

# Socio-economic disparities in access to treatment and their impact on colorectal cancer survival

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**Background** Significant socio-economic disparities have been reported in survival from colorectal cancer in a number of countries, which remain largely unexplained. We assessed whether possible differences in access to treatment among socio-economic groups may contribute to those disparities, using a population-based approach.

**Methods** We retrospectively studied 71 917 records of colorectal cancer patients, diagnosed between 1997 and 2000, linked to area-level socio-economic information (Townsend index), from three cancer registries in UK. Access to treatment was measured as a function of delay in receipt of treatment. We assessed socio-economic differences in access through logistic regression models. Based on relative survival  $\leq 3$  years after diagnosis, we estimated excess hazard ratios (EHRs) of death for different socio-economic groups.

**Results** Compared with more affluent patients, deprived patients had poorer survival [EHR = 1.20; 95% confidence interval (CI) 1.16–1.25], were less likely to receive any treatment within 6 months [odds ratio (OR) = 0.87, 95% CI 0.82–0.92] and, if treated, were more likely to receive late treatment. No disparities in survival were detected among patients receiving treatment within 1 month from diagnosis. Disparities existed among patients receiving later or no treatment (EHR = 1.30; 95% CI 1.22–1.39), and persisted after adjustment for age and stage at diagnosis (EHR = 1.15; 95% CI 1.08–1.24).

**Conclusions** Tumour stage helped explain socio-economic disparities in colorectal cancer survival. Disparities were also greatly attenuated among patients receiving early treatment. Aspects other than those captured by our measure of access, such as quality of care and patient preferences in relation to treatment, might contribute to a fuller explanation.

**Keywords** Colorectal neoplasms, mortality, social class

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## Introduction

Colorectal cancer is one of the most common causes of cancer-related death in most industrialized countries, with 640 000 deaths worldwide per year.<sup>1</sup> In many parts of the world, there is now strong evidence that colorectal cancer survival differs between socio-economic groups.<sup>2–4</sup> Disparities are found even in countries with universal entitlement to health care, like the UK, where the health system is inspired by an egalitarian ethos, which prompts challenging questions on the origins of such disparities. It has been suggested that disparities in survival may be driven by differences in stage at diagnosis,<sup>5</sup> although a number of studies using ecological measures of socio-economic condition failed to establish such a link.<sup>6–8</sup> Differences in treatment are also among the factors that may contribute to explaining disparities in survival from colorectal cancer,<sup>2,4</sup> but limited evidence of this has been produced so far. Socio-economic disparities in type of, and access to, treatment have been examined in a number of studies.<sup>7,9–11</sup> These studies, however, did not assess the impact of disparities in treatment on survival and used heterogeneous measures of socio-economic status and access to treatment, which makes comparisons across studies very difficult.

Given this background, we designed a new population-based study to explore the associations between deprivation, access to treatment and survival for colorectal cancer in the areas covered by three regional cancer registries in the UK. The final aim of the study was to assess whether differences in access to treatment contribute to explaining socio-economic disparities in survival from colorectal cancer.

## Methods

### Patient-level data

We obtained patient-level cancer registration data from the Thames Cancer Registry, the Eastern Cancer Registration and Information Centre and the Northern and Yorkshire Cancer Registry and Information Service in the UK, covering populations of ~13.5, 2.7 and 6.6 million, respectively. Patients diagnosed with a first primary invasive colorectal cancer between January 1997 and 2000 and registered by one of the three cancer registries were deemed eligible for inclusion. Pathways of care and vital status for these patients were observed through to 31 December 2003. We identified 76 078 eligible patients, 3751 (4.9%) of these were excluded because tumour registration was based on a death certificate only. A further 410 patients were excluded because they could not be assigned to a socio-economic group. The statistical analyses were conducted on the remaining 71 917 patients (38 085 for the Thames Cancer Registry, 9785 for the Eastern Cancer Registration and Information Centre and

24 047 for the Northern and Yorkshire Cancer Registry and Information Service).

