Lung cancer on Haugalandet, Norway

A long term follow-up study

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Scientific environment

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2. Aknowledgement

After some years work from 1990 as the only chest physician at Haugesund County Hospital the question emerged from a clinical point of view: How are the lung cancer patients doing?

Professor Amund Gulsvik kindly invited me to discuss possible research questions, and how these questions could be answered by an epidemiological study. Gradually a project protocol was formed. Later Amund has supported me through the various phases of the study, and I want to express my sincere thanks. You always found an opportunity for a meeting the many times when I needed guidance. A population based long term follow up study needs time, and when most of the work is done outside ordinary working hours it takes additional time, but you have always encouraged me through these years.

Likewise I want to thank my second supervisor professor Geir Egil Eide for the guidance through the statistics needed for this study. You have patiently taken me through the various analyses of the data and the interpretation of the results. In addition you have given advises regarding study protocols, in making tables and figures, and worked with the manuscripts in details.

At The Regional Centre for Clinical Research I was always welcomed both in the coffee breaks and during the statistical sessions with Geir. Thanks to all of you under the leadership of my good friend professor Ernst Omenaas. From this centre I was granted a 50% scholarship for 3 months from The Health Region West in the early phase of the study, which helped me to collect the data for the first paper.

In Haugesund hospital the daily work load could be heavy in periods. It has however been a positive experience to work in this environment where colleges care for each other. I thank specially dr. Sverre Fluge who in spite of much work supported me all the time both in the clinical work and in participating in the study itself. Also thanks to our present director Laila Nehmeth for support in the final stage of this project. Our research coordinator Doris Gundersen has been of help in various ways, especially when finishing the first paper, and by applying for economical support in the beginning of the study.

The Institute of Internal Medicine at the University of Bergen has been my part time employer the last 11 years in teaching and administrative work with the medical students. In periods

between the student groups I have sometimes got opportunities to do research work within the ordinary working time. The contact with the university and also with the university clinic, Department of Thoracic Medicine at Haukeland University Hospital, under the leadership of dr. Kahtan Al-Azawy, has been stimulating for me in the scientific and clinical work.

I also thank GlaxoSmithKline who invited me to participate at the yearly congresses at The American Thoracic Society for some years, thus giving me the opportunity to present parts of this work.

Most of all I thank my dear wife Sigdis for supporting me through the years with this project. Your positive encouragement has been most important to fulfill this thesis.

3. Summary

3.1 Background

Little was known on long term survival, the use of hospital days, symptoms both initially and terminally, and the quality of lung cancer care for the population of the patients with lung cancer in Haugalandet, Norway.

3.2 Material and methods

In a retrospective study we followed a cohort of all incident lung cancer patients from 01.01.1990 to 31.12.1996 in the hospital area of Haugesund hospital (Haugalandet). To study the predictors for long term survival we followed the patients either to death or to the last follow up to 31.12.2008. All hospital admissions and hospitalization days were recorded for all patients up to 01.12.2003. We studied the terminal symptoms in the last eight weeks of patients' lives who died before that date. Finally, we compared for the same time period four quality indicators in the patient cohort from the local hospital-based lung cancer registry (LCR) with the patient cohort in the Cancer Registry of Norway (CRN) both from the same geographical area (Haugalandet), and a cohort of all lung cancer patients from the rest of Norway.

3.3 Results

A total of 271 patients were diagnosed with lung cancer in these seven years. The long term survival was poor, with one-year survival of 29.2% and five- and ten-year survival of 8.5% and 5.5%, respectively. The median (IQR) survival time was 5.7 (1.9,14.1) months. No weight loss, young age, limited stage, good performance status and surgical treatment were predictors for long survival, which were also not influenced by the diagnostic delay time.

Furthermore, we found that all 271 patients had a median number (inter quartile range, IQR) of 3 (2,5) admissions and 35 (18,58) hospitalization days. Those who did not survive spent 19% of their remaining life time in institutions. Young age, limited disease and good performance status were associated with high number of hospital days, but these effects were not significant when adjusted for treatment.

Information on symptoms in the terminal 8 weeks was obtained in 247 of the patients who died before 1st December 2003. Pain was observed in 85%, psychological symptoms (anxiety, insomnia and/or depression) in 71%, dyspnea in 54%, neurologic symptoms in 28%, cough in 24%, nausea in 21%, and hemoptysis in 9%. Young age and small cell cancer (SCLC) were risk the factors for psychological symptoms, and initial stage III disease was a risk factor for terminal dyspnea. Terminal cough was associated with NSCLC and nausea with SCLC.

The average minimal difference of clinical importance judged by 26 physicians for four lung cancer quality indicators (histological/cytological verification, staging, surgery and one year survival) varied from 18% to 23% from the national average of the indicators.

The level of the four quality indicators studied was in agreement with the patient cohort from Haugalandet and the cohort from the rest of Norway. However, the sample sizes necessary to detect a 20% difference from the national average (power 0.80, $p<0.05$) varied from 435 to 2826 cases depending on the prevalence of the indicators.

3.4 Conclusions

The long term survival of lung cancer is poor, with only less than 10% of the patients surviving after five years. The patients who died spent one fifth of their remaining time after

diagnosis in health care institutions. Those with limited disease and young age had most days in the hospital. All patients had one or more symptoms requiring treatment in the terminal stage of the disease, and pain was the most frequent symptom in 85% of the patients. The quality of lung cancer care is difficult to evaluate in small management units. The small decentralized units should thus be merged to larger cooperative units with standardized routines. A national quality registry on lung cancer would then be a powerful tool contributing to improved quality of local lung cancer care.

4. List of abbreviations

CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRF	Case record form
CRN	Cancer Registry of Norway
CT	Computer tomography
EUS	Endoscopic ultrasound
EGFR	Epidermal growth factor receptor
F	Female
HR	Hazard ratio
ICD	International Classification of Diseases
IQR	Inter quartile range
LCR	Local cancer registry
M	Male
MCID	Minimal clinical important difference
MID	Minimal important difference
NSCLC	Non-small cell lung cancer
PET	Positron emission tomography
PS	Performance status
QOL	Quality of life
RCT	Randomized controlled trials
SCLC	Small cell lung cancer
SD	Standard deviation
UICC	Union for International Cancer Control

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7. List of papers

1. Skaug, K., Eide, G.E., Gulsvik, A. (2011) "Predictors of long-term survival of lung cancer patients in a Norwegian community." Clin Respir J **5**(1): 50-8.

2. Skaug, K., Eide, G.E., Gulsvik, A. (2009). "Hospitalisation days in patients with lung cancer in a general population." Respir Med **103**(12): 1941-8.

3. Skaug, K., Eide, G.E., Gulsvik, A. (2007). "Prevalence and predictors of symptoms in the terminal stage of lung cancer: A community study." Chest 131(2): 389-94.

4. Skaug,K. , Eide,G.E, Langmark,F. and Gulsvik, A. (2011): "National registry and control of care of lung cancer. Experiences from a Norwegian community." Submitted for publication.

8. Introduction

8.1 Incidence, mortality and survival of lung cancer

Until 1990 no data were published on lung cancer from an entire population in defined hospital areas in Norway. The hospital area belonging to Haugesund hospital, Haugalandet, consists of municipalities both from Rogaland and Hordaland county. In these two counties there was a steady increase in the incidence of lung cancer from the start of registration in the Cancer Registry of Norway (CRN) until the present study (1) (figure 1 and figure 2).

Figure 1 Age adjusted incidence rate of lung cancer in trachea, bronchus and lung per 100 000 in Rogaland county 1956 – 1995

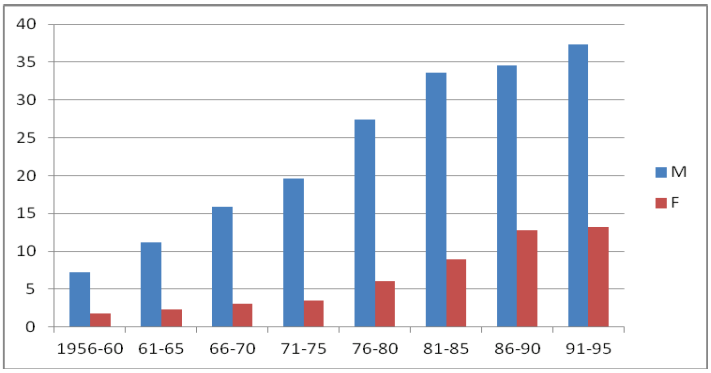
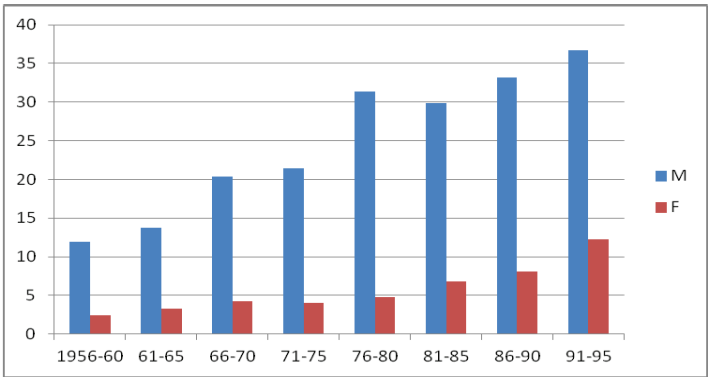
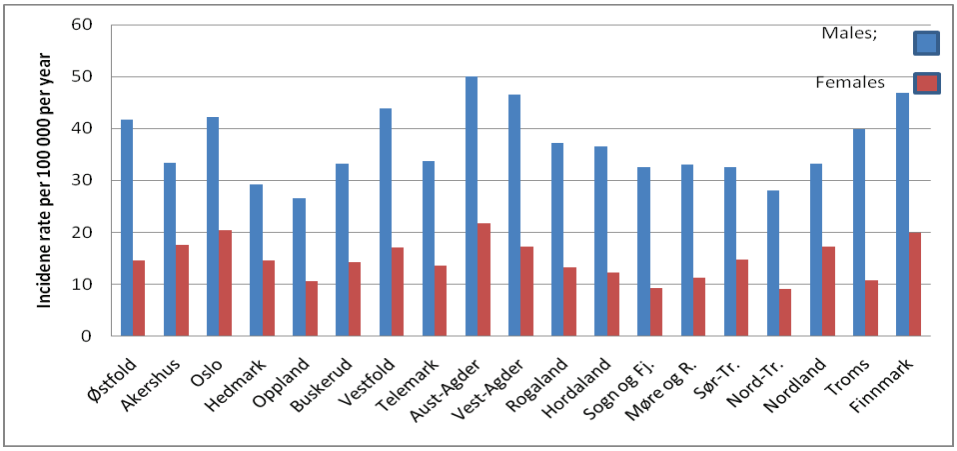


Figure 2 Age adjusted incidence rate of lung cancer in trachea, bronchus and lung per 100 000 in Hordaland county 1956 – 1995



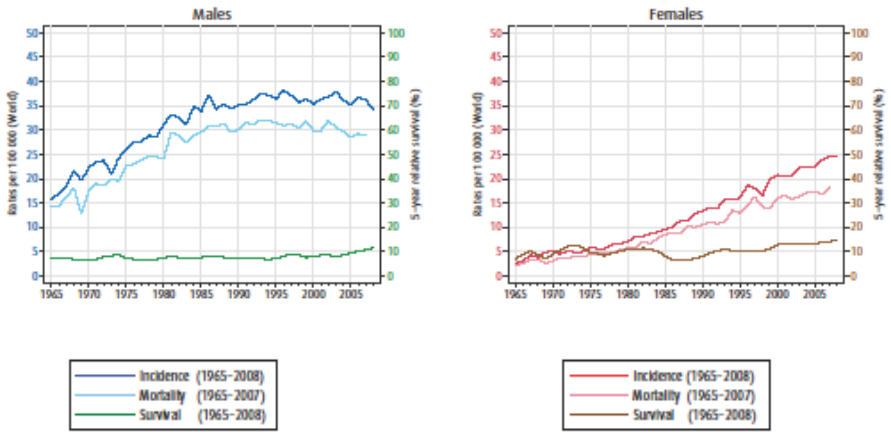
Within Norway (2) there are marked differences in the incidence between the counties (3), as it was at the time of this study (figure 3), but there is no valid explanation for this (1), therefore it will be discussed in chapter 12.1.4.

