Patients' symptom experiences before and after lung cancer surgery
- predictors of patients' symptom burden

Trine Oksholm

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Summary

The purpose of this study was to explore multiple symptoms in lung cancer patients before and after surgery and to identify predictors of patients' symptom burden (including age). In total, 264 lung cancer patients were recruited from 3 university hospitals. They completed questionnaires preoperatively, and 1 and 5 months after surgery.

The study revealed that patients' experienced a mean of 10 symptoms before surgery, with only small differences in the older patients compared to the younger ones (>65 years). When comparing the occurrence of symptoms before and after surgery, there was a significant increase in the mean number of symptoms at 1 month. However, the only characteristic that was associated with a higher number of symptoms 1 month after surgery was the number of symptoms reported before surgery. At 5 months, the number of symptoms was reduced compared to the 1 month assessment, but it was still significantly higher compared to the preoperative assessment. A total of 79% of the patients experienced shortness of breath (SOB) 5 months after surgery, while 71% experienced lack of energy, and 56% reported pain. Some of the symptoms were intense. Our findings show that patients with more comorbidities and a higher number of preoperative symptoms need special attention, as they tend to experience a higher number of postoperative symptoms. Even though it is recommended in guidelines, only 32% of the patients had physical therapy after surgery and 16% had inpatient rehabilitation. While 30% of the patients were working preoperatively, only 9% worked at 5 months.

This study provides important information about the symptom burden of patients that underwent lung cancer surgery, and about the most vulnerable patients. The results can be used to educate patients about the normal course of postoperative recovery. Clinicians need to perform a comprehensive symptom assessment prior to surgery and at regular intervals after surgery.

List of papers

Article 1:

Oksholm, T., Miaskowski, C., Kongerud, J. S., Cooper, B., Paul, S. M., Laerum, L., Rustoen, T. (2013). Does age influence the symptom experience of lung cancer patients prior to surgery? Lung Cancer, 82 (1), 156-161.
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Article 2:

Oksholm, T., Miaskowski, C., Solberg, S., Lie, I., Cooper, B., Paul, S. M., Kongerud, J., Rustoen, T. (2014). Changes in symptom occurrence and severity before and after lung cancer surgery. Cancer Nursing. 38(5):351-357, September/October 2015.
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Article 3:

Oksholm, T., Rustoen, T., Cooper, B., Paul, S. M., Solberg, S., Henriksen, K., Kongerud, J., Miaskowski, C. Trajectories of symptom occurrence and severity from before through five months after lung cancer surgery. Journal of Pain and Symptom Management, 49 (6), 995-1015.
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Abbreviations

CTX	Chemotherapy
EORTC- QOL	Quality of life questionnaire developed by the European Organization for Research and Treatment of Cancer
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
LC13	A disease specific module of the EORTC QOL questionnaire that assesses lung cancer specific symptoms
MSAS	Memorial Symptom Assessment Scale
NSCLC	Non-small cell lung cancer
PORT	Postoperative adjuvant radiotherapy
pTNM	A system for cancer staging based on tumor (T), node (N), and metastasis (M), when the staging is done by pathologist, normally after surgery
QOL	Quality of life
SCQ	Self-administered Comorbidity Questionnaire
SOB	Shortness of breath
TNM	A system for cancer staging based on tumor (T), node (N), and metastasis (M)
TSM	Theory of Symptom Management

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1.0 INTRODUCTION

Lung cancer is an important cause of morbidity and mortality across the world. It is a leading cause of cancer deaths (1, 2). Surgical resection is considered the treatment of choice for patients with early stage, non-small cell lung cancer (2). Lung cancer patients are normally diagnosed shortly before surgery and the operation is extensive. After 7 to 10 days, patients are discharged to their homes. Transitioning from one care setting to another is a risky part of patient care (3, 4). The transfer increases the risk for medications errors, discontinuity in patients' follow-up visits, and worsening of symptoms (5-7).

Both preoperatively and before discharge from the hospital, patients want information about the usual course of recovery of their physical and mental health (8, 9). However, limited information is available on lung cancer patients' specific preferences following surgical treatment. In one study that presented hypothetical scenarios to 64 patients to assess their preferences for information following lung surgery (8), patients wanted information about postoperative outcomes (e.g., need for nursing home placement, oxygen dependence, restrictions in mobility, limitations in activities of daily living) before surgery to help them decide whether or not they want to have the surgery (8).

At hospital discharge, patients need information about common symptoms and when to seek care for unrelieved symptoms (9). Patients often experience several symptoms simultaneously. The co-occurrence of multiple symptoms is reported to be associated with significant decreases in functional status and quality of life (QOL) (10). In addition to the occurrence of the symptom, its frequency, severity, and associated distress are described to influence the patient's symptom experience (11).

Therefore, it is assumed to be of importance to assess more than the occurrence of the symptom to capture the symptom experience.

The idea and inspiration for the study came from results of a previous study at Oslo University Hospital (OUH). In that study, data were collected using semi-structured qualitative interviews with 11 patients, 3 months after lung cancer surgery (12). The patients described a postoperative period characterized by discomfort and lack of support from clinicians. They expressed a need for information about the normal postoperative period and when to contact a clinician (12). However, there is limited research about these patients rehabilitation phase.

At the initiation of this dissertations research, a literature review was done. The literature search focused on patients who underwent surgery for lung cancer, because patients who are not offered surgery are described to experience different symptoms (13-15). A significant gap in the literature on patients' symptoms and predictors of symptoms before and after lung cancer surgery was identified. Only four studies had evaluated symptoms in lung cancer patients prior to and after surgery (14, 16-18). In addition, only one study evaluated the severity and predictors of six symptoms at 1 and 4 months after lung cancer surgery (19).

Although the previous studies provided interesting information, several limitations were noted. First, these studies evaluated a limited number of symptoms (14, 16-19) , mainly because their main focus was to assess QOL (16-18). In addition, these evaluations were limited to either ratings of symptom severity (16-19) or symptom distress (14). Only two of the previous studies reported predictors of patients' symptom burden (14, 19). Assessment of predictors of patients' symptom burden is important for identifying vulnerable groups of patients. The literature review

revealed a need for a more comprehensive study that assed multiple symptoms and predictors of these symptoms; evaluated multiple dimensions of symptoms (i.e., occurrence of, frequency, severity, distress), in a larger sample patients, from prior to and following lung cancer surgery.

Lung cancer is a disease of the elderly (20). Older lung cancer patients have a higher number of comorbid conditions (21) and a higher number of comorbid conditions is associated with that patients report an increase the number of symptoms (14, 18). This study was conducted to gain knowledge about the symptom burden of elderly lung cancer patients from before through 5 months after surgery. Based on previous studies (15, 22, 23), patients in this study who were ≥ 65 years of age were categorized as older. Due to the limited information about symptoms in lung cancer patients who undergo surgery and for comparative purposes, both older and younger patients were included in this study. Since in the first paper, few differences were found in the majority of symptoms between the two age groups; age was not the main theme in the other two papers.

The Theory of Symptom Management (TSM) was chosen as the theoretical framework for this study, because it can be used as a guide to understand the patient's symptom experience, particularly in terms of the multiple dimensions of symptoms (10). The three essential dimensions of the TSM are symptom experience, symptom management strategies, and symptom status outcomes. Due to the lack of evidence about surgically treated lung cancer patients' symptoms, the main focus of the study was on patients' symptom experience. Symptom experience is defined as a simultaneous perception, evaluation, and response to a change in one's usual feeling (10). Knowledge about a patient's symptom experience is necessary to develop and

test interventions to improve patients' symptom management (10, 24, 25) and to change patients' symptom status outcomes.

2.0 BACKGROUND

2.1 Lung cancer

More than 600.000 patients are diagnosed with lung cancer in the United States and Europe annually (26, 27). In Norway, at the time of this study in 2011, 2842 patients were diagnosed with lung cancer and 57% of them were men and 43% women (28). As the incidence of lung cancer increases, especially in women, the social and economic burden of this disease increases as well (29, 30). Factors like occupational and environmental exposures and genetic characteristics are risk factors for the development of lung cancer (31, 32). However, smoking is the main cause of lung cancer. Approximately 10% to 20% of smokers develop lung cancer (32). The duration of smoking, the number of cigarettes smoked per day, and the age when smoking was initiated are some of the determinants associated with this risk factor.

Lung cancer is difficult to detect because in the early stages of the disease patients are often asymptomatic (32). As a result, patients diagnosed with lung cancer often have regional or distant spread at the time of diagnosis. Cancer statistics from the United States report that only 15.3% of lung cancer patients are diagnosed with localized disease (i.e., cancer found only in the part of the body where it started) (33).

Lung cancer is broadly categorized into small cell lung cancer (SCLC) and non–small cell cancer (NSCLC), based on histological differences in the tumor cells. NSCLC accounts for 80% of the cases while SCLC makes up 20% (31). NSCLC is further divided into three major and several minor histologic classes. The major histologic classes are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma (34). NSCLC is staged based on the TNM system (i.e., tumor (T), node

(N), and metastasis (M)). SCLC is not TNM staged but divided into limited or extensive disease (35).

The TNM classification system is used to stage the extent of NSCLC lung cancer. The T category describes the size and extent of the primary tumor; the N category describes the extent of involvement of regional lymph nodes; while the M category describes the presence or absence of distant metastasis (36). The TNM classification provides an indication of prognosis and aids clinicians in treatment planning (31). Based on the combinations of TNM staging, NSCLC is divided into stages from 0 – IV (i.e. Stage 0, Stage IA, Stage IB, Stage IIA, Stage IIB, Stage IIIA, Stage IIIB, Stage IV). While the staging system was revised in 2010, Stage 0 indicates no evidence of primary tumor and Stage IV indicates the presence of metastatic spread (31).

Lung cancer is the most frequent cause of cancer deaths in Europe (26). In Norway in 2011, the 5 year survival rates for lung cancer patients were 12.1% for men and 16.8% for women (28). The survival rates for patients with early stage lung cancer (both NSCLC and SCLC) have improved over the past 25 years, due to improved surgical procedures, better patient selection and follow-up, and the use of adjuvant chemotherapy (CTX) (37-39).

The 5 year survival rates for NSCLC depend on both the time of diagnose (stage of the disease) and sex (40-42). Based on the literature (40-42), the 5 year survival rates for women and men with different stages of disease are summarized in Table 1.