Tumours were characterized according to their anatomic site,<sup>12</sup> their morphology and behaviour [International Classification of Diseases-O-2] and their stage. The morphology grouping was based on the classification proposed by Gatta *et al.*<sup>13</sup> Tumour stage was classified on the basis of American Joint Committee on Cancer (AJCC) stage groupings (I, local extension; II, extension beyond organ; III, regional lymph node involvement; and IV, metastatic disease).<sup>14</sup>

Two measures reflecting access to treatment were used in the analyses. The first is receipt of any treatment within 6 months from the first known contact with the National Health Service (NHS). The second, for patients who did receive a treatment within 6 months, is time-to-treatment, i.e. the time elapsed between the first known contact and the time of the first treatment received (surgery for 95% of the patients in the study). In many cases, the date of first contact corresponded to the date of diagnosis recorded in cancer registries, and normally corresponds to a specialist consultation or a diagnostic investigation. No primary care consultations are recorded in the three participating registries.

### Area-level socio-economic data

Cancer registries in the UK do not routinely collect information on individual socio-economic status. Therefore, research on socio-economic disparities in cancer normally relies on ecological measures of deprivation. We selected a measure of area deprivation widely used in health and health-care research in the UK, the Townsend index,<sup>15</sup> calculated at the ward level using data from the 2001 census.<sup>16</sup> The average population of a ward in the UK is approximately 5500 individuals. Townsend scores were assigned to patients on the basis of postcodes of residence at the time of diagnosis (full postcodes include an average of 15–20 households). Patients were then assigned to quintiles of the national distribution of wards by level of deprivation. Therefore, a patient in the highest socio-economic group, for instance, is one living in an area that is part of the most affluent fifth of wards in the country. The five categories were labelled from the least deprived (1 = affluent) to the most deprived (5 = poor).

### Statistical analysis

The association between socio-economic condition and receipt of treatment within 6 months was investigated with a logistic model, whereas a multinomial logistic model was used to assess the relationships between deprivation and time-to-treatment. The latter was categorized as follows: no treatment received within 6 months from the first known contact with the NHS; treatment received within 1 week; treatment in 2–4 weeks; treatment in 2–3 months and treatment in 4–6 months. The following covariates

were introduced into both models: age (five age groups); tumour stage at diagnosis; and type of treatment (surgery, chemotherapy, radiotherapy).

Relative survival was estimated  $\leq 3$  years after diagnosis using a maximum likelihood approach for individual-level data records.<sup>17</sup> Relative survival is the standard approach to estimating population-based survival. It is calculated as the ratio of the observed probability of survival to the probability that would have been expected for an individual with the same characteristics (age, gender, socio-economic condition) in the general population. Background mortality was derived from population life tables. Because of wide variations in background mortality between deprivation groups, complete life tables were built by deprivation category for 1998 using mid-year population estimates and the mean annual number of deaths during a period of 3 years centred on the index year.<sup>18</sup> We used life tables defined by quintiles of the income domain score of the Index of Multiple Deprivation (IMD 2000)<sup>19</sup> because life tables by Townsend Index were not available. A generalized lineal model with Poisson error<sup>20</sup> was used to estimate the excess hazard ratio (EHR) of death associated with deprivation, and the confounding effects of age, receipt of treatment and time-to-treatment and stage at diagnosis. Interactions between deprivation and access variables and between deprivation and follow-up time were also investigated.

Tumour stage at diagnosis was missing for 12 139 (17%) patients. A 10-fold multiple imputation approach was applied to the data to account for this incompleteness.<sup>21–24</sup> The associations between missing values and recorded values enable the imputation model to fill in the missing values, using records in which stage information is available. The imputation model, in this case an ordered logistic regression, was iteratively applied to generate 10 ‘completed’ datasets, generally deemed sufficient to obtain reliable estimates. The parameters of interest and their variance were estimated in each dataset and then pooled using multiple imputation rules.

## Results

Cancer patients in the five socio-economic groups had similar distributions by age and gender. No differences among socio-economic groups were found in relation to tumour characteristics, with the exception of stage at diagnosis, with overall slightly more advanced disease in more deprived groups (17% of local tumour and 29% of metastatic tumour in the bottom group vs 24 and 25%, respectively, in the most affluent group). Patients in lower socio-economic groups were slightly less likely to have received treatment within 6 months after the first known contact with the NHS. Generally, more affluent patients had received treatment earlier than most deprived patients (Table 1). The proportion of missing

tumour stage tended to increase, though very little, with deprivation (Table 1). When limited on the 59 848 complete cases, the proportion of advanced stages increased a little and this increase was slightly more markedly with deprivation. The patterns observed on the completed data sets (Table 1) between deprivation and treatment, were also slightly accentuated among the complete cases.