Figure 3 Incidence of lung cancer in Norwegian counties 1990 – 95



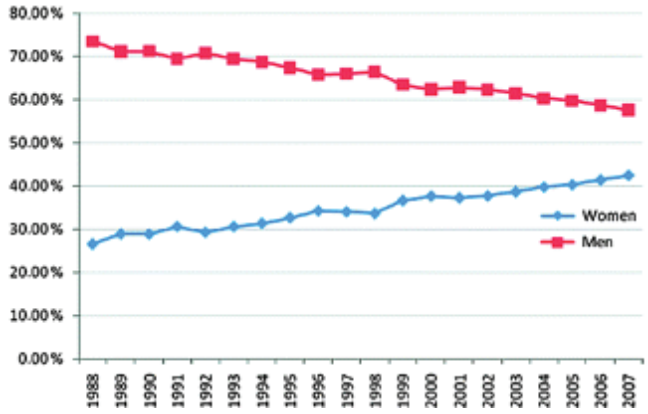
The mortality rate in lung cancer among men in Norway has reached a plateau (4, 5) while the incidence in women continues to increase (figure 4)(6).

Figure 4 Trends in incidence and mortality rates and 5-year relative survival proportions in lung cancer in Norway (ICD-10, C33-34, from Cancer Registry of Norway, 2008)



Thus, the lung cancer incidence between young males and females in Norway in from the years 1954 – 1998 was converging the last 20 years of this period (figure 5) (6).

Figure 5 Sex specific incidence fraction of lung cancer in Norway from 1988 – 2007 (Sagerup et al 2011)



Globally, 1.35 millions new patients were estimated to be diagnosed with lung cancer in 2002, which is the most frequent cause of cancer death (7). In developed countries the incidence is declining in males (7-10) while there is a lower but increasing incidence in women (11-14). There are great differences in the incidence of lung cancer among the countries (11, 15).

Squamous cell carcinoma was previously the most frequent histological subtype, but there has been a shift to adenocarcinoma as the most prominent subtype in Norway (6). This is also in agreement with the findings in a Sweden (13), Finland (16) and the U.S. A. (8). No data were available for the Haugesund hospital area for the incidence and mortality of lung cancer by sex, age, stage, histology and performance status.

8.2 Etiology of lung cancer

8.2.1 Tobacco smoking.

A connection between tobacco smoking and lung cancer was found early in Norwegian studies (17), and was later well established (18). A dose-response relation between tobacco consumption and lung cancer is found in most studies (4, 19, 20). In Northern Sweden, an increase in the smoking prevalence was followed by an increase in lung cancer mortality (21). Smoking was strongly associated with lung cancer risk in a large prospective American study (22). Among 219 Norwegian lung cancer patients referred to a central hospital only six (3%) were non-smokers (23). This strong association between tobacco smoking and lung cancer may explain that the incidence of lung cancer in men is declining following a decrease in tobacco smoking (7-10). There is an increasing incidence of lung cancer in women following the increased use of cigarettes in females (6, 11).

8.2.2 Other risk factors.

Passive smoking represents a risk factor for lung cancer according to evidence found in studies of non-smoking women exposed to passive smoking from their spouses (8, 24). Adenocarcinoma in a woman's lung exposed to passive smoking was recognized as an occupational disease (25). The risk for lung cancer was associated with passive smoking at their homes in Japanese non-smoking women, and if they were exposed to additionally passive smoking at the workplace (26).

Occupation exposures are known to be important etiological factors for lung cancer, and it is the most known work-related cancer (27). In a national cohort study from Norway on 53 occupational groups after adjusting for active smoking, an excessive risk of lung cancer was found in 26 groups, and 20% were considered to be related to exposure of asbest, polycyclic aromatic hydrocarbons, arsenics, certain metal compounds and radon (28). The population

etiological fraction attributed to occupation was estimated to 9% in a case-control study from Sweden (29). Two recent case-control studies from the New-Zealand and Italy found increased risk of lung cancer associated both with current and past occupational exposures (30, 31).

Radon exposure is known for a long time as a risk factor for lung cancer both as occupational risk (32, 33) and as a risk factor due to domestic exposure (34). In a study of indoor radon exposure in 427 municipalities in Norway the incidence of small-cell anaplastic lung cancer (SCLC) increased with increasing radon exposure (35). However, measurements of radon concentrations showed great variations between counties, and municipalities, as well as between houses within the municipalities (36). The counties Hedmark and Oppland with the highest radon measurements were among those with the lowest lung cancer incidence (figure 3), and Aust-Agder with the highest lung cancer incidence had low radon measurements.

Socioeconomic factors have been studied in a meta-analysis. A low level of education, low income and socioeconomic occupation were associated with increased risk for lung cancer, after adjusting for tobacco smoking (37). In a Danish study the incidence rate of lung cancer has increased with social disadvantages as poor employment status, being unmarried, urbanization and the presence of somatic or psychiatric diseases (38). In two studies of European countries a higher lung cancer mortality rate in men was found in the groups with low educational level compared to those with high education. However, in women in Southern Europe low lung cancer mortality was associated with low educational level (39, 40). The question is always how well these studies have adjusted for tobacco smoking. Both studies suggest that differences in prevalence and intensity of smoking contribute to variations in the lung cancer mortality.

8.3 Predictors of long term survival in lung cancer

In 1981-85 a five year overall survival of lung cancer in Norway was 8.5% for men and 8.1% for women, according to CRN. In 1986-90, the corresponding percentages were 8.6% and 10.0%, respectively (41). Age and anatomical stage were prognostic factors for survival. In West Sweden, the 5-year survival rate was 8.3% in 1976-85 (42). In a population-based study of all incident lung cancer patients in Scotland in 1995 the 3 year survival was 7%, and predictors for survival were localized disease, active treatment within 6 months after diagnosis, young age, and involvement of a lung cancer specialist (43). In lung cancer patients diagnosed in USA between 1995 and 1998 Tammemagi found that adverse symptoms such as weight loss, fatigue, neurological symptoms and extensive stage were negative predictive factors for survival (44). The influence of delay time from symptom onset to diagnosis on survival was examined in lung cancer in patients from 1987-89 in Spain. Surprisingly, a long delay time was associated with better survival (45). This conflicting evidence for predictors of long term survival was of importance for the lung cancer population of Haugalandet.

8.4 Hospital admissions and days in lung cancer care

There are great variations in most studies of the use of resources in lung cancer patient populations depending on the items of costs which are included (46). However, a common finding is that hospitalizations are a main cost driver (47-49) counting for 40 – 70% of the expenses in lung cancer. Some cost studies included only patients given chemotherapy (50), and other at certain stages of the disease (51).

The resources used on all lung cancer patients were not available in a community which included admissions and hospital days in the whole course of the disease. Hospitalization (admissions and hospital days) was the major cost driver in a retrospective study on patients with SCLC referred to hospital from 1994-97 (52).

Lung cancer is a serious disease, and many patients are asking the physicians about the time necessary to stay in the hospital. Knowledge on such data was not available at the time of the study.

8.5 Terminal symptoms in lung cancer

Symptoms are the main causes for patients seeking health care services and physicians. Studies on terminals symptoms in all lung cancer patients were not available. In a study in England on patients with NSCLC recruited from chest clinics, 80% experienced cough, 60% chest pain, 90% dyspnea and 20% hemoptysis the last two months before death (53). As much as 90% of lung cancer patients referred to a palliative care service in Italy had pain (54). In the recent years most studies on the effect of various treatment options include quality of life (QOL) as one of the end-points (55-57). Methods used to get information on QOL are poorly applicable in terminal care, since many of the terminally ill patients are too sick to fill out the questionnaires (58). In a prospective population-based study on lung cancer in South-Norway, about 40% of the patients did not answer the health related QOL-questionnaires (59) already at the time of the diagnosis. The patients not answering were older and had poorer performance status than those who answered. A usual exclusion criterion of patients with advanced lung cancer invited to multicenter studies is: no ability to fill out the quality of life questionnaire. Knowledge on the prevalence and predictors of terminal symptoms is one prerequisite for good palliative care management.

8.6 Quality of lung cancer care

8.6.1 Quality indicators

Lung cancer care is a complex disease, and there is no agreement how to measure quality (60). In a study among the Nordic countries the aim was to do benchmarking on the quality of care both in lung cancer and other important diseases by using quality indicators. However,

the conclusion was that the differences between the countries in e.g. legislation and reporting data were so great that comparisons were impossible and that present modern health care systems were not able to report their quality (61).

Quality indicators may be focused on firstly structure of care, e.g. which resources are available to do the diagnostic work and treatment, and secondly on process of care which refers to the treatment actually given to the patient (62), which is often based on guidelines. The third type is the outcome indicators, as 30 days survival after lung cancer surgery, or one year mortality (60, 63). Much of the work with quality indicators in lung cancer care is done on surgically treated patients as in Denmark. Indicators are here used in a quality registry which seems to have contributed to an improvement in the quality of lung cancer surgery (64). Such registries for lung cancer are also in use in England (65). In Norway a quality registry was made for all operated lung cancer patients in a 10-year period from 1993-2002 (66), but there are otherwise no nationwide quality registry for lung cancer. No knowledge was available on the quality of lung cancer care in a defined hospital region in Norway.

