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Factors behind favorable long-term lung cancer survival in Norway compared to Denmark: a retrospective cohort study

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ABSTRACT

Background: Long-term survival of patients with non-small cell lung cancer (NSCLC) is considerably higher in Norway compared to Denmark, even though diagnostic work-up, treatment, and follow-up are comparable. We aim to explore factors behind favorable long-term survival for lung cancer patients in Norway compared to Denmark.

Method: A retrospective cohort study of patients with NSCLC diagnosed between 2014 and 2016. From the Danish Lung Cancer Registry, 1000 patients were randomly selected, and 974 patients were included. From the Norwegian Vestfold Hospital Trust, 220 patients were randomly selected, and 218 were included. Data from medical records were obtained for all patients. The Danish and Norwegian cohorts were compared using the Pearson chi squared test and multivariate logistic regression analysis.

Results: The two cohorts were comparable in terms of age, sex, and smoking history. However, the Danish patients had a higher number of pack-years (43.5 vs 34.5 $p < 0.001$) and more comorbidities. The Norwegian patients had less advanced disease stage ($p < 0.001$), and a larger proportion was treated with curative intent (90 (41.3%) vs 343 (35.2%), $p = 0.063$). One-year survival was similar, but the 5-year survival was superior in the Norwegian cohort (58 (26.6%) vs 177 (18.2%), $p = 0.005$). In a multivariate logistic regression model, adjusted for sex, smoking history, performance status, TNM stage and comorbidity, the odds ratio of being a five-year survivor in Norway was 1.81 (95% CI: 1.11–2.94) compared to Denmark.

Conclusions: We found a higher proportion of Norwegian patients diagnosed at potential curable stage and fewer heavy smokers compared to Danish patients. This could contribute to the superior long-term survival found in Norwegian NSCLC patients.

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Lung cancer; Scandinavian and Nordic countries; Epidemiology; Survival; Smoking; Treatment

Introduction

Lung cancer is the main cause of cancer-related deaths in Denmark and Norway as well as in the rest of the world [1,2]. Since 2008, Danish lung cancer patients have been diagnosed and staged through fast-track cancer pathways and received treatment in high-volume centers with minimal delay. Furthermore, after therapy, Danish lung cancer patients are monitored with short-interval CT scans as part of the most comprehensive follow-up program among the Nordic countries [3]. Nevertheless, the survival rate of Danish lung cancer patients remains lower than in Norway [4]. Common milestones when assessing cancer-related outcomes are 1- and 5-year overall survival. The Norwegian National Quality Registry of Lung Cancer (NLCR) annual report provides relative survival for Norwegian lung cancer patients with 1- and 5-year survival of 59.4% and 30%, respectively, in 2022 [5], whereas according to the Danish Lung Cancer Registry (DLCR) annual report, the overall 1- and 5-year survival for Danish lung cancer patients was 57.3% and 24%, respectively, in 2022 [6]. However, the use of different survival measures, relative in Norway versus overall in Denmark, may bias direct comparison [7]. The latest results from the Association of The Nordic Cancer Registries are from 2017 to 2021; they report just two percent points better 5-year relative survival in Norway compared to Denmark [1]. The cause(s) for the superior long-term survival in Norway is currently unknown.

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The health-care systems in Denmark and Norway are tax-funded and provide equal access to healthcare for all citizens regardless of social status or income. Patients with suspicion of lung cancer are referred to the nearest pulmonary department at a university hospital or local community hospital for diagnostic procedures and evaluation. In Denmark, there are 13 departments of pulmonology involved in lung cancer evaluation, 4 departments of cardiothoracic surgery, and 12 departments of oncology treating lung cancer in Denmark. Fast-track pathways for lung cancer were introduced in 2008. The Danish Health Authority publishes guidelines for fast-track lung cancer work-up and treatment [8]. The Danish Lung Cancer Group provides updated detailed guidelines for lung cancer work-up and treatment. In Norway, there are 19 departments of pulmonology involved in lung cancer evaluation, 8 departments of thoracic surgery and systemic treatment are given by either oncologists or pulmonologists in 19 health trust centers in Norway. The Norwegian Directorate of Health publishes guidelines for lung cancer treatment, which are assessed yearly and updated when deemed necessary [9]. The authors of the guidelines are representatives from the clinical community. In 2015, the Norwegian Directory of Health introduced fast-track pathway for lung cancer [3]. Furthermore, Denmark and Norway evaluate lung cancer patients in similar high-quality multidisciplinary team meetings [10].

