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Cancer of Unknown Primary (CUP): a Cancer Registry study of factors affecting access to diagnosis

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Abstract

A potential impact of the centralisation of cancer services in the UK is difficulty in gaining access for members of the population living far from them. This could lead to delayed presentation of cancer with more advanced disease and clinical deterioration at diagnosis. A patient may be recorded in the cancer registry as having cancer of unknown primary (CUP) if the clinical state at presentation precludes investigation. Other patients may be so recorded if investigation identifies sites of metastatic tumour but the primary is not found. We hypothesised that the first group would include more patients who experienced difficulties in gaining access to health services through residing in deprived areas or through poorer geographical access to healthcare facilities. To test this, we compared the diagnosis of CUP with a comparator tumour, carcinoma of the rectum where diagnosis is facilitated by an alarm symptom and where variations in access are lower. Records from the Northern and Yorkshire Cancer Registry from 1994-2002 with ICD 10 C77-C80 (CUP, including categories where investigations may have been incomplete or no primary cancer was found) and C20 (malignant neoplasm of rectum) were combined with travel time to services (primary care, secondary and tertiary services) and the Index of Multiple Deprivation (IMD). Logistic regression modelled predictors of CUP compared to C20 and, within CUP, the odds of a histological basis of diagnosis.

The registry classified 7,428 patients as C80, 8,849 as C77-79, and 10,804 as C20. Compared to C20, the number of cases of C80 showed a statistically significant increasing trend with

increasing travel time to primary care. Risk also increased strongly with age, and deprivation. Results for C77-C79 were similar to those for C80, except that the travel time to primary care showed no effect. Considering all CUP alone, histological diagnosis significantly declined with travel time to the nearest hospital. There was no association with sex and the likelihood of histological diagnosis, but a marked decline with age, a downward trend with deprivation, and an increase when the nearest hospital was a cancer centre. These findings facilitate the understanding of factors associated with the group of patients that includes those with the least effective access to cancer services.

Keywords

Cancer of Unknown Primary, Cancer diagnosis, Rectal Cancer, Socioeconomic Deprivation, Access to Health Services, Primary Care.

Introduction

Policy for the management of cancer in the UK has been driven by the observation that at the end of the previous century, survival rates from cancer were worse in the UK than in comparable European countries [1]. The reasons continue to be debated but, following the *NHS Cancer Plan* [2] policies sought to improve the quality of care by increasing specialist recruitment and enhancing services in selected centres. Some specialist diagnostic and therapeutic services for cancer have been concentrated in selected large hospitals, known as Designated Cancer Centres. Typical district general hospitals, known as Designated Cancer Units, focus on the management of common cancers where high volumes can be sustained.

A possible disadvantage of centralising services in this manner is that populations living further from specialist centres may have difficulties, including gaining transport to provide access to them for treatment, and such difficulties may consequently be associated with poorer disease prognosis [3,4]. Rural GPs have complained of the problems of gaining access to treatment for patients living in remoter areas far from cancer treatment centres [5] and a report from the Commission for Rural Communities has illustrated some adverse experiences of cancer sufferers and their carers living in rural England, with some patients facing round trips of 100 miles and the topography and quality of local roads further lengthening journey times [6]. There is accumulating evidence that longer travel times have negative effects on access to treatment and the outcome of care for patients with diagnosed cancer [7].

Campbell et al. [4] examined the relationship between survival and distance to cancer centres amongst 64,000 patients diagnosed with common cancers in Scotland between 1991 and 1995. They found that increasing distance from a cancer centre was associated with less chance of diagnosis before death for stomach, breast, and colorectal cancers and poorer survival after

diagnosis for prostate and lung cancers. A study of 5,147 cases of colorectal cancer in southern England [8] also found post-operative survival declined with increasing distance from a treatment centre.

Our previous study of cancers of the breast, bowel, lung, prostate and ovary, which used records from the former Northern and Yorkshire Cancer Registry and Information Service (NYCRIS), added to the evidence. We found that survival from cancers of the prostate was adversely associated with travel time to the patient's GP, as was the likelihood of presenting at late stage for breast or colorectal cancer [9]. Access to the centralised services of radiotherapy and thoracic surgery was shown to be reduced with increasing travel time, as was some chemotherapy [10] and the type of surgery used to treat breast cancer was influenced by access to radiotherapy [11]. These analyses adjusted for deprivation of the area of residence but more detailed analyses for lung cancer showed that the issues of access were minimal for the least deprived localities and greatest for the most deprived [12]. Similar observations were made for colonic but not rectal cancer; the symptom patterns of these tumours suggest that difficulty in suspecting the diagnosis was key [13]. There was also a tendency for those living furthest from a hospital to be recorded as having been diagnosed on the date of death [14].

