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Patient-reported outcomes (PROs) in lung cancer: Experiences from a nationwide feasibility study

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ABSTRACT

Objectives: Our objectives were to examine the feasibility of a nationwide collection of patient-reported outcomes (PROs) in a lung cancer population as well as in various sub-populations, and to describe the characteristics of responders compared to non-responders.

Materials and methods: All patients diagnosed with lung cancer in Denmark are registered in the Danish Lung Cancer Registry (DLCR). The 7,295 patients registered in DLCR from 1 October 2013 until 30 September 2015 who had received treatment were eligible. Using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-LC13 questionnaires, we employed two different methods of delivery, resulting in two different project parts. In project part 1, the baseline questionnaire was handed out at the hospital departments before treatment. The following questionnaires were sent out as paper versions three times within one year. In project part 2, all questionnaires were electronic versions delivered in association with planned hospital visits.

Results: Of the 7,295 lung cancer patients 4,229 (58%) completed at least one questionnaire, and 2,459 completed two or more. Only 562 baseline questionnaires were returned before treatment (7.7%), whereas 43.4%–57.4% of the potential responders completed the following questionnaires. The best response rates were achieved among patients treated with surgery and among patients who discussed their questionnaires with health care personnel. When comparing patient characteristics, responders had a significantly better health and a higher socioeconomic position than non-responders.

Conclusion: A decentralised model used for delivering the initial questionnaire to the patients was insufficient. It is our estimation that sending out electronic versions of the baseline questionnaires, as was done with the following questionnaires, would result in a significantly better patient coverage. Despite the severe morbidity and high mortality rate in lung cancer, reasonable response rates were achieved at follow-ups to this method, and PRO collection in this population was feasible.

1. Introduction

Lung cancer is the most frequent cancer-related cause of death in Denmark and Europe. Approximately 3,600 people die of the disease each year in Denmark [1], and in Europe in year 2017, the predicted number of deaths from lung cancer was > 275,000 [2]. Survival has improved significantly during the past 10 years. Improved survival, meaning more years lived with lung cancer, makes it imperative to increase the focus on the course of the disease from the patients' perspective.

An accepted way to gain information about patients' symptoms and quality of life is through patient-reported outcomes (PROs). The

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American Food and Drug Administration (FDA), U.S., has defined PRO as *"…a measurement of any aspect of a patient's health status that comes directly from the patient (*i.e. *without the interpretation of the patient's responses by a physician or anyone else)"* [3]. Through many years, PROs have been used in randomised clinical trials (RCTs) for comparison of different treatment regimens or in studies describing the burden of different diseases. Furthermore, PROs have helped predict survival in cancer patients [4,5].

To find out more about the use of PROs in cancer treatment, and specifically about PROs used as measures of quality in lung cancer healthcare at the national level (e.g. PROs used in hospital benchmarking), we carried out a systematic review in which the literature search was done in collaboration with a research librarian. Searches were performed in three different databases (PubMed, Embase, and Cinahl), and we used search filters to include studies published in 2005-2015. The literature review protocol was registered in the PROSPERO database, registration number CRD42015016822 (where further details about the searches can be found). We searched for studies using PROs for the purpose of improving quality in both general cancer treatment and in lung cancer treatment in particular, e.g. PROs used as performance indicators for benchmarking. We found one study only in which Vickers et al. [6] described a surgeon performance feedback system after radical prostatectomy. However, not a single study was found on the use of PROs for performance measurement in lung cancer, and consequently the results have not been recorded for publication.

In Denmark, treatment of lung cancer has been audited on an annual basis for many years at the at the national level using performance indicators such as survival/mortality rates via the Danish Lung Cancer Registry (DLCR) [7]. These national performance indicators are based on data from the entire population of Danes diagnosed with lung cancer. Data in the DLCR originates primarily from national patient registries, actively supplemented by data from the clinicians; all Danish hospitals diagnosing and treating patients with lung cancer are obliged to report data to the DLCR continuously. The result is a complete and highly reliable national registry. However, no data in the DLCR contains information from the *patients'* perspective on life quality with the disease.

