



**Social differences in lung cancer management and survival
in South East England -A cohort study.**

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2 **Social differences in lung cancer management and survival in South East England - a**
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4 **cohort study.**
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52 **Key words:** lung neoplasm, management, treatment, survival, socioeconomic status
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Article focus

- Social differences in management and survival in lung cancer patients.
- Particular focus on possible social variations in lung cancer survival and assess if any such gradients can be attributed to social differences in co-morbidity, stage at diagnosis or treatment.

Key messages

- There were no detectable socioeconomic differences in stage at diagnosis among lung cancer patients in South East England between 2006 and 2008.
- Socioeconomic differences in lung cancer management and survival existed. The observed inequalities in survival could not fully be explained by social differences in stage at diagnosis, co-morbidity and treatment factors.
- In early stage disease, social gradients in survival existed throughout follow-up, whereas in advanced disease variations in survival were confined to the period immediately after diagnosis.

Strengths and limitations

- Strengths included the population-based cohort design. The material at hand allowed analyses that accounted for comorbidity, stage at diagnosis and treatment factors.
- Limitations included the absence of data on smoking history and life style factors.

ABSTRACT

Objective: To examine possible social variations in lung cancer survival and assess if any such gradients can be attributed to social differences in co-morbidity, stage at diagnosis or treatment.

Design: Population-based cohort identified in the Thames Cancer Registry.

Setting: South East England.

Participants: 15,582 lung cancer patients diagnosed between 2006 and 2008.

Main outcome measures: Stage at diagnosis, surgery, radiotherapy, chemotherapy and survival.

Results: The likelihood of being diagnosed with early stage disease did not vary by socioeconomic quintiles ($p=0.58$). In early stage non-small cell lung cancer, the likelihood of undergoing surgery was lowest in the most deprived group. There were no socioeconomic differences in the likelihood of receiving radiotherapy in stage III disease, while in advanced disease and in small cell lung cancer, receipt of chemotherapy differed over socioeconomic quintiles ($p<0.01$). In early stage disease and following adjustment for confounders, the hazard ratio between the most deprived and the most affluent group was 1.24 (95% confidence interval 0.98 to 1.56). Corresponding estimates in stage III and advanced disease or small cell lung cancer were 1.16 (95% confidence interval 1.01 to 1.34) and 1.12 (95% confidence interval 1.05 to 1.20), respectively. In early stage disease, the crude hazard ratio between the most deprived and the most affluent group was approximately 1.4 and constant through follow-up, while in patients with advanced disease or small cell lung cancer no difference was detectable after three months.

Conclusion: We observed socioeconomic variations in management and survival in patients diagnosed with lung cancer in South East England between 2006 and 2008, differences which could not fully be explained by social differences in stage at diagnosis, co-morbidity and treatment. The survival observed in the most affluent group should set the target for what is achievable for all lung cancer patients, managed in the same health care system.

INTRODUCTION

The overall prognosis of lung cancer is particularly poor in the United Kingdom with recent estimates showing a five year relative survival of 6.5% and 8.4% for men and women, respectively [1]. Observed national differences appear to be most pronounced early in the period of follow-up [1, 2]. Outcome in early stage lung cancer is highly dependent on management, where pulmonary resection offers a potentially curative treatment modality [3, 4]. Approximately 10% of all lung cancer patients in the United Kingdom underwent surgical resection between 2004 and 2006 [5], which is lower than corresponding estimates in some other European countries and the United States [6-7]. Previous studies have found evidence of both regional variations in treatment intensity and socioeconomic inequalities in lung cancer survival in the United Kingdom [8-12]. While one important aim of the National Health Service Cancer Plan in 2000 was to reduce social inequalities in cancer survival [13], marked differences persisted 10 years later [14]. Several factors may contribute to social gradients in cancer survival including the patient's general health status, knowledge and health care seeking behaviours, characteristics of the tumour at time of diagnosis, and clinical management. Differences in the management of patients in relation to socioeconomic factors, including the use of surgery in non-small cell lung cancer patients, have previously been reported in the United Kingdom and in other countries [15, 16]. The present study was based on patients diagnosed with lung cancer identified in the Thames Cancer Registry between 2006 and 2008 and aimed to examine possible social gradients in lung cancer survival and assess if any such variation can be attributed to social differences in co-morbidity, stage at diagnosis and treatment.

METHODS

Data collection

The Thames Cancer Registry is population based and currently covers a population of 12 million people in South East England (London, Kent, Surrey and Sussex). The Thames Cancer Registry registers approximately 57,000 incident cancer cases annually. Cancer registration is based on clinical and pathological information received from hospitals and from death certificates provided

1 by the Office for National Statistics. Hospital episode statistics data are obtained from hospital
2 patient administration systems and include information on the patient, as well as clinical and
3 administrative details. The UK National Lung Cancer Audit was set up in 2004 as a clinical
4 database for all new lung cancer patients. The number of trusts participating in this audit increased
5 from 40% in 2005 to 85% in England and Wales in 2008 [17]. While information on items such as
6 stage at diagnosis and treatment details are incompletely recorded in the cancer registry dataset,
7 these can be supplemented by means of record-linkage to the National Lung Cancer Audit and
8 hospital episode statistics [18]. The large majority of the relevant healthcare providers in South
9 East England are part of a national tax-funded health system, with only a minority of lung cancer
10 patients being managed by private providers.
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26 For the purpose of the present study we identified lung cancer cases registered with International
27 Classification of Diseases-10th Revision codes C33 and C34 from the Thames Cancer Registry
28 database. Data on surgery and radiotherapy were retrieved from hospital episode statistics and
29 supplemented with data from Thames Cancer Registry, whilst information on stage and
30 chemotherapy was obtained from the Cancer Registry and supplemented with data from the
31 National Lung Cancer Audit. Information on stage at diagnosis was available for 72.7% of the
32 patients. The definition of primary initial treatment (surgical resection, radiotherapy and
33 chemotherapy) was based on simple binary indicators. No treatment and no record of treatment
34 cannot be distinguished in these data.
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48 **Study population**

49 A total of 16,183 patients with a diagnosis of lung cancer between 2006 and 2008 were identified
50 in the Thames Cancer Registry. Following exclusion of death-certificate-only cancer registrations
51 (601 cases or 3.7% of the total), the final study population consisted of 15,582 cases. Patients were
52 subdivided into three subgroups according to disease status; early stage (stage IA-IIIB) non-small
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2 cell lung cancer (n=1,828), stage III non-small or small cell lung cancer (n=2,771) and advanced
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4 stage (stage IIIA-IV) disease or all stages of small cell lung cancer (n=10,039).
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8 **Co-morbidity**

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10 A modified version of the Charlson comorbidity index was used to assess the burden of
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12 concomitant disease for each patient, following retrieval of information on co-morbidity from the
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14 hospital episode statistics in a three-year period preceding the lung cancer diagnosis. The original
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16 Charlson comorbidity index consists of 19 disease groups, and has been used in earlier studies that
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18 have assessed the role of concomitant disease in cancer patients [19-21]. In the present study, all
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20 groups except cancer were included. Each disease group was then assigned a specific weight (1, 2,
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22 3 and 6) depending of the severity of the medical condition. The Charlson index was derived by
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24 summing the weighted scores for all comorbidities. On the basis of the distribution of the
25
26 Charlson score the patients were classified into three co-morbidity categories; no (0), mild (1), and
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28 severe co-morbidity (2+). Information was available for 88.4% of the patients. For 1,808 patients
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30 no link to the hospital episode statistics data could be established.
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36 **Socioeconomic quintile**

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38 Socioeconomic status recorded in the Thames Cancer Registry is based on the income domain of
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40 the 2007 Indices of Deprivation [22] in which patients are classified based on their postcode of
41
42 residence and are categorised into quintiles of socioeconomic deprivation. The most affluent
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44 group was labelled Q1 and the most deprived, Q5.
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49 **Statistical methods**

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51 Among all patients, crude and adjusted binary logistic regression models with odds ratios and 95%
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53 confidence intervals were used for prediction of the probability of being diagnosed with early stage
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55 disease by socioeconomic quintile. In a subsequent step, the likelihood to undergo surgical
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57 resection (in early stage non-small cell lung cancer), to receive radiotherapy (in stage III disease)
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1 and to receive chemotherapy (in advanced disease or small cell lung cancer) were assessed by using
2 crude and adjusted binary logistic regression models. All models were adjusted for sex, age at
3 diagnosis and the Charlson comorbidity index.
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10 In time to event analysis, the outcome of interest was all-cause mortality. Survival time was defined
11 as the interval between the date of the lung cancer diagnosis and the date of death, emigration or
12 end of follow-up on December 31, 2009. For each clinical subgroup (early stage non-small cell
13 lung cancer, stage III disease, and advanced stage or small-cell lung cancer), Cox regression models
14 were used to calculate hazard ratios and 95% confidence intervals for all-cause mortality in relation
15 to socioeconomic quintiles. Both univariate and multivariate models adjusted for sex, age at
16 diagnosis, co-morbidity and treatment factors were used. We used multiple imputation to account
17 for missing information on co-morbidity using chained equations with 60 imputed datasets [23].
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30 The relative contribution (%) of adding each covariate separately in explaining the possible social
31 variation in mortality between the most affluent and the most deprived patients in each subgroup
32 was calculated as follows: $((\text{HR for SES}_{Q_5} \text{ in Model A} - \text{HR for SES}_{Q_5} \text{ in model B}) / (\text{HR for SES}_{Q_5}$
33 $\text{in Model A} - 1)) * 100$, where Model A is the basic model (socioeconomic quintiles and adjusted
34 for sex) and in Model B, with each covariate being added to Model A.
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43 Cumulative survival and mortality rates (per 100 person-years) were estimated by subgroups and
44 socioeconomic quintile. The mortality rates were calculated as number of deaths divided by the
45 person-years at risk. These estimates were modelled with flexible parametric survival models using
46 a restricted cubic spline for the baseline mortality rate [24]. These models, similar to Cox
47 regression models, provide hazard ratios as measures of association between exposures and
48 outcome. By modelling the underlying rate parametrically, it is possible to estimate fitted curves
49 from the model, such as the cumulative survival function. In the Cox regression models, we
50 estimated a single hazard ratio between socioeconomic quintiles, assumed to be constant
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1 throughout follow-up. In the flexible parametric survival framework, the hazard ratio between the
2 most deprived versus most affluent patients was estimated in pre-defined segments of the follow-
3 up, using a second spline function. The hazard ratio is then time-dependent on the underlying
4 timescale which was time since diagnosis of lung cancer. All flexible parametric survival models
5 were estimated using the stpm2-package in STATA [25].
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14 In all analyses, we computed χ^2 tests and *p*-values for trend by fitting a linear categorical variable.
15 All *p*-values are two-sided and statistical significance was considered at *p*<0.05. The statistical
16 analyses were performed using STATA 11 and graphical displays were produced using R 10.2 [26].
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23 RESULTS

24 Demographic and clinical characteristics

25 **Table 1** shows the demographic and clinical characteristics by socioeconomic quintile. The most
26 affluent patients were generally older than the most deprived patients (*p*<0.01). The proportion of
27 patients with severe co-morbidity was higher in people categorised as deprived (29.6%) in Q5 than
28 in people belonging to the affluent (23.8%) in Q1 (*p*<0.01). The ratio of small cell to non-small
29 cell lung cancer decreased with socioeconomic deprivation. No statistically significant trend over
30 the socioeconomic quintiles was observed with regard to the likelihood to be diagnosed with early
31 stage disease (*p*=0.44) (**Table 2**). However, patients with co-morbidity were more likely to be
32 diagnosed with early stage disease (*p*<0.01).
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47 Treatment modality

48 About half of patients (49.2%) with early stage non-small cell lung cancer underwent surgical
49 resection. Surgery decreased from 55.8% in the most affluent group to 46.9% in the most deprived
50 group (*p*=0.29) (**Table 3**). There was a significant reduction in surgical resection with increasing
51 age at diagnosis (trend *p*<0.01), but not in relation to co-morbidity (trend *p*=0.21), once other
52 variables were adjusted for. In patients with stage III disease, 1,054 (38.0%) had radiotherapy
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1 treatment recorded (**Table 3**). In this subgroup, there was no association between socioeconomic
2 quintile and receipt of radiotherapy ($p=0.67$). In 10,039 patients registered with advanced disease
3 or small cell lung cancer, 36.5% had a record of chemotherapy (**Table 3**). A statistically significant
4 trend of reduced odds to receive chemotherapy was observed not only with increasing levels of
5 socioeconomic deprivation ($p<0.01$), but also with increased age at diagnosis ($p<0.01$) and co-
6 morbidity burden ($p<0.01$).
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14 Survival

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17 **Figure 1** shows estimated cumulative survival functions by socioeconomic quintile generated by
18 flexible parametric models. In patients with early stage non-small cell lung cancer, the three-year
19 survival in the most affluent and the most deprived group was 50% and 39%, respectively. While
20 survival in stage III disease and in advanced disease or small cell lung cancer was poor in all
21 socioeconomic quintiles, the prognosis was somewhat better in the most affluent group.
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32 **Table 4** shows the risk of all-cause mortality in patients with early stage non-small cell lung cancer,
33 in stage III disease and advanced disease or small cell lung cancer. In early stage non-small cell
34 lung cancer, the hazard ratio between the most deprived versus most affluent group was 1.24 (95%
35 confidence interval 0.98 to 1.56) following adjustment for potential confounders. The
36 corresponding estimates in stage III disease and advanced disease or small cell lung cancer was
37 1.16 (95% confidence interval 1.01 to 1.34) and 1.12 (95% confidence interval 1.05 to 1.20),
38 respectively. In none of the three clinical subgroups, no independent statistically significant trend
39 by socioeconomic quintiles could be detected.
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52 The relative contribution of age at diagnosis explaining the social inequality in survival between the
53 most affluent and the most deprived patients was 34.6% in stage III disease and 13.9% in
54 advanced disease or small cell lung cancer, respectively (**Table 4**). The corresponding percentages
55 of co-morbidity burden explaining the social inequality between the most affluent and the most
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2 deprived patients was 17.4% in stage III disease and 11.0% in advanced disease or small cell lung
3 cancer, respectively. Resection explained 42.3% in early stage disease, and chemotherapy explained
4 23.4% in advanced disease or small cell lung cancer of the social variation in survival.
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10 **Figure 2** illustrates the variation in overall mortality rates by time since diagnosis in the five
11 socioeconomic quintiles, and the variation of hazard ratios between the most deprived and the
12 most affluent group. In early stage non-small cell lung cancer, socioeconomic variations in the
13 mortality rates were most pronounced in the first months after diagnosis, but the differences
14 persisted twelve months after diagnosis. A hazard ratio of approximately 1.4 between the most
15 deprived and the most affluent group remained constant during follow-up.
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25 In stage III disease, and in advanced disease or small cell lung cancer, the mortality rates peaked
26 and varied by socioeconomic quintiles primarily during the first month post diagnosis, but after
27 twelve months only a minor social difference was observed. The same pattern was observed in the
28 time-dependent hazard ratio between the most deprived and the most affluent group.
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36 DISCUSSION

37 Main findings

38 Our study clearly demonstrates the presence of social differences in management, and in survival
39 in patients diagnosed with lung cancer in South East England between 2006 and 2008, and
40 observed social differences could not fully be explained by differences in stage at diagnosis, co-
41 morbidity and treatment factors. In early stage disease, the social gradients existed throughout
42 follow-up, whereas in advanced disease variations in survival were confined to the period
43 immediately after diagnosis.
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Methodological strengths and limitations

Strengths of our study included the population-based approach where the analyses were based on a cohort that included virtually all lung cancer patients diagnosed and managed in South East England between 2006 and 2008. For the purpose of the present study, additional information was obtained from other sources than the Thames Cancer Registry, including information on stage at diagnosis and co-morbidity. A weakness was the absence of stage at diagnosis for one fourth of the patients, which varied from 25.4% (Q5) to 27.9% (Q1) by socioeconomic quintiles. Patients with missing information on stage at diagnosis had particularly poor prognosis, which indicates that they often had advanced disease. Co-morbidity burden was assessed by using the Charlson comorbidity index which previously has been shown to be associated with the management of and outcomes in cancer patients [20], including lung cancer [27]. However, since no information was available on medical conditions not requiring in-hospital care and on other types of malignancies, it cannot be excluded that the influence of concomitant disease was underestimated. Thus, concomitant disease may have been both more common and more severe in patients with low socioeconomic status, ultimately influencing choice of treatment.

