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Comparison of quadrant-specific breast cancer incidence trends in the United States and England between 1975 and 2013

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ABSTRACT

Background: UK breast cancer incidence rates suggest that upper outer quadrant (UOQ) cancers have risen disproportionately compared with other areas over time. We aimed to provide a comparison of the trend in quadrant-specific breast cancer incidence between the United States (US) and England, and determine whether a disproportionate UOQ increase is present.

Methods: Surveillance Epidemiology and End Results (SEER) cancer registry data were obtained on 630,007 female breast cancers from 1975 to 2013. English cancer registry data were obtained on 1,121,134 female breast cancers from 1979 to 2013. Temporal incidence changes were analysed using negative binomial regression. Interaction terms determined whether incidence changes were similar between sites.

Results: English breast cancer incidence in the UOQ rose significantly from 13% to 28% from 1979 to 2013 whereas no significant increase was observed among SEER data. The significant interaction between quadrant and year of diagnosis ($p < 0.001$) in both SEER and English data indicates that breast cancer incidence in each quadrant changed at a different rate. Incidence in the UOQ rose disproportionately compared to the nipple (SEER IRR = 0.81, $p < 0.001$; England IRR = 0.78, $p < 0.001$) and axillary tail (SEER IRR = 0.87, $p = 0.018$; England IRR = 0.69, $p < 0.001$) in both SEER and England. In addition, incidence rose disproportionately in the UOQ compared to non-site-specific tumours in England (Overlapping lesions IRR = 0.81, $p = 0.002$; NOS IRR = 0.78, $p < 0.001$). The proportion of non-site-specific tumours was substantially higher in England than SEER throughout the study period (62% in England; 39% in SEER).

Conclusions: Breast cancer incidence in the UOQ increased disproportionately compared to non-site-specific tumours in England but not in SEER, likely due to the decrease in non-site-specific tumours observed in England over time. There may be real differences in incidence between the two countries, possibly due to differences in aetiology, but is much more likely to be an artefact of changing data collection methods and improvements in site coding in either country.

1. Introduction

The Upper Outer Quadrant (UOQ) is the most frequent tumour site of breast cancer [1–4], comprising 25% of all breast cancers in the UK [1] and 36% in a SEER-based study [5]. It is unclear why breast cancer is more frequently diagnosed in the UOQ than in any other quadrant although it is generally accepted that the greater proportion of epithelial tissue in this region is the main contributor [2,3]. Previous research has shown that the reported incidence of breast cancer in the UOQ is not only greater, but according to data from the UK, is also rising disproportionately over time compared to other quadrants [6]; suggesting that the higher incidence in this quadrant may be due to other causes, rather than just the greater amount of epithelial tissue.

The Surveillance Epidemiology and End Results (SEER) program collect and provide information on cancer registrations for a subset of the population in the United States of America (US). English cancer registries and the SEER program provide large population-based cohorts of breast cancer survivors. Previous studies [7,8] have suggested that breast cancer incidence is higher in the SEER

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program than English registries due to differing rules for defining multiple primary breast cancers. SEER have developed their own rules for defining multiple primary cancers [9], whereas England closely follow the International Agency for Research on Cancer (IARC) rules [10], which tend to be more stringent. The introduction of breast screening in the US and the UK, together with advances in diagnostic testing, have led to improvements in the accuracy of data collection [11,12]. Changes in accuracy of data over time and differing definitions have been shown to have an influence on cancer intelligence and must be taken into consideration throughout this study [7,8,11,13–15].

The aim of this study was to provide a comparison of the trend in quadrant-specific breast cancer incidence between the US and England, and to investigate whether the apparent disproportionate increase in incidence of female breast cancer in the UOQ previously reported in the UK was also observed in the US. Findings are reported from the first study to investigate quadrant-specific breast cancer incidence data in the US.

2. Methods

2.1. Data collection—SEER

Data was collected from the SEER 9 program of the National Cancer Institute (NCI) in the US. The SEER 9 program collects information on cancer incidence from 9 population-based registries in the US (Connecticut, Hawaii, Iowa, New Mexico, Utah, San Francisco-Oakland, Seattle-Puget Sound, Michigan and Atlanta) [16]. The SEER 9 registries account for approximately 9.4% of the US population, have a standard case ascertainment of 98% and are considered to be the standard for quality control worldwide [9]. The number of malignant female breast cancers reported (1973–2013) were obtained through the SEER*stat statistical software [17]. Information on age at diagnosis (5-year bands) and quadrant of the breast were also obtained. Quadrant information was extracted using the following ICD-O-3 topography codes: C50.0 Nipple, C50.1 Central portion, C50.2 Upper Inner Quadrant (UIQ), C50.3 Lower Inner Quadrant (LIQ), C50.4 Upper Outer Quadrant (UOQ), C50.5 Lower Outer Quadrant (LOQ), C50.6 Axillary Tail, C50.8 Overlapping lesions and C50.9 Not otherwise specified (NOS). Data submitted to SEER in previous versions of ICD-O, were converted by SEER into ICD-O-3. Cancer site definitions were consistent over time due to no changes occurring between ICD-O-2 and ICD-O-3 regarding the definition of breast cancer [9].