This feasibility study is the first of two studies aiming to investigate the possibilities of using PROs as performance indicators in an entire national population with lung cancer. In this first study, our objective was to examine the feasibility of nationwide PRO collection in this disease-burdened population. We employed two different methods of PRO collection, in the following explained as *project parts 1 and 2*, and we evaluated and compared data completeness. Furthermore, we investigated whether responders to PROs were representative of the whole population of eligible patients with lung cancer, and whether response rates were different between the two data collection methods and according to the type of treatment for lung cancer.

2. Method

We designed a prospective cohort study, with collection of PROs from all newly diagnosed Danish lung cancer patients in treatment. Patients were included through two years, and each patient included was encouraged to respond to a questionnaire at least four times within the first year after diagnosis. Data from all questionnaires returned was entered into the DLCR (described further below).

2.1. Patient population

Since the year 2000, the DLCR has monitored and evaluated the quality of treatment of all Danish lung cancer patients. Data in the DLCR includes information regarding the lung cancer diagnosis, the patient's performance status, comorbidity, initiation of the patient's first treatment and related events, including examinations, treatments and death. The comprehensiveness of the registry regarding patient population is estimated to be > 95%, for cancer stage 87%, pathology 95%, treatment variables concerning oncologic treatment 85% and surgical treatment 99% [7,8].

All patients registered with lung cancer in the DLCR from 1 October 2013 until 30 September 2015 were eligible for the project if they received treatment for their lung cancer. Patients without pathological verification of the lung cancer diagnosis were excluded.

2.2. Tools for the collection of PROs

As measures of PROs, we used the Danish versions of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 ("Quality of Life Questionnaire Core 30″) [9] and EORTC QLQ-LC13 ("Quality of Life Questionnaire Lung Cancer 13″) [10].

The QLQ-C30 version 3.0 is a generic cancer questionnaire assessing physical and emotional well-being, symptoms, side effects, social life, general health and quality of life (QoL) during the past week. It contains 30 items in 15 subscales (functional scales, symptom scales and global health/QoL). Scores from the scales can be estimated according to the Scoring Manual [11] and range between 0 and 100: a high score for a function scale or overall quality of life indicates good health, a high score for a symptom scale indicates a high level of symptoms.

The QLQ-LC13 is a disease-specific lung cancer questionnaire made to accompany the QLQ-C30. It contains 13 items about symptoms and medication during the past week (one multi-item scale to assess dyspnoea and 9 single items assessing e.g. coughing, sore mouth or pain in chest). Scoring the questionnaire is done the same way as with the symptoms scales/single items of the QLQ-C30, i.e. a high score indicates a high level of symptoms.

2.3. PRO data collection procedures in project parts 1 and 2

Questionnaires were delivered to the patients in two ways: either *(1)* as paper versions of the questionnaires sent out four times within one year, or *(2)* as electronic versions delivered several times in association with treatment and follow-ups (see next section).

All 17 hospital departments treating patients for lung cancer in Denmark participated. The hospitals were divided into two groups, collecting PROs according to two different routines, called project parts 1 and 2. The 12 hospitals participating in project part 1 included both surgical (all 4 departments in Denmark performing lung surgery) and oncological departments; the five hospitals participating in project part 2 included oncological departments only.

2.3.1. Project part 1

Patients had their first paper questionnaire ("QoL0″) handed out at their first visit to the outpatient clinic, before initiation of first treatment. The next three PROs were collected 3 months ("QoL1″), 6 months ("QoL2″) and 12 months ("QoL3″) after the date of first treatment. These points in time were chosen to follow the times for outpatient follow-up defined in the national follow-up programme for lung cancer patients in Denmark [12]. The questionnaires QoL1-3 were sent out to the patients by mail. However, the patient was also given the opportunity to log on to an internet site and fill out the questionnaire electronically. Once a month, the project collaborator "WestChronic™" received a file from DLCR containing all new registered cancer patients in DLCR, including information about the date of first treatment for each patient, and WestChronic™ sent the questionnaires to the patients. Prior to sending out questionnaires QoL1-3, the patient's vital status was checked in The Danish Civil Registration System [13], using the PINs. All paper questionnaires filled out by patients were received and scanned using optical character recognition by WestChronic™. WestChronic™ also received the electronic data submitted via web. Patients not returning questionnaires were sent a reminder by letter after 14 days, and a new questionnaire after 42 days.