Table 1 Five year survival rates for women and men with different stages of lung cancer

Gender	Stage I	Stage II	Stage III
Women	47 – 69 %	41 – 63 %	15 – 46 %
Men	33 – 64 %	32 – 52 %	6 – 37 %

Lung cancer appears to be a more aggressive disease in men compared to women at the same stage of the disease. In SCLC, 60–70% of the patients have extensive disease at the time of diagnosis (43). These patients have median survival of 7–12 months and the proportion alive at 5 years is approximately 2%. Among patients with limited-stage disease, median survival is about 23 months and 5 years survival is approximately 12–17% (43).

2.2 Treatment of lung cancer

Surgical resection, radiotherapy, and CTX are the main curative treatments for NSCLC and SCLC. The specific treatment depends on the stage of the cancer, histology of the tumor, patients' preferences, and patients' physical condition (31). In previous years, single treatments were used. Currently, these patients receive a combination of treatments (31).

The treatments for NSCLC and SCLC differ. SCLC is treated primarily with CTX or CTX combined with radiotherapy (35). Surgery is offered to only 5% of patients with SCLC who are diagnosed in very early stages of the disease (35, 44). In NSCLC, surgical resection is offered to patients with stage I, II, and IIIA cancer (2). In addition to surgery, patients with NSCLC are offered treatment with CTX or

radiotherapy. Adjuvant treatment is given before and/or after surgery, depending of the stage of the disease (37, 45-47).

Because comorbidity increases with increasing age, the choice of optimal treatment for older patients with lung cancer can be challenging (48). The inability to predict which elderly patients are “fit” for treatment often results in under treatment (23, 48). The likelihood of receiving any kind of treatment for NSCLC decreases significantly with age (49). Older patients with lung cancer are less likely to be offered surgery (22, 50, 51), even though long term survival rates for older and younger patients are comparable (50, 52). Recently, recommendations about how to make treatment decisions seems to be based less on patients’ chronological age and more on the estimated absolute benefits of treatment, life expectancy, treatment tolerance, cognition, presence of comorbidities, and patient preferences (49).

2.2.1 Surgery

As discussed above, surgery is the main treatment for NSCLC. This approach is used unless the preoperative assessment reveals dissociated disease or the primary lesion is inoperable (2, 35, 44).

Historically, open thoracotomy was the only surgical approach for resection of tumor, lung tissue, and lymph nodes (31). During the last two decades, minimally invasive access - Video-Assisted Thoracic Surgery (VATS) has become more widespread. An increasing percentage of the patients are operated on using this method which is less traumatic and seems to offer the same survival advantage as open thoracotomy (53). The extent of resection performed during each operation is dependent mainly on tumor size and localization. Other factors include pre-exiting lung disease and the occurrence of comorbidities. Therefore, the extent of surgery

can vary from a wedge resection, segmentectomy, (bi-) lobectomy, to removal of the entire lung (pneumonectomy). In addition, reconstruction of airways and blood vessels can be performed in order to reduce the amount of lung tissue that needs to be removed. While removal of lymph nodes does not appear to improve survival (54), guidelines recommend that quite extensive dissection and removal of lymph nodes should be performed during these operations (54). If the surgeon determines that the tumor is too extensive to remove during surgery, the incision will be closed without tumor removal; which is referred to as exploratory surgery (55, 56).

2.2.2 Adjuvant chemotherapy (CTX)

Patients are offered CTX before (neoadjuvant) or/and after (adjuvant) surgery depending of the stage of their disease (37, 45-47). Because only four of the patients who participated in this study received neoadjuvant CTX (i.e. treatment before surgery), the focus of this section is on adjuvant CTX. Adjuvant CTX is recommended after surgery for patients with more advanced cancer (57). In general, the majority of patients with stage II or III NSCLC benefit from adjuvant CTX. However, evidence about its benefit in patients with stage 1B is inconclusive (57, 58). The Norwegian guidelines (i.e., Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av lungekreft) recommend adjuvant CTX for stage II or III NSCLC (44), but not for stage 1B.

Adjuvant CTX is usually started 4 to 6 weeks after surgery (57). The Norwegian guidelines recommend that treatment be initiated within 8 weeks (44). Vinorelbine with cisplatin is the most common adjuvant CTX regimen for lung cancer (57, 58). Usually, the treatment is given over 4 cycles. On day 1, patients receive a combination of vinorelbine with cisplatin, then a supplementary dose of vinorelbine

on day 8. This cycle is repeated every 21 days. The total duration of adjuvant CTX treatment is usually 10 weeks. Not every patient is able to complete all 4 cycles of CTX due to the toxic effects of the CTX. In some studies, only 50% of patients were able to complete all 4 cycles at the planned doses (57, 58).

Treatment with CTX can increase symptoms and decrease QOL (57, 58). The most frequent toxic effects of adjuvant CTX for NSCLC are neutropenia, anemia, and febrile neutropenia (58). Other common side effects are asthenia (i.e., weakness), nausea, vomiting, anorexia, and infection (57, 58).

2.2.3 Postoperative adjuvant radiotherapy (PORT)

Postoperative adjuvant radiotherapy (PORT) is recommended after adjuvant CTX for patients with resected NSCLC who have cancer cells present in two lymph nodes (i.e., N2 disease) and disease at Stage III A with N1 – N2 to reduce local recurrence (59). If the patient has N0 / pN1 disease, PORT is recommended if there is a suspicion of residual cancer (44). PORT is not recommended after pneumonectomy.

Treatment with PORT is normally given 25 to 30 times (44). No studies were found that explored symptom burden in patients treated with surgery and PORT, respectively (60). However, usual side effects of PORT are dermatitis, esophagitis, gastrointestinal symptoms, and neurologic toxic reactions (60). An increased risk of death from non-cancer causes has occurred after PORT. However, the toxicity has decreased with improvements in planning and in treatment technology (60). Both the severe disease and its treatments can cause symptoms in lung cancer patients(61)

2.3 Definition of a symptom and symptom experience of oncology patients

A symptom and patients' symptoms experiences are defined and described in different ways (11). In this study, we have chosen to define a symptom, as defined in the TMS, as a subjective experience that reflects changes in the biopsychosocial functioning, sensation, or cognition of an individual (62). In contrast, a sign is defined as any abnormality indicative of disease that is detectable by the individual or others (62). Both signs and symptoms are important aspects of health and illness. However, a symptom is the patient's own subjective experience and cannot be measured by others.

Knowledge about symptoms is important for cancer patients for several reasons. Symptoms are the most common reason why patients seek healthcare (10). Unrelieved symptoms are associated with increased psychological distress, decreased physical functioning, and reduced QOL (14). Symptoms can be produced by the disease itself, by treatments for the disease, from comorbid medical conditions, or from acute injuries (61).

Each symptom is a multidimensional experience (11). In addition to the occurrence of the symptom, its frequency, severity, and associated distress can influence the patient's symptom experience (11). The multidimensionality of the symptom experience is important because patients evaluate their symptoms, not only by their occurrence, but by making judgements about the severity, cause, treatability, and effects of symptoms on their lives (62). Previous research reports that the most prevalent symptoms are not necessarily the most severe or distressing (63, 64). Symptom distress is defined as the degree or amount of physical or mental upset, anguish, or suffering that in associated with a specific symptom (65).

Symptoms can be measured either individually or in combination with other symptoms (11). However, patients rarely experience a single symptom. Often, they experience multiple symptoms simultaneously (66). For example, patients with cancer were found to experience an average of 11 symptoms (67). The risk of experiencing multiple, concurrent symptoms after lung cancer surgery are high, since these patients can have both cancer-related symptoms as well as symptoms associated with surgery. The co-occurrence of multiple symptoms has a significant impact on patients' level of functioning (61). Further research is warranted to examine the experience of multiple symptoms in these patients.

2.4 Symptoms in lung cancer patients before and after surgery

To our knowledge, only five studies have evaluated changes in symptom occurrence, severity, and distress before and after lung cancer surgery (14, 16-19). All of these studies were published before the present study. Four of these studies reported symptoms preoperatively (14, 16-18), and one reported only symptoms after surgery (19). The most common preoperative symptoms were: cough, pain, dyspnea, loss of appetite, fatigue, and insomnia. One month after surgery, the most frequently reported symptoms were: fatigue, nausea, vomiting, insomnia, pain, and dyspnea (14, 16-19). The occurrence rates for all of these symptoms increased significantly after surgery. However, findings regarding the occurrence rates for the symptom at 4 to 6 months after surgery were inconsistent. While one study reported that the symptom rates at 4 to 6 months after surgery were back to preoperative levels (18), others reported that patients still experienced high rates of pain, dyspnea, fatigue, and cough at 4 to 6 months (14, 16, 17, 19) . All five studies used a longitudinal design, were well executed, and had a response rate of approximately 80% during

the first 4-6 moths (14, 16-19). A higher response rate is preferable because the missing data occurs at random (68). In addition, a response rate of approximate 80% is acceptable response rate for this patient population. Across these five studies, three different questionnaires were used to assess patients' symptoms. Three of studies assed symptoms using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 and the EORTC QLQ-LC13 lung cancer-specific questionnaire (16-18). One study used the Symptom Distress Scale (SDS) (14) and the other study used the Lung Cancer Symptom Scale (LCSS) (19). While all three questionnaires have acceptable psychometric properties, the major purpose of the EORTC QLQ questionnaires is to measure patients' QOL and not symptoms.

While these five studies provided interesting information, several limitations warrant considerations. For three of the previous studies the main focus was to assess QOL (16-18). These studies reported data on a limited number of symptoms and restricted the findings to only occurrence or severity rates for this limited number of symptoms (16-18). The first study of 110 patients reported on the severity of only two symptoms, namely cough and dyspnea (18). The second study had a limited sample (i.e. 60) and a very limited age range (i.e., only patients between 70 and 80 years) (16). Small sample sizes reduce the studies statistical power; which reduces the chance of detecting a true effect, as well as reduces the likelihood that a statistically significant result reflects a true effect (68). In addition, the restricted age range of the second study, limits the generalizability of the study findings. In the third study (n=173), patients were divided into two groups; namely one that remained disease free at 2 years and one with patients with recurrent cancer diagnosed during follow-up (18). Although, this division is an interesting one, it is difficult to use the

results to inform patients about symptoms, because it is difficult to know who will have recurrent cancer several years after cancer surgery.