The definition of primary treatment (surgical resection, radiotherapy and chemotherapy) was based on the registration of 'Yes' or 'Unknown'. Thus, it was unclear if 'Unknown' was registered as meaning no treatment or missing information. However, it appears unlikely that there would be a systematic misclassification of treatment modality, favouring the most affluent patients. We acknowledge that our study included no information on second line treatments or smoking history. Although the income domain of the Indices of Deprivation used in the present study is an established indicator of socioeconomic status, it might not cover all aspects that contribute to the meaning of social status. In analyses without multiple imputation for missing values on co-morbidity, results remained virtually unchanged with regard to social gradients in management and survival. Finally, the interpretation of results in some subgroups (e.g. early stage disease) may have been hampered by a small number of events.

Comparison with other studies

Patients diagnosed with lung cancer are predominantly elderly smokers or ex-smokers who often have other smoking associated illnesses. We observed social variations in co-morbidity burden, but there were no differences with regard to stage at diagnosis between socioeconomic quintiles, a finding which corroborates with results from earlier studies [16, 28]. In the present study, early stage disease was more common in patients with severe co-morbidity, which may reflect that the lung malignancy was detected in the course of medical attention for other conditions.

In the present as well as in earlier studies conducted in Europe, choice of lung cancer management appears to vary by social group [16, 29]. Corroborating results from earlier studies [15, 16], we observed social gradients in the likelihood to undergo surgery, a finding which was independent of age at diagnosis and co-morbidity burden. The majority of lung cancer patients are diagnosed with advanced disease, where the primary goal of treatment is to control the cancer and alleviate symptoms, such as cough or breathlessness. Recommended initial treatments in advanced disease include radiotherapy and/or chemotherapy. The 2005 Guidelines on the management of lung cancer from the National Institute for Health and Clinical Excellence (NICE) and updated in 2011, recommend chemotherapy in small cell lung cancer, given that patients are fit enough [3]. In line with our findings, socioeconomic factors have previously been shown to be associated with chemotherapy use in lung cancer in South East England [30].

Social variations in management may be a result of several factors. In addition to possible differences between deprivation groups in general health status and health care seeking behaviours, there may be subtle differences in the doctor-patient interaction related to socioeconomic factors. Also, more affluent patients may have better support and knowledge resulting in increased expectations and demands on the health provider. Furthermore, patients' own willingness to accept treatment and acceptance of risks associated with surgical resection may

1 differ by level of deprivation. Finally, socioeconomic status has been associated with access to
2 cancer services, with less affluent patients having poorer access to specialist services and treatment
3 modalities, referred to in the United Kingdom as a 'postcode lottery' [31]. A recent study
4 concluded that living in a deprived locality in northern England reduced the likelihood of
5 undergoing treatment for lung cancer, and suggested that centralisation of services (thus increasing
6 travelling distances to specialist centres) would lead to further disadvantages for these patients [32].
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17 Our findings of social gradients in lung cancer survival corroborate results from several earlier
18 studies [8-10, 16]. Also, a recent report has documented persisting socioeconomic inequalities in
19 cancer survival in England after the introduction of the National Health Service Cancer Plan [14].
20 While social differences in tumour stage at time of diagnosis have often been put forward as an
21 explanation for social inequalities in cancer survival [33], both the present and recent results from
22 Sweden do not support this notion [16]. One English study has even suggested that deprived lung
23 cancer patients are more likely to be diagnosed with localized disease [34]. However, possible
24 social differences in diagnostic intensity, such as a higher likelihood to be examined by PET-CT or
25 CT-scan in affluent groups, could have resulted in stage migration ('Will Rogers phenomenon')
26 [35], which could inflate observed findings of social variations in survival. We have previously
27 observed a higher diagnostic intensity in lung cancer patients in Sweden with high socioeconomic
28 status [16], which may result in more accurate staging. Host factors that may contribute to social
29 differences in survival include co-morbidity and lifestyle factors, both pre- and post- diagnosis. In
30 the present study, adjustment for concomitant disease contributed only marginally to the
31 difference in the survival estimates between social groups. While no information was available on
32 lifestyle, it cannot be excluded that the observed inequalities in survival in early stage disease
33 throughout follow-up may reflect social differences in smoking cessation following diagnosis. Our
34 findings indicate that the relative contribution of differences in treatment to social inequalities in
35 survival appears to be high, foremost in early stage disease. This may play a particularly important
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2 role in explaining social differences in short-term mortality rates. Thus, increased treatment
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4 intensity among deprived patients is likely to help reduce social inequalities in survival.
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8 **Conclusion and policy implications**

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10 We observed socioeconomic differences not only in the clinical management, but also in survival
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12 in patients diagnosed with lung cancer in the South East England between 2006 and 2008. While
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14 efforts to eliminate social differences in lung cancer incidence will take many years, concerted
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16 action could reduce socioeconomic inequalities in management and survival more quickly. Areas
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18 of importance include efforts to guarantee equal access to health services and monitoring of
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20 adherence to guidelines. The survival observed in the most affluent patient group should set the
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22 target for what is achievable in the short-term for all lung cancer patients managed in the same
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24 health care system.
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30 **CONTRIBUTORS**

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32 Henrik Møller, Lars Holmberg, Mats Lambe and Anders Berglund designed and collected the data
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34 of the study. Anders Berglund did the statistical analyses. All authors participated in interpretation
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36 of the data. Anders Berglund wrote the first draft of the paper. All authors had full access to all the
37
38 data and approved the final draft. Henrik Møller is the guarantor for the study.
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48
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51 results; preparation, review, or approval of the manuscript.
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1 The funders did not have any involvement in the design of the study, the collection, analysis, and
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4 grant on behalf of all authors, an exclusive license on a worldwide basis to the BMJ publishing
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19 **CONFLICT OF INTEREST**

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21 Competing interests: All authors have completed the Unified Competing Interest form at
22 www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and
23 declare: that the for the specific matter of this research, no support from any organisation for the
24 submitted work; no financial relationships with any organisations that might have an interest in the
25 submitted work in the previous 3 years; no other relationships or activities that could appear to
26 have influenced the submitted work.
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37 **ETHICAL APPROVAL**

38 The study was approved by the Research Ethics Committee at Karolinska Institute.
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43 **DATA SHARING**

44 No additional data is available. Consent was not obtained but the presented data are anonymous
45 and the risk of identification is low.
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REFERENCES

1. Holmberg L, Sandin F, Bray F, *et al.* National comparisons of lung cancer survival in England, Norway and Sweden 2001-2004: differences occur early in follow-up. *Thorax* 2010;65:436-41.
2. Coleman MP, Forman D, Bryant H, *et al.* Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet* 2011;377:127-38.
3. Baldwin DR, White B, Schmidt-Hansen M, *et al.* Diagnosis and treatment of lung cancer: summary of updated NICE guidance. *Bmj* 2011;342:d2110.
4. Pearson, FG. Current status of surgical resection for lung cancer. *Chest* 1994;106:337S-339S.
5. National Cancer Intelligence Network. NHS treated cancer patients receiving major surgical resections - NCIN Data Briefing 2010.
6. Fry WA, Phillips JL, Menck HR. Ten-year survey of lung cancer treatment and survival in hospitals in the United States: a national cancer data base report. *Cancer* 1999;86:1867-76.
7. Myrdal G, Lamberg K, Lambe M, *et al.* Regional differences in treatment and outcome in non-small cell lung cancer: a population-based study (Sweden). *Lung Cancer* 2009;63:16-22.
8. Riaz SP, Horton M, Kang J, *et al.* Lung Cancer Incidence and Survival in England: An Analysis by Socioeconomic Deprivation and Urbanization. *J Thorac Oncol* 2011;1:1.
9. Jack RH, Davies EA, Moller H. Lung cancer incidence and survival in different ethnic groups in South East England. *Br J Cancer* 2011;105:1049-1053.
10. Coleman MP, Rachet B, Woods LM, *et al.* Trends and socioeconomic inequalities in cancer survival in England and Wales up to 2001. *Br J Cancer* 2004;90:1367-73.
11. Jack RH, Gulliford MC, Ferguson J, *et al.* Geographical inequalities in lung cancer management and survival in South East England: evidence of variation in access to oncology services? *Br J Cancer* 2003;88:1025-31.
12. NHS Information Centre. The National Lung Cancer Audit: 2011 report. Available via: http://www.ic.nhs.uk/webfiles/Services/NCASP/audits%20and%20reports/NHS_IC_Lung_Cancer_AUDIT_2011_Interactive_PDF_V1.0.pdf (last accessed 15.01.12)
13. Department of Health. The NHS Cancer plan: a plan for investment, a plan for reform. 2000.
14. Rachet B, Ellis L, Maringe C, *et al.* Socioeconomic inequalities in cancer survival in England after the NHS cancer plan. *Br J Cancer* 2010;103:446-53.
15. McMahon M, Barbiere JM, Greenberg DC, *et al.* Population-based trends in use of surgery for non-small cell lung cancer in a UK region, 1995-2006. *Thorax* 2011;66:453-5.
16. Berglund A, Holmberg L, Tishelman C, *et al.* Social inequalities in non-small cell lung cancer management and survival: a population-based study in central Sweden. *Thorax* 2010;65:327-33.
17. The NHS Information Centre. National Lung Cancer Audit 2010. 2009.
18. National Cancer Intelligence Network. National Cancer Data Repository. http://www.ncin.org.uk/collecting_and_using_data/national_cancer_data_repository/default.aspx.

19. Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83.
20. Berglund A, Garmo H, Tishelman C, *et al.* Comorbidity, treatment and mortality: a population based cohort study of prostate cancer in PCBaSe Sweden. *J Urol* 2011;185:833-9.
21. Janssen-Heijnen ML, Smulders S, Lemmens VE, *et al.* Effect of comorbidity on the treatment and prognosis of elderly patients with non-small cell lung cancer. *Thorax* 2004;59:602-7.
22. Department of Communities and Local Government. Indices of deprivation 2007. <http://www.communities.gov.uk/communities/neighbourhoodrenewal/deprivation/deprivation07/>.
23. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30:377-99.
24. Royston P, Parmar MK. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. *Stat Med* 2002;21:2175-97.
25. Lambert PC, Royston P. Further development of flexible parametric models for survival analysis. *Stata Journal* 2009;9:265-290.
26. Team R.D.C. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna Austria, 2008.
27. Asmis TR, Ding K, Seymour L, *et al.* Age and comorbidity as independent prognostic factors in the treatment of non small-cell lung cancer: a review of National Cancer Institute of Canada Clinical Trials Group trials. *J Clin Oncol* 2008;26:54-9.
28. Louwman WJ, Aarts MJ, Houterman S, *et al.* A 50% higher prevalence of life-shortening chronic conditions among cancer patients with low socioeconomic status. *Br J Cancer* 2010;103:1742-8.
29. Riaz SP, Luchtenborg M, Jack RH, *et al.* Variation in surgical resection for lung cancer in relation to survival: Population-based study in England 2004-2006. *Eur J Cancer* 2011;24:24.
30. Patel N, Adaita R, Mellempgaard A, *et al.* Variation in the use of chemotherapy in lung cancer. *Br J Cancer* 2007;96:886-90.
31. Bungay H. Cancer and Health Policy: the postcode lottery of care. *Soc Policy Adm* 2005;39:35-48.
32. Crawford SM, Sauerzapf V, Haynes R, *et al.* Social and geographical factors affecting access to treatment of lung cancer. *Br J Cancer* 2009;101:897-901.
33. Kogevinas M, Pearce N, Susser M, *et al.* Social Inequalities and Cancer. Vol. 138. 1997, Lyon: IARC Scientific Publications, International Agency for Research on Cancer.
34. Brewster DH, Thomson CS, Hole DJ, *et al.* Relation between socioeconomic status and tumour stage in patients with breast, colorectal, ovarian, and lung cancer: results from four national, population based studies. *BMJ* 2001;322:830-1.
35. Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon. Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. *N Engl J Med* 1985;312:1604-8.

LEGENDS FIGURES

Figure 1. Cumulative survival estimated by flexible parametric models by tumour subgroups and socioeconomic quintile.

Figure 2. Estimated mortality rates by socioeconomic quintile (allowing socioeconomic quintile to vary by follow-up) and the hazard ratio between the most deprived versus the most affluent patients within 12 months of diagnosis by tumour subgroups using flexible parametric models

Table 1. Demographic and clinical characteristics of 15,582 patients diagnosed with lung cancer between 2006 and 2008, by socioeconomic quintile.