8.6.2 Minimal important difference (MID)

MID is defined as the smallest benefit in an outcome that has an impact on the management of the disease by clinicians (67). Some use the term 'minimally clinically important difference' (MCID) (68, 69), and underline the importance of participation of the patients to judge the difference in care (70). Such a difference must be meaningful for the patient in addition to have an influence on the management of the disease (70, 71). MID can be applied on outcome variables in chronic obstructive pulmonary disease (COPD) as six-minutes walk test (72) or as quality of life (QOL) (73). In oncology, response to the treatment can give meaningful differences for the physicians in endpoints as tumor volume (68), while in a QOL instrument as the Functional Assessment of Cancer Therapy – Lung (FACT-L) the patients perception of

QOL is taken into account (74). The MID and MCID are important in the calculation of the sample size in a study (67, 75). The sample size has to be higher to detect a MID for an outcome of low prevalence compared to a high prevalence (76). At the time of the present study (1990 – 96) there were no available studies in Norway based on the whole population of lung cancer patients in a hospital defined geographical area. The only source of data was The Cancer Registry of Norway (CRN). In spite of a high quality of the data (77) one could question how complete the data were, since NCR did not get access to the hospital registries before 1998.

To ensure the quality of the lung cancer management it was a great demand to do a careful follow up study on the whole population of lung cancer patients. By applying scientific methods a basis was build for comparative studies, both with other parts of Norway and with future studies in our own geographical area. Furthermore, it was a demand to get experience in applying scientific methods in the daily clinical work in a non-university institution with little tradition in this matter.

On this background we initiated this retrospective study on all lung cancer patients in the hospital area of Haugesund hospital to get answers to the research questions of chapter 9.

9. Research questions

The aims of this study including all lung cancer patients in a defined community were to find answers to the following research questions:

9.1 a) What was the incidence of lung cancer by age, gender, UICC anatomical stage of tumor and performance status of lung cancer? b) What predicted the survival in the population of lung cancer patients at Haugalandet, Norway?

9.2 How many hospital admissions and hospital days have lung cancer patients from diagnosis until death?

9.3 Which symptoms require treatment in the terminal stage of lung cancer?

9.4 a) How is the quality of lung cancer care in our hospital area compared with the rest of Norway? b) What are the minimal important differences of lung cancer quality indicators for physicians to change their management?

10. Materials and methods

10.1 Study design

This is a retrospective study of a patient cohort of all incident lung cancer patients at Haugalandet in seven years 1990-1996. It is also a longitudinal follow up study of the same patient cohort until 31.12.2008.

10.2 Geographical area

Haugalandet is located in southwest Norway and included the city of Haugesund and 10 surrounding municipalities at the time of the study; three from Hordaland County and the rest from Rogaland county (figure 6)

.

Figure 6 Map of Haugalandet, Norway, with the 11 municipalities

Haugalandet with the municipalities Bokn, Etne, Haugesund, Karmøy. Sauda, Suldal (northern part), Sveio,Tysvær, Utsira, Vindafjord and Ølen (later Ølen and Vindafjord have later merged to one municipality).

10.3 Population

In 1992 the hospital district had 98 316 inhabitants, 49 507 men and 49 809 women (table 1).

Table 1 Population by gender and age by 11 municipalities at Haugalandet 1. January 1994 (source: Statistics of Norway)

Age		0 - 15	16 - 66	67+	Total
Municipality					
Bokn	M	84	255	50	389
	F	89	223	74	386
Etne	M	449	1247	291	1 987
	F	441	1109	377	1 927
Haugesund	M	3 013	9 137	1 676	13 826
	F	2 907	9 026	2 911	14 844
Karmøy	M	4 434	11 823	1 612	17 869
	F	4 392	11 162	2 222	17 776
Sauda	M	574	1 657	360	2 591
	F	552	1 566	490	2 608
Suldal	M	502	1 266	323	2 091
	F	468	1 161	377	2 006
Sveio	M	644	1468	245	2 357
	F	572	1365	343	2 280
Tysvær	M	1 109	2 644	380	4 133
	F	1 029	2 423	487	3 939
Vindafjord	M	621	1 584	346	2 551
	F	561	1 351	434	2 346
Ølen	M	384	995	213	1592
	F	368	924	309	1601
Utsira	M	31	67	23	121
	F	17	49	30	96
Total	M	11 845	32 143	5 519	49 507
	F	11 396	30 359	8 054	49 809

10.4 Management of lung cancer patients in Haugesund hospital 1990-96

Of the patients 63% were referred from primary care physicians and 24% from other specialists (table 2). The hospital had only one authorized chest physician who was part of the team doing general internal medicine (principal investigator). Younger physicians assisted the chest physician. Medical history and clinical examination were obtained on the day of admission. Spirometry and chest X-ray were performed on the same or following day, followed by computer tomography (CT) scanning and bronchoscopy. In two patients we did not obtain the reports from x-ray thorax, but CT was performed. A higher proportion of the patients not examined with spirometry (37%) or bronchoscopy (16%, table 2) were older, had poorer performance status, more extensive disease and got supportive care only compared to those who underwent these procedures (data not shown). Transcutaneous biopsies of peripheral tumors were guided by CT. These procedures were in agreement with international textbook recommendations (78). Mediastinoscopy was performed by referral to university hospitals. Anatomical staging was done on the basis of X-ray, CT, bronchoscopy, biopsies and cytological specimens (79).

Radiation treatment was given at Haukeland University Hospital, Bergen. The capacity for radiology treatment was low, and the patients had to wait six to eight weeks for palliative treatment like other hospitals in Norway (80). Thoracic surgery was for the 5 first years done at Haukeland University Hospital or at Stavanger University Hospital depending on the patient's residence. Lung cancer surgery was also performed at Haugesund Hospital in 1994-96. The role of chemotherapy in NSCLC was not yet established (81) and it was given mainly to patients with SCLC.

Table 2 Reference pattern, diagnostic procedures and initial treatment in 271 lung cancer patients of Haugalandet 1990-96

N(%)	271(100)
Referral to hospital from	
Primary care doctors	171(63)
The National Mass Radiography Service	7(3)
Other hospitals and health institutions	17(6)
Other specialists (ENT, radiologists, surgeons)	64(24)
Direct contact to lung specialist from the patient	12(4)
X-ray thorax (report present)	
Yes	269(99)
No	2(1)
CT thorax	
Yes	227(84)
No	44(16)
Spirometry	
Yes	171(63)
No	100(37)
Bronchoscopy	
Yes	226(84)
No	45(16)
Initial treatment	
Surgery (resection)	31(11)
Chemo- and/ or radiotherapy	141(52)
Best supportive care	99(37)

After diagnostic procedures and initial treatment the patients were discharged from the hospital, and thereafter ambulant followed as outpatients twice a year. Patients with relapse of the disease were only given best supportive care. Regular treatment with opioids was initiated in hospital and followed up in a primary health care setting. Second line chemotherapy was only given in exceptional cases. Haugalandet had no separate hospice institution, and terminal care was provided in the local hospital, in local nursing homes and at home. The 16 nursing homes in the municipalities were staffed with nurses and served by a physician at least once

weekly. A palliative care nurse at the hospital made home visits to the patients on a direct request by patients or his/hers general practitioner. Patients with advanced disease and metastasis were offered direct admission to the local hospital at their own request.

10.5 Sources of data

10.5.1 Haugaland Local Lung Cancer Registry (LCR).

All incident lung cancer patients admitted to the hospital in 1990 – 1996 were included in the study. Three patients were diagnosed at Haukeland University Hospital, one at Stavanger University Hospital and the other 267 at Haugesund hospital. The medical reports from all 128 patients with 192 admissions in other hospitals (table 3) were collected together with all records from Haugesund hospital in one single journal for each patient and stored in a patient archive.

Table 3 Distribution of incident patients with lung cancer 1990-96 admitted in other hospitals than Haugesund County Hospital

	Surgical resection	Radio- and/or chemotherapy	Supportive care only	Total
Haukeland University Hospital	15	78	4	103[b]
Stavanger University Hospital and other hospitals[a]	11	21	2	28[b]

[a]Stord county Hospital, The Norwegian Radium Hospital

[b]Three patients were admitted both in Haukeland University Hospital and other hospitals

From the archive the patients' journals were brought to the physicians performing the study. The medical records from all patients given from CRN were found in the hospital archives and could thus be studied. Patients misdiagnosed or double recorded were excluded (figure 7). The diagnosis of lung cancer was defined by neoplastic histology, cytology or convincing radiologic signs (chest radiography, CT).

10.5.2 The Cancer Registry of Norway (CRN)

This is population based and receives clinical and pathology reports for all cancer patients in Norway. From 1998 information from hospital patient administrative systems and other centers dealing with cancer patients are also sources of information. Information from death certificates comes in addition. It is mandatory to report cancer to CRN, and patient's consent is not needed. Therefore, the completeness of CRN is estimated to be very high (77). The data from the CRN are readily available for the whole country and for each of the 19 counties via annual reports and on the website (2), and on the request for health regions and municipalities. The stages of solid tumors in CRN consist of three categories which is different from the International System of Staging Lung Cancer (appendix 17.1). About 30 physicians at Haugesund hospital had participated in filling out the routine forms for CRN, according to the law. Information was subtracted regarding gender, age, histology and stage for all new patients with lung cancer, as well as on the number of patients that were operated on, and their overall survival after 1, 5 and 10 years. Data on other treatment options were not sufficiently complete for a further analysis.

10.6 Inclusion and exclusion of patients

Inclusion criteria in this hospital area survey were as follows: 1. All new patients in the hospital records of Haugesund Hospital with lung cancer in ICD 9 (1990-96). 2. All new patients in the CRN with lung cancer in ICD 7, (1990–92) and ICD 9 (1993–96). Hospitalized patients diagnosed with lung cancer in the same period but resident outside this hospital area were excluded (figure 7). From the hospital records in 1990-96 we found 312 patients (figure 7) by searching on the diagnosis number according to the International Classification of Diseases 9 (ICD-9). However, 21 patients were diagnosed before 1990 (prevalent). Of the remaining 291 patients 24 had diagnosis like lymphoma, thymoma, tuberculosis, embolus of

the lung, neuroectodermal tumor in mediastinum and liver cirrhosis with ascites. Examples of patients reported to CRN with incorrect diagnosis according to the hospital records were patients with pleural fluid in heart failure with possible atypical cells, or lung infiltrate with atypical squamous cell in bronchial biopsy proven to be tuberculosis. On the other side some patients with serious concomitant diseases as the main diagnosis and who also had lung cancer were not initially reported to CRN, e.g. a patient with leukemia or patients seriously ill from heart disease. Among the patients with initially incorrect diagnosis from CRN were three with metastasis, but without localization of primary tumor, and one with prostate cancer. Such patients later got the initial diagnosis changed and were no longer registered as lung cancer patients in CRN.

Twenty-one patients had been diagnosed before 1990 (prevalent cases). Eight patients were living outside our hospital area. From the hospital records 259 patients were thus included in the study, and 15 of these were not found in the records from CRN where 264 patients were reported. Three were double recorded and in five patients the diagnosis was not correct. Thus 256 patients were included from CRN, but 12 of these were not found in the hospital records diagnosed with lung cancer and thus 244 patients were common in both records. We were however able to trace all these 12 patients in the records of Haugesund Hospital because of their birth number, and they had lung cancer. Thus the total number of eligible patients then became 271 (figure7, and figure 8). Altogether 214 (78%) were men and 57(22%) were women (table 4a, figure 8).

