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Geographical differences in risk of advanced breast cancer: Limited evidence for reductions over time, Queensland, Australia 1997–2014

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ABSTRACT

Background: Reducing geographical inequalities in breast cancer stage remains a key focus of public health policy. We explored whether patterns of advanced breast cancer by residential accessibility and disadvantage in Queensland, Australia, have changed over time.

Methods: Population-based cancer registry study of 38,706 women aged at least 30 years diagnosed with a first primary invasive breast cancer of known stage between 1997 and 2014. Multilevel logistic regression was used to examine temporal changes in associations of area-level factors with odds of advanced disease after adjustment for individual-level factors.

Results: Overall 19,401 (50%) women had advanced breast cancer. Women from the most disadvantaged areas had higher adjusted odds (OR = 1.23 [95%CI 1.13, 1.32]) of advanced disease than those from least disadvantaged areas, with no evidence this association had changed over time (interaction p = 0.197). Living in less accessible areas independently increased the adjusted odds (OR = 1.18 [1.09, 1.28]) of advanced disease, with some evidence that the geographical inequality had reduced over time (p = 0.045). Sensitivity analyses for un-staged cases showed that the original associations remained, regardless of assumptions made about the true stage distribution.

Conclusions: Both geographical and residential socioeconomic inequalities in advanced stage diagnoses persist, potentially reflecting barriers in accessing diagnostic services. Given the role of screening mammography in early detection of breast cancer, the lack of population-based data on private screening limits our ability to determine overall participation rates by residential characteristics. Without such data, the efficacy of strategies to reduce inequalities in breast cancer stage will remain compromised.

1. Introduction

Breast cancer is the most common invasive cancer affecting women worldwide [1]. One of the strongest predictors of survival is stage at diagnosis [2,3], with disparities in stage being shown to be a key driver of inequalities between population subgroups in long-term prognosis [2,4]. There is substantial evidence that the proportion of women diagnosed with advanced disease varies by geographical location, with numerous studies reporting an association between increasing area-level disadvantage and more advanced disease [3,5–11], although this was not always significant [12,13]. Two recent systematic reviews [14,15] concluded that women from rural areas were more likely to experience advanced disease than their urban counterparts, despite inconsistencies across some individual studies.

We have previously reported that the risk of presenting with

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Abbreviations

Queensland Cancer Registry QCR
Statistical Area Level 2 SA2

advanced breast cancer in Queensland, Australia from 1997 to 2006 was higher among women from more remote and disadvantaged areas [6]. Since then, various initiatives designed to improve cancer services across Australia for women from remote and other underserved areas have been implemented, including the deployment of mobile digital screening units [16] and the expansion of regional cancer infrastructure [17]. However, to the best of our knowledge, there has been no assessment at a population level of whether such initiatives have impacted stage distribution across geographical areas over time.

This study examines whether variations in the risk of advanced breast cancer by geographical accessibility and residential disadvantage have reduced over time in Queensland.

2. Material and methods

Approval was obtained from the data custodian, Queensland Health to use these de-identified routinely collected incidence data.

Information for all women aged at least 30 years diagnosed with a histologically verified first primary invasive breast cancer (ICD-O3 C50) in Queensland between January 1, 1997 and December 31, 2014 (inclusive) were extracted from the Queensland Cancer Registry (QCR) [18]. The choice of lower age limit was based on the small number of cases among women younger than 30 years ($n = 228$, <0.05% of cases). Notification of all cancers diagnosed in Queensland to the QCR is a statutory requirement. Data quality is high, with 99% of all female breast cancer cases histologically verified and only 0.6% diagnosed through death certificates in 2013 [18].