	Q1 (Affluent)		Q2		Q3		Q4		Q5 (Deprived)		Total		Test	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	χ^2 (d.f)	p-value
All patients	2111	(100.0)	2550	(100.0)	3035	(100.0)	3817	(100.0)	4069	(100.0)	15582	(100.0)		
Sex														
Male	1208	(57.2)	1458	(57.2)	1708	(56.3)	2165	(56.7)	2358	(58.0)	8897	(57.1)		
Female	903	(42.8)	1092	(42.8)	1327	(43.7)	1652	(43.3)	1711	(42.0)	6685	(42.9)	0.31 (1)	0.57
Age at diagnosis														
0-59	310	(14.7)	329	(12.9)	430	(14.2)	637	(16.7)	752	(18.5)	2458	(15.8)		
60-69	497	(23.5)	617	(24.2)	743	(24.5)	990	(25.9)	1086	(26.7)	3933	(25.2)		
70-79	751	(35.6)	869	(34.1)	1009	(33.2)	1241	(32.5)	1302	(32.0)	5172	(33.2)		
80+	553	(26.2)	735	(28.8)	853	(28.1)	949	(24.9)	929	(22.8)	4019	(25.8)	66.7 (1)	<0.01
Charlson Score														
0	897	(49.8)	1065	(47.5)	1217	(45.5)	1496	(43.8)	1494	(41.1)	6169	(44.8)		
1	476	(26.4)	621	(27.7)	754	(28.2)	942	(27.6)	1064	(29.3)	3857	(28.0)		
2+	428	(23.8)	555	(24.8)	704	(26.3)	981	(28.7)	1075	(29.6)	3743	(27.2)	53.8 (1)	<0.01
Missing	310	-	309	-	360	-	398	-	436	-	1813	-		
Histologic type														
NSCLC	961	(45.5)	1058	(41.5)	1236	(40.7)	1515	(39.7)	1623	(39.9)	6393	(41.0)		
Other specified	39	(1.8)	47	(1.8)	54	(1.8)	61	(1.6)	60	(1.5)	261	(1.7)		
SCLC	197	(9.3)	259	(10.2)	311	(10.2)	440	(11.5)	485	(11.9)	1692	(10.9)		
Unspecified	914	(43.3)	1186	(46.5)	1434	(47.2)	1801	(47.2)	1901	(46.7)	7236	(46.4)	27.4 (12)	<0.01
Stage at diagnosis														
IA-IIIB	236	(15.4)	341	(18.6)	369	(16.9)	492	(17.9)	480	(15.8)	1918	(16.9)		
IIIA-IV	1296	(84.6)	1496	(81.4)	1812	(83.1)	2250	(82.1)	2556	(84.2)	9410	(83.1)	0.18 (1)	0.67
Unknown	579	-	713	-	854	-	1075	-	1033	-	4254	-		

Table 2. The likelihood of being diagnosed with early stage disease¹ estimated by crude and adjusted regression models with odds ratios (OR) and 95% confidence intervals (CI).

	No.	(%)	Crude		Adjusted	
			OR	95% CI	OR	95% CI
Socioeconomic quintile						
Q1 (Affluent)	236	(15.4)	1.00	reference	1.00	reference
Q2	341	(18.6)	1.25	(1.04 to 1.50)	1.24	(1.04 to 1.49)
Q3	369	(16.9)	1.12	(0.93 to 1.34)	1.11	(0.93 to 1.33)
Q4	492	(17.9)	1.20	(1.01 to 1.42)	1.18	(1.00 to 1.40)
Q5 (Deprived)	480	(15.8)	1.03	(0.87 to 1.22)	1.01	(0.85 to 1.20)
<i>Test for trend (χ^2, p-value)</i>			<i>0.18</i>	<i>0.67</i>	<i>0.59</i>	<i>0.44</i>
Sex						
Male	1037	(15.9)	1.00	reference	1.00	reference
Female	881	(18.3)	1.19	(1.08 to 1.30)	1.10	(1.10 to 1.33)
<i>Test for trend (χ^2, p-value)</i>			<i>11.5</i>	<i><0.01</i>	<i>12.6</i>	<i><0.01</i>
Age at diagnosis						
0-59	300	(15.2)	1.00	reference	1.00	reference
60-69	550	(17.6)	1.19	(1.02 to 1.39)	1.16	(0.99 to 1.35)
70-79	694	(18.4)	1.26	(1.08 to 1.46)	1.18	(1.01 to 1.37)
80+	374	(15.3)	1.01	(0.85 to 1.19)	0.93	(0.78 to 1.10)
<i>Test for trend (χ^2, p-value)</i>			<i>2.75</i>	<i>0.10</i>	<i>0.29</i>	<i>0.59</i>
Charlson Score						
0	719	(15.0)	1.00	reference	1.00	reference
1	511	(17.6)	1.19	(1.05 to 1.34)	1.19	(1.05 to 1.34)
2+	504	(19.0)	1.29	(1.14 to 1.47)	1.31	(1.15 to 1.49)
<i>Test for trend (χ^2, p-value)</i>			<i>20.0</i>	<i><0.01</i>	<i>21.7</i>	<i><0.01</i>

¹ The binary outcome was categorized into early stage disease (stage IA-IIIB at diagnosis) or advanced disease (stage IIIA-IV at diagnosis).

Table 3. The likelihood to undergo surgical resection in the subgroup of patients with early stage non-small cell lung cancer, to receive radiotherapy (stage III disease), or chemotherapy (advanced disease or small cell lung cancer) estimated by crude and adjusted logistic regression models with odds ratios (OR) and 95% confidence interval (CI).

	Surgical resection in early stage NSCLC (No. 1,828)						Radiotherapy in stage III disease (No. 2,771)						Chemotherapy in advanced or SCLC (No. 10,039)					
	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI
Eligible patients	899	(49.2)	-	-	-	-	1054	(38.0)	-	-	-	-	3661	(36.5)	-	-	-	-
Socioeconomic quintile																		
Q1 (Affluent)	126	(55.8)	1.00	reference	1.00	reference	146	(36.2)	1.00	reference	1.00	reference			1.00	reference	1.00	reference
Q2	156	(48.0)	0.73	(0.52 to 1.03)	0.74	(0.51 to 1.06)	179	(39.3)	1.14	(0.87 to 1.51)	1.16	(0.88 to 1.54)	555	(40.4)	0.87	(0.75 to 1.01)	0.90	(0.77 to 1.06)
Q3	171	(48.7)	0.75	(0.54 to 1.05)	0.71	(0.49 to 1.02)	215	(39.1)	1.13	(0.87 to 1.47)	1.17	(0.90 to 1.53)	591	(37.0)	0.78	(0.68 to 0.90)	0.78	(0.67 to 0.91)
Q4	230	(49.5)	0.78	(0.56 to 1.07)	0.73	(0.52 to 1.03)	263	(39.7)	1.16	(0.90 to 1.49)	1.18	(0.91 to 1.53)	666	(34.5)	0.83	(0.72 to 0.95)	0.77	(0.66 to 0.89)
Q5 (Deprived)	216	(46.9)	0.70	(0.51 to 0.96)	0.67	(0.48 to 0.95)	251	(35.9)	0.98	(0.76 to 1.27)	0.99	(0.77 to 1.29)	869	(35.9)	0.83	(0.73 to 0.95)	0.75	(0.65 to 0.87)
<i>Test for trend (χ², p-value)</i>			2.32	0.13	1.13	0.29			0.10	0.75	0.18	0.67			5.30	0.02	15.9	<0.01
Sex																		
Male	475	(47.9)	1.00	reference	1.00	reference	632	(37.8)	1.00	reference	1.00	reference	2195	(37.7)	1.00	reference	1.00	reference
Female	424	(50.7)	1.12	(0.93 to 1.35)	1.16	(0.95 to 1.41)	422	(38.3)	1.02	(0.87 to 1.19)	1.02	(0.87 to 1.20)	1466	(34.8)	0.88	(0.81 to 0.96)	0.90	(0.82 to 0.98)
<i>Test for trend (χ², p-value)</i>			2.28	0.13	2.63	0.11			0.07	0.80	0.85	0.36			8.76	<0.01	4.84	0.03
Age at diagnosis																		
0-59	203	(71.7)	1.00	reference	1.00	reference	197	(45.4)	1.00	reference	1.00	reference	1089	(60.4)	1.00	reference	1.00	reference
60-69	320	(61.3)	0.62	(0.46 to 0.85)	0.65	(0.48 to 0.89)	303	(39.5)	0.79	(0.62 to 1.00)	0.81	(0.64 to 1.03)	1357	(49.1)	0.63	(0.56 to 0.71)	0.66	(0.58 to 0.75)
70-79	318	(47.8)	0.36	(0.27 to 0.49)	0.38	(0.28 to 0.52)	362	(38.2)	0.74	(0.59 to 0.94)	0.79	(0.62 to 1.00)	1020	(30.9)	0.29	(0.26 to 0.33)	0.32	(0.28 to 0.36)
80+	58	(16.3)	0.08	(0.05 to 0.11)	0.08	(0.05 to 0.12)	192	(30.8)	0.54	(0.42 to 0.69)	0.56	(0.43 to 0.73)	195	(9.0)	0.06	(0.05 to 0.08)	0.07	(0.06 to 0.08)
<i>Test for trend (χ², p-value)</i>			39.0	<0.01	31.1	<0.01			17.2	<0.01	9.01	<0.01			869.4	<0.01	677.2	<0.01
Charlson Score																		
0	398	(58.4)	1.00	reference	1.00	reference	466	(41.5)	1.00	reference	1.00	reference	1960	(45.1)	1.00	reference	1.00	reference
1	257	(52.8)	0.82	(0.65 to 1.03)	0.87	(0.68 to 1.12)	288	(39.0)	0.90	(0.75 to 1.09)	0.93	(0.76 to 1.12)	943	(37.0)	0.72	(0.65 to 0.79)	0.82	(0.74 to 0.92)
2+	215	(44.8)	0.60	(0.48 to 0.76)	0.78	(0.60 to 1.01)	216	(32.7)	0.70	(0.57 to 0.85)	0.75	(0.61 to 0.92)	616	(26.9)	0.46	(0.41 to 0.51)	0.61	(0.54 to 0.68)
<i>Test for trend (χ², p-value)</i>			5.12	<0.01	1.57	0.21			12.9	<0.01	8.20	<0.01			217.1	<0.01	74.3	<0.01

Table 4. The risk of all-cause mortality in patients with early stage non-small cell lung cancer, in stage III disease, advanced disease or small cell lung cancer estimated by crude and adjusted Cox regression models with relative risks expressed as hazard ratios (HR)

	Early stage NSCLC (No. = 1,828)					Stage III disease (No. = 2,771)					Advanced disease or SCLC (No. = 10,039)				
	Crude		Adjusted		*% ¹	Crude		Adjusted		*% ¹	Crude		Adjusted		*% ¹
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
Socioeconomic quintile															
Q1 (Affluent)	1.00	reference	1.00	reference		1.00	reference	1.00	reference		1.00	reference	1.00	reference	
Q2	1.22	(0.95 to 1.56)	1.09	(0.85 to 1.40)		1.16	(1.00 to 1.34)	1.20	(1.03 to 1.39)		1.16	(1.08 to 1.25)	1.17	(1.08 to 1.26)	
Q3	1.25	(0.98 to 1.60)	1.18	(0.93 to 1.51)		1.15	(0.99 to 1.33)	1.14	(0.99 to 1.32)		1.16	(1.08 to 1.25)	1.13	(1.05 to 1.22)	
Q4	1.19	(0.94 to 1.50)	1.15	(0.91 to 1.46)		1.14	(0.99 to 1.30)	1.15	(1.00 to 1.32)		1.15	(1.07 to 1.23)	1.16	(1.08 to 1.25)	
Q5 (Deprived)	1.35	(1.07 to 1.70)	1.24	(0.98 to 1.56)	-	1.15	(1.01 to 1.32)	1.16	(1.01 to 1.34)	-	1.15	(1.08 to 1.24)	1.12	(1.05 to 1.20)	-
<i>Test for trend (χ², p-value)</i>	<i>4.18</i>	<i>0.04</i>	<i>2.56</i>	<i>0.11</i>		<i>2.38</i>	<i>0.12</i>	<i>0.14</i>	<i>0.70</i>		<i>9.35</i>	<i><0.01</i>	<i>1.92</i>	<i>0.17</i>	
Sex															
Male	1.00	reference	1.00	reference		1.00	reference	1.00	reference		1.00	reference	1.00	reference	
Female	0.84	(0.74 to 0.96)	0.85	(0.75 to 0.97)	-	0.97	(0.89 to 1.06)	0.95	(0.87 to 1.03)	-	0.95	(0.91 to 0.99)	0.92	(0.88 to 0.96)	-
<i>Test for trend (χ², p-value)</i>	<i>6.57</i>	<i>0.01</i>	<i>7.13</i>	<i><0.01</i>		<i>0.49</i>	<i>0.48</i>	<i>3.46</i>	<i>0.06</i>		<i>5.34</i>	<i>0.02</i>	<i>12.6</i>	<i><0.01</i>	
Age at diagnosis															
0-59	1.00	reference	1.00	reference	5.8%	1.00	reference	1.00	reference	34.6%	1.00	reference	1.00	reference	13.9%
60-69	1.41	(1.11 to 1.80)	1.25	(0.98 to 1.59)		1.15	(1.01 to 1.32)	1.09	(0.95 to 1.25)		1.14	(1.07 to 1.22)	1.07	(1.00 to 1.14)	
70-79	2.05	(1.64 to 2.58)	1.54	(1.22 to 1.95)		1.51	(1.33 to 1.72)	1.29	(1.12 to 1.47)		1.42	(1.33 to 1.51)	1.15	(1.08 to 1.22)	
80+	3.61	(2.85 to 4.58)	1.78	(1.39 to 2.28)		2.17	(1.89 to 2.49)	1.47	(1.26 to 1.70)		1.82	(1.71 to 1.95)	1.16	(1.08 to 1.25)	
<i>Test for trend (χ², p-value)</i>	<i>101.1</i>	<i><0.01</i>	<i>16.0</i>	<i><0.01</i>		<i>92.8</i>	<i><0.01</i>	<i>19.0</i>	<i><0.01</i>		<i>245.3</i>	<i><0.01</i>	<i>13.6</i>	<i><0.01</i>	
Charlson Score															
0	1.00	reference	1.00	reference	7.3%	1.00	reference	1.00	reference	17.4%	1.00	reference	1.00	reference	11.0%
1	1.10	(0.93 to 1.30)	0.98	(0.82 to 1.16)		1.10	(1.00 to 1.22)	1.03	(0.92 to 1.14)		1.08	(1.02 to 1.13)	0.99	(0.94 to 1.05)	
2+	1.35	(1.15 to 1.59)	1.03	(0.87 to 1.23)		1.32	(1.19 to 1.47)	1.09	(0.97 to 1.22)		1.22	(1.16 to 1.29)	1.00	(0.95 to 1.06)	
<i>Test for trend (χ², p-value)</i>	<i>13.5</i>	<i><0.01</i>	<i>0.04</i>	<i>0.84</i>		<i>30.9</i>	<i><0.01</i>	<i>3.05</i>	<i>0.08</i>		<i>58.6</i>	<i><0.01</i>	<i>0.17</i>	<i>0.90</i>	
Resection															
<i>Test (χ², p-value)</i>	<i>557.2</i>	<i><0.01</i>	<i>422.3</i>	<i><0.01</i>	42.3%	-	-	-	-	-	-	-	-	-	-
Radiotherapy															
<i>Test (χ², p-value)</i>	-	-	-	-	-	0.78	(0.72 to 0.85)	0.81	(0.73 to 0.88)	12.9%	0.71	(0.67 to 0.74)	0.73	(0.70 to 0.76)	1.2%
<i>Test (χ², p-value)</i>	-	-	-	-	-	<i>34.1</i>	<i><0.01</i>	<i>22.4</i>	<i><0.01</i>		<i>236.8</i>	<i><0.01</i>	<i>205.3</i>	<i><0.01</i>	
Chemotherapy															
<i>Test (χ², p-value)</i>	-	-	-	-	-	0.48	(0.44 to 0.52)	0.54	(0.49 to 0.59)	18.0%	0.42	(0.40 to 0.44)	0.44	(0.42 to 0.46)	23.4%
<i>Test (χ², p-value)</i>	-	-	-	-	-	<i>301.7</i>	<i><0.01</i>	<i>179.6</i>	<i><0.01</i>		<i>1564.7</i>	<i><0.01</i>	<i>179.6</i>	<i><0.01</i>	