Figure 7 Inclusion and exclusion of patients

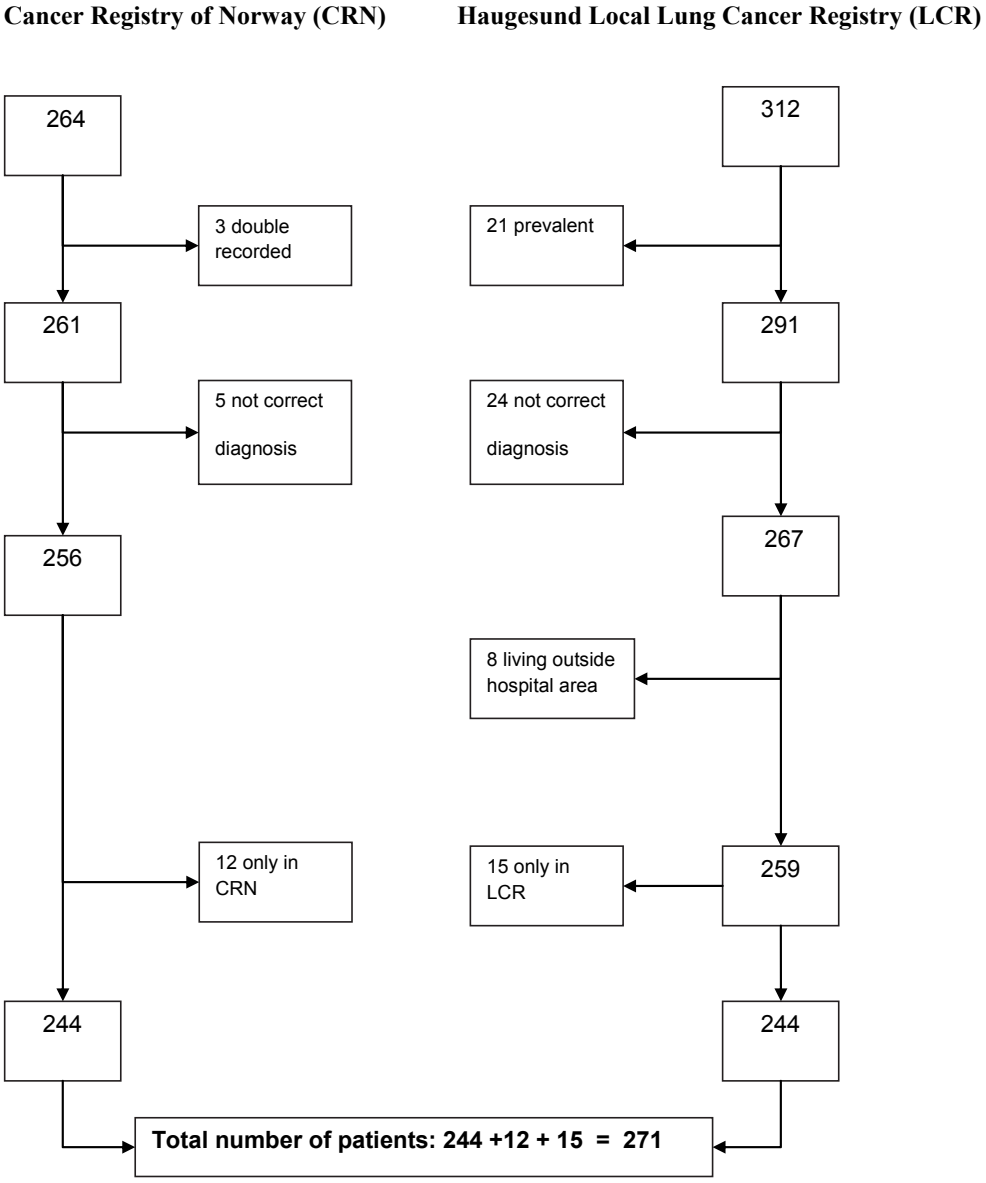
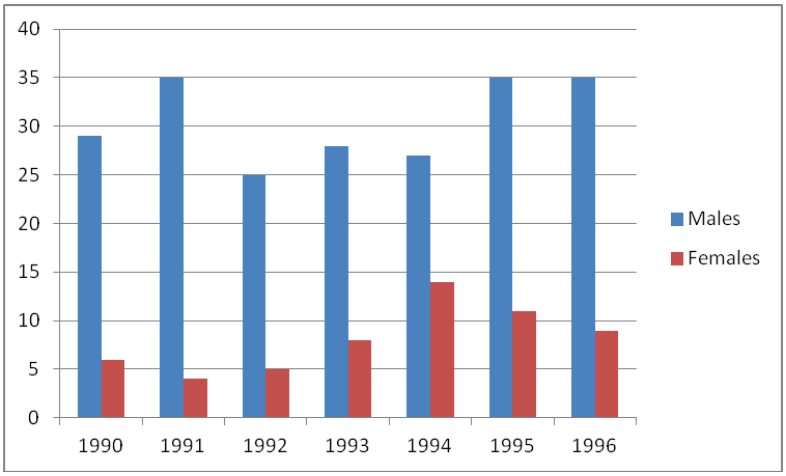


Figure 8 Incident cases of lung cancer in 214 men and 57 women in Haugalandet area 1990 – 96



This gives in average 30.6 cases per year in men and 8.1 cases per year in women, in total 38.7 cases per year.

10.7 Case record form (CRF) (Appendix 17.6)

The CRF was developed to collect information about demography, referring procedures, number and length of hospital admissions, diagnosis, co morbidity, occupational history, smoking status, symptoms and clinical signs. The date for symptoms, diagnosis and deaths were noticed. Furthermore laboratory results, X-ray-findings, diagnostic procedures, diagnosis, staging and treatment were recorded. The symptoms and treatment in the terminal eight weeks were given special emphasis. A pilot study was performed on 20 patient records by an experienced specialist in internal medicine using the case record form, and a semi quantification of symptom load was added. Dates of death were collected from the Cancer Registry of Norway (1). Altogether 31 variables of a total of 139 variables regarding municipality, referral, comorbidity at diagnosis, occupational history, tobacco history and laboratory results were not analyzed for this thesis.

Table 4a Variation of patient characteristics of lung cancer among the participating physicians extracting data from the patient journals. Demography,stage, performance status, histology, treatment, comorbidities and symptoms.

Variable	Participating physicians			Total	P (Exact Pearson chi-square)
	I	II	III		
	N(%)	N(%)	N(%)	N(%)	
Total	204(75.3)	44(16.2)	23(8.5)	271(100)	
Gender					0.54
Male	161(79)	33(75)	20(87)	214(79)	
Female	43(21)	11(25)	3(13)	57(21)	
Age (years)					0.67
<65	72(35)	11(25)	9(39)	92(39)	
65-74	73(37)	20(46)	8(35)	101(35)	
75+	59(29)	13(30)	6(26)	78(100)	
Stage (UICC)					0.33
1 and 2	61(30)	7(16)	5(22)	73(27)	
3	67(33)	19(43)	10(44)	96(35)	
4	76(37)	18(41)	8(35)	102(38)	
Performance status (WHO)					0.33
0 and 1	90(44)	23(52)	12(52)	125(46)	
2	69(34)	15(34)	4(17)	88(33)	
3 and 4	45(22)	6(14)	7(30)	58(21)	
Histology					0.91
NSCLC	137(67)	28(64)	16(70)	181(67)	
SCLC	45(22)	12(27)	4(17)	61(23)	
No histology verified	22(11)	4(9)	3(13)	29(11)	
Treatment					0.69
Surgery (resection)	25(12)	5(11)	1(4)	31(11)	
Chemo- and/or radiotherapy	103(51)	23(52)	15(65)	141(52)	
Best supportive therapy only	76(37)	16(36)	7(30)	99(37)	
Heart disease					0.72
Yes	50(25)	13(30)	7(30)	70(26)	
No	154(76)	31(71)	16(70)	201(74)	
Obstructive lung disease					0.04
Yes	47(23)	16(36)	2(9)	65(24)	
No	157(77)	28(64)	21(91)	206(75)	
Cough					0.15
Yes	80(39)	24(55)	8(35)	112(41)	
No	124(61)	20(46)	15(65)	159(59)	
Dyspnea					0.003
Yes	80(39)	29(66)	8(35)	117(43)	
No	124(61)	15(34)	15(65)	154(57)	
Chest pain					0.59
Yes	56(28)	15(34)	8(35)	79(29)	
No	148(73)	29(66)	15(65)	192(71)	
Weight loss					0.49
Yes	56(28)	16(36)	7(30)	79(29)	
No	148(73)	28(64)	16(70)	192(71)	
Reduced general condition					0.17
Yes	104(51)	29(66)	11(48)	144(53)	
No	100(49)	15(34)	12(52)	127(47)	
Skeletal pain					0.08
Yes	21(10)	2(5)	5(22)	28(10)	
No	183(90)	42(96)	18(78)	243(90)	

We counted all the symptoms at the time of the diagnosis mentioned in the CRF, and when nothing was mentioned e.g. on chest pain, this was counted as 'no chest pain'. The three physicians who extracted data from the hospital records into the CRF carried out meetings to discuss this process. The principal investigator examined 204 cases, the second 44 cases and the third 23 cases (tables 4a and 4b). No overt differences were observed among the three recording physicians for the patient characteristics of demography, staging, histology, treatment, comorbidity and initial symptoms. However, the prevalence of treatment symptoms like pain, cough, anxiety and depression varied between the physicians (table 4 b).

The grouping of lung cancer in four stages was done according to International Union of Cancer Control (UICC) based on the extent of the primary tumor and lymph nodes and the presence of distant metastasis (appendix 17.1) (82). Performance status was graded into five groups (appendix 17.2); from zero with the ability to carry out all normal activities without restriction to four where the patient is completely disabled (83). To get complete data about the staging and the performance status was a challenge since it was done several years after the initial examination of the patients (this problem is also discussed in the method chapter 12.1.4).