2.3.2. Project part 2

The format of the questionnaires was electronic versions only. The additional purpose of this part of the project (beyond the collection of data for quality assessment) was to develop and test a model for systematic collection and use of PROs in the outpatient clinic [14]. Patients were asked to respond to questionnaires prior to each of their hospital visits, and they could choose to fill out the questionnaire from a computer at home or on a tablet in the waiting room before the outpatient clinical consultation. The department staff reminded the patients to fill out the questionnaires. Before the date of first treatment, the patient was informed about the project and was asked to fill out the baseline questionnaire online. Through the course of the 12-month data collection period, some patients filled out more than 4 questionnaires in total.

For the analyses of this paper, we used data from both parts of the project, but with the constraint that each patient could submit only four questionnaires. For patients participating in project part 2 (who could have more assessments than in part 1) we used the PRO data returned closest to the four time points in part 1, as described in detail below.

2.4. Dividing questionnaires in groups and defining “potential responders”

Questionnaires were divided into four groups according to the date of their return. Baseline questionnaires (QoL0) were only included in the analysis if they had been filled out no later than the day *before* initiation of first treatment. The follow-up questionnaires (QoL1-3) had to be filled out within the intervals 31–135, 136–240 and 300–420 days after initial treatment, respectively. If a patient had returned more than one questionnaire during a time window, only the one closest to a scheduled visit at 3 months (90 days), 6 months (180 days) or 12 months (360 days) after treatment was included. If a questionnaire was filled out outside the intervals, it was excluded. Questionnaires returned blank were considered a “non-response” and classified as missing.

Patients were considered “potential responders” to the four questionnaires if they were alive on the day of initiation of first treatment (QoL0) and at 90 days (QoL1), 180 days (QoL2) and 360 days (QoL3) after first treatment, respectively. Patients who died before these time points were excluded from the *potential responder* group unless they (before their death) had answered a questionnaire within the planned time period.

As WestChronic™ ended the data collection in the summer of 2016, not all QoL3 questionnaires from patients diagnosed in 2015 were collected.

2.5. Data from DLCR

Based on pathology data registered in DLCR, patients were divided into four groups: *small cell carcinoma*, *squamous cell carcinoma*, *adenocarcinoma* and *other*. Lung cancer stages were registered in DLCR according to the 7th edition of the TNM classification for lung cancer [15] as follows: *IA, IB, IIA, IIB, IIIA, IIIB* or *IV,* defined by location and extent of primary and metastatic tumour involvement. First treatment after diagnosis, labelled “initial treatment”, was categorised as *surgery*, *curative oncology* or *palliative oncology*. The Eastern Cooperative Oncology Group (ECOG) Performance Status was also available in DLCR along with patients’ pulmonary function test of FEV1 (forced expiratory volume in 1 s). Both variables had been estimated before treatment, and they were used without further sub-classification. Charlson Comorbidity Index (CCI) [16] scores were grouped as 0, 1 and ≥ 2.

2.6. Socioeconomic and demographic variables

Even though the Danish health care system is tax-funded and provides free access to medical examinations and hospital treatment, differences remain between patients with different socioeconomic position. Studies have shown variability in outcomes according to social characteristics among lung cancer patients [17–21], and we therefore found it important to include data on patients’ socioeconomy in our analyses. At birth, every Danish citizen is given a 10-digit unique personal identification number (PIN) which is used in all patient identification processes in the Danish health care system (thus, PIN correlates to a combined version of the social security number, SSN, and the Medical Record Number, MRN). By means of the PIN, we obtained information from Statistics Denmark about socioeconomic position, including the highest attained educational level, disposable income, affiliation to employment market and cohabitation [22,23] at the time of inclusion. Using the PINs, we were able to merge the two datasets from Statistics Denmark and DLCR.