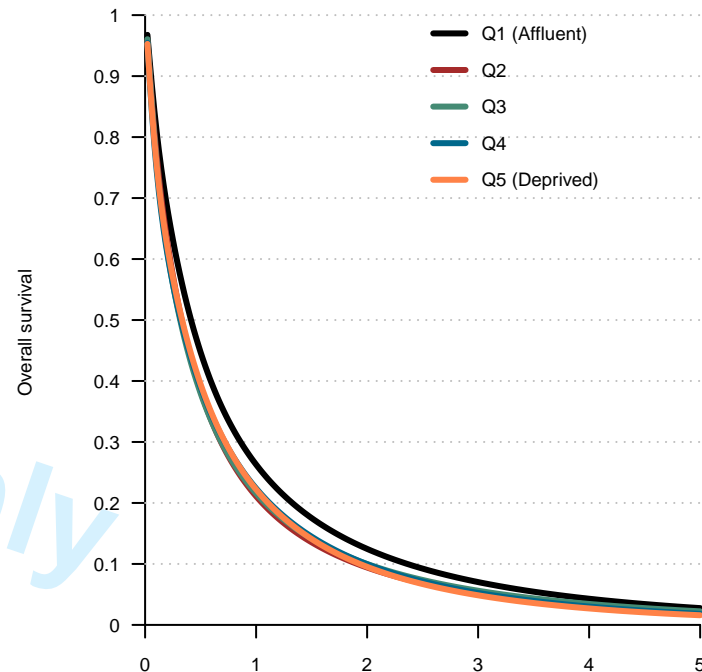
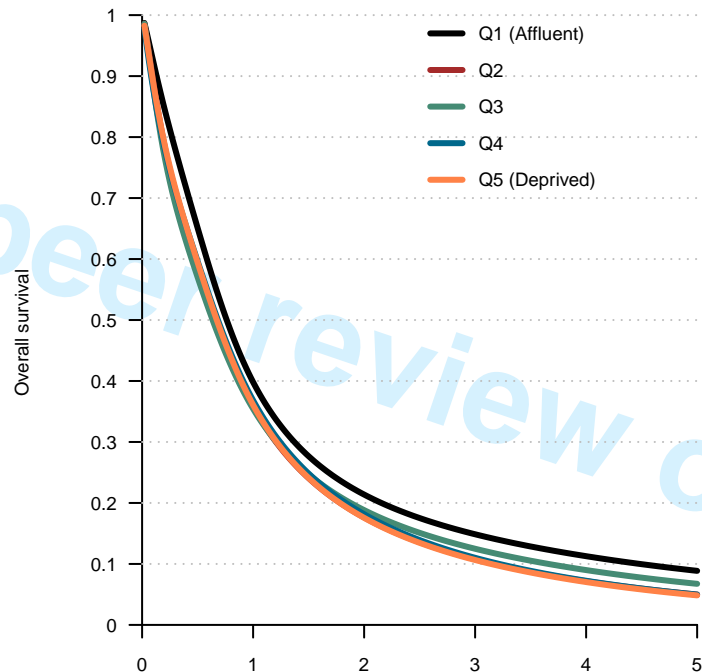
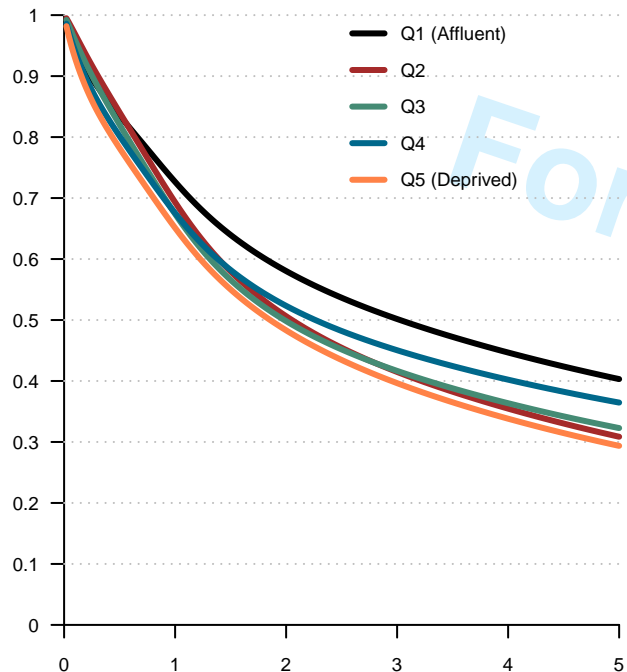
1. The relative contribution for each covariate in each subgroup was calculated as follows: ((HR for SES_{Q5} in a model adjusted for sex - HR for SES_{Q5} in a model adjusted for sex + covariate) / (HR for SES_{Q5} in a model adjusted for sex - 1)) * 100

Figure 1a. Early stage NSCLC (cumulative survival)

Figure 1b. Stage III disease (cumulative survival)

Figure 1c. Advanced disease or SCLC (cumulative survival)

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Page 24 of 24
Figure 2a. Early stage NSCLC (mortality rate)

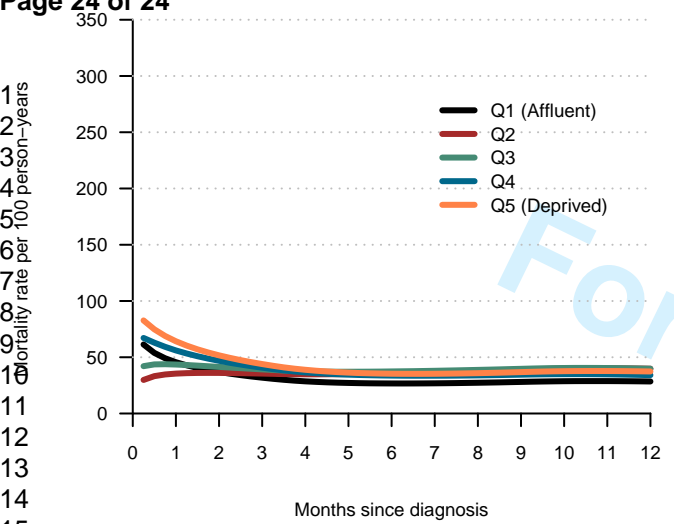


Figure 2b. Stage III disease (mortality rate)

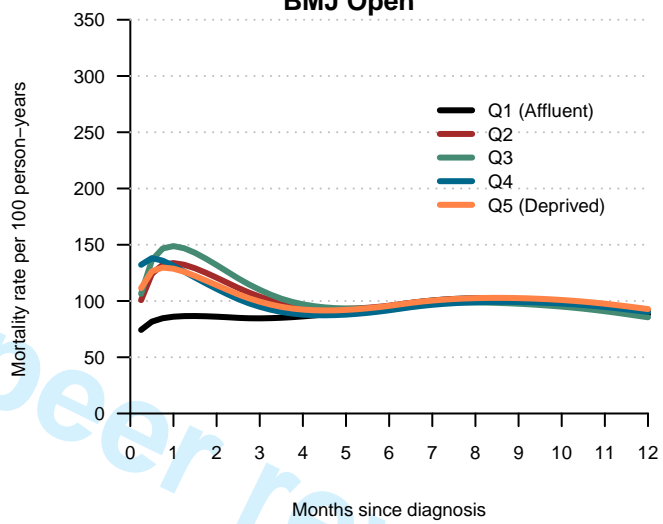


Figure 2c. Advanced disease or SCLC (mortality rate)

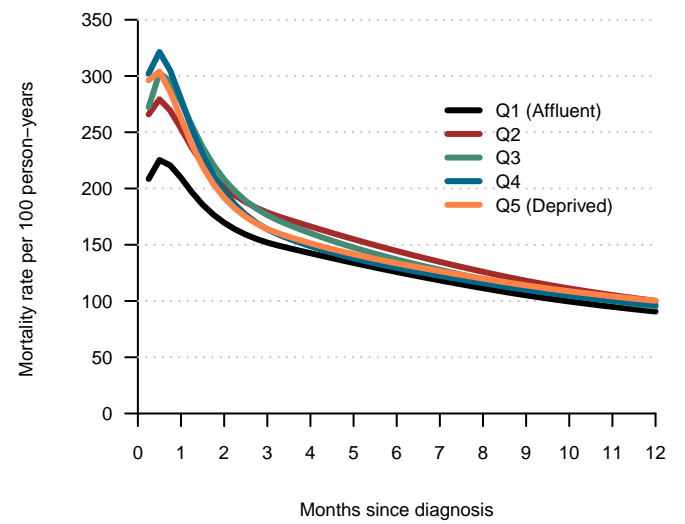


Figure 2d. Early stage NSCLC (hazard ratio)

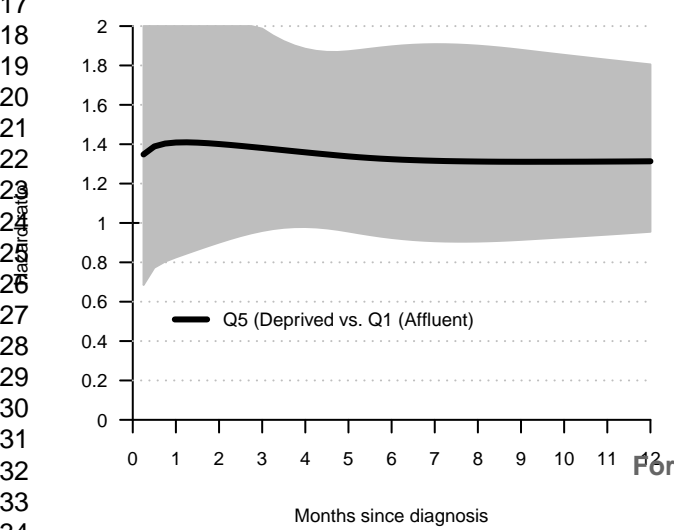


Figure 2e. Stage III disease (hazard ratio)

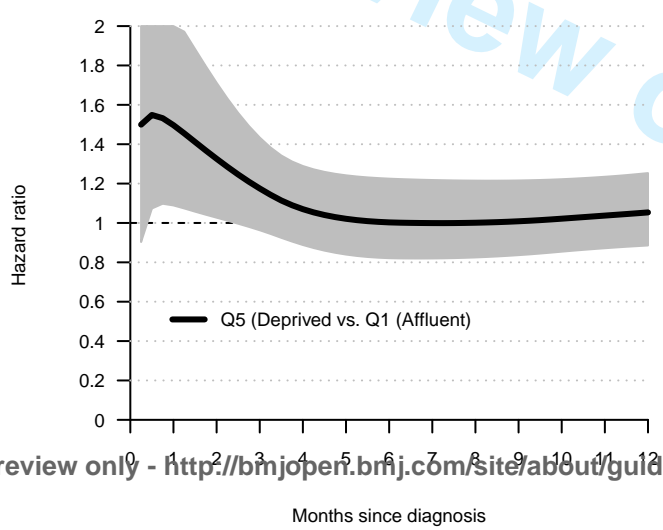
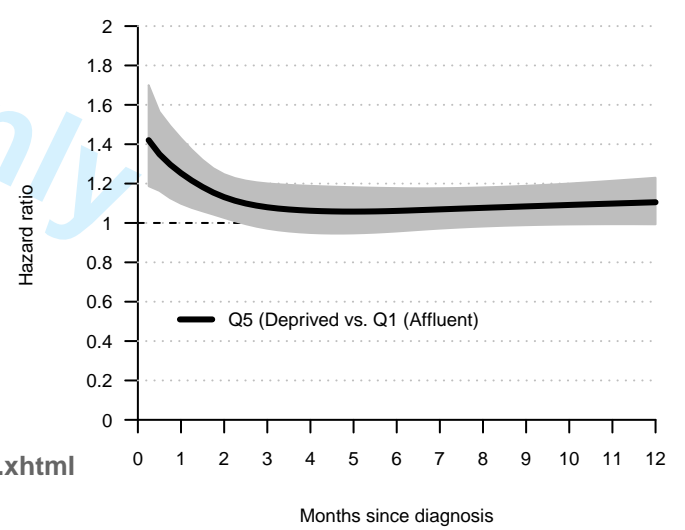


Figure 2f. Advanced disease or SCLC (hazard ratio)





**Social differences in lung cancer management and survival
in South East England -A cohort study.**

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2 **Social differences in lung cancer management and survival in South East England - a**
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4 **cohort study.**
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52 **Key words:** lung neoplasm, management, treatment, survival, socioeconomic status
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Article focus

- Social differences in management and survival in lung cancer patients.
- Particular focus on possible social variations in lung cancer survival and assess if any such gradients can be attributed to social differences in co-morbidity, stage at diagnosis or treatment.

