5%)    | 42 (7.2%)       | 19 (4.4%)     | 367 (12.6%)        |         |
| Non-cancer                       | 341 (47.6%)   | 370 (31.2%)    | 80 (13.8%)      | 26 (6.0%)     | 817 (27.9%)        |         |

Vital status and cause of death from cancer registry, censoring on 31 December 2014.

\*P value from one-way analysis of variance for age in years and  $\chi^2$  or ranked tests for others (see the Methods section).

IRSD, Index of Relative Socioeconomic Disadvantage; SEIFA, Socioeconomic Index for Areas.

country of birth, 70% were born in Australia, 17% in other predominantly English-speaking countries and 13% in predominantly non-English-speaking countries. SACR data indicated that 30% of the cohort were born outside of Australia. Of these, 50% were born in the UK/Ireland, 21% in Southern or Eastern Europe, 11% in Western Europe, 9% in Asia and 9% elsewhere. Almost three quarters (74%) resided in a major city, 11% in inner regional locations and 14% in outer regional, remote or very remote areas. The percentage by residential socioeconomic disadvantage ranged from 17% for the most disadvantaged to 22% for the least disadvantaged quintile. The percentage by diagnostic period increased from 31% for 2000–2004 to 35% for 2005–2009 and 2010–2014.

### Cancer stage

The TNM stage distribution was: stage I, 46%; stage II, 39%; stage III, 12%; and stage IV, 4%. Differences in stage were found in unadjusted analysis by age ( $p < 0.001$ ),

country of birth ( $p = 0.002$ ) and SEIFA disadvantage ( $p < 0.001$ ), but not by residential remoteness ( $p = 0.310$ ) or diagnostic period ( $p = 0.346$ ; [table 1](#)).

Compared with women aged  $< 50$  years at diagnosis, the adjusted OR for advanced stage was: 0.70 (95% CI 0.62 to 0.80) for ages 50–59 years, 0.60 (95% CI 0.53 to 0.69) for 60–69 years and 0.85 (95% CI 0.74 to 0.98) for 70–79 years. Higher adjusted risks of advanced stage tended occur in ages  $< 50$  years and 80+ years, although the difference for ages 80+ years compared with  $< 50$  years did not achieve statistical significance (OR 1.11, 95% CI 0.95 to 1.31; [table 2](#)).

Adjusted ORs for advanced cancer were lower among women of least residential socioeconomic disadvantage (Q4/Q5) than most disadvantage (Q1; OR 0.79 95% CI 0.68 to 0.92) for Q4 and OR 0.75 (95% CI 0.65 to 0.87) for Q5 (least disadvantage). Risk of advanced stage did

**Table 2** ORs (95% CIs) for diagnosis with advanced (tumour, node and metastases (TNM) III or IV) as opposed to more localised (TNM I or II) breast cancers diagnosed in 2000–2014 in South Australia\* (n=14 759)

