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Time spans from first symptom to treatment in patients with lung cancer – The influence of symptoms and demographic characteristics

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Abstract

Background. Cancer stage at diagnosis is the most important prognostic factor for lung cancer (LC), but most patients are diagnosed with advanced disease with many and intense symptoms. This study explores relationships between LC patients' first symptoms, symptoms triggering health care system (HCS) contact, demographic/clinical characteristics, and time spans in the care trajectory from first symptom(s) to treatment start. *Materials and Methods.* Medical records were examined from all 314 patients diagnosed with primary LC in 2003 at a Department of Respiratory Medicine, in Stockholm Sweden. Descriptive analysis was used to examine symptoms and time spans in the care trajectory. Cox regression analysis was conducted to explore the influence of symptoms and demographic/clinical characteristics on the time spans. *Results.* Tumor-specific symptoms led to HCS visits to a greater extent than did systemic symptoms, despite reports of weight loss, fatigue and appetite loss as common first symptoms. Minor differences between women and men were found regarding specific symptoms. The study confirms that the time spans from first symptoms reported to treatment start are extensive, exceeding Swedish national recommendations. A lump/resistance, neurological symptoms, appetite loss, hemoptysis and non-thoracic related pain were associated with significantly shorter time spans in the care trajectory. People >74 years old risked longer time span from first HCS visit to treatment start. *Conclusion.* This study indicates a need for a more efficient LC care trajectory. Elderly patients could be particularly vulnerable for longer time spans.

Lung cancer (LC) is the most common cause of cancer death among men and the third most common among women in the European Union [1]. The demographic panorama in LC is rapidly changing from predominantly affecting older men to increasingly affecting women and younger people [2]. Although the most important prognostic factor for LC is resectable disease at diagnosis, most patients are still diagnosed with advanced cancer with poor prognosis. This is the case, although circa 90% of LC patients have many and varied symptoms at diagnosis [3,4].

A variety of factors related to patients, providers and health care systems (HCS) contribute to late diagnosis and treatment [4–8]. Studies from differ-

ent European and Nordic countries show wide variation in the length of time spans between different key events in the care trajectory [5–9]. Variation has also been found between different areas of Sweden. Myrdal et al. [6] reported time between the first symptom perceived by the patient and treatment start as approximately 4.6 months for non-small cell lung cancer (NSCLC) in one region of Sweden, while Koyi et al. [7] found this period averaged 7 months for all LC in an adjacent region, with 43 days representing the time span from first reported symptom to first visit at the HCS. The Swedish national recommendations for 80% of all patients with LC are as follows: waiting time to

specialist: <7 days; time from first visit at a lung specialist to determination of treatment plan: <21 days; and <10 days from determination of treatment plan to treatment start [10,11]. The available national data from 2003 [10] lack time points for treatment start, thus limiting investigation of the time spans along the care trajectory.

Reasons for late diagnosis and treatment are poorly understood. Smith et al. [12] suggest that patient's interpretation of health changes and/or symptoms is one reason for late diagnosis. Symptoms can often exist for lengthy periods, without being perceived as threatening and without health care being sought [5–9,13]. In a Swedish qualitative study, Leveälahti et al. [13] also found that LC could be suspected but not perceived as readily curable, which might delay HCS contact. These data raise questions about how the occurrence of specific symptoms and patterns in symptom recognition and interpretation relate to diagnosis and treatment, and how factors related to patients' lives and backgrounds influence the time spans leading to diagnosis and treatment of LC. Potential gender differences are also of interest in this investigation, due to the changing demographics of LC.

The aims of this study are therefore to explore early symptoms in women and men with primary LC and investigate relationships between different symptoms and time spans in the care trajectory. An additional aim is to examine how demographic and clinical characteristics are related to these time spans. We tried to answer the following questions:

1. Which are the first symptoms patients diagnosed with LC report?
2. Which symptoms triggered HCS contact?
3. To what extent are the symptoms triggering HCS contact identical with the first symptoms reported?
4. Are there any differences between men and women with regard to the above?
5. What is the total time span between first reported symptoms and treatment start, examined as time span between:
   a. first reported symptoms and first HCS visit?
   b. first HCS visit and referral to lung specialist?
   c. referral to lung specialist and first visit with specialist?
   d. first visit with lung specialist and diagnosis?
   e. diagnosis and determination of treatment plan?
   f. determination of treatment plan and treatment start?
6. How are specific symptoms, demographic and clinical characteristics associated with the length of the above time spans?

