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The European Journal of Public Health, Vol. 31, No. 5, 967–974

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doi:10.1093/eurpub/ckab071 Advance Access published on 3 May 2021

Factors associated with emergency-related diagnosis, time to treatment and type of treatment in 5713 lung cancer patients

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Background: International and national differences exist in survival among lung cancer patients. Possible explanations include varying proportions of emergency presentations (EPs), unwanted differences in waiting time to treatment and unequal access to treatment. **Methods:** Case-mix-adjusted multivariable logistic regressions the odds of EP and access to surgery, radiotherapy and systemic anticancer treatment (SACT). Multivariable quantile regression analyzed time from diagnosis to first treatment. **Results:** Of 5713 lung cancer patients diagnosed in Norway in 2015–16, 37.9% ($n = 2164$) had an EP before diagnosis. Higher age, more advanced stage and more comorbidities were associated with increasing odds of having an EP ($P < 0.001$) and a lower odds of receiving any treatment ($P < 0.001$). After adjusting for case-mix, waiting times to curative radiotherapy and SACT were 12.1 days longer [95% confidence interval (CI): 10.2, 14.0] and 5.6 days shorter (95% CI: –7.3, –3.9), respectively, compared with waiting time to surgery. Patients with regional disease experienced a 4.7-day shorter (Coeff: –4.7, 95% CI: –9.4, 0.0) waiting time to curative radiotherapy when compared with patients with localized disease. Patients with a high income had a 22% reduced odds [odds ratio (OR) = 0.78, 95% CI: 0.63, 0.97] of having an EP, and a 63% (OR = 1.63, 95% CI: 1.20, 2.21) and a 40% (OR = 1.40, 95% CI: 1.12, 1.76) increased odds of receiving surgery and SACT, respectively. **Conclusion:** Patients who were older, had advanced disease or increased comorbidities were more likely to have an EP and less likely to receive treatment. While income did not affect the waiting time for lung cancer treatment in Norway, it did affect the likelihood of receiving surgery and SACT.

Introduction

Although lung cancer survival is modest, it has improved significantly over the last decade, and substantial variation exists both internationally and nationally.^{1–3} In patients diagnosed in 2015–19, the 5-year survival was estimated to be 22.7% in men and 29.2% in women in Norway.⁴ The proportion of patients diagnosed through an emergency presentation (EP), waiting times from diagnosis to treatment, as well as access to treatment may explain some of the observed variations in survival.

There are different explanations for why patients may have an emergency visit. Patients may experience a disease that rapidly manifests symptoms, or they may have delayed health-seeking behaviour which could result in a worsened condition (patient-delay). It is also

possible that an emergency visit may be associated with a prolonged diagnostic interval by the general practitioner or hospital (system-delay). During their emergency visit, patients may be diagnosed with lung cancer due to lung-specific symptoms, or incidentally diagnosed when examined for an unrelated condition. Internationally, the proportion of lung cancer patients who are diagnosed during an emergency visit varies.^{5,6}

The timeliness of and access to treatment are of great importance to the prognosis. In order to ensure a timely treatment, not only does there need to be sufficient capacity in terms of medical staff and equipment but there should also be a well-organized and structured healthcare system where unnecessary delays to treatment are kept at a minimum. In Norway from 2007 to 2016 waiting time from diagnosis to lung cancer treatment (surgery and radiotherapy)

decreased, but differences between different regions still exist.^{7,8} Also, in 2015, Norway implemented cancer patient pathways (CPPs) in order to reduce waiting time and regional variation, and to increase the predictability of the cancer care for patients and their relatives. However, earlier research showed that there are additional factors not mentioned in the national guidelines that may affect the odds of receiving surgery and radiotherapy, internationally and in Norway.^{9,10} One such factor was socioeconomic status (SES), which may be increasingly relevant as the number and availability of medical treatments have substantially increased and these come with a large economic cost. Hence, this study aimed to describe the pattern of care among lung cancer patients through identifying factors associated with EP, waiting time to treatment and access to treatment.

Methods

Cancer registry of Norway

Since 1953 it has been mandatory for all hospitals, pathology laboratories and general practitioners in Norway to report all newly diagnosed malignant diseases to the Cancer Registry of Norway (CRN). The CRN also receives death certificates for all patients with a cancer diagnosis from the Cause of Death Registry. Using the personal identification number assigned to all Norwegian citizens since 1964, the CRN is linked monthly with the National Population Register to update vital status (death or emigration), and three times per year with the Norwegian Patient Registry (NPR) to ensure completeness of cancer cases. The quality, comparability, completeness, validity and timeliness of the data in the CRN have been evaluated to be high, with an estimated completeness of 98.8% for all cancer sites together.¹¹

Norwegian patient registry

The NPR is a national health register that holds data on all patient visits to government-funded hospitals in Norway. Reporting to the NPR is mandatory, and its database covers over 99% of all patient visits to specialized healthcare services.¹² These also include data regarding CPPs. From 2008, the NPR data also include personal identification numbers, thus enabling researchers and health authorities to follow patients and their disease trajectories between different sectors and hospitals.

Statistics Norway

The national statistics institute, Statistics Norway, holds individual-level information in areas, such as population, health, finance and education for the entire Norwegian population. Education data have been collected from various national databases since 1970. The tax authorities provide Statistics Norway with personal income data, while are available from 1967, and household type and income, which are available from 2004 onwards.

