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ORIGINAL ARTICLE

The role of receipt and timeliness of treatment in socioeconomic inequalities in lung cancer survival: population-based, data-linkage study

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ABSTRACT

Background Lung cancer survival is socioeconomically patterned, and socioeconomic inequalities in receipt of treatment have been demonstrated. In England, there are target waiting times for the referral (14 days) and treatment intervals (31 days from diagnosis, 62 days from GP referral). Socioeconomic inequalities in the time intervals from GP referral have been found. Cancer registry, Hospital Episode Statistics and lung cancer audit data were linked in order to investigate the contribution of these inequalities to socioeconomic inequalities in lung cancer survival.

Methods Logistic regression was used to examine the likelihood of being alive 2 years after diagnosis, by socioeconomic position, for 22 967 lung cancer patients diagnosed in 2006–2009, and in a subset with stage recorded (n=5233).

Results Socioeconomic inequalities in survival were found in a multivariable analysis adjusted for age, sex, histology, year, timely GP referral, performance status and comorbidity, with those in the most deprived socioeconomic group significantly less likely to be alive after 2 years (OR=0.77, 95% CI 0.66 to 0.88, p<0.001). When receipt of treatment was included in the analysis, the association no longer remained significant (OR=0.87, 95% CI 0.75 to 1.00, p=0.06). Addition of timeliness of treatment did not alter the conclusion. Patients treated within guideline targets had lower likelihood of two-year survival.

Conclusions Socioeconomic inequalities in survival from lung cancer were statistically explained by socioeconomic inequalities in receipt of treatment, but not by timeliness of referral and treatment. Further research is required to determine the currently unexplained socioeconomic variance in treatment rates.

Key messages

What is the key question?
- What role does receipt of, and time to, treatment play in socioeconomic inequalities in lung cancer survival?

What is the bottom line?
- Socioeconomic inequalities in survival from lung cancer were statistically explained by socioeconomic inequalities in receipt of treatment, but not by timeliness of treatment.

Why read on?
- Although current clinical guidelines focus on target times for referral and treatment, our results suggest that a clinical focus on ensuring equity of treatment for lung cancer is likely to reduce socioeconomic inequalities in survival, and improve overall survival.

Linked

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▶ http://dx.doi.org/10.1136/thoraxjnl-2014-205841
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INTRODUCTION

Intervention-generated inequalities have been described as unintended variations in outcome that result from the way that health interventions are organised and delivered.[1] Although overall health may improve as the result of an intervention, differences in access to the intervention, differential uptake, delays in time to uptake and differential compliance with, or effectiveness of, an intervention may result in inequalities in outcome.[1 2] There may also be inequalities in timeliness of the offer of the intervention and to whom it is offered.

Lung cancer is the most common incident cancer, worldwide. In the USA and the UK, it is the second most incident cancer,[3 4] as well as the most common cause of cancer mortality.[4 5] In the UK, the 5-year lung cancer survival rate is less than 10%.[5 6] There are socioeconomic inequalities in lung cancer survival,[7 8] and it has been estimated that over 1300 deaths could be avoided annually in England and Wales if the survival rate in the more deprived socioeconomic groups were similar to that of the most affluent.[8]

Socioeconomic inequalities in receipt of treatment for lung cancer have been demonstrated in a systematic review and meta-analysis[9] and in previous analyses of the dataset used here.[10] It has been suggested that socioeconomic inequalities in receipt of treatment may at least partially contribute to socioeconomic inequalities in cancer survival,[11] although there is little definitive evidence to support this.

In England, there are target waiting times for the referral (14 days from general practitioner (GP) referral to first hospital appointment (FHA)) and treatment intervals (31 days from diagnosis, 62 days from GP referral). Socioeconomic inequalities in the time intervals from referral to FHA, diagnosis and treatment were found in our previous lung cancer analyses, but no linear pattern by socioeconomic position (SEP) emerged. Those in the middle SEP groups were least likely to receive timely referral and treatment (Forrest *et al*, unpublished data,

2014). Although there is some speculation that inequalities in delay might contribute to socioeconomic differences in cancer survival,[12] again, it is not known what role socioeconomic inequalities in referral, diagnostic and treatment intervals may play in survival inequalities.

Cancer registry, Hospital Episode Statistics (HES) and lung cancer audit (LUCADA) datasets were linked in order to investigate the factors that may influence socioeconomic inequalities in survival for lung cancer, specifically examining the influence of receipt of treatment, and timely GP referral and treatment, taking into account age, sex, histology, year of diagnosis, comorbidity, stage and performance status.

