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Lung cancer treatment is influenced by income, education, age and place of residence in a country with universal health coverage

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Selection of lung cancer treatment should be based on tumour characteristics, physiological reserves and preferences of the patient. Our aims were to identify and quantify other factors associated with treatment received. Lung cancer patient data from 2002 to 2011 were obtained from the national population-based Cancer Registry of Norway, Statistics Norway and the Norwegian Patient Register. Multivariable logistic regression examined whether year of diagnosis, age, sex, education, income, health trust, smoking status, extent of disease, histology and comorbidities were associated with choice of treatment; surgery or radical or palliative radiotherapy, within 1 year of diagnosis. Among the 24,324 lung cancer patients identified, the resection rate remained constant while the proportion of radical radiotherapy administered increased from 8.6 to 14.1%. Older patients, those with lower household incomes and certain health trusts were less likely to receive any treatment. Lower education and the male gender were identified as negative predictors for receiving surgery. Smoking history was positively associated with both radical and palliative radiotherapy, while comorbidity and symptoms were independently associated with receiving surgery and palliative radiotherapy. Although Norway is a highly egalitarian country with a free, universal healthcare system, this study indicates that surgery and radical and palliative radiotherapy were under-used among the elderly, those with a lower socioeconomic status and those living in certain health trusts.

According to Norwegian guidelines, lung cancer treatment should be based on extent of disease (EOD), tumor histology, comorbidities, performance status and preferences of the patient.[1] Surgical resection is considered a prerequisite for the cure of lung cancer, but a benefit has only been shown for patients with localized disease, that is, disease that does not extend beyond the intrapulmonary or hilar lymph nodes.

Key words: lung cancer, surgery, radiotherapy, national population-based
Abbreviations: CCI: Charlson comorbidity index; CI: confidence interval; CRN: Cancer Registry of Norway; EOD: extent of disease; ICD: international classification of diseases; OR: odds ratio; SES: socioeconomic status; TNM: tumour, node, metastasis
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Stereotactic radiotherapy has recently become an alternative for selected patients.[2,3] If a patient is deemed ineligible for surgical treatment due to EOD or significant comorbidities, radiotherapy and/or chemotherapy can be offered. For patients with mediastinal lymph node metastasis, this combination is offered with curative intent, while for patients whose tumours have spread beyond the lung and mediastinum, in the majority of patients, palliative radiotherapy and/or chemotherapy are offered for symptom relief, to slow disease progression and improve medium term survival.

Likelihood of both receiving surgical treatment and radiotherapy as treatment for lung cancer has previously been shown to be affected by factors not mentioned in guidelines. A number of studies have found that socioeconomic status (SES) and/or place of residence may influence the likelihood of receiving surgical treatment.[4–8] However, the influence of SES on radiotherapy remains inconclusive.[4,9–11]

Previous studies have been unable to examine the association between lung cancer treatment and factors not mentioned in the guidelines, using individual measures of SES. To date there has been no population-based study examining

What's new?
According to Norwegian guidelines, lung cancer treatment should be based on extent of disease, tumour histology, comorbidities, performance status and preferences of the patient. Here, the authors present the first nationwide population-based study to examine and quantify the association between nonguideline-specified factors and surgical treatment and radical radiotherapy or palliative radiotherapy for lung cancer patients. The results suggest that even in a highly egalitarian country with a free, universal healthcare system such as Norway, lung cancer patients with low socioeconomic status, advanced age and living in certain areas are less likely to receive surgery, radical radiotherapy and palliative radiotherapy.

radiotherapy as a treatment for lung cancer, stratified by treatment intention (*i.e.*, radical and palliative radiotherapy).[6] If factors other than EOD, histology and presence of comorbidities are found to be independently associated with treatment received, it may suggest that some subgroups are over- or under-treated. This study is unique in so far as it is a nationwide population-based study that examines and quantifies the association between nonguideline specified factors and surgical treatment and radical radiotherapy or palliative radiotherapy for lung cancer patients.

Material and Methods

Cancer registry of Norway

All hospitals, pathology laboratories and general practitioners in Norway must report all newly diagnosed malignant neoplasms to the Cancer Registry of Norway (CRN). The CRN also receives death certificates from the Cause of Death Registry. Using the personal identification number assigned to each Norwegian citizen, the CRN is linked monthly to the National Population Register to update vital status (death or emigration) and yearly to the National Patient Register to ensure completeness of cancer cases. The CRN contains clinical reports from hospitals, which include individual information on surgical treatment, smoking status and symptoms. However, smoking status and symptoms are only available for patients diagnosed in 2004–2010. The CRN also contains patient-identifiable radiotherapy data, which it receives annually from all radiotherapy centres in Norway.

All cases with malignant neoplasm of bronchus and lung (International Classification of Diseases, Revision 10 (ICD-10) code C34) diagnosed between 1 January 2002 and 31 December 2011 and recorded in the CRN were eligible for inclusion in this study. The quality, comparability, completeness, validity and timeliness of the data in the CRN are high, with a 96.9% estimated completeness for lung cancer.[12]

Classification of variables

Year and age at diagnosis, sex, smoking status, symptoms, EOD and histology were extracted from the CRN, as was information on surgical treatment and radiotherapy.[13] Duration of symptoms was defined as the number of days from when the first symptom occurred to date of diagnosis. EOD was grouped into localized, regional or metastatic, according to the condensed tumor, node, metastasis (TNM) status.[14] Before 2008, EOD was coded as unknown if it was based solely on the pathology report (*i.e.*, no valid clinical notification) and there was no information about metastases at the time of diagnosis. After 2008, these cases were coded as localized if they received curative surgery, but to avoid bias in this study, we classified all post-2008 information about EOD as unknown. Treatment intention for radiotherapy was categorized as radical (including curative, local control and prophylactic) or palliative.[15] When treatment intention was missing (5.3% of patients), it was assigned based on the radiotherapy dose, in accordance with the national guidelines available during the study period.[1] Small-cell carcinoma patients receiving doses of $\geq$42 Gy and $<$42 Gy were categorized as radical and palliative, respectively. Nonsmall cell carcinoma patients were categorized as radical if they received doses of $\geq$60 Gy, otherwise radiotherapy was classified as palliative. If the total dose given was $\geq$45 Gy and given in 3 fractions, it was defined as stereotactic and classified as curative.