Key messages

- There were no detectable socioeconomic differences in stage at diagnosis among lung cancer patients in South East England between 2006 and 2008.
- Socioeconomic differences in lung cancer management and survival existed. The observed inequalities in survival could not fully be explained by social differences in stage at diagnosis, co-morbidity and treatment factors.
- In early stage disease, social gradients in survival existed throughout follow-up, whereas in advanced disease variations in survival were confined to the period immediately after diagnosis.

Strengths and limitations

- Strengths included the population-based cohort design. The material at hand allowed analyses that accounted for comorbidity, stage at diagnosis and treatment factors.
- Limitations included the absence of data on performance status, forced expiratory volume, smoking history and life style factors.

ABSTRACT

Objective: To examine possible social variations in lung cancer survival and assess if any such gradients can be attributed to social differences in co-morbidity, stage at diagnosis or treatment.

Design: Population-based cohort identified in the Thames Cancer Registry.

Setting: South East England.

Participants: 15,582 lung cancer patients diagnosed between 2006 and 2008.

Main outcome measures: Stage at diagnosis, surgery, radiotherapy, chemotherapy and survival.

Results: The likelihood of being diagnosed with early stage disease did not vary by socioeconomic quintiles ($p=0.58$). In early stage non-small cell lung cancer, the likelihood of undergoing surgery was lowest in the most deprived group. There were no socioeconomic differences in the likelihood of receiving radiotherapy in stage III disease, while in advanced disease and in small cell lung cancer, receipt of chemotherapy differed over socioeconomic quintiles ($p<0.01$). In early stage disease and following adjustment for confounders, the hazard ratio between the most deprived and the most affluent group was 1.24 (95% confidence interval 0.98 to 1.56). Corresponding estimates in stage III and advanced disease or small cell lung cancer were 1.16 (95% confidence interval 1.01 to 1.34) and 1.12 (95% confidence interval 1.05 to 1.20), respectively. In early stage disease, the crude hazard ratio between the most deprived and the most affluent group was approximately 1.4 and constant through follow-up, while in patients with advanced disease or small cell lung cancer no difference was detectable after three months.

Conclusion: We observed socioeconomic variations in management and survival in patients diagnosed with lung cancer in South East England between 2006 and 2008, differences which could not fully be explained by social differences in stage at diagnosis, co-morbidity and treatment. The survival observed in the most affluent group should set the target for what is achievable for all lung cancer patients, managed in the same health care system.

INTRODUCTION

The overall prognosis of lung cancer is particularly poor in the United Kingdom with recent estimates showing a five year relative survival of 6.5% and 8.4% for men and women, respectively [1]. Observed national differences appear to be most pronounced early in the period of follow-up [1, 2]. Outcome in early stage lung cancer is highly dependent on management, where pulmonary resection offers a potentially curative treatment modality [3, 4]. Approximately 10% of all lung cancer patients in the United Kingdom underwent surgical resection between 2004 and 2006 [5], which is lower than corresponding estimates in some other European countries and the United States [6-7]. Previous studies have found evidence of both regional variations in treatment intensity and socioeconomic inequalities in lung cancer survival in the United Kingdom [8-12]. While one important aim of the National Health Service Cancer Plan in 2000 was to reduce social inequalities in cancer survival [13], marked differences persisted 10 years later [14]. Several factors may contribute to social gradients in cancer survival including the patient's general health status, knowledge and health care seeking behaviours, characteristics of the tumour at time of diagnosis, and clinical management. Differences in the management of patients in relation to socioeconomic factors, including the use of surgery in non-small cell lung cancer patients, have previously been reported in the United Kingdom and in other countries [15, 16]. The present study was based on patients diagnosed with lung cancer identified in the Thames Cancer Registry between 2006 and 2008 and aimed to examine possible social gradients in lung cancer survival and assess if any such variation can be attributed to social differences in co-morbidity, stage at diagnosis and treatment.

METHODS

Data collection

The Thames Cancer Registry is population based and currently covers a population of 12 million people in South East England (London, Kent, Surrey and Sussex). The Thames Cancer Registry registers approximately 57,000 incident cancer cases annually. Cancer registration is based on

1 clinical and pathological information received from hospitals and from death certificates provided
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3
4 by the Office for National Statistics. Hospital episode statistics data are obtained from hospital
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6 patient administration systems and include information on the patient, as well as clinical and
7
8 administrative details. The UK National Lung Cancer Audit was set up in 2004 as a clinical
9
10 database for all new lung cancer patients. The number of trusts participating in this audit increased
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12 from 40% in 2005 to 85% in England and Wales in 2008 [17]. While information on items such as
13
14 stage at diagnosis and treatment details are incompletely recorded in the cancer registry dataset,
15
16 these can be supplemented by means of record-linkage to the National Lung Cancer Audit and
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18 hospital episode statistics [18]. The large majority of the relevant healthcare providers in South
19
20 East England are part of a national tax-funded health system, with only a minority of lung cancer
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22 patients being managed by private providers.
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28 For the purpose of the present study we identified lung cancer cases registered with International
29
30 Classification of Diseases-10th Revision codes C33 and C34 from the Thames Cancer Registry
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32 database. Data on surgery and radiotherapy were retrieved from hospital episode statistics and
33
34 supplemented with data from Thames Cancer Registry, whilst information on stage and
35
36 chemotherapy was obtained from the Cancer Registry and supplemented with data from the
37
38 National Lung Cancer Audit. Information on stage at diagnosis was available for 72.7% of the
39
40 patients. The definition of primary initial treatment (surgical resection, radiotherapy and
41
42 chemotherapy) was based on simple binary indicators. No treatment and no record of treatment
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44 cannot be distinguished in these data.
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49 **Study population**

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51 A total of 16,183 patients with a diagnosis of lung cancer between 2006 and 2008 were identified
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53 in the Thames Cancer Registry. Following exclusion of death-certificate-only cancer registrations
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55 (601 cases or 3.7% of the total), the final study population consisted of 15,582 cases. Patients were
56
57 subdivided into three subgroups according to disease status; early stage (stage IA-IIIB) non-small
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2 cell lung cancer (n=1,828), stage III non-small or small cell lung cancer (n=2,771) and advanced
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4 stage (stage IIIA-IV) disease or all stages of small cell lung cancer (n=10,039). These three groups
5
6 were created on the basis of the most commonly used initial treatment modalities in every
7
8 subgroup.
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10 11 12 **Co-morbidity**

13
14 A modified version of the Charlson comorbidity index was used to assess the burden of
15
16 concomitant disease for each patient, following retrieval of information on co-morbidity from the
17
18 hospital episode statistics in a three-year period preceding the lung cancer diagnosis. The original
19
20 Charlson comorbidity index consists of 19 disease groups, and has been used in earlier studies that
21
22 have assessed the role of concomitant disease in cancer patients [19-21]. In the present study, all
23
24 groups except cancer were included. Each disease group was then assigned a specific weight (1, 2,
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26 3 and 6) depending of the severity of the medical condition. The Charlson index was derived by
27
28 summing the weighted scores for all comorbidities. On the basis of the distribution of the
29
30 Charlson score the patients were classified into three co-morbidity categories; no (0), mild (1), and
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32 severe co-morbidity (2+). Information was available for 88.4% of the patients. For 1,808 patients
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34 no link to the hospital episode statistics data could be established.
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40 41 **Socioeconomic quintile**

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43 Socioeconomic status recorded in the Thames Cancer Registry is based on the income domain of
44
45 the 2007 Indices of Deprivation [22] in which patients are classified based on their postcode of
46
47 residence and are categorised into quintiles of socioeconomic deprivation. The most affluent
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49 group was labelled Q1 and the most deprived, Q5.
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52 53 **Statistical methods**

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55 Among all patients, crude and adjusted binary logistic regression models with odds ratios and 95%
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57 confidence intervals were used for prediction of the probability of being diagnosed with early stage
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1 disease by socioeconomic quintile. In a subsequent step, the likelihood to undergo surgical
2 resection (in early stage non-small cell lung cancer), to receive radiotherapy (in stage III disease)
3 and to receive chemotherapy (in advanced disease or small cell lung cancer) were assessed by using
4 crude and adjusted binary logistic regression models. All models were adjusted for sex, age at
5 diagnosis and the Charlson comorbidity index.
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14 In time to event analysis, the outcome of interest was all-cause mortality. Survival time was defined
15 as the interval between the date of the lung cancer diagnosis and the date of death, emigration or
16 end of follow-up on December 31, 2009. For each clinical subgroup (early stage non-small cell
17 lung cancer, stage III disease, and advanced stage or small-cell lung cancer), Cox regression models
18 were used to calculate hazard ratios and 95% confidence intervals for all-cause mortality in relation
19 to socioeconomic quintiles. Both univariate and multivariate models adjusted for sex, age at
20 diagnosis, co-morbidity and treatment factors were used. We used multiple imputation to account
21 for missing information on co-morbidity using chained equations with 60 imputed datasets [23].
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34 The relative contribution (%) of adding each covariate separately in explaining the possible social
35 variation in mortality between the most affluent and the most deprived patients in each subgroup
36 was calculated as follows: $((\text{HR for SES}_{Q5} \text{ in Model A} - \text{HR for SES}_{Q5} \text{ in model B}) / (\text{HR for SES}_{Q5}$
37 $\text{in Model A} - 1)) * 100$, where Model A is the basic model (socioeconomic quintiles and adjusted
38 for sex) and in Model B, with each covariate being added to Model A.
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47 Cumulative survival and mortality rates (per 100 person-years) were estimated by subgroups and
48 socioeconomic quintile. The mortality rates were calculated as number of deaths divided by the
49 person-years at risk. These estimates were modelled with flexible parametric survival models using
50 a restricted cubic spline for the baseline mortality rate [24]. These models, similar to Cox
51 regression models, provide hazard ratios as measures of association between exposures and
52 outcome. By modelling the underlying rate parametrically, it is possible to estimate fitted curves
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1 from the model, such as the cumulative survival function. In the Cox regression models, we
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3
4 estimated a single hazard ratio between socioeconomic quintiles, assumed to be constant
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6 throughout follow-up. In the flexible parametric survival framework, the hazard ratio between the
7
8 most deprived versus most affluent patients was estimated in pre-defined segments of the follow-
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10 up, using a second spline function. The hazard ratio is then time-dependent on the underlying
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12 timescale which was time since diagnosis of lung cancer. All flexible parametric survival models
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14 were estimated using the stpm2-package in STATA [25].
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19 In all analyses, we computed χ^2 tests and *p*-values for trend by fitting a linear categorical variable.
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21 All *p*-values are two-sided and statistical significance was considered at *p*<0.05. The statistical
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23 analyses were performed using STATA 11 and graphical displays were produced using R 10.2 [26].
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28 RESULTS

29 Demographic and clinical characteristics

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32 **Table 1** shows the demographic and clinical characteristics by socioeconomic quintile. The most
33
34 affluent patients were generally older than the most deprived patients (*p*<0.01). The proportion of
35
36 patients with severe co-morbidity was higher in people categorised as deprived (29.6%) in Q5 than
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38 in people belonging to the affluent (23.8%) in Q1 (*p*<0.01). Among patients with classifiable
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40 disease, the proportion of non-small cell lung cancer was higher in the most affluent group. No
41
42 statistically significant trend over the socioeconomic quintiles was observed with regard to the
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44 likelihood to be diagnosed with early stage disease (*p*=0.44) (**Table 2**). However, patients with co-
45
46 morbidity were more likely to be diagnosed with early stage disease (*p*<0.01).
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51 Treatment modality

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53 About half of patients (49.2%) with early stage non-small cell lung cancer underwent surgical
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55 resection. Surgery decreased from 55.8% in the most affluent group to 46.9% in the most deprived
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57 group (*p*=0.29) (**Table 3**). There was a significant reduction in surgical resection with increasing
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1 age at diagnosis (trend $p < 0.01$), but not in relation to co-morbidity (trend $p = 0.21$), once other
2 variables were adjusted for. In patients with stage III disease, 1,054 (38.0%) had radiotherapy
3 treatment recorded (**Table 3**). In this subgroup, there was no association between socioeconomic
4 quintile and receipt of radiotherapy ($p = 0.67$). In 10,039 patients registered with advanced disease
5 or small cell lung cancer, 36.5% had a record of chemotherapy (**Table 3**). A statistically significant
6 trend of reduced odds to receive chemotherapy was observed not only with increasing levels of
7 socioeconomic deprivation ($p < 0.01$), but also with increased age at diagnosis ($p < 0.01$) and co-
8 morbidity burden ($p < 0.01$).

21 Survival

22 **Figure 1** shows estimated cumulative survival functions by socioeconomic quintile generated by
23 flexible parametric models. In patients with early stage non-small cell lung cancer, the three-year
24 survival in the most affluent and the most deprived group was 50% and 39%, respectively. While
25 survival in stage III disease and in advanced disease or small cell lung cancer was poor in all
26 socioeconomic quintiles, the prognosis was somewhat better in the most affluent group.

27 **Table 4** shows the risk of all-cause mortality in patients with early stage non-small cell lung cancer,
28 in stage III disease and advanced disease or small cell lung cancer. In early stage non-small cell
29 lung cancer, the hazard ratio between the most deprived versus most affluent group was 1.24 (95%
30 confidence interval 0.98 to 1.56) following adjustment for potential confounders. The
31 corresponding estimates in stage III disease and advanced disease or small cell lung cancer was
32 1.16 (95% confidence interval 1.01 to 1.34) and 1.12 (95% confidence interval 1.05 to 1.20),
33 respectively. In none of the three clinical subgroups, no independent statistically significant trend
34 by socioeconomic quintiles could be detected.

