**Socioeconomic differences and lung cancer survival in Germany:**

**Investigation based on population-based clinical cancer registration**

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**Words:** Main text: 3404, Abstract: 236, Tables: 4, Figures: 1, Supplementary Material, Supplementary Tables: 7, Supplementary Figures: 3

**Classification:** Epidemiology and Prevention

**Abstract**

**Objectives:** Studies from several countries reported socioeconomic inequalities in lung cancer survival. Hypothesized reasons are differences in cancer care or tumor characteristics. We investigated associations of small-area deprivation and lung cancer survival in Germany and the possible impact of differences in patient, tumor or treatment factors.

**Materials and Methods:** Patients registered with a primary tumor of the lung between 2000-2015 in three German population-based clinical cancer registries were included. Area-based socioeconomic deprivation on municipality level was measured with the categorized German Index of Multiple Deprivation. Association of deprivation with overall survival was investigated with Cox regression models.

**Results:** Overall, 22,905 patients were included. Five-year overall survival from the least to the most deprived quintile were 17.2%, 15.9%, 16.7%, 15.7%, and 14.4%. After adjustment for patient and tumor factors, the most deprived group had a lower survival compared to the least deprived group (Hazard Ratio (HR) 1.06, 95% confidence interval (CI) 1.01-1.11). Subgroup analyses revealed lower survival in the most deprived compared to the least deprived quintile in patients with stage I-III [HR: 1.14, 95% CI: 1.06-1.22]. The association persisted when restricting to patients receiving surgery but was attenuated for subgroups receiving either chemotherapy or radiotherapy.

**Conclusion:** Our results indicate differences in lung cancer survival according to area deprivation in Germany, which were more pronounced in patients with I-III stage cancer. Future research should address in more detail the underlying reasons for the observed inequalities and possible approaches to overcome them.

**Keywords:** Area-based socioeconomic deprivation, survival, lung cancer, stage at diagnosis, treatment, Germany

**List of Abbreviations:**

FU Follow-up

GIMD German Index of Multiple Deprivation

HR Hazard ratio

ICD International Classification of Diseases

N Number of observations

n/a Not applicable

NSCLC Non-small cell lung cancer

SCLC Small cell lung cancer

SD Standard deviation

US United States

1. **Introduction**

Lung cancer is the leading cause of cancer related death globally, accounting for approximately 1.76 million deaths in 2018.1 Prognosis used to be generally very poor, with 5-year survival rates ranging between 10 and 20 % in different countries.2 Numerous prognostic factors have been investigated which include tumor-related but also patient-related factors, as well as smoking status and cancer treatment.3 For example, a later stage at diagnosis, male gender and current smoking at diagnosis have been shown to predict particularly poor prognosis in lung cancer patients.4,5

Social inequalities in lung cancer survival have been reported for countries with and without universal health care systems.6,7 Irrespective of the type of socioeconomic measurement, studies reported lower survival for lower socioeconomic groups.8 Stage at diagnosis, comorbidity, cancer therapy and smoking status have been found to at least partly explain the association between socioeconomic status and lung cancer survival.9-11 A study including lung cancer patients resident in Denmark reported smaller hazard ratio estimates when additionally adjusting for stage at diagnosis, first-line treatment and comorbidities.10

Area-based measurements such as indices of multiple deprivation can be used to investigate associations of area-specific indicators with the health of a population independent of socioeconomic status in a population subgroup such as patients with a given disease.12 In addition, such indices are also used as a proxy if the individual socioeconomic status is not available.12

In a recent study from Germany, the associations between area-based socioeconomic deprivation and cancer survival was analyzed for 25 cancer sites using data from population-based cancer registries covering 200 of 439 districts (median population: 126,000 residents in 2006) in Germany.13 For cancers of the trachea, lung and bronchus, results showed lower 5-year relative survival in patients living in the most deprived districts compared to patients living in all other districts [5-year age-standardized relative survival (standard error in % units): Quintile 1 (Q1, least deprived) 18.0 % (0.5), Q2 17.8 % (0.5), Q3 16.1 % (0.4), Q4 16.5 % (0.4), Q5 (most deprived) 14.4 % (0.4)]. Effect sizes were largest in the first three months after diagnosis and even increased after adjustment for stage at diagnosis.13 However, measurement of socioeconomic deprivation at county level does no take potential variation of socioeconomic deprivation across municipalities within counties into account. Whereas possible interventions to reduce differences in lung cancer survival could be organized on municipality level.

The objective of the current analysis is to investigate the association between area-based socioeconomic deprivation on municipality level (median population: 2,200 residents, range 130-520,000)14 and lung cancer survival by using data from German population-based clinical cancer registries. Furthermore, we examined whether the association between area deprivation and lung cancer survival depended on the age or sex of the cancer patients, clinical prognostics factors or utilization of cancer therapy.

1. **Materials and Methods**
	1. Study population

For our retrospective cohort study, data were used from three regional population-based clinical cancer registries in Germany (located in Regensburg, Erfurt, and Dresden and covering parts of the German states Bavaria, Thuringia and Saxony, respectively, Supplementary Figure B1). These cancer registries cover regions in the south and east of Germany (Population size ≈ 4 million residents in 2015).14 The cities of Dresden (523,058 residents), Erfurt (204,994 residents) and Regensburg (135,520 residents) comprise 13.4 %, 5.2 % and 3.5 % of the total underlying study population, respectively.14 The catchment areas of the Erfurt and Regensburg registries include five other cities with a population of 42,000 to 51,000 residents. Patients at the age of 15 years or older and resident in the catchment areas of one of the above-mentioned registries with a malignant primary tumor of the lung (International Classification of Diseases 10 C34) diagnosed in 2000-2015 were eligible for the analysis. Death certificate or autopsy only cases were excluded (Supplementary Figure B2).