In 2011, Norway consisted of 21 health trusts which are responsible for general healthcare treatment and management of all patients residing in its geographical catchment area. The study variable denoting health service region was based on the patients' place of residence, independent of where the patient was treated. Due to centralization, the number of hospitals performing surgery has decreased.[16] In 2002, there were 14 health trusts that had hospitals performing surgery and 7 that were providing radiotherapy, while the comparable numbers in 2011 were 7 (Ahus, OUS, Helse Stavanger, Helse Bergen, St.Olavs Hospital, Nordlandssykehuset and UNN) and 9 (OUS, Innlandet, Sørlandet, Helse Stavanger, Helse Bergen, Helse Møre og Romsdal, St.Olavs Hospital, Nordlandssykehuset and UNN).

Data on the highest education level achieved and household income during the year before lung cancer diagnosis were obtained through linkage with Statistics Norway. Data on household income was only available after 2004. The cut-points were set at the 33rd (low) and 66th (high) percentiles with an intermediate group between these cut-points and were redefined every year to account for increasing income over time.

Comorbidity information was measured using a modified version of the Charlson comorbidity index (CCI), which is constructed by using diagnostic codes (ICD-10) from hospitalizations within one year prior to and including, the date of diagnosis. A score is determined for each of a patient's recorded comorbid diseases based on its severity and the

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combination of these scores results in a modified CCI. Comorbidity information is only available for patients diagnosed after 1 January 2009 and it is collected from the Norwegian Patient Register which only contains person-identifiable data from January 2008 onwards. The index was categorized into: "no hospital admissions before lung cancer diagnosis" (CCI = −1), low (CCI = 0), intermediate (CCI = 1, 2) and high (CCI ≥3).[17,18]

Data on chemotherapy were not available; hence "no treatment" refers to patients who received neither surgery nor radiotherapy.

Statistical analysis

Multiple imputation is a statistical method that uses available data to model the likely distribution of missing data and was used to handle incomplete data on education, income, smoking status, symptoms, EOD and histology. The imputation model was run 30 times using the mi impute chained command in STATA 13.1.[19,20]

Likelihood ratio tests were performed using complete case data (*i.e.*, excluding patients with missing information), to assess which variables to include in the final models. Multivariable logistic regression models examined possible predictors of the first treatment received within 1 year of diagnosis. All models included year of diagnosis, age, sex, education, income, place of residence (*i.e.*, health trust), EOD and histology. The same analysis, stratified by histology, was performed to find predictors for receiving treatment. Since SCLC patients very seldom undergo surgery, the outcomes considered here were only radical and palliative radiotherapy. To estimate the proportion of patients experiencing different treatments, a competing risk model was created.[21] For all treatment modalities, multivariable subanalyses were performed for patients diagnosed in 2004–2010 and 2009–2011, to be able to account for smoking and comorbidity, respectively. Statistical significance ($p < 0.05$) of the individual explanatory variables was obtained from Wald tests. The correlation between the proportions of patients treated with radical and palliative radiotherapy between patients residing in different health trusts was measured using Pearson's correlation coefficient. To measure how the changes in treatment rates affect the odds of receiving treatment between all health trusts over time, we measured the median difference between the estimated odds ratios (OR) for each health trust and the national average (OR =1). This is calculated in 2002–2006 and 2007–2011, for all three treatment modalities.

Results

We identified 25,082 patients with a diagnosis of primary lung cancer in 2002–2011. We excluded 29 (0.1%) with a registered date of diagnosis or surgical treatment after the date of death and 8 (0.03%) due to surgery occurring outside Norway. An additional 151 (0.6%) patients diagnosed through autopsy, 524 (2.1%) registered solely based on death certificates and 46 (0.2%) registered with "other specified histologies" (80.4% of which were sarcoma) were also excluded. The final study sample was 24,324 lung cancer patients. The proportion of C33-34 patients with a histologically verified diagnosis in 2002–2011 was 78.7%.

The proportion of patients with "no treatment" decreased from 50.0 to 38.7% over the study period and ranged overall between 36.1 and 54.6% across health trusts. This decrease was offset by a corresponding increase in radical and palliative radiotherapy, while the proportion of patients who received surgical treatment remained fairly constant (Table 1). A higher proportion of patients with high education and/or high household income were treated with surgery or radiotherapy (Table 1).

Within 1 year of diagnosis, 16.5, 9.7 and 30.7% of patients were treated with surgery, radical radiotherapy and palliative radiotherapy, respectively (Fig. 1). While the proportion treated with surgery and radical radiotherapy reached a plateau after 3–4 months, this pattern was not seen for patients treated with palliative radiotherapy (Fig. 1). There was a small increase over time in the proportion of patients initially treated with radical or palliative radiotherapy (Fig. 2).

Surgery

Men were less likely than women to undergo surgery (odds ratio [OR] = 0.84, 95% confidence interval [CI]:0.77–0.93; Table 2). Patients with high education or high household income were more likely to undergo surgery than those with low education or low household income after adjusting for case mix [OR = 1.28, 95% CI: (1.08–1.51) and OR =1.66, 95% CI: (1.43–1.94), respectively] (Table 2). Across health trusts the OR for surgery varied from 0.74 to 1.63 when compared with the national average (Fig. 3). The median differences in OR between health trusts were calculated to be 0.28 in the first period and 0.29 in the second period.

The inclusion of symptoms, smoking or comorbidity in the multivariable model had only a minimal effect on the ORs for the other explanatory variables (data not shown). Current and former smokers were indicated to have a reduced odds of receiving surgery compared with never smokers; however the results did not achieve statistical significance (Table 2). Patients with "no hospital admissions before lung cancer diagnosis" were less likely to undergo surgery than patients with low comorbidities (OR = 0.53, 95% CI: 0.30–0.93), although this difference was non-significant when presence and duration of symptoms were included in the model (OR = 1.06, 95% CI: 0.44–2.52).

