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Socio-economic patterning in early mortality of patients aged 0–49 years diagnosed with primary bone cancer in Great Britain, 1985–2008

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ABSTRACT

Background: Studies have shown marked improvements in survival between 1981 and 2000 for Ewing sarcoma patients but not for osteosarcoma. This study aimed to explore socio-economic patterning in early mortality rates for both tumours.

Procedure: The study analysed all 2432 osteosarcoma and 1619 Ewing sarcoma cases, aged 0–49 years, diagnosed in Great Britain 1985–2008 and followed to 31/12/2009. Logistic regression models were used to calculate risk of dying within three months, six months, one year, three years and five years after diagnosis. Associations with Townsend deprivation score and its components were examined at small-area level. Urban/rural status was studied at larger regional level.

Results: For osteosarcoma, after age adjustment, mortality at three months, six months and one year was associated with higher area unemployment, OR = 1.05 (95% CI 1.00, 1.10), OR = 1.04 (95% CI 1.01, 1.08) and OR = 1.04 (95% CI 1.02, 1.06) respectively per 1% increase in unemployment. Mortality at six months was associated with greater household non-car ownership, OR = 1.02 (95% CI 1.00, 1.03). For Ewing sarcoma, there were no significant associations between mortality and overall Townsend score, nor its components for any time period. For both tumours increasing mortality was associated with less urban and more remote rural areas.

Conclusions: This study found that for osteosarcoma, early mortality was associated with residence at diagnosis in areas of higher unemployment, suggesting risk of early death may be socio-economically determined. For both tumours, distance from urban centres may lead to greater risk of early death.

1. Introduction

Initiatives by the National Cancer Research Institute (NCRI), the National Cancer Intelligence Network (now the National Cancer Registration and Analysis service) and the National Awareness and Early Diagnosis Initiative (NAEDI) have highlighted the need for early diagnosis of cancer to improve survival [1]. Studies have suggested that childhood bone cancer has a longer time to diagnosis compared to some other childhood cancers and that a longer time to diagnosis is associated with older age for bone cancer in children, teenagers and young adults (TYA) [2,3]. The TYA age (13–24 years) group represents a unique challenge to the UK National Health Service as they often straddle paediatric and older adult services, experience variation in treatment protocols compared to younger children and have to cope with a cancer diagnosis during a key developmental part of their lives [4].

Previous studies have analysed incidence and survival from primary bone tumours using data from the northern part of England. In those analyses, over the twenty year period from 1981 to 2000 there were marked improvements in survival from Ewing sarcoma for children and for all patients aged less than 40 years at time of diagnosis, whereas no improvements were seen in survival from osteosarcoma [5,6]. A

Abbreviations: AIC, Akaike information criterion; CI, confidence interval; ICD-O-3, International Classification of Diseases for Oncology Third Edition; NAEDI, National Awareness and Early Diagnosis Initiative; NCIN, National Cancer Registration and Analysis Service; NCRI, National Cancer Research Institute; OR, odds ratio; pph, persons per hectare; SAU, small area unit; TYA, teenagers and young adults

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previous national study of osteosarcoma and Ewing sarcoma survival data for those aged 0–39 years did not fully investigate geographical patterns in survival rates [7]. A study from Germany showed that delays in diagnosis of bone tumours may be greater for patients resident in rural areas [8]. Differences in survival between countries have also been demonstrated. A comparative survival analysis of Ewing sarcoma patients between the UK and Germany found that survival rates were lower for UK patients [9]. Furthermore, a recent study from the USA suggested that socioeconomic factors influence overall survival for osteosarcoma [10]. Taken together these previous findings suggest that there are geographically determined factors which are related to mortality and survival amongst patients diagnosed with bone tumours.

The aims of the present study were to determine if socio-economic patterning in early mortality rates for osteosarcoma and Ewing sarcoma were modulated by age, gender, area based measures of deprivation, and residence in urban or rural areas. This should provide better understanding of the possible reasons for longer time to diagnosis in the UK compared to other similar countries. It should also allow the reasons for lack of improvement in early mortality, especially for osteosarcoma, to be elucidated.

2. Methods

2.1. Study subjects

The study population consisted of patients diagnosed with osteosarcoma or Ewing sarcoma in Great Britain between 1985 and 2008. Patients were followed to 31/12/2009 or date of death if earlier. The age range was limited to 0–49 years since there were very few Ewing sarcoma cases above this age and osteosarcoma over 50 years is most often associated with Paget's disease or is usually secondary to radiotherapy [11,12].