In the last two of the five studies (14, 19); the primary focus was on an evaluation of patients' symptoms. However, one study focused on symptom distress in lung cancer patients who received different treatments (i.e., surgery, CTX, radiotherapy). Of note, the surgery group in this sample consisted of only 45 patients (14). In the fifth study (19), symptoms severity in 94 patients were assessed at 1 and 4 months after surgery. The lack of a preoperative symptom assessment makes it difficult to distinguish the symptoms that the patients experienced before and after surgery. The lack of preoperative symptom assessment is a significant limitation because lung cancer patients seem to have a high number of comorbidities than other patients (21). These two studier only focused on either symptom distress (14) or symptom severity (19). Therefore, we wanted determine if, multiple dimensions of the patients' symptoms experience change from before to following lung cancer surgery.

2.5 Symptoms influence on rehabilitation

This study follows the patients' from before to five months after surgery. At five months after surgery is the period of time when patients start the rehabilitation process. Cancer rehabilitation is defined as helping a person with cancer to help himself or herself obtain maximum physical, social, psychological, and vocational functioning (e.g., optimal working performance) within the limits imposed by the disease and its treatment (69). The aim of rehabilitation is to improve the quality of survival so that patients will be as comfortable and productive as possible and can function at a minimum level of dependency regardless of life expectancy (70).

Findings from two studies suggest that, compared to the general population, lung cancer patients have a poorer QOL prior to surgery (71, 72). In addition, one month after surgery, their QOL decreases compared to preoperative ratings (14, 17, 18, 73). However, findings regarding changes in QOL scores in months following surgery are inconsistent. While some studies found that patients' QOL returned to pre-surgical levels at 3 to 6 months after surgery (16, 18, 73, 74), others reported that QOL remained impaired for up to 2 years after surgery (17, 75). A reduction in QOL can have a major impact on patients' lives because it is associated with difficulties in fulfilling family roles; reductions in their inability to work; and reductions in their ability to participate in common social activities (76).

If patients experience multiple symptoms in the rehabilitation period, it could affect the progress of their rehabilitation, because multiple symptoms are associated with significant decreases in functional status and QOL (77). In addition, while symptoms are a major problem for patients, they can be a problem for their family caregivers. Due to a lack of follow-up care for these patients, symptom management often becomes a family member's responsibility (78). Cancer and its treatments may cause physical impairments and psychological distress in survivors (79). While limited research is available on lung cancer patients lives after surgery, the findings suggest that lung cancer patients have a poorer performance status after surgery compared to other cancer patients (80).

Rehabilitation and physical activity can help patients recover from surgery. The European Respiratory Society (ERS) and the European Society of Thoracic Surgery (ESTS) clinical guidelines on fitness for radical therapy in lung cancer patients (45) recommend early pre- and postoperative rehabilitation in patients with

operable lung cancer. Factors that are important in rehabilitation of surgically treated lung cancer patients include; increased physical activity, smoking cessation, and avoidance of malnutrition (81). In a recent study (82), the introduction of a standardized aerobic endurance training program as part of the inpatient rehabilitation of patients with lung cancer resulted in significant improvements in both physiological and psychological parameters after lung cancer surgery.

2.6 Comorbidities effect on symptoms

Comorbidity is the presence of one or more additional medical conditions that can co-occur with a primary disease or disorder (83). The prevalence of comorbidities among lung cancer patients is about twice as high as in the general population (21). Findings regarding whether the presence of comorbidities affect survival in patients with NSCLC are inconclusive (84, 85). In one study (84), the presence of comorbidities reduced survival. In another study (85), no association was found. The most common comorbidities in patients with lung cancer are cardiovascular disease, emphysema/chronic obstructive pulmonary disease (COPD), and hypertension (19, 85).

The presence of comorbidities is associated with a variety of symptoms and can influence the severity of symptoms in lung cancer patients (16, 19). However, studies on the relationships between comorbid conditions and the QOL of patients following lung cancer report divergent results (86-88). Two of these studies found that a higher number of comorbid conditions was associated with poorer physical and mental QOL (87, 88). In contrast, another study found no association between number of comorbid conditions and QOL (86). Additional research is needed to

confirm or refute these findings, and to examine further the impact that comorbid conditions have on symptoms.

2.7 Summary and critique of previous research on symptoms in patients undergoing surgery for lung cancer

Few studies have evaluated patients' symptom burden before and after lung cancer surgery (14, 16-19). Symptoms like; cough, pain, dyspnea, loss of appetite, fatigue, and insomnia were most common before surgery. The occurrence rates of several of these symptoms increased significantly after surgery (14, 16-19). Findings regarding further change in symptoms after surgery are inconsistent. The studies reported either that the symptom rates were back to preoperative levels 4-6 months after surgery (18), or that patients still experienced a high symptom burden (14, 16, 17, 19). These previous studies provided interesting information (14, 16-19), but had several limitations (i.e., reported data on a limited number of symptoms and only occurrence, distress or severity rates for these symptoms). However, it seems like lung cancer patients have a poorer performance status after surgery compared to other cancer patients (80).

2.8 Theory of Symptom Management (TSM)

The Theory of Symptom Management (TSM) was chosen as the theoretical framework for this study (10). The TSM is a middle range theory that can be used to guide symptom assessment and treatment in nursing practice. In addition, the TSM can be used to guide the development of hypotheses for nursing research (10). A middle range theory is a theory with limited scope, that explains a specific set of phenomena, in a discipline (89).

The TSM was first introduced as the Symptom Management Model by faculty members at the University of California, San Francisco (UCSF) in 1994 (78). The theory was further tested and discussed by students and faculty members at UCSF. Revised models were published in a journal in 2001 (62), and later as a chapter entitled “Theory of Symptom Management” in the third edition of the book “Middle Range Theory for Nursing”(10).

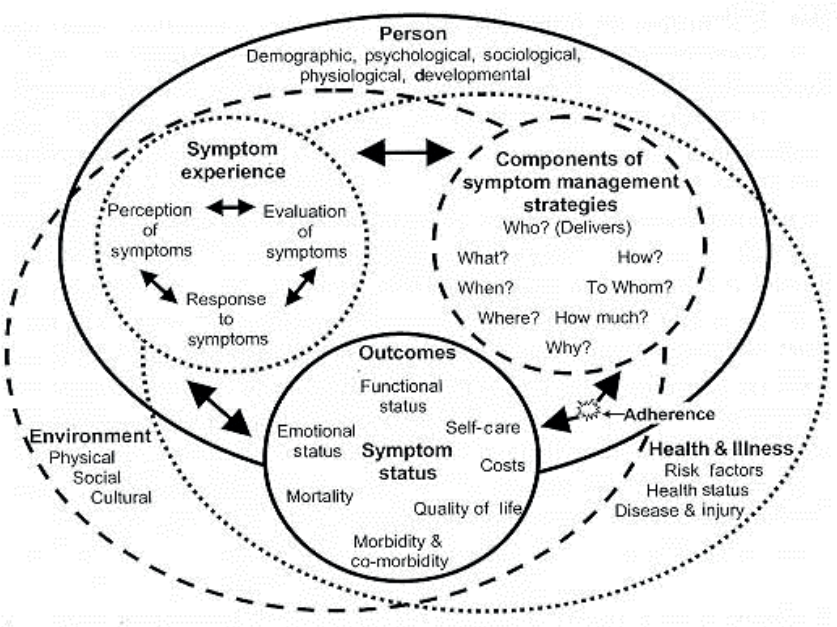

Figure 1. Model of the three essential dimensions of the TSM, the symptom experience, symptom management strategies, and symptom status outcomes.

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As illustrated in Figure 1, the three essential dimensions of the TSM are symptom experience, symptom management strategies, and symptom status outcomes (10). The symptoms experience dimension is defined as a perception, evaluation, and a response to a change in the person’s usual feelings (10). Patients

evaluate their symptoms by making judgement about the severity, cause, treatability, and effect of symptoms on their lives (62). The symptom management strategies dimension is defined as efforts to avert, delay, or minimize the symptom experience. Interventions to manage symptoms can be initiated by the health care provider or by patient or family members. The reduction in symptoms can be done by either reducing the frequency, the severity, or the distress associated with a symptom (90). The final dimension (i.e., symptom outcome) is defined as a change in a symptom's status. The change in symptom status can be that the symptom is less frequent, less intense, or less distressing. Factors like functional status, QOL, comorbidity, and morbidity will influence patients' symptom outcomes.

The three essential dimensions are nested within the three domains of nursing science (i.e., person, environment, health/illness). Personal factors, environmental factors, and a person's health/illness will influence a person's symptom experience. For instance, a woman's symptom experience is described to vary by age (person domain), her cultural beliefs about the symptom (environmental domain), and her current state of health (health/illness domain) (10). A simultaneous interaction exists among the symptom experience, symptom management strategies, and symptom status outcomes.

The TSM has been used in different ways in several studies (10, 91, 92). However, to our knowledge this study is the first to use the TSM in a sample of patients with lung cancer who were evaluated before and following surgery. The TSM illustrates the complexity of the patients' symptom experience. The TSM was used when the study was planned; it guided both the longitudinal design of the study, the selection of questionnaires, and which demographic and clinical characteristics were

collected. Further, the TSM guided the data analysis and the interpretation of the results. The TSM provided guidance on the important variables to evaluate both in this research study and in the clinic. Given the limited amount of evaluation on multiple dimensions of the symptom experience of lung cancer patients and how the symptoms change from before to following surgery, this study focused on the symptom experience dimension. Based on the findings from this study, subsequent intervention studies can be planned to decrease symptoms and improve rehabilitation outcomes in these patients.

AIMS OF THE STUDY

The main aims of this clinical, interdisciplinary, multi-center, and international research study with 264 lung cancer patients were to evaluate patients' symptom experiences before and after lung cancer surgery and to explore how demographic and clinical factors influenced these symptom experiences.

The specific aims were:

The aim of paper 1 was to evaluate for differences in the symptom experience (i.e., occurrence, severity, distress) between older (≥65 years) and younger (<65 years) patients using a multidimensional symptom assessment scale (i.e., Memorial Symptom Assessment Scale (MSAS)).

The aim of paper 2 was to evaluate for changes in symptom occurrence and severity from the preoperative period to 1 month after surgery. In addition, the associations between select demographic (i.e., age, gender, living situation) and clinical characteristics (i.e., preoperative FEV1, comorbidity, stage of cancer, extent of surgery, postoperative complications), as well as the number of preoperative symptoms, and the number of symptoms reported at 1 month after surgery were evaluated.

The aim of paper 3 was to evaluate for changes in symptom occurrence and severity from the preoperative period to 5 months after surgery and to evaluate for predictors of symptom occurrence and severity for seven of the most common symptoms.