Radical radiotherapy

The odds of receiving radical radiotherapy increased over time and decreased with increasing age (Table 2). While 0.7% of patients were treated with stereotactic radiotherapy during the study period, 2.4% received it in 2011 (data not shown). High household income was associated with increased odds of receiving radical radiotherapy (OR = 1.35, 95% CI: 1.15-1.58; Table 2). Compared with the national

Table 1. Characteristics of lung cancer patients diagnosed in Norway in 2002–2011 according to treatment received within 1 year after diagnosis ($n = 24{,}324$)

	All	Not treated[1]		Resected		Radiotherapy			
						Radical[2]		Palliative	
	n	*n*	%	*n*	%	*n*	%	*n*	%
Number of patients	24 324	10 878	44.7	4 424	18.2	2 634	10.8	7 617	31.3
Year of diagnosis									
2002	2 116	1 058	50.0	386	18.2	183	8.6	617	29.2
2003	2 286	1 119	49.0	400	17.5	227	9.9	676	29.6
2004	2 283	1 093	47.9	385	16.9	222	9.7	710	31.1
2005	2 305	1 063	46.1	417	18.1	198	8.6	733	31.8
2006	2 437	1 076	44.2	462	19.0	238	9.8	809	33.2
2007	2 524	1 138	45.1	468	18.5	270	10.7	771	30.5
2008	2 515	1 117	44.4	450	17.9	283	11.3	795	31.6
2009	2 553	1 065	41.7	462	18.1	315	12.3	844	33.1
2010	2 644	1 118	42.3	444	16.8	324	12.3	856	32.4
2011	2 661	1 031	38.7	550	20.7	374	14.1	806	30.3
Age (years)									
$\leq$49	923	227	24.6	265	28.7	130	14.1	379	41.1
50–59	3 575	1 081	30.2	826	23.1	537	15.0	1 413	39.5
60–69	7 239	2 599	35.9	1 646	22.7	939	13.0	2 552	35.3
70–79	8 252	3 996	48.4	1 466	17.8	803	9.7	2 314	28.0
$\geq$80	4 335	2 975	68.6	221	5.1	225	5.2	959	22.1
Sex									
Female	10 100	4 447	44.0	1 967	19.5	1 136	11.2	3 061	30.3
Male	14 224	6 431	45.2	2 457	17.3	1 498	10.5	4 556	32.0
Stage									
Localized	4 210	1 231	29.2	2 139	50.8	585	13.9	554	13.2
Regional	6 833	2 462	36.0	1 788	26.2	1 449	21.2	1 869	27.4
Metastatic	11 698	6 320	54.0	266	2.3	423	3.6	4 831	41.3
Unknown	1 571	865	55.1	231	14.7	170	10.8	358	22.8
Education									
Low	11 619	5 579	48.0	1 923	16.6	1 136	9.8	3 471	29.9
Intermediate	10 127	4 263	42.1	1 978	19.5	1 189	11.7	3 280	32.4
High	2 285	885	38.7	496	21.7	278	12.2	774	33.9
Unknown	293	151	51.5	27	9.2	31	10.6	92	31.4
Household income[3]									
Low	3 412	1 890	55.4	402	11.8	286	8.4	909	26.6
Intermediate	10 578	4 577	43.3	1 973	18.7	1 208	11.4	3 327	31.5
High	3 580	1 102	30.8	868	24.2	503	14.1	1 360	38.0
Unknown	69	39	56.5	10	14.5	5	7.2	18	26.1
Histology									
Squamous-cell carcinoma	4 881	1 548	31.7	1 350	27.7	616	12.6	1 710	35.0
Adenocarcinoma	7 882	3 222	40.9	2 165	27.5	611	7.8	2 513	31.9
Small-cell carcinoma	3 959	1 986	50.2	68	1.7	855	21.6	1 095	27.7
Large-cell carcinoma	1 078	392	36.4	293	27.2	98	9.1	399	37.0
Other specified carcinoma	3 084	1 202	39.0	493	16.0	269	8.7	1 206	39.1
Carcinoma, not specified	1 032	482	46.7	54	5.2	91	8.8	427	41.4

Table 1. Characteristics of lung cancer patients diagnosed in Norway in 2002–2011 according to treatment received within 1 year after diagnosis ($n = 24{,}324$) (Continued)

	All	Not treated[1]		Resected		Radiotherapy			
						Radical[2]		Palliative	
	n	*n*	%	*n*	%	*n*	%	*n*	%
Unknown	2 408	2 046	85.0	1	0.0	94	3.9	267	11.1
Health trust									
Østfold	1 532	751	49.0	274	17.9	150	9.8	440	28.7
Ahus	2 208	1 037	47.0	480	21.7	232	10.5	588	26.6
OUS	828	383	46.3	159	19.2	65	7.9	268	32.4
Lovisenberg sykehus	597	299	50.1	112	18.8	48	8.0	174	29.1
Diakonhjemmet sykehus	406	207	51.0	64	15.8	27	6.7	127	31.3
Innlandet	2 123	910	42.9	368	17.3	279	13.1	686	32.3
Vestre Viken	2 039	920	45.1	312	15.3	222	10.9	650	31.9
Vestfold	1 305	536	41.1	211	16.2	146	11.2	474	36.3
Telemark	964	453	47.0	162	16.8	112	11.6	288	29.9
Sørlandet	1 762	767	43.5	303	17.2	198	11.2	553	31.4
Helse Stavanger	1 290	545	42.2	222	17.2	150	11.6	432	33.5
Helse Fonna	840	393	46.8	136	16.2	94	11.2	256	30.5
Helse Bergen	1 810	729	40.3	294	16.2	247	13.6	621	34.3
Helse Førde	521	247	47.4	74	14.2	54	10.4	173	33.2
Helse Møre og Romsdal	1 279	556	43.5	271	21.2	149	11.6	371	29.0
St Olavs Hospital	1 387	659	47.5	288	20.8	138	9.9	373	26.9
Nord-Trøndelag	710	388	54.6	121	17.0	62	8.7	166	23.4
Helgeland	456	235	51.5	83	18.2	36	7.9	126	27.6
Nordlandssykehuset	737	289	39.2	188	25.5	58	7.9	268	36.4
UNN	1 008	364	36.1	202	20.0	106	10.5	400	39.7
Finnmark	481	193	40.1	91	18.9	53	11.0	173	36.0
Comorbidity[4]									
No admissions	214	82	38.3	24	11.2	32	15.0	87	40.7
CCI = 0	4 480	1 673	37.3	873	19.5	547	12.2	1 603	35.8
CCI [1, 2]	2 667	1 161	43.5	507	19.0	372	13.9	721	27.0
CCI ≥ 3	497	298	60.0	52	10.5	62	12.5	95	19.1
Symptoms[5]									
None	1 555	548	35.2	696	44.8	228	14.7	238	15.3
Yes	8 208	3 618	44.1	1 287	15.7	882	10.7	2 828	34.5
Unknown	7 498	3 504	46.7	1 105	14.7	740	9.9	2 452	32.7
Smoking status[5]									
Never	1 347	679	50.4	276	20.5	88	6.5	354	26.3
Current	7 538	3 183	42.2	1 393	18.5	900	11.9	2 462	32.7
Former	4 052	1 749	43.2	806	19.9	463	11.4	1 284	31.7
Unknown	4 324	2 059	47.6	613	14.2	399	9.2	1 418	32.8