Table 4b Distribution of characteristics of lung cancer patients among the three examining physicians according to place of death in 253 patients and terminal symptoms in 247 patients with lung cancer

Variable	Participating physicians			Total	P (Exact Pearson chi-square)
	I	II	III		
	N(%)	N(%)	N(%)	N(%)	
Place of death (total)	187(100)	43(100)	23(100)	**253**(100)	0.06
At home	19(10)	6(14)	4(17)	29(12)	
In Haugesund hospital	106(57)	23(54)	13(57)	142(56)	
In nursing home	57(31)	13(30)	3(13)	73(29)	
Other hospitals	4(2)	0(0)	3(13)	7(3)	
Unknown	1(1)	1(2)	0(0)	2(1)	
Terminal symptoms	185(100)	39(100)	23(100)	**247** (100)	
Terminal pain					0.01
No pain	21(11)	11(28)	4(17)	36(15)	
Pain, but not treated	2(1)	0(0)	0(0)	2(1)	
Peripheral analgetics	38(21)	2(5)	4(17)	44(18)	
Opiates	109(59)	17(44)	12(52)	138(56)	
Opiates via pain infuser	15(8)	9(23)	3(13)	27(11)	
Terminal dyspnea					0.28
Central obstruction	34(18)	7(18)	7(30)	48(19)	
Pleural fluid	30(16)	7(18)	2(9)	39(16)	
Other reasons	30(16)	11(28)	6(26)	47(19)	
No dyspnea	91(49)	14(36)	8(38)	113(46)	
Terminal cough					0.02
Present, but not treated	35(19)	6(15)	3(13)	44(18)	
Treated	11(6)	8(21)	5(22)	24(10)	
No cough	139(75)	25(64)	15(65)	179(73)	
Terminal nausea					0.38
Present, but not treated	6(3)	1(3)	2(9)	9(4)	
Treated	47(25)	7(18)	3(13)	57(23)	
Not present	132(71)	31(80)	18(78)	181(73)	
Terminal hemoptysis					0.24
Present, but not treated	9(5)	5(13)	2(9)	16(7)	
Treated	5(3)	0(0)	0(0)	5(2)	
Not present	171(92)	34(87)	21(91)	226(92)	
Terminal anxiety/depression					<0.01
Present, but not treated	0(0)	4(10)	1(4)	5(2)	
Treated	139(75)	16(41)	16(70)	171(69)	
Not present	46(25)	19(49)	6(26)	71(29)	
Terminal neurological signs					0.10
Present, but not treated	12(7)	1(3)	0(0)	13(5)	
Treated	47(25)	4(10)	4(17)	55(22)	
Not present	126(68)	34(87)	19(83)	179(73)	

10.8 Tobacco smoking and occupational exposure

The incompleteness of the routine hospital records on tobacco smoking and occupational exposure is given in table 5, and with this high proportion of insufficient history no further analyses were done on this data.

Table 5 Hospital information on smoking and occupational history of 271 lung cancer patients in the case histories of Haugesund county hospital 1990 – 96

	N(%)
Tobacco history	
Absent	16(6)
Poor	80(30)
Good (information about amount or duration)	107(30)
Very good (information in pack years)	68(25)
Occupational history	
Not present	55(20)
Poor (only one occupation, no duration)	129(48)
Good (both more occupations and duration)	61(23)
Very good (detailed from start of work to the last occupation)	26(10)

10.9 Survival

The survival time was counted as the number of days between the date of confirmed diagnosis and the date of death. Date of diagnosis was the date of confirmed histological or cytological confirmation, or if morphological data were not available, the date of radiological diagnosis. For those patients who died outside the hospital, the date of death was obtained from the central population registry and the CRN. The specific causes of death were obtained from Statistics Norway. The delay time was defined as the time between onset of the first symptom caused by the lung cancer and diagnosis as stated above.

10.10 Hospital admissions and days

The stays were categorized in three groups: 1. Diagnostic hospitalization, i.e. days in hospital necessary for acquiring a definite diagnosis; 2. Terminal hospitalization, i.e. hospital days

within the last 8 weeks of life; and 3. Other hospital days. Admission and departure days were counted as whole hospital days. The days in nursing homes were counted separately.

10.11 Terminal symptoms

Terminal symptoms during the last eight weeks of life were extracted from the patients' records (page five in the case record form, appendix 17.6). Pain was graded according to its intensity defined by the use of peripheral analgesics, opioids or a morphine infuser. The presence and possible causes of dyspnea were recorded (central stenosis when a tumor was observed on bronchoscopy, pleural fluid observed on chest x-rays or other reasons). Psychological symptoms were recorded in patients' files and defined according to the prescribed drugs in the ATC-classification system (84): depression, when given antidepressive medication (N 06), anxiousness, when given diazepam (N05 B A 01) or other anxiolytic treatments (N05 B A 04), or insomnia when given hypnotics (N 05 C). Dizziness, headache or signs of paresis were defined as neurological symptoms but the records did not require treatment intervention. Additional terminal symptoms recorded were nausea, cough and hemoptysis. The number of weeks in the terminal 8 weeks treated for pain, psychological symptoms and dyspnea was recorded. The principal investigator visited the nursing homes and interviewed the primary care doctors to get this information of the patients who died outside hospital.

10.12 Quality of lung cancer care

10.12.1Quality indicators

We compared four quality indicators: Staging, histology, resectional surgery and one year survival. Lung cancer care should be performed according to evidence based guidelines (85), and quality indicators are then developed to measure the adherence to guidelines and to make comparisons of the quality of lung cancer care between management units possible (60, 86). Thus we had to find quality indicators possible to measure both in CRN and LCR. About 30 physicians at the Haugesund county hospital participated in filling out the routine forms for CRN, according to the law. Information was subtracted regarding gender, age, histology and stage for all new patients with lung cancer, ICD 7 (1990–92) and ICD 9 (1993–96), as well as on the number of patients that were operated on, and their overall survival after 1, 5 and 10 years. Data on other treatment options were very incomplete for further analysis

10.12.2 Minimal important differences (MID) in quality indicators

Twenty-six physicians at the Department of Thoracic Medicine, Haukeland University Hospital, Bergen, filled out a questionnaire on what they felt was a meaningful and relevant percentage difference from the national average regarding quality indicators that should lead to the implementation of changes in their own management of lung cancer (appendix 17.3). These indicators included the proportion of patients with no histological confirmation, unknown staging, surgical treatment, and one-year survival. The mean age of the physicians was 41.3 (SD 10.6) years. Seven physicians were women and 14 had four years or more of training in a chest clinic. They were informed on the national average of the four quality indicators for the period from 1990 to 1996. Each physician was asked to tick a box of pre-recorded relative differences (5, 10, 20, 30, 40, 50, 75 or 100%) that would change their own management program.

10.13 Data handling

The records from hospitals, nursing homes and general practitioners were reviewed randomly by three physicians following instructions given by the principal author. During this process they had meetings where the interpretation and coding were discussed. The CRF forms were then scanned optically into an Excel work sheet, before analysis. The overall agreement among the three physicians in the recorded characteristics of the lung cancer patients is given in table 4a and 4b.

10.14 Statistical analyses

The case record forms were scanned into a Microsoft Excel worksheet and then imported into a statistical software package (SPSS for Windows; SPSS, Inc; Chicago IL, versions 11.5 - 17.0) for analyses.

Pearson's Chi-Square test was used to analyze the differences in categorical variables between groups of patients defined by gender, age groups, anatomical stage, performance status, histology, treatment and symptoms.

Kaplan-Meier (87) curves and log rank tests (88) were used in analyzing differences in continuous variables with censored observations as days in hospital and survival time between the groups of patients.

The unadjusted hazard ratio (HR) and 95% confidence interval (CI) were estimated for each factor in a Cox proportional hazards regression model (89) both for hospital days (paper II) and survival time (paper III). Adjusted HR and 95% CI were estimated from a multiple Cox regression model using backward stepwise selection of variables.

The Mantel-Haenszel test (90) was used to compare the one-year survival in the two patient cohorts between Haugalandet and the rest of Norway, stratified for gender, age, stage and histology (paper IV).

A logistic regression analysis (91) of one-year survival adjusted for gender, age, histology, stage and living place was done in paper IV and reported as odds ratios (OR) and 95% CIs.

To calculate the sample size (paper IV) to obtain a deviation of 20% on 5% significance level with a power of 80% from the national average the SPSS program Sample Power 2.0 was used.

A significance level of 0.05 was applied for all statistical tests.

10.15 Ethics

Our study was approved by the Regional Committee for Medical Research Ethics of Western Norway.

11 Synopsis of the papers/main results

Paper I

The aims of this paper were to study the survival and the predictors of survival in all lung cancer patients in a defined population and to determine whether and how the length of time from symptom onset to confirmed diagnosis (delay time) influenced survival. All incident cases from the Norwegian Cancer Registry and the hospital records in the Haugalandet area from 1990–1996 were followed until 31 December 2008. The dates of symptom onset, diagnosis, death and information about demographics, initial stage, performance status, histology, and initial symptoms were recorded.

There were 271 incident lung cancer patients from 1990 to 1997. The mean age (SD) at the diagnosis was 67.4 (11.2) years, and 57 (21%) were women. The diagnosis was confirmed by histology in 242 patients (89%). The distribution of age, stage, performance status and histology at the time of initial diagnosis (table 6a) did not differ between genders ($p > 0.05$).

Eighteen (6.6%) were alive by January 1st 2000. One-year survival was 29.2%, and five- and 10-year survival was 8.5% and 5.5%, respectively. The median (inter quartile range, IQR) survival time was 5.7 (1.9,14.1) months and the median (IQR) delay time was 2.2 (1.1,3.7) months. Twenty-five patients (10% of those who died) had a non-lung cancer cause of death. No weight loss, at the time of diagnosis, was a significant predictor for long survival in addition to younger age, limited stage, good functional performance and surgical treatment, but delay time for diagnosis had no effect on survival time for lung cancer.

We conclude that in the whole population of lung cancer patients, long-term survival remains poor and is not influenced by diagnostic delay time.

Paper II

All incident lung cancer patients in the Haugalandet area in South West Norway from 1990 through 1996 were followed from diagnosis till either death or end of follow-up 1 Dec 2003. Initial symptoms, anatomical stage, functional performance status, histology, initial treatment, terminal care, number of admissions as well as days of hospitalization were recorded. Of a total of 271 patients (57 women) only 16 were still alive at end of follow up. Median survival time was 170 days. Mean age at the first admission was 67.4 years (range 21 - 89 years). Median number (inter quartile range, IQR) of admissions was 3 (2, 5) and total hospitalization days were 35 (18, 58). Altogether 26% of the days in institutional care were spent in nursing homes. Thirty one patients surgically treated had 75 (56, 96) days of hospitalization, which is the highest number of admission days. Young age, low anatomical stage and good performance status at time of diagnosis were associated with increased hospitalization days. The effects of age, tumor stage and performance status were non-significant in a Cox regression analysis when adjusting for treatment interventions.

We conclude that in a population-based cohort of incident lung cancer patients, days in health care institutions involved a considerable part (19%) of all survival time for those who died. However the absolute number was greater for those with small tumors and high functional performance status which initiated other interventions than only palliative treatment.

Paper III

We examined, retrospectively, all the cases of lung cancer diagnosed from 1990 to 1996 in a defined hospital area in Norway with regard to the symptoms in the terminal 8 weeks of life. All medical records from general practitioners, nursing homes, and hospitals were investigated. A total of 271 cases were diagnosed, and 247 of 253 deaths (98%) were

analyzed. One patient died abroad, and the records of 5 patients were not available. Only 53 (22%) of the 247 deaths were women.

Pain was recorded in 85% of the patients, psychological symptoms (anxiety, insomnia, and/or depression) in 71%, dyspnea in 54%, neurologic symptoms in 28%, cough in 24%, nausea in 21%, and hemoptysis in 9%. Young age ($p \leq 0.02$) and small cell lung carcinoma (SCLC) ($p \leq 0.03$) were risk factors for psychological symptoms. Terminal dyspnea was more frequent in patients with stage III ($p \leq 0.002$) and nausea in stage IV ($p \leq 0.02$) at the time of diagnosis, while cough ($p \leq 0.04$) occurred more often in non-small cell lung carcinoma (NSCLC).