These descriptive findings were confirmed by univariable regression analyses of the effects of socio-economic status on access to treatment, showing that the odds of late treatment, or no treatment within 6 months, increase as deprivation increases (upper section of Table 2). Adjusting for age at diagnosis and tumour stage did not meaningfully alter the association between deprivation and treatment (lower section of Table 2). In summary, socio-economic status was associated with access to treatment. More deprived patients were more likely to receive late treatment (4–6 months) or no treatment within 6 months, and less likely to receive treatment within one month from their first contact with the NHS.

We investigated the impact of differences in access to treatment on disparities in survival among socio-economic groups  $\leq 3$  years after diagnosis. We calculated EHRs of death, reflecting relative risks of cancer-related mortality, for most deprived socio-economic groups relative to the most affluent group. EHRs increased with increasing deprivation, up to a value of 1.20, 95% confidence interval (95% CI) 1.16–1.25, for the most deprived socio-economic group (Table 3). Of the patient and tumour characteristics accounted for in the analysis, only tumour stage had a confounding effect on socio-economic disparities in survival, with a small reduction of EHRs for the lower socio-economic groups, from 1.20; 95% CI 1.16–1.25 to 1.13; 95% CI 1.09–1.16 for the most deprived group (data not shown). Accounting for receipt of treatment within 6 months had hardly any effect on overall EHRs (for all patients). However, patterns of excess mortality hazard varied among patients treated with different degrees of delay. The socio-economic gradient in mortality was substantially reduced, or even disappeared, among patients who had received early treatment (within the first month). Conversely, the gradient was steeper among patients who had not been treated within 6 months. Adjusting for age at diagnosis and tumour stage once again attenuated, but did not eliminate, excess mortality for the lower socio-economic groups. We did not find any strong evidence for an interaction between deprivation and time since diagnosis over the 3-year follow-up.

## Discussion

Using a population-based approach, we found an important socio-economic gradient in 3-year survival from colorectal cancer, with lowest mortality among the most affluent patients. This gradient was only

**Table 1** Characteristics of study population by deprivation category

	<b>All</b>		<b>Most affluent</b>		<b>2</b>		<b>3</b>		<b>4</b>		<b>Most deprived</b>	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
	71 917		11 070		12 848		14 406		14 461		19 132	
<b>Sex</b>												
Men	38 385	53	5944	54	6795	53	7581	53	7669	53	10 396	54
Women	33 532	47	5126	46	6053	47	6825	47	6792	47	8736	46
<b>Age in years at diagnosis</b>												
15–49	3533	5	530	5	560	5	667	5	701	5	1075	6
50–59	8195	11	1393	13	1467	11	1597	11	1621	11	2117	11
60–69	17 038	24	2758	25	2991	23	3258	23	3340	23	4691	24
70–79	25 288	35	3698	33	4561	36	5066	35	5134	36	6829	36
≥80	17 863	25	2691	24	3269	25	3818	26	3665	25	4420	23
<b>Stage at diagnosis<sup>a</sup></b>												
Local	14 476	20	2599	24	2815	22	2956	21	2796	19	3310	17
Extension beyond organ	18 930	26	2753	25	3346	26	3746	26	3902	28	5183	27
Regional lymph node involvement	19 053	27	2925	26	3385	26	3882	27	3818	26	5044	27
Metastasis (missing) <sup>b</sup>	19 457	27 (17)	2793	25 (17)	3302	26 (15)	3822	26 (15)	3945	27 (17)	5595	29 (19)
<b>Tumour site</b>												
Colon	50 935	71	7939	72	9093	71	10 238	71	10 198	71	13 467	70
Rectum	20 982	29	3131	28	3755	29	4168	29	4263	29	5665	30
<b>Morphology group</b>												
Adenocarcinoma in polyp/adenoma	2565	4	339	3	421	3	499	4	533	4	773	4
Mucinous adenocarcinoma	4720	7	761	7	864	7	998	7	963	7	1134	6
Other adenocarcinoma	54 941	76	8529	77	9887	77	10 998	76	10 944	76	14 583	76
Other carcinoma and carcinoma NOS	8542	12	1340	12	1537	12	1707	12	1769	12	2189	11
Sarcoma and unspecified	1149	1	101	1	139	1	204	1	252	1	453	3
<b>Treatment</b>												
Within first week	14 089	20	2367	21	2678	21	2851	20	2615	18	3578	19
Within 2–4 weeks	14 930	21	2431	22	2629	20	3017	21	2928	20	3925	20
Within 2–3 months	20 482	28	3078	28	3723	29	4146	29	4202	29	5333	28
Within 4–6 months	5621	8	769	7	925	7	1141	8	1235	9	1551	8
No treatment within 6 months	16 795	23	2425	22	2893	23	3251	22	3481	24	4745	25