Previous studies have compared survival trends from registries in a Nordic setting [11]. The national lung cancer registries of both Norway and Denmark have a high degree of completeness and cover 96% and 95% of incident lung cancer patients, respectively [12,13]. Data concerning tobacco use and comorbidities are included in the DLCR while this is not registered in the NLCR, making patient comparisons based on registry data difficult and potentially biased [7,14–17].

In this study, we aim to compare Danish and Norwegian cohorts of non-small cell lung cancer (NSCLC) patients in terms of characteristics at the time of diagnosis (age, gender, smoking, alcohol consumption, burden of comorbidity, and histopathology) as well as diagnostic procedures and treatment. Our hypothesis is that lung cancer patients in Norway have a better overall health status with regard to comorbidities, performance status, smoking, etc., at the time of diagnosis, which may explain their higher 5-year survival rate relative to Danish lung cancer patients. However, we also aim to identify potential differences in clinical practice, which could contribute to differences in outcome.

Method

Study method

This study is a comparative retrospective cohort study between a Danish and a Norwegian cohort of lung cancer patients. The Danish cohort was a nationwide sample of all patients diagnosed with NSCLC between 1 January 2014 and 31 December 2016 in the DLCR. A sample of 1000 patients were selected at random by STATA®v18.0. Electronic medical records for the included patients were reviewed across the country by utilizing the unique personal identification number provided to all Danish Citizens at birth or immigration [18]. Data collection was performed from June 2022 through March 2023, by trained clinical physicians. Results from this cohort have previously been used to validate the Danish Lung Cancer Registry [19].

The Norwegian cohort was a single-center cohort from the Vestfold Hospital Trust in Tønsberg, Norway. Of the patients diagnosed with lung cancer in the hospital between 1 January 2014 and 31 December 2016, 220 lung cancer patients, excluding small cell lung cancer, were randomly selected for the study. Data were obtained from electronic medical records in July 2023. Patients who were alive at the time of data collection were contacted by mail with information about the study and the possibility of not participating. We expected approximately 40 patients to be alive and that half of them would withdraw consent.

For both cohorts, we collected data on patient-specific information (including age, sex, civil status, height, weight), comorbidity (including smoking history, alcohol consumption, and Charlson Comorbidity Index (CCI) [20]), information on lung cancer diagnosis (including date, symptoms at diagnosis, diagnostic work-up, histology and stage), information on treatment (surgical, radiation, etc., and treatment intent), information on vital status five years after diagnosis and cause of death.

Statistical analysis

With a sample size of 1,000 Danish patients and 200 Norwegian patients, we have with a two-sided significance level of 5% a power of at least 80% for detecting a difference of 10% in prevalence of active smoking at time of diagnosis (assuming a prevalence of between 10–35% for Danish patients and 5–25% for Norwegian patients). Likewise for difference in proportion of patients with a comorbidity index of 3 or more. Continuous data with normal distribution were compared by Student's t-test. Categorical variables were compared by Pearson chi squared test. Associations between countries and study variables were analyzed by logistic regression, adjusted for TNM stage,

sex, CCI, Eastern Cooperative Oncology Group performance status (ECOG PS), and smoking status (never/ever). Kaplan–Meier analyses and log-rank tests were conducted to evaluate overall survival in both cohorts. Missing data were handled using the missing indicator method [21]. In brief, for categorical variables, missing values were grouped into a 'missing' category in order to retain the full dataset for analyses. The results are reported as odds ratios (OR) with 95% confidence intervals (95% CI). A p-value of < 0.05 was considered significant. All analysis were performed by using STATA® V.18.0.

Results

Danish and Norwegian cohorts

Figure 1 presents the flowchart of the Danish and Norwegian NSCLC cohorts. In the DLCR, 11.575 patients were registered with NSCLC in the study period. The 1000 patients-sample thus constituted 9% of the underlying cohort. Of the random sample, all 1000 medical records were retrieved and reviewed. Sixteen were duplicates, three were lost to follow-up due to emigration after diagnosis (0.3%), one was diagnosed in a following year, and six were misclassified. Consequently, of the 1000 patients in the sample, 974 were included in the following analysis.

In the Vestfold Hospital Trust, 489 patients were diagnosed with lung cancer during the study period, and $n = 220$ NSCLC patients (45%) were randomly selected. Thirty-four of the patients (15.5%) were still alive at the time of data collection and were contacted by mail. Of the selected patients, one emigrated after lung cancer diagnosis and one patient did not want to participate in the study (0.9%). Ultimately, data on 218 patients were included in the following analysis. Both cohorts were similar to the underlying nationwide register-based cohorts with regards to age, gender distribution, treatment intent, and survival (Supplementary Table A). During the period 2014 to 2016, the NLCR used the Surveillance, Epidemiology, and End Results (SEER) staging and not the Tumor, Node and Metastasis (TNM) classification used in the DLCR.