METHODS

Data sources and linkage

We analysed a linked dataset reported previously (Forrest *et al*, unpublished data, 2014).[10] Over the time that these data were collected, the Northern and Yorkshire Cancer Registry and Information Centre (NYCRIS) was one of eight English regional cancer registries that collect a common minimum cancer dataset of information.[13] Data on SEP, age, sex, histology, tumour, year of diagnosis, GP referral date, FHA date, diagnosis date, treatment dates, details of receipt of treatment (surgery, chemotherapy and radiotherapy) within 1 year of diagnosis, and survival time were obtained for patients with lung cancer.

Comorbidity may be a factor influencing whether treatment is offered[14] and may also influence survival. Details of comorbidity are not collected by UK cancer registries. However, data that can be used to calculate a comorbidity score can be obtained from HES.

As stage data is incomplete in UK cancer registry datasets we used stage data contained in the Lung Cancer Audit (LUCADA), a non-mandatory register of clinical information on patients diagnosed with lung cancer in the UK. The audit initially included only a subset of registry patients (66% nationally in 2006, increasing to 93% in 2010).[15]

Records were allocated a unique, randomly generated key number, derived from the NHS number by NYCRIS. Data from the three data sources (cancer registry, HES and LUCADA) were anonymised and supplied by NYCRIS. The HES and LUCADA data were then linked to the registry data using this key number.

Variables of interest

The Index of Multiple Deprivation (IMD) is an area-based, composite measure of SEP. Postcodes of residences are used to assign individuals to small administrative areas known as lower-level super output areas (LSOA) containing an average of 1500 individuals. Areas are ranked from least deprived to most deprived, on seven different dimensions of deprivation including: income employment, health and disability, education, crime; barriers to housing and services, and living environment.[16]

SEP was assigned according to the agreed methodology for all English cancer registries, as the rank of the income domain of IMD, grouped into quintiles, based on the England-wide distribution of this variable, where Q5 is the most deprived and Q1 the least deprived. The income domain of IMD2010 was used for patients diagnosed between 2007 and 2009. For those diagnosed in 2006, the income domain of IMD2007 was used.

Age at diagnosis was categorised into four groups: age <60, 60–69, 70–79 and 80+ years.

Histology was classified as non-small cell lung cancer (NSCLC), including adenocarcinoma, large cell carcinoma, squamous cell carcinoma and non-small cell carcinoma (not otherwise specified) subtypes; small cell lung cancer (SCLC); and other histology (including unspecified carcinoma, neoplasm, other specified carcinomas and carcinoid tumours).

Since 2000, urgent referrals for suspected cancer in England and Wales have been required to have a FHA within 14 days of the date of referral (referral interval) and, since 2005, a target interval of first treatment within 31 days from decision to treat/diagnosis (treatment interval) has been in place.[17] Time from GP referral date to FHA was categorised as ≤14 days (within target), >14 days, or no referral interval recorded (either no GP referral date or no FHA date recorded). Time from diagnosis to first treatment was categorised as: ≤31 days (within target), >31 days (32–62 days, >62 days), or no treatment received. Diagnosis date was determined by cancer registry personnel as the first time the tumour was identified either by imaging or histology in the case notes.

A weighted comorbidity score was calculated by NYCRIS using a validated instrument, the Charlson Comorbidity Index (CCI),[18] using the number of inpatient HES admissions for 17 specified conditions (other than lung cancer) in the 3–18 months prior to diagnosis. HES-linked comorbidity data were unavailable for patients diagnosed in 2009 as, due to national problems in calculating the comorbidity score, there was a time lag in data availability. Comorbidity score was categorised as 0, 1–2, 3+, missing, or unavailable.

Performance status (PS) and stage data were obtained from LUCADA. Stage was assigned using the TNM staging system[19] and categorised as I, II, III, IV, or missing. PS is a measure of general well-being for cancer patients, as assessed by the Multi-Disciplinary Team, on a scale of 0 (asymptomatic) to 4 (bedridden) using the Eastern Co-operative Group performance status scale,[20] and categorised as 0, 1–2, 3–4, or missing.

Survival was flagged as yes or no at 2 years after diagnosis. Two-year survival was chosen to allow a minimum of 1 year follow-up after treatment for patients who had treatment within 1 year of diagnosis.