<sup>a</sup>Frequencies and proportions derived from the 10 completed data sets.

<sup>b</sup>Proportions of missing stage observed in the original data set.

NOS = not otherwise specified.

partially explained by differences in stage at diagnosis among socio-economic groups. We also showed important socio-economic differences in access to treatment, with more deprived patients more likely to receive late treatment or no treatment within 6 months from their first contact with the NHS, even after accounting for differences in stage at diagnosis. Socio-economic disparities in survival were greatly attenuated among patients receiving early treatment, and persisted otherwise.

The existence of a socio-economic gradient in survival from colorectal cancer in the UK has been shown in previous studies.<sup>3,25,26</sup> The role played by

tumour stage in explaining socio-economic disparities in survival remains controversial,<sup>6–8,27</sup> although our findings are consistent with evidence reported in several recent studies confirming that differences in stage at diagnosis are responsible for at least part of the observed socio-economic gradient in survival.<sup>28–30</sup> Socio-economic disparities in access to care in the UK have been documented with reference to a range of health services,<sup>31</sup> and specifically with reference to treatment for colorectal cancer. Tumour stage, however, does not appear to play a key role in the choice of surgical procedure in colorectal cancer.<sup>10</sup> Our study is probably the first population-based

**Table 2** Association of receipt of treatment and time-to-treatment (absence of treatment<sup>a</sup> taken as reference category) with deprivation ( $n = 71\,917$ )

	Receipt of treatment (Yes vs No) <sup>a</sup>	Time-to-treatment (vs no treatment)			
		Treatment in first week (95% CI)	Treatment within first month (95% CI)	Treatment within 2–3 months (95% CI)	Treatment within 4–6 months (95% CI)
<b>Unadjusted OR</b>					
1 (most affluent)	1.00	1.00	1.00	1.00	1.00
2	0.97 (0.91–1.03)	0.95 (0.88–1.02)	0.91 (0.84–0.98)	1.01 (0.94–1.09)	1.01 (0.90–1.13)
3	0.96 (0.91–1.02)	0.90 (0.83–0.97)	0.93 (0.86–1.00)	1.00 (0.94–1.08)	1.11 (1.00–1.23)
4	0.88 (0.83–0.94)	0.77 (0.71–0.83)	0.84 (0.78–0.90)	0.95 (0.89–1.02)	1.12 (1.01–1.24)
5 (most deprived)	0.85 (0.80–0.90)	0.77 (0.72–0.83)	0.83 (0.77–0.89)	0.89 (0.83–0.95)	1.03 (0.93–1.14)
<b>Adjusted OR<sup>b</sup></b>					
1 (most affluent)	1.00	1.00	1.00	1.00	1.00
2	0.99 (0.93–1.06)	0.97 (0.89–1.05)	0.93 (0.86–1.01)	1.05 (0.97–1.13)	1.04 (0.93–1.16)
3	1.01 (0.95–1.08)	0.93 (0.86–1.01)	0.97 (0.90–1.05)	1.06 (0.99–1.15)	1.17 (1.05–1.30)
4	0.91 (0.86–0.97)	0.79 (0.73–0.85)	0.87 (0.80–0.94)	0.99 (0.92–1.07)	1.16 (1.05–1.30)
5 (most deprived)	0.87 (0.82–0.92)	0.78 (0.72–0.84)	0.84 (0.78–0.90)	0.91 (0.85–0.98)	1.07 (0.96–1.18)

<sup>a</sup>Treatment within 6 months after first contact within the NHS.