* 1. Area-based socioeconomic deprivation

The area-based socioeconomic deprivation of the patients was assessed using the German Index of Multiple Deprivation (GIMD)15 on municipality level. The GIMD is based on data of official statistics and consists of seven single domains (income, employment, education, municipality revenue, social capital, environment, and security deprivation), and a composite index. Up to now, two editions of this deprivation index are available based on data from 2006 and from 2010 (or the next year available), respectively. All included municipalities were assigned the composite index as deprivation score. Using the population size, deprivation quintiles were then computed twice involving either all included municipalities (main analyses) or calculating registry-specific values over all municipalities within the registry. For the latter calculation, the large cities Dresden and Erfurt were assigned a separate category. All patients were assigned to a deprivation quintile according to the municipality of residence at the time of diagnosis. In the catchment areas of included registries, there were 792 municipalities with a median population of 2205 residents (range 137-504,795) in 2006 and 779 municipalities with a median population of 2189 residents (range 128-523,058) in 2010.14 Supplementary Table B1 and Figure B1 show cutoffs for the categorized GIMD quintiles, the original GIMD quintiles and a map of the categorized 2010 GIMD quintiles over all included municipalities.

* 1. Covariates

Cancer registries provided information on age, sex, place of residence, year of diagnosis, stage, histology, grade, vital status of cancer patients, and primary treatment, which referred to first treatment of the primary tumor and was defined as either receiving surgery, chemotherapy or radiotherapy (we did not consider treatment combinations). During data quality checks, strong differences in treatment utilization proportions across registries and calendar periods were detected which could not be excluded to be based on differences in the completeness of treatment registration and might result in biases in regional analyses. However, if the treatment variable explicitly indicated that a specific therapy was actually given, this information was expected to be reliable. We therefore used treatment factors for subgroup analyses by restricting the sample to patients receiving specific treatments. Additionally, we included cancer registry (Dresden, Erfurt, Regensburg) as adjustment or stratification variable in our models.

* 1. Outcome

Overall survival was computed from date of cancer diagnosis to death from any cause. Vital status was ascertained using death certificates and information from the registration offices. Patients lost to follow-up before death or still alive at the last vital status assessment were right-censored at the date of the last vital status assessment or end of 2015 whichever came first.

* 1. Statistical analysis

Demographic and clinical characteristics by area-based deprivation quintile were described and distribution across deprivation quintiles were compared using Chi-square tests. Missing values in relevant variables were imputed using Multiple Imputation by Chained Equations (more detail in the Supplementary Material A).16 The distribution of these variables before and after imputation is shown in supplementary Table B2. Overall survival curves by area-based deprivation quintile were computed with the Kaplan-Meier method. The median follow-up length was estimated with reverse Kaplan-Meier method.17

Cox proportional hazards regression was used to investigate the association between area-based deprivation and survival in detail. Various models were fitted and compared: The base model included adjustment for age, sex and year of diagnosis. The second model additionally included cancer subtype and grading. In a third model, cancer stage was added. Using the third model, subgroup analyses were conducted by restricting the patient sample to patients who received specific treatments. We additionally performed subgroup analyses stratified by patient and tumor characteristics. Results were visualized by showing adjusted survival curves which are estimated using marginal survival functions.18 In an additional fourth model we adjusted for registry. In a sensitivity analysis, we calculated the Cox models by using a category for Dresden city additionally to area-based deprivation quintiles. To account for immortal time bias, we repeated the analysis stratified by treatment using fixed follow-up start dates at 30, 60, and 90 days after diagnosis. We additionally excluded patients who received their first treatment more than one year after diagnosis. Multiple imputation was conducted in R (Version 3.5.2)19, all other analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

1. **Results**

Overall, 22,905 patients were included (Supplementary Figure B2) of whom 47.1 % were registered in the clinical cancer registry located in Regensburg, 72.9 % were male, 23.8 % were over 75 years of age, 49.5 % had stage IV cancer, 45.3 % had a lung cancer of the upper lobe and 82.7 % had a non-small cell lung cancer (NSCLC; Table 1). Chi-square test revealed significant differences for all factors except subtype, however, there were only marginal differences for most factors when comparing across area-based socioeconomic deprivation groups (Table 1). Patients resident in most deprived municipalities were more often males, less often diagnosed with an adenocarcinoma, more often diagnosed with squamous cell carcinoma or small-cell lung cancer (SCLC) and had more often undetermined grading. Within the catchment areas of registries, municipalities in the Dresden and Erfurt region were more deprived on average than municipalities in the Regensburg region (Table 1). Median time from diagnosis to first neoadjuvant or adjuvant treatment in days was 20, 21, 26, 24, and 23 for Q1 (least deprived), Q2, Q3, Q4, and Q5 (most deprived), respectively.