Terminal pain was independent of gender, age, performance status, stage, and histology. We concluded that in a community health service encompassing all lung cancer patients, pain, psychological symptoms, and dyspnea were frequent complaints in the terminal phase. Terminal dyspnea and nausea were associated with staging at the time of diagnosis, terminal cough with NSCLC and nausea with SCLC.

Paper IV

We compared four quality indicators (staging, histology, resectional surgery and one year survival) in 271 patients recorded in a local lung cancer registry (LCR) with 266 patients recorded in the Cancer Registry of Norway (CRN) from Haugalandet hospital area and 12 428 patients from the rest of Norway for an identical period of time. The average minimal difference of clinical importance, as judged by the physicians, for the four lung cancer quality indicators varied between 18% and 23%. Percentages regarding histology, resectional surgery and one year survival did not differ between LCR and CRN. However, fewer patients had localized disease in the LCR than in the CRN. The differences in relative percentage between Haugalandet and the rest of Norway were 3% for unknown stage, -6% for unknown histology,

-20% for surgery and -5% for one year survival. The sample sizes necessary to detect a relative 20 % difference from the national average (power 0.80, $p<0.05$) were from 435 cases to 2826 cases depending on which indicator was chosen.

Quality indicators from two lung cancer registries were in agreement in a population recorded for the same time and area, and did not differ from the rest of the country with the exception of stage. Small regional management units should merge to a larger unit with standardized procedures which include at least 250 incident lung cancer patients per year. We could thus estimate quality indicators of lung cancer care for comparisons with national averages, and with other management units. A national lung cancer quality registry should be established. In addition to quality indicators of today discussed in this study one should include: 1. Modern TNM-classification (UICC), 2. Performance status, and 3. More accurate information on interventions, follow up and final outcome. Such a registry could then be a tool to improve the quality of lung cancer care in Norway.

12 Discussion

12.1 Methodological considerations

12.1.1 Study design.

The study is retrospective, which implies some limitations. In a retrospective study one can observe connection between variables, and thus it can generate hypothesis, but not give information about causal relationship.

12.1.2 Patient selection

The patients were found by searching in the hospital records on the ICD-diagnosis number, either as main diagnosis or additional diagnosis. Also the search from CRN was based on diagnosis number. At the time of the study, CRN had no access to the hospital registries, and was based on cancer reports from institutions and doctors in addition to death certificates. A lung cancer patient missing in LCR and not reported, e.g. due to misdiagnosis, could therefore also be missed in CRN (see chapter 10.6).

Originally we had an intention to estimate the completeness of the data in both CRN and the LCR. Since these two institutions had some communication during the planning of the study and extraction of data, this may have improved the quality and the completeness in the patient cohorts which we examined, by removing some mistakes. At the first contact between the hospital and CRN there were errors in both registries (figure 7) with incorrect diagnosis or lack of records in the registries. No records were available for 15 (5.5%) lung cancer patients in CRN and for 12 (4.4%) of the lung cancer patients in LCR.

Two measures have the potential to improve the quality of CRN and thus obtain high quality data in future studies. Firstly, in the new electronic journal systems in the hospital the report form may now be filled out electronically at the same time as the doctor makes the report to

the referring doctor. This improves the quality of the reports compared to the earlier ones when the paper forms were filled out separately often a long time after the initial examinations. Secondly, from 1998 CRN got access directly to the hospital registries, thus improving the completeness in the reporting.

12.1.3 Case record form

Hospital admissions and days were recorded on the CRF (appendix 17.5), but outpatient visits were not recorded. From 1995 – 1996, some of the bronchoscopy procedures were done ambulant. Future studies should record outpatient visits and procedures applied at outpatient visits as well as procedures at hospital admissions.

12.1.4 Validity

12.1.4.1 Internal validity

Internal validity may be threatened by 1. Selection bias, and 2. Information bias

1. *Selection bias.* We attempted to get the cohort of lung cancer patients as complete as possible by a careful search in our own hospital registry and by repeatedly contacting with CRN (figure 7). Since we were able to retrieve all patients from CRN, also those who had not got the lung cancer diagnosis from the beginning in our hospital registry, we consider the selection bias to be small. Two patients living in the Haugesund hospital area were initially diagnosed at Haukeland University hospital and one patient diagnosed at Stavanger University Hospital the CRF-forms filled out on account of the records in these hospitals (table 3).

2. *Information bias.* Retrospective data based on the routine work in a busy local hospital may be incomplete for scientific purpose due to both missing information and missing notes (92). Both occupational and smoking history were significantly incomplete

(table 5). To extract the information from the original hospital notes from the patients (notes from doctors and nurses, referring letters, x-ray pictures and descriptions, results from laboratory and other examinations) into a structured case record form could also imply inaccuracy. To get complete information on performance status we searched not only in the doctors' records, but also in the hand written records from the nurses, who carefully had recorded the general condition of the patients, e.g. if they were linked to bed, or if they could walk and be able to care for themselves in activities of the daily life. To minimize bias the three physicians had meetings both before and during this process to discuss how to transfer the findings in the patient records into the CRF-forms.

12.1.4.2 External validity

Are these results applicable to a population outside Haugalandet, as to the Norwegian population?

There was a slightly higher proportion of younger people at Haugalandet than in the whole Norway but no difference in the gender (table 6).

Table 6 Distribution of men and women and age groups in the population at Haugalandet compared to the whole population of Norway in 1994 (source: Statistics Norway)

	Haugalandet N(%)	Norway N(%)
Gender		
Males	49 507(49.8)	2 138 628(49.5)
Females	49 809(50.2)	2 186 187(50.5)
Age (years)		
0-15	23 241(23.4)	888 561(20.5)
16-66	62 502(62.9)	2 815 503(65.1)
67+	13 573(13.7)	620 751(14.4)
Total	99 316(100.0)	4 324 815(100.0)

We compared our lung cancer patient cohort with all patients in the rest of Norway, based on information from CRN (paper 4). There were less female lung cancer patients at Haugalandet compared to the rest of Norway, but histology, stage, surgical treatment and one year survival did not differ. As seen in figure 3 there are variations in the incidence of lung cancer between the counties in Norway. It is difficult to find evidence based knowledge for these differences. Some possibilities are suggested. There may be different cigarette consumption in various counties. In the Agder counties 88% of ever-smokers had smoked primarily hand-rolled cigarettes (93). Melting industry and ship-yard industry with potential occupational exposures are more frequent at the coastal area in West-Norway than in the inland. There are differences in radon exposures between geographical areas in Norway, as discussed in the introduction (chapter 8.2.2). We hypothesize that cigarette smoke and occupations with lung cancer risks were less prevalent for women at Haugalandet compared with the rest of the country before the 1990-ties.

However, since distribution in the population in Haugalandet and the whole Norway is similar regarding age of men, we may assume that the results from the local patient cohort are comparable to the results from other population-based lung cancer patient cohorts in Norway regarding men.

When comparing the number of hospital days, the management units in other regions with more dense population than Haugalandet may have more of the lung cancer care on an outpatient basis.

12.2 Discussion of main results

12.2.1 Incidence of lung cancer

In this population based study we found 271 incident cases of lung cancer in 11 municipalities at Haugalandet from 1990-96 of whom 57 (21%) were women (table 4a). This means in average 38.7 new cases per year; 8.1 women and 30.6 men in a total population of 99 316 inhabitants in 1993 (figure 8).

From CRN the total number of new cases in the same period of time was 260 (table 7). There may be various reasons why the CRN has a lower total incidence of lung cancer patients than LCR. Before 1998, this registry had no direct access to the hospital registries. Furthermore CRN is never closed, which means that when new information about patients becomes available even years after first registration the register may be adjusted.

There was a lower incidence of women with lung cancer at Haugalandet compared with the rest of the country both in LCR and CRN (paper 4). The proportion of women was also higher (27%) in a hospital-based cohort diagnosed at Nordland Central Hospital 1987-92 (23) compared to Haugalandet. In a prospective study from Aust- and Vest-Agder counties, 42% of the patients diagnosed from 2002 - 2005 were women (94). In addition to a possible higher proportion of women in Agder compared to 21% at Haugalandet, this difference may also reflect the increasing number of women with lung cancer since the inclusion was 10 years after our study. Several studies from Norway have shown the association between cigarette smoking and lung cancer (20, 95). Recent national data show that the proportion of women has increased and the proportion of men with lung cancer has decreased the last years (figure 5), and this is also our clinical experience from Haugalandet the last decade.

Comparisons of incidence rates have to use age-adjusted incidence rate according to WHO World Standard Population (96). When comparing Haugalandet with the counties Rogaland and Hordaland, it was a trend towards a lower incidence rate in women at Haugalandet, and this was more pronounced when compared with all patients in Norway (table 7).

Table 7 Number of new cases and age adjusted incidence rates per 100 000 per year in Haugalandet and Norway for 1990-96, and Rogaland and Hordaland counties for 1991-1995 (source: Cancer Registry of Norway)

		Males	*Females*
Haugalandet 1990-1996	Number	202	58
	Age-adjusted incidence rate	39.9	10.8
Norway 1990-1996	Number	8 557	3874
	Age-adjusted incidence rate	36.3	15.3
Rogaland 1991-1995	Number	427	168
	Age-adjusted incidence rate	37.3	13.2
Hordaland 1991-1995	Number	572	211
	Age-adjusted incidence rate	36.7	12.3

The trend of a lower proportion of women at Haugalandet compared with the whole country was also seen when comparison was made for each year. In men the age-adjusted incidence rate was similar for the two cohorts (tables 7 and 8).

Table 8 New cases per year and age-adjusted incidence per 100 000 per year at Haugalandet compared with Norway 1990-1996 in 260 patients with lung cancer reported in the Cancer Registry of Norway.

		Haugalandet		Norway	
		Number	*Age-adjusted rate*	*Number*	*Age-adjusted rate*
	Males	30	43.3	1175	35.0
1990	***Females***	6	9.7	478	13.3
	Total	36	25.3	1653	23.1
	Males	32	47.2	1160	35.1
1991	***Females***	4	6.8	511	14.0
	Total	36	25.9	1671	23.6
	Males	23	31.3	1203	35.8
1992	***Females***	6	7.6	502	13.9
	Total	29	18.5	1705	23.8
	Males	29	39.9	1244	37.3
1993	***Females***	5	5.8	545	15.5
	Total	34	21.7	1789	25.3
	Males	24	32.9	1244	36.7
1994	***Females***	14	17.8	565	15.7
	Total	38	24.6	1809	25.1
	Males	34	47.8	1241	36.2
1995	***Females***	11	13.1	598	15.8
	Total	45	29.4	1839	25.0
	Males	30	39.1	1290	37.7
1996	***Females***	12	14.5	675	18.6
	Total	42	25.7	1965	27.2

The average age at the diagnosis of 67.4 years in Haugalandet correspond with the rest of Norway (paper 4), and also with the population based study from Aust- and Vest-Agder counties 10 years later with a mean age of 67.9 years (94). In the hospital based cohort in secondary care in Nordland county the mean age was 65.5 years (23), and in tertiary care at Rikshospitalet, Oslo, the mean age of patients discharged with lung cancer 1962 – 71 was 65 years for men and 60 years for women (97). However, the oldest and most sick patients were probably not referred to this tertiary care hospital for further diagnosis and treatment in these time periods.