[1]Patients may have received chemotherapy.
[2]Includes local control, curative and prophylactic radiotherapy.
[3]2005–2011, $n = 17\ 639$.
[4]2009–2011, $n = 7\ 858$.
[5]2004–2010, $n = 17\ 261$.
Patients can receive multiple treatments, so that the sum of the rows may exceed 100%. The "no treatment" group excludes patients who received surgery or radiotherapy. "'No admissions' means that patients are not registered with any diseases or hospitalizations in the Norwegian Patient Register during the one year prior to lung cancer diagnosis (including the date of diagnosis)."
Abbreviation: CCI: Charlson comorbidity index.

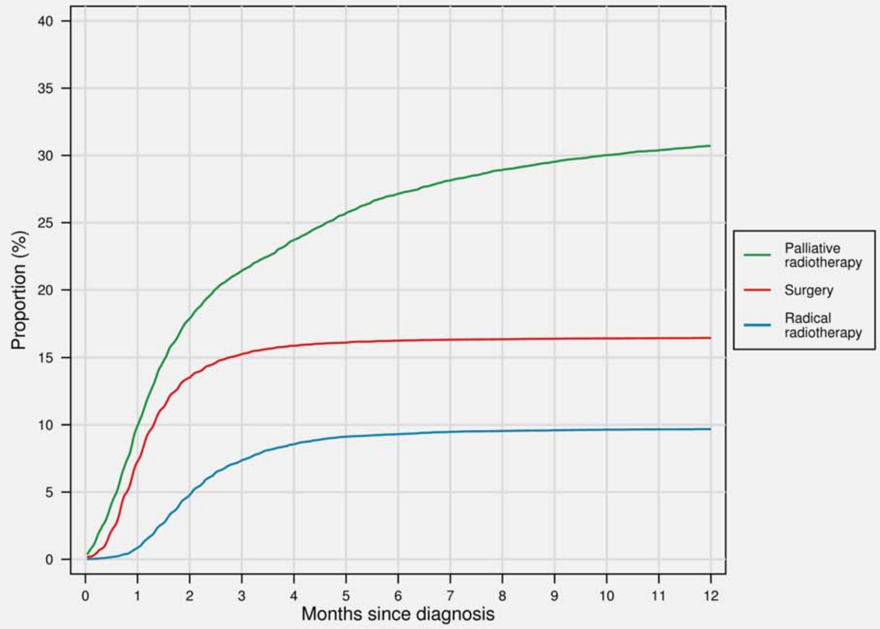

Figure 1. Proportions of lung cancer patients in Norway diagnosed in 2002–2011 receiving surgery, radical and/or palliative radiotherapy within 1 year of diagnosis ($n = 24{,}324$). Footnote: These estimates come from a competing risk model, which takes into account that patients can receive multiple treatments. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

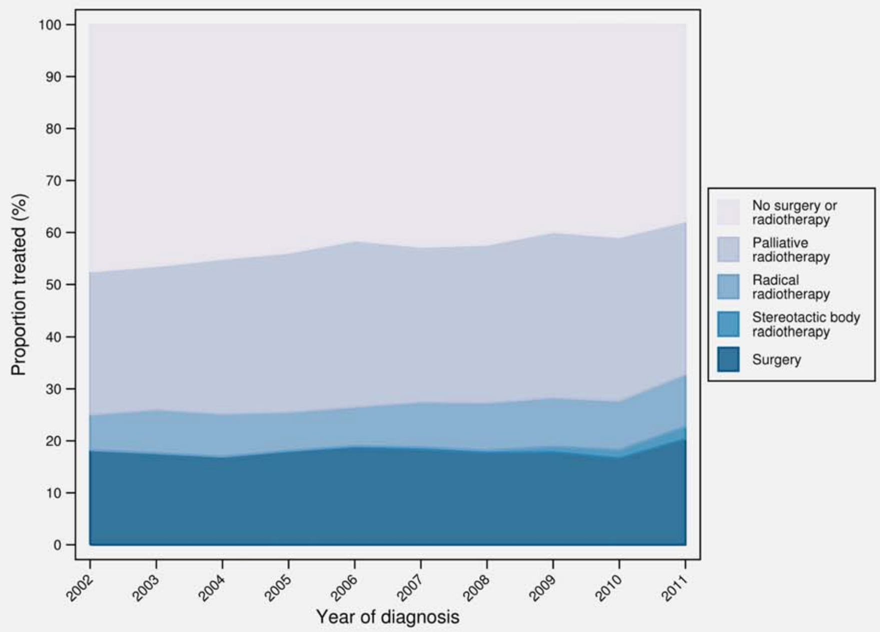

Figure 2. Trends in the proportion of lung cancer patients in Norway diagnosed in 2002–2011 initially treated with surgery, radical, palliative and stereotactic body radiotherapy ($n = 24{,}324$). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

average, the OR for receiving radical radiotherapy varied across health trusts (from 0.56 to 1.50; Fig. 3). The Pearson's correlation coefficient comparing the proportions of patients treated with radical and palliative radiotherapy between patients residing in different health trusts was 0.22 (95%CI: −0.23 – 0.60). The median differences in OR between health trusts were calculated to be 0.37 in the first period and 0.36 in the second period.