For the total population, the number of observed deaths was 18,277 (79.8 %) and median follow-up time in months was 72.0 (69.0-73.0). Figure 1 shows non-standardized overall survival curves for the total study population stratified by stage and area-based deprivation quintiles. The corresponding one-, three-, and five-year overall survival rates are displayed in Table 2. For the total study population, survival was at each time point lowest for most deprived areas but no gradient across deprivation groups was observed (5-year survival difference to Q1: Q2 1.3%, Q3 0.5%, Q4 1.5%, Q5 2.8%, Figure 1, Table 2). In patients with stage I/II, survival was highest in the least deprived quintiles and in patients with stage III, survival was lowest in the most deprived quintile. There was no difference for other quintiles in these subgroups and no difference in patients with stage IV patients (Figure 1, Table 2).

Pre-defined multivariable models for the total study population consistently showed a statistically significantly lower survival in the most deprived quintile (HR 1.06, 95% CI 1.01-1.11, Figure B3, Table 3). Additionally adjusting for cancer registry attenuated the association (Table 3). Stratified analyses showed lower survival in the most deprived municipalities for patients with stage I/II (HR 1.13, 95% CI 1.00-1.28) and stage III (1.13, 1.03-1.24) lung cancer but no gradient across area-based deprivation quintiles (Figure B3, Table 3). We observed medium-sized differences in survival between the most and least deprived municipalities for these subgroups and no difference for patients with stage IV lung cancer (stage I+II: 2.2-4.1 % units, stage III: 3.0-4.0 % units, Figure B3, Table B3). When adjusting for cancer registry, effect estimates were slightly larger in the subgroup diagnosed with stage I/II (Table 3). Stratified analyses by patient and tumor factors revealed lower survival in the most deprived municipalities for men, age group 15-69 years, low/intermediate grade, NSCLC, period of diagnosis 2011-2015, and follow-up length of 1 year and 5 years (Table B4). A significant trend towards lower survival in the most deprived areas in subgroups with overall better prognosis was observed (Tables 3 and B4).

Patients receiving surgery showed a lower survival when resident in the more deprived municipalities (Q4: HR 1.13. 95% CI 1.00-1.27, Table B4). This association strengthened for Q4, when further restricting to patients with stages I-III for whom surgery is indicated according to German recommendations (Q4: 1.19, 1.05-1.36, Supplementary Table B5). Further restriction to patients receiving chemotherapy or radiotherapy changed effect estimates and were not statistically significant. However, confidence intervals were large for these subgroups (Tables B4 and B5).

Table 4 shows the association of the area-specific socioeconomic deprivation quintiles with survival within each region. In neither region, significant differences between the least and most deprived areas were observed. Survival was significantly lower than in Q1 in Erfurt city but not in Dresden city.

The sensitivity analysis for the Cox models including an additional category for Dresden city revealed similar results for deprivation quintiles compared to our main analysis (Table 3 and Supplementary Tables B4 and B6). Dresden city had significantly lower survival in subgroups with high grading and SCLC and better survival in subgroups receiving chemotherapy or surgery compared to the least deprived municipalities (Table B6).

The sensitivity analysis for treatment groups using follow-up start 30, 60, and 90 days after diagnosis showed marginal differences to our main analysis (Supplementary Tables B4 and B7).

1. **Discussion**

This is the first study on the association between small-area socioeconomic deprivation and survival after lung cancer in Germany considering clinical prognostic factors and cancer therapy. Most patients’ characteristics were rather similar across the area-based socioeconomic deprivation quintiles. There were small differences for sex, subtype and grading. Regarding survival, we observed no clear gradient across deprivation quintiles but lowest survival in the most deprived areas. After full adjustment, a significant association between area-based socioeconomic deprivation and lung cancer survival was found for all stages combined. There was an indication for a lower survival for the most deprived municipalities in subgroups diagnosed in stage I-III, lower grading and with NSCLC.

One previous study investigated associations between socioeconomic deprivation and lung cancer survival in 200 of 439 districts in Germany using a broader assignment of deprivation on district rather than municipality level and computing relative instead of absolute survival. This study reported lower survival in lung cancer patients living in the most deprived districts compared to all other districts, only adjusting for age and stage.13 Our analysis revealed a significant association for all stages combined after adjusting for a wider range of factors.

A recent systematic review including 94 studies observed lower lung cancer survival for lower socioeconomic groups irrespective of the socioeconomic measure.8 When comparing our study to area-level index studies using similar levels of adjustment, effect estimates were larger in countries both with and without universal health care systems (e.g. The Netherlands: HR 1.09-1.16, 20,21, United States (US): 1.05-1.38, 22-26, our study: 1.06). Two US studies that were restricted to patients with a better prognosis (NSCLC stage I), observed overall stronger associations (HR 1.27-1.34). 25,26 In contrast to one US study22, we observed lower survival for the most deprived compared to the least deprived municipalities for men but not for women. A possible explanation might be the higher all-cause mortality27 and higher smoking prevalence28 in men compared to women in Germany. Due to missing life tables and information on smoking behavior, it was not possible to account for this in the current study. Adjusted 1-, 3- and 5-year survival rates were 1.7, 1.5, and 1.2 % units lower for the most compared to the least deprived regions and effect estimates were smaller than for other cancer types.29-31 Compared to other common cancers, such as breast or colon cancer, lung cancer has a much poorer prognosis2, leaving less room for the impact of socioeconomic deprivation on survival differences and resulting in smaller effect sizes for lung cancer.32 Supporting this hypothesis, a French study reported lower age-standardized net survival in patients resident in the most deprived areas for almost all 19 solid tumor sites with smaller differences for lung cancer patients.33 Future analyses should focus on lung cancer patients with better prognoses to further investigate social inequalities reported for these patients.