Data analysis

Full details regarding the methods employed in examining inequalities in receipt of treatment[10] and inequalities in referral and treatment intervals (Forrest *et al*, unpublished data, 2014) using logistic regression have been previously reported. Here, univariable and multivariable logistic regression were used to examine the likelihood of being alive 2 years after diagnosis, by SEP, in the full cohort (22 967) and in the subset with stage recorded (5233). As the aim was to develop an explanatory model for socioeconomic inequalities in survival, the variable selection procedure was based on an underlying conceptual framework rather than on formal stepwise methods.[21] Variables known a priori to be important confounders were included first. Other variables that had not previously been well studied, but were thought likely to be important, were then included, and their influence on socioeconomic inequalities in survival examined. The amount of outcome variance explained by each variable was also considered. A number of models were produced, varying the order in which variables were added, to determine whether it was a particular variable, and not the order in which it was added, that was important.

A likelihood ratio test was performed to determine the overall significance of each categorical variable. The R^2 statistic was examined as a measure of 'model fit', to determine the amount of variance in two-year survival explained by each model. Analysis was carried out in Stata V.12.0.

RESULTS

Descriptive analysis

Data for 23 497 patients with a primary diagnosis of lung cancer (ICD10 C33 and C34), diagnosed between 1 Jan 2006 and 31 December 2009, were obtained from NYCRIS. Of these, 530 had tumour registration based on death certification only (DCO), and so were excluded from analyses, leaving an eligible cohort of 22 967. Of the 22 967 patients examined, 5233 (23%) had stage, and 6127 (27%) had a PS score recorded in LUCADA, and 7488 (33%) had a comorbidity score recorded in HES.

The demographic and clinical characteristics of the lung cancer patients included in the study have been reported previously.[10] In the full cohort, 15.3% of patients (3513) were still alive 2 years after diagnosis (table 1). In the unadjusted analysis, those in the most deprived group were significantly less likely to still be alive after 2 years, than those in the least deprived group (OR=0.79, 95% CI 0.70 to 0.89) (table 1). Likelihood of two-year survival was also better for younger patients, women, those diagnosed with NSCLC, those with no comorbidity, those with early stage cancer, those with good PS, those referred by their GP and those receiving any treatment. Patients treated within the 14-day referral target had reduced likelihood of two-year survival (OR=0.76, 95% CI 0.69 to 0.84) compared to those who received later referral, as did those who were treated within 31 days of diagnosis (OR=0.37, 95% CI 0.34 to 0.41) compared to those who were treated later (table 1).

Multivariable analysis

In a multivariable analysis adjusted for age, sex, histology, year of diagnosis, timely GP referral and comorbidity, inequalities in survival by SEP were observed in the full cohort, with reduced likelihood of two-year survival in the lowest compared to the highest SEP group (OR=0.74, 95% CI 0.66 to 0.84) (table 2). Model fit was poor (R^2=5.77). Adding stage and PS improved model fit (R^2=12.31) but did not substantially change the SEP OR (OR=0.77, 95% CI 0.66 to 0.88). However, if treatment type was included, the association no longer remained significant (OR=0.87, 95% CI 0.75 to 1.00). Receipt of treatment also made the greatest contribution to model fit (R^2=27.97). Further, addition of timeliness of treatment did not alter the outcome (OR=0.87, 95% CI 0.75 to 1.00).

In the staged subset (n=5233), socioeconomic inequalities in survival were found in a multivariable analysis including age, sex, histology, year of diagnosis, comorbidity and timely GP referral, with those in the most deprived group having a significantly lower likelihood of two-year survival than those in the most affluent (OR=0.76, 95% CI 0.61 to 0.96), but with poor model fit (R^2=3.72) (table 3). However, the association was no longer significant when stage was added (OR=0.79, 95% CI 0.61 to 1.02), with a large increase in R^2 to 24.39. The addition of PS (OR=0.90, 95% CI 0.70 to 1.17) and treatment (OR=1.03, 95% CI 0.78 to 1.36) further attenuated the OR (table 3). Stage and receipt of treatment made the greatest contribution in explaining survival variance, but PS and treatment had the greatest influence on likelihood of survival by SEP.

DISCUSSION

Principal findings

To our knowledge, this is the first study to examine referral and treatment intervals, as well as receipt of treatment, on lung cancer survival, using multiple dataset linkage (NYCRIS, HES and LUCADA). Socioeconomic inequalities in lung cancer survival were found when patient, tumour and system factors were included in the multivariable model, but not with the addition of receipt of treatment. Socioeconomic inequalities in receipt of treatment statistically explained socioeconomic inequalities in lung cancer survival. Time to treatment had no significant effect on socioeconomic inequalities in survival. However, those who received treatment within the 31-day target, and those who received a hospital appointment within 14 days of referral, had poorer survival than those who had later referral or treatment, in the full cohort.