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56 The relative contribution of age at diagnosis explaining the social inequality in survival between the
57 most affluent and the most deprived patients was 34.6% in stage III disease and 13.9% in
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1 advanced disease or small cell lung cancer, respectively (**Table 4**). The corresponding percentages
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4 of co-morbidity burden explaining the social inequality between the most affluent and the most
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6 deprived patients was 17.4% in stage III disease and 11.0% in advanced disease or small cell lung
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8 cancer, respectively. Resection explained 42.3% in early stage disease, and chemotherapy explained
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10 23.4% in advanced disease or small cell lung cancer of the social variation in survival.
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15 **Figure 2** illustrates the variation in overall mortality rates by time since diagnosis in the five
16
17 socioeconomic quintiles, and the variation of hazard ratios between the most deprived and the
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19 most affluent group. In early stage non-small cell lung cancer, socioeconomic variations in the
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21 mortality rates were most pronounced in the first months after diagnosis, but the differences
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23 persisted twelve months after diagnosis. A hazard ratio of approximately 1.4 between the most
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25 deprived and the most affluent group remained constant during follow-up.
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30 In stage III disease, and in advanced disease or small cell lung cancer, the mortality rates peaked
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32 and varied by socioeconomic quintiles primarily during the first month post diagnosis, but after
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34 twelve months only a minor social difference was observed. The same pattern was observed in the
35
36 time-dependent hazard ratio between the most deprived and the most affluent group.
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39 40 41 **DISCUSSION**

42 43 **Main findings**

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45 Our study clearly demonstrates the presence of social differences in management, and in survival
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47 in patients diagnosed with lung cancer in South East England between 2006 and 2008, and
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49 observed social differences could not fully be explained by differences in stage at diagnosis, co-
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51 morbidity and treatment factors. In early stage disease, the social gradients existed throughout
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53 follow-up, whereas in advanced disease variations in survival were confined to the period
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55 immediately after diagnosis.
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Methodological strengths and limitations

Strengths of our study included the population-based approach where the analyses were based on a cohort that included virtually all lung cancer patients diagnosed and managed in South East England between 2006 and 2008. For the purpose of the present study, additional information was obtained from other sources than the Thames Cancer Registry, including information on stage at diagnosis and co-morbidity. A weakness was the absence of stage at diagnosis for one fourth of the patients, which varied from 25.4% (Q5) to 27.9% (Q1) by socioeconomic quintiles. Patients with missing information on stage at diagnosis had particularly poor prognosis, which indicates that they often had advanced disease. Co-morbidity burden was assessed by using the Charlson comorbidity index which previously has been shown to be associated with the management of and outcomes in cancer patients [20], including lung cancer [27]. However, since no information was available on medical conditions not requiring in-hospital care and on other types of malignancies, it cannot be excluded that the influence of concomitant disease was underestimated. The introduction of the 7th edition of the TNM classification in 2009 provides better prognostic differentiation [28]. Since our study included cases diagnosed between 2006 and 2008, some caution should be taken when a reader generalise the findings to the situation of today. Also, the data at hand did not allow for assessment of performance status, forced expiratory volume, smoking history and life style factors. Thus, concomitant disease, poor performance status and impaired lung function may have been both more common and more severe in patients with low socioeconomic status, ultimately influencing choice of treatment.

The definition of primary treatment (surgical resection, radiotherapy and chemotherapy) was based on the registration of 'Yes' or 'Unknown'. Thus, it was unclear if 'Unknown' was registered as meaning no treatment or missing information. However, it appears unlikely that there would be a systematic misclassification of treatment modality, favouring the most affluent patients. We acknowledge that our study included no information on second line treatments or smoking history. Although the income domain of the Indices of Deprivation used in the present study is an

1 established indicator of socioeconomic status, it might not cover all aspects that contribute to the
2 meaning of social status. Using an area-based deprivation index is likely to lead to an
3
4 meaning of social status. Using an area-based deprivation index is likely to lead to an
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6 underestimation of social differences in survival [29]. The variability in socioeconomic status based
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8 on area characteristics will always be smaller than that on the individual level [30]. In analyses
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10 without multiple imputation for missing values on co-morbidity, results remained virtually
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12 unchanged with regard to social gradients in management and survival. Finally, the interpretation
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14 of results in some subgroups (e.g. early stage disease) may have been hampered by a small number
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16 of events.
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21 **Comparison with other studies**

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23 Patients diagnosed with lung cancer are predominantly elderly smokers or ex-smokers who often
24
25 have other smoking associated illnesses. We observed social variations in co-morbidity burden, but
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27 there were no differences with regard to stage at diagnosis between socioeconomic quintiles, a
28
29 finding which corroborates with results from earlier studies [16, 31]. However, a recent
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31 population-based Danish study found associations between level of education and stage at
32
33 diagnosis [32], which is in line with results from a study from United States [33]. In the present
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35 study, early stage disease was more common in patients with severe co-morbidity, which may
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37 reflect that the lung malignancy was detected in the course of medical attention for other
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39 conditions.
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45 In the present as well as in earlier studies conducted in Europe, choice of lung cancer management
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47 appears to vary by social group [16, 34]. Corroborating results from earlier studies [15, 16], we
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49 observed social gradients in the likelihood to undergo surgery, a finding which was independent of
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51 age at diagnosis and co-morbidity burden. The majority of lung cancer patients are diagnosed with
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53 advanced disease, where the primary goal of treatment is to control the cancer and alleviate
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55 symptoms, such as cough or breathlessness. Recommended initial treatments in advanced disease
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57 include radiotherapy and/or chemotherapy. The 2005 Guidelines on the management of lung
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1 cancer from the National Institute for Health and Clinical Excellence (NICE) and updated in
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4 2011, recommend chemotherapy in small cell lung cancer, given that patients are fit enough [3]. In
5
6 line with our findings, socioeconomic factors have previously been shown to be associated with
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8 chemotherapy use in lung cancer in South East England [35].
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12 Social variations in management may be a result of several factors. In addition to possible
13
14 differences between deprivation groups in general health status and health care seeking
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16 behaviours, there may be subtle differences in the doctor-patient interaction related to
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18 socioeconomic factors. A recent Danish study found evidence of associations between educational
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20 level and time between referral and diagnosis [32], findings that corroborate results from Sweden
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22 [16]. Also, more affluent patients may have better support and knowledge resulting in increased
23
24 expectations and demands on the health provider. Furthermore, patients' own willingness to
25
26 accept treatment and acceptance of risks associated with surgical resection may differ by level of
27
28 deprivation. Finally, socioeconomic status has been associated with access to cancer services, with
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30 less affluent patients having poorer access to specialist services and treatment modalities, referred
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32 to in the United Kingdom as a 'postcode lottery' [36]. A recent study concluded that living in a
33
34 deprived locality in northern England reduced the likelihood of undergoing treatment for lung
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36 cancer, and suggested that centralisation of services (thus increasing travelling distances to
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38 specialist centres) would lead to further disadvantages for these patients, and the same
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40 phenomenon was observed in respect of access through a local hospital to any treatment and to
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42 histological diagnosis [37].
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50 Our findings of social gradients in lung cancer survival corroborate results from several earlier
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52 studies [8-10, 16]. Also, a recent report has documented persisting socioeconomic inequalities in
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54 cancer survival in England after the introduction of the National Health Service Cancer Plan [14].
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56 While social differences in tumour stage at time of diagnosis have often been put forward as an
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58 explanation for social inequalities in cancer survival [38], both the present and recent results from
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Sweden do not support this notion [16]. One English study has even suggested that deprived lung cancer patients are more likely to be diagnosed with localized disease [39]. However, possible social differences in diagnostic intensity, such as a higher likelihood to be examined by PET-CT or CT-scan in affluent groups, could have resulted in stage migration ('Will Rogers phenomenon') [40], which could inflate observed findings of social variations in survival. We have previously observed a higher diagnostic intensity in lung cancer patients in Sweden with high socioeconomic status [16], which may result in more accurate staging. Host factors that may contribute to social differences in survival include co-morbidity and lifestyle factors, both pre- and post- diagnosis. In the present study, adjustment for concomitant disease contributed only marginally to the difference in the survival estimates between social groups. While no information was available on lifestyle, it cannot be excluded that the observed inequalities in survival in early stage disease throughout follow-up may reflect social differences in smoking cessation following diagnosis. Our findings indicate that the relative contribution of differences in treatment to social inequalities in survival appears to be high, foremost in early stage disease. This may play a particularly important role in explaining social differences in short-term mortality rates. Thus, increased treatment intensity among deprived patients is likely to help reduce social inequalities in survival.

Conclusion and policy implications

We observed socioeconomic differences not only in the clinical management, but also in survival in patients diagnosed with lung cancer in the South East England between 2006 and 2008. While efforts to eliminate social differences in lung cancer incidence will take many years, concerted action could reduce socioeconomic inequalities in management and survival more quickly. Areas of importance include efforts to guarantee equal access to health services and monitoring of adherence to guidelines. The survival observed in the most affluent patient group should set the target for what is achievable in the short-term for all lung cancer patients managed in the same health care system.

CONTRIBUTORS

Henrik Møller, Lars Holmberg, Mats Lambe and Anders Berglund designed and collected the data of the study. Anders Berglund did the statistical analyses. All authors participated in interpretation of the data. Anders Berglund wrote the first draft of the paper. All authors had full access to all the data and approved the final draft. Henrik Møller is the guarantor for the study.

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NOTES

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CONFLICT OF INTEREST

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: that the for the specific matter of this research, no support from any organisation for the

1 submitted work; no financial relationships with any organisations that might have an interest in the
2
3 submitted work in the previous 3 years; no other relationships or activities that could appear to
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5 have influenced the submitted work.
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10 **ETHICAL APPROVAL**

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12 The study was approved by the Research Ethics Committee at Karolinska Institute.
13
14

15 **DATA SHARING**

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17 No additional data is available. Consent was not obtained but the presented data are anonymous
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19 and the risk of identification is low.
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REFERENCES

1. Holmberg L, Sandin F, Bray F, *et al.* National comparisons of lung cancer survival in England, Norway and Sweden 2001-2004: differences occur early in follow-up. *Thorax* 2010;65:436-41.
2. Coleman MP, Forman D, Bryant H, *et al.* Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet* 2011;377:127-38.
3. Baldwin DR, White B, Schmidt-Hansen M, *et al.* Diagnosis and treatment of lung cancer: summary of updated NICE guidance. *Bmj* 2011;342:d2110.
4. Pearson, FG. Current status of surgical resection for lung cancer. *Chest* 1994;106:337S-339S.
5. National Cancer Intelligence Network. NHS treated cancer patients receiving major surgical resections - NCIN Data Briefing 2010.
6. Fry WA, Phillips JL, Menck HR. Ten-year survey of lung cancer treatment and survival in hospitals in the United States: a national cancer data base report. *Cancer* 1999;86:1867-76.
7. Myrdal G, Lamberg K, Lambe M, *et al.* Regional differences in treatment and outcome in non-small cell lung cancer: a population-based study (Sweden). *Lung Cancer* 2009;63:16-22.
8. Riaz SP, Horton M, Kang J, *et al.* Lung Cancer Incidence and Survival in England: An Analysis by Socioeconomic Deprivation and Urbanization. *J Thorac Oncol* 2011;1:1.
9. Jack RH, Davies EA, Moller H. Lung cancer incidence and survival in different ethnic groups in South East England. *Br J Cancer* 2011;105:1049-1053.
10. Coleman MP, Rachet B, Woods LM, *et al.* Trends and socioeconomic inequalities in cancer survival in England and Wales up to 2001. *Br J Cancer* 2004;90:1367-73.
11. Jack RH, Gulliford MC, Ferguson J, *et al.* Geographical inequalities in lung cancer management and survival in South East England: evidence of variation in access to oncology services? *Br J Cancer* 2003;88:1025-31.
12. NHS Information Centre. The National Lung Cancer Audit: 2011 report. Available via: http://www.ic.nhs.uk/webfiles/Services/NCASP/audits%20and%20reports/NHS_IC_Lung_Cancer_AUDIT_2011_Interactive_PDF_V1.0.pdf (last accessed 15.01.12)
13. Department of Health. The NHS Cancer plan: a plan for investment, a plan for reform. 2000.
14. Rachet B, Ellis L, Maringe C, *et al.* Socioeconomic inequalities in cancer survival in England after the NHS cancer plan. *Br J Cancer* 2010;103:446-53.
15. McMahon M, Barbiere JM, Greenberg DC, *et al.* Population-based trends in use of surgery for non-small cell lung cancer in a UK region, 1995-2006. *Thorax* 2011;66:453-5.
16. Berglund A, Holmberg L, Tishelman C, *et al.* Social inequalities in non-small cell lung cancer management and survival: a population-based study in central Sweden. *Thorax* 2010;65:327-33.
17. The NHS Information Centre. National Lung Cancer Audit 2010. 2009.
18. National Cancer Intelligence Network. National Cancer Data Repository. http://www.ncin.org.uk/collecting_and_using_data/national_cancer_data_repository/default.aspx.

19. Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83.
20. Berglund A, Garmo H, Tishelman C, *et al.* Comorbidity, treatment and mortality: a population based cohort study of prostate cancer in PCBaSe Sweden. *J Urol* 2011;185:833-9.
21. Janssen-Heijnen ML, Smulders S, Lemmens VE, *et al.* Effect of comorbidity on the treatment and prognosis of elderly patients with non-small cell lung cancer. *Thorax* 2004;59:602-7.
22. Department of Communities and Local Government. Indices of deprivation 2007. <http://www.communities.gov.uk/communities/neighbourhoodrenewal/deprivation/deprivation07/>.
23. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30:377-99.
24. Royston P, Parmar MK. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. *Stat Med* 2002;21:2175-97.
25. Lambert PC, Royston P, Further development of flexible parametric models for survival analysis. *Stata Journal* 2009;9:265-290.
26. Team R.D.C. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna Austria, 2008.
27. Asmis TR, Ding K, Seymour L, *et al.* Age and comorbidity as independent prognostic factors in the treatment of non small-cell lung cancer: a review of National Cancer Institute of Canada Clinical Trials Group trials. *J Clin Oncol* 2008;26:54-9.
28. Travis WD. Reporting lung cancer pathology specimens. Impact of the anticipated 7th Edition TNM classification based on recommendations of the IASLC Staging Committee. *Histopathology* 2009;54:3-11.
29. Smith GD, Hart C, Watt G *et al.* Individual social class, area-based deprivation, cardiovascular disease risk factors, and mortality: the Renfrew and Paisley Study. *J Epidemiol Community Health* 1998;52:399-405.
30. Smith GD, Hart C. Re: "Use of census based aggregate variables to proxy for socioeconomic group: evidence from national samples". *Am J Epidemiol* 1999;150:996-7.
31. Louwman WJ, Aarts MJ, Houterman S, *et al.* A 50% higher prevalence of life-shortening chronic conditions among cancer patients with low socioeconomic status. *Br J Cancer* 2010;103:1742-8.
32. Dalton SO, Frederiksen BL, Jacobsen E, *et al.* Socioeconomic position, stage of lung cancer and time between referral and diagnosis in Denmark, 2001-2008. *Br J Cancer* 2011;105:1042-8.
33. Halpern MT, Ward EM, Pavluck AL, *et al.* Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: a retrospective analysis. *Lancet Oncol* 2008;9:222-31.
34. Riaz SP, Luchtenborg M, Jack RH, *et al.* Variation in surgical resection for lung cancer in relation to survival: Population-based study in England 2004-2006. *Eur J Cancer* 2011;24:24.
35. Patel N, Adaita R, Mellempgaard A, *et al.* Variation in the use of chemotherapy in lung cancer. *Br J Cancer* 2007;96:886-90.