| Characteristic                   | Case numbers—<br>advanced/all stages | OR for advanced<br>stage (unadjusted) | OR for advanced<br>stage* (adjusted) |
|----------------------------------|--------------------------------------|---------------------------------------|--------------------------------------|
| <b>Age at diagnosis (years)</b>  |                                      |                                       |                                      |
| <50                              | 587/3166                             | 1.00                                  | 1.00                                 |
| 50–59                            | 532/3902                             | 0.69 (0.61 to 0.79)                   | 0.70 (0.62 to 0.80)                  |
| 60–69                            | 475/3940                             | 0.60 (0.53 to 0.69)                   | 0.60 (0.53 to 0.69)                  |
| 70–79                            | 391/2392                             | 0.86 (0.75 to 0.99)                   | 0.85 (0.74 to 0.98)                  |
| 80+                              | 279/1359                             | 1.13 (0.98 to 1.33)                   | 1.11 (0.95 to 1.31)                  |
| <b>Country of birth</b>          |                                      |                                       |                                      |
| Australia                        | 1370/8918                            | 1.00                                  | 1.00                                 |
| Other English-speaking countries | 301/2144                             | 0.90 (0.79 to 1.03)                   | 0.91 (0.80 to 1.04)                  |
| Non-English-speaking countries   | 280/1695                             | 1.09 (0.95 to 1.26)                   | 1.08 (0.93 to 1.24)                  |
| Unknown                          | 316/2002                             | 1.04 (0.91 to 1.18)                   | 1.02 (0.89 to 1.16)                  |
| <b>Diagnostic period</b>         |                                      |                                       |                                      |
| 2000–2004                        | 649/4560                             | 1.00                                  | 1.00                                 |
| 2005–2009                        | 853/5102                             | 1.21 (1.08 to 1.35)                   | 1.20 (1.07 to 1.34)                  |
| 2010–2014                        | 762/5097                             | 1.06 (0.95 to 1.19)                   | 1.06 (0.95 to 1.19)                  |
| <b>Residential remoteness</b>    |                                      |                                       |                                      |
| Major city                       | 1078/10 979                          | 1.00                                  | 1.0                                  |
| Inner regional                   | 243/1654                             | 0.93 (0.81 to 1.08)                   | 0.96 (0.82 to 1.11)                  |
| Outer region/remote/very remote  | 313/2126                             | 0.94 (0.82 to 1.07)                   | 0.88 (0.77 to 1.02)                  |
| <b>SEIFA IRSD quintile</b>       |                                      |                                       |                                      |
| 1 (most disadvantaged)           | 450/2570                             | 1.00                                  | 1.00                                 |
| 2                                | 457/2987                             | 0.85 (0.74 to 0.98)                   | 0.87 (0.75 to 1.00)                  |
| 3                                | 467/2974                             | 0.88 (0.76 to 1.01)                   | 0.88 (0.76 to 1.01)                  |
| 4                                | 429/2939                             | 0.81 (0.70 to 0.93)                   | 0.79 (0.68 to 0.92)                  |
| 5 (least disadvantaged)          | 461/3287                             | 0.77 (0.67 to 0.89)                   | 0.75 (0.65 to 0.87)                  |

\*Adjusted ORs from logistic regression model including age, country of birth, diagnosis period, SES quintile and residential remoteness. IRSD, Index of Relative Socioeconomic Disadvantage; SEIFA, Socioeconomic Index for Areas.

not differ in adjusted analyses by country of birth or residential remoteness (table 2).

While the adjusted OR for advanced cancer was higher in 2005–2009 than the 2000–2004 baseline (OR 1.20, 95% CI 1.07 to 1.34), the difference between 2010–2014 and 2000–2004 was not significant (OR 1.06 95% CI 0.95 to 1.19).

Analyses by age showed heterogeneity for advanced stage by diagnostic period. During 2000–2004, women aged 80+ years were significantly more likely to have advanced stage than the reference age (<50 years; OR 1.50 95% CI 1.12 to 2.01) but significant corresponding associations were not observed in 2005–2009 (OR 1.16, 95% CI 0.90 to 1.50) or 2010–2014 (OR 0.82, 95% CI 0.62 to 1.10).

### Supplementary analysis

When the analysis was repeated subclassifying age <50 years as <40 and 40–49 years, adjusted ORs for advanced stage were essentially unchanged for sociodemographic factors. Compared with <40 years, the adjusted ORs were: 0.79 (0.64 to 0.97) for 40–49 years; 0.59 (0.48 to 0.72) for 50–59 years; 0.50 (0.41 to 0.62) for 60–69 years; 0.71 (0.58 to 0.88) for 70–79 years; and 0.93 (0.75 to 1.16) for 80+ years.