Material and methods

This study is based on data from one university hospital specialist Department of Respiratory Medicine. Patients with LC present to the University Hospital Department of Respiratory Medicine in several ways. Most patients are referred to this regional specialist department from their primary care general practitioner (GP) with suspected or x-ray verified LC. Patients can also be referred from other specialists or after health checkups. Diagnostic workup and treatment decisions are coordinated by lung specialists in consultation with oncologists/thoracic surgeons. It should be recognized that most health care in Sweden is provided by the national HCS and financed by a combination of local income tax, national health insurance and government subsidies, with only limited fee-for-service payment.

All 314 patients referred to this university hospital specialist Department of Respiratory Medicine in Stockholm Sweden who received a diagnosis of primary LC during 2003 were included in this study. Four lung specialists were responsible for initial patient visits including an assessment of medical history. This assessment included demographic characteristics, smoking habits, other diseases, medications, performance status, asbestos exposure and experienced symptoms. The data analyzed here were based on physician's documentation in medical records.

Data from medical records were collected about the following seven time points in the disease trajectory: first reported symptoms; first visit at the HCS; receipt of referral at Respiratory Medicine Department; first visit to the lung specialist; diagnosis; determination of treatment plan; and treatment start. Date of PAD/cytology results during diagnostic work-up were used as diagnosis date when available (n =291). When necessary, time point for first symptom occurrence was approximated as follows: if reported in the middle of the month, the 15th was used as proxy time point. The 6th was used for early in the month, and the 26th used for symptoms originating late in the month.

The study was approved by the regional research Ethics review board 2005/1115-31/3.

Data analysis

Categorizations

Education level was classified according to the Swedish Standard Classification of Occupations and performance status according to the World Health Organization. Smoking status was classified in terms

of "current smokers", "ex-smokers" (smoking cessation >1 year) and "never smokers", according to Regional Oncologic Centre norms. In all regressions described below, the following dichotomized variables were used: civil status = living alone versus living with a spouse; type of LC = NSCLC versus SCLC; and stage of LC as early (Ia-IIb) versus late (IIIa-IV) based on praxis for surgical resection in Sweden.

Statistical analysis

Clustering within the first occurring symptoms and trigger symptoms to HCS contact was explored using a hierarchic cluster analysis [14] (research questions 1–2). Descriptive statistics were used to examine each symptom category (research questions 1–3). To examine whether symptoms differed between women and men, χ^2 test or Fischer's exact test was used (research question 4). Independent sample t-test, χ^2 test or Fischer's exact test were also used to examine differences between women and men regarding to demographic and clinical characteristics. The lengths of all time spans were analyzed descriptively (research question 5). Research question 6 was examined with Cox's proportional hazard regression model [15] because assumptions for linear regression analysis were not met. Results of these analyses are presented as Hazard Ratio (HR), a type of relative risk.

Cox's regression analysis were conducted for five time spans which are between key events: a) from first reported symptom to first HCS visit, b) from first HCS visit to referral to the Respiratory Medicine Department, c) from referral to diagnosis, d) from diagnosis to treatment start; and e) from first HCS visit to treatment start. In regression a, first reported symptoms and demographic characteristics were included in the model. In regression b, c and d, first reported symptoms, symptoms that triggered the visit with the HCS, and demographic characteristics were included in the model. In regression e, demographic and clinical characteristics were included. "Other symptoms" (see Table II) does not represent a homogeneous category, and was therefore excluded from all regression models.

Variables were added to the Cox proportional hazards model in descending order on the basis of significance (p ≤0.05). The assumptions of the model were tested as follows: The continuous variable age was investigated by examining scatter-plots, partial residuals versus time but did not meet the statistical assumptions. Age was therefore formulated as a variable with four groups (<55, 55–64, 65–74, >75 years). All variables were investigated by examining the differences in log cumulative baseline hazards rate by time to check the proportional hazards assumption. Estimated change in a coeffi-

cient when a case was removed was used to investigate the influence of individual observations. If a single observation changed the model, the variable was excluded from the model. If removal of a single observation strengthened the model, the variable was included in the model. All models presented in the result section met all statistical assumptions.