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36. Bungay H. Cancer and Health Policy: the postcode lottery of care. *Soc Policy Admini* 2005;39:35-48.
 37. Crawford SM, Sauerzapf V, Haynes R, *et al.* Social and geographical factors affecting access to treatment of lung cancer. *Br J Cancer* 2009;101:897-901.
 38. Kogevinas M, Pearce N, Susser M, *et al.* Social Inequalities and Cancer. Vol. 138. 1997, Lyon: IARC Scientific Publications, International Agency for Research on Cancer.
 39. Brewster DH, Thomson CS, Hole DJ, *et al.* Relation between socioeconomic status and tumour stage in patients with breast, colorectal, ovarian, and lung cancer: results from four national, population based studies. *BMJ* 2001;322:830-1.
 40. Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon. Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. *N Engl J Med* 1985;312:1604-8.

LEGENDS FIGURES

Figure 1. Cumulative survival estimated by flexible parametric models by tumour subgroups and socioeconomic quintile.

Figure 2. Estimated mortality rates by socioeconomic quintile (allowing socioeconomic quintile to vary by follow-up) and the hazard ratio between the most deprived versus the most affluent patients within 12 months of diagnosis by tumour subgroups using flexible parametric models

Table 1. Demographic and clinical characteristics of 15,582 patients diagnosed with lung cancer between 2006 and 2008, by socioeconomic quintile.

	Q1 (Affluent)		Q2		Q3		Q4		Q5 (Deprived)		Total		Test	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	χ^2 (d.f)	p-value
All patients	2111	(100.0)	2550	(100.0)	3035	(100.0)	3817	(100.0)	4069	(100.0)	15582	(100.0)		
Sex														
Male	1208	(57.2)	1458	(57.2)	1708	(56.3)	2165	(56.7)	2358	(58.0)	8897	(57.1)		
Female	903	(42.8)	1092	(42.8)	1327	(43.7)	1652	(43.3)	1711	(42.0)	6685	(42.9)	0.31 (1)	0.57
Age at diagnosis														
0-59	310	(14.7)	329	(12.9)	430	(14.2)	637	(16.7)	752	(18.5)	2458	(15.8)		
60-69	497	(23.5)	617	(24.2)	743	(24.5)	990	(25.9)	1086	(26.7)	3933	(25.2)		
70-79	751	(35.6)	869	(34.1)	1009	(33.2)	1241	(32.5)	1302	(32.0)	5172	(33.2)		
80+	553	(26.2)	735	(28.8)	853	(28.1)	949	(24.9)	929	(22.8)	4019	(25.8)	66.7 (1)	<0.01
Charlson Score														
0	897	(49.8)	1065	(47.5)	1217	(45.5)	1496	(43.8)	1494	(41.1)	6169	(44.8)		
1	476	(26.4)	621	(27.7)	754	(28.2)	942	(27.6)	1064	(29.3)	3857	(28.0)		
2+	428	(23.8)	555	(24.8)	704	(26.3)	981	(28.7)	1075	(29.6)	3743	(27.2)	53.8 (1)	<0.01
Missing	310	-	309	-	360	-	398	-	436	-	1813	-		
Histologic type														
NSCLC	961	(45.5)	1058	(41.5)	1236	(40.7)	1515	(39.7)	1623	(39.9)	6393	(41.0)		
Other specified	39	(1.8)	47	(1.8)	54	(1.8)	61	(1.6)	60	(1.5)	261	(1.7)		
SCLC	197	(9.3)	259	(10.2)	311	(10.2)	440	(11.5)	485	(11.9)	1692	(10.9)		
Unspecified	914	(43.3)	1186	(46.5)	1434	(47.2)	1801	(47.2)	1901	(46.7)	7236	(46.4)	27.4 (12)	<0.01
Stage at diagnosis														
IA-IIIB	236	(15.4)	341	(18.6)	369	(16.9)	492	(17.9)	480	(15.8)	1918	(16.9)		
IIIA-IV	1296	(84.6)	1496	(81.4)	1812	(83.1)	2250	(82.1)	2556	(84.2)	9410	(83.1)	0.18 (1)	0.67
Unknown	579	-	713	-	854	-	1075	-	1033	-	4254	-		

Table 2. The likelihood of being diagnosed with early stage disease¹ estimated by crude and adjusted regression models with odds ratios (OR) and 95% confidence intervals (CI).

	No.	(%)	OR	Crude 95% CI	Adjusted OR	Adjusted 95% CI
Socioeconomic quintile						
Q1 (Affluent)	236	(15.4)	1.00	reference	1.00	reference
Q2	341	(18.6)	1.25	(1.04 to 1.50)	1.24	(1.04 to 1.49)
Q3	369	(16.9)	1.12	(0.93 to 1.34)	1.11	(0.93 to 1.33)
Q4	492	(17.9)	1.20	(1.01 to 1.42)	1.18	(1.00 to 1.40)
Q5 (Deprived)	480	(15.8)	1.03	(0.87 to 1.22)	1.01	(0.85 to 1.20)
<i>Test for trend (χ^2, p-value)</i>			<i>0.18</i>	<i>0.67</i>	<i>0.59</i>	<i>0.44</i>
Sex						
Male	1037	(15.9)	1.00	reference	1.00	reference
Female	881	(18.3)	1.19	(1.08 to 1.30)	1.10	(1.10 to 1.33)
<i>Test for trend (χ^2, p-value)</i>			<i>11.5</i>	<i><0.01</i>	<i>12.6</i>	<i><0.01</i>
Age at diagnosis						
0-59	300	(15.2)	1.00	reference	1.00	reference
60-69	550	(17.6)	1.19	(1.02 to 1.39)	1.16	(0.99 to 1.35)
70-79	694	(18.4)	1.26	(1.08 to 1.46)	1.18	(1.01 to 1.37)
80+	374	(15.3)	1.01	(0.85 to 1.19)	0.93	(0.78 to 1.10)
<i>Test for trend (χ^2, p-value)</i>			<i>2.75</i>	<i>0.10</i>	<i>0.29</i>	<i>0.59</i>
Charlson Score						
0	719	(15.0)	1.00	reference	1.00	reference
1	511	(17.6)	1.19	(1.05 to 1.34)	1.19	(1.05 to 1.34)
2+	504	(19.0)	1.29	(1.14 to 1.47)	1.31	(1.15 to 1.49)
<i>Test for trend (χ^2, p-value)</i>			<i>20.0</i>	<i><0.01</i>	<i>21.7</i>	<i><0.01</i>

¹ The binary outcome was categorized into early stage disease (stage IA-IIB at diagnosis) or advanced disease (stage IIIA-IV at diagnosis).

Table 3. The likelihood to undergo surgical resection in the subgroup of patients with early stage non-small cell lung cancer, to receive radiotherapy (stage III disease), or chemotherapy (advanced disease or small cell lung cancer) estimated by crude and adjusted logistic regression models with odds ratios (OR) and 95% confidence interval (CI).

	Surgical resection in early stage NSCLC (No. 1,828)						Radiotherapy in stage III disease (No. 2,771)						Chemotherapy in advanced or SCLC (No. 10,039)					
	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI	No.	(%)	Crude OR	95% CI	Adjusted OR	95% CI
Eligible patients	899	(49.2)	-	-	-	-	1054	(38.0)	-	-	-	-	3661	(36.5)	-	-	-	-
Socioeconomic quintile																		
Q1 (Affluent)	126	(55.8)	1.00	reference	1.00	reference	146	(36.2)	1.00	reference	1.00	reference			1.00	reference	1.00	reference
Q2	156	(48.0)	0.73	(0.52 to 1.03)	0.74	(0.51 to 1.06)	179	(39.3)	1.14	(0.87 to 1.51)	1.16	(0.88 to 1.54)	555	(40.4)	0.87	(0.75 to 1.01)	0.90	(0.77 to 1.06)
Q3	171	(48.7)	0.75	(0.54 to 1.05)	0.71	(0.49 to 1.02)	215	(39.1)	1.13	(0.87 to 1.47)	1.17	(0.90 to 1.53)	591	(37.0)	0.78	(0.68 to 0.90)	0.78	(0.67 to 0.91)
Q4	230	(49.5)	0.78	(0.56 to 1.07)	0.73	(0.52 to 1.03)	263	(39.7)	1.16	(0.90 to 1.49)	1.18	(0.91 to 1.53)	666	(34.5)	0.83	(0.72 to 0.95)	0.77	(0.66 to 0.89)
Q5 (Deprived)	216	(46.9)	0.70	(0.51 to 0.96)	0.67	(0.48 to 0.95)	251	(35.9)	0.98	(0.76 to 1.27)	0.99	(0.77 to 1.29)	869	(35.9)	0.83	(0.73 to 0.95)	0.75	(0.65 to 0.87)
<i>Test for trend (χ^2, p-value)</i>			2.32	0.13	1.13	0.29			0.10	0.75	0.18	0.67			5.30	0.02	15.9	<0.01
Sex																		
Male	475	(47.9)	1.00	reference	1.00	reference	632	(37.8)	1.00	reference	1.00	reference	2195	(37.7)	1.00	reference	1.00	reference
Female	424	(50.7)	1.12	(0.93 to 1.35)	1.16	(0.95 to 1.41)	422	(38.3)	1.02	(0.87 to 1.19)	1.02	(0.87 to 1.20)	1466	(34.8)	0.88	(0.81 to 0.96)	0.90	(0.82 to 0.98)
<i>Test for trend (χ^2, p-value)</i>			2.28	0.13	2.63	0.11			0.07	0.80	0.85	0.36			8.76	<0.01	4.84	0.03
Age at diagnosis																		
0-59	203	(71.7)	1.00	reference	1.00	reference	197	(45.4)	1.00	reference	1.00	reference	1089	(60.4)	1.00	reference	1.00	reference
60-69	320	(61.3)	0.62	(0.46 to 0.85)	0.65	(0.48 to 0.89)	303	(39.5)	0.79	(0.62 to 1.00)	0.81	(0.64 to 1.03)	1357	(49.1)	0.63	(0.56 to 0.71)	0.66	(0.58 to 0.75)
70-79	318	(47.8)	0.36	(0.27 to 0.49)	0.38	(0.28 to 0.52)	362	(38.2)	0.74	(0.59 to 0.94)	0.79	(0.62 to 1.00)	1020	(30.9)	0.29	(0.26 to 0.33)	0.32	(0.28 to 0.36)
80+	58	(16.3)	0.08	(0.05 to 0.11)	0.08	(0.05 to 0.12)	192	(30.8)	0.54	(0.42 to 0.69)	0.56	(0.43 to 0.73)	195	(9.0)	0.06	(0.05 to 0.08)	0.07	(0.06 to 0.08)
<i>Test for trend (χ^2, p-value)</i>			39.0	<0.01	31.1	<0.01			17.2	<0.01	9.01	<0.01			869.4	<0.01	677.2	<0.01
Charlson Score																		
0	398	(58.4)	1.00	reference	1.00	reference	466	(41.5)	1.00	reference	1.00	reference	1960	(45.1)	1.00	reference	1.00	reference
1	257	(52.8)	0.82	(0.65 to 1.03)	0.87	(0.68 to 1.12)	288	(39.0)	0.90	(0.75 to 1.09)	0.93	(0.76 to 1.12)	943	(37.0)	0.72	(0.65 to 0.79)	0.82	(0.74 to 0.92)
2+	215	(44.8)	0.60	(0.48 to 0.76)	0.78	(0.60 to 1.01)	216	(32.7)	0.70	(0.57 to 0.85)	0.75	(0.61 to 0.92)	616	(26.9)	0.46	(0.41 to 0.51)	0.61	(0.54 to 0.68)
<i>Test for trend (χ^2, p-value)</i>			5.12	<0.01	1.57	0.21			12.9	<0.01	8.20	<0.01			217.1	<0.01	74.3	<0.01

Table 4. The risk of all-cause mortality in patients with early stage non-small cell lung cancer, in stage III disease, advanced disease or small cell lung cancer estimated by crude and adjusted Cox regression models with relative risks expressed as hazard ratios (HR)