### Breast cancer mortality

Of the 14 759 women, 2924 (19.8%) had died from any cause and 1740 (11.8%) from breast cancer by the end of the study (table 1). Adjusted sub-HRs (SHRs; table 3) varied by: (1) stage—increasing with more advanced stage to 41.97 (95% CI 34.78 to 50.65) for stage IV compared with stage I; (2) age at diagnosis—increasing with age to 2.24 (95% CI 1.88 to 2.66) for age 80+ compared with <50 years; and (3) residential socioeconomic disadvantage—reducing to 0.73 (95% CI 0.62 to 0.87) for the least compared with most disadvantaged quintile. The adjusted risk of breast cancer death reduced, independently of stage and sociodemographic factors, in the later diagnostic periods compared with the 2000–2004 reference (SHR 0.75, 95% CI 0.67 to 0.83) for 2005–2009 and 0.57 (95% CI 0.48 to 0.67) for 2010–2014. Significant differences were not found in unadjusted or adjusted analyses by country of birth or residential remoteness.

### Supplementary analysis

When the analysis was repeated subclassifying age <50 years as <40 and 40–49 years, adjusted SHRs were essentially the same as in the earlier analysis by other sociodemographic factors and stage. Compared with <40 years, the adjusted SHRs were: 0.64 (0.52 to 0.80) for 40–49 years; 0.80 (0.65 to 0.97) for 50–59 years; 0.77 (0.62 to 0.94) for 60–69 years; 1.04 (0.84 to 1.28) for 70–79 years; and 1.63 (1.30 to 2.03) for 80+ years.

## DISCUSSION

A very similar stage distribution was found for staged invasive female breast cancers in South Australia in 2000–2014 to that for the Australian national study for 2011.<sup>5</sup>

This may reflect the common standards for screening, treatment and accreditation, and similar although not identical screening participation.<sup>20–22</sup>

Stage distributions were also similar in South Australia to distributions for staged breast cancers in Canada and England.<sup>5</sup> The distributions in South Australia (2000–2014) compared with Australia (2011), Canada (2013) and England (2012) were: (1) stage I—46% compared with 46%, 47% and 44% respectively; (2) stage II—39% compared with 37%, 35% and 39%, respectively; (3) stage III—12% compared with 13%, 12% and 10%, respectively; and (4) stage IV—4% compared with 5%, 6% and 7%, respectively<sup>5</sup> (figure 1).

These differences appear minor and smaller than anticipated, given potential effects of methodological and geographic differences.<sup>5</sup> The marginally higher proportion of early stage I and II of 85% for South Australia compared with 82% for Australia may also have been influenced by a marginally higher screening participation in South Australia.<sup>20 21</sup>

The proportion with advanced cancers (stage III or IV) was lower for ages 50–79 years than younger or older women. A similar pattern was seen for staged cancers in Australia (2011) where the age-standardised percentage with stages III or IV was 16% compared with 21% for younger and 25% for older women.<sup>5</sup> This likely reflects targeting of women aged 50–69 years for screening in 2000–2013 and availability of screening on demand from 70 years during the study period.<sup>1 2</sup> In addition, women aged 80+ years, through a higher prevalence of frailty and comorbidity, may have been slower to access clinical services.<sup>5</sup> Notably, a higher OR for advanced cancers presented in ages 80+ years than in younger women in 2000–2014, although this was less obvious for later diagnostic periods, especially 2010–2014, potentially reflecting a growing emphasis on early diagnosis in older women.<sup>22</sup> Supplementary analysis showed a lower OR for advanced cancer in women aged 40–49 than <40 years and in the 50–79 year age range, likely reflecting screening availability and potentially biological factors.<sup>1 2</sup>

Among women with breast cancer, the proportion by age ranged from 17% for the most disadvantaged quintile to 22% for the least disadvantaged, consistent with the Australia-wide gradient for 2010–2014.<sup>5</sup> Residents of the most disadvantaged quintile were at higher risk of advanced cancers than the least disadvantaged quintile in this study, which is confirmatory of the difference found nationally in 2011 (21% vs 16%).<sup>5</sup> Screening participation could have contributed, it being lower for disadvantaged than advantaged areas.<sup>5</sup> Although screening services have introduced initiatives to address needs of women from disadvantaged areas, more research into barriers and opportunities would be desirable.