Data linkage

The study population included all patients with a lung cancer diagnosis (ICD-10 code C33–34) registered at the CRN between 1 January 2015 and 31 December 2016. Information from the NPR was linked to identifying which patients were included in a CPP, the patient's level of co-existing diseases (i.e. comorbidities) and all registered episodes from specialist healthcare. Information about a patient's SES, measured through household income and education, was obtained from Statistics Norway.

Classification of variables

Date of diagnosis was defined as the date of the first clinically or pathologically confirmed diagnosis registered at the CRN. The proportion of diagnoses morphologically verified (either histologically

or cytologically) was 90.5%. Radiologically confirmed diagnoses without morphological confirmation represented 6.1% of lung cancer diagnoses. The remaining diagnoses were confirmed by NPR data and/or radiotherapy data.

Stage

Stage of disease was categorized as localized, regional, metastatic or unknown.¹³ Notifications received at the CRN within the diagnosis period, which was defined as the month of diagnosis plus an additional four months, were used for staging.

Region

Norway consists of four regional health authorities that are responsible for specialized healthcare in their catchment areas: Southern and Eastern Norway, Western Norway, Central Norway and Northern Norway. Regional affiliation was based on a patient's place of residence at the time of diagnosis, independent of where the patient was diagnosed or treated. In practice, the proportion of patients diagnosed outside their own region is small.

Socioeconomic (income, education) and marital status

A patient's SES was measured using individual information about household income and the highest level of education obtained. Household income included wages, self-employment capital income, pension and social benefits earned the year prior to diagnosis. The equalized household income (square root scale), a measure adjusting for the number of people living in the household, was used and categorized as low, intermediate or high, based on the 20th and 80th sex-specific percentiles of household income among patients diagnosed with colorectal, lung, breast or prostate cancer.¹⁴ Education was categorized as low (<10 years of school), intermediate (10–12 years of school) or high (>12 years of school). A patient's marital status was categorized as single (registered as not married, widow, divorced or separated) or married (registered as married or partner).

Comorbidity

Co-existing diseases were measured using a modified version of the Charlson Comorbidity Index (CCI) using diagnostic codes (ICD-10) from hospitalizations within 2 years prior to and including the date of diagnosis.^{15,16} A score was determined for each co-existing disease based on its severity, and the combination of these scores resulted in a modified CCI. The index was grouped into 'no hospital admissions', low (CCI = 0), intermediate (CCI = 1, 2) or high (CCI = 3+).

Cancer patient pathways

A CPP is a set of the maximum days that patients should wait from a hospital referral to the first specialist visit, to a clinical decision and finally to the start of treatment.¹⁷ The patients who are included in a CPP are assigned a cancer pathway coordinator who becomes their primary contact in the health system. In Norway, it has been shown that over 80% of all lung cancer patients were included in a CPP during 2015–2016.¹⁸

Emergency presentation

The NPR collects the urgency of a patient's visit to the hospital as either 'acute' or 'planned'. A cancer diagnosis was defined as an 'EP' if an inpatient attendance with an acute urgency was registered in the NPR in the period 30 days before and 2 days after the date of diagnosis.

Table 1 Patient characteristics and the proportion treated with surgery, curative or palliative radiotherapy or systemic anticancer treatment, among lung cancer patients diagnosed in 2015–16 in Norway