Highest educational level was categorised into three groups as in the study by Starr et al. [24]: *short* (i.e. mandatory education of up to 7 or 9 years for people born before or after 1 January 1958, respectively), *medium* (between 8/10 and 12 years, last grades of primary, secondary and vocational education) and *higher* education (> 12 years). Disposable income was defined as household income after taxation and interest per person, and based on the total population of eligible patients in the study period, we categorised disposable income by quartiles into *low* (first quartile), *medium* (second and third quartiles), and *high* (fourth quartile). Affiliation to the employment market was categorised into *in work (including studying)*, *unemployed* and *pensioner (including early retirement)*. Cohabitation status was defined as *living with a partner* if the patient was living with another adult person (> 25 years of age) in the household irrespective of marital status, or *living alone,* if the patient was the only adult person in the household.

2.7. Statistical analyses

The statistical analyses used to compare responders with non-responders in the different categories were the *t*-test and the chi-squared test. The significance level was set at $p \leq 0.05$. All statistical analyses were conducted in STATA statistical software, using the research servers at Statistics Denmark.

3. Results

3.1. Characteristics of patients with at least one questionnaire response (responders)

Fig. 1, shows the patients registered in DLCR during the 2-year study period. In total, 4,229 lung cancer patients (58% of the eligible patients) completed a least one questionnaire within our chosen time windows. Clinical and demographic characteristics of the participating patients are shown in Table 1. The characteristics of the 3,066 non-responders (living patients not completing a questionnaire or with no questionnaires within our chosen time periods) are shown for comparison as is the total population of eligible patients in DLCR during the 2-year study period.

The mean age of responders was 68 years (range 17–96), and the group consisted of a few more women than men (48.8% male and 51.2% female). Most of the patients had stage IV cancer (35.5%) at diagnosis, and lung cancer cell type was predominantly adenocarcinoma (45.3%). FEV1 was 73% of expected, performance status was 0 in 48.5% of the patients, and Charlson Comorbidity Index was 0 in 47.8% of the patients. Initial treatment was predominantly palliative oncology (42.4%) or surgery (31.1%). Most patients had attained a high or medium educational level, and patients were predominantly pensioners (77.8%) living with a partner (66.7%).

3.2. Non-responders compared to responders

Characteristics of the responders and the non-responders are presented for comparison in Table 1, and only differences with statistical

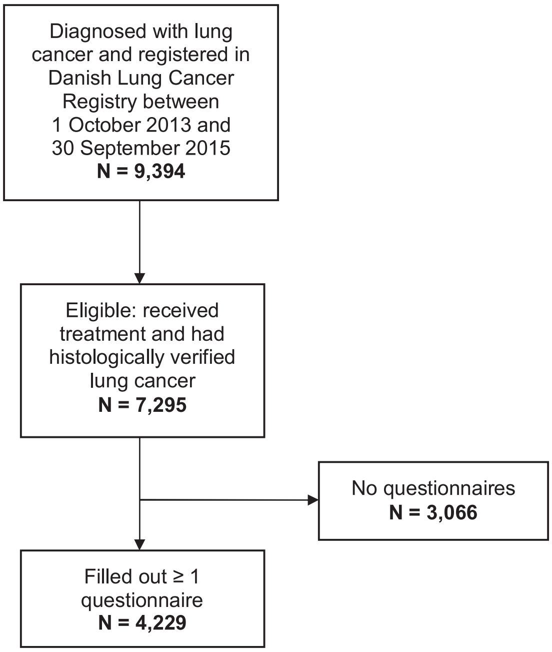

Fig. 1. Flowchart of the study population.