Results

Patient demographic and clinical characteristics

The age distribution for the patients in this study was similar to national data for the same time period [10]. Eighty-seven percent of the patients had NSCLC and 72% had advanced LC, which is also in line with national data [10], although adenocarcinoma occurred more in both women and men in this study than nationally. Women lived alone significantly more often than men did and were more often non-smokers or ex-smokers. Women and men differed significantly with regard to level of education, as shown in Table I. Patients without PAD/cytology results were significantly older (p =0.004) than others.

First symptom and reason to visit the HCS

No clusters of symptoms were found. Frequencies are therefore shown by symptom category in Table II. The five most commonly reported first symptoms were cough, dyspnea, weight loss, fatigue and thoracic pain, although not in the same order for women and men. Women reported the occurrence of edema as first symptom significantly more often than men did. The four symptoms which most commonly led to first HCS visit for both women and men were cough, dyspnea and thoracic pain, with 10% of women reporting neurological symptoms and 8% of men reporting hemoptysis as the fourth most common symptom triggering HCS contact. Significantly more men than women visited the HCS for hoarseness, although it should be noted that few people reported this symptom.

Both women and men reported more first symptoms than symptoms triggering HCS contact. Symptoms triggering the HCS visit were often not identical with the first reported symptom; for example, systemic symptoms did not lead to a HCS visit to the same degree as tumor-specific symptoms. Patients who reported hemoptysis or neurological symptoms as their first symptom also visited the HCS for that symptom to a high degree (73% respectively 64%).

Time span from first reported symptom to treatment start

Most patients followed the chronology of the care trajectory depicted in Figure 1. Data from patients

Table I. Patient demographic and clinical characteristics, with comparisons between men and women.

	Total n = 314	Men n = 153 (49%)	Women n = 161 (51%)	p-values
Age Mean (SD)	68.3 (10.7)	69.5 (10.2)	67.1 (11.1)	NS
Median	69	71	67	
Min-Max	38–92	41–92	38–90	
Smoking habits N (%)				
Smoker	167 (53.2)	81 (52.9)	86 (53.4)	p = 0.027
Ex-smoker	116 (36.9)	66 (43.1)	50 (31.1)	p = 0.001
Never smoker	31 (9.9)	6 (3.9)	25 (15.5)	NS
Civil status N (%)				
Live alone	83 (26.7)	29 (19.2)	54 (33.8)	p = 0.004
Married or cohabiting	193 (62.1)	116 (76.8)	77 (48.1)	p < 0.001
Widow/er	28 (9.0)	5 (3.3)	23 (14.4)	p = 0.01
Other	7 (2.3)	1 (0.7)	6 (3.8)	NS
Missing data	3	2	1	
Education (SSYK 96)				
<High school (9 years)	43 (15.6)	11 (8.1)	32 (23.0)	p = 0.001
High school or equivalent (12 years)	151 (54.9)	84 (61.8)	67 (48.2)	p = 0.024
University ≤3 years or similar	45 (16.4)	25 (18.4)	20 (14.4)	NS
Academic degree (university more than 3–5 years)	36 (13.1)	16 (11.8)	20 (14.4)	NS
Missing data	39	17	22	
Type of lung cancer N (%)				
NSCLC				
Squamous cell carcinoma	62 (19.7)	38 (24.8)	24 (14.9)	NS
Adenocarcinoma	142 (45.4)	64 (41.8)	78 (48.8)	NS
Lung cancer (clinical diagnosis)	24 (7.6)	11 (7.2)	13 (8.1)	NS
Undifferentiated carcinoma	30 (9.6)	12 (7.8)	18 (11.3)	NS
Large cell carcinoma	17 (5.4)	11 (7.2)	6 (3.7)	NS
Non specific cytology	2 (0.6)	2 (1.3)	0	NS
SCLC	36 (11.5)	15 (9.8)	21 (13.0)	NS
Missing data	1	0	1	
Stage of lung cancer N (%)				
Ia	30 (9.6)	9 (5.9)	21 (13.0)	NS
Ib	42 (13.4)	23 (15.0)	19 (11.8)	NS
IIb	7 (2.2)	4 (2.6)	3 (1.9)	NS
IIIa	36 (11.5)	21 (13.7)	15 (9.3)	NS
IIIb	83 (26.4)	36 (23.5)	47 (29.2)	NS
IV	116 (36.9)	60 (39.2)	56 (34.8)	NS
Treatment N (%)				
Operation	51 (16.2)	23 (15.0)	28 (17.4)	NS
Chemotherapy	105 (33.4)	43 (28.1)	62 (38.5)	NS
Chemotherapy + Radiotherapy (curative intent)	42 (13.4)	25 (16.3)	17 (10.6)	NS
Radiotherapy for metastases	17 (5.4)	8 (5.2)	9 (5.6)	NS
Radiotherapy primary tumour	27 (8.6)	14 (9.2)	13 (8.1)	NS
Pleura centesis. pleurodesis	3 (1.0)	2 (1.3)	1 (0.6)	NS
SCLC limited (ct+rt)	6 (1.9)	1 (0.7)	5 (3.1)	NS
SCLC extensive (ct alone)	14 (4.5)	7 (4.6)	7 (4.3)	NS
No treatment	49 (15.6)	30 (19.6)	19 (11.8)	NS
Performance status[a] WHO N (%)				
0	104 (33.2)	46 (30.1)	58 (36.3)	NS
1	112 (35.3)	53 (34.6)	59 (36.9)	NS
2	65 (20.8)	37 (24.2)	28 (17.5)	NS
3	27 (8.6)	14 (9.2)	13 (8.1)	NS
4	5 (1.6)	3 (2.0)	2 (1.3)	NS
Missing data	1	0	1	