	All	Surgery		Curative radiotherapy		Palliative radiotherapy		Systemic anticancer treatment	
	N (%)	N (%)	% treated	N (%)	% treated	N (%)	% treated	N (%)	% treated
Year of diagnosis									
2015	2861 (50.1)	588 (49.8)	20.6	306 (52.4)	10.7	411 (50.0)	14.4	919 (50.0)	32.1
2016	2852 (49.9)	592 (50.2)	20.8	278 (47.6)	9.7	411 (50.0)	14.4	918 (50.0)	32.2
Age group									
18–49	135 (2.4)	44 (3.7)	32.6	2 (0.3)	1.5	17 (2.1)	12.6	57 (3.1)	42.2
50–59	564 (9.9)	156 (13.2)	27.7	47 (8.0)	8.3	83 (10.1)	14.7	227 (12.4)	40.2
60–69	1808 (31.6)	448 (38.0)	24.8	163 (27.9)	9.0	228 (27.7)	12.6	739 (40.2)	40.9
70–79	2129 (37.3)	486 (41.2)	22.8	233 (39.9)	10.9	298 (36.3)	14.0	690 (37.6)	32.4
80–89	982 (17.2)	46 (3.9)	4.7	137 (23.5)	14.0	181 (22.0)	18.4	123 (6.7)	12.5
90+	95 (1.7)	0 (0.0)	0.0	2 (0.3)	2.1	15 (1.8)	15.8	1 (0.1)	1.1
Sex									
Female	2728 (47.8)	569 (48.2)	20.9	290 (49.7)	10.6	371 (45.1)	13.6	879 (47.8)	32.2
Male	2985 (52.2)	611 (51.8)	20.5	294 (50.3)	9.8	451 (54.9)	15.1	958 (52.2)	32.1
Stage									
Localized	1049 (18.4)	607 (51.4)	57.9	273 (46.7)	26.0	34 (4.1)	3.2	42 (2.3)	4.0
Regional	1611 (28.2)	533 (45.2)	33.1	161 (27.6)	10.0	165 (20.1)	10.2	529 (28.8)	32.8
Metastasis	2300 (40.3)	34 (2.9)	1.5	31 (5.3)	1.3	510 (62.0)	22.2	1048 (57.0)	45.6
Unknown	753 (13.2)	6 (0.5)	0.8	119 (20.4)	15.8	113 (13.7)	15.0	218 (11.9)	29.0
Marital status									
Single	2759 (48.3)	506 (42.9)	18.3	286 (49.0)	10.4	390 (47.4)	14.1	800 (43.5)	29.0
Married	2954 (51.7)	674 (57.1)	22.8	298 (51.0)	10.1	432 (52.6)	14.6	1037 (56.5)	35.1
Income									
Low	894 (15.6)	150 (12.7)	16.8	105 (18.0)	11.7	124 (15.1)	13.9	234 (12.7)	26.2
Intermediate	3908 (68.4)	785 (66.5)	20.1	408 (69.9)	10.4	561 (68.2)	14.4	1235 (67.2)	31.6
High	911 (15.9)	245 (20.8)	26.9	71 (12.2)	7.8	137 (16.7)	15.0	368 (20.0)	40.4
Education									
Low	2357 (41.3)	439 (37.2)	18.6	263 (45.0)	11.2	323 (39.3)	13.7	687 (37.4)	29.1
Intermediate	2682 (46.9)	566 (48.0)	21.1	261 (44.7)	9.7	393 (47.8)	14.7	938 (51.1)	35.0
High	674 (11.8)	175 (14.8)	26.0	60 (10.3)	8.9	106 (12.9)	15.7	212 (11.5)	31.5
Region									
Southern and Eastern Norway	3160 (55.3)	618 (52.4)	19.6	317 (54.3)	10.0	520 (63.3)	16.5	921 (50.1)	29.1
Western Norway	1223 (21.4)	246 (20.8)	20.1	135 (23.1)	11.0	139 (16.9)	11.4	489 (26.6)	40.0
Central Norway	736 (12.9)	187 (15.8)	25.4	67 (11.5)	9.1	69 (8.4)	9.4	238 (13.0)	32.3
Northern Norway	594 (10.4)	129 (10.9)	21.7	65 (11.1)	10.9	94 (11.4)	15.8	189 (10.3)	31.8
Comorbidity									
No admissions	90 (1.6)	28 (2.4)	31.1	9 (1.5)	10.0	15 (1.8)	16.7	24 (1.3)	26.7
0	3104 (54.3)	676 (57.3)	21.8	215 (36.8)	6.9	495 (60.2)	15.9	1136 (61.8)	36.6
1–2	2109 (36.9)	426 (36.1)	20.2	297 (50.9)	14.1	268 (32.6)	12.7	597 (32.5)	28.3
3+	410 (7.2)	50 (4.2)	12.2	63 (10.8)	15.4	44 (5.4)	10.7	80 (4.4)	19.5
Emergency presentation									
No	3549 (62.1)	1046 (88.6)	29.5	475 (81.3)	13.4	391 (47.6)	11.0	1154 (62.8)	32.5
Yes	2164 (37.9)	134 (11.4)	6.2	109 (18.7)	5.0	431 (52.4)	19.9	683 (37.2)	31.6
CPP									
No	1081 (18.9)	70 (5.9)	6.5	53 (9.1)	4.9	149 (18.1)	13.8	256 (13.9)	23.7
Yes	4632 (81.1)	1110 (94.1)	24.0	531 (90.9)	11.5	673 (81.9)	14.5	1581 (86.1)	34.1

First/ever treatment

The first treatment was defined as the first registered occurrence of surgery, curative or palliative radiotherapy or systemic anticancer treatment (SACT) within 1 year of the date of diagnosis. Comprehensive information for surgery and radiotherapy were obtained from the CRN, while information on SACT was obtained from the NPR. Radiotherapy intention was obtained by data collected directly from the radiotherapy centres. For those with unknown intention (11.6%), the total dose received was used to categorize radiotherapy as curative or palliative. Among small cell lung cancer, total doses greater than or equal to 42 Gray (Gy) were categorized as curative, while doses under 42 Gy were categorized as palliative. Among non-small cell lung cancer patients who had and did not have surgery, the cut-offs were 60 Gy and 50 Gy, respectively. SACT included chemotherapy, immunotherapy and any other public hospital-administered anticancer medication. All medical procedure codes with the prefix WBOC and WML000 were included. Every treatment referred to all the cancer-related treatments a patient received within a year of diagnosis.

Statistical analysis

Pearson's chi-squared test was used to assess differences between the categories of the explanatory variables and a dichotomous variable indicating whether a patient was diagnosed due to an EP. Six multivariable logistic regressions were performed, with EP, surgery, curative and palliative radiotherapy, SACT and any treatment as the dependent variable, respectively.¹⁹ These were all adjusted for case-mix, i.e. year of diagnosis, age group and stage at diagnosis, sex, region, income group, marital status and comorbidity index. Education was not adjusted for as the regressions would have given the marginal effects of income and education. The analysis of receiving treatment (surgery, curative and palliative radiotherapy, SACT, and any) was additionally adjusted for CPP-status. Multivariable quantile (median) regressions of waiting time from date of diagnosis to surgery, curative and palliative radiotherapy, SACT, and any treatment were performed individually for all patients adjusted for case-mix and CPP-status. The regression analyzing any treatment, has additionally been adjusted for treatment modality. Wald test was used to assess the significance of the different explanatory variables.