4.0 METHODS

A longitudinal study that included 270 patients with presumptive primary lung cancer over 12 months was initiated in 2010. A longitudinal design is appropriate to study a phenomenon's development over time (93). Patients were recruited from three University Hospitals in different health regions in Norway. Data on demographic and clinical characteristics, comorbidities, symptoms, and QOL outcome were collected and used in this thesis. Patients filled in the Memorial Symptom Assessment Scale (MSAS), the European Organization for Research and Treatment of Cancer (EORTC) QOL questionnaire with its lung specific module (LC13), and the Self-administered Comorbidity Questionnaire (SCQ) preoperatively, and again at 1 and 5 months after surgery. Only data from the 3 item dyspnea scale of the EORTC QOL-LC13 (i.e., SOB at rest, SOB walking, SOB climbing stairs) were used in this thesis.

Patients were assessed prior to surgery, and at 1, 5, 9, and 12 months after surgery. Due to the time constraints of doctoral study, only data from the preoperative, one month, and 5 month assessment were analyzed for this thesis. Results from the 9 and 12 month assessments will be published after the thesis is completed. Most patients completed the preoperative assessment in the hospital. For the remaining assessments, patients received the questionnaires at home and returned them to the research office by mail. The one and five month time frames were chosen to evaluate the patients' symptom experience following surgery, as well as prior to and after the administration of adjuvant CTX.

4.1 Patients and settings

Patients were recruited from three university hospitals in Norway (i.e., Oslo University Hospital, St. Olav University Hospital in Trondheim, Haukeland University

Hospital in Bergen). The recruitment of patients started in October 2010 at Oslo University Hospital (OUS). Patients were recruited on the surgical ward prior to surgery (i.e., the pulmonary division at Rikshospitalet, patient hotel at Ullevål). At each institution, two nurses were trained to assist with patient recruitment when the PhD student was not present. A check list and a description of the information that needed to be provided to the patients were developed and used by these recruitment nurses (Appendix 1 and 2).

In November 2010, recruitment started at St. Olav University Hospital and in March 2011 at Haukeland University Hospital. The recruitment of patients at these clinics was done by nurses in the pulmonary outpatient clinics and in the division of thoracic surgery. The PhD student insured that identical procedures were followed at all of the recruitment sites. The recruitment of patients was completed in March 2012.

4.1.1 Inclusion criteria

Patients were included if they were adults ≥18 years of age; were able to read, write, and understand Norwegian; and were scheduled for surgery for primary lung cancer. Patients were excluded if they were cognitively impaired; their surgery was cancelled; or if the histological examination after surgery revealed that they had benign or metastatic disease. The research staff discussed with the responsible nurse and physician if the patient was cognitively impaired and if they were able to read, write, and understand Norwegian. If the clinicians were uncertain, patients were asked if they thought they were able to complete the questionnaires.

4.2 Study procedures

Research staff approached the patient and explained the purpose of the study. After obtaining written informed consent (Appendix 3), patients completed the

enrollment questionnaires (Appendix 4). The majority of the patients (91%) were recruited in the hospital one to three days before surgery. The remaining 9% of the sample was recruited in the outpatient clinic prior to surgery. At one and five months after surgery, patients were sent the study questionnaires and asked to return them using a postage paid envelope. The patients who did not return the questionnaires were sent one reminder after about 2 weeks.

When they enrolled in the study, patients were offered support to complete the questionnaires from the PhD student or the research nurse; if they expressed problems. The patients were given a mobile phone number and an e-mail address they could use to contact the staff if they had any questions about or reactions to the questionnaires that were mailed to them at 1 and 5 months after surgery (Appendix 5). The information about the possibility to withdraw from the study was repeated at all measurements points.

4.3 Study Variables and Instruments

Study measures were obtained through a set of multi-item questionnaires. In addition, data were abstracted from patients' charts. Measures and data collection time points are listed in Table 2. When the questionnaires were completed and returned, the forms were scanned by a company, and the results were transformed to a SPSS data file. Then, the PhD student checked the questionnaires against the scanned data file for any errors.

Table 2. Measures and data collection time points

Concepts measured	Instruments	Data source	Study months		
			0	1	5
Patient demographics	Study specific	Qnaire / charts	X	X	X
Clinical and medical information	Study specific	Qnaire / charts	X	X	X
Comorbidity	SCQ	Charts	X		X
Symptoms (general)	MSAS	Qnaire	X	X	X
Quality of life	EORTC QLQ-C30+LC13	Qnaire	X	X	X

4.3.1 Demographic and clinical characteristics

Information about demographic and clinical characteristics were collected either from the patients or from their medical records. Patients provided information on gender, marital status, living situation, level of education, and employment status. Patients' medical records were reviewed for information on age, lung function, height, weight, and use of preoperative medications, tumor histology, type of surgery, and TNM classification (94). A case report form (CRF) was developed to ensure that this information was collected from the medical records of all patients (Appendix 1). The PhD student or the research nurse completed the CRF based on information found in the patient's medical record. The PhD student picked up the CRFs at the different hospitals and brought the forms to OUS. The PhD student evaluated all of the CRF forms for completions and obtained any missing data prior to entering the information into the SPSS database.

Information on smoking status was collected at all three assessments. The initial information on smoking status (i.e., pre-operative assessment) was obtained

from the patients' medical records. At the 1 and 5 month assessments, the patients provided information about smoking. Preoperative information about smoking status included: when they started and eventually stopped smoking and the number of cigarettes smoked daily. This information is important for the calculation of number of pack-years, which is the unit to measure the amount a person has smoked over time. One pack-year is 20 cigarettes smoked/day for one year (95). Based on information about smoking history, the patients were divided into three groups; never smoked, previous smokers, and current smokers. At one and 5 months after surgery, the patients were asked if they were smoking (i.e., yes/no) and if they had stopped smoking in the period since the last assessment.

Patients' lung function was measured by spirometry preoperatively and their FEV1 (forced expiratory volume in 1 second) and FVC (forced vital capacity) values were recorded in their medical records. FVC is the volume of air that can forcibly be blown out after full inspiration. FEV1 is the volume of air that can forcibly be blown out in the first second after full inspiration. Predicted normal values for FEV1 and FVC are calculated based on an individual's age, sex, height, weight, and ethnicity. By comparing the measured FEV1 and FVC with the predicted normal values, the percent of expected FEV1 and FVC were calculated (96).

Patients' height and weight were recorded from the medical records. Body mass index (BMI) was calculated. BMI is a formula that determines whether an individual has the correct weight for their height (97).

4.3.2 Comorbidity questionnaire

To measure comorbidity, the Self-administered Comorbidity Questionnaire (SCQ) was chosen because it was used in another study of Norwegian cancer

patients and found to be a useful and reliable scale (98, 99). The SCQ was completed at the preoperative and 5 month assessments (Appendix 4). The SCQ includes 16 common comorbidities and three optional conditions (100). Patients indicated whether or not they had the comorbid condition (yes/no); if they had the condition they were asked if they received treatment for it (yes/no); and finally if it limited their activities (yes/no). The SCQ can be scored in two different ways (i.e., a sum score, a total score). The sum score is a count of the number of comorbid conditions and can range from 0 to 19. The total SCQ-19 score ranges from 0-57. An individual can receive a maximum of 3 points for each medical condition: 1 point for the presence of the condition, another point if he/she receives treatment for it, and an additional point if the condition causes a limitation in function. Because the SCQ contains 16 defined medical conditions and 3 optional conditions, the maximum score totals 57 points if the open ended items are used and 48 points if only the close-ended items are used (100, 101). A higher total score indicates a more severe comorbidity profile.

The SCQ was used to assess comorbidity in Norwegian oncology patients in previous studies (98, 99). The SCQ was translated into Norwegian using a standard forward backward translation procedure. The SCQ was tested on medical and surgical patients; test-retest reliability of the SCQ was shown to be 0.94 calculated by the intraclass correlation coefficient and 0.81 by the Spearman correlation coefficient (100).

4.3.3 Symptoms assessment scale

Several instruments are available to measure multiple symptoms in cancer patients. In one review (67), three questionnaires were considered to be valid and

reliable instruments to measure multiple symptoms in cancer patients at different stages of their disease. The three instruments were: Symptom Distress Scale (102), M. D. Anderson Symptom Inventory (103), and Memorial Symptom Assessment Scale (MSAS) (90). The Symptom Distress Scale is a 13-item self-report instrument that assesses the level of distress associated with 13 symptoms. The M. D. Anderson Symptom Inventory measures the severity of 10 physical symptoms, three psychological symptoms, and six interference items (103). The MSAS assesses the occurrence, frequency, severity, and distress of 32 symptoms (90). The MSAS was selected because it assesses a broad range of symptoms across multiple dimensions of the symptom experience.

The Memorial Symptom Assessment Scale (MSAS) is a patient-rated instrument that was developed to provide multidimensional information about common symptoms (Appendix 4). The scale contains a list of 32 physical and psychological symptoms. Patients completed the questionnaire prior to surgery and at 1 and 5 months. Patients were asked to indicate whether or not they had the symptom during the past week (i.e., symptom occurrence). If they experienced the symptom, they were asked to rate its frequency, severity, and distress. Symptom frequency was rated using a four-point Likert scale (1= rarely, 2 = occasionally, 3 = frequently, 4 = almost constantly). Symptom severity was rated using a four-point Likert scale (1= slight, 2 = moderate, 3 = severe, 4 = very severe). Symptom distress was rated using a five-point Likert scale (i.e., 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much).

The MSAS is a reliable and valid instrument for the assessment of symptom occurrence, severity, and distress (90). During its development the validity of MSAS

was tested using a number of approaches. To test the concurrent validity of the MSAS, relationships between symptoms scores and functional status (measured using the Karnofsky Performance Status (KPS) scale) and QOL (measured using the FLIC) scores were evaluated. Patients with an increased symptom burden had lower functional status and QOL scores (90). The construct validity of MSAS was evaluated by comparing MSAS scores in different subpopulations. As expected, inpatients had higher distress scores than outpatients. In addition, patients with more advanced disease were more symptomatic than patients with earlier stage disease (90).

Previous research used the MSAS to evaluate symptoms in Norwegian oncology patients (63). It was translated into Norwegian using a standard forward-backward translation procedure. Before it was used in a longitudinal study with 188 breast cancer patients (63), it was pilot tested with 10 breast cancer patients. Only minor linguistic adjustments were needed after the pilot testing.