Hypothesized determinants for socioeconomic inequalities in cancer survival were age, sex, year of diagnosis, stage, subtype, grading, and treatment.8,10,11 Cox models consistently revealed significantly lower survival for most deprived municipalities across all levels of adjustment unless cancer registry was added. We therefore assume that subtype, grading and stage might not have an impact on the association between socioeconomic deprivation and lung cancer survival in our study population. However, since the distribution of socioeconomic deprivation of municipalities was quite different across registries, the attenuation of associations by adjusting for registry catchment area or in analyses stratified by cancer registry suggests that part of the deprivation differences might be mediated by factors acting on the “supra-municipality-level”. Such factors might include, for example, quality of hospital care, which would be assumed to act on a district rather than municipality level because most municipalities do not have their own hospital.

Due to data quality, we could not investigate the probability of receiving a certain therapy. Recent studies from England reported lower odds for receiving surgery 34,35 but a higher probability of receiving radical radiotherapy 35 in more deprived regions. Inequalities in treatment explained area-based socioeconomic differences in lung cancer survival for both universal and non-universal health care systems.11,36,37 Our study revealed lower survival for most deprived municipalities in patients receiving surgery after restricting to patients with stage I-III but effects were attenuated by further restricting to chemotherapy or radiotherapy. This might indicate survival differences by receipt of treatment. In order to provide reliable evidence for all of Germany and appropriately adjust for treatment, a larger sample size and high-quality data is needed.

Sensitivity analyses revealed a better survival in patients receiving chemotherapy or surgery and resident in Dresden city compared to the least deprived municipalities. As there is a comprehensive cancer center in Dresden city, access to health care might be better compared to less deprived municipalities. However, it is unclear why patients residing in Dresden city and diagnosed with high grading or SCLC have a worse survival in comparison with less deprived municipalities. Further research regarding direct regional variations might provide more explanations to our findings.

One limitation was potential residual confounding by smoking due to the lack of data on smoking behavior which is associated with socioeconomic status.38 Another limitation was the data quality of therapy. However, if the treatment variable explicitly indicated that a specific therapy was actually given, this information was expected to be reliable and usable by restricting our analyses to subgroups receiving certain therapies. Analyzing both individual and area-based socioeconomic measures is preferable. However, individual information was not available. Therefore, we could not investigate if the effects in our study originated from individual socioeconomic status or to area-based deprivation. The use of two GIMD editions based on data from 2006 and 2010 might have affected our results regarding a change of the distribution of the GIMD across registries. From 2006 to 2010, the underlying population changed towards a slightly higher proportion in less deprived municipalities. Due to missing life tables or cause of death information, we reported overall survival and therefore cannot distinguish between cancer and other causes of death. However, as the prognosis of lung cancer patients is generally poor, survival might be similar to cause-specific or relative survival.39 If we would have used cause-specific or relative survival instead of overall survival, the effect could be smaller compared to hazard ratios reported in our study. A reason could be differences between deprivation groups in, for example, comorbidities.40 However, as most lung cancer patients do not die from causes other than lung cancer41,42, this is unlikely to affect our results to a relevant degree. Furthermore, the underlying population for our study comprises only three federal states. We assume these regions as representative for most parts of Germany, as they cover both rural and urban regions as well as the eastern and western part of Germany.

One main strength of our study is the inclusion of data from three population-based clinical cancer registries. Compared to epidemiological registries, the completeness of variables for important prognostic factors is higher in clinical cancer registries and further variables like treatment are available with improving data quality.13,43 Another strength is that we were able to investigate for the first time in Germany the association between lung cancer survival and socioeconomic deprivation at the municipality level (median population ≈ 2,200 residents)14 which is comparable to countries routinely using small-area levels such as England (median population ≈ 1,500 residents).36 Although only including three registries, the analyzed cohort was still large and comparable to other studies investigating lung cancer survival.8 When data completeness of clinical cancer registries has improved, more detailed analyses with a more comprehensive set of variables are possible.43

1. **Conclusions**

Our study could show lower survival in most deprived regions for the total study population after adjusting for prognostic factors. Furthermore, we observed associations between survival and area-based deprivation for patients diagnosed in earlier stages, lower grading and with NSCLC. Thus, social inequalities in cancer survival might especially be relevant for lung cancer patients with better prognoses. Future research on socioeconomic differences in lung cancer survival should focus on these patients and explore possible inequalities in the receipt of cancer treatment in detail.