	Early stage NSCLC (No. = 1,828)					Stage III disease (No. = 2,771)					Advanced disease or SCLC (No. = 10,039)				
	Crude		Adjusted		*% ¹	Crude		Adjusted		*% ¹	Crude		Adjusted		*% ¹
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
Socioeconomic quintile															
Q1 (Affluent)	1.00	reference	1.00	reference		1.00	reference	1.00	reference		1.00	reference	1.00	reference	
Q2	1.22	(0.95 to 1.56)	1.09	(0.85 to 1.40)		1.16	(1.00 to 1.34)	1.20	(1.03 to 1.39)		1.16	(1.08 to 1.25)	1.17	(1.08 to 1.26)	
Q3	1.25	(0.98 to 1.60)	1.18	(0.93 to 1.51)		1.15	(0.99 to 1.33)	1.14	(0.99 to 1.32)		1.16	(1.08 to 1.25)	1.13	(1.05 to 1.22)	
Q4	1.19	(0.94 to 1.50)	1.15	(0.91 to 1.46)		1.14	(0.99 to 1.30)	1.15	(1.00 to 1.32)		1.15	(1.07 to 1.23)	1.16	(1.08 to 1.25)	
Q5 (Deprived)	1.35	(1.07 to 1.70)	1.24	(0.98 to 1.56)	-	1.15	(1.01 to 1.32)	1.16	(1.01 to 1.34)	-	1.15	(1.08 to 1.24)	1.12	(1.05 to 1.20)	-
<i>Test for trend (χ², p-value)</i>	4.18	0.04	2.56	0.11		2.38	0.12	0.14	0.70		9.35	<0.01	1.92	0.17	
Sex															
Male	1.00	reference	1.00	reference		1.00	reference	1.00	reference		1.00	reference	1.00	reference	
Female	0.84	(0.74 to 0.96)	0.85	(0.75 to 0.97)	-	0.97	(0.89 to 1.06)	0.95	(0.87 to 1.03)	-	0.95	(0.91 to 0.99)	0.92	(0.88 to 0.96)	-
<i>Test for trend (χ², p-value)</i>	6.57	0.01	7.13	<0.01		0.49	0.48	3.46	0.06		5.34	0.02	12.6	<0.01	
Age at diagnosis															
0-59	1.00	reference	1.00	reference	5.8%	1.00	reference	1.00	reference	34.6%	1.00	reference	1.00	reference	13.9%
60-69	1.41	(1.11 to 1.80)	1.25	(0.98 to 1.59)		1.15	(1.01 to 1.32)	1.09	(0.95 to 1.25)		1.14	(1.07 to 1.22)	1.07	(1.00 to 1.14)	
70-79	2.05	(1.64 to 2.58)	1.54	(1.22 to 1.95)		1.51	(1.33 to 1.72)	1.29	(1.12 to 1.47)		1.42	(1.33 to 1.51)	1.15	(1.08 to 1.22)	
80+	3.61	(2.85 to 4.58)	1.78	(1.39 to 2.28)		2.17	(1.89 to 2.49)	1.47	(1.26 to 1.70)		1.82	(1.71 to 1.95)	1.16	(1.08 to 1.25)	
<i>Test for trend (χ², p-value)</i>	101.1	<0.01	16.0	<0.01		92.8	<0.01	19.0	<0.01		245.3	<0.01	13.6	<0.01	
Charlson Score															
0	1.00	reference	1.00	reference	7.3%	1.00	reference	1.00	reference	17.4%	1.00	reference	1.00	reference	11.0%
1	1.10	(0.93 to 1.30)	0.98	(0.82 to 1.16)		1.10	(1.00 to 1.22)	1.03	(0.92 to 1.14)		1.08	(1.02 to 1.13)	0.99	(0.94 to 1.05)	
2+	1.35	(1.15 to 1.59)	1.03	(0.87 to 1.23)		1.32	(1.19 to 1.47)	1.09	(0.97 to 1.22)		1.22	(1.16 to 1.29)	1.00	(0.95 to 1.06)	
<i>Test for trend (χ², p-value)</i>	13.5	<0.01	0.04	0.84		30.9	<0.01	3.05	0.08		58.6	<0.01	0.17	0.90	
Resection															
<i>Test (χ², p-value)</i>	0.19	(0.16 to 0.22)	0.21	(0.18 to 0.25)	42.3%	-	-	-	-		-	-	-	-	
<i>Test (χ², p-value)</i>	557.2	<0.01	422.3	<0.01		-	-	-	-		-	-	-	-	
Radiotherapy															
<i>Test (χ², p-value)</i>	-	-	-	-	-	0.78	(0.72 to 0.85)	0.81	(0.73 to 0.88)	12.9%	0.71	(0.67 to 0.74)	0.73	(0.70 to 0.76)	1.2%
<i>Test (χ², p-value)</i>	-	-	-	-		34.1	<0.01	22.4	<0.01		236.8	<0.01	205.3	<0.01	
Chemotherapy															
<i>Test (χ², p-value)</i>	-	-	-	-	-	0.48	(0.44 to 0.52)	0.54	(0.49 to 0.59)	18.0%	0.42	(0.40 to 0.44)	0.44	(0.42 to 0.46)	23.4%
<i>Test (χ², p-value)</i>	-	-	-	-		301.7	<0.01	179.6	<0.01		1564.7	<0.01	179.6	<0.01	

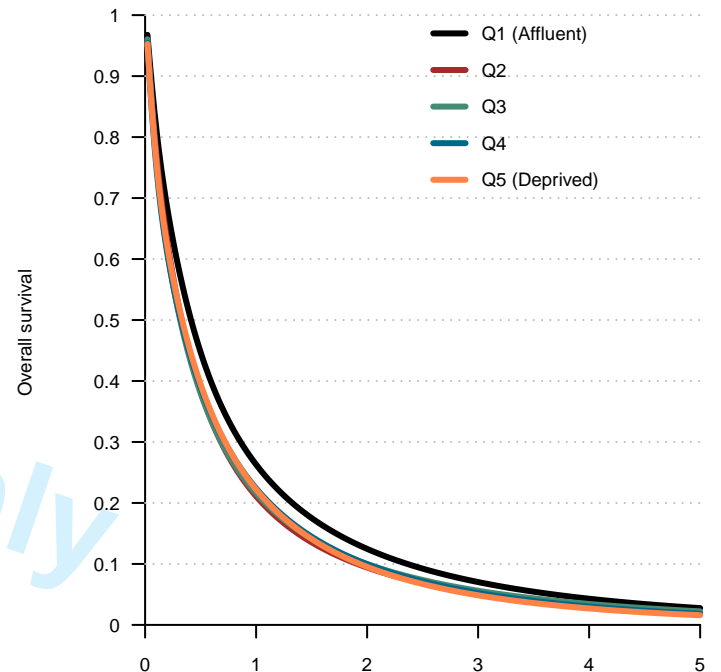
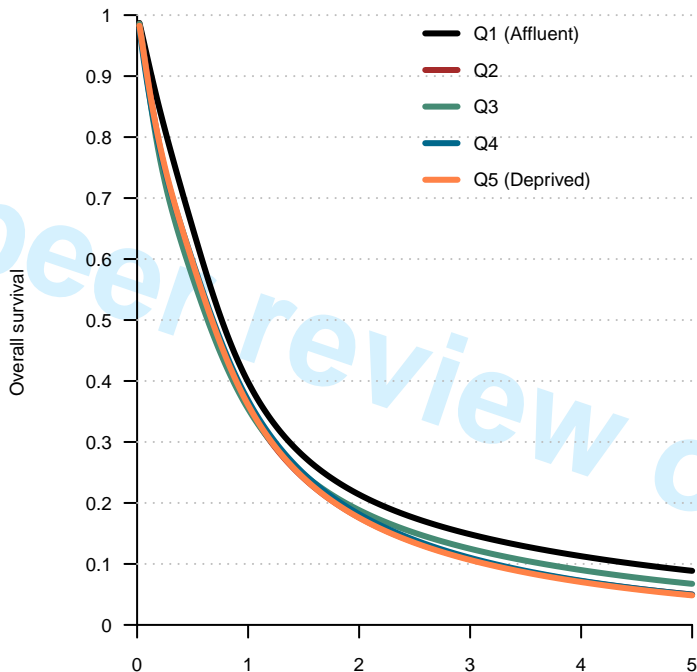
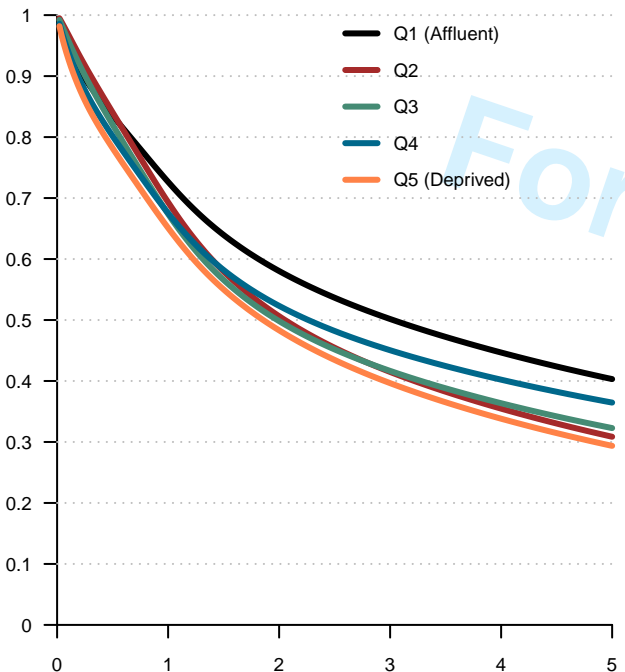
1. The relative contribution for each covariate in each subgroup was calculated as follows: ((HR for SES_{Q5} in a model adjusted for sex - HR for SES_{Q5} in a model adjusted for sex + covariate) / (HR for SES_{Q5} in a model adjusted for sex - 1)) * 100

Figure 1a. Early stage NSCLC (cumulative survival)

Figure 1b. Stage III disease (cumulative survival)

Figure 1c. Advanced disease or SCLC (cumulative survival)

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Page 26 of 26 Figure 2a. Early stage NSCLC (mortality rate)

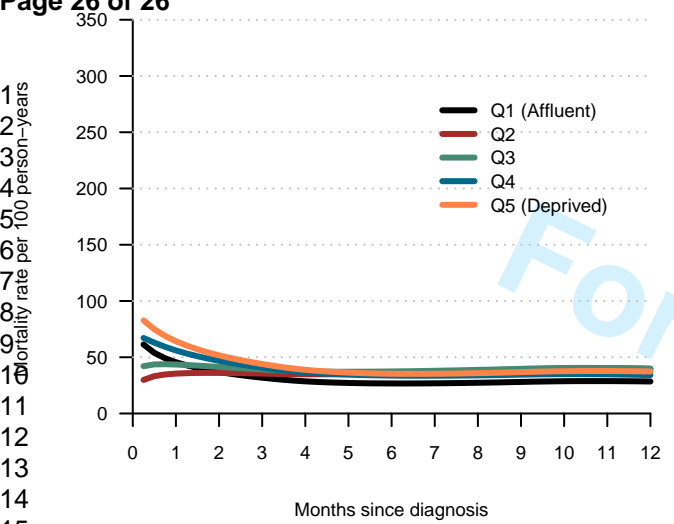


Figure 2b. Stage III disease (mortality rate)

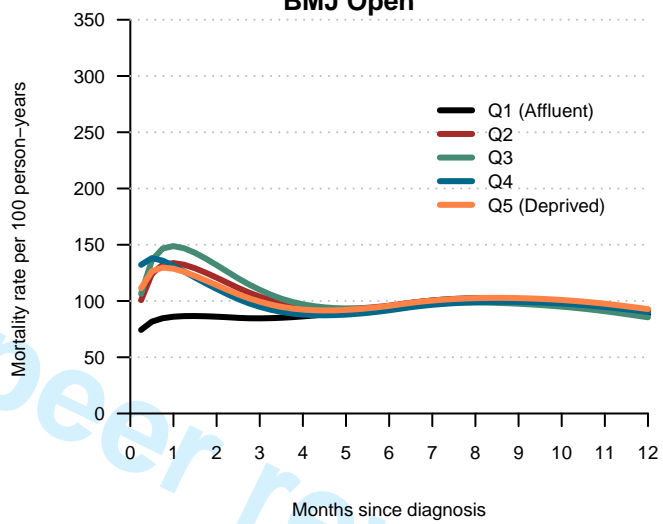


Figure 2c. Advanced disease or SCLC (mortality rate)

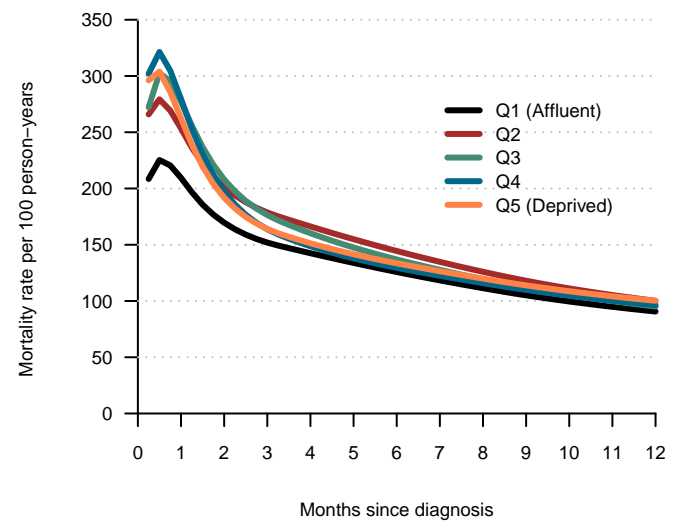


Figure 2d. Early stage NSCLC (hazard ratio)

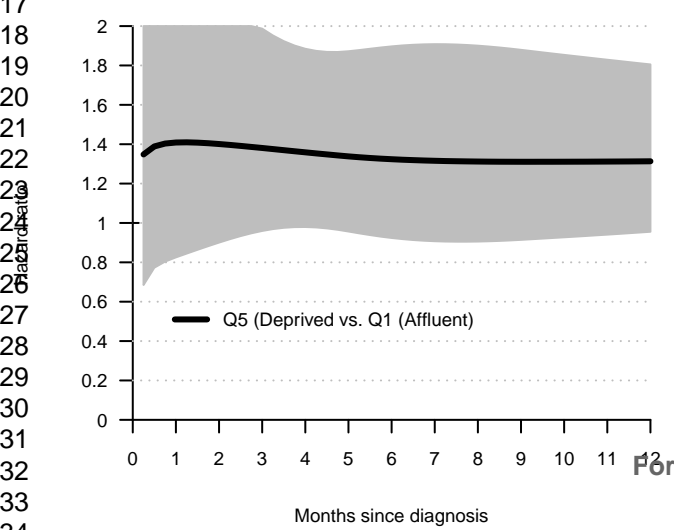


Figure 2e. Stage III disease (hazard ratio)

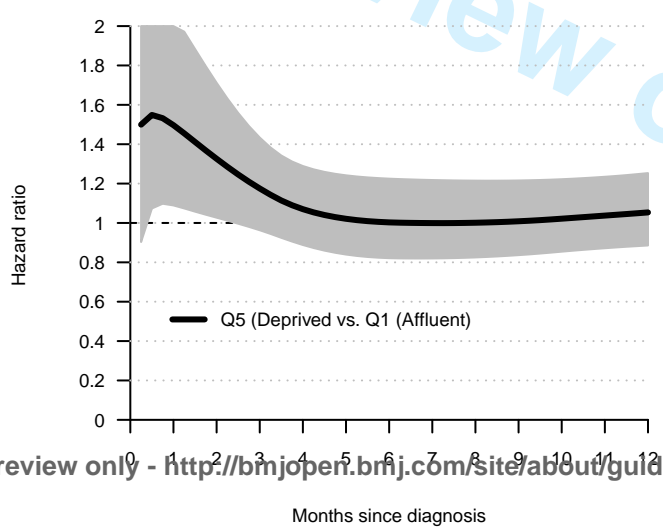


Figure 2f. Advanced disease or SCLC (hazard ratio)