4.3.4 Quality of life questionnaire with a lung cancer specific module

Numerous instruments are available to assess QOL in oncology patients. The most frequently used questionnaires to measure the QOL of lung cancer patients before and after surgery are the Medical Outcomes Study - Short Form Health Survey 36 (SF 36) (55) and the European Organization for Research and Treatment of Cancer (EORTC) QOL questionnaire (55, 104). In this study, the EORTC QOL questionnaire (Appendix 4) (105) was selected because this questionnaire was developed to measure QOL in cancer patients, and to be able to compare the results from our study with previous research. In addition, it has a lung cancer specific module (i.e., LC13) that measures lung cancer associated symptoms and side effects

from treatment (106). However, in this study, only the lung cancer specific module (i.e., LC13) was used because it has specific items for lung cancer patients.

The EORTC QOL core questionnaire consists of 30 items (105). It includes five functional scales (i.e., physical, role, emotional, social, cognitive), three symptom scales (i.e., fatigue, pain, nausea/vomiting), a global health status/QOL scale, and a number of single items that assess additional symptoms and perceived financial impact. This cancer specific, multidimensional questionnaire was tested in different cultures and was translated into several languages, including Norwegian (107).

The EORTC QOL-LC13 is a disease specific module, that assesses lung cancer specific symptoms including cough, hemoptysis, dyspnea, and pain as well as side effects associated with CTX and RT therapy (106). Patients were asked to rate the severity of the symptom using a four-point Likert scale (i.e., 1 = not at all, 2 = a little, 3 = quite a bit, 4 = very much). Responses to the QLQ-LC13 questionnaire were scored according to procedures specified in the EORTC scoring manual (108). EORTC QLQ-LC13 was validated in Norwegian patients. It was found to be a clinically valid and a useful tool to assess disease- and treatment-specific symptoms in lung cancer patients when it was combined with the EORTC QOL core questionnaire (106). In this thesis, only the three item dyspnea scale from the EORTC QOL-LC13 was used (i.e., SOB at rest, SOB walking, SOB climbing stairs).

4.4 Statistics

All analyses were done using SPSS version 20 and STATA Version 13. For all tests, a p-value of <0.05 was considered statistically significant. Descriptive statistics were used to present demographic and clinical characteristics of the sample. Means

and standard deviations were generated for quantitative variables and frequencies and percentages for categorical variables.

Paper 1

In the first paper, a cross sectional design was used. Cross-sectional studies are appropriate for describing the status of a phenomenon, or the relationship between phenomena, at a fixed point in time (93). This paper evaluated for differences in symptom occurrence, severity, and distress between older (≥65 years) and younger (<65 years) patients, preoperatively. Mean scores for severity and distress ratings were calculated for those patients who reported a symptom. Independent Student's t-tests, Mann-Whitney U tests, and Chi Square analyses were used to evaluate for differences in demographic and clinical characteristics between the two age groups. Differences between the two age groups in demographic characteristics with multiple levels (e.g., employment status) were further examined using post hoc contrasts with a Bonferroni correction (68). Post-hoc analyses are concerned with finding patterns and/or relationships between subgroups (e.g., working full or part-time, being on sick leave or disability, or being retired).

Logistic regression analysis was used to evaluate the effect of increasing age on the occurrence of each symptom. Significant differences in the occurrence of each symptom were evaluated using binary logistic regression analyses. To evaluate for differences between the two age groups in the severity and distress ratings for each symptom, ordinal logistic regression was utilized. Deviance tests were used for the binary logistic regression to determine whether the set of covariates improved the fit of the model. Ordinal logistic regression was done with bootstrapping that used at least 1000 repetitions for each analysis. Bootstrapping is done to assign measures of

accuracy to sample estimates (109). Significance was evaluated with bias-corrected bootstrapped confidence intervals.

Paper 2

The purposes of this paper were to assess for changes in symptom occurrence rates and severity scores from the preoperative period to 1 month after surgery. Mean scores for severity ratings were calculated for those patients who reported a symptom.

McNemar's tests were used to evaluate for changes in symptom occurrence rates (110). This test determined whether changes in symptom occurrence rates in one direction were significantly greater than in the opposite direction (i.e., was the number of patients who went from not reporting the symptom preoperatively to reporting it postoperatively higher than those who went from reporting the symptom preoperatively to not reporting it postoperatively). A paired t-test was used to evaluate for changes over time in symptom severity ratings. This analysis was done only for symptoms where patients reported severity scores either preoperatively, postoperatively, or on both occasions.

The General Linear Model procedure was used to determine whether select demographic and clinical characteristics, as well as total number of preoperative symptoms were associated with the total number of symptoms reported after surgery. A multivariable model was created and the analysis was performed twice. First an unadjusted analysis was done with all factors in the model. Second, a final model was created with the predictors that were significant in the unadjusted model or were found to be important covariates to include based on previous research.

Paper 3

This paper evaluated the six most common physical symptoms and the most common psychological symptom for changes over time in symptom occurrence and severity by using a multilevel growth model (MGM). Symptom occurrence was examined using multilevel logistic regression (111). Changes in symptom severity were examined with multilevel proportional odds ordinal logistic regression. For both types of models, random intercepts were estimated, with the first assessment being treated as the baseline (or intercept) for the growth trajectory.

Unconditional models were examined first to estimate the linear change in the symptom reports. Since the growth trajectory might not be only linear, quadratic effects were examined. Based on previous research (19), age, gender, comorbidity (i.e., SCQ total score), and receipt of adjuvant CTX were included as covariates in the conditional models for both symptom occurrence and severity. After identifying the best fitting growth trajectory for each symptom, conditional models were fit to examine the associations for each of the covariates on the reported symptom dimensions at enrollment (i.e., prior to surgery) and on the change in symptom dimensions over time (cross-level interaction) (112).

Supplementary analyzes

To present more detailed information on the frequency, severity, and distress dimensions of this patients' symptom experience, additional analyses was done and are presented in the front ("cappa"). In addition, differences in the symptom experience of patients who did and did not receive physiotherapy or rehabilitation were evaluated.

Mean scores for symptom frequency and distress ratings were calculated and presented for all three assessments for those patients who reported a symptom. Differences in the total number of symptom at five months were examined with paired T test between patients who had and had not received physiotherapy or rehabilitation.

4.5 1.1 Ethical considerations

This study was approved by the Regional Ethical Review Committee (REK), with REK number 2010/1508b, and supported by the Institutional Review Boards (Personvernombudet) at the hospitals involved in the study. New REK permissions were obtained before the recruitment of patients started at Haukeland University Hospital. Patients signed an informed consent when they agreed to participate in the study (Appendix 3).

The patients who participated in this study were a vulnerable group, because lung cancer is a serious and stigmatizing illness. They were included in the study at a difficult time of their life; shortly after being diagnosed with cancer and facing surgery. To ensure that patients did not feel pressured to participate in the study; they were asked by a familiar nurse if they wanted information about the study. An information brochure were developed and given to the patients to inform them about the study (Appendix 6).

Some of the questions about psychological factors could be sensitive for patients to answer, and this could be experienced as a burden for the patients. Patients were informed that participation in the study was voluntary, that their treatment would be the same whether they participated or not, and that they could withdraw from the study at any time. The patients were given an email address and a

telephone number when they enrolled in the study. This information was repeated in the information letter that was sent with the questionnaires (Appendix 5). If the patients did not answer the questionnaire, they were sent only one reminder. Patients who did not respond to two consecutive assessments were not sent any additional questionnaires. If the patient contacted the PhD student with questions, they were given the necessary information about the topic, and were informed about the possibility to withdraw from the study.

To ensure the patients' anonymity and confidentiality, the questionnaires were marked with a code. The list that connected patients' names and the code was kept in a locked safe in a locked room in the hospital. The data files were stored according to Oslo University Hospitals' safety rules.

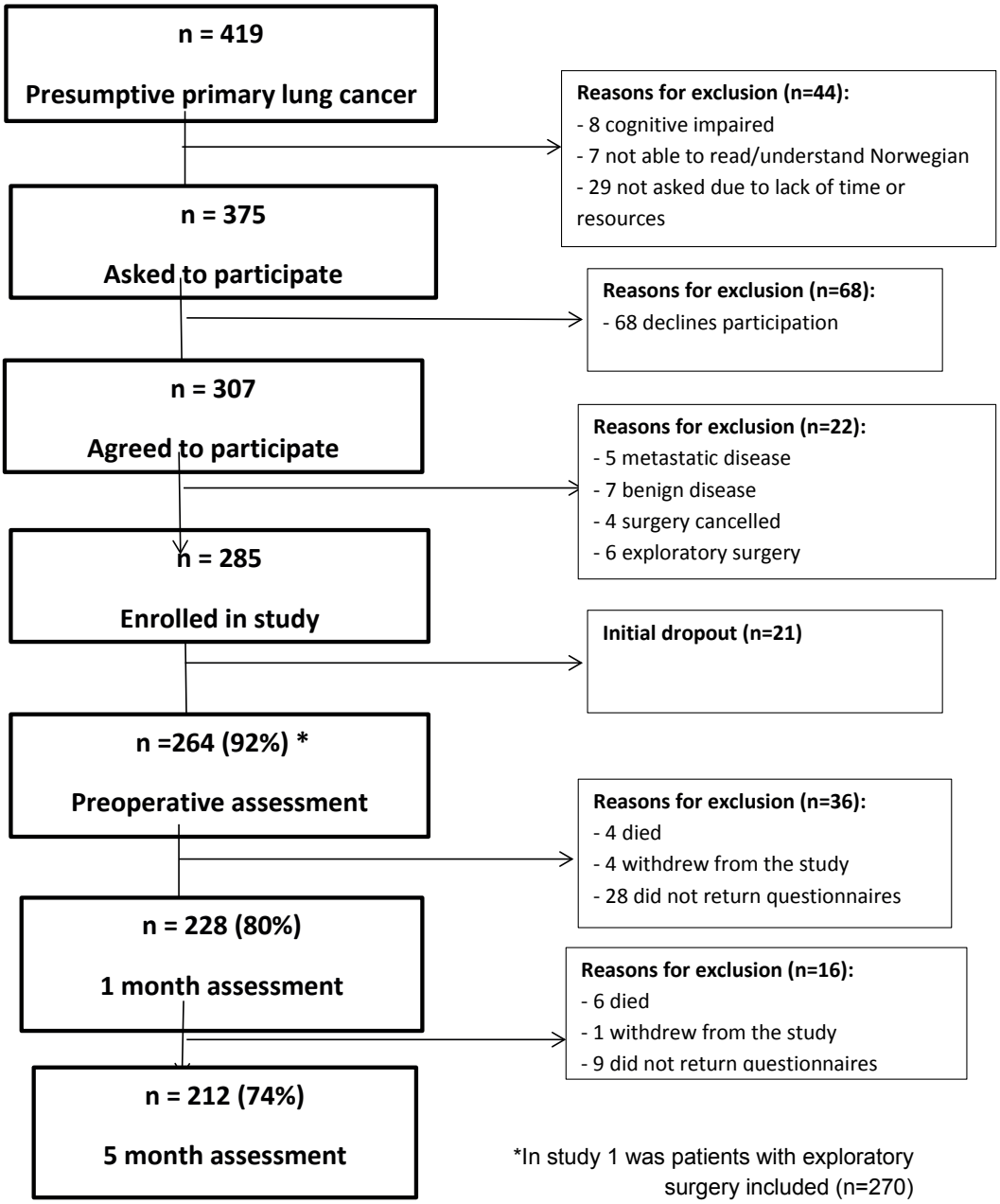

Figure 2. Flow chart inclusion and exclusion.