Although the QCR does not record stage information, routinely collected data since 1997 on maximum tumour diameter and lymph node status allowed a proxy measure of stage at diagnosis to be determined [6]. Cases were defined as 'localised' (Stage I) if ≤ 20 mm diameter with no evident nodal spread or metastases while Stage II, III and IV cancers which could not be distinguished based on available information were collectively combined as 'advanced' [6]. For women with multiple primary breast cancers, we included only the most advanced case. Around 5% of cases were un-staged and these were excluded from the primary analysis, consistent with our previous work [6]. However, as changing proportions of un-staged cases may affect the proportion of advanced stage diagnoses, sensitivity analyses were performed with an expanded cohort of women including un-staged cases to assess the impact of various assumptions about their true stage.

The geographical unit was the Statistical Area Level 2 (SA2) [19]. Each woman's geocoded residential address at diagnosis was mapped to the 2011 SA2 boundaries. Women were then classified into three accessibility groups (Table 1) based on the travel time from their SA2 to the closest radiation treatment facility, which are typically located in major hospitals in Queensland [20] and as such better reflect access from the viewpoint of optimal cancer care than more generic area-based remoteness classifications [21]. Area-level disadvantage was quantified using the 2011 census-based Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD [22]. Women lacking geographical information ($n = 44$, 0.2%) were excluded.

2.1. Analyses

2.1.1. Model development

Multilevel logistic regression was used to simultaneously evaluate the independent association of area- and individual-level predictors with advanced breast cancer while accounting for between-area variance. Models were fitted with Markov chain Monte Carlo (MCMC) simulations [23] in MLwiN [24] version 2.35 (University of Bristol, United Kingdom) interfaced with Stata 14 (StataCorp, Texas) [25]. Chain convergence was checked with Raftery-Lewis and Brooks-Draper diagnostics and visual inspection of the trace, density and autocorrelation plots of the posterior distributions for monitored parameters [23]. Parameter estimates were based on 80,000 iterations (with every 10th iteration kept) after the initial 40,000 iterations. Models were compared using the Bayesian deviance information criterion (DIC) with smaller values (≤ 7) indicating better fit [26].

Age was collapsed into 5-year age groups from 30 to 34 to 75–79 years with those aged above 80 years included in the 80 + category. Exploratory analyses found little difference in model fit between various transformations of the continuous age variable or collapsing it into categories. Women aged at least 40 are eligible for publicly-funded mammography screening in Australia, while those aged 50–69 were actively recruited for screening during the study period [27].

Year of diagnosis was transformed using restricted cubic splines to allow for non-linearity, with four degrees of freedom. Trend analyses were performed by including this transformed measure in the models, along with interaction terms for areal-level covariates, to examine whether the trends varied by these covariates.

Models were developed systematically. First, a null model (Model 1) consisting of individuals nested in SA2s without covariates was fitted to quantify the variance between areas. Individual-level characteristics (Model 2) were then added followed by area-level accessibility (Model 3) or disadvantage (Model 4) with the full main-effects model (Model 5) being simultaneously adjusted for all covariates. Interactions were assessed by adding relevant second-order terms for geographical accessibility (Model 6) or residential disadvantage (Model 7) to Model 5.

Additional linear regression models were used to explore covariate effects for continuous variable tumour size, transformed to the log scale to reduce its skewness.

2.1.2. Model predictions

Statistical analyses were performed using Stata/SE version 14 (StataCorp, TX, USA). Significance of individual coefficients, interaction terms and area-level random effect were assessed with the Wald test (significant if $p \leq 0.05$, two-sided).

Fixed parameter estimates are presented as odds ratios (OR) with their 95% confidence intervals (CI) [28]. Adjusted OR's for the transformed year of diagnosis were estimated from the predicted probabilities. The model-derived probabilities of women with advanced breast cancer diagnoses were obtained by an inverse-transformation of the linear predictor (and associated CI) to the probability scale, and expressed as a percentage.

Sensitivity analyses to explore the impact of unknown stage on observed associations were performed by repeating analyses with an expanded cohort assuming that all un-staged cases were (i) localised; (ii) advanced or (iii) randomly distributed equally over both these categories. Associations of covariates with odds of unknown (versus known) stage at diagnosis were also assessed with multilevel logistic regression.