<sup>b</sup>Adjustment for age at first attendance and stage at diagnosis.

OR = odds ratio.

assessment of the impact of differences in access to treatment on socio-economic disparities in cancer survival. No socio-economic disparities in survival were found among colorectal cancer patients enrolled in clinical trials, who therefore received the same treatments.<sup>32</sup> The absence of a socio-economic gradient in survival in patients receiving early treatment in our study is in line with the latter evidence.

Information on tumour stage was not available for almost one-fifth of the patients. These patients tended to be slightly more deprived, older, and had lower relative survival. This suggests that the missingness mechanism was not completely random, and analyses limited to complete cases would likely be biased. Multiple imputation approaches aim at providing unbiased estimates on the assumption of a random distribution of missing observations. Therefore, the imputation model incorporated all the relevant available information such as socio-demographic and tumour variables as well as time since diagnosis and vital status.<sup>33</sup> Compared with the observed cases, the imputed values were more likely to be of advanced stage: on average, 15% local stage and 36% metastatic stage, compared with 21 and 25%, respectively, among the complete cases. All analyses were repeated on the 59 848 complete cases and results compared with those derived from the 10 imputed datasets.<sup>34</sup> The associations between deprivation and the receipt of treatment or time to treatment were less strong, but followed similar patterns. The conclusions based on the excess hazard models estimated from the complete cases would be the same as those based on the results shown in Table 3.

There were a number of limitations in our data concerning treatments received by colorectal cancer patients. It was not possible to distinguish between elective and emergency treatment. We assumed that treatments received within 1 week from diagnosis are highly likely to have been delivered in emergency circumstances. Unexpectedly, we found that a larger proportion of patients in the upper socio-economic groups were treated within 1 week, relative to more disadvantaged patients. This finding might be partly explained by a larger use of the private health-care sector by more affluent patients in their pursuit of a diagnosis. A similar problem might exist at the opposite end of the time-to-treatment spectrum, if treatments delivered privately were not recorded in cancer registries. However, all the registries concerned have established links with private health-care facilities, which make these potential sources of bias unlikely to affect our findings to any meaningful extent. More generally, it was not possible to distinguish cases for which information on treatment was missing from those which genuinely received no treatment within the relevant timeframe.

Our study provides evidence of a persistent socio-economic gradient in survival among patients receiving late treatment. This finding may reflect differences in unobserved tumour or treatment characteristics among socio-economic groups. Unfortunately, the information recorded in the three cancer registries was too often not detailed enough or missing on aspects such as the nature of surgical interventions (e.g. curative vs palliative; different types of resection) or the nature of neo-adjuvant and adjuvant therapies

**Table 3** EHR of death  $\leq 3$  years since diagnosis by deprivation category ( $n = 71\,917$ )

	EHR of death (95% CI)					
	All patients <sup>a</sup>	Treatment in first week	Treatment within first month	Treatment within 2–3 months	Treatment within 4–6 months	No treatment
<b>Unadjusted</b>						
Deprivation						
1 (most affluent)	1.00					
2	1.07 (1.02–1.12)					
3	1.12 (1.07–1.17)					
4	1.18 (1.13–1.23)					
5 (most deprived)	1.20 (1.16–1.25)					
<b>Model including treatment</b>						
Deprivation						
1 (most affluent)	1.00	1.00	1.00	1.00	1.00	1.00
2	1.07 (1.03–1.12)	1.00 (0.91–1.10)	1.03 (0.92–1.14)	1.14 (1.02–1.27)	1.04 (0.82–1.32)	1.11 (1.03–1.19)
3	1.15 (1.10–1.20)	1.06 (0.97–1.16)	1.09 (0.98–1.20)	1.13 (1.01–1.25)	1.07 (0.85–1.35)	1.25 (1.17–1.33)
4	1.20 (1.15–1.25)	1.12 (1.02–1.23)	1.17 (1.06–1.30)	1.12 (1.01–1.24)	1.10 (0.88–1.37)	1.31 (1.22–1.39)
5 (most deprived)	1.20 (1.16–1.25)	1.06 (0.97–1.16)	1.11 (1.01–1.22)	1.24 (1.13–1.37)	1.17 (0.94–1.45)	1.30 (1.22–1.39)
<b>Model including treatment, age at first attendance and stage at diagnosis</b>						
Deprivation						
1 (most affluent)	1.00	1.00	1.00	1.00	1.00	1.00
2	1.04 (0.99–1.08)	0.99 (0.90–1.09)	0.99 (0.89–1.10)	1.13 (1.02–1.25)	1.01 (0.81–1.27)	1.04 (0.96–1.12)
3	1.09 (1.05–1.14)	1.08 (0.99–1.19)	1.02 (0.93–1.13)	1.11 (1.01–1.22)	1.04 (0.85–1.29)	1.14 (1.06–1.22)
4	1.15 (1.10–1.20)	1.12 (1.02–1.24)	1.12 (1.01–1.23)	1.14 (1.03–1.26)	1.03 (0.84–1.26)	1.20 (1.12–1.29)
5 (most deprived)	1.12 (1.07–1.17)	1.05 (0.96–1.14)	1.04 (0.95–1.15)	1.20 (1.09–1.31)	1.14 (0.93–1.39)	1.15 (1.08–1.24)