The distribution of stages in our patient cohort was 38% for stage IV (82) similar to the rest of Norway as found in CRN (paper 4). Lower stages are impossible to compare since CRN has a different staging. In our cohort from Haugalandet 38 % were in stage Ia – IIIa, and 62% in IIIb – IV (table 9), slightly different to the population based study from Agder counties with corresponding proportions of 28% and 72% (59) and similar to the selected cohort from Nordland county with 63% of the patients in stage IIIb and IV (23).

The proportion of SCLC of 23% (Table 9) in Haugalandet corresponds with 19% in the rest of Norway and with 24% and 21% in the two other recent Norwegian studies (23, 93). Initial surgical treatment was given to 11% of our patients (table 9) which is a lower percentage than in the recent population-based study from Agder county with 16% (98), and in the rest of Norway (paper 4) with 16%. One reason for this could be different attitudes to and indications for lung cancer surgery at Haukeland University Hospital in 1990-96 compared to other units of thoracic surgery in Norway.

Table 9 Age, gender, anatomical stage, performance status, histology, initial treatment, and referral sources in 271 lung cancer patients 1990-96, Haugesund County Hospital.

Total n (%)	271(100)
Age (years) mean(SD)	67.4(11.2)
Men	214(79.0)
Women	57(21.0)
Anatomical stage (UICC 1997)	
Ia n(%)	13(4.8)
Ib n(%)	37(13.7)
IIa n(%)	2(0.7)
IIb n(%)	21(7.7)
IIIa n(%)	29(10.7)
IIIb n(%)	67(24.7)
IV n(%)	102(37.6)
Performance status	
0 and 1	125(46.1)
2	88(32.5)
3 and 4	58(21.4)
Histology	
Small cell carcinoma	61(22.5)
Adenocarcinoma	75(27.7)
Squamous cell carcinoma	59(21.8)
Non-differentiated carcinoma	34(12.5)
Other lung cancer.	13(4.8)
No tissue diagnosis	29(10.7)
Initial treatment	
Surgery resection)	31(11.4)
Chemo- and/ or radiotherapy	141(52.0)
Best supportive care	99(36.5)
Referral to hospital from	
Primary care doctors	171(63.1)
The National Mass Radiography Service	7(2.6)
Other hospitals and health institutions	17(6.3)
Other specialists (ENT, radiologists, surgeons)	64(23.6)
Direct contact to lung specialist from the patient	12(4.4)

12.2.2 Survival in lung cancer

In this study of an unselected cohort of lung cancer patients from a defined geographical area we found a median survival of 5.7 months, and a one year and five year survival of 29.2% and 8.5%, respectively. Younger age, limited disease, surgical treatment, good performance status and no initial weight loss were predictors of long survival. We did not find that the time between symptom onset and diagnosis predicted survival. In an early Norwegian study from tertiary care in 1053 patients with lung cancer diagnosed from 1962 to 1971, the five year survival was 15.5% (99). The duration of symptoms when present did not influence the survival, and extensive disease and old age were unfavorable prognostic factors as in our study from Haugalandet.

The overall five-year survival in lung cancer has not changed markedly in Norway the last 40 years (figure 1), but a trend in the last years of a moderate increase in survival in women is observed (5). In a recent study from Norway female gender was a predictor for long time survival in a selected population of lung cancer patients offered surgery (100). We have found 17 clinical lung cancer studies from Norway published in the last 10 years (table 10a+10b), and we want to discuss their observations in the context of lung cancer patients at Haugalandet.

Table 10a Clinical studies of lung cancer patients in Norway published 2001- 2007

Author/ year of publication (reference)	Years of patient diag-nosis	Number of patients	Mean age (years)	Gender % women	Stage	Histo-logy	Median suvival (months)	One year sur-vival %	Five year sur-vival %
Alexandersen 2001 (23)	1987-92	219	65.5	25	163 NSCLC 28% stageI+II 72% stageIII+IV	76% NSCLC 24% SCLC	NA	NA	10
Bremnes 2001 (101) Chemo-therapy	1996-98	39	Median: 63	46	L.D.	SCLC	21	69	NA
Dahle 2003 (102) Surgery	1993-98	99	63	31	I-IIIa 89 IIIB-IV 9	NSCLC	30	NA	NA
Bremnes 2003 (103) Chemo-therapy	1989-94	436	Median: 64	36	51% E.D.	SCLC	9 (LD – 13 ED - 7)	NA	NA
Sundstrøm 2004 (104) Palliative radiotherapy	1993-98	421	Median: 68	23	St. III : 77% IV: 23%	NSCLC	NA	29	NA
Batevik 2005 (105) Surgery	1988-2002	351	64	32	I : 71% II: 15% III: 15%	NSCLC	NA	NA	46
von Plessen 2006 (106) (Chemo-therapy)	2000-02	297	65	37	IIIb: 24% IV: 76%	NSCLC	7.7	C3:25 C6:25	NA
Sundstrøm 2006 (107) Pall. radioth. (A,B and C)	1993-98	301	Median: 68	23	St. IIIa: 18% IIIB: 82%	NSCLC	A: 9.2 B:7.5 C:7.5		0 6 3
Hellbekkmo 2007 (108) Chemo-therapy	2003-04	432	Median: 67	39	IIIb: 39% IV: 61%	NSCLC	NA	29	NA

SCLC = Small cell lung cancer, NSCLC = Non-small cell lung cancer, L.D. = Local disease, E.D. = Extensive disease, m = months, NA = Not available

Table 10b Clinical studies of lung cancer patients in Norway published since 2008

Author/year of publication	Years of patient diag-nosis	Number of patients	Mean age (years)	Gender % women	Stage	Histo-logy	Medi-an sur-vival months	1 y Sur-vival %	5y Sur-vival %
Hermes, A 2008 (109) Irin+carbo Etopo+carbo	2001-05	209	Median 67 68	34	E.D.	SCLC	8.5m 7.1m	NA	NA
von Plessen 2008 (110) Chemo-therapy	1994-2005	13 757	67.5	35	Regional ly advanced 27% Met 23%	NSCLC	94-97: 5 2000-05: 6	NA	2.5
Roth 2008 (111) Surgery	1993-2006	148	67.3	32	IA:43% IB:46% II-IV: 11%	NSCLC	71	82	42
Al-Shibli 2009 (112) Surgery	1990-2004	335	Median 67	25	I : 27% II : 65% IIIa: 8%	NSCLC	109	NA	57
Grønberg 2009 (113) Chemo-therapy	2005	36	Median 61	29	LD	SCLC	4 1/2	NA	NA
Grønberg 2009 (114) Chemo-therapy	2005-06	436	Median 65	42	St IIIB : 40% Stad IV: 60%	NSCLC	7.1	32	NA
Strand 2010 (115) Radiation	1993-2001	497	65	32	I+II: 29% IIIa+IIIb: 70%	NSCLC	NA	53	9
Hjelde 2010 (116) Surgery	1994-2001	190	66	39	I+II:81% III+IV: 19%	NSCLC	NA	NA	42
Skaug 2011 (117) Population based	1990-96	271	67.4 Median: 69	21	I+II : 27% III+IV 73%	Un-selected	5.7	29	8.5

SCLC = Small cell lung cancer, NSCLC = Non-small cell lung cancer, L.D. = Local disease, E.D. = Extensive disease, m = months, NA = Not available

These studies are heterogeneous, with different criteria for patient selection according to the planned treatment intervention. All these clinical studies had a higher proportion of women

than our population based study from Haugalandet (table 10a and 10b). The majority had a younger mean age. With the exception of our study all were selected on the basis of histology; four were based only SCLC and 12 only NSCLC. Median survival was not available in 6 studies, one-year survival not in 10 studies and 5 year survival not in 9 studies. Three of the studies are retrospective of all surgically treated patients referred to Akershus University Hospital (102), Haukeland University Hospital in Bergen (105) and from Møre and Romsdal and Trøndelag counties in Norway (111). The five-year survival in the two last studies was 46% and 42 % respectively, which is comparable to 52% in our study. This trend of longer survival in our patients may indicate a strong selection, since only 11.4% of all our patients were operated. In a study from Northern Norway on patients with NSCLC recruited from 1990 - 2004 (112) the five year survival after operation for lung cancer was as high as 57%.

Nine of the studies were on chemotherapy, and four of these on SCLC (101, 103, 109, 113). In the study of Hermes the patients with performance status (PS) up to WHO 4 were also included (109); otherwise only patients with PS 0-2 were studied, as in the chemotherapy trials with NSCLC (106, 108, 118). These various selection criteria illustrate one of the difficulties in comparing a population based patient cohort with cohorts selected for chemotherapy. Differences in patient selection are also seen in radiotherapy, where only some stages of NSCLC are selected in therapeutic trials (104, 107, 115).

In one study (23) 10% were alive after 5 years, compared to 8.5% in our patient cohort. This was, however, a hospital based cohort and not all patients were referred to the major county hospital. In a national patient cohort from CRN based on 13 757 patients with advanced NSCLC, the median survival was 149 days for the patients included from 1994-97, and 176 days for those from 2000-2005 (110). In our total population the median survival for stage III patients was 179 days and for stage IV 96 days. Again a complete comparison is difficult,

since we included also SCLC and those without histological confirmation of the diagnosis who are mostly associated with a short survival. A recent study of lung cancer patients in Norway from CRN indicates that survival is lower in men than in women (6). This was also found in the study of the operated lung cancer patients from Bergen (105). In this study there were no gender differences in age, but a higher proportion of the men had been treated for cardiovascular disease prior to the lung cancer treatment, compared to the women. Future intervention studies on lung cancer must be more complete on survival including median, one year and five years survival.

The prognostic factors found in our study correspond with other studies (119), and in SCLC weight loss and performance status had previously been found to have prognostic significance both in local and extensive disease (103). Low stage has long been known to be a good prognostic factor after lung cancer surgery as reported in an early study which also included SCLC (120). A five year relative survival of 10.9% was found in population based studies on lung cancer patients diagnosed in year 2000 - 2002 based on national cancer registries from 47 European countries, but there were marked differences between the countries (121). Denmark, England and Scotland have a lower five year survival rate than many other countries. In Denmark this has partly been explained by a less favorable stage at the time of diagnosis (122). For other European countries less access to specialist care is considered to be part of the explanation (123). Future population based studies in lung cancer should be done to estimate which impact the new therapeutic interventions have on survival of the total lung cancer population in the community.

12.2.3 Hospitalizations and hospital days in lung cancer

Earlier studies on costs of lung cancer care are very heterogeneous. Some include only insured patients (124, 125), SCLC (52, 126), NSCLC (50, 127), special treatment

interventions (128, 129), or the focus is only on the final part of the course of the disease (51, 130, 131). There are also great variations on which costs are counted. We found therefore that a retrospective study of hospitalization days and admissions could give us valid measures. Hospitalizations are regarded as a main cost driver with more than a half of the total expenses in cancer care (46, 49). This is in agreement for what is observed in COPD-care (132).