[a]Performance status: 0 = Fully active. Able to carry on all activities. 1 = Able to carry out most activities. Restrictions apply to physically strenuous activity. 2 = Active and able to care for self. Unable to perform work activity. Up and about at least 50% of waking hours. 3 = Capable of only limited self-care. Confined to a bed or chair at least 50% of waking hours. 4 = Cannot care for self. Confined to bed or chair.

Table II. First symptoms and symptoms that triggered a Health Care System (HCS) appointment. Note that each person can report more than one symptom.

	First reported symptoms			Symptoms triggering HCS- appointment			First reported symptom = Trigger symptom		
	Total n =314 n (%)	Men n =153 n (%)	Women n =161 n (%)	Total n =314 n (%)	Men n =153 n (%)	Women n =161 n (%)	Total n (%)	Men n (%)	Women n (%)
Cough	130 (41.8)	61 (40.4)	69 (43.1)	84 (27.0)	40 (26.5)	44 (27.5)	69 (54.8)	30 (50.8)	39 (58.2)
Dyspnea	102 (32.3)	55 (36.4)	47 (29.4)	71 (22.8)	37 (24.5)	34 (21.3)	55 (55.0)	29 (54.7)	26 (55.3)
Thoracic related pain	55 (17.7)	33 (21.9)	22 (13.8)	43 (13.8)	19 (12.6)	24 (15.0)	30 (55.6)	18 (56.3)	12 (54.5)
Non thoracic related pain	28 (9.0)	10 (6.6)	18 (11.3)	25 (8.0)	12 (7.9)	13 (8.1)	15 (55.6)	5 (55.6)	10 (55.6)
Weight loss	100 (32.1)	52 (34.4)	48 (30.0)	10 (3.2)	6 (4.0)	4 (2.5)	10 (10.3)	6 (11.8)	4 (8.7)
Fatigue	80 (25.7)	35 (23.2)	45 (28.1)	17 (5.5)	8 (5.3)	9 (5.6)	15 (19.5)	6 (18.8)	9 (20.0)
Appetite loss	40 (12.9)	19 (12.6)	21 (13.1)	1 (0.3)	0	1 (0.6)	1 (2.6)	0	1 (4.8)