significance are mentioned here. In the group of non-responders, more patients were men (51.3% compared to 48.8% in the responders' group), cancer stages were higher (57.7% vs. 35.5% patients with stage IV), and more patients had small cell lung cancer (17.3% vs. 14.4%). FEV1 were lower (68% vs. 73%), and performance status poorer (30.2% vs. 48.5% with PF 0). More patients received palliative oncological treatment (72.2% vs. 42.4%), and fewer received surgical treatment (13.1% vs. 31.1%). Educational level and disposable income were lower (4.6% vs. 3.4% with a short education, and 28.6% vs. 22.5% with a low disposable income). More patients were pensioners (81.1% vs. 77.8%), and fewer patients were living with a partner (57.1% vs. 66.7%).

3.3. PRO questionnaires over time

The response rates for the four different time periods are shown in Table 2. As the first questionnaire was administered to patients by health care personnel in the hospital departments, it cannot be concluded how many of the 7,295 patients alive at this time point actually received QoL0 (the staff may have forgotten to hand out the questionnaires). The "true"/actual response rate at baseline is therefore unknown; nevertheless, as only 562 QoL0 questionnaires were received from 7,295 "potential responders", the response rate could be as low as 7.7%.

Response rates for QoL1-3 were 43.4%, 57.4% and 48.9%, respectively.

A minimum of two questionnaires was completed by 2,459 patients, predominantly the combination QoL1 and QoL2.

3.4. Response rates according to different methods of PRO delivery

The response rates divided according to mode of PRO delivery (project parts 1 and 2) are shown in Table 3. For QoL0, response rate was almost 8% higher for project part 1 (no use in the clinic), but for QoL1, response rate was almost 10% higher for project part 2 (use in the clinic). For QoL2 and QoL3, response rates were similar.

3.5. Response rates in different treatment groups

Response rates according to treatment group are shown in Table 4. The subgroup of patients treated with surgery had a remarkably better response rate than the groups with oncological treatment throughout the study, and response rates were lowest in the group receiving palliative treatment.

4. Discussion

This feasibility study showed a very poor patient participation at baseline (7.7%) when the hospital departments were responsible for PRO collection. Nonetheless, 58% of the eligible patients completed a least one of the four questionnaires, enabling us to compare responders to non-responders as well as two different methods of PRO collection and subgroups of patients receiving different types of treatment.

Responders and non-responders differed significantly on almost all variables (Table 1). Lung cancer stages were much lower in the responders' group, in which 27.8% had been diagnosed with stage I and only 35.5% with stage IV disease, compared to respectively 11.8% and 57.7% in the non-responders' group. Almost half of the patients (48.5%) in the responders' group had performance status 0 at diagnosis compared to less than one third (30.2%) of the non-responders. Initial treatment was also very different between the groups as 68.9% of the patients in the responders' group received some form of oncological treatment compared to 86.9% of the non-responders. The most remarkable differences in the socioeconomic variables were seen for income (28.4% of responders had a high income compared to 20.1% of non-responders) and cohabitation (66.7% of responders were living with a partner compared to 57.1% of non-responders). Because of all these differences, it would not be reasonable to assume that the responders' group is a representative sample of the total eligible population, and great caution should be made to avoid generalisations. However, the population of patients with lung cancer is known to be burdened with considerable morbidity and poor quality of life [25,26].

In this study, the poor patient participation at baseline clearly shows that the method of collection of this questionnaire failed. This is unfortunate as it makes it impossible to analyse changes in PROs over time for the whole population. We asked different department staff in our study about the missing baseline questionnaires, and their explanations for not handing out QoL0 were (among others) lack of time, insufficient information about the project from the project managers and individual decisions from the health care personnel not to burden very sick patients with 'time-consuming research'. From this, we concluded that the missing baseline questionnaires were not just missing at random, and imputational statistics were not applied.