Patient characteristics

Patient, tumor, and treatment characteristics are presented in Table 1. The Norwegian and Danish NSCLC patients were similar in age, gender distribution, forced expiratory volume in 1 second (FEV1), and smoking history. The mean number of pack-years (20 cigarettes per day for one year) was significantly higher for Danish patients, 43.5 (95% CI: 42.0–45.0) compared to 34.5 (95% CI: 31.3–37.7) and the Danish patients had higher consumption of alcohol ($p < 0.001$). The Norwegian cohort had a larger proportion of patients diagnosed with stage I disease compared to the Danish (30.7% vs. 17.8%, $p < 0.001$). Symptoms at time of diagnosis (first clinical visit) were different. The Danish NSCLC patients had a higher burden of symptoms, especially in terms of systemic symptoms (weight-loss, fatigue, fever), whereas a larger proportion of Norwegian patients had no symptoms at time of diagnosis. In the Danish cohort, a larger proportion of patients with a CCI score of 3+ compared to the Norwegian cohort (22.7%vs. 7.8%, $p < 0.001$).

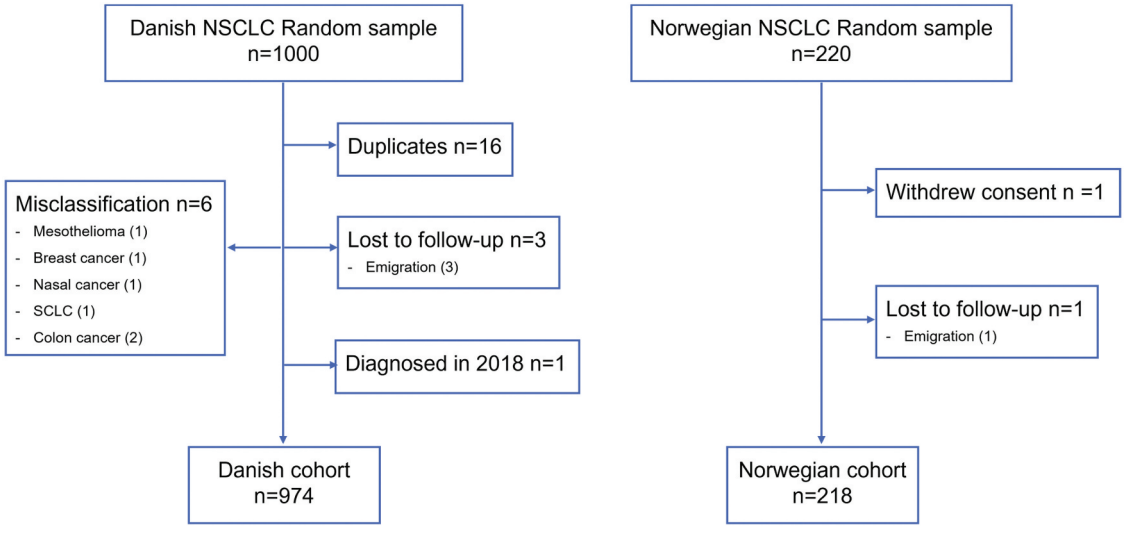


Figure 1. Flow chart of Danish and Norwegian cohort.

NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer.

Table 1. Clinical characteristics of Danish and Norwegian patients with NSCLC.