5.0 RESULTS

5.1 Sample

Of the 419 patients with presumptive primary lung cancer, 375 were eligible to be approached about participation, and 307 agreed to participate (81% response rate). Based on our pre-specified exclusion criteria, 15 patients were excluded (i.e., 5 for metastatic disease, 7 for benign disease, 4 had surgery cancelled,) (Figure 2). The 6 patients who had exploratory surgery were included in the sample in paper 1 (n=270) because this paper presented preoperative data. However, these patients were excluded from the preoperative sample in papers 2 and 3, because they did not have a tumor removed (n=264). The recruitment was planned so that all eligible patients would be asked about participation, but due to lack of time or resources, 29 of the potential patients were not invited to participate.

The demographic and clinical characteristics of the patients at the different assessment points are summarized in Table 3. Approximately 45% of the patients smoked preoperatively, 10% after one month, while 13% smoked five months after surgery. The number of patients who worked decreased from 30% preoperatively to 9% five months after surgery (Table 3). In this study, 77% of the patients were transported to a local hospital before coming home. At five months, 36% of the patients were using analgesics, compared to 15% at the preoperative and 75% at the postoperative assessments (i.e., one month).

A total of 85% of the patients reported comorbid conditions; 23% had one comorbid condition, 25% had 2, and 37% had 3 or more comorbid conditions. The most frequent comorbid condition was back/neck pain (46%), followed by

hypertension (34%), and COPD (32%). Approximately 30% of the patients received CTX after surgery.

Patients who declined participation in the study was significantly older (mean age 70.0 years, SD 7.4, $p < .001$) compared to those who participated. No gender differences were found between participants and non-participants ($p=0.41$). Of the 264 who completed the preoperative assessment; 10 patients died during the first 5 months.

Table 3: The demographic and clinical characteristics of the patients at the different assessment points.

Characteristics	Assessment		
	Preoperative n=270*	1 month n=228	5 months n=212
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	65.8 (8.5)	65.8 (8.5)	66.1 (8.3)
SCQ-19 score	4.4 (3.8)	4.3 (3.8)	4.2 (3.8)
Mean number of MSAS symptoms	9.1 (7.0)	12.8 (6.7)	11.0 (6.9)
	% (n)	% (n)	% (n)
Gender- Female	41.5 (112)	43.4 (99)	42.9 (91)
Lives alone	23.1 (59)	23.1 (50)	21.7 (46)
Partnered/married	73.0 (189)	73.4 (160)	72.9 (148)
Education			
Primary School	36.6 (94)	36.6 (79)	35.6 (72)
Secondary school	47.1 (121)	48.1 (104)	48.0 (97)
University/ College	16.3 (42)	15.3 (33)	16.3 (33)
Employment status:			
Full or part-time	29.9 (60)	13.1 (26)	8.8 (17)
Sick leave or disability	23.9 (48)	32.2 (64)	35.2 (68)
Retired or other	43.9 (93)	54.8 (109)	56.0 (108)
Smoking (% yes)	45.3 (96)	10.1 (20)	12.6 (26)
Tumor type			
Adenocarcinoma	56.3 (152)	56.1 (128)	55.2 (117)
Squamous cell	30.7(83)	30.7 (70)	30.7 (65)
Small cell	2.2(6)	2.2 (5)	2.4 (5)
Carcinoid	2.2(6)	2.2 (5)	2.8 (6)
Other	8.5 (23)	8.8 (20)	9.0 (19)
Stage of cancer disease			
IA	32.0 (80)	31.8 (68)	33.3 (66)
IB	31.6 (79)	33.2 (71)	31.8 (63)
II	18.8 (47)	18.7 (40)	19.7 (39)
IIIA	16.0 (40)	15.9 (34)	14.6 (29)
IIIB - IV	1.6 (4)	0.5 (1)	0.5 (1)
Type of surgery			
Lobectomy	183 (68.0)	69.3 (158)	67.5 (143)
Bi-lobectomy	19 (7.1)	6.1 (14)	7.1 (15)
Pneumonectomy	23 (8.6)	9.6 (22)	9.4 (20)
Wedge resection	24 (8.9)	8.8 (20)	9.4 (20)
Video-assisted thoracoscopic surgery	14 (5.2)	6.1 (14)	6.6 (14)
Exploratory surgery	2.2 (6)	0	0
Used analgesic (% yes)	14.6 (31)	74.8 (169)	36.0 (73)

5.2 Results of paper 1

This paper evaluated for differences in symptom occurrence, severity, and distress between older (≥65 years) and younger (<65 years) patients prior to surgery. No significant differences were found in the total number of symptoms reported by older (mean=9.15, SD=7.64) and younger (mean =10.11, SD=6.96) patients. Looking at the individuals with symptoms; in the bivariate analyses, older patients reported significantly lower occurrence rates for difficulty concentrating ($p<.01$), feeling drowsy ($p<.01$), feeling nervous ($p<.05$), feeling sad ($p<.05$), and worrying ($p<.05$). In the multivariable analyses, after adjusting for employment status, analgesic use, and the use of anticholinergic medicines, older patients reported a significantly lower occurrence rate for only one symptom, namely feeling drowsy.

Symptom severity scores ranged from slight to moderate. In the bivariate analyses, older patients reported significantly lower severity scores for difficulty concentrating ($p=.049$), feeling nervous ($p=.044$), and feeling sad ($p=.045$). In the multivariable analyses, only the severity score for feeling nervous ($p=.049$) was significant in that older patients were 71% less likely to report a higher severity score for feeling nervous

Mean distress scores ranged from a “little bit” to “somewhat”. In the bivariate analyses, older patients reported significantly lower distress ratings for five symptoms (i.e., feeling drowsy ($p=.012$), pain ($p=.018$), lack of energy ($p=.029$), shortness of breath ($p=.044$), worrying ($p=.036$)). In the multivariable analyses, only lack of energy ($p=.035$) was significant in that older patients were 71% less likely to report a higher distress score.

5.3 Results of paper 2

This paper evaluated for changes in symptom occurrence rates and severity ratings from the preoperative period to 1 month after surgery. The total number of symptoms increased significantly from the preoperative (mean = 9.4) to the postoperative (mean = 13.1) assessment (p<.001). Of the 11 symptoms that occurred in ≥50% of the patients at 1 month, 8 of them increased significantly in both occurrence rates and severity ratings from the preoperative assessment. The occurrence rates for SOB (p<.001), lack of energy (p<.001), pain (p<.001), feeling drowsy (p<.001), dry mouth (p<.001), sweats (p=.003), feeling bloated (p=.021), and lack of appetite (p<.001) increased significantly from the preoperative to the postoperative assessment.

Severity scores for SOB (CI 0.69 to 1.17), lack of energy (CI 0.74 to 1.21), pain (CI 0.86 to 1.28), feeling drowsy (CI 0.64 to 1.03), dry mouth (CI 0.14 to 0.67), sweats (CI 0.18 to 0.82), feeling bloated (CI 0.05 to 0.71), and lack of appetite (CI 1.01 to 1.59) increased significantly from the preoperative to the postoperative assessment. The only symptom that had a significant reduction in its severity score was cough (CI -0.58 to -0.06).

In both the unadjusted and final models, the only variable that was associated with a higher number of postoperative symptoms was the number of preoperative symptoms reported by the patient.

5.4 Results of paper 3

This paper evaluated for changes in symptom occurrence rates and severity ratings from the preoperative period to 1 and 5 months after surgery. The total number of symptoms increased significantly from the preoperative (mean=9.1

SD=7.0) to the 1 month (mean=12.8, SD=6.7, p<.001) assessment. At 5 months, the number of symptoms was lower than at 1 month but significantly higher (mean=11.0, SD=6.9, p<.001) than at the preoperative assessment.

The patterns in the occurrence and severity of symptoms varied for the seven symptom evaluated in this paper. For example, in the unconditional model, trajectories for the occurrence of pain, lack of energy, SOB, feeling drowsy, and worrying increased significantly from prior to through the first month after surgery and then decreased over time. In contrast, the occurrence of cough and difficulty sleeping did not change over time. In terms of the patterns observed for the symptom severity ratings, in the unconditional model, the severity of SOB at rest and during walking and climbing stairs changed over time. SOB when resting, walking, and climbing stairs increased significantly from enrollment to one month and then decreased over time. In contrast, the severity of cough decreased from enrollment to one month after surgery and then increased over time. Of note, severity ratings for pain, lack of energy, feeling drowsy, difficulty sleeping, and worrying did not change over time.

Overall, the four covariates (i.e., comorbidity score, age, gender, receipt of adjuvant CTX) influenced the occurrence of symptoms preoperatively. Comorbid conditions influenced the occurrence of all symptoms except cough preoperatively and it influenced the occurrence of difficulty sleeping over time.

Patients who were older were less likely to report pain and feeling drowsy preoperatively. In addition, age influenced changes over time in the severity ratings for SOB when climbing stairs. From the preoperative assessment to one month after surgery, younger patients' severity ratings for SOB when climbing stairs increased and then decreased at a faster rate than those of the older patients.

In this paper, women reported higher occurrence rates for worrying preoperatively, and a greater increase in the severity scores for pain at one month. From the preoperative to the one month assessment, women's pain severity scores increased while men's pain severity scores decreased. The opposite patterns were observed from the one month to the 5 month assessment.