Another explanation for the missing questionnaires could be the short time span from diagnosis to treatment in Denmark. As an example, patients having surgery for lung cancer are usually admitted on the day before treatment, and if they receive the questionnaires upon admittance, they have only the rest of the same day to complete them. For these reasons, we conclude that the responsibility to deliver questionnaires should not lie with the departments. It would have been a better solution to systematically send out these questionnaires by mail or as electronic versions as was done with QoL1-3. However, this solution is not without problems, either: the way the registration process of newly diagnosed lung cancer patients in DLCR is configured today, it is not possible to retrieve information on patients until they start treatment. Therefore, most QoL0 responses would take place *after* initiation of first treatment, not prior to.

If QoL0 were sent out electronically, as soon as the patient is booked for an examination for lung cancer in the patient health record system, the questionnaire would get to the patient much sooner. In Denmark (and in Norway and Sweden as well), the use of an online digital mailbox, called "e-Boks", has become the established electronic communication path between the health care system and patients [27]. *e-Boks* is an electronic mail system free of charge. It is linked to a patient's Danish PIN and is a secure way for the public authorities to communicate with Danish people. Thus, it is commonly used when patients are referred to hospital appointments. Since the introduction of the system

Table 1
Characteristics of responders, non-responders, and the total population of patients in DLCR treated for lung cancer during the study inclusion period.

	Responders (≥1 questionnaire)		Non-responders			Total	
	N =	%	N =	%	*p-value*	N =	%
Total	4229	**58.0**	3066	**42.0**		7295	**100**
Sex					0.033		
Male	2,063	48.8	1,573	51.3		3,636	49.8
Female	2,166	51.2	1,493	48.7		3,659	50.2
Age					0.008		
Mean	68		69			69	
Range	17 - 96		23 - 93			17 - 96	
Stage					< 0.001		
IA	757	17.9	236	7.7		993	13.6
IB	420	9.9	126	4.1		546	7.5
IIA	200	4.7	78	2.5		278	3.8
IIB	206	4.9	124	4.0		330	4.5
IIIA	511	12.1	286	9.3		797	10.9
IIIB	435	10.3	279	9.1		714	9.8
IV	1,500	35.5	1,768	57.7		3,268	44.8
Not reported	200	4.7	169	5.5		369	5.1
Cell type					< 0.001		
Small cell carcinoma	608	14.4	530	17.3		1,138	15.6
Squamous cell carcinoma	835	19.7	587	19.1		1,422	19.5
Adenocarcinoma	1,914	45.3	1,191	38.8		3,105	42.6
Other	872	20.6	758	24.7		1,630	22.3
Lung function, median					< 0.001		
FEV1 - % of expected value	73		68			71	
Not reported	707	16.7	689	22.5		1,396	19.1
ECOG Performance status					< 0.001		
0	2,051	48.5	926	30.2		2,977	40.8
1	1,287	30.4	937	30.6		2,224	30.5
2	371	8.8	487	15.9		858	11.8
3	105	2.5	279	9.1		384	5.3
4	17	0.4	50	1.6		67	0.9
Not reported	398	9.4	387	12.6		785	10.8
Charlson Comorbidity Index					0.153		
0	2,020	47.8	1,405	45.8		3,425	46.9
1	918	21.7	663	21.6		1,581	21.7
≥ 2	1,291	30.5	998	32.6		2,289	31.4
Initial treatment					< 0.001		
Surgery	1,315	31.1	403	13.1		1,718	23.6
Curative oncology	1,122	26.5	450	14.7		1,572	21.5
Palliative oncology	1,792	42.4	2,213	72.2		4,005	54.9
Highest attained educ. level					0.001		
High	643	15.2	402	13.1		1,045	14.3
Medium	3,343	79.0	2,428	79.2		5,771	79.1
Short	145	3.4	142	4.6		287	3.9
Not reported	98	2.3	94	3.1		192	2.6
Disposable income					< 0.001		
High	1,172	28.4	585	20.1		1,757	25.0
Medium	2,025	49.1	1,492	51.3		3,516	50.0
Low	926	22.5	831	28.6		1,757	25.0
Not reported	106		159			265	
Affiliation to work market					< 0.001		
In work	792	18.7	416	13.6		1,208	16.6
Unemployed	144	3.4	159	5.2		303	4.2
Pensioner (incl. early retirement)	3,290	77.8	2,485	81.1		5,775	79.2
Not reported	3	0.1	6	0.2		9	0.1
Cohabitation					< 0.001		
Living with partner	2,820	66.7	1,751	57.1		4,571	62.7
Living alone	1,409	33.3	1,315	42.9		2,724	37.3