In a recent retrospective study from The Netherlands in patients with advanced NSCLC hospitalizations counted for most of the expenses (133). When comparing the costs after initial treatment between those who got only best supportive care and those who were additionally treated with chemotherapy, drugs represented the second largest cost driver. This is also confirmed in studies from France (134). We found like other studies (135, 136) that most resources were given to young patients with limited disease and good performance status. They are offered the most active treatment.

An additional important aspect of hospitalization in lung cancer care is the time these patients have to spend away from their homes and families, as in our study where those with the shortest survival after first admission spent more than 30% of their remaining lifetime in institutions. Studies have shown that the majority would prefer to stay in their homes when given good palliative care (137). High quality palliative care at home would probably give those patients a higher quality of life and may reduce the expenses of hospitalizations.

12.2.4 Terminal symptoms in lung cancer

Terminal care is important in lung cancer with a one year mortality rate of 70% and five year mortality rate of about 90%. We found that altogether 99% of the lung cancer patients in our study had one or more symptoms in the terminal eight weeks. The most frequent was pain in 85%, and two-third of the patients had psychological symptoms, and more than half had

dyspnea. When we compare with other studies (table 11) there are considerable inconsistencies (138-141).

Table 11 Previous studies on symptoms in the terminal stage of lung cancer

Author and year of publication (reference)	**Skaug** (2007) (142)	**Edmonds** (2001) (138)	**McCarthy** (2000) (139)	**Vaino** (1996) (141)	**Lutz** (2001) (140)
N	247	449	749	387	69
Pain (%)	85	85	45	54	80
Dyspnea (%)	54	78	70	46	92
Nausea (%)	27	NA	10	14	NA
Cough (%)	28	56	NA	NA	90
Hemoptysis (%)	9	NA	NA	NA	22
Anxiety, insomnia, depression (%)	71	60	NA	10	NA
Dizziness, head-ache or paresis (%)	28	NA	Confusion 28	Confusion 9	NA
Time window in the course of the disease	Terminal eight weeks	Terminal year	0-3 terminal days, 3days-1month, 1-3months , 3–6 months before death	In the last phase after cancer treatment, but poorly defined	4-6 months, 0-3 terminal months
Patient selection	All	A random sample of deaths, from 20 districts in England.	Died within one year. SCLC in 5 hospitals	Referred to seven palliative centres in several countries	69 consecutive patients, referred to radiation oncology
Methods	Retrospec-tive data extraction from hospital records	Retrospective post-bereavement structured interviews	Prospective. Interviewed 2 and 6 months. after inclusion, and survivors 4 – 10 weeks after death. Medical records examined by nurses	Prospective. Patient interview by nurse or physician. Excluded those not able to be interviewed	Prospective. Symptom scale using interview with patients and health care givers

NA: Not available

There is great variation between the studies in the selection of patients, methods, and examined time window in the course of the disease. These differences make comparisons difficult and may explain the inconsistencies in the findings.

A literature search was performed in MEDLINE on the term “lung cancer” and when combined with “end stage” 14 papers were found, with “terminal care” 8 papers, and in EMBASE combined with “terminally ill patients” 13 papers. None of these were population based. When searching on “lung cancer” and “terminal symptoms” only the present study was found (142). No new studies were addressing these terms.

Lung cancer patients have a high burden of symptoms which change over time in the course of the disease (143). Furthermore, these patients experience more severity and distress than other cancer patients (144). To give high quality palliative treatment to lung cancer patients is a great challenge for health care providers, both regarding symptom control (145-148) and ethical issues (149).

Quality of life has been found to be a predictor for survival in lung cancer (150, 151), and those who are giving care to the lung cancer patients should be aware of recent studies that early palliative care not only improves quality of life, but also gives prolonged survival (152, 153). With a median survival of less than six months focus must also be given to palliative care of already when lung cancer is diagnosed.

12.2.5 Quality of lung cancer care

12.2.5.1 Quality indicators

We compared four indicators on lung cancer care (staging, histology, surgery, one year survival) and found no differences between our local cohort from LRC and the local cohort from CRN and the lung cancer patients from the rest of Norway.

There is so far no agreement in Norway about which quality indicators to use in lung cancer care for all patients, all though a quality registry was established for surgically treated lung cancer patients from 1993-2002 (66). Since 1953, notification to CRN on every patient with cancer has been mandatory. The staging system used in the CRN reports was established in 1953, and consists of three categories: localized disease, regional spread and distant metastasis. CRN does not get sufficient information on the staging to stage according to the Union for International Cancer Control (UICC) (82, 154, 155). While there is a high completeness regarding diagnosis, the information on treatment applied is incomplete in CRN since the decisions on other treatment options than surgery are not made at the time of reporting. Further CRN report forms should include both UICC staging, performance status, more detailed information on interventions other than surgery, palliative care of the patients and final outcome.

12.2.5.2 Minimal important difference

When searching in Pub med on MID or MCID and “lung cancer” no references were found. In one study, however, on the Functional Assessment of Cancer Therapy – Lung (FACT-L) measuring the quality of life in a 7-item scale, an increase in the score of 2 point was found meaningful when the patient improved, and reduction of 2.75 when the patient worsened (74).

Various methods are used to estimate the minimal important difference (MID) in an outcome measure, giving sufficient benefit for the patient to change the management of the disease. Some use the expression minimal clinical important difference (MCID) (69, 73). One method is to make an estimate of MID based on patients' preference. This has been done when measuring health status in pulmonary rehabilitation in COPD, either by asking about the judgment of the patient before and after intervention (73) or the judgment relative to a group of other patients (156). Another method in estimating MID is to use expert judgments to assess which size in differences in health status as in COPD are of importance (157). There was good agreement between these two methods (73). A third way to calculate the MID is the anchor-based method. A well established test with known MID is the reference, and the MID in the test of interest may be calculated via logistic regression analysis (158). A linear relationship between these two tests is required. A fourth method is the distribution-based estimate of MID based on statistical calculations without judgment from patients or experts (159), which is also discussed in ERS/ATS statement on outcomes for COPD in pharmacological trials (160). In a recent study the MID in severe COPD after lung volume surgery patient outcome measure (6 minute walking distance) was determined using the anchor based method (158). The value of MID may however be different in different interventions as lung volume surgery, pulmonary rehabilitation or pharmacological treatment in COPD patients, or in patient groups with different degree of serious disease. Furthermore, MID obtained at a group level may not be appropriate to judge the improvement of the individual patient (161).

We attempted to find the MID for four outcome measures by the use of the expert-preference method (chapter 10.12.2). The thoracic physicians estimated MID in deviation in relative

percent from the national average of about 20% as sufficient to make an impact on their management of lung cancer (paper 4 and appendix 17.3, 17.4, 17.5).

To get a sufficient number obtaining a relative change of 20% with a power of 80% we would need a sample size to estimate the quality which is much higher than the number of incident lung cancer patients observed in our hospital area in five years. We concluded that it is difficult within a reasonable time to get good estimates of the quality of lung cancer care in a hospital with 40 incident lung cancer patients per year.

A model to overcome this problem and use the quality indicators from CRN is to merge hospitals within a health region to a larger unit with standardized routines for diagnosis and treatment of lung cancer. To a certain degree this is done in Norway, since lung cancer surgery now is centralized to six university hospitals, but little standardizations are done so far for palliative care. In Denmark, a report on an indicator project on lung cancer indicated a better quality on lung cancer surgery in hospitals with more than 170 new cases yearly (162), and in a recent article from Germany it was suggested that a center treating lung cancer should have at least 200 new cases per year (14).

13. Main conclusions

1a.The age-adjusted yearly incidence rate of lung cancer in Haugalandet was 39.9 per 100000 in men and 10.8 per 100 000 in women.

1b.The long term survival in the whole population of lung cancer patients is poor, with a five-year survival of 8.5% and median survival time of 5.7 months. Young age, limited disease, good performance status and no weight loss were predictors for longer survival, which was not influenced by the diagnostic delay time.

2. The 271 incident lung cancer patients in the Haugalandet area 1990-96 had a median of three admissions and 35 hospital days, and most was spent on those surgically treated. For those 253 patients who died before December 1st, 2003, 19% of their survival time was spent in health institutions.

3. A very high proportion of the lung cancer patients have symptoms requiring treatment in the terminal stage, and pain, dyspnea and psychological symptoms were the most frequent. Nausea is more present in SCLC, and nausea and dyspnea are more frequent when the disease is extensive at diagnosis. Younger patients have more often psychological symptoms than patients older than 65 years. Health care workers giving palliative treatment should be aware of these predictors.

4. No differences were found of the quality indicators available in CRN when comparing the lung cancer care at Haugalandet with the rest of the Norwegian population. However, to get sufficient sample sizes to detect a 20% different estimate from the national average in quality indicators, smaller management units need to merge into network with standardized programs for diagnosis and curative and palliative treatment of lung cancer. A national lung cancer quality registry would be favorable.

14. Future perspectives

The last patients included in our retrospective study were diagnosed with their lung cancer at the end of 1996. At that time the use of chemotherapy in advanced NSCLC was not routinely established, even if studies were ongoing, and the role of neoadjuvant chemotherapy after surgery for stage 2 disease was not yet clarified (163). The value of lung cancer surgery was questioned (164). Considering the importance of lung cancer as cause of mortality, the disease had received too little attention (165).

Since 1996 there have been marked changes in the management of lung cancer (166). The Norwegian Lung Cancer Group has published guidelines for diagnosis and treatment (167). Important changes are the extensive use of chemotherapy in NSCLC and positron emission tomography before potential surgical treatment.

14.1 Consequences of our observations

14.1.1 Clinical issues

Centralizing of lung cancer patients eligible for radical treatment should continue. Thus it seems appropriate that lung cancer surgery is concentrated to only six university hospitals in Norway and radiation therapy to seven hospitals. Palliative chemotherapy should be given as far as possible locally in order to keep the patient near to home and family as much as possible in the remaining life time. In spite of new treatment options, it remains to estimate how this will improve the long term survival for the whole community population of lung cancer.

14.1.2 Research issues

This study forms a base for further comparative studies. In spite of increased emphasis in the treatment of NSCLC the last 15 years it remains to observe which impact with regard to survival and quality of life this has on the whole population of lung cancer patients in the community. A new study of the population from the same geographical area may provide answers on that question, in addition also to show if the manifestations of the patients has changed lately, as well as the management. A prerequisite for future community studies is however a more valid registration of all intervention procedures, records of all outpatients visits and quality of life.

Further studies should be performed on costs of lung cancer, including direct as well as indirect costs, in the community. Such studies should also include the procedures on diagnosis and treatment of lung cancer done by the primary health care.

Future research questions could be:

1. What is the optimal individual management of lung cancer in a local hospital area?
2. What is the most effective use of a multidisciplinary team for lung cancer?
3. What is the value of investigations of molecular-genetic markers for the treatment of lung cancer?
4. What is the effect of different palliative lung cancer treatments on quality of life and health economy in a general population?
5. What lung cancer patients are invited to participate in controlled clinical trials?

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