Neurological symptoms	34 (10.9)	15 (9.9)	19 (11.9)	23 (7.4)	7 (4.6)	16 (10.0)	21 (63.6)	7 (50.0)	14 (73.7)
Hemoptysis	16 (5.1)	10 (6.6)	6 (3.8)	21 (6.8)	13 (8.6)	8 (5.0)	11 (73.3)	6 (66.7)	5 (83.3)
Hoarseness	7 (2.2)	4 (2.6)	3 (1.9)	5 (1.6)★	5 (3.3)	0	4 (57.1)★★	4 (100.0)	0
Respiratory infection	15 (4.8)	5 (3.3)	10 (6.3)	2 (0.6)	1 (0.7)	1 (0.6)	1 (7.1)	0	1 (11.1)
Fever	16 (5.1)	6 (4.0)	10 (6.3)	14 (4.5)	7 (4.6)	7 (4.4)	8 (50.0)	3 (50.0)	5 (50.0)
General malaise	15 (4.8)	4 (2.6)	11 (6.9)	3 (1.0)	2 (1.3)	1 (0.6)	1 (6.7)	1 (25.0)	0
Lump/resistance	9 (2.9)	2 (1.3)	7 (4.4)	6 (1.9)	1 (0.7)	5 (3.1)	5 (55.6)	1 (50.0)	4 (57.1)
Edema	20 (6.4)★	5 (3.3)	15 (9.4)	10 (3.2)	3 (2.0)	7 (4.4)	9 (45.0)	3 (60.0)	6 (40.0)
GI symptoms	15 (4.8)	4 (2.6)	11 (6.9)	5 (1.6)	2 (1.3)	3 (1.9)	4 (26.7)	1 (25.0)	3 (27.3)
Other symptoms	35 (11.3)	12 (7.9)	23 (14.4)	17 (5.5)	8 (5.3)	9 (5.6)	10 (28.6)★	6 (50.0)	4 (17.4)
No symptoms	11 (3.5)	5 (3.3)	6 (3.8)	–	–	–	–	–	–
For other reason visited the HCS	–	–	–	21 (6.8)	13 (8.6)	8 (5.0)	–	–	–
Missing	3	2	1	3	2	1	–	–	–

Significant difference between men and women: ★ p <0.05. ★★ p <0.01.
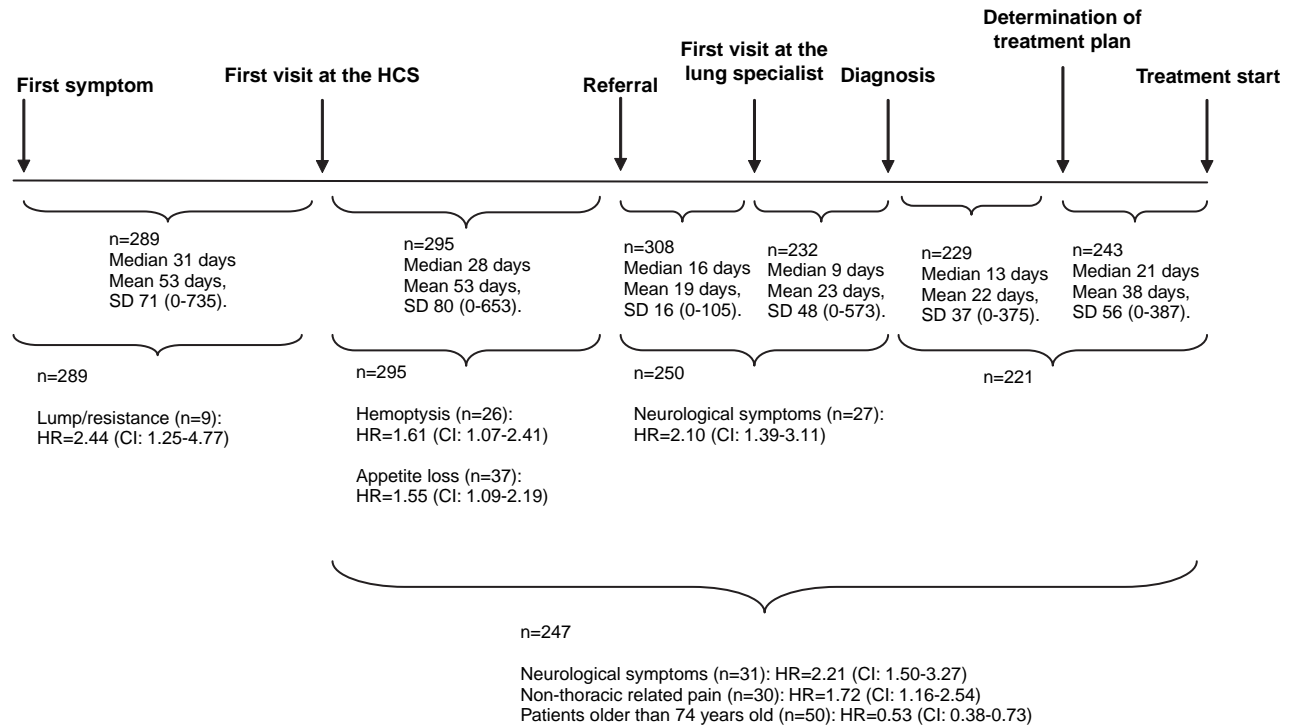
Figure 1. Median, mean, SD and min-max in days for the time spans from first symptom to treatment start, and influence of symptoms and demographic/clinical characteristics on the time spans presented here as Hazard Ratio (HR) and Confidence Interval (CI). HR >1 is associated with significantly shorter time spans, while HR<1 is associated with significantly longer time spans.