in 2001, Danes have become increasingly used to communicating electronically with their health caregivers, and it has now become mandatory for public authorities to use this type of communication with the population. Our study implicates that an electronic method of collection of PROs might be superior to a decentralised method, and it has already been proposed by the Danish health authorities that collection of PROs be implemented using e-Boks. Naturally, an electronic collection will cause a skew in responders with regard to e.g. age, disposable income and educational level, however, it has been shown in a report from Statistics Denmark that in 2017 e-Boks was by > 90% of the Danish population [28]. Only 21% of age group 65–89 years stated that they were not using the internet, which indicates that there might

Table 2
Potential responders (patients alive) and response rates (number of responses from potential responders) for the four questionnaires.

	Potential responders	Responders	
	N =	N =	%
QoL0	7,295	562	7.7
QoL1	6,121	2,656	43.4
QoL2	5,230	3,000	57.4
QoL3	3,899	1,908	48.9
Questionnaires in total		8,126	

Table 3
Inclusion and response rates in project parts 1 and 2.

	Project part 1			Project part 2		
	Potential responders	Responders		Potential responders	Responders	
	N =	N =	%	N =	N =	%
QoL0	5,027	507	10.1	2,268	55	2.4
QoL1	4,268	1,732	40.6	1,851	924	49.9
QoL2	3,709	2,143	57.8	1,521	857	56.3
QoL3	2,867	1,405	49.0	1,032	503	48.7
Questionnaires in total		5,787			2,339	

still be a demand for the choice of a paper version of the PRO questionnaires to achieve the best patient coverage among the elderly.

Regarding the choice between paper vs. electronic versions of questionnaires, the International Society for Quality of Life Research (ISOQOL) has released a user's guide for implementing PROs in clinical practice [29], which (among other things) describes the advantages and disadvantages of an electronic administration of questionnaires. The advantages are many, e.g. the possibility of linking PRO data to the patient's electronic health record and the enabling of adaptive testing. The electronic version saves resources and has fewer missing data, and with the new computerized adaptive testing (CAT) for the EORTC QLQ-C30 [30], patient burden will be reduced and measurement precision at patient level increased. As the EORTC CAT was not yet developed at the beginning of our study, we chose the "traditional" version of QLQ-C30, and it is possible that the length of the questionnaires (in total 30 + 13 = 43 questions) caused fewer patients to respond in this considerably disease-burdened population.

Response rates for QoL1-3 were considerably higher than for QoL0, and we compared rates between project parts. For the QoL1 questionnaire, response rates in the two project parts revealed a difference close to 10% in favour of project part 2, where patients were reminded of the questionnaires during each visit to the hospital, and health care personnel often discussed the patients' answers with the patient, to take care of problems arising during treatment. This was not the case in project part 1, where PROs were never planned to be discussed with health care personnel and were not available to the staff. This difference in setup is a reasonable explanation for the higher response rates in project part 2, however, it does not explain why the response rates did not continue to be higher in QoL2-3. The different composition of the populations in the two project parts might play a role here, too. Patients receiving surgery had higher response rates than patients receiving oncological treatment, and this could probably be explained by better health in this group. Patients who are offered surgery have lower cancer stages, better performance status and a better prognosis [8] than patients receiving oncological treatment. In project part 2, all of the participating hospital departments were oncological, no patients received surgery.