Table 2 Univariable and multivariable analysis of having an emergency presentation among lung cancer patients diagnosed in 2015–16 in Norway

	Univariable Odds ratio [95% CI]	Multivariable Odds ratio [95% CI]
Year of diagnosis		
2015	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
2016	0.87 [0.78, 0.97]	0.84 [0.75, 0.94]
P-value	0.012	0.003
Age group		
18–49	0.82 [0.55, 1.22]	0.84 [0.55, 1.29]
50–59	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
60–69	0.93 [0.77, 1.14]	0.91 [0.73, 1.12]
70–79	1.02 [0.84, 1.23]	1.01 [0.81, 1.24]
80–89	1.51 [1.22, 1.87]	1.34 [1.06, 1.70]
90+	1.95 [1.26, 3.01]	1.71 [1.06, 2.75]
P-value	<0.001	<0.001
Sex		
Female	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Male	1.03 [0.92, 1.14]	1.01 [0.90, 1.13]
P-value	0.649	0.895
Stage		
Localized	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Regional	2.32 [1.88, 2.87]	2.40 [1.94, 2.97]
Metastasis	8.49 [6.97, 10.34]	9.02 [7.38, 11.03]
Unknown	4.70 [3.73, 5.91]	4.52 [3.57, 5.71]
P-value	<0.001	<0.001
Marital status		
Single	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Married	0.80 [0.72, 0.89]	0.83 [0.74, 0.94]
P-value	<0.001	0.003
Income		
Low	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Intermediate	0.89 [0.77, 1.04]	0.88 [0.75, 1.04]
High	0.74 [0.61, 0.90]	0.78 [0.63, 0.97]
P-value	0.009	0.079
Region		
Southern and Eastern Norway	1.07 [1.02, 1.12]	1.05 [1.00, 1.11]
Western Norway	0.98 [0.88, 1.08]	1.00 [0.89, 1.11]
Central Norway	0.93 [0.81, 1.08]	0.91 [0.78, 1.06]
Northern Norway	0.81 [0.69, 0.96]	0.86 [0.72, 1.03]
P-value	0.023	0.138
Comorbidity		
No admissions	0.12 [0.05, 0.28]	0.11 [0.05, 0.25]
0	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
1–2	1.05 [0.94, 1.17]	1.21 [1.07, 1.38]
3+	1.53 [1.24, 1.88]	1.79 [1.42, 2.25]
P-value	<0.001	<0.001

P-values < 0.05 were considered significant. The statistical program Stata 16.1 was used for all analyses.²⁰

Results

Study population

Between 1 January 2015 and 31 December 2016, 6154 patients were identified with a primary lung cancer diagnosis. Patients registered based on either autopsy ($n=22$) or death certificate alone ($n=143$) were excluded. Patients under 18 years of age ($n=2$), unknown place of residence ($n=88$), unknown education ($n=50$) and unknown type of household ($n=62$) were also excluded from the analyses. In addition, patients with a registered negative time between diagnosis and first treatment were excluded ($n=74$). As a result, 5713 cases were eligible for this study.

Patient characteristics

The proportion of men were 52.3% and the median age at diagnosis was 71 [IQR: 65–77] years [71 (IQR: 65–78) years for men, 70 (IQR: 64–77) years for women]. The proportion of lung cancer patients with localized, regional, metastatic and unknown diseases was 18.4,

28.2, 40.3 and 13.3, respectively (table 1). A total of 37.9% of all patients were diagnosed at EPs (table 1, Supplementary table S1). The first treatment was surgery for 20.7%, radiotherapy for 24.6% (curative radiotherapy for 10.2%, palliative radiotherapy for 14.4%), and SACT for 32.2% of all patients. The proportion of patients ever treated with surgery, radiotherapy (curative and palliative) and SACT were 21.1, 46.2 (17.9 and 28.3%) and 45.3%, respectively (Supplementary figure S1). Within 1 year of diagnosis, 1290 (22.6%) patients did not receive any form of treatment, and of these, 1064 patients (82.5%) died, and 226 patients (17.5%) (median age 78 years, IQI: [69–85]) were alive, but remained untreated.

Emergency presentation

Older age and higher level of comorbidity were significantly associated with increasing odds of being diagnosed through an EP ($P < 0.001$). Patients with regional (OR = 2.40, 95% CI: 1.94, 2.97) or metastatic (OR = 9.07, 95% CI: 7.38, 11.03) disease had over a 2- and 9-fold increased odds, respectively, of being diagnosed following an emergency visit compared to patients with localized disease (table 2). High-income patients had a 22% reduced odds of an EP (OR = 0.78, 95% CI: 0.63, 0.97) opposed to those with a low income. Patients who were married had a 17% reduced odds of an EP (OR = 0.83, 95% CI: 0.74, 0.94) compared with those who were single.

Waiting time to treatment

Compared to patients with localized disease, patients with regional disease had on median a 4.7-day (95% CI: –9.4, 0.0) shorter waiting time from diagnosis to curative radiotherapy (table 3, univariable results in Supplementary table S2). The waiting times to palliative radiotherapy and SACT were 18.5 days longer (95% CI: 11.3, 25.6) and 10 days longer (95% CI: 4.3, 15.7), respectively, among the small groups of patients with localized disease who received these treatment modalities as their first treatment compared to those with metastatic disease (table 3). Patients with an EP had a 7.2- and 4.6-day shorter median waiting time to palliative radiotherapy and SACT, respectively, compared to those with a non-EP. Being included in a CPP was associated with an increased median waiting time to curative radiotherapy of 7 days (95% CI: 0.7, 13.3). Compared with time to surgery, the waiting times to curative radiotherapy and SACT were 12.1 days longer (95% CI: 10.2, 14.0) and 5.6 days shorter (95% CI: –7.3, –3.9), respectively.