who deviated from this chronology were excluded from both the descriptive and regression analyses of the time spans. Descriptive data for six time spans are presented in Figure 1. The median time of the entire span from first reported symptom(s) to treatment start was 155 days (n =237, mean 173 days, SD 126, min-max: 6-892, not in Figure), of which a median of 31 days was prior to the first HCS visit (often termed "patient delay"). The median time between first HCS visit to referral (also known as "first doctor delay") was 28 days. The median time between referral and treatment start (a.k.a. "second doctor delay") was 58 days (n =245, mean 77, SD 74, not shown in Figure). The median time from first HCS visit to treatment start (often termed "HCS delay") was 94 days (n = 247, mean 122 days, SD 103, not in Figure).

This data was compared with Swedish national recommendations [11]. The time span from referral to specialist contact was <7 days for 27% of patients. The time from first visit with lung specialist to determination of treatment plan was <21 days for 56% of patients, while <10 days elapsed from determination of treatment plan to treatment start for 25% of these patients. These time spans all exceed the Swedish national recommendations [10,11].

Extreme values

As a large number of patients were found to have unusually long time spans along the care trajectory,

we returned to the medical records to find possible explanations for this. We defined an unusually long time spans as >3 box-lengths from the 75th or 25th percentile in any time span, which means that the length of time defined as unusually long varies by time span. Data for the 48 cases with unusually long time spans are summarized in Table III. Due to the large number of such cases, they were included in analyses.

Factors that influenced the time spans from first symptom to treatment

Presence of a lump/resistance, hemoptysis, appetite loss, neurological symptoms and non-thoracic related pain were all associated with a significantly shorter time span in the care trajectory (see Figure 1). Age also influenced one time span; the patient group >74 years old was associated with a significantly longer time spans from first HCS visit to treatment start, than was the case for other age groups. No statistically differences in time spans were found in relation to histology types or stage of LC.

Discussion

This study confirms the existence of extensive time spans from the first symptoms reported to treatment start, indicating that many patients waited longer for care than is recommended by the Swedish lung cancer study group [11]. The patient group aged

Table III. Possible explanations for the extreme long time spans (from first reported symptom to treatment start) based on information from the medical records.