Strengths and weaknesses

The population-based approach is a strength of this study. Linking data from NYCRIS, with its excellent population coverage, to HES and LUCADA, allowed inclusion of variables that had previously not been well explored. However, we used local, north of England data only, which may limit the generalisability of the findings to other settings.

The validity of CCI score and PS as proxy measures of general wellbeing is unclear.[10] PS is a measure of patients' functional status. Although it has been shown to have good prognostic predictive validity,[22] only moderate agreement in allocating PS score was found in an interobserver reliability study. However, there was good agreement when allocating patients to good (PS 0–2) compared to poor PS (PS 3–4),[23] and we used similar groupings.

The CCI is a validated instrument for measuring comorbidity[18] but, in deriving it, we used only details of conditions recorded during episodes of in-patient care. Patients who are never admitted to hospital or who suffer from relevant conditions which were not recorded during such an admission will have a score of O, thus resulting in potential underestimation of total comorbidity.[10] It is also a crude measure, as patients with relatively mild and severe forms of a comorbid disease receive the same score.

High levels of missing data for CCI score, PS and stage were a limitation. Stage was recorded for 12% of patients in 2006 and data completeness improved over time. However, by 2009, stage was still only recorded for 36% of participants. Multiple imputation was considered but is not recommended where over 50% of values for a variable are missing.[24] An alternative way to address the problem of missing data is to analyse only complete cases, although results from complete-case analyses can be biased.[25] We looked at the subset of patients who had stage recorded (as an analysis of complete-case stage patients, the majority of whom also had PS recorded) and also analysed the full cohort and included 'missing' categories for stage, PS and CCI.

Survival time in days from date of diagnosis was not available from the registry dataset as this variable could be used to calculate date of death, which is considered a potentially identifiable data item. Survival time in weeks was used which was accurate to within 4 days of death. Thus, there is a low level of error but not bias in the accuracy of survival time.

We investigated a wide range of factors that may be important in the relationship between SEP and survival. We were unable to examine smoking status or geographical distance to treatment centre[26] as these variables are not recorded in UK cancer registry datasets. There may be residual confounding from these and other factors.

Interpretation of results and comparison with other studies

Inequalities in receipt of treatment (surgery and chemotherapy but not radiotherapy) were previously found in this dataset[10]

Table 1 Descriptive data and univariable ORs of still being alive two years after diagnosis, for full cohort

Variable	Cohort n	Alive at 2 years n	%	Univariable regression analysis (n=22 967) OR	95% CI		p Value
Deprivation (IMD) quintile	22 967	3513	15.3				0.004
1 (least deprived)	2698	474	17.6	1.00			
2	3303	520	15.7	0.88	0.76	1.00	0.059
3	3827	586	15.3	0.85	0.74	0.97	0.015
4	5387	815	15.1	0.84	0.74	0.95	0.005
5 (most deprived)	7752	1118	14.4	0.79	0.70	0.89	<0.001
Age group (years)	22 967	3513	15.3				<0.001
<60	3041	651	21.4	1.00			
60–69	6016	1199	19.9	0.91	0.82	1.02	0.100
70–79	8219	1210	14.7	0.63	0.57	0.70	<0.001
80+	5691	453	8.0	0.32	0.28	0.36	<0.001
Sex	22 967	3513	15.3				<0.001
Female	10 510	1770	16.8	1.00			
Male	12 457	1743	14.0	0.80	0.75	0.86	<0.001
Histology	22 967	3513	15.3				<0.001
NSCLC	12 152	2463	20.3	1.00			
SCLC	2829	236	8.3	0.36	0.31	0.41	<0.001
Other	7986	814	10.2	0.45	0.41	0.49	<0.001
Year of diagnosis	22 967	3513	15.3				<0.001
2006	5533	783	14.2	1.00			
2007	5712	844	14.8	1.05	0.95	1.17	0.347
2008	5851	861	14.7	1.05	0.94	1.16	0.392
2009	5871	1025	17.5	1.28	1.16	1.42	<0.001
Comorbidity (CCI) score	22 967	3513	15.3				0.001
0	3597	601	16.7	1.00			
1–2	3125	453	14.5	0.85	0.74	0.97	0.013
3+	766	89	11.6	0.66	0.52	0.83	<0.001
Missing	10 133	1509	14.9	0.87	0.79	0.97	0.009
Unavailable	5346	861	16.1	0.96	0.85	1.07	0.450
Timely GP referral	22 967	3513	15.3				<0.001
FHA>14 days from referral	3669	803	21.9	1.00			
FHA≤14 days from referral	8284	1456	17.6	0.76	0.69	0.84	<0.001
No GP referral date	11 014	1254	11.4	0.46	0.42	0.51	<0.001
Stage	22 967	3513	15.3				<0.001
I	864	504	58.3	1.00			
II	332	128	38.6	0.45	0.35	0.58	<0.001
III	1587	276	17.4	0.15	0.12	0.18	<0.001
IV	2450	139	5.7	0.04	0.03	0.05	<0.001
Missing	17 734	2,466	13.9	0.12	0.10	0.13	<0.001
Performance status	22 967	3,513	15.3				<0.001
0	1,298	481	37.1	1.00			
1–2	3414	635	18.6	0.39	0.34	0.45	<0.001
3–4	1415	65	4.6	0.08	0.06	0.11	<0.001
Missing	16 840	2332	13.9	0.27	0.24	0.31	<0.001
Type of treatment	22 967	3513	15.3				<0.001
no treatment	10 675	459	4.3	1.00			
Surgery	1427	1041	73.0	60.02	51.68	69.71	<0.001
Surgery + chemotherapy and/or radiotherapy	809	521	64.4	40.26	33.91	47.80	<0.001
Chemotherapy	2759	267	9.7	2.38	2.04	2.79	<0.001
Chemotherapy + radiotherapy	3236	701	21.7	6.15	5.43	6.98	<0.001
Radiotherapy	4061	524	12.9	3.30	2.89	3.76	<0.001
Timely 1st treatment	22 967	3513	15.3				<0.001
>31 days from diagnosis	7443	2346	31.5	1.00			
≤31 days from diagnosis	4849	708	14.6	0.37	0.34	0.41	<0.001
No treatment	10 675	459	4.3	0.10	0.09	0.11	<0.001