	Danish	Norwegian	p-value
	N = 974	*N* = 218	
Age mean in years (95% CI)	69.4 (68.8-70.0)	69.4 (68.1-70.8)	0.933
Gender female/male (%)	475/499 (49/51%)	108/110 (50/50%)	0.836
TNM Stage (%)	173 (17.8%)	67 (30.7%)	<0.001
I	78 (8.0%)	16 (7.3%)	
II	198 (20.3%)	31 (14.2%)	
III	490 (50.3%)	93 (42.7%)	
IV	35 (3.6%)	11 (5.2%)	
Missing			
ECOG PS (%)	368 (37.8%)	44 (20.2%)	<0.001
0	299 (30.7%)	66 (30.3%)	
1	139 (14.3%)	31 (14.2%)	
2	70 (7.2%)	13 (6.0%)	
3	15 (1.5%)	13 (6.0%)	
4	83 (8.5%)	51 (23.4%)	
Missing			
FEV1 in percent expected mean (95% CI)	71.1 (69.5-72.7)	69.7 (66.4-73.0)	0.4535
Smoking history (%)	76 (7.8%)	19 (8.7%)	0.910
Never	414 (42.5%)	94 (43.1%)	
Former	75 (7.7%)	18 (8.3%)	
Cessation (6 months)	387 (39.7%)	84 (38.5%)	
Active	22 (2.3%)	3 (1.4%)	
Missing			
Pack years mean (95% CI)	43.5 (42.0-45.0)	34.5 (31.3-37.7)	<0.001
Missing (%)	9.4%	37.8%	
Alcohol consumption (%)	570 (58.5%)	122 (56.0%)	0.001
0-7	136 (14.1%)	21 (9.6%)	
7-14	44 (4.5%)	18 (8.3%)	
14-21	86 (8.8%)	10 (4.6%)	
>21	138 (14.2%)	47 (21.6%)	
Missing			
CCI	392 (40.3%)	95 (43.6%)	<0.001
0	186 (19.1%)	70 (32.1%)	
1	175 (18.0%)	36 (16.5%)	
2	221(22.7%)	17 (7.8%)	
3+			
BMI mean (95% CI)	24.8 (24.4-25.7)	25.0 (24.5-25.2)	0.687
Marital status (%)	553 (56.8%)	122 (56.0%)	0.172
Married/cohabiting	355 (36.5%)	88 (40.4%)	
Living alone	66 (6.8%)	8 (3.7%)	
Missing			
Psychiatric comorbidity (%)	731 (75.1%)	191 (87.6%)	<0.001
None	55 (5.7%)	11 (5.1%)	
Depression	11 (1.1%)	1 (0.5%)	
Anxiety	10 (1.0%)	1 (0.5%)	
Substance addiction	167 (17.1%)	14 (6.4%)	
Other/missing			
Symptoms at diagnosis (%)	84 (8.6%)	35 (16.1%)	0.001
None	421 (43.2%)	74 (33.9%)	0.012
Cough	87 (8.9%)	10 (4.6%)	0.034
Hemoptysis	164 (16.8%)	35 (16.1%)	0.779
Chest pain	349 (35.8%)	90 (41.3%)	0.131
Dyspnea	300 (30.8%)	39 (17.9%)	<0.001
Weight loss	221 (22.7%)	34 (15.6%)	0.021
Fatigue	60 (6.2%)	9 (4.1%)	0.246
Night sweat	26 (2.7%)	2 (0.9%)	0.123
Pleural effusion	27 (2.8%)	4 (1.8%)	0.432
Lymph node	34 (3.5%)	17 (7.8%)	0.005
CNS symptoms	12 (1.2%)	1 (0.5%)	0.320
Anemia	18 (1.9%)	5 (2.3%)	0.666
Fever	211 (21.7%)	25 (11.5%)	0.001
Other			

TNM =Tumor, Node, Metastasis. ECOG PS = Eastern Cooperative Oncology Group performance status. FEV1 = Forced expiratory volume in one second. CCI = Charlson Comorbidity Index.

Tumor characteristics and NSCLC treatment

As shown in Table 2, the distribution of histopathology was comparable between the cohorts except for proportion of missing. Of the Danish cohort, $n = 38$ (3.9%) did not have a histologically verified diagnosis, whereas this was the case for $n = 32$ (14.7%) of the Norwegian patients ($p < 0.001$). All Danish patients without a biopsy-verified diagnosis received treatment with palliative intent or which the intent was not clearly stated in the medical record. Eight (25% of non-biopsied) Norwegian patients received stereotactic

Table 2. Tumor characteristics, work-up, treatment, and survival of Norwegian and Danish patients with NSCLC.

	Danish	Norwegian	p-value
	N = 974	*N* = 218	
Histology (%)	600 (61.6%)	109 (50.0%)	<0.001
Adenocarcinoma	265 (27.2%)	63 (28.9%)	
Squamous	13 (1.3%)	0 (0.0%)	
Large cell carcinoma	34 (3.5%)	8 (3.7%)	
Neuroendocrine tumor	24 (2.5%)	6 (2.8%)	
Other	38 (3.9%)	32 (14.7%)	
Missing			
MDT discussion (%)	721 (74.0%)	165 (75.7%)	
Curative treatment intent (%)	343 (35.2%)	90 (41.3%)	0.063
Missing	15.7%	17.0%	
Treatment (%)	185 (19.0%)	51 (23.4%)	0.294
Surgical	161 (16.5%)	40 (18.4%)	
Oncology – curative	491 (50.4%)	94 (43.1%)	
Oncology – palliative	3 (0.3%)	0 (0%)	
Microwave Ablation	134 (13.8%)	33 (15.1%)	
None/palliative			
Adjuvant chemotherapy	45/185 (24.3%)	10/51 (19.6%)	0.481
Curative oncology treatment n (%)	68 (42.2%)	29 (72.5%)	<0.001
SBRT	93 (57.8%)	11 (27.5%)	<0.001
CCRT			
Palliative oncology treatment n (%)*	301 (61.3%)	38 (40.4%)	<0.001
Chemotherapy	221 (45.0%)	69 (73.4%)	<0.001
Radiotherapy	15 (3.1%)	0 (0%)	0.080
Chemotherapy+radiation	36 (7.3%)	2 (2.1%)	0.044
Targeted/Immunotherapy			
Survival (%)	487 (50.0%)	112 (51.4%)	0.713
1-year	333 (34.2%)	78 (35.3%)	0.655
2-year	269 (27.6%)	68 (31.2%)	0.289
3-year	213 (21.9%)	61 (28.0%)	0.052
4-year	177 (18.2%)	58 (26.6%)	0.005
5-year			