Cancer service development since 2000 initially concentrated on hospital services but more recently the focus has shifted to the timing of diagnosis [15]. This requires improvement in the interface between primary care, where GPs have to decide if it is appropriate to consider the diagnosis in a patient, and secondary care, where the facilities for investigation are located. For patients with common epithelial cancers, those from deprived areas have been shown to be more likely to have their first hospital admission as an emergency event [16]. Current understanding of the role of primary care in the process is discussed in the Lancet Oncology

Commission on the subject [17]. Practitioners in this discipline have a role throughout the cancer patient's journey but it is especially important leading up to the diagnosis.

There is concern about patients being admitted to hospital with previously undiagnosed cancer. The National Institute for Health and Care Excellence has issued a guideline for management of patients with malignancy of unknown primary [18], a decade after the Cancer Plan [2]. That document addresses the fact that this group of patients comprises two distinct entities; those patients whose primary site has not been identified because of presentation with very advanced disease and those in whom a primary cannot be identified. The first entity suggests that timely access to the diagnostic services of the Health Service has not been attained and in this study we investigate that process. We therefore decided to approach this entity in the same way and for the same time period over which we had looked at data concerning common cancer sites as an addition to the previous work. Taken as a whole, our body of work provides a detailed picture of the state of services at an important time point.

We hypothesised that cancers of unknown primary would include more patients who faced difficulties in gaining access to health services through residing in deprived areas or through having to travel further to cancer facilities. To test this we compared the diagnosis of Cancer of Unknown Primary (CUP) with a comparator tumour, carcinoma of the rectum, where associations with access are not strong [13]. Indeed, few patients with rectal cancer require multiple consultations before a diagnosis is reached [19], most likely because it has a signature symptom of rectal bleeding. Undiagnosed rectal cancer is therefore unlikely to contribute greatly to the total of CUP patients. The data we have analysed are from the time the Cancer Plan was being introduced and our results therefore form a historically relevant baseline against which the effects of that plan can be measured.

Materials and Methods

Setting

The study drew patients from the area covered by the former Northern and Yorkshire Cancer Registry & Information Service NYCRIS, which extended from the Scottish border to the Humber Estuary. The population covered was around 6.7 million. Approximately 17,500 new malignant cancer patients were assessed annually within this region during the period of study, and five year survival figures were lower than the national average for the majority of sites [20]. As well as widely distributed primary care services operated by general practitioners (GPs), the region contains 32 main acute hospitals (secondary care units) providing diagnostic and basic therapeutic services. Cancer Centres (specialist tertiary care units) are located in Hull, Leeds, Middlesbrough and Newcastle. The study area is predominantly rural and, in the counties of Northumberland and Cumbria, contains some of the most remote parts of Great Britain. The populations of some districts in those counties live an average distance of over 35km from their nearest main acute hospital, compared to a national average distance of under 9km [2]. The area also includes the urban conurbations of Leeds and Tyneside and other industrial cities, with significant pockets of inner-city deprivation. Among the hospitals that are not cancer centres we have not separately analysed data concerning those that had an in-house oncology service. These include several in West Yorkshire and Carlisle Infirmary, which has a radiotherapy facility.

Subjects

Records were supplied by NYCRIS for cancers registered from 1994 to 2002. This period was chosen so that the findings were comparable with our previous work looking at different stages of the treatment/diagnosis pathway, described earlier [9-14]**.** NYCRIS supplied anonymous

records of patients registered with the following ICD 10 classifications: C77 (Secondary and unspecified malignant neoplasm of lymph nodes), C78 (Secondary malignant neoplasm of respiratory and digestive organs), C79 (Secondary malignant neoplasm of other sites), and C80 (Malignant neoplasm without specification of site). C80 has the highest proportion of death certificate only and zero survival registrations and is likely to contain the patients whose presentation was with a clinical state that precluded further investigation. Data from ICD C20 Carcinoma of rectum were supplied and used as a comparator site.

The study was approved by the South Yorkshire Research Ethics Committee of the National Research Ethics Service.