**Acknowledgement**

Members of the German Cancer Survival Working Group: Mark Möller, Karin Jäger (Cancer Registry of Bavaria, Regional Center Erlangen-Nürnberg), Carmen Werner (Clinical Cancer Registry Dresden), Paul Strecker (Clinical Cancer Registry Thuringia, Regional Center Erfurt), Michael Gerken (Cancer Registry of Bavaria, Regional Center Regensburg), Karla Geiss, Dorothee Twardella, Martin Meyer (Cancer Registry of Bavaria), Andrea Eberle, Sabine Luttmann (Cancer Registry of Bremen), Heide Wilsdorf-Köhler, Roland Stabenow (Cancer Registry of Berlin and the New Federal States), Cynthia Erb, Alice Nennecke, Stefan Hentschel (Hamburg Cancer Registry), Eunice Sirri, Joachim Kieschke (Cancer Registry of Lower Saxony), Bernd Holleczek (Saarland Cancer Registry), Katharina Emrich (Cancer Registry of Rhineland-Palatinate), Hiltraud Kajüter, Volkmar Mattauch (Cancer Registry of North Rhine-Westphalia), Alexander Katalinic, Ron Pritzkuleit, Johann Mattutat (Cancer Registry of Schleswig-Holstein), Volker Arndt (Cancer Registry of Baden-Württemberg), Werner Maier, Lars Schwettmann (Institute of Health Economics and Health Care Management, Helmholtz Zentrum München), Hermann Brenner, Gundula Behrens, Lina Jansen and Isabelle Finke (German Cancer Research Center).

We want to thank Tobias Terzer and Axel Benner from the Division of Biostatistics at the German Cancer Research Center for their valuable input regarding our analyses.

**Funding**

This research is supported by the German Cancer Aid (grant number 70112090).

**Ethics approval**

The study was approved by ethics committee of the University of Heidelberg. Data collection within the Cancer Registries has been carried out according to state cancer registry laws. The study was conducted in accordance with the recommendations of the Declaration of Helsinki by the World Medical Association.

**Authors’ contributions**

Designed research (project conception, development of overall research plan, and study oversight): LJ, RP, BH, HB; conducted research (hands-on conduct of the experiments and data collection): IF, LJ, GB, LS, MG; analyzed data or performed statistical analysis: IF, LJ; wrote paper: IF, LJ, HB; had primary responsibility for final content: IF, LJ, HB. All authors read and approved the final manuscript.

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**Figure 1** Kaplan Meier curves stratified by area-based socioeconomic deprivation and by stage at diagnosis for the total population of lung cancer patients registered in three German clinical cancer registries.