*Patients can receive more than one type of palliative treatment.
SBRT = stereotactic body radiation therapy. CCRT = concurrent chemoradiotherapy.

body radiation therapy (SBRT) with curative intent without biopsy confirming a malignant diagnosis (Table 3). Six of these patients were in stage IA, one in stage IB, and one unknown. Overall, 5-year survival was not altered by exclusion of this group of patients from analysis.

Treatment of NSCLC is displayed in Table 2. A larger proportion of Norwegian patients were treated surgically compared to the Danish patients (23.4% vs 19.0%). Surgical approaches and techniques were similar (data not shown). The use of adjuvant treatment was also similar in both cohorts. Significant differences emerged in oncological treatment. Among Danish patients receiving curative oncologic treatment, 57.8% underwent a combination of chemotherapy and radiation, compared to 27.5% in Norway ($p < 0.001$). Conversely, 72.5% of the Norwegian patients were treated with SBRT vs. 42.2% in Denmark ($p < 0.001$). Differences were also found in terms of palliative treatment, with Norway using radiation therapy more frequently than Denmark ($p < 0.001$). Thirty-six (7.3%) Danish, but only two (2.1%) Norwegian patients, received immunotherapy or targeted treatment (this treatment was not introduced in Norway in the study period).

Survival

Median overall survival was 408 days for the Norwegian cohort and 376 days for the Danish cohort. Cause of death was similar in both cohorts (data not shown). Overall survival at one, two, three, four and five years after diagnosis was higher for the Norwegian

Table 3. Danish and Norwegian NSCLC patients without biopsy.

	Danish	Norwegian	p-value
	N = 38	*N* = 32	
Treatment intent n (%)	0 (0.0%)	8 (25.0%)	<0.001
Curative	22 (58.9%)	8 (25.0%)	
Palliative	16 (42.1%)	16 (50.0%)	
Unknown			
1-year survival	9 (23.1)	13 (40.6%)	0.112
5-year survival	1 (2.6%)	2 (6.3%)	0.442

cohort compared to the Danish (Table 2), but only significantly so in terms of five-year survival (26.6% vs 18.2%, $p = 0.005$). Kaplan–Meier survival graphs for both cohorts are presented in Figure 2. There were no statistically significant stage-specific differences in survival between the two cohorts; however, there was a trend towards better survival of stage I NSCLC patients in the Norwegian cohort (64.2% vs 54.3%, $p = 0.167$). The Norwegian NSCLC patients had a fully adjusted OR of 1.81 (95%CI: 1.11–2.94) for being a 5-year survivor compared to the Danish patients (Table 4). Male gender had lower odds for 5-year survival compared to women. Increasing TNM stage and ECOG PS were associated with lower odds for being a 5-year survivor. In contrast, the burden of comorbidity (CCI) was not associated with long-term survival.