Accessibility and deprivation measures

The travel time from the patients' home postcode to their GP and the nearest cancer centre and hospital was calculated using the ArcGIS v9.3 Geographical Information System (GIS) package (ESRI Inc). In order to do this, a digital representation of the road network was constructed using the Ordnance Survey Meridian dataset [21] and network routing algorithms were used in the GIS to identify the most direct route along the road network from each patient's home to their GP, the nearest cancer centre and nearest hospital. The total travel time in minutes for that route was then computed based on route length and the mix of road types. All calculations assumed car travel.

As a measure of neighbourhood material deprivation, an Index of Multiple Deprivation (IMD) score [22] was calculated for each individual based on the Census Lower Super Output Area zone that their postcode fell within. We computed scores for the index minus the access to

services domain contribution to avoid duplication with our own access measures. To preserve anonymity, postcodes were removed from the records before they left the Registry for statistical analysis.

Analysis

Logistic regression was used to model predictors of CUP compared to carcinoma of the rectum. Models for C77-79 and C80 separately were adjusted for sex, age group, material deprivation quartile, and travel time to GP quartile. For CUP patients only, we also modelled the travel time to the nearest hospital and whether the nearest hospital was a cancer centre. Both of these models were adjusted for sex, age group and deprivation quartile. Tests for trend were carried out by fitting the values of the quartile number as a continuous variable. All analyses were carried out in Stata (version 14).

Results

In the dataset studied, 7,428 patients were classified as C80, 8,849 as C77-79, and 10,804 as C20. Characteristics of patients in the analyses are summarised in Table 1. C20 patients were disproportionately male (62.2%). CUP patients tended to be older, especially those classified as C80. The table shows that fewer of the participants had travel time to their GP available than had the other travel time measurements as the postcode of the GP that these patients attended was not recorded in the cancer registry records.

Table 2 gives the results from the logistic regression model, with the odds ratios for C80 compared to C20 for sex, age group, deprivation quartile and travel time to GP quartile. Travel time to GP showed a shallow gradient; odds ratios (ORs) (1.00, 1.09, 1.14) for quartiles 2-4

respectively, compared to the closest quartile 1, with p(trend)=0.007. Compared to C20, there was a significant protective effect against being classified as C80 in males, but this is partly an artefact of the high number of males in the C20 group which reflects the known sex ratio for rectal cancer. Risk of classification as C80 compared to C20 increased strongly with age, with the test for trend being highly significant (<0.001). Risk of diagnosis of C80 compared to C20 also increased with deprivation, p(trend)<0.001.

Table 3 shows the corresponding results for C77-C79. These were similar to those for C80, except that the travel time to GP showed no association, p(trend)=0.241.

Table 4 shows the results of a logistic regression considering all CUP patients alone, and modelling the chance of a histological basis of diagnosis. There was no association with sex and the likelihood of histological diagnosis, but an extremely strong association with age, with an OR as low as 0.063 for the 80+ group and p(trend)<0.001. Histological diagnosis declined with deprivation, p(trend) <0.001 and less markedly with travel time to the nearest hospital; ORs (0.96, 0.88, 0.87) for quartiles 2-4, p(trend)=0.001. There was a small but significant increased chance of a histological diagnosis if the nearest hospital was a cancer centre, OR=1.096 (95% CI 1.012-1.087).

The fitting of interaction terms suggested that deprivation did not moderate the association with travel time in any of the models.

Discussion

Main findings of the study

Compared to rectal cancer, risk of CUP diagnosis increased with age, deprivation and, for C80, travel time to GP. For CUP patients, the chance of a histological basis of diagnosis decreased with age, deprivation and travel time to hospital and whether or not the nearest hospital was a cancer centre.

What is already known on this topic?

An American study found that a higher proportion of CUP was diagnosed in the elderly, females, black people and residents of less affluent or less educated counties [23]. A recent study of Scottish Cancer Registry data from 1961–2010 found that during 2001–2010, age-standardised rates of CUP were higher in the most compared with the least deprived quintile of the population [24]. They also found that CUP was unusual in people younger than 40 years and that rates increased quite steeply with age, although with some variation by sex and decade of incidence.

What this study adds

To our knowledge, no other studies have looked at travel time to locations of healthcare provision and CUP, or investigated the factors associated with the likelihood of a histological diagnosis in CUP patients. This is the last in a series of studies based on cancer registry data from NYCRIS covering the period at the turn of the 20th century when the leadership of the NHS was recognising the shortfall in cancer survival that characterised the UK in comparison with other Western European economies. Whilst the Cancer Plan [2] was a major step in the process of improving hospital-based services concerned with cancer treatment, the question of what happens before the patient is seen in a hospital was not a focus until later that decade [15].