The patient data were accessed from the ten former regional cancer registries that covered the whole of Great Britain. Patient data from the National Registry of Childhood Tumours [13] were also extracted and used to cross-check accuracy of data for those aged 0–14 years obtained from the regional registries. Analyses of these data showed similar results, and thus provided reassurance regarding data accuracy. The necessary regulatory and ethical approvals were obtained (UK National Research Ethics Service reference number 11/NE/0298).

2.2. Diagnostic groups

Cases were classified into diagnosis groups using the International Classification of Diseases for Oncology, third edition (ICD-O-3) [14]. The coding used information on both morphology and topography. Two specific diagnostic groups were specified a priori: (i) osteosarcoma (ICD-O-3 topography codes for sites classified as bones and joint: C400-C403, C408-C414, C418-C419 and associated morphology codes 9180/3, 9181/3, 9182/3, 9183/3, 9184/3, 9185/3, 9186/3, 9187/3, 9192/3, 9193/3, 9194/3, 9195/3) and (ii) Ewing sarcoma (ICD-O-3 topography codes for sites classified as bones and joint: C400-C403, C408-C414, C418-C419, C760-C768 and associated morphology codes 9260/3, 9261/3).

2.3. Outcome

The possibility that time to diagnosis could increase in older age groups suggested that survival time might not be a robust outcome measure and mortality, as defined by the number of deaths in specified time intervals, would be more appropriate. Survival was recorded in the dataset as time in days from date of diagnosis to date of death or 31/12/2009 if vital status was recorded as alive at that date. Extremely early death is unusual in bone sarcoma and therefore patients with survival time equal to 0 days were excluded from the analysis on the assumption that their true survival time was unknown. Mortality at each time point after diagnosis of three months, six months, one year, three years and five years was calculated where vital status was recorded as died and survival time was not greater than 91, 182, 365, 1096, or 1826 days respectively.

2.4. Boundary data

Widespread boundary changes impede analyses over a prolonged time span, particularly at the small area level. Geo-referenced bone cancer registration data were linked to 2001 census boundaries [15]. The census boundaries consisted of wards in England and Wales (0–49 population ranges from 297 to 29,300, median = 3090) and postcode sectors in Scotland (0–49 population ranges from 23 to 15,916, median = 3201). In England and Wales analyses were performed at the small area census ward level and in Scotland at the postcode sector level. The term small area unit (SAU) is used for convenience throughout this article.

There are no formal urban/rural classifications of wards/postal sectors or other small areas that cover the whole of Great Britain and therefore two ways of examining the urban/rural nature of areas were chosen. First, a scheme developed in 1991 by Office of Population Censuses and Surveys and updated by Champion and Norman was used. This grouped local authority areas into 13 area types ranging from 'Inner London' to 'Remoter rural'. Secondly, a measure was created using 'persons per hectare' (pph) in the following way; a SAU with > 33 pph was classified as 'Most urban', 26–33 pph 'Very urban', 13–26 pph 'Urban', 1–13 pph 'Rural' and < 1 pph 'Most rural'.

2.5. Demographic data

Adjustment for deprivation was made using an area based, time-series of cross-sectional indicators. These were obtained from each of the censuses during the study period and geographically converted to be compatible with the 2001 SAUs [15]. The Townsend index is often used in similar geographical studies and comprises four components on unemployment, non-car ownership, non-home ownership and household overcrowding. To take account of any changes in deprivation for every SAU at the different time points, each Townsend component was expressed as a z-score relative to the GB average level over the study period. At each census time point, the z-scores were summed, equally weighted, to provide a set of deprivation scores in every SAU [16].

2.6. Statistical analysis

Logistic regression models analysed the odds of dying within three months, six months, one year, three years and five years after diagnosis. Three year and five year follow up data were only available for patients diagnosed 1985–2006 and 1985–2004 respectively and therefore the analyses of these time periods were carried out on a subset of the patients analysed at the shorter time periods.

Associations with a time series of Townsend deprivation score and its components were examined at small-area level. The ecological (independent) variables were the census-derived small-area characteristics, which were allocated to the 2001 census geography using Norman's method [15].

A series of univariable and multivariable models were fitted separately for osteosarcoma and Ewing sarcoma and included the following independent variables: sex, age group at diagnosis (0–14, 15–19, 20–39 and 40–49 years), area based population density, Townsend score (as a composite). The four components of the Townsend score (percentage of overcrowded homes, percentage of households without a car, percentage of persons unemployed and percentage of homes that are not owner occupied) were included in separate models that did not include the composite score. Multivariable models comprised those variables which had shown a statistically significant relationship with mortality in a univariable model but only fitted if one of the variables was a