Missing data

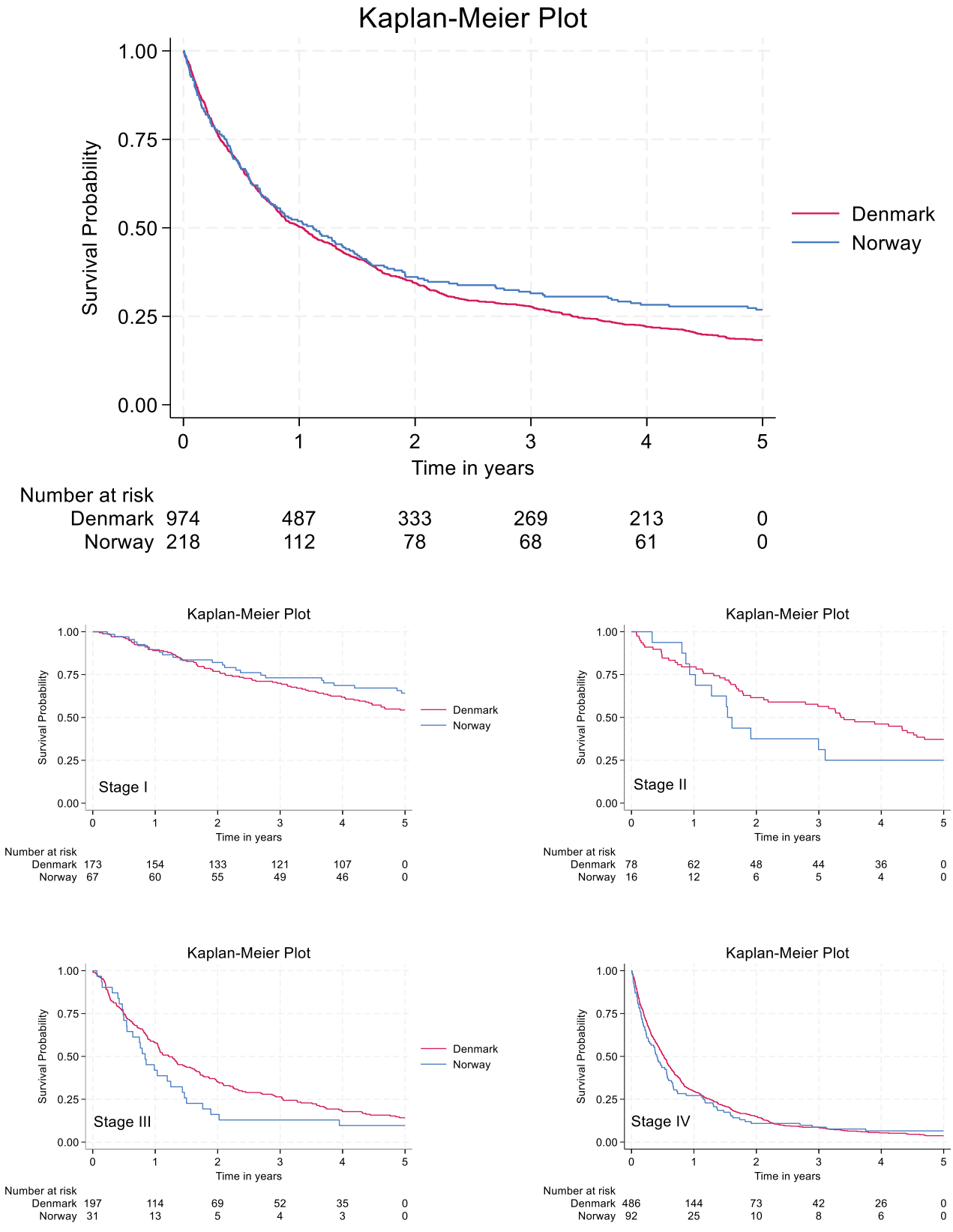
The dataset was complete with respect to survival, sex, and comorbidity. For TNM stage, the data were more than 95% complete (96.4% for the Danish cohort and 94.8% for the Norwegian). However, there were variables with a large proportion of missing data. In 37.8% of the Norwegian cohort's' medical records, information on pack-year was missing. Similarly, a larger proportion of Norwegian NSCLC patients had no information on ECOG PS (23.4 vs. 8.5%, p-value <0.001) and alcohol consumption (21.6% vs. 14.2%, p-value <0.001) compared to Danish NSCLC patients. For both cohorts, treatment intent was unclear/missing in the medical records for 15–17%. Descriptive results without missing can be found in the supplementary data (Table B).

Discussion

In this study, we compared cohorts of patients with NSCLC from Denmark and Norway to explore differences in stage distribution, patient characteristics, disease burden, and treatment patterns that could explain the difference in 5-year survival between these countries. We found that the two cohorts were very comparable in age, sex, FEV1, and smoking history. However, the Danish NSCLC patients had a higher number of pack-years and a greater burden of symptoms at diagnosis and of comorbidity. Furthermore, the Norwegian patients had a more favorable stage distribution, and a higher proportion was treated with curative intent. We found that unlike in Denmark, Norwegian patients with suspicion of NSCLC were treated with SBRT without biopsy confirmation. Five-year survival was higher in the Norwegian cohort, and even after adjusted for stage, smoking status, ECOG PS, and comorbidity, the odds ratio of being a long-term survivor in Norway was 1.81 compared to Denmark.