Even now, GPs are aware of their paramount role as gatekeepers of the NHS whilst acting appropriately to allow timely diagnosis of cancer [17].

Paramount in the development of understanding the importance of the timing of diagnosis was the recognition that much of the international difference in survival was accounted for by deaths in the first year. Møller et al showed that differences in survival of patients with bowel cancer within England between socioeconomic groups were also apparent in the short term, that is poorer people are more likely to experience early death and the difference in survival between socioeconomic groups is much less for those who survive the first year [25]. Early death is likely to be a consequence of very advanced disease at the time of diagnosis. Our previous work has shown that there are differences in access to treatment for bowel cancer associated with socioeconomic status but these are relatively small for rectal cancer [13]. This led us to use rectal cancer as the reference group in this study.

In studying patients registered as having cancer without a primary site being specified we acknowledge that when the diagnosis is not confirmed histologically, some patients will not actually have cancer; the diagnosis is inferred from clinical and radiological findings. Indeed, we have two groups of patients which overlap in the ICD classifications. Some patients are not fully investigated, commonly because of severe comorbidity or because the underlying cancer is causing them to be very ill. This category is expected to form the bulk of the C80 classification. It represents patients in whom the cancer diagnostic services have, for whatever reason, been least successful.

The second group consists of patients in whom investigations fail to reveal the primary; this is a recognised entity requiring specialist treatment. These patients will mostly be included in categories C77-C79 along with some patients in C80. For these patients palliative systemic

therapy is available but this should not be given without a histological diagnosis. Attainment of this step is therefore a measure of active management of the patient. In addition to the strong effects of age and deprivation, we have shown that whether or not the nearest hospital is a cancer centre influences it. This is likely to reflect the perceived utility of the precise diagnosis which in turn reflects what treatment is thought potentially appropriate. Whether or not an oncological opinion is brought is readily available will be relevant here. In the period since these patients were registered we have seen the development of multidisciplinary teams, in fulfilment of the Cancer Plan [2] and of acute oncology services. These should reduce the difference between the types of institutions.

It may be argued that new investigative techniques may decrease the number of patients designated CUP. The NICE Guidance proposes a conservative approach to investigation in the light of limited evidence [18]. It does not advocate the use of magnetic resonance imaging except in the assessment of lymphadenopathy that might be due to breast cancer. Similarly, recommendations for imaging that includes positron emission tomography advises its use only in cervical lymphadenopathy when an aerodigestive primary is possible. It is therefore not likely that their introduction to routine practice will have had an impact on the situation we have found.

The delivery of up-to-date cancer services has been a major endeavour within the National Health Service within the past 20 years after it became apparent that there were weaknesses compared with comparable European countries. Lyratzopoulos et al have explored the issue of diagnostic delay when patients have come to the attention of a GP [26]. They argue that diagnosis may be swifter if facilitated by decision support interventions, better interactions between generalists and specialists, and easier access to diagnostics. In this respect, the

characteristics we have found to be associated with a higher likelihood of being diagnosed with CUP are very similar to the characteristics associated with early death after a diagnosis of lung cancer [27].

Much has been done to improve the process for patients who come to specialist attention and current efforts are aimed at improving the timeliness of the initiation of diagnostic processes. To this must be added the need to understand the barriers that prevent potential cancer patients from seeking an explanation for their symptoms. We have studied a group of patients which includes those who are least well served by the process. This sets a baseline against which improvements in access to diagnosis can be measured. In particular, we found a higher likelihood of histological confirmation of CUP, with the implication of greater diagnostic endeavour and expertise, when the nearest hospital was a cancer centre; yet this disparity may become less pronounced with enhanced performance throughout the NHS. Further, our findings suggest that the increased travel times typically experienced by patients attending cancer units may be detrimental to some. In addition, whilst the association between CUP and socioeconomic status has been noted before, with CUP generally being over-represented by those from more deprived backgrounds [28], we believe this is one of the first studies to assess socioeconomic status in connection with access to services.

Limitations of this study

We were not able to separate those patients presenting too unwell for investigation to be appropriate from those who were able to be investigated and were not, and those who were thoroughly investigated but no primary tumour was found. We would anticipate that C80 would mostly contain the first group and that most of the second and third groups would be in C77-79.