The last covariate; receipt of adjuvant CTX increased the occurrence of the following symptoms; lack of energy, difficulty sleeping, pain, and feeling drowsy preoperatively, as well as the severity of cough. The administration of adjuvant CTX was associated with higher severity ratings for cough at the preoperative assessment followed by a decline in the severity ratings for cough and then a subsequent increase in the severity of cough.

5.5 Results of the additional analyses

The additional analyses revealed that the symptoms with the highest occurrence rates at the different assessments were not necessarily the most frequent, severe or distressing at five months after surgery (Table 4 and 5). The five symptoms with the highest occurrence rates at five months were: SOB, lack of energy, feeling drowsy, cough, and pain. The five symptoms with the highest frequency rates at five months were; problems with sexual interest, SOB, hair loss, lack of energy, and changes in skin.

Problems with sexual interest had the ninth highest occurrence rate at the 5 months assessment. However, for patients who reported this symptom, it had the highest ratings for frequency, severity and distress. Of note, some of the symptoms that were rated as very severe or distressing were only experienced by a few patients. Symptoms like "I don't look like myself" and "problems with urination" were

among the top five most severe and distressing symptoms, but were only experienced by a limited number of patient (i.e., n=13 and n= 33, respectively). While different symptoms were among the most common as well as among the most frequent, severe or distressing symptom, two symptoms, namely SOB and lack of energy were among the top five for all of the symptom dimensions at 5 months.

Additional analysis was done to further explore patients' symptom experience at five months for the 8 symptoms with the highest severity and distress ratings (Table 6 and 7). The purpose of this analysis was to obtain more detailed information about the distribution of the severity and distress scores for these symptoms. These analyses revealed that the majority of the patients reported relative low levels of severity and/or distress for these symptoms. However, between 5% and 10% of the patients reported high severity and/or distress scores for the 8 symptoms. These patients may be at particularly high risk and warrant more aggressive symptom management. SOB and lack of energy were the two symptoms associated with high severity and distress ratings for the majority of the patients.

Finally, an analysis was done that compared the total number of symptoms at five months, between patients who did and did not receive physical therapy and/or rehabilitation. The purpose of this analysis was to evaluate if physiotherapy and/or rehabilitation reduced the number of symptoms. Forty-two percent of the patients (n=89) received physical therapy and/or inpatient rehabilitation after surgery. When the total number of symptoms was compared between patients' who received and did not receive physiotherapy/rehabilitation, no differences were found. In addition, no between group differences were found on gender, age and number of comorbidities.

Table 4. The symptoms with the highest occurrence rates and the highest frequency, sever, frequent, and distress rating at different assessment points

OCCURRENCE RATES				
Rank†	Symptoms	**Preoperative (n=264)**	**1 month (n=228)**	**5 months (n=212)**
		% of patients	% of patients	% of patients
1	Shortness of breath	51.1	85.5	78.8
2	Lack of energy	54.9	83.8	70.8
3	Feeling drowsy	52.7	82.5	67.0
4	Cough	64.0	61.4	59.9
5	Pain	38.6	83.3	55.7
6	Difficulty sleeping	46.6	51.8	50.5
7	Feeling bloated	44.7	51.8	49.1
8	Dry mouth	45.8	58.8	48.1
9	Problems with sexual int.	43.6	49.6	46.7
10	Worrying	51.5	56.6	46.7
FREQUENCE RATINGS¤				
Rank†	Symptom	**Preoperative**	**1 month**	**5 months**
		Mean score (SD)	Mean score (SD)	Mean score (SD)
1	Problems with sexual interest	2.63 (1.03)	2.87 (1.13)	2.79 (.99)
2	Shortness of breath	2.47 (.92)	2.64 (.93)	2.60 (.94)
3	Hair loss	2.58 (1.22)	2.56 (1.29)	2.54 (1.14)
4	Lack of energy	2.50 (.97)	2.71 (.88)	2.52 (.86)
5	Changes in Skin	2.05 (.90)	2.06 (1.09)	2.52 (.95)
6	Feeling drowsy	2.36 (.80)	2.47 (.82)	2.36 (.80)
7	Pain	2.60 (1.06)	2.48 (.97)	2.28 (.96)
8	Feeling bloated	2.14 (.80)	2.18 (.84)	2.28 (.87)
9	Changes in way food tastes	1.75 (.91)	2.46 (1.03)	2.23 (.83)
10	Difficulty sleeping	2.49 (.90)	2.55 (.91)	2.21 (.92)
SEVERITY RATINGS*				
Rank†	Symptom	**Preoperative**	**1 month**	**5 months**
		Mean score (SD)	Mean score (SD)	Mean score (SD)
1	Problems with sexual int.	2.46 (.90)	2.43 (.85)	2.53 (.90)
2	I don't look like myself	2.25 (.87)	2.27 (.80)	2.38 (.96)
3	Shortness of breath	2.14 (.74)	2.20 (.73)	2.25 (.82)
4	Lack of energy	2.08 (.74)	2.21 (.74)	2.19 (.69)
5	Problems with urination	2.07 (.92)	1.77 (.85)	2.15 (.83)
6	Constipation	2.06 (.72)	2.11 (.90)	2.14 (.81)
7	Hair loss	2.64 (1.15)	2.36 (1.13)	2.12 (1.09)
8	Changes in Skin	1.62 (.62)	1.77 (.60)	2.10 (.63)
9	Difficulty sleeping	2.31 (.84)	2.23 (.77)	2.09 (.73)
10	Difficulty Swallowing	1.92 (1.08)	1.79 (.88)	2.09 (1.07)

¤Frequency ratings = rarely (1), occasionally (2), frequently (3), almost constantly (4). *Severity ratings= slight (1), moderate (2), severe (3), very severe (4). †The ranking were done based on the results of the assessment at 5 months.

Table 5. The symptoms with the highest distress ratings at different assessments

		DISTRESS RATINGS†		
Rank	Symptom	**Preoperative**	**1 month**	**5 months**
		Mean score (SD)	Mean score (SD)	Mean score (SD)
1	Problems with sexual interest	1.78 (1.36)	1.36 (1.12)	1.70 (1.19)
2	Lack of energy	1.57 (1.07)	1.58 (.97)	1.62 (1.01)
3	I don't look like myself	1.71 (1.38)	1.63 (1.46)	1.62 (1.26)
4	Shortness of breath	1.73 (1.09)	1.72 (1.12)	1.59 (1.11)
5	Problems with urination	1.35 (1.25)	1.00 (1.15)	1.45 (1.30)
6	Difficulty Swallowing	1.14 (1.35)	1.29 (1.13)	1.45 (1.18)
7	Pain	1.63 (1.09)	1.36 (.93)	1.42 (.91)
8	Feeling sad	1.63 (1.07)	1.20 (.87)	1.40 (1.00)
9	Worrying	1.65 (1.07)	1.45 (1.02)	1.38 (.91)
10	Constipation	1.15	1.34	1.35

†Distress ratings = not at all (0), a little bit (1), somewhat (2), quite a bit (3), very much (4). ᵀ The ranking were done based on the results of the assessment at 5 months.

Table 6. Severity ratings at 5 months

Symptom	Sample size	Mean score	Severity ratings % (n)			
			Slight	Moderate	Severe	Very severe
Shortness of breath	131	2.25	15 (20)	53 (69)	24 (29)	7 (9)
Lack of energy	118	2.19	12 (14)	62 (73)	22 (26)	4 (5)
Feeling drowsy	107	2.0	20 (21)	62 (66)	17 (18)	2 (2)
Cough	100	1.81	34 (34)	52 (52)	13 (13)	1 (1)
Pain	100	1.98	22 (22)	59 (59	17 (17)	2 (2)
Difficulty sleeping	77	2.09	14 (18)	58 (45)	20 (15)	4 (3)
Worrying	82	1.84	32 (26)	54 (44)	12 (10)	2 (2)
Problems with sexual int.	74	2.53	10 (7)	46 (34)	27 (20)	18 (13)

†Severity ratings= slight (1), moderate (2), severe (3), very severe (4)

Table 7. Distress ratings at 5 months

Symptom	Sample size	Mean score	Distress ratings % (n)				
			Not At All	A Little Bit	Some what	Quite A Bit	Very Much
Shortness of breath	128	1.59	13 (17)	43 (55)	23 (29)	14 (18)	7 (9)
Lack of energy	115	1.62	10 (11)	42 (48)	32 (37)	10 (12)	6 (7)
Feeling drowsy	105	1.10	29 (30)	43 (45)	20 (21)	7 (7)	2 (2)
Cough	92	0.97	34 (32)	47 (43)	11 (10)	7 (6)	2 (2)
Pain	95	1.42	11(10)	51 (48)	30 (28)	5 (5)	4 (4)
Difficulty sleeping	81	1.31	22 (18)	41 (33)	26 (21)	6 (5)	5 (4)
Worrying	82	1.38	11 (9)	55 (45)	23 (19)	7 (6)	4 (3)
Problems with sexual interest	76	1.70	16 (12)	34 (26)	22 (17)	20 (15)	8 (6)

†Distress ratings =not at all (0), a little bit (1), somewhat (2), quite a bit (3), very much (4)

6.0 DISCUSSION

6.1 Methodological considerations

6.1.1 Sample

Approximately 850 patients went through lung cancer surgery in Norway during the period of this study. With 270 patients included in the present study (113), approximately 30% of the total number of lung cancer patients who underwent surgery in Norway were included. This finding suggests that this sample is representative of surgically treated lung cancer patients in Norway. However, patients from only 4 of the 8 hospitals performing this surgery in Norway were included. Across these 4 hospitals, 29 of the eligible patients were not invited to participate due to lack of time or resources. The main reason for not asking these patients to participate was because they came to the hospital on Sunday afternoon. No differences in demographic characteristics were found between these patients and the ones who were invited to participate in this study.

The sample sizes varied at the different measurement points because of the reasons listed in Figure 2. The dropout rate over the first 5 months of the study was approximately 15% (i.e. 5 withdrew their informed consent, 35 did not answer the mailed questionnaires). This attribute could cause sampling bias; because a major problem with self-report data is that data may be lost from patients who are not doing well (23). However, no differences in demographic and clinical characteristics were found between patients who did and did not complete the 5 month assessment.