Compared with never smokers, current and former smokers had at least 75% greater odds of receiving radical

Table 2. OR and 95% confidence interval (CI) for receiving (a) surgery, (b) radical radiotherapy (RT) or (c) palliative RT within 1 year after diagnosis for lung cancer patients diagnosed in Norway in 2002–2011 ($n = 24,324$)

	Surgery		Radical radiotherapy		Palliative radiotherapy	
Variables	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Diagnostic year						
2002	1.00	(ref)	1.00	(ref)	1.00	(ref)
2003	0.87	(0.71,1.07)	1.14	(0.88,1.47)	1.07	(0.93,1.24)
2004	0.81	(0.66,0.99)	1.28	(0.99,1.65)	1.21	(1.04,1.39)
2005	0.87	(0.71,1.07)	1.12	(0.86,1.45)	1.25	(1.08,1.44)
2006	0.93	(0.76,1.13)	1.13	(0.88,1.47)	1.39	(1.21,1.60)
2007	0.93	(0.76,1.13)	1.30	(1.01,1.67)	1.25	(1.09,1.44)
2008	0.90	(0.74,1.10)	1.48	(1.16,1.89)	1.26	(1.09,1.45)
2009	0.87	(0.71,1.08)	1.73	(1.35,2.23)	1.46	(1.26,1.69)
2010	0.74	(0.59,0.92)	1.86	(1.45,2.38)	1.39	(1.21,1.61)
2011	0.91	(0.73,1.13)	1.97	(1.54,2.52)	1.28	(1.10,1.48)
p-value	0.25		<0.01		<0.01	
Age (year)						
≤49	1.28	(1.02,1.61)	0.76	(0.57,1.01)	1.18	(0.99,1.41)
50–59	1.00	(ref)	1.00	(ref)	1.00	(ref)
60–69	0.84	(0.73,0.96)	0.70	(0.60,0.81)	0.80	(0.72,0.88)
70–79	0.53	(0.46,0.61)	0.47	(0.40,0.55)	0.53	(0.48,0.58)
≥80	0.10	(0.08,0.12)	0.23	(0.18,0.28)	0.37	(0.33,0.41)
p-value	<0.01		<0.01		<0.01	
Sex						
Female	1.00	(ref)	1.00	(ref)	1.00	(ref)
Male	0.84	(0.77,0.93)	0.93	(0.84,1.04)	0.99	(0.93,1.06)
p-value	<0.01		0.21		0.81	
Stage						
Localized	67.15	(56.51,79.79)	3.00	(2.39,3.76)	1.00	(ref)
Regional	14.83	(12.64,17.40)	7.73	(6.40,9.34)	4.78	(3.96,5.77)
Metastasis	1.00	(ref)	1.00	(ref)	6.91	(5.83,8.19)
p-value	<0.01		<0.01		<0.01	
Education						
Low	1.00	(ref)	1.00	(ref)	1.00	(ref)
Intermediate	1.20	(1.08,1.33)	1.13	(1.01,1.26)	1.03	(0.97,1.11)
High	1.28	(1.08,1.51)	1.12	(0.93,1.37)	1.02	(0.91,1.15)
p-value	<0.01		0.10		0.62	
Household income						
Low	1.00	(ref)	1.00	(ref)	1.00	(ref)
Intermediate	1.48	(1.29,1.71)	1.27	(1.10,1.48)	1.21	(1.10,1.33)
High	1.66	(1.43,1.94)	1.35	(1.15,1.58)	1.42	(1.29,1.57)
p-value	<0.01		<0.01		<0.01	
Histology						
Squamous cell carcinoma	1.00	(ref)	1.00	(ref)	1.00	(ref)
Adenocarcinoma	1.43	(1.28,1.60)	0.51	(0.43,0.59)	0.61	(0.56,0.67)
Small-cell carcinoma	0.06	(0.05,0.08)	3.28	(2.76,3.90)	0.49	(0.44,0.55)
Large-cell carcinoma	1.77	(1.44,2.18)	0.63	(0.46,0.86)	0.78	(0.66,0.92)

Table 2. OR and 95% confidence interval (CI) for receiving (a) surgery, (b) radical radiotherapy (RT) or (c) palliative RT within 1 year after diagnosis for lung cancer patients diagnosed in Norway in 2002–2011 ($n = 24,324$) (Continued)

	Surgery		Radical radiotherapy		Palliative radiotherapy	
Variables	OR	95% CI	OR	95% CI	OR	95% CI
Other specified carcinoma	0.49	(0.42,0.58)	0.83	(0.69,1.00)	0.86	(0.77,0.96)
Carcinoma, not specified	0.25	(0.18,0.35)	1.17	(0.88,1.56)	0.82	(0.70,0.96)
p-value	<0.01		<0.01		<0.01	
Health trust[1]						
p-value	<0.01		<0.01		<0.01	
Comorbidity[2]						
No admissions	0.53	(0.30,0.93)	1.78	(1.04,3.07)	1.40	(0.99,1.98)
CCI = 0	1.00	(ref)	1.00	(ref)	1.00	(ref)
CCI ϵ [1,2]	1.03	(0.86,1.23)	1.14	(0.95,1.36)	0.70	(0.62,0.79)
PRI ≥ 3	0.60	(0.41,0.89)	1.07	(0.75,1.52)	0.45	(0.34,0.58)
p-value	0.01		0.14		<0.01	
Smoking[3]						
Never	1.00	(ref)	1.00	(ref)	1.00	(ref)
Current	0.88	(0.72,1.08)	1.76	(1.34,2.30)	1.17	(1.00,1.37)
Former	0.94	(0.76,1.16)	1.84	(1.38,2.45)	1.33	(1.12,1.58)
p-value	0.39		0.01		<0.01	
Symptoms[3]						
No	1.00	(ref)	1.00	(ref)	1.00	(ref)
Yes	0.41	(0.35,0.48)	1.04	(0.85,1.27)	1.91	(1.61,2.25)
p-value	<0.01		0.71		<0.01	

[1]Estimates can be found in Figure 3.
[2]Patients diagnosed in 2009–2011, model includes all other covariates that are available in 2002–2011.
[3]Patients diagnosed in 2004–2010, model includes all other covariates that are available in 2002–2011.
Footnote: The multivariable logistic models included health trust as well, but the estimates for radical and palliative radiotherapy are presented graphically in Figure 3.
Abbreviation: OR: odds ratio; CI: confidence interval, CCI: Charlson comorbidity index.

radiotherapy (Table 2). Patients with "no hospital admissions before their lung cancer diagnosis" had 78% higher odds of receiving radical radiotherapy than patients with low comorbidities, but when duration of symptoms was accounted for, this difference disappeared (OR = 1.03, 95% CI: 0.37–2.89; Table 2). Inclusion of smoking, symptoms or comorbidity in the model only marginally affected the estimated ORs for other explanatory variables (data not shown).