Likelihood of different first treatment modalities

The odds of receiving surgery and SACT decreased with increasing age ($P < 0.001$) (table 4, univariable results in Supplementary table S3). In contrast, patients aged 80–89 years had a 75% (OR = 1.75, 95% CI: 1.19, 2.57) and 46% (OR = 1.46, 95% CI: 1.08, 1.99) increased odds, respectively, of receiving curative and palliative radiotherapy than patients aged 50–59 years. Patients with regional or metastatic disease had a 35% (OR = 0.65, 95% CI: 0.49, 0.86) and 67% (OR = 0.33, 95% CI: 0.25, 0.43), respectively, reduced odds of any treatment compared to patients with localized disease. Patients with a high income had a 63% (OR = 1.63, 95% CI: 1.20, 2.21) and 40% (OR = 1.40, 95% CI: 1.12, 1.76) increased odds of receiving surgery and SACT, respectively. Compared with the national mean, patients living in Central Norway had a 66% increased odds (OR = 1.66, 95% CI: 1.35, 2.05) of surgery, and a 37% reduced odds (OR = 0.63, 95% CI: 0.50, 0.79) of palliative radiotherapy. Patients from Western Norway had a 58% increased odds (OR = 1.58, 95% CI: 1.41, 1.78) of SACT and a 22% (OR = 0.78, 95% CI: 0.66, 0.91) decreased odds of palliative radiotherapy (table 4). Those patients who were included in a CPP experienced over a 3-fold increased odds of any form of treatment (OR = 3.35, 95% CI: 2.83, 3.98).

Table 3 Multivariable analyses of median time from diagnosis to first treatment (surgery, curative or palliative radiotherapy, systemic anticancer treatment or any treatment) among lung cancer patients diagnosed in 2015–16 in Norway

	Surgery Coeff [95% CI]	Curative radiotherapy Coeff [95% CI]	Palliative radiotherapy Coeff [95% CI]	Systemic anticancer treatment Coeff [95% CI]	Any Coeff [95% CI]
Year of diagnosis					
2015	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
2016	-0.5 [-2.6, 1.6]	-4.3 [-8.0, -0.7]	-0.1 [-2.9, 2.7]	1.6 [-0.1, 3.3]	-0.5 [-1.6, 0.6]
P-value	0.662	0.020	0.949	0.065	0.351
Age group					
18–49	2.3 [-3.8, 8.4]	-14.0 [-44.3, 16.3]	0.7 [-9.7, 11.1]	-2.9 [-8.3, 2.5]	-1.0 [-4.6, 2.7]
50–59	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
60–69	0.5 [-2.9, 3.8]	-1.0 [-8.0, 6.0]	1.4 [-3.7, 6.5]	0.9 [-1.9, 3.6]	0.2 [-1.6, 2.0]
70–79	1.8 [-1.6, 5.2]	3.7 [-3.2, 10.6]	0.5 [-4.6, 5.6]	2.1 [-0.7, 4.9]	1.7 [-0.2, 3.5]
80–89	0.6 [-5.4, 6.6]	1.0 [-6.4, 8.4]	4.9 [-0.6, 10.4]	0.1 [-4.0, 4.2]	1.6 [-0.7, 4.0]
90+	-	14.3 [-16.7, 45.3]	1.3 [-10.0, 12.5]	12.1 [-24.0, 48.3]	5.9 [-2.7, 14.6]
P-value	0.740	0.255	0.282	0.314	0.117
Sex					
Female	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
Male	1.0 [-1.1, 3.1]	0.7 [-2.9, 4.3]	-1.7 [-4.6, 1.1]	-0.4 [-2.2, 1.3]	-0.3 [-1.4, 0.7]
P-value	0.360	0.716	0.236	0.607	0.532
Stage					
Localized	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	18.5 [11.3, 25.6]	10.0 [4.3, 15.7]	0.0 [0.0, 0.0]
Regional	2.5 [0.3, 4.6]	-4.7 [-9.4, 0.0]	1.7 [-2.0, 5.4]	1.2 [-0.8, 3.2]	0.4 [-1.2, 2.0]
Metastasis	7.9 [1.6, 14.1]	10.7 [2.4, 19.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	-1.8 [-3.8, 0.2]
Unknown	79.7 [65.1, 94.3]	1.7 [-3.1, 6.4]	2.7 [-1.5, 6.9]	1.9 [-0.9, 4.6]	1.3 [-1.0, 3.6]
P-value	<0.001	0.002	<0.001	0.004	0.005
Marital status					
Single	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
Married	0.3 [-1.9, 2.4]	-2.3 [-6.0, 1.3]	0.7 [-2.1, 3.6]	-0.7 [-2.4, 1.0]	-0.3 [-1.4, 0.8]
P-value	0.808	0.206	0.617	0.428	0.581
Income					
Low	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
Intermediate	-2.3 [-5.5, 0.9]	-1.0 [-5.7, 3.7]	-0.5 [-4.5, 3.4]	2.0 [-0.5, 4.6]	-0.0 [-1.6, 1.6]
High	-2.5 [-6.3, 1.3]	-2.0 [-8.5, 4.5]	-2.1 [-7.2, 3.0]	1.6 [-1.5, 4.7]	-0.9 [-2.9, 1.0]
P-value	0.352	0.832	0.691	0.30	0.460
Region					
Southern and Eastern Norway	-0.0 [-1.6, 1.6]	1.8 [-1.0, 4.5]	4.8 [2.6, 7.0]	3.3 [1.9, 4.6]	2.8 [2.0, 3.7]
Western Norway	1.7 [-0.3, 3.7]	-0.3 [-3.7, 3.2]	-3.5 [-6.5, -0.5]	-1.2 [-2.7, 0.3]	-1.5 [-2.5, -0.5]
Central Norway	-0.6 [-2.8, 1.7]	3.1 [-1.2, 7.4]	0.6 [-3.2, 4.4]	-1.3 [-3.3, 0.6]	-0.2 [-1.5, 1.0]
Northern Norway	-1.1 [-3.7, 1.5]	-4.6 [-8.9, -0.3]	-1.9 [-5.3, 1.6]	-0.7 [-2.8, 1.4]	-1.1 [-2.4, 0.2]
P-value	0.432	0.129	<0.001	<0.001	<0.001
Emergency presentation					
0	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
1	2.4 [-0.9, 5.7]	1.7 [-3.0, 6.3]	-7.2 [-10.1, -4.3]	-4.6 [-6.4, -2.7]	-3.6 [-4.9, -2.3]
P-value	0.151	0.484	<0.001	<0.001	<0.001
Comorbidity					
No admissions	5.7 [-1.2, 12.5]	5.7 [-9.1, 20.5]	4.8 [-5.6, 15.3]	19.3 [11.8, 26.7]	8.7 [4.6, 12.9]
0	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
1–2	0.7 [-1.5, 3.0]	-1.7 [-5.6, 2.2]	2.8 [-0.3, 5.9]	-1.3 [-3.2, 0.6]	0.6 [-0.6, 1.8]
3+	0.3 [-5.0, 5.6]	0.3 [-5.9, 6.5]	3.9 [-2.4, 10.2]	-0.1 [-4.3, 4.1]	1.4 [-1.1, 3.9]
P-value	0.422	0.641	0.206	<0.001	<0.001
CPP					
0	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]
1	1.6 [-2.8, 6.0]	7.0 [0.7, 13.3]	1.5 [-2.2, 5.3]	-1.8 [-4.3, 0.7]	0.7 [-1.0, 2.4]
P-value	0.478	0.030	0.417	0.157	0.435
Treatment					
Surgery					0.0 [0.0, 0.0]
Curative radiotherapy					12.1 [10.2, 14.0]
Palliative radiotherapy					0.8 [-1.3, 2.9]
Chemotherapy					-5.6 [-7.3, -3.9]
P-value					<0.001