For comparison with previous results, this study was based on data for patients diagnosed between 1994 and 2002. This has the advantage, however, of establishing a baseline to measure the effects of changes in policy and practice. In fact, the focus on diagnosis in UK policy and the formulation of a policy for Metastasis of Unknown Origin (MUO) occurred much more recently with guidance being published in 2010 [18] and so our observations are likely to have retained their relevance until the start of the current decade. Studies of current patients will assess what effect they are having. Our own recent work in lung cancer confirms that major geographical variations in access to services persisted at least until 2010 in spite of the efforts to develop services [29].

Our study is cross-sectional in nature, so we cannot determine if the associations we have seen are causal. We had no information on patient ethnicity or individual conditions or characteristics beyond age and sex, and we relied on an area-based measure of deprivation, the IMD. This was a surrogate for individual measures of disadvantage, which were unavailable. Our measure of deprivation may thus be subject to the ecological fallacy [30], where patients living in a deprived area were not themselves deprived, but our large sample size reduces the expected effects of this factor. We had data on travel time to GP for a smaller number of patients (5697, 64% of the total); those for whom this information was available may not be representative of all patients.

Much of the cancer registry information is obtained by individuals who are not clinicians and who may not have access to every detail of the patient's clinical record. This will result in some patients inappropriately being recorded as CUP. One Australian study [31] audited 574 cancer registry CUP diagnoses (C80.9) and found that 30.0% of cases were reclassified to a known primary site, mostly cutaneous, and 1.6% were found to be non-malignant; some of our patients

will not have had cancer and some will have had diagnoses unknown to us. If the distribution of such error is random, the effect will have been to dilute the associations between age, travel time, deprivation and institution type that we have seen.

Conclusions

We have found that, in the time period we have studied and compared to rectal cancer, risk of CUP diagnosis increases for C80 with travel time to GP. For all registry categories of CUP patients, the chance of a histological basis of diagnosis decreases with travel time to hospital and increases when that hospital is a cancer centre. As the NHS continues to press for timelier ascertainment of cases of cancer in order that patients can best benefit from treatment it should be expected that the adverse trends that we have shown for deprivation and travel time to care will be reduced. It is also important to recognise that the gateway to care will be through the hospital first encountered, so all NHS institutions providing a diagnostic service should be able to do this effectively whether or not they are designated cancer centres.

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Table 1: Characteristics of study participants

	C77-C79		C80		C20	
	n	%	n	%	n	%
Sex						
Female	4,459	50.4	4,057	54.6	4,085	37.8
Male	4,390	49.6	3,371	45.4	6,719	62.2
Age at diagnosis (y)						
<50	395	4.5	269	3.6	591	5.5
50-59	919	10.4	590	7.9	1,432	13.3
60-69	1,989	22.5	1,310	17.6	2,890	26.8
70-79	3,215	36.3	2,647	35.6	3,626	33.6
80+	2,331	26.3	2,612	35.2	2,265	21.0
Deprivation (IMD Score)						
Quartile 1 (least deprived)	2,140	24.2	1,556	21.0	3,080	28.5
Quartile 2	2,227	25.2	1,882	25.3	2,655	24.6
Quartile 3	2,260	25.5	1,906	25.7	2,607	24.1
Quartile 4 (most deprived)	2,222	25.1	2,084	28.1	2,462	22.8
Estimated travel time to GP						
Quartile 1 (0-<2.9 mins)	1,433	25.2	1,081	25.4	2,333	24.8
Quartile 2 (2.9-<5.3 mins)	1,472	25.8	1,018	23.9	2,353	25.0
Quartile 3 (2.3-<9.1 mins)	1,368	24.0	1,101	25.9	2,382	25.3
Quartile 4 (9.1-231.7 mins)	1,424	25.0	1,056	24.8	2,357	25.0
Travel time to nearest cancer centre						
Quartile 1 (0.1-<6.1 mins)	2,209	25.0	1,970	26.5	2,649	24.5
Quartile 2 (6.1-<27.4 mins)	2,260	25.5	1,909	25.7	2,640	24.4
Quartile 3 (27.4-<38.8 mins)	2,156	24.4	1,795	24.2	2,737	25.3
Quartile 4 (38.8-195.0 mins)	2,224	25.1	1,754	23.6	2,778	25.7
Travel time to nearest hospital						
Quartile 1 (0.1-<7.6 mins)	2,272	25.7	1,889	25.4	2,416	22.4
Quartile 2 (7.6-<11.6 mins)	2,194	24.8	1,908	25.7	2,754	25.5
Quartile 3 (11.6-<17.1 mins)	2,214	25.0	1,854	25.0	2,771	25.7
Quartile 4 (17.1-117.5 mins)	2,169	24.5	1,777	23.9	2,863	26.5
Histological basis of diagnosis						
No	4,542	51.3	5,639	75.9		
Yes	4,307	48.7	1,789	24.1		