Time span	Time span in days	Woman/Man & Age	Possible explanation from medical records for extreme long time spans
First symptom-First visit at the HCS	735	M 76	Never previously sick, no prior contacts with the HCS
	281	W 82	Presented with several co-morbidities
	426, 275, 269, 242, 313	W 55, 68, 58, 80 M 79	No probable explanations found
First visit at the HCS- Referral to Respiratory Medicine Department	653	M 89	Initial workup for pain in shoulder, with extended diagnostic process.
	580	M 76	Unclear, stable change on x-ray.
	393, 370, 216, 210,	M 55, 76 W 72, 85	Initially treated for respiratory infections
	376	W 74	Unclear delegation of responsibility between hospital specialist departments
	218,369, 269	W 89, M 63, 77	Presented with other previously diagnosed cancers (mammae, larynx, bladder)
	372, 379	W 85, M 73	Initially examined at other hospitals or departments
	214	M 77	No probable explanations found.
Referral- First visit with lung specialist	105	W 82	Unclear, stable change on x-ray.
First visit with the lung specialist-Diagnosis	573, 181	W 82, M 68	Unclear, stable change on x-ray.
	277, 107	W 85, 59	Patient refused bronchoscopy.
	153	M 75	Presented with other previously diagnosed cancer (renal).
	134	W 52	Initially diagnosed as sarcoidosis
	115	M 81	Surgery for colon cancer during diagnostic process for LC
	104	W 75	Additional diagnostic procedures for suspected liver metastases
	99	M 59	Additional procedures to evaluate possible surgery
Diagnosis-Determination of treatment plan	685, 429, 375, 250	M 86, 84, 63, 77, 82	Presented with deteriorated general condition
	118, 498, 191	W 73, 87	Presented with deteriorated general condition
	325, 98, 121,	W 82, 82, 73	Unclear disease picture
	140	W 80	Refused treatment
	100	M 76	Presented with several co-morbidities
	142	M 78	No probable explanations found
Determination of treatment plan-Treatment start	387, 358	W 60, 65	Changed treatment plan due to deteriorating general condition
	380	M 74	Additional procedures to evaluate possible surgery
	372	M 75	Patient choose to delay treatment start
	299	W 64	No probable explanations found

>74 years differed significantly from other age groups in that their trajectory through the HCS to treatment was longer than that in other age groups. Minor differences between women and men regarding symptoms were found, although no explanation for these differences is readily apparent from the available data. While symptoms such as weight loss, fatigue and appetite loss were relatively common, patients more commonly first visited the HCS for tumor-specific symptoms than for such systemic symptoms. In the analyses conducted, a lump/ resistance, hemoptysis, appetite loss, neurological symptoms and non-thoracic related pain were associated with significantly shorter time spans in the care trajectory. Although only a limited number of observations were available for each symptom, to the best of our knowledge no prior study has investigated the influence of symptoms in the care trajectory of

this patient group. These results therefore provide a first exploration of these issues.

No statistically significant relationships were found between length of time span and histology or stage of LC in this study. While Myrdal et al. [6] found some differences in time spans related to disease stage; Jensen et al.'s review [16] shows contradictory results regarding influence of stage and histology on the length of time span. The notable differences in clinical and demographic patient characteristics as well as analysis methods may explain the lack of consistency in findings. It should also be noted that our study has equal numbers of men and women, which is not the case in the other studies.

The demographic and clinical characteristics of this sample are comparable with present national data, with the exception of the slightly higher prevalence of adenocarcinoma in this urban study.

The methods for data collection used here follow the same structure as those in Koyi et al.'s [7,17], representing a systematic initial detailed assessment of all patients by a limited number of physicians at first specialist visit. Cough, dyspnea, fatigue and thoracic pain were found to be more prevalent first symptoms in this study than in Koyi el al.'s study [17], with fewer asymptomatic patients compared with other studies [4,17]. Cough, dyspnea and thoracic pain were more commonly reported as triggering HCS contact in this study compared with others [4,17], while hemoptysis was less common [4]. These data are from a large city as opposed to Koyi et al.'s [7,17] and Myrdal et al.'s [6] studies conducted over five years previously in small-town and rural regions of Sweden. It is unclear if time and geography adequately explain differences in symptom recognition and presentation, but they may explain the longer time span from contact with specialists to treatment start. For example, a recent report on waiting times in cancer care emphasizes that while the Stockholm region has the country's greatest capacity for radiotherapy, fewer patients were treated there in 2003 than in other regions [18]. Similar logistical problems may affect LC patients' trajectories in other ways. In addition, in recent years primary care has been given the responsibility for primary diagnosis and referral of many diseases, including LC [19]. It is possible that availability and access to GPs in the Stockholm region is not adequate to meet these increasing demands.