Bearing in mind the disease burden and lung cancer prognosis, we are relatively content with the response rates for QoL1-3. Regarding QoL3, WestChronic™ ended data collection around summer 2016, and therefore not all QoL3-questionnaires from patients diagnosed in 2015 were collected. As a consequence, there was a drop in response rates during the fall season of 2015 which affects the overall mean response rate. It is an unfortunate limitation of the study that the data collection did not continue until all four questionnaires were collected. Different approaches could be chosen to increase response rates. If health care professionals had placed greater emphasis on the importance of high compliance to completion of PROs when presenting it to patients (and on remembering the study), response rates could undoubtedly have been increased in this study. However, it would require a substantial amount of resources and personnel, during enrolment as well as later. The Clinical Trials Group (CTG) of the National Cancer Institute of Canada (NCIC) has accomplished very high response rates for PROs from cancer patients during treatment (> 90%) [31], and this was made possible because of several initiatives, e.g. educational sessions for personnel, consent forms for patients before collection of PROs, regular meetings for data managers, different kinds of compliance monitoring during collection and phone calls to remind patients of completing the questionnaires. Without this resource-demanding setting, other initiatives could be shortening of questionnaires or administration of questionnaires through an app for smartphones and tablets. In the future electronic versions of PROs might be introduced as a routine part of all visits to a hospital, and with the following increased awareness, response rates will undoubtedly increase as well.

The present study has several limitations some of which are already mentioned. We showed that responders and non-responders to the questionnaires differed significantly, which was an important finding. Our study population therefore does not reflect the entire cohort of patients diagnosed with lung cancer, and this is crucial to bear in mind when PROs are analysed and results are interpreted.

The most important strength of this study is the large national cohort of patients linked to a national quality database, which means that we have precise knowledge of the target population. To our knowledge, no studies have repeatedly collected PROs from lung cancer patients with the purpose of quality evaluation on this scale before. We have shown that collection of PROs is possible in a national setting and that import to a clinical database is feasible.

Table 4
Response rates by treatment group.

	Total		Curatively intended surgery			Curatively intended oncological treatment			Palliative oncological treatment		
	Responders		Potential responders	Responders		Potential responders	Responders		Potential responders	Responders	
	N =	%	N =	N =	%	N =	N =	%	N =	N =	%
QoL0	562	7.7	1,718	327	19.0	1,572	83	5.3	4,005	152	3.8
QoL1	2,656	43.3	1,658	787	47.5	1,503	683	45.4	2,960	1,186	40.1
QoL2	3,000	57.4	1,618	1,019	63.0	1,399	810	57.9	2,213	1,171	52.9
QoL3	1,908	48.9	1,537	765	49.8	1,145	582	50.8	1,217	561	46.1
Question-naires in total	8,126			2,898			2,158			3,070	

In our next study, we will analyse the PROs collected, and because of the heterogeneity of the total population of lung cancer patients (e.g. different prognoses), patients will be divided into groups according to their treatment. From the analyses of patients treated with surgery, we wish to develop a model which can convert PROs into measures of quality in the surgical treatment of lung cancer.

5. Conclusion

Despite severe morbidity and a high mortality rate in lung cancer, reasonable response rates were achieved at follow-ups. The best response rates were achieved among patients treated with surgery and among patients that discussed their questionnaires with health care personnel. The decentralised method of collection of baseline questionnaires used in this study is not recommendable unless a large effort is made to inform, educate and support the hospital departments in handing out the questionnaires. As an alternative, we propose electronic administration of questionnaires sent through the online digital mailbox e-Boks used in the Scandinavian countries and linked to the health record system. To increase patient coverage, patients could be offered the possibility of using a paper version of the questionnaire received in a letter.

Non-responders differed significantly from responders. At diagnosis, responders had lower lung cancer stage, higher performance status, fewer had NSCLC, more were treated with surgery, income was higher, and more were living with a partner. Therefore, the collected PROs do not provide a representative picture of how the whole population of patients with lung cancer perceives their health, symptoms and quality of life during the course of disease. However, if efforts are made to increase response rates further, particularly at baseline, collection of PROs in a national setting is definitely feasible.

Conflict of interest statement

The authors declare no conflict of interest.

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