CCI score, Charlson Comorbidity Score; FHA, first hospital appointment; IMD, Index of Multiple Deprivation; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

Table 2 Likelihood of still being alive two years after diagnosis, by SEP, adjusted for selected patient, tumour and system factors, for full cohort

	Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral (n=22 967, R^2=5.77)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS (n=22 967, R^2=12.31)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS, treatment (n=22 967, R^2=27.97)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS, treatment, timely 1st treatment (n=22 967, R^2=28.74)			
Variable	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**
Deprivation quintile				<0.001				0.002				0.345				0.336
1 (least deprived)	1.00				1.00				1.00				1.00			
2	0.87	0.76	1.00	0.054	0.87	0.76	1.01	0.073	0.88	0.75	1.04	0.130	0.88	0.75	1.04	0.137
3	0.86	0.75	0.98	0.026	0.87	0.75	1.00	0.054	0.90	0.77	1.06	0.222	0.90	0.76	1.05	0.180
4	0.80	0.70	0.91	0.001	0.83	0.72	0.95	0.005	0.94	0.81	1.09	0.410	0.94	0.81	1.09	0.394
5 (most deprived)	0.74	0.66	0.84	<0.001	0.77	0.68	0.88	<0.001	0.87	0.75	1.00	0.056	0.87	0.75	1.00	0.053
Age group (years)				<0.001				<0.001				0.115				0.040
<60	1.00				1.00				1.00				1.00			
60–69	0.93	0.83	1.03	0.168	0.92	0.82	1.03	0.140	1.04	0.91	1.18	0.601	1.02	0.89	1.16	0.801
70–79	0.65	0.58	0.73	<0.001	0.64	0.57	0.71	<0.001	0.94	0.82	1.07	0.334	0.90	0.79	1.03	0.121
80+	0.35	0.31	0.41	<0.001	0.34	0.30	0.39	<0.001	0.88	0.74	1.03	0.119	0.84	0.71	1.00	0.048
Sex				<0.001				<0.001				<0.001				<0.001
Female	1.00				1.00				1.00				1.00			
Male	0.74	0.69	0.80	<0.001	0.73	0.67	0.79	<0.001	0.72	0.66	0.79	<0.001	0.71	0.65	0.78	<0.001
Histology				<0.001				<0.001				<0.001				<0.001
NSCLC	1.00				1.00				1.00				1.00			
SCLC	0.34	0.30	0.40	<0.001	0.36	0.31	0.42	<0.001	0.46	0.40	0.54	<0.001	0.57	0.49	0.67	<0.001
Other	0.60	0.55	0.66	<0.001	0.64	0.58	0.71	<0.001	1.28	1.14	1.44	<0.001	1.33	1.18	1.50	<0.001
Year of Diagnosis				0.082				0.204				0.009				0.009
2006	1.00				1.00				1.00				1.00			
2007	1.06	0.95	1.18	0.301	1.05	0.94	1.18	0.351	1.02	0.90	1.15	0.765	1.00	0.88	1.13	0.954
2008	1.06	0.95	1.19	0.274	1.08	0.96	1.21	0.183	1.08	0.95	1.23	0.221	1.02	0.90	1.16	0.753
2009	1.19	1.04	1.36	0.010	1.16	1.01	1.33	0.036	0.83	0.71	0.98	0.025	0.80	0.68	0.93	0.005