One issue for consideration is that the frequently used concept of "patient delay" may be a misnomer as this time span can represent more than patients' actions alone. Nearly two thirds of patients contacting primary care in Sweden receive an appointment time based on professionals' assessment of the severity of their health needs [19]. The time span between first symptom and HCS visit may be related to whether specific symptoms are considered "alarming" enough to trigger immediate action by patients and/or health care professionals [13]. The HCS may thus contribute to patient delay through its' varied response in determining the time point for first HCS visit. For example in this study, a lump/resistance, hemoptysis and neurological symptoms were found to be associated with shorter time spans, possibly because they are relatively dramatic discrete occurrences that led to immediate action from both patient and provider. Based on these and other data, more nuanced investigation of "patient delay" is warranted. The term "patient delay" implies that a particular individual is responsible and has a derogatory and morally normative tone.

The term "delay" does not always adequately represent other time spans either. Different types of diagnostic procedures and examinations are often carried out during different time spans [18], which should not be considered undue prolongations or waiting times. Patient's behaviors have also been found here to influence the length of other time spans in the trajectory to diagnosis, as illustrated in Table IV.

With the exception of Koyi et al. [7,17], the different designs used to study the time spans in the care trajectory hinder direct comparison. For example, Neal and Allgar [20] present data from a patient survey, whereas Corner et al. [9] base their conclusions on detailed interviews with a smaller number of patients. While our data is systematically collected and robust, it should be recognized that it represents only that which is assumed to be of relevance by patient and/or physician at the first visit with a specialist physician in respiratory medicine. It is possible that clinical assessments in this patient group previously dominated by men may have a gender bias. Data probing patients' experiences would be likely to provide further information, as suggested by Strömgren et al.'s [21] finding that symptoms omitted from medical records were documented in patients' self-reports.

There is little literature about the relationship between demographic factors and time spans in diagnosis and treatment of cancer, with only one British study found which was in part based on LC patients [20]. Much of the research has explored the time span from first symptom(s) to first HCS visit in breast cancer [22–24], although other time spans and patient groups have also been studied to a more limited extent [20,22,23,25]. Results are in consistent, with some studies indicating an influence of age [24] and marital status [23] on the time span from first symptom(s) to first HCS visit, while other find these variables to be without significant influence [22]. Such contradictory results might be explained by different HCSs in different countries, different type of cancers, as well as the lack of consistent design.

Neal and Allgar's [20] data on LC patients in UK indicated that age, marital status, ethnic groups and gender influenced time spans. They found that younger patients had longer total times in all time spans assessed, which is contrary to our data indicating longer time spans for the oldest patients. Although "ageism" is not formally acceptable in Sweden, it may informally exist [26].

We did not find that any time span in this study was influenced by gender. In their meta-ethnographic study Smith et al. [12] found that men viewed help-seeking as unmasculine and believed that women found it easier since they had more contact with the HCS, both for their own needs and for their families. Women, on the other hand, could

refer to work and family as priorities competing with their own health [12]. This could mean that while some women may have shorter time spans before contacting the HCS, others may prioritize differently, allowing longer time spans contacting the HCS. It is possible that these divergent patterns neutralize any apparent gender influence in studies such as ours and Neal and Allgar's [20]. A qualitative or person-oriented design might allow for a more nuanced understanding of patterns within groups of women and men.

In summary, the results of this study indicate the need to maintain and optimize effective care trajectories for persons with potential and newly diagnosed LC. Elderly people may be particularly vulnerable for extended time periods prior to diagnosis/treatment. Salander et al. [25] suggest that some symptoms are so common in everyday life, for example fatigue, that patients may be less inclined to identify them as an indicator of a serious disease. A more detailed and nuanced picture of symptom perception, patterns, characteristics and interactions is needed to help both patients and providers distinguish symptoms that may indicate LC. Regardless of possible effects on survival, access and contact with the HCS can be important for psychological well-being in this patient group with palliative needs.

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