Direct comparison between Danish and Norwegian lung cancer patients, including information on patient characteristics and treatment, has not previously been published. Several Nordic register-based studies, have described trends in survival over time and compared countries [1,11,22]. In a recent paper, Tichanek et al. reports upwards trends in lung cancer survival in all of the Nordic countries since the year 2000 and that Norway has the highest 5-year survival rate [11]. However, as the paper is based on data from national registries and does not include information on histology, disease stage, comorbidity or treatment, further associations cannot be assessed. In the present study we have obtained data concerning these potential confounders. However, the present Norwegian cohort is from a single center and does not cover the whole nation. We found a more favorable stage distribution, and accordingly a larger proportion of patients treated with curative intent in our cohort compared to the underlying national cohort in the time period (supplement Table A), but comparable to the stage distribution described in a paper with patients from another single center in Norway at the same time period [23].

All Nordic countries have implemented preventive tobacco policies [24], but with dissimilar success. In the year 2023, there were 7% daily smokers in Norway and 13% in Denmark [25,26]. In this study, we report a similar prevalence of ever-smokers (active or former smokers) and never-smokers in the cohorts of NSCLC patients. However, the Danish ever-smokers had a higher number of pack-years, which have previously been reported as an independent prognostic factor of NSCLC survival [27,28]. We found an impact of smoking intensity on 5-year survival in this study, in line with previous research. However, we must take into an account that there were substantial missing data regarding number of pack-years in the Norwegian cohort. As with smoking, Danes generally have a higher alcohol consumption [29,30] and also years of life lost due to alcohol compared to Norwegians [31]. In our study, we found a larger proportion of heavy drinkers in the Danish cohort. Similarly, the NSCLC patients in the Danish cohort had a higher burden of comorbidity including mental illness and substance abuse compared to the Norwegian cohort. On average, the life expectancy for Norwegian men and women are higher than for Danish men and women by approximately 1.5 years [32,33] probably attributable to



a) Survival analysis on all patients by country

b) Survival estimates by stage and country.

Figure 2. Survival analysis on Danish and Norwegian patients with NSCLC.

(a) Survival analysis on all patients by country. (b) Survival estimates by stage and country.

Table 4. Odds ratio of being 5-year survivor.

	Unadjusted OR	95% CI	Adjusted OR	95% CI
Country				
Denmark	Ref.		Ref.	
Norway	1.63	1.16-2.30	1.81	1.11-2.94
TNM Stage				
I	Ref.		Ref.	
II	0.41	0.25-0.67	0.37	0.22-0.65
III	0.12	0.07-0.19	0.11	0.07-0.18
IV	0.03	0.02-0.05	0.04	0.02-0.06
Missing	0.21	0.10-0.44	0.42	0.17-1.00
Sex				
Women	Ref.		Ref.	
Men	0.54	0.40-0.72	0.45	0.31-0.65
CCI				
0	Ref.		Ref.	
1	1.07	0.74-1.55	1.32	0.81-2.15
2	1.10	0.74-1.62	1.13	0.68-1.88
3+	0.57	0.37-0.89	0.86	0.49-1.49
ECOG PS				
0	Ref.		Ref.	
1	0.44	0.32-0.61	0.46	0.31-0.70
2	0.09	0.04-0.19	0.09	0.04-0.21
3	0.02	0.00-0.16	0.03	0.00-0.24
4	(too few patients)		(too few patients)	
Missing	0.18	0.10-0.34	0.13	0.06-0.29
Smoking status Never	Ref.		Ref.	
Ever	0.53	0.33-0.84	0.76	0.41-1.41

TNM =Tumor, Node, Metastasis. ECOG PS = Eastern Cooperative Oncology Group performance status. CCI = Charlson Comorbidity Index.

a combination of smoking, alcohol and other lifestyle differences between the populations [34,35]. We know e.g. from a Danish study on NSCLC patients diagnosed 2018–2023 [36], that 21% of patients with stage I-IIIA did not receive treatment with curative intent and 10% of patients with stage IIIB-IV did not receive any treatment. Advanced stage, comorbidity, age above 80 years, reduced ECOG PS, and living alone were associated with less likelihood of guideline recommended treatment. In the present study, we found significant differences in comorbidity between the cohorts, where a larger proportion of Danish lung cancer patients had a high burden of comorbidity, potentially affecting treatment possibilities.

In the present study, we found noticeable differences in treatment of NSCLC patients. During the study period immunotherapy and targeted treatment were used in Denmark, whereas immunotherapy was not implemented in Norway until 2017. In Norway, a higher proportion of patients underwent radiation therapy with curative (SBRT) as well as palliative intent. We found eight patients treated with SBRT on tumors that were not histopathologically verified as malignant. Empirical SBRT, hence undergoing treatment without a biopsy-verified diagnosis was not and continues not to be generally used in Denmark. However, in Norway empirical SBRT is an option for patients with volume progression on successive CT scans and positive uptake of fluorodeoxyglucose on positron emission tomography (PET), if they are not physically fit for biopsy or if a biopsy did not yield a conclusive result in accordance with guidelines from the American Society for Therapeutic Radiology (ASTRO). The American Society of Clinical Oncology supports the ASTRO guideline [37] and in a study on American veterans, 14.9% of early-stage NSCLC patients were treated without pathology confirmation [38]. The present study, was not powered to investigate differences in biopsy confirmation on survival rates. However, this is a point of interest in differences between clinical practice in Denmark and Norway and this could contribute to differences in long term survival rates between the two countries.