**Table 1** Characteristics of the total study population stratified by area-based socioeconomic deprivation quintiles

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  | **Deprivation quintile** |  |
|  | **Total** |  | **Q1****(Least deprived)** | **Q2** | **Q3** | **Q4** | **Q5****(Most deprived)** | **p-valuea** |
|  | **N (%)** |  | **N (%)** | **N (%)** | **N (%)** | **N (%)** | **N (%)** |  |
| **Cases** | 22,905 (100.0) |  | 3,904 (17.0) | 4,662 (20.4) | 4,690 (20.5) | 4,622 (20.2) | 5,027 (22.0) |  |
| **Cancer Registry** |  |  |  |  |  |  |  |  |
| Dresden | 6,752 (29.5) |  | 551 (14.1) | 1,730 (37.1) | 1,722 (36.7) | 794 (17.2) | 1,955 (38.9) |  |
| Erfurt | 5,373 (23.5) |  | 160 (4.1) | 260 (5.6) | 1,270 (27.1) | 1,893 (41.0) | 1,790 (35.6) |  |
| Regensburg | 10,780 (47.1) |  | 3,193 (81.8) | 2,672 (57.3) | 1,698 (36.2) | 1,935 (41.9) | 1,282 (25.5) | <.0001 |
| **Sex** |  |  |  |  |  |  |  |  |
| Men | 16,690 (72.9) |  | 2,816 (72.1) | 3,298 (70.7) | 3,391 (72.3) | 3,335 (72.2) | 3,850 (76.6) |  |
| Women | 6,215 (27.1) |  | 1,088 (27.9) | 1,364 (29.3) | 1,299 (27.7) | 1,287 (27.8) | 1,177 (23.4) | <.0001 |
| **Age at diagnosis****(years)** |  |  |  |  |  |  |  |  |
| 15-54 | 3,007 (13.1) |  | 581 (14.9) | 584 (12.5) | 587 (12.5) | 617 (13.3) | 638 (12.7) |  |
| 55-59 | 2,508 (10.9) |  | 467 (12.0) | 475 (10.2) | 512 (10.9) | 516 (11.2) | 538 (10.7) |  |
| 60-64 | 3,452 (15.1) |  | 565 (14.5) | 720 (15.4) | 675 (14.4) | 714 (15.4) | 778 (15.5) |  |
| 65-69 | 4,099 (17.9) |  | 710 (18.2) | 831 (17.8) | 828 (17.7) | 831 (18.0) | 899 (17.9) |  |
| 70-74 | 4,398 (19.2) |  | 714 (18.3) | 922 (19.8) | 928 (19.8) | 853 (18.5) | 981 (19.5) |  |
| 75+ | 5,441 (23.8) |  | 867 (22.2) | 1,130 (24.2) | 1,160 (24.7) | 1,091 (23.6) | 1,193 (23.7) | 0.022 |
| Mean (years ± SD) | 67.2 ± 10.3 |  | 66.4 ± 10.4 | 67.5 ± 10.3 | 67.5 ± 10.3 | 67.1 ± 10.3 | 67.3 ± 10.2 |  |
| **Period of Diagnosis** |  |  |  |  |  |  |  |  |
| 2000-2010 | 14,769 (64.5) |  | 2,383 (61.0) | 2,873 (61.6) | 3,107 (66.2) | 2,982 (64.5) | 3,424 (68.1) |  |
| 2011-2015 | 8,136 (35.5) |  | 1,521 (39.0) | 1,789 (38.4) | 1,583 (33.8) | 1,640 (35.5) | 1,603 (31.9) | <.0001 |
| **Diagnosis (ICD-10)**  |  |  |  |  |  |  |  |  |
| C34.0 Main bronchus | 2,765 (12.1) |  | 539 (13.8) | 607 (13.0) | 504 (10.7) | 538 (11.6) | 577 (11.5) |  |
| C34.1 Upper lobe | 10,375 (45.3) |  | 1,730 (44.3) | 2,155 (46.2) | 2,150 (45.8) | 2,097 (45.4) | 2,243 (44.6) |  |
| C34.2 Middle lobe | 947 (4.1) |  | 162 (4.1) | 176 (3.8) | 181 (3.9) | 215 (4.7) | 213 (4.2) |  |
| C34.3 Lower lobe | 5,591 (24.4) |  | 925 (23.7) | 1,139 (24.4) | 1,153 (24.6) | 1,125 (24.3) | 1,249 (24.8) |  |
| C34.8 Overlappinglesion | 838 (3.7) |  | 129 (3.3) | 163 (3.5) | 204 (4.3) | 142 (3.1) | 200 (4.0) |  |
| C34.9 Unspecified | 2,389 (10.4) |  | 419 (10.7) | 422 (9.1) | 498 (10.6) | 505 (10.9) | 545 (10.8) | <.0001 |
| **Stage at diagnosis**  |  |  |  |  |  |  |  |  |
| I | 3,321 (16.2) |  | 532 (15.3) | 654 (15.5) | 748 (18.0) | 684 (16.9) | 703 (15.5) |  |
| II | 1,625 (7.9) |  | 298 (8.6) | 319 (7.6) | 323 (7.8) | 328 (8.1) | 357 (7.9) |  |
| III | 5,384 (26.3) |  | 924 (26.6) | 1,068 (25.3) | 1,076 (25.9) | 1,047 (25.9) | 1,269 (28.0) |  |
| IV | 10,111 (49.5) |  | 1,723 (49.6) | 2,184 (51.7) | 2,011 (48.4) | 1,987 (49.1) | 2,206 (48.6) |  |
| Missing | 2,464 (10.8) |  | 427 (10.9) | 437 (9.4) | 532 (11.3) | 576 (12.5) | 492 (9.8) | 0.003 |
| **Histological subtype** |  |  |  |  |  |  |  |  |
| NSCLC |  |  |  |  |  |  |  |  |
|  Adenocarcinoma | 6,912 (30.2) |  | 1,243 (31.9) | 1,566 (33.6) | 1,405 (30.0) | 1,345 (29.1) | 1,353 (26.9) |  |
|  Squamous cell carcinoma | 7,081 (31.0) |  | 1,165 (29.9) | 1,389 (29.8) | 1,403 (30.0) | 1,419 (30.7) | 1,705 (34.0) |  |
|  Other | 4,910 (21.5) |  | 803 (20.6) | 897 (19.3) | 1,091 (23.3) | 1,063 (23.0) | 1,056 (21.0) |  |
| SCLC3 | 3,975 (17.4) |  | 685 (17.6) | 807 (17.3) | 785 (16.8) | 791 (17.1) | 907 (18.1) |  |
| Missing | 27 (0.1) |  | 8 (0.2) | 3 (0.1) | 6 (0.1) | 4 (0.1) | 6 (0.1) | 0.522b |
| **Grading** |  |  |  |  |  |  |  |  |
| Low/intermediategrade | 7,168 (41.1) |  | 1,313 (47.9) | 1,475 (45.7) | 1,470 (40.3) | 1,346 (35.6) | 1,564 (38.9) |  |
| High grade | 7,158 (41.1) |  | 1,319 (48.1) | 1,572 (48.7) | 1,427 (39.1) | 1,476 (39.1) | 1,364 (33.9) |  |
| Undetermined | 3,094 (17.8) |  | 109 (4.0) | 180 (5.6) | 751 (20.6) | 961 (25.4) | 1,093 (27.2) |  |
| Missing | 5,485 (23.9) |  | 1,163 (29.8) | 1,435 (30.8) | 1,042 (22.2) | 839 (18.2) | 1,006 (20.0) | <.0001 |
| **Chemotherapy** | 10,819 (50.6) |  | 2,065 (54.5) | 2,123 (48.7) | 2,141 (49.8) | 2,083 (48.2) | 2,407 (52.3) | NA |
| **Radiotherapy** | 6,928 (30.2) |  | 1,060 (27.2) | 1,396 (29.9) | 1,450 (30.9) | 1,376 (29.8) | 1,646 (32.7) | NA |
| **Surgery** | 5,752 (25.1) |  | 990 (25.4) | 1,100 (23.6) | 1,227 (26.2) | 1,207 (26.1) | 1,228 (24.4) | NA |

Abbreviations: ICD, International Classification of Diseases; N, number of observations; NA, not applicable; NSCLC, non-small-cell lung cancer; SCLC, small-cell lung cancer; SD, standard deviation; 3N=12 patients had an additional diagnosis of NSCLC; aP-value from Chi-square test comparing the distribution of the factors and deprivation quintiles; bComparing NSCLC and SCLC.