Conclusions

The likelihood of a patient experiencing a hospital emergency visit leading to a lung cancer diagnosis increased with increasing age, more advanced stage, and more comorbidities, while having a high income was associated with a reduced likelihood. Shorter waiting time to curative radiotherapy was seen among patients with a regional disease and a shorter waiting time to any treatment was also observed among those who had an EP prior to diagnosis. In addition, patients treated with curative radiotherapy had a longer waiting time than patients treated with surgery. Access to surgery and SACT were associated with the patient's income level.

The results around EP in this study are well supported in previous literature. Patients with lung cancer can present with symptoms such as coughing, shortness of breath, blood in spit, pain in chest or between shoulder blades, fatigue, reduced appetite and weight loss,^{21,22} and the odds of experiencing symptoms are higher among patients with more advanced stage.²³ A report from Ireland showed that 76.8% of cancer patients were diagnosed in stage III/IV at an emergency visit compared to 37.9% when the visit was elective.²⁴ Hence, it seems reasonable that patients with more advanced stages at diagnosis have more emergency visits. A previous study also showed that the likelihood of hospital admissions increased with increasing age.¹⁶ While the relationship between smoking and

Table 4 Multivariable analyses for being treated with surgery, curative or palliative radiotherapy, systemic anticancer treatment or any treatment among lung cancer patients diagnosed in 2015–16 in Norway