<sup>a</sup>Presence of treatment within 6 months after first contact within the NHS.

received by patients. Patients in the most affluent groups, who are also likely to be better educated, may be able to obtain more appropriate and higher quality treatments. For instance, data from one of the registries covered by our study show a lower likelihood of breast conserving surgery in socio-economically disadvantage women.<sup>35</sup> There is at least some evidence that physician perceptions of patients may be influenced by the patients' socio-demographic characteristics, which may ultimately affect referral patterns, diagnostic pathways and treatment recommendations.<sup>36</sup> Other non-clinical factors, such as willingness to participate in treatment, might contribute to a higher colorectal cancer mortality in the lower socio-economic groups.<sup>37</sup> All of these hypotheses warrant further investigation.

Our measure of access to treatment was based on the time elapsed between the date of the first known contact within the NHS (excluding primary care) and the date of first treatment. However, the time since the onset of clinical symptoms or the first contact with a general practitioner, not available in our data, may also affect survival. The latter, which may be a reflection of awareness of cancer risk, is also likely to vary by socio-economic condition.<sup>38</sup> Time-to-treatment has been defined in a variety of

ways in previous studies, making comparisons across studies difficult. Examples include time elapsed between first symptoms,<sup>9,39</sup> first medical consultation<sup>39</sup> or outpatient attendance,<sup>40</sup> or first presentation of initial symptoms to a doctor,<sup>41</sup> and hospital admission<sup>42</sup> or treatment.<sup>9,40,41</sup>

Individuals were assigned to socio-economic groups on the basis of an ecological measure of socio-economic status, the Townsend index, measured at the ward level. Life tables for different socio-economic groups were based on a different ecological measure, the income domain of the IMD.<sup>19</sup> However, previous research has shown that different indices of area deprivation lead to similar estimates of socio-economic gradients, and what makes the largest difference is the geographical level at which they are measured.<sup>43</sup> Assessing area deprivation at the ward level is likely to underestimate socio-economic gradients in cancer treatment and survival to a certain degree, relative to what would have been observed if individual-level or smaller-area-level information had been available.

In conclusion, we showed how access to treatment for colorectal cancer varies in different socio-economic groups. Differences in access to treatment did not seem to play a direct role in explaining overall

socio-economic disparities in colorectal cancer survival, whereas tumour stage at diagnosis partly explained these disparities. However, our findings also suggested that disparities in survival were greatly attenuated among patients receiving early treatment. This observation reinforces the idea that equal treatment may lead to equal outcomes, whatever the socio-economic level. Access to treatment is a multidimensional concept and factors other than those captured by our measure of access, such as quality of care and patient preferences in relation to treatment might play a role in generating socio-economic disparities in survival.

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**Conflict of interest:** None declared.

### KEY MESSAGES

- In the UK, access to treatment for colorectal cancer and 3-year relative survival vary according to a socio-economic gradient.
- More deprived patients are more likely to receive late treatment (4–6 months) or no treatment within 6 months since their first contact with the NHS, compared with less deprived patients.
- The socio-economic gradient in relative survival is greatly reduced among patients receiving early treatment (within the first month), even after accounting for differences in age at diagnosis and tumour stage.

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