The odds for receiving radical radiotherapy did not differ between NSCLC and SCLC patients (p-value = 0.25) (data not shown). The odds for receiving radical radiotherapy had a steeper trend with higher levels of education for SCLC patients compared to NSCLC patients (SCLC: intermediate *vs*. low: OR = 1.20, 95% CI: 0.95–1.51, high *vs*. low: OR = 1.58, 95% CI: 1.03–2.43; NSCLC: intermediate *vs*. low: OR = 1.11, 95% CI: 0.98–1.27, high *vs*. low: OR = 1.06, 95% CI: 0.85–1.34). The odds for receiving radical radiotherapy had a steeper trend with higher levels of income for SCLC patients compared with NSCLC patients (SCLC: intermediate *vs*. low: OR = 1.67, 95% CI: 1.22–2.28, high *vs*. low: OR = 2.07, 95% CI: 1.52–2.82; NSCLC: intermediate *vs*. low: OR = 1.16, 95% CI: 0.97–1.39, high *vs*. low: OR = 1.18, 95% CI: 0.98–1.44). The other results were comparable and consistent between NSCLC and SCLC patients.

Palliative radiotherapy

Patients aged ≥80 years were less likely than those aged 50–59 years to receive palliative radiotherapy (OR = 0.37, 95% CI: 0.33–0.41; Table 2). Patients with a high household income were more likely to receive palliative radiotherapy than those with low income (OR = 1.42, 95% CI: 1.29–1.57). Figure 3 shows geographical differences for receiving palliative radiotherapy, with ORs ranging from 0.64 to 1.47 across the health trusts. The median differences in OR between health trusts were calculated to be 0.23 in the first period and 0.28 in the second period.

Former smokers had increased odds of receiving palliative radiotherapy compared to never smokers [OR = 1.33, 95% CI: (1.12–1.58)] and a high comorbidity score was negatively associated with palliative radiotherapy (OR = 0.45, 95% CI: 0.34–0.58 for high vs. low comorbidity; Table 2). Including smoking and comorbidity only marginally affected the

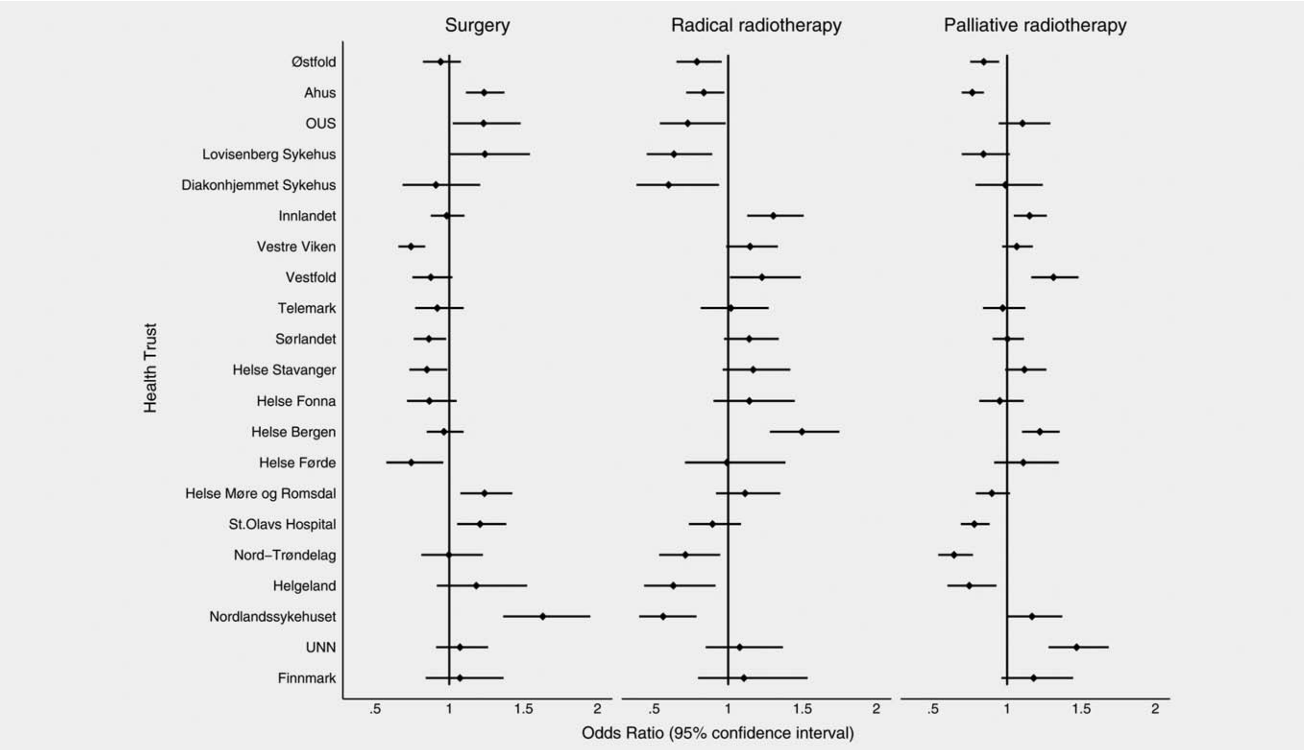

Figure 3. ORs (black diamonds) with 95% confidence intervals for receiving surgery, radical and palliative radiotherapy in all health trusts compared with the country average of Norway for lung cancer patients diagnosed in 2002–2011 ($n = 24{,}324$). Footnote: These estimates come from a multivariable logistic regression model including year of diagnosis, age, sex, education, income, health trust, EOD and histology. In 2011, there were 7 health trusts that had hospitals performing surgery (Ahus, OUS, Helse Stavanger, Helse Bergen, St.Olavs Hospital, Nordlandssykehuset and UNN) and 9 that were providing radiotherapy (OUS, Innlandet, Sørlandet, Helse Stavanger, Helse Bergen, Helse Møre og Romsdal, St.Olavs Hospital, Nordlandssykehuset and UNN).

estimated ORs for the other explanatory variables (data not shown).