Table 2: Odds ratio for cancer of unknown primary (compared to C20, rectal carcinoma), adjusted for sex, age group, deprivation quartile and travel time to GP quartile for ICD code C80 (n=13,681)

	Odds ratio	95% CI	P-value	P-trend
Sex				
Female	1.000			
Male	0.561	0.520-0.605	<0.001	
Age at diagnosis (y)				
<50	1.000			
50-59	1.030	0.819-1.294	0.802	
60-69	1.219	0.990-1.503	0.063	
70-79	1.841	1.504-2.253	<0.001	
80+	2.455	2.000-3.014	<0.001	<0.001
Deprivation (IMD Score)				
Quartile 1 (least deprived)	1.000			
Quartile 2	1.532	1.371-1.712	<0.001	
Quartile 3	1.739	1.557-1.941	<0.001	
Quartile 4 (most deprived)	2.067	1.853-2.305	<0.001	<0.001
Travel time to GP				
Quartile 1 (0-<2.9 mins)	1.000			
Quartile 2 (2.9-<5.3 mins)	1.003	0.902-1.115	0.959	
Quartile 3 (2.3-<9.1 mins)	1.091	0.983-1.212	0.102	
Quartile 4 (9.1-231.7 mins)	1.135	1.020-1.262	0.020	0.007

Table 3: Odds ratio for cancer of unknown primary (compared to rectal carcinoma, C20), adjusted for sex, age group, deprivation quartile, travel time to GP quartile for ICD codes C77-C79 (n=15,122)

	Odds ratio	95% CI	P-value	P-trend
Sex				
Female	1.000			
Male	0.612	0.572-0.655	0.000	
Age at diagnosis (y)				
<50	1.000			
50-59	1.029	0.852-1.241	0.769	
60-69	1.165	0.981-1.385	0.082	
70-79	1.458	1.232-1.725	<0.001	
80+	1.594	1.341-1.895	<0.001	<0.001
Deprivation (IMD score)				
Quartile 1 (least deprived)	1.000			
Quartile 2	1.342	1.219-1.477	<0.001	
Quartile 3	1.415	1.285-1.557	<0.001	
Quartile 4 (most deprived)	1.598	1.453-1.758	<0.001	<0.001
Travel time to GP				
Quartile 1 (0-<2.9 mins)	1.000			
Quartile 2 (2.9-<5.3 mins)	1.061	0.966-1.166	0.214	
Quartile 3 (2.3-<9.1 mins)	0.992	0.902-1.091	0.862	
Quartile 4 (9.1-231.7 mins)	1.087	0.988-1.196	0.088	0.241

Table 4: Odds ratio for histological basis of diagnosis adjusted for sex, age group, deprivation quartile, travel time to nearest hospital quartile and whether the nearest hospital was a cancer centre for ICD codes C77-C80 (n=16,277)

	Odds ratio	95% CI	P-value	P-trend
Sex				
Female	1.000			
Male	0.978	0.913-1.048	0.543	
Age at diagnosis (y)				
<50	1.000			
50-59	0.521	0.422-0.644	<0.001	
60-69	0.321	0.264-0.390	<0.001	
70-79	0.152	0.126-0.184	<0.001	
80+	0.063	0.052-0.076	<0.001	<0.001
Deprivation (IMD score)				
Quartile 1 (least deprived)	1.000			
Quartile 2	0.752	0.681-0.830	<0.001	
Quartile 3	0.667	0.604-0.736	<0.001	
Quartile 4 (most deprived)	0.618	0.559-0.684	<0.001	<0.001
Travel time to nearest hospital				
Quartile 1 (0.1-<7.6 mins)	1.000			
Quartile 2 (7.6-<11.6 mins)	0.956	0.868-1.052	0.358	
Quartile 3 (11.6-<17.1 mins)	0.881	0.800-0.971	0.011	
Quartile 4 (17.1-117.5 mins)	0.876	0.792-0.968	0.010	0.003
Nearest hospital was a cancer centre				
No	1.000			
Yes	1.096	1.012-1.187	0.025	

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