The absence of differences in risk of advanced stages in our study by residential remoteness may reflect the reach of mobile screening clinics in rural areas. Differences also appeared small in the national survey with 18% of staged cases having advanced cancers among major city

**Table 3** Sub-HRs (SHRs; 95% CIs) for breast cancer-specific mortality in South Australia for invasive breast cancers diagnosed in 2000–2014 (n=14 759)

| Characteristic                    | Breast cancer death/death | Unadjusted SHR*        | Adjusted SHR†          |
|-----------------------------------|---------------------------|------------------------|------------------------|
| <b>TNM stage</b>                  |                           |                        |                        |
| I                                 | 209/720                   | 1.00                   | 1.00                   |
| II                                | 680/1186                  | 3.99 (3.42 to 4.65)    | 3.87 (3.32 to 4.53)    |
| III                               | 460/582                   | 10.69 (9.09 to 12.57)  | 10.87 (9.22 to 12.81)  |
| IV                                | 391/436                   | 45.82 (38.15 to 55.03) | 41.97 (34.78 to 50.65) |
| <b>Age at diagnosis (years)</b>   |                           |                        |                        |
| <50                               | 365/405                   | 1.00                   | 1.00                   |
| 50–59                             | 404/526                   | 0.83 (0.77 to 1.02)    | 1.10 (0.95 to 1.27)    |
| 60–69                             | 342/556                   | 0.78 (0.68 to 0.90)    | 1.05 (0.91 to 1.22)    |
| 70–79                             | 329/699                   | 1.31 (1.13 to 1.52)    | 1.43 (1.22 to 1.67)    |
| 80+                               | 300/738                   | 2.22 (1.89 to 2.59)    | 2.24 (1.90 to 2.66)    |
| <b>Country of birth</b>           |                           |                        |                        |
| Australia                         | 1049/1777                 | 1.00                   | 1.00                   |
| Other English-speaking countries  | 247/412                   | 0.98 (0.85 to 1.12)    | 1.01 (0.87 to 1.17)    |
| Non-English-speaking countries    | 200/346                   | 1.02 (0.87 to 1.18)    | 0.98 (0.84 to 1.15)    |
| Unknown                           | 244/389                   | 1.08 (0.94 to 1.25)    | 1.15 (1.00 to 1.33)    |
| <b>Diagnostic period</b>          |                           |                        |                        |
| 2000–2004                         | 884/1512                  | 1.00                   | 1.00                   |
| 2005–2009                         | 654/1076                  | 0.81 (0.73 to 0.90)    | 0.75 (0.67 to 0.83)    |
| 2010–2014                         | 202/336                   | 0.62 (0.53 to 0.72)    | 0.57 (0.48 to 0.67)    |
| <b>Residential remoteness</b>     |                           |                        |                        |
| Major city                        | 1302/2186                 | 1.00                   | 1.00                   |
| Inner regional                    | 185/313                   | 0.99 (0.85 to 1.16)    | 1.01 (0.86 to 1.20)    |
| Outer regional/remote/very remote | 253/425                   | 1.01 (0.88 to 1.15)    | 0.97 (0.84 to 1.13)    |
| <b>SEIFA IRSD quintile</b>        |                           |                        |                        |
| 1 (most disadvantaged)            | 364/605                   | 1.00                   | 1.00                   |
| 2                                 | 371/604                   | 0.88 (0.76 to 1.02)    | 0.93 (0.79 to 1.09)    |
| 3                                 | 353/613                   | 0.80 (0.69 to 0.93)    | 0.85 (0.72 to 0.99)    |
| 4                                 | 328/544                   | 0.79 (0.68 to 0.92)    | 0.85 (0.73 to 1.00)    |
| 5 (least disadvantage)            | 324/558                   | 0.67 (0.58 to 0.78)    | 0.73 (0.62 to 0.87)    |