The odds for receiving palliative radiotherapy differed between NSCLC and SCLC patients over time (p-value < 0.01), with an increase only observed among SCLC patients (data not shown). The odds for receiving palliative radiotherapy had a steeper trend with higher levels of education for SCLC patients compared with NSCLC patients (SCLC: intermediate *vs*. low: OR = 1.15, 95% CI: 0.96 – 1.37, high *vs*. low: OR = 1.41, 95% CI: 1.03–1.94; NSCLC: intermediate *vs*. low: OR = 1.01, 95% CI: 0.94–1.09, high *vs*. low: OR = 0.97, 95% CI: 0.85–1.10). The odds for receiving palliative radiotherapy had a steeper trend with higher levels of income for SCLC patients compared with NSCLC patients (SCLC: intermediate *vs*. low: OR = 1.49, 95% CI: 1.16–1.90, high *vs*. low: OR = 1.90, 95% CI: 1.47–2.45; NSCLC: intermediate *vs*. low: OR = 1.17, 95% CI: 1.05–1.29, high *vs*. low: OR = 1.35, 95% CI: 1.21–1.50). The other results were comparable and consistent between NSCLC and SCLC patients (data not shown).

Discussion

Together with the criteria for treatment specified in the national guidelines (EOD, histology and comorbidity), we found that education, household income and place of residence (*i.e*., health trust) were independent predictive factors for receiving surgical treatment among lung cancer patients in Norway in 2002–2011. We also found that age, household income and health trust were independently associated with both radical and palliative radiotherapy. Furthermore, smokers were less likely than nonsmokers to receive surgery, but more likely to receive radical radiotherapy.

While it is well-known that the guideline factors are predictors for treatment, our finding that education and income are positively associated with receiving surgical treatment for lung cancer is rather surprising in a country with free, universal healthcare. However, a positive association between income and surgery has also been reported in England, where they have universal healthcare as well.[6,9] Only one other study is directly comparable as it also uses individual measures of SES to investigate treatment among lung cancer patients.[22] This study used education as a proxy for SES and reported that higher education was associated with an almost 2-fold increase in the likelihood of receiving surgical treatment. As lower SES is often associated with poorer general health and greater smoking prevalence, these factors may also contribute to the observed differences in surgical treatment for lung cancer.[23] However, our results coincide with previous research that reduced general health in lower SES groups does not explain observed differences in the likelihood of receiving surgery.[9]

High household income was also associated with increased odds of receiving both radical and palliative radiotherapy. A recent systematic review showed that countries with nonuniversal healthcare, such as the USA, experience SES differences with respect to radiotherapy while most of the studies in countries with universal healthcare, such as Norway and other European countries did not.[4] The one study that used individual measures of education to categorise SES found a pattern similar to ours, although it did not distinguish between radical and palliative radiotherapy.[22] A possible explanation for the differences in results is the use of individual measures versus area-based measures of SES. Differences in smoking consumption and performance status between the household income categories may also explain varying radiotherapy use.[23] It can be argued that education and income are both proxies for SES and that their corresponding estimates often measure the same effect. However, previous studies, including our study, argue that education and income measure different aspects of SES, and that, they should both be treated as independent predictors for treatment.[24,25]

Place of residence was found to be an independent predictor for receipt of each of the three treatment modalities. The geographical differences we found coincide with other international studies.[7,26–29] In our study, when the location where surgery was performed (within or outside of the health trust) was included in the model, it did not affect the differences by health trust (data not shown). The observed geographical differences for radiotherapy were found for both radical and palliative intentions. When we explored differences in the odds for treatment between health trusts over time, there was no change for surgery and radical radiotherapy, however a small increase was observed for palliative radiotherapy.

We found that men had a 15% reduced odds of receiving surgery compared with women. A Danish study[30] reported the opposite result, while other studies reported no significant differences between the sexes.[5,9,26,31] A possible explanation for these results could be historical differences in smoking habits, although this seems unlikely as the difference persisted after adjustment for smoking status. Another possibility could be that as men tend to smoke more heavily than women, they present with more advanced stages of lung cancer, more comorbidities and poorer performance status, making surgery less viable.[32]

Increasing age was associated with a reduced likelihood of receiving any of the treatment modalities. Other studies have also reported that the elderly have a reduced chance of receiving palliative radiotherapy.[33–37] It is possible that the elderly are being evaluated for radiotherapy solely based on their age, instead of all the criteria specified in treatment guidelines, and hence are being under-treated. The elderly also have poorer performance status hence lower life expectancy which might explain some of the lower use of treatment.

Our results also showed that current and former smokers were less likely to undergo surgery and more likely to receive radical and palliative radiotherapy compared to never smokers. In addition, current and former smokers had more comorbidities than never smokers (data not shown), which might explain why never smokers were more likely to receive surgery, since high comorbidity is a contra-indication for surgery.

We were only able to adjust for EOD and comorbidities through condensed TNM status and CCI, respectively, thus the observed sex and smoking difference might be a result of residual confounding of EOD and comorbidity.

Patients with “no hospital admissions before lung cancer diagnosis” had 50% lower odds for undergoing surgery, and 80% higher odds for undergoing radical radiotherapy when compared to patients with low comorbidity. Within this small group of patients with “no hospital admissions before lung cancer diagnosis,” a higher proportion had symptoms, but the symptom duration was shorter. This could indicate that these patients generally had more aggressive tumors, and thus were ineligible for surgery. One could also speculate that these patients may choose to avoid hospitals, in general, and therefore are less likely to undergo surgery. In line with other studies, we also found that general health as measured by the CCI was negatively associated with receiving palliative radiotherapy.[35,37] This could indicate that patients with a number of comorbidities have a shorter life expectancy and do not live long enough to receive palliative radiotherapy or they are too weak to endure it.

This study has some limitations. We had no information on receipt of chemotherapy, and as nearly half of all patients are diagnosed at a stage that calls for chemotherapy, this information would have provided a more complete picture of the treatment patterns in the Norwegian population. Moreover, detailed TNM status was not available for unresected lung cancer patients and we did not have information on comorbidity and smoking for the whole study period. Finally, we have no information about performance status, which is important when considering patients’ treatment options, and which may have been useful for explaining the results on smoking status, comorbidity and symptoms. Despite these limitations, this study provides unique and important information on lung cancer treatment in Norway through the use of complete information on surgery and radiotherapy classified by treatment intent, and of individual-level information on education and income. The study’s population-based design and the use of national, comprehensive, high-quality data provide results that are widely representative.