Comorbidity score				0.007				0.011				<0.001				<0.001
0	1.00				1.00				1.00				1.00			
1–2	0.95	0.83	1.09	0.503	0.94	0.81	1.08	0.376	1.10	0.93	1.29	0.253	1.10	0.93	1.29	0.253
3+	0.84	0.66	1.07	0.158	0.79	0.61	1.03	0.077	0.96	0.72	1.28	0.787	0.96	0.72	1.29	0.807
Missing	0.82	0.74	0.92	<0.001	0.83	0.74	0.93	0.001	0.84	0.73	0.95	0.006	0.83	0.73	0.95	0.006
Unavailable	0.94	0.82	1.07	0.324	0.97	0.85	1.11	0.659	1.37	1.17	1.60	<0.001	1.38	1.18	1.61	<0.001
Timely GP referral				<0.001				<0.001				<0.001				<0.001
No GP referral date	1.00				1.00				1.00				1.00			
FHA≤14 days	1.44	1.32	1.58	<0.001	1.40	1.28	1.53	<0.001	1.16	1.05	1.29	0.004	1.14	1.03	1.26	0.015
FHA>14 days	1.98	1.79	2.19	<0.001	1.80	1.62	2.01	<0.001	1.40	1.25	1.58	<0.001	1.36	1.20	1.53	<0.001
Stage								<0.001				<0.001				<0.001
I					1.00				1.00				1.00			
II					0.38	0.29	0.50	<0.001	0.48	0.35	0.68	<0.001	0.49	0.35	0.69	<0.001
III					0.13	0.11	0.16	<0.001	0.29	0.23	0.36	<0.001	0.30	0.24	0.38	<0.001
IV					0.04	0.03	0.05	<0.001	0.12	0.09	0.15	<0.001	0.13	0.10	0.17	<0.001
Missing					0.17	0.14	0.20	<0.001	0.31	0.25	0.38	<0.001	0.33	0.27	0.41	<0.001
Performance status								<0.001				0.001				
0					1.00				1.00				1.00			
1–2					0.55	0.47	0.65	<0.001	0.88	0.73	1.05	0.157	0.89	0.74	1.07	0.201
3–4					0.18	0.14	0.24	<0.001	0.59	0.43	0.81	0.001	0.61	0.44	0.83	0.002
Missing					0.45	0.38	0.54	<0.001	0.73	0.60	0.90	0.002	0.72	0.59	0.88	0.002
Type of treatment												<0.001				<0.001
No treatment									1.00				1.00			
Surgery									49.77	41.93	59.07	<0.001	60.95	51.12	72.66	<0.001
Surgery + chemotherapy and/or radiotherapy									33.00	26.99	40.34	<0.001	40.47	32.96	49.69	<0.001
Chemotherapy									3.25	2.71	3.91	<0.001	4.19	3.47	5.05	<0.001
Chemotherapy + radiotherapy									7.83	6.65	9.22	<0.001	10.03	8.48	11.86	<0.001
Radiotherapy									3.34	2.89	3.87	<0.001	4.12	3.55	4.78	<0.001
Timely 1st treatment																<0.001
>31 days from diagnosis													1.00			
<31 days from diagnosis													0.50	0.45	0.56	<0.001

CCI score, Charlson Comorbidity Score; FHA, first hospital appointment; IMD, Index of Multiple Deprivation; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

Table 3 Likelihood of still being alive 2 years after diagnosis, by SEP, adjusted for selected patient, tumour and system factors, for those with stage recorded

	Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral (n=5233, R^2=3.72)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS (n=5233, R^2=26.59)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS, treatment (n=5233, R^2=31.73)				Adjusted—IMD, age, sex, histology, year, CCI, timely GP referral, stage, PS, treatment, timely 1st treatment (n=5233, R^2=32.04)			
Variable	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**	**OR**	**95% CI**		**p Value**
Deprivation quintile				0.017				0.221				0.761				0.800
1 (least deprived)	1.00				1.00				1.00				1.00			
2	0.92	0.71	1.20	0.544	0.97	0.72	1.31	0.834	1.02	0.74	1.40	0.923	1.01	0.73	1.39	0.966
3	0.92	0.72	1.19	0.534	1.00	0.75	1.34	0.993	1.08	0.79	1.47	0.641	1.07	0.78	1.46	0.672
4	0.72	0.56	0.91	0.007	0.77	0.58	1.02	0.064	0.90	0.67	1.21	0.505	0.91	0.67	1.22	0.511
5 (most deprived)	0.76	0.61	0.96	0.019	0.90	0.70	1.17	0.452	1.03	0.78	1.36	0.849	1.02	0.77	1.34	0.900
Age group (years)				<0.001				<0.001				0.687				0.668
<60	1.00				1.00				1.00				1.00			
60–69	1.06	0.86	1.31	0.601	1.03	0.81	1.32	0.793	1.12	0.86	1.45	0.411	1.11	0.85	1.44	0.452
70–79	0.79	0.64	0.97	0.026	0.75	0.59	0.96	0.024	1.03	0.78	1.34	0.853	1.00	0.77	1.31	0.989
80+	0.53	0.41	0.68	<0.001	0.49	0.36	0.67	<0.001	0.95	0.68	1.33	0.786	0.94	0.67	1.31	0.712
Sex				<0.001				<0.001				<0.001				<0.001
Female	1.00				1.00				1.00				1.00			
Male	0.75	0.65	0.86	<0.001	0.70	0.59	0.82	<0.001	0.69	0.58	0.82	<0.001	0.69	0.58	0.82	<0.001
Histology				<0.001				<0.001				0.0005				0.007
NSCLC	1.00				1.00				1.00				1.00			
SCLC	0.32	0.22	0.47	<0.001	0.49	0.32	0.76	0.001	0.48	0.31	0.74	0.001	0.55	0.35	0.85	0.008
Other	0.65	0.54	0.78	<0.001	0.80	0.64	1.00	0.047	1.19	0.93	1.52	0.176	1.18	0.92	1.51	0.190
Year of diagnosis				0.698				0.931				0.431				0.411
2006	1.00				1.00				1.00				1.00			
2007	1.03	0.80	1.33	0.831	1.07	0.80	1.43	0.660	1.02	0.75	1.38	0.910	1.00	0.73	1.36	0.993
2008	0.91	0.72	1.15	0.423	1.09	0.83	1.44	0.523	1.02	0.77	1.37	0.868	0.98	0.74	1.31	0.918
2009	0.95	0.72	1.25	0.704	1.09	0.79	1.50	0.594	0.82	0.59	1.14	0.242	0.79	0.57	1.11	0.175
Comorbidity score				0.071				0.218				0.025				0.021
0	1.00				1.00				1.00				1.00			
1–2	1.22	0.95	1.58	0.123	1.21	0.90	1.64	0.202	1.35	0.99	1.84	0.060	1.35	0.99	1.84	0.060
3+	1.00	0.63	1.58	0.998	0.83	0.49	1.40	0.479	1.06	0.61	1.83	0.843	1.02	0.59	1.78	0.934
Missing	0.85	0.68	1.07	0.168	0.93	0.71	1.21	0.575	0.90	0.68	1.18	0.455	0.90	0.68	1.18	0.434
Unavailable	1.05	0.83	1.34	0.663	1.19	0.91	1.58	0.209	1.40	1.04	1.88	0.025	1.40	1.05	1.89	0.024
Timely GP referral				<0.001				<0.001				0.137				0.165
No GP referral date	1.00				1.00				1.00				1.00			
FHA≤14 days	1.44	1.22	1.70	<0.001	1.36	1.12	1.66	0.002	1.23	1.00	1.52	0.048	1.22	0.99	1.50	0.059
FHA>14 days	1.87	1.52	2.30	<0.001	1.33	1.05	1.70	0.019	1.16	0.90	1.50	0.252	1.15	0.89	1.48	0.288
Stage								<0.001				<0.001				<0.001
I					1.00				1.00				1.00			
II					0.40	0.30	0.53	<0.001	0.47	0.34	0.63	<0.001	0.47	0.35	0.64	<0.001
III					0.14	0.12	0.17	<0.001	0.23	0.18	0.29	<0.001	0.24	0.19	0.30	<0.001
IV					0.04	0.04	0.06	<0.001	0.09	0.07	0.12	<0.001	0.10	0.07	0.13	<0.001
Performance status								<0.001				<0.001				<0.001
0					1.00				1.00				1.00			
1–2					0.53	0.44	0.64	<0.001	0.75	0.61	0.92	0.007	0.76	0.62	0.94	0.011
3–4					0.18	0.13	0.25	<0.001	0.44	0.30	0.65	<0.001	0.46	0.31	0.67	<0.001
Missing					0.47	0.35	0.64	<0.001	0.70	0.51	0.97	0.034	0.72	0.52	0.99	0.045
Type of treatment												<0.001				<0.001
No treatment									1.00				1.00			
Surgery									11.24	7.78	16.24	<0.001	12.86	8.84	18.70	<0.001
Surgery + chemotherapy and/or radiotherapy									13.13	8.78	19.63	<0.001	14.94	9.93	22.49	<0.001
Chemotherapy									2.48	1.70	3.62	<0.001	2.81	1.92	4.11	<0.001
Chemotherapy + radiotherapy									4.75	3.41	6.61	<0.001	5.43	3.87	7.60	<0.001
Radio									2.24	1.67	3.00	<0.001	2.47	1.83	3.32	<0.001
Timely 1st treatment																<0.001
>31 days from diagnosis													1.00			
<31 days from diagnosis													0.63	0.51	0.79	<0.001