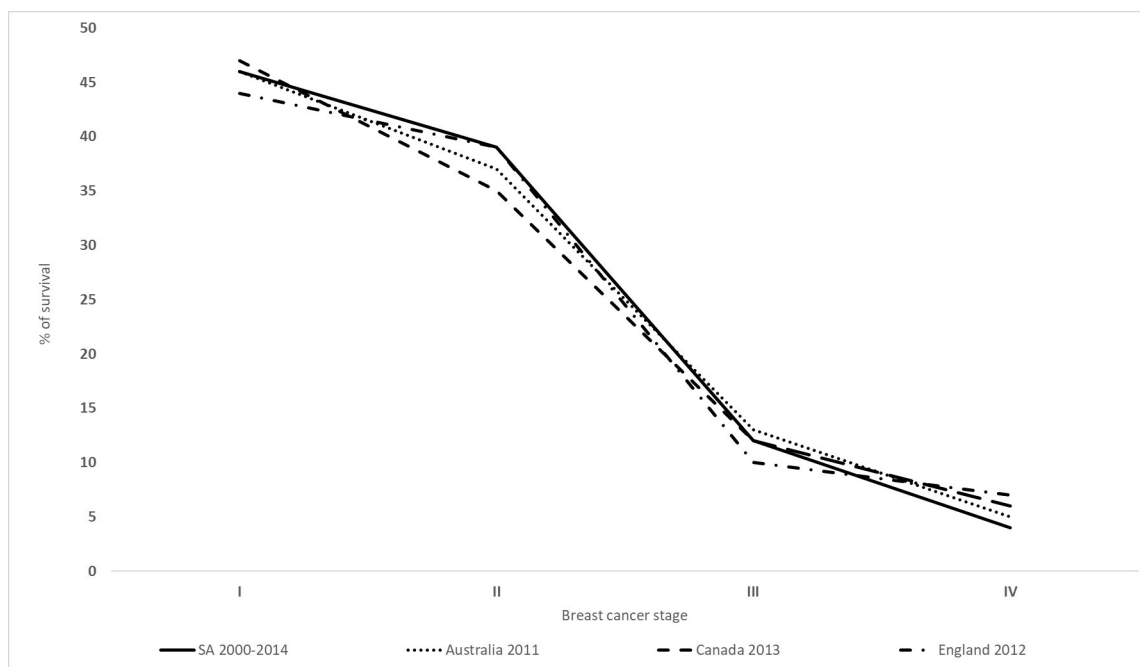
\*Unadjusted SHRs derived from univariate competing risk regression modelling, deaths followed to 31 December 2014.

†Adjusted SHRs derived from multivariate competing risk regression model adjusting by including cancer stage, age, country of birth, diagnosis period, residential remoteness and Socioeconomic Index for Areas (SEIFA) quintile. IRSD, Index of Relative Socioeconomic Disadvantage.

residents compared with 17% for regional areas and 20% for remote and very remote areas.<sup>5</sup> The absence of a difference in risk by country of birth in the present study is reassuring from an equity perspective.

Predictably the proportion of cases dying from breast cancer increased with TNM stage (from 3% for stage I to 70% for stage IV). Adjusted analyses confirmed stage to be the strongest predictor of survival. The National BreastScreen Evaluation Report of 2009, using data sourced from the Victorian Cancer Registry, indicated that the percentage of breast cancers with diameters  $\leq 15$  mm was higher at 64% in women notified through BreastScreen

than the 39% for other women in the 50–69 year age range, which likely contributed to the BreastScreen-related survival advantage.<sup>23</sup> An Expert Panel from 16 countries assembled by the International Agency for Research on Cancer reported in 2015 that participation of women aged 50–69 years in mammography screening can reduce the risk of breast cancer death by approximately 40%.<sup>24</sup> In addition, the national study showed a 5-year relative survival of 91% for 2011–2015 for all stages combined, but varying markedly by stage (ie, >95% of women with stages TNM I and II survived 5 years compared with 81% for stage III and 32% for stage IV).<sup>5</sup>