	Surgery Coeff [95% CI]	Curative radiotherapy Odds ratio [95% CI]	Palliative radiotherapy Odds ratio [95% CI]	Systemic anticancer treatment Odds ratio [95% CI]	Any Odds ratio [95% CI]
Year of diagnosis					
2015	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
2016	0.97 [0.82, 1.14]	0.86 [0.72, 1.04]	0.98 [0.84, 1.14]	0.94 [0.83, 1.07]	0.82 [0.71, 0.96]
<i>P</i> -value	0.696	0.119	0.781	0.376	0.013
Age group					
18–49	1.45 [0.83, 2.54]	0.17 [0.04, 0.74]	0.83 [0.47, 1.47]	1.01 [0.67, 1.54]	0.67 [0.34, 1.31]
50–59	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
60–69	0.76 [0.58, 1.02]	0.98 [0.68, 1.41]	0.86 [0.65, 1.14]	1.08 [0.87, 1.34]	0.68 [0.48, 0.96]
70–79	0.66 [0.50, 0.88]	1.08 [0.76, 1.55]	1.07 [0.81, 1.42]	0.79 [0.64, 0.98]	0.44 [0.31, 0.61]
80–89	0.10 [0.07, 0.15]	1.75 [1.19, 2.57]	1.46 [1.08, 1.99]	0.22 [0.17, 0.29]	0.12 [0.09, 0.17]
90+	1.00 [1.00, 1.00]	0.27 [0.06, 1.18]	1.22 [0.65, 2.27]	0.02 [0.00, 0.12]	0.03 [0.01, 0.05]
<i>P</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001
Sex					
Female	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Male	1.15 [0.97, 1.36]	0.91 [0.75, 1.10]	1.12 [0.96, 1.31]	0.94 [0.83, 1.06]	1.02 [0.87, 1.19]
<i>P</i> -value	0.119	0.317	0.146	0.316	0.815
Stage					
Localized	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Regional	0.30 [0.25, 0.36]	0.36 [0.29, 0.44]	3.32 [2.27, 4.85]	13.24 [9.51, 18.42]	0.65 [0.49, 0.86]
Metastasis	0.01 [0.01, 0.01]	0.05 [0.04, 0.08]	7.55 [5.24, 10.87]	30.87 [22.17, 43.00]	0.33 [0.25, 0.43]
Unknown	0.01 [0.00, 0.01]	0.66 [0.51, 0.85]	4.77 [3.19, 7.14]	16.44 [11.50, 23.51]	0.25 [0.19, 0.34]
<i>P</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001
Marital status					
Single	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Married	1.25 [1.05, 1.49]	0.98 [0.81, 1.19]	1.10 [0.94, 1.28]	1.25 [1.10, 1.42]	1.75 [1.50, 2.05]
<i>P</i> -value	0.010	0.870	0.253	<0.001	<0.001
Income					
Low	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Intermediate	1.33 [1.04, 1.71]	0.84 [0.65, 1.07]	1.08 [0.87, 1.35]	1.31 [1.09, 1.57]	1.63 [1.34, 1.98]
High	1.63 [1.20, 2.21]	0.78 [0.55, 1.11]	1.19 [0.90, 1.58]	1.40 [1.12, 1.76]	2.82 [2.08, 3.83]
<i>P</i> -value	0.008	0.299	0.478	0.007	<0.001
Region					
Southern and Eastern Norway	0.95 [0.88, 1.02]	1.03 [0.95, 1.12]	1.18 [1.10, 1.27]	0.82 [0.78, 0.87]	0.86 [0.81, 0.92]
Western Norway	0.87 [0.74, 1.02]	1.07 [0.90, 1.27]	0.78 [0.66, 0.91]	1.58 [1.41, 1.78]	1.46 [1.25, 1.70]
Central Norway	1.66 [1.35, 2.05]	0.90 [0.70, 1.15]	0.63 [0.50, 0.79]	1.02 [0.87, 1.19]	0.96 [0.79, 1.17]
Northern Norway	0.96 [0.76, 1.22]	0.83 [0.64, 1.08]	1.23 [0.99, 1.53]	1.08 [0.90, 1.30]	1.06 [0.85, 1.33]
<i>P</i> -value	<0.001	0.383	<0.001	<0.001	<0.001
Emergency presentation					
0	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
1	0.42 [0.33, 0.52]	0.61 [0.48, 0.77]	1.50 [1.28, 1.77]	0.66 [0.57, 0.75]	0.41 [0.35, 0.48]
<i>P</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001
Comorbidity					
No admissions	1.35 [0.70, 2.59]	1.03 [0.49, 2.15]	1.29 [0.72, 2.33]	0.64 [0.38, 1.08]	0.95 [0.48, 1.87]
0	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
1–2	0.70 [0.59, 0.84]	1.84 [1.51, 2.25]	0.85 [0.72, 1.00]	0.86 [0.75, 0.99]	0.73 [0.62, 0.86]
3+	0.39 [0.26, 0.56]	2.25 [1.62, 3.14]	0.66 [0.47, 0.93]	0.59 [0.45, 0.78]	0.37 [0.28, 0.48]
<i>P</i> -value	<0.001	<0.001	0.029	<0.001	<0.001
CPP					
0	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
1	2.07 [1.51, 2.84]	2.24 [1.63, 3.08]	1.55 [1.26, 1.90]	1.64 [1.38, 1.95]	3.35 [2.83, 3.98]
<i>P</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001

lung cancer has been well-known since the 1950s, and the proportion of daily smokers in Norway has significantly decreased to less than 10%, data from the Norwegian Institute of Public Health show that 24% among people with low education and 5% for those with high education are smokers.²⁵ In addition, patients with high SES are known to have a more active and healthy lifestyle than low-SES patients. Therefore, the results appear feasible since high-income patients smokeless, leading to a lower proportion of patients who may be affected by smoking-related symptoms, which in turn would reduce the likelihood of an EP.

It appears as though patients with a more advanced disease were more quickly prioritized for palliative radiotherapy and SACT to reduce pain and avoid serious complications such as paralysis, while patients with a localized disease may have had less urgency and had more time to undergo additional examinations e.g. PET-CT, cardiac evaluation, lung physiology, in order to determine appropriate

treatment.²¹ These results were similar to a previous study that showed that there was a shorter time to first treatment among stages III and IV lung cancer patients, and for those undergoing SACT compared with surgery.²⁶

Although CPP guidelines advise the same number of days from start of CPP to radiotherapy and surgery, our results show the time from diagnosis to curative radiotherapy was 12 days longer than the time to surgery. Patients receiving curative radiotherapy may have undergone clinical examinations which deemed them surgically inoperable. The additional time taken to decide, plan and start curative radiotherapy may contribute to the longer waiting time. This study also found that patients included in a CPP had a longer time to start of curative radiotherapy compared with those not included in a CPP. This result is consistent with a recent Norwegian study that showed that the odds of not being included in a CPP were significantly increased among older patients and patients with a

regional or metastatic disease.¹⁸ Hence, the shorter waiting time among non-CPP patients is likely to reflect more advanced disease and possibly more medically acute conditions requiring a quicker diagnosis and an earlier start of curative radiotherapy.