**Table 2** Kaplan-Meier estimates stratified by area-based socioeconomic deprivation and by stage at diagnosis for the total population of lung cancer patients registered in three German clinical cancer registries.

|  |  |
| --- | --- |
| **Area-based****socioeconomic deprivation quintile** | **Overall Survival in % (95 % Confidence Interval)** |
| **1 year** | **3 years** | **5 years** |
| Total population |  |  |  |
|  Q1 (=least deprived)  | 48.8 (47.2-50.4) | 22.6 (21.1-24.0) | 17.2 (15.8-18.5) |
|  Q2  | 47.7 (46.2-49.2) | 22.0 (20.7-23.3) | 15.9 (14.8-17.2) |
|  Q3  | 47.9 (46.5-49.4) | 23.5 (22.2-24.8) | 16.7 (15.5-17.9) |
|  Q4  | 47.7 (46.2-49.1) | 22.6 (21.3-23.9) | 15.7 (14.5-16.9) |
|  Q5 (=most deprived)  | **46.6 (45.2-48.0)** | **20.7 (19.6-22.0)** | **14.4 (13.3-15.5)** |
| Stage I + II |  |  |  |
|  Q1 (=least deprived)  | 81.3 (78.4-83.9) | 59.0 (55.3-62.5) | 48.1 (44.2-51.9) |
|  Q2  | 80.2 (77.4-82.7) | 58.3 (54.9-61.5) | 46.9 (43.4-50.4) |
|  Q3  | 79.3 (76.7-81.7) | 55.3 (52.2-58.4) | 42.9 (39.7-46.2) |
|  Q4  | **76.8 (74.0-79.3)** | 52.8 (49.5-55.9) | **40.1 (36.8-43.4)** |
|  Q5 (=most deprived)  | 78.3 (75.6-80.7) | **52.5 (49.3-55.6)** | 40.7 (37.5-43.9) |
| Stage III |  |  |  |
|  Q1 (=least deprived)  | 53.7 (50.3-56.9) | 21.1 (18.4-23.9) | 15.2 (12.8-17.8) |
|  Q2  | 54.2 (51.2-57.2) | 18.8 (16.4-21.3) | 12.0 (10.0-14.2) |
|  Q3  | 52.5 (49.4-55.4) | 20.9 (18.4-23.4) | 14.2 (12.0-16.6) |
|  Q4  | 53.6 (50.5-56.5) | 20.7 (18.3-23.2) | 13.5 (11.4-15.8) |
|  Q5 (=most deprived)  | **47.9 (45.1-50.7)** | **17.7 (15.6-19.9)** | **10.9 (9.2-12.8)** |
| Stage IV |  |  |  |
|  Q1 (=least deprived)  | 30.6 (28.4-32.8) | **6.2 (5.0-7.5)** | 3.7 (2.8-4.9) |
|  Q2  | 29.4 (27.5-31.4) | 7.1 (6.0-8.4) | 3.9 (3.0-5.0) |
|  Q3  | **28.9 (26.9-30.9)** | 8.1 (6.9-9.4) | 4.3 (3.4-5.4) |
|  Q4  | 29.3 (27.3-31.3) | 7.8 (6.6-9.2) | 4.0 (3.0-5.2) |
|  Q5 (=most deprived)  | 30.3 (28.4-32.3) | 7.0 (5.9-8.2) | **3.6 (2.8-4.6)** |

Lowest overall survival among the quintiles is printed in bold.

**Table 3** Association between area-based socioeconomic deprivation and lung cancer survival overall in a German population and stratified by stage at diagnosis with different levels of adjustment.