2.2. Data collection—England

The Office for National Statistics provided the number of malignant female breast cancers along with information on quadrant and age at diagnosis (5-year bands) from 1979 to 2013 for England. England collects information on cancer incidence on a national basis with the use of regional cancer registries. It was estimated that in 2006 ascertainment of cancer in England was 98–99% complete [13] and so comparable to SEER. Quadrant information was extracted using the following ICD-9 (for cancers diagnosed 1979–1994) and ICD-10 (for cancers diagnosed 1995–2013) codes: 174.0/C50.0 Nipple, 174.1/C50.1 Central portion, 174.2/C50.2 Upper Inner Quadrant (UIQ), 174.3/C50.3 Lower Inner Quadrant (LIQ), 174.4/C50.4 Upper Outer Quadrant (UOQ), 174.5/C50.5 Lower Outer Quadrant (LOQ), 174.6/C50.6 Axillary Tail, 174.8/C50.8 Overlapping lesions and 174.9/C50.9 Not otherwise specified (NOS). ICD-9 and ICD-10 for malignant breast cancer are comparable to ICDO-3 topography codes that are used by the SEER program.

2.3. Statistical analysis

Seattle (Puget Sound) and Atlanta (Metropolitan) registries joined SEER 9 in 1974 and 1975, respectively, therefore to ensure all registries were included for the entire time frame 1973 and 1974 were excluded from all analyses using SEER data. Incidence rates for all malignant female breast cancers combined as well as for each quadrant were calculated by dividing the observed number of breast cancers by the mid-year general population estimates for each age stratum (5-year bands) and year of diagnosis (SEER: 1975–2013; England: 1979–2013). Incidence rates presented graphically were age-standardised to the World (WHO 2000–2025) Standard Population [18]; this enabled a direct comparison between rates in SEER 9 and England.

Changes in breast cancer incidence over time by age group (<40, 40–44, 45–49.....75–79, 80–84, 85+), quadrant and year of diagnosis were explored using negative binomial regression. Negative binomial regression was preferred to Poisson regression due to over-dispersion from non-zero counts yielding better model fit. A model was fitted to estimate the incidence rate ratios (IRR) adjusting for age group (<40 years taken as baseline), year of diagnosis and quadrant (UOQ baseline). Year of diagnosis was centered and multiplied by 10 to provide IRR by decade, to enable easier interpretation. Linearity of year of diagnosis was tested and higher powers were also considered (quadratic and cubic). Interactions were tested between age group and year, age group and quadrant and year and quadrant. IRRs for interactions can be interpreted as ratios of IRRs. Interactions were tested between $(\text{year})^2$ and quadrant, and $(\text{year})^3$ and quadrant, however these were not significant. Akaike's Information Criterion [19] values were also virtually identical for non-linear terms for year of diagnosis, so the simpler linear model without non-linear interactions was chosen to allow easier interpretation. IRR and the percentage change in incidence of breast cancer in each quadrant were calculated per decade, using the following calculation: the change in baseline incidence multiplied by the change in incidence within each quadrant. To provide an overall estimate of whether UOQ increases were different to all other quadrants combined, we refitted the negative binomial regression with a new definition of quadrant (UOQ, specific quadrant excluding UOQ and non-specific [overlapping and NOS]). All statistical analyses were carried out in Stata v.14.0 [20].

2.4. Sensitivity analysis—improvement in site-coding over time

To investigate how much of an effect the improvement in site-coding accuracy contributed to the change in incidence for specific sites, sensitivity analyses were conducted. The proportion of each specific site (excluding overlapping lesions and NOS) was calculated for the years 1975, 1996 and 2013 for the SEER registry and 1979, 1996 and 2013 for England. This proportion was then used to equally distribute the non-specific-site codes (overlapping lesions and NOS) across specific sites (results can be found in Online Tables 3–4).

In cancer registries, it is unlikely that 100% of cancer registrations would have a specific site code; therefore further sensitivity analyses were conducted accounting for a proportion of non-site-specific tumours. The proportion of non-site-specific tumours for the most recent year (2013) was used as the standard level of missingness across all other years. The proportion of non-site-specific tumours over this standard level of missingness was then distributed equally among all other sites (results can be found in Online Tables 5–6).