Supporting the results of earlier studies, this study showed that patients with a high income in a country with universal healthcare had over a 60% and 40% increased odds of receiving surgery and SACT, respectively.^{9,26–28} Some of the observed SES effects in SACT may be explained by the patient's smoking status, since the risk of infection is significant for patients receiving chemotherapy, and especially large among patients with smoking-related lung cancer. In addition, these results may suggest that higher income patients are more active in their treatment decisions than lower income patients. Other factors that may explain some of the observed SES effects are performance status and residual confounding in comorbidity. However, a recent study that adjusted for performance status still showed significant SES effects on access to treatment.²⁷ Therefore, the effect of these factors may not alter the overall conclusions of the SES results.

Regional differences in waiting time to treatment and type of treatment provided were also observed. Despite having a common national guideline for diagnosis and treatment of lung cancer, systemic variation may include differences in local traditions in treatment choices, access to treatment equipment and capacity, and level of knowledge of new treatment options.²⁹ The latest report from the Norwegian Lung Cancer Registry showed variation in proportion treated with surgery and curative radiotherapy between health trusts and between years.³⁰

This study had some limitations. First, the symptomatology of patients would have been helpful in separating those eligible to start treatment immediately after diagnosis from those who should receive palliative treatment once symptoms develop, but unfortunately this was unavailable. Second, information about a patient's smoking status would have enabled a better estimate the effect of income on access to treatment. However, this information is not available at an individual-level. Third, SACT information in this study do not provide details about treatment provided outside of the hospital setting (e.g. tyrosine kinase inhibitors). In order to add this level of detail, data linkage with the Prescription Registry would be required. This may bias our results as the number of SACTs in this study may be an underestimation. And finally, the level of a patient's comorbidity may be underestimated as some diseases are managed by the general practitioner only and not by the hospital.¹⁶ Despite these limitations, this study has several strengths. First, the study utilized comprehensive treatment information regarding all three treatment modalities: surgery, radiotherapy, and SACT. The study was also able to use individual-specific information about SES measures such as income and education. And finally, the study uses population-based design and national, comprehensive, high-quality data to generate results that are widely representative.

This study showed that patients who were older, had advanced disease or increased comorbidities were more likely to have an EP and less likely to receive treatment. While income did not affect the waiting time for lung cancer treatment in Norway, it did affect the likelihood of receiving surgery and SACT. Therefore, public health awareness campaigns should aim to improve the health literacy throughout the Norwegian population to encourage earlier hospital attendance, diagnosis and possibly treatment.

Funding

This study was funded by the Norwegian Cancer Society through Open Call 2016 (reference number: 182809). The funders did not have any influence on any aspects of the study (i.e. design, data collection, analyses, interpretation or writing the manuscript).

Conflicts of interest: None declared.

Key points

- 37.9% of all lung cancer patients had an emergency presentation within a month prior to diagnosis
- High-income patients were less likely to present at emergency
- No apparent differences in waiting times to treatment across socioeconomic groups
- High income increased the odds of surgery and systemic anticancer treatment
- Public health awareness campaigns should aim to improve the health literacy throughout the Norwegian population to encourage earlier hospital attendance, diagnosis and possibly treatment.

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The European Journal of Public Health, Vol. 31, No. 5, 974–979

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 doi:10.1093/eurpub/ckab129 Advance Access published on 4 August 2021

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Development of medicines consumption in Portugal before and during the financial crisis

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Background: In May 2011, the Portuguese Government signed a Memorandum of Understanding with the European Commission, the European Central Bank and the International Monetary Fund, including detailed measures to control health costs, allowing Portugal to receive a financial rescue package. This study aims to investigate medicines utilization in the outpatient sector during Troika's financial rescue. **Methods:** Using Defined Daily Dose per million inhabitants per year as a measurement unit, we compared medicines utilization with other relevant indicators over 5-year intervals for a total period of 20 years, based on a built-in inventory of national outpatient drug use using the Intercontinental Medical Statistics Health and Anatomical Therapeutic Chemical index of the World Health Organization databases. The calculation was made on the basis of both compound and year-on-year growth rates. **Results:** With the exception of the interval 2009–11, an absolute rise in consumption was observed over the 20-year period. The downturn occurred prior to financial rescue, when expenditure management mechanisms were already in place, and coincided with an increase in out-of-pocket spending. With the decline of cost for patients, the access trend returned to being positive, but at a slower pace. **Conclusion:** The rise in out-of-pocket and austerity measures may have led to decreased access to medicines. The findings of this study suggest that this impact was influenced by public cost-saving policies implemented even before the financial rescue. The results show that price reduction attenuated the repercussion of the measures.

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Introduction

The Portuguese constitutional law establishes a universal public health service, the Portuguese National Health Service (PNHS).¹ In addition, other health care sub-systems (for specific sectors or professions) and private voluntary insurance coexist with the PNHS.²

The PNHS reimburses outpatient prescription-only medicines at different levels (level A, 90%; level B, 69%; level C, 37%; and level D, 15%). Additional co-payments are available for pensioners with low income.^{2,3}

The 2009 financial crisis, along with chronic budgetary deficits, led to increased market pressure on the Portuguese debt.