**Figure 1** % of breast cancer survival by cancer stage in South Australia (SA) comparing with other countries during 2000–2014. Data source: Cancer Australia.<sup>5</sup>

Older age at diagnosis was predictive of lower survival in the present study, with the lowest survival applying to ages 80+ years. The national study provided consistent findings with the lowest 5-year relative survival of 81% applying to women aged 75+ years.<sup>5</sup> Supplementary analysis with a finer age breakdown confirmed the lowest survival to apply to 80+ ages in the present study.

Socioeconomic status was also predictive with residents of the least disadvantaged areas having the highest survival. This is consistent with national data for 2006–2010.<sup>5</sup> Factors potentially responsible warrant further study and could include artificial effects of lead time and overdiagnosis, plus real effects due to differences in health literacy, variations in engagement with health protection, competing pressures on time and resources by level of disadvantage, and a tendency for lower screening participation in the most disadvantaged areas.<sup>5</sup>

A major increase in survival outcomes was evident in more recent diagnostic periods, which is also seen in the national data where 5-year relative survival increased from 72% in 1984–1988 to 91% in 2010–2014.<sup>5</sup> This may reflect combination effects of artificial influences from differences in lead time and overdiagnosis, plus real benefits from screening and treatment advances, among them an increased use of specialised breast cancer centres and advances in adjuvant therapies.<sup>24</sup> The more advanced breast cancer stage distribution for South Australia in 2005–2009 was unexpected and warrants further investigation. These years represented the end of the film-reading era prior to transfer to digital technology. Despite this peak in advanced cases, it is reassuring to see a steady secular increase in survival.

The present study follows the national study of stage.<sup>5</sup> Stage was derived from pathology reporting and hospital reporting and stage distributions were checked with statistical profiles from the Quality Audit of Breast Surgeons of Australia and New Zealand.<sup>7</sup> Results complement earlier data: from New South Wales, Australia, based on localised, regional and distant Surveillance, Epidemiology, and End Results program (SEER) Summary Stage, where a similar survival gradient was observed with higher stage for follow-up limited to  $\leq 3$  years from diagnosis<sup>25 26</sup>; and on breast cancer mortality trends for Australia which did not include data on stage or survival.<sup>27</sup>

Limitations included restricting stage to four major categories to avoid inconsistencies due to changes at a more detailed level across versions of AJCC TNM coding. Further efforts are needed to improve accuracy of staging, although the 96% coverage of invasive cancers with staging was high and similar to coverage observed in other studies in Australia, Canada and England.<sup>5</sup> Another limitation was lack of adjustment for postdiagnostic explanatory variables such as treatment practices, which may have affected sociodemographic survival differences. We plan to address these aspects in a further investigation of linked data.

Data on race and ancestry were not available for this study. While Indigenous status is recorded, numbers were too small for meaningful analysis. We therefore used country of birth as a crude marker of diversity according to whether predominantly English speaking. It is important with increasing ethnic diversity in Australia that greater attention be given to ethnic descriptors in health data collections.

## CONCLUSIONS

Stage was a stronger predictor of survival outcome than sociodemographic predictors. Achieving earlier diagnosis outside the original screening target of 50–69 years and in residents of socioeconomically disadvantaged areas likely would further increase cancer survival at a population level. The present data show plausible stage distributions and effects on survival, using readily available data for staging. The uptake of voluntary screening from age of 40 years may improve outcomes for patients under 50 years and more targeted screening for patients with genetic risk and breast density may have positive impacts.

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