Norway is considered to be an egalitarian society, with a GINI-index in the first quintile that varied between 26.5 and 30.2 in 2002–2011.[38] In such a society, where by law all citizens have equal access to the healthcare system regardless of their social class or place of residence, the differences in the likelihood of receiving surgery and radiotherapy that we found may indicate the existence of social inequality in health services depending on where one lives in the country. One could speculate that patients with high education or high income are better informed about their treatment options, and may be more active in the decision making process with their doctor.

In conclusion, this study showed that even in a country with a free, universal healthcare system, lung cancer patients with low SES, advanced age and living in certain areas were less likely to receive surgery, radical radiotherapy and palliative radiotherapy.

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References

1. The Norwegian Directorate of Health. [Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfolgning av lungekreft]. Oslo. 2014.
2. Zhang B, Zhu F, Ma X, et al. Matched-pair comparisons of stereotactic body radiotherapy (SBRT) versus surgery for the treatment of early stage non-small cell lung cancer: a systematic review and meta-analysis. *Radiother Oncol* 2014;112: 250–5.
3. Solda F, Lodge M, Ashley S, et al. Stereotactic radiotherapy (SABR) for the treatment of primary non-small cell lung cancer; systematic review and comparison with a surgical cohort. *Radiother Oncol.* 2013;109:1–7.
4. Forrest LF, Adams J, Wareham H, et al. Socioeconomic inequalities in lung cancer treatment: systematic review and meta-analysis. *PLoS Med* 2013;10:e1001376.
5. Currow DC, You H, Aranda S, et al. What factors are predictive of surgical resection and survival from localised non-small cell lung cancer? *Med J Aust* 2014;201:475–80.
6. Forrest LF, White M, Rubin G, et al. The role of patient, tumour and system factors in socioeconomic inequalities in lung cancer treatment: population-based study. *Br J Cancer* 2014;111: 608–18.
7. 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* 2012;48:54–60.
8. Strand TE, Bartnes K, Rostad H. National trends in lung cancer surgery. *Eur J Cardiothorac Surg* 2012;42:355–8.
9. Berglund A, Lambe M, Luchtenborg M, et al. Social differences in lung cancer management and survival in South East England: a cohort study. *BMJ Open* 2012;2.
10. 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.
11. Johnson AM, Hines RB, Johnson JA, III, et al. Treatment and survival disparities in lung cancer: the effect of social environment and place of residence. *Lung Cancer* 2014;83:401–7.
12. Larsen IK, Smastuen M, Johannesen TB, et al. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. *Eur J Cancer* 2009;45: 1218–31.
13. Parkin DM, Whelan SL, Ferlay J, et al. Cancer Indidence in Five Continents, vol. VIII. Lyon: International Agency for Research on Cancer, 2002. 782 p.
14. U.S. Department of Health and Human Services. SEER program: comparative staging guide for cancer. U.S. Department of Health and Human Services, Bethesda, MD, 1993.
15. Asli LM, Kvaloy SO, Jetne V, et al. Utilization of radiation therapy in Norway after the implementation of the national cancer plan–a national, population-based study. *Int J Radiat Oncol Biol Phys* 2014;90:707–14.
16. National Quality Register for Lung Cancer. [Aarsrapport 2014]. Oslo: Cancer Registry of Norway, 2014.
17. 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.
18. Nilssen Y, Strand TE, Wiik R, et al. Utilizing national patient-register data to control for comorbidity in prognostic studies. *Clin Epidemiol* 2014;6:395–404.
19. StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP.
20. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30:377–99.
21. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *J Am Stat Assoc* 1999;94:496–509.
22. 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.
23. Tal om tobakk 1973-2012 [database on the Internet]. Available at: https://helsedirektoratet.no/Lists/Publikasjoner/Attachments/319/Tal-om-tobakk-1973-2012-IS-2064.pdf. Accessed on July 2, 2015.
24. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Commun Health* 2006;60:7–12.
25. Dalton SO, Steding-Jessen M, Jakobsen E, et al. Socioeconomic position and survival after lung cancer: influence of stage, treatment and comorbidity among Danish patients with lung cancer diagnosed in 2004-2010. *Acta Oncol* 2015;54:797–804.
26. Wouters MW, Siesling S, Jansen-Landheer ML, et al. Variation in treatment and outcome in patients with non-small cell lung cancer by region, hospital type and volume in the Netherlands. *Eur J Surg Oncol* 2010;36:S83–92.
27. Sant M, Minicozzi P, Allemani C, et al. Regional inequalities in cancer care persist in Italy and can influence survival. *Cancer Epidemiol* 2012;36:541–7.
28. 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.
29. Strand TE, Brunsvig PF, Johannessen DC, et al. Potentially curative radiotherapy for non-small-cell lung cancer in Norway: a population-based study of survival. *Int J Radiat Oncol Biol Phys* 2011;80:133–41.
30. Kaergaard Starr L, Osler M, Steding-Jessen M, et al. Socioeconomic position and surgery for early-stage non-small-cell lung cancer: a population-based study in Denmark. *Lung Cancer* 2013;79:262–9.
31. Rich AL, Tata LJ, Free CM, et al. Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service. *Thorax* 2011;66: 1078–84.
32. Sitas F, Weber MF, Egger S, et al. Smoking cessation after cancer. *J Clin Oncol* 2014;32:3593–5.
33. Tyldesley S, Zhang-Salomons J, Groome PA, et al. Association between age and the utilization of radiotherapy in Ontario. *Int J Radiat Oncol Biol Phys* 2000;47:469–80.
34. Chen AB, Cronin A, Weeks JC, et al. Palliative radiation therapy practice in patients with metastatic non-small-cell lung cancer: a Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) Study. *J Clin Oncol* 2013;31:558–64.
35. Hayman JA, Abrahamse PH, Lakhani I, et al. Use of palliative radiotherapy among patients with metastatic non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2007;69:1001–7.
36. Wong J, Xu B, Yeung HN, et al. Age disparity in palliative radiation therapy among patients with advanced cancer. *Int J Radiat Oncol Biol Phys* 2014;90:224–30.
37. Murphy JD, Nelson LM, Chang DT, et al. Patterns of care in palliative radiotherapy: a population-based study. *J Oncol Pract* 2013;9: e220–7.
38. GINI Index. Available at: http://data.worldbank.org/indicator/SI.POV.GINI/. Accessed 7 Oct 2015.