| **Subgroup****(deprivation quintile)** |  | **Events****N (%)** |  | **Model****Hazard ratio (95% confidence interval)\*** |  | **Adjusted 5-year survival rate %c** | **Model 3 plus cancer registryd****Hazard ratio****(95% confidence interval)\*** |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Model 1a** | **Model 2b** | **Model 3c** |  |  |
| Total population |  | 18,277 (79.8) |  |  |  |  |  |  |  |
| Q1 (Least deprived) |  |  |  | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |  | 17.1 (16.2-18.0) | 1.00 (ref.) |
| Q2 |  |  |  | 1.02 (0.97-1.07) | 1.02 (0.97-1.07) | 1.02 (0.97-1.07) |  | 16.7 (15.9-17.5) | 1.00 (0.96-1.06) |
| Q3 |  |  |  | 1.00 (0.95-1.05) | 1.01 (0.96-1.06) | 1.02 (0.97-1.07) |  | 16.7 (15.9-17.5) | 1.00 (0.95-1.05) |
| Q4 |  |  |  | 1.03 (0.98-1.08) | 1.03 (0.98-1.08) | 1.05 (1.00-1.10) |  | 16.1 (15.3-17.0) | 1.02 (0.97-1.08) |
| Q5 (Most deprived) |  |  |  | **1.06 (1.01-1.11)** | **1.06 (1.01-1.11)** | **1.06 (1.01-1.11)** |  | 15.9 (15.1-16.7) | 1.03 (0.98-1.08) |
| Stage I/II |  | 3,182 (56.8) |  |  |  |  |  |  |  |
| Q1 (Least deprived) |  |  |  | 1.00 (ref.) | 1.00 (ref.) |  |  | 47.0 (43.7-50.2) | 1.00 (ref.) |
| Q2 |  |  |  | 0.93 (0.82-1.06) | 0.94 (0.83-1.07) |  |  | 49.0 (45.9-51.9) | 0.97 (0.85-1.10) |
| Q3 |  |  |  | 1.10 (0.97-1.24) | 1.11 (0.98-1.26) |  |  | 43.5 (40.7-46.3) | **1.14 (1.00-1.30)** |
| Q4 |  |  |  | **1.16 (1.03-1.31)** | **1.17 (1.04-1.32)** |  |  | 41.8 (38.9-44.6) | **1.19 (1.05-1.35)** |
| Q5 (Most deprived) |  |  |  | 1.12 (0.99-1.26) | **1.13 (1.00-1.28)** |  |  | 42.9 (40.0-45.6) | **1.17 (1.03-1.32)** |
| Stage III |  | 4,978 (82.3) |  |  |  |  |  |  |  |
| Q1 (Least deprived) |  |  |  | 1.00 (ref.) | 1.00 (ref.) |  |  | 15.6 (13.6-17.8) | 1.00 (ref.) |
| Q2 |  |  |  | 1.00 (0.91-1.10) | 1.00 (0.91-1.10) |  |  | 15.6 (13.7-17.6) | 1.00 (0.91-1.10) |
| Q3 |  |  |  | 1.03 (0.94-1.13) | 1.03 (0.94-1.14) |  |  | 14.8 (12.9-16.7) | 1.02 (0.92-1.12) |
| Q4 |  |  |  | 1.02 (0.93-1.12) | 1.01 (0.92-1.12) |  |  | 15.3 (13.4-17.3) | 0.99 (0.90-1.10) |
| Q5 (Most deprived) |  |  |  | **1.13 (1.03-1.23)** | **1.13 (1.03-1.24)** |  |  | 12.6 (11.0-14.2) | **1.11 (1.00-1.22)** |
| Stage IV |  | 10,117 (89.9) |  |  |  |  |  |  |  |
| Q1 (Least deprived) |  |  |  | 1.00 (ref.) | 1.00 (ref.) |  |  | 4.7 (3.9-5.6) | 1.00 (ref.) |
| Q2 |  |  |  | 1.03 (0.97-1.11) | 1.03 (0.96-1.10) |  |  | 4.3 (3.6-5.0) | 1.01 (0.94-1.08) |
| Q3 |  |  |  | 1.00 (0.93-1.07) | 1.00 (0.93-1.06) |  |  | 4.8 (4.1-5.6) | 0.96 (0.89-1.03) |
| Q4 |  |  |  | 1.03 (0.97-1.10) | 1.02 (0.96-1.10) |  |  | 4.4 (3.7-5.2) | 0.99 (0.93-1.06) |
| Q5 (Most deprived) |  |  |  | 1.01 (0.94-1.07) | 1.00 (0.94-1.07) |  |  | 4.7 (4.0-5.4) | 0.96 (0.89-1.03) |

Abbreviations: N, number of events;

aAdjusted for age group (15-54 years, 55-59 years, 60-64 years, 65-69 years, 70-74 years, 75+ years), sex (males, females) and year of diagnosis.

bSame adjustment as model 1 plus cancer subtype (NSCLC, SCLC) and grading (well- or moderately differentiated, poorly or undifferentiated).

cSame adjustment as model 2 plus stage at diagnosis (I, II, III, IV). In stage stratified analyses, this is the same model as model 2.

dSame adjustment as model 3 plus registry (Dresden, Erfurt, Regensburg).

\*Hazard ratios with p<0.05 are printed in bold;

**Table 4** Association between region-specific area-based socioeconomic deprivation and lung cancer survival overall stratified by three German clinical cancer registries

| **Registry** |  | **Events****N (%)** |  | **Deprivation quintile****Hazard ratio (95% confidence interval)**a,\* |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Q1****(Least deprived)** | **Q2** | **Q3** | **Q4** | **Q5****(Most deprived)** | **Dresden/Erfurt cityb** |
| Dresden |  | 5,470 (81.0) |  | 1.00 (ref.) | 0.94 (0.83-1.05) | 1.00 (0.89-1.12) | 0.91 (0.82-1.02) | 1.09 (0.98-1.21) | 0.94 (0.85-1.03) |
| Erfurt |  | 4,344 (80.9) |  | 1.00 (ref.) | 1.10 (0.97-1.25) | 1.11 (0.98-1.26) | 1.08 (0.95-1.22) | 1.11 (0.98-1.26) | **1.15 (1.04-1.29)** |
| Regensburg |  | 8,463 (78.5) |  | 1.00 (ref.) | 0.97 (0.90-1.04) | 1.01 (0.94-1.08) | 0.98 (0.92-1.06) | 0.99 (0.92-1.06) | - |

Abbreviations: N, number of events;

aAdjusted for age group (15-54 years, 55-59 years, 60-64 years, 65-69 years, 70-74 years, 75+ years) and sex (males, females), year of diagnosis, cancer subtype (NSCLC, SCLC), grading (well- or moderately differentiated, poorly or undifferentiated), stage at diagnosis (I, II, III, IV).

bFor the cancer registry Dresden and Erfurt, the cities Dresden and Erfurt were classified separately, as they would otherwise dominate the classification of the quintiles. The deprivation value for Dresden lies between Q1 and Q2 in 2006 and in Q2 in 2010. For Erfurt, it lies in Q1 in 2006 and in Q2 in 2010.

\*Hazard ratios with p<0.05 are printed in bold