We found an overall superior survival in the Norwegian NSCLC cohort compared to the Danish. This is in line with the results of the national registries (supplement Table A). The superior Norwegian survival was probably driven by a more preferable stage distribution and less smoking intensity in the Norwegian cohort. However, even after adjusting for these predictors, Norwegian NSCLC patients had better odds for 5-year survival. The 5-year survival rates for women were comparable for the Danish and Norwegian cohorts. However, there were notable discrepancies between men, with the Danish men exhibiting significantly lower 5-year survival compared to Norwegian men. These results are in line with results reported in previous studies [1,11,22].

In this study, missing data were handled by the missing data indicator method to show the differences in proportion of missing data between the cohorts [21]. The dataset was complete concerning information on country, survival, sex, or comorbidity. However, there were some missing data on important variables such as treatment intent and number of pack-years. The Norwegian NSCLC patients generally had more missing data on important confounders. Culturally, there is a stigma associated to smoking in Norway [39] and neither smoking status nor pack-years are included in the Norwegian registries unlike the DLCR, as well as often not noted in the patient medical record. Likewise, there were substantial missing data on ECOG PS in the Norwegian cohort. In the years 2019–2023, 25% of lung cancer patient were ECOG 0 at diagnosis, with only 11% missing data [40]. Thus, the missing data could have introduced bias into our results.

Clinical implications of findings

The NSCLC patients in Norway were diagnosed at an earlier stage, had less symptoms at the time of diagnosis, and had a lower burden of comorbidity compared to the Danish patients, leaving a larger proportion of patients eligible for curative treatment strategies. Currently, screening is still pending in both countries [41,42]. In contrary to Norway, empirical SBRT in Denmark is rarely undertaken and is currently not included in the clinical practice guidelines. Norway has the highest prices on tobacco and at present time just 7% daily smokers, nearly half the prevalence in Denmark. This study supports the legislative proposal on further restriction on tobacco sales made by the Danish Medical Association [43].

Strengths and limitations

This study is the first comparative study of NSCLC patient cohorts in Denmark and Norway, not based on registry data. We present data from medical records, with very few patients lost to follow-up and no information bias. We have included important well-established prognostic covariates in our comparisons and analyses. We have also evaluated differences in clinical practice, e.g. treatment patterns, which also potentially could contribute to different survival patterns between the two countries. There are, however, also several limitations to this study. The most important limitation is not having a nationwide cohort from Norway. The cohort from Vestfold is not completely representative of the Norwegian NSCLC patients with regards to stage (supplementary Table A). Data are solely from electronic medical records. If there were no information on, i.e., weight-loss or fatigue in the record, it was reported as 'no'. However, we do not know if the patient truly did not experience weight loss, or it was lack of documentation. The Norwegian cohort was underpowered to look at stage-specific parameters.

Conclusion

Norwegian patients with NSCLC were similar to Danish patients on many characteristic parameters. However, more Norwegian patients were diagnosed in a curable stage, they smoked fewer cigarettes, and had a greater proportion surviving 5 years. After adjusting for sex, stage, smoking, ECOG PS, and CCI, the odds ratio of being a 5-year survivor remained higher for Norwegian NSCLC patients.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Authors' contributions

AG: Conceptualization, Data curation, Formal analysis, Methodology, Writing original draft, Writing reviewing and editing. JB: Conceptualization, Writing reviewing and editing. AK: Writing reviewing and editing. SD: Writing reviewing and editing. TRR: Conceptualization, Methodology, Writing reviewing and editing. NC: Conceptualization, Formal analysis, Methodology, Writing reviewing and editing. The work reported in the paper has been performed by the authors.

Data availability statement

The data collected for this study can be made available to others in de-identified form. Requests for data sharing can be made to the corresponding author.

Ethical approvals

All information were found in the patient medical records. The present study was approved by the Danish Data Protection Agency (registration no. 1–45-70-80-21) and the Norwegian Regional committees for medical and health research ethics (REK, registration no. 557036). In accordance with Norwegian approval, patients alive on the time of the data collection were informed of the study by mail with the possibility of not participating.

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