CCI score, Charlson Comorbidity Score; FHA, first hospital appointment; IMD, Index of Multiple Deprivation; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

and these treatment inequalities appear to substantially explain inequalities in lung cancer survival. A similar finding was shown in a small study of 695 patients that did not include comorbidity or PS in the multivariable analysis.[27] Number of comorbidities and PS vary by SEP[28] and might help explain socioeconomic inequalities in receipt of treatment and survival. However, we were able to adjust for comorbidity and PS in a multivariable analysis, and survival inequalities were still observed. It was only on addition of receipt of treatment that the association no longer remained significant. In the subset with stage recorded, PS also substantially accounted for socioeconomic inequalities in survival. Patients were more likely to be younger and had higher rates of treatment in the staged subset, compared to the full cohort.[10]

Lung cancer survival is lower in the UK than in other European countries with similar healthcare systems which, it has been suggested, may be due to differences in management and access to treatment[29] and to longer diagnostic delay.[30] However, two literature reviews found the evidence of an association between timely care and survival for lung cancer inconclusive.[31 32] Contradictory results were found in the studies examined, but the quality of the studies included was mixed.[32] Lack of control for important confounding factors, such as age, stage, histology and comorbidity may account for why those with more timely care appear to have poorer survival in previous studies. The waiting time paradox suggests that sicker people are referred and treated more quickly but have shorter survival.[33]

Adequately controlling for stage, comorbidity and PS should eliminate this 'sicker quicker' effect. In a small study of colorectal cancer patients, shorter diagnostic interval was associated with higher mortality for those who appeared more ill, but not for those presenting with 'vague' symptoms.[33] In our study, we found that those who had a FHA within 14 days of GP referral had poorer survival than those who waited longer to be seen in secondary care in the full cohort, but not in the staged subset. Patients who had a shorter diagnostic to treatment interval had a lower likelihood of survival 2 years after diagnosis, compared to those with later treatment, and this association remained after age, stage, histology, comorbidity and PS were taken into account in the multivariable analysis. It may be that uncontrolled confounding remains, or that the measures of 'sickness' used—PS and comorbidity—have poor validity.

Implications for policy and practice, and further research

Socioeconomic inequalities in receipt of treatment appear to substantially account for socioeconomic inequalities in lung cancer survival. However, clinical guidelines focus on target times for referral and treatment rather than receipt of treatment. A clinical focus on ensuring that those who are eligible for treatment receive it, rather than on time-interval targets, might have a greater impact on improving survival, as well as reducing inequalities in survival.

As patients who were treated within the guideline targets had poorer survival than those who had later treatment, the effectiveness of the guidelines in improving survival appears unclear. A time-series analysis examining lung cancer survival preguideline and postguideline implementation could be used to investigate this.

Patients with early stage lung cancer are likely to be the patients for whom application of the guidelines, resulting in earlier referral and treatment, might improve survival. Further research on this group of patients is required to help determine whether delays in referral and treatment lead to poorer lung cancer survival, without the confounding effect of the waiting time paradox. Further research is also required to determine whether this interval effect on survival is also seen in other cancers.

Further examination of the patient, tumour and system factors that determine receipt and timeliness of treatment is warranted to determine why those who have later treatment have better survival, and to develop interventions to reduce inequalities in treatment and improve cancer survival.

CONCLUSIONS

Socioeconomic inequalities in lung cancer survival appear to be statistically explained by inequalities in receipt of treatment but not by inequalities in time from GP referral to FHA, or from diagnosis to treatment. However, patients who were treated within the time-to-treatment guideline targets had poorer survival compared to those who had later treatment.

Interventions that address socioeconomic inequalities in receipt of treatment may help to reduce socioeconomic inequalities in survival and improve survival rates overall.

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