To increase the sample's homogeneity, all of the patients in this study were diagnosed with primary lung cancer; they were all surgically treated; and none of them had any evidence of metastases when they were included in the study. The

reason for only including surgically treated lung cancer patients without metastasis, was that the prognosis for these patients is different than for inoperable lung cancer patients and/or for patients with metastatic lung cancer (31). This inclusion criteria was considered as important when following patients for a relatively long period of time after surgery.

The patients in this study had different stages of disease, had different histological types, and had different types of surgery; which provides a representative and varied sample of lung cancer patients. The distribution of types of surgery are quite similar to the total distribution of lung cancer surgery in Norway that was provided by the Norwegian Association for Cardiothoracic Surgery (113). Even though the distribution of VATS in our sample was similar to the Norwegian sample, some countries have a higher percentage of VATS (114). This difference may decrease the generalizability of the study findings to other countries because VATS seems to improve patients' perioperative outcomes, as well as reduce complication rates and duration of hospitalization (53, 55). However, the significance of these differences is uncertain. A meta-analysis reported a lack of well-designed randomized controlled trials and longitudinal studies that assessed for differences in QOL outcomes between patients who underwent a VATS compared to a thoracotomy (53).

6.1.2 Recruitment of patients

The PhD student recruited the majority of the patients (54%). The remaining patients were recruited by nurses who were trained in the recruitment processes. To ensure that the enrollment procedure was standardized, a written procedure for the recruitment process was given to the nurses who assisted with recruitment (Appendix

2). The procedures for recruitment were slightly different at each hospital, due to different hospitalization practice and work schedules for the nurses assigned to do the recruitment. However, these differences did not seem to influence the percentage of patients recruited to the study at each hospital.

The majority of the patients (91%) were recruited from the hospital where they had the surgery, one to three days before surgery. They were asked to complete the study questionnaires the day before surgery. This time may be a vulnerable period for the patients and may influence their responses. The timeframe was chosen for practical reasons because the decision about the tumor's operability was often made shortly before surgery at a local hospital. Therefore, it was difficult to contact the patient before surgery. We made the decision to recruit the patients at the time of hospitalization. Another advantage to this approach is that the patients had to wait for different tests and for different examiners on the day before the surgery. Therefore, they had time to complete the questionnaires.

The remaining 9% of the sample was recruited in the outpatient clinic after receiving their cancer diagnosis, approximately 1-4 weeks prior to surgery. They completed the enrollment questionnaires at home and mailed it back to the hospital where they were recruited. The fact that the patients completed questionnaires at different times and places may influence their responses. However, all of the patients had received information about a serious cancer diagnosis and were awaiting surgery which is a quite stressful period for them. Even if this sample was small (n=24), an analysis was done to evaluate for differences in the patients based on location of recruitment. No significant differences in symptom occurrence rates and

frequency, severity, or distress ratings were found between the groups recruited in the outpatient clinic and in the hospital.

6.1.3 Data collections

The majority of the demographic and clinical information was found easily in the medical records. However, information about the patients' smoking history was somewhat incomplete in the medical records in some cases. In many cases, information on previous smoking history and number of cigarettes smoked daily was not recorded. This information is important for the calculation of number of pack-years. Initially, we planned to evaluate if the number of pack-years influenced symptom burden, but due to the incomplete data this analysis was not possible.

When designing this study, the selection of questionnaires was discussed. It was important to collect sufficient data, but at the same time to limit the number of questions to reduce respondent burden (93). Because of the paucity of research about changes in symptom burden over time in patients with lung cancer, we chose to focus our data collecting on symptoms. This approach would provide the foundation for future research. Because we are a research group that is focused on the evaluating of symptoms in different patient groups, we chose to use similar questionnaires across these studies for comparative purposes. One questionnaire that was not included was the Karnofsky Performance Status scale (KPS), which assesses the patients' level of physical functioning. The KPS scale was not used because the EORTC QOL-LC13 assessed how SOB influenced patients' ability to function (i.e., SOB at rest, SOB walking, SOB climbing stairs). In retrospect, having data from the KPS scale would have allowed us to compare the findings from this study to other symptom studies that included this scale (67). In addition, information

on symptom management interventions should have been collected. With these data, analyses could have been done to evaluate for differences in the symptom experience of patients who did and did not receive treatments for their symptoms.

Furthermore, we knew at the start of the study that the majority of the patients would be elderly. Therefore, efforts were made to design questionnaires that were easy to read. This approach was used because poorly designed questionnaires can make the respondent confused and affect the quality of the study results (93). When completing the MSAS, some patients did not answer all of the questions. This questionnaire asks patients to indicate whether or not they had the symptom during the past week (i.e., symptoms occurrence). If they experienced the symptom, they were asked to rate its severity and distress. Some patients did not indicate if they had the symptoms, even though they indicated that it was a severe or distressing symptom. As was done in a previous study (63), in these cases, we chose to interpret that they experienced the symptom, because the first question about symptom occurrence may have been misunderstood.

6.1.4 Design and statistical analysis

This thesis presents data at 3 measurement points. Patients were enrolled preoperatively and followed for 5 months. One challenge with longitudinal studies is to decide on the number of and the interval between the assessments. Too many or too frequent assessments may be a burden for the patients. However, too long a time between the assessments may result in lost information about changes in the phenomenon of interest (93). In this study, data were collected before and 1 and 5 months after surgery, to measure the symptoms before and after the potential administration of adjuvant CTX. Adjuvant CTX is usually started 4 to 6 weeks after

surgery and the duration of treatment is normally 10 weeks *(57)*. However, it may be that we lost some information about changes in symptoms in the 4 month interval between the 1 and 5 month assessment. For instance, when symptoms decreased from 1 month to 5 months; it is not clear if the symptom decreased steadily from 1 to 5 months or if symptom remained high until 4 months and then decreased.

Because the three papers had different foci and different assessments points were included, different statistical procedures were used in each paper to answer its specific goal. The statistical analyses varied based on the type of data collected and if the study was cross sectional or longitudinal. On MSAS, the ratings of symptoms occurrence, frequency, severity, and distress are all categorical. However, while symptom occurrence is a dichotomous variable with two categories (i.e., yes, no), the frequency, severity, and distress were ordinal variables measured using four or five point Likert scales. These differences in the variables required the use of different types of statistical analyses.

In the first paper, a cross sectional design was used. This design was the best approach because we wanted to describe patients' symptoms before surgery. The benefit of a cross-sectional design is that it allows researchers to compare many different variables at the same time. A limitation with cross-sectional studies is that it does not provide definite information about cause-and-effect relationships (93). A comparison was done of the occurrence rates and severity and distress ratings of 32 symptoms between younger and older patients before surgery. In order to evaluate the effect of age on the severity of each symptom, we divided the patients into two age groups and utilized ordinal logistic regression. Because surgery is not done on severely ill patients (31), and all the patients in this study had surgery, some of the

symptoms had very low occurrence rates. Since regression analyses should not be performed on small samples (68), this analysis was performed only when 40 patients reported the occurrence of a specific symptom. In addition, symptom severity and distress ratings were not analyzed if fewer than 10 responses were available in the upper two categories. With this approach, we may have lost some information about age differences in patients' symptom experience. However, this conservative approach to the statistical analysis provided confidence that we would not draw erroneous conclusions.

The second paper evaluated for changes in symptom occurrence and severity from the preoperative period to 1 month after surgery. To make the presentation of these data manageable and clinically relevant, only the eleven symptoms that occurred in more than 50% of the patients at the postoperative assessment were analyzed and the analysis of symptom distress was not included. However, by not including analyses of the distress and frequency ratings in papers 2 and 3, we lost some information about two dimensions of the patients' symptom experience. Data on patients' distress and frequency ratings are presented in this thesis to give a more comprehensive picture of the patients' symptom experience.

Different analysis methods can be used to evaluate for changes in symptom occurrence rates from before to 1 month after surgery. Since symptom occurrence is a dichotomous variable, the McNemar's test was chosen. The McNemar's test determined whether changes in symptom occurrence rates in one direction were significantly greater than in the opposite direction. McNemar's test provides more detailed information than a Chi-square test that was another alternative (68) side

220. The McNemar's test was done because some symptoms were not present at the preoperative assessment and or 1 month assessment and vis a versa.

In paper two, a general linear model was used to determine whether select demographic and clinical characteristics, as well as the number of preoperative symptoms, were associated with the total number of symptoms reported after surgery. The specific characteristics were used because previous research found that they were associated with reductions in QOL after surgery (55, 86, 115). Predictors from QOL studies were chosen because of the paucity of symptoms studies in surgically treated lung cancer patients. While the analysis was done with a number of demographic (i.e., age, gender, living situation) and clinical characteristics (i.e., preoperative FEV1, comorbidity, stage of cancer, extent of surgery, postoperative complications), other predictors not assessed in this study (e.g., number of pack years) may influence the occurrence or severity of symptoms. Further research is needed to identify additional predictor of symptom occurrence rates and/or severity ratings.

In the third paper, a multilevel growth model was developed (111). Multilevel growth modelling is a complicated statistical analysis that may be unfamiliar to many clinicians. However, this kind of analysis has several advantages. In addition, it is important to use this type of analysis to the advance of the science of symptom management. The first advantage with this method is that it provides information about how demographic and clinical characteristics influence a phenomenon both preoperatively and over time (cross-level interaction) (111). Another advantage of using multilevel growth modeling is that this kind of analysis provides information on both the observed and the predicted values of a symptom. The observed values for

the individual data are the raw scores. The predicted values are the scores derived from the regression equation (model). When one illustrates both the predicted and the observed values, one can see how the predicted model fits with the observed values. If the observed and predicted values are similar, the model fits well with the observations.

6.1.5 Reliability and validity of the study

To insure a study's quality, it is important to evaluate the validity and reliability of the instruments used in the study. An instrument's reliability is the consistency with which it measures the target topic (93). In this case, it is how accurately an instrument measures symptom burden, comorbidity, and QOL. Reliability evaluates both the reproducibility as well as the internal consistency of a scale. Reproducibility is that repeated measurement gives the same results. Internal consistency is that all items in a questionnaire measure the same concept (116). As pointed out in all the papers in this thesis, all of the instruments used in this study were tested and found to be reliable (63, 90, 98-100, 105, 106). Cronbach's alphas for MSAS are: physical subscale (.82), psychological subscale (.81), global distress index (.82), and total MSAS score (.88) (90, 117). Previous reliability testing in one study does not insure its reliability in a new study (93), because the questionnaires' reliability depends on the patient groups that are assessed and the context of the study. However, since these instruments were used in a previous study of Norwegian cancer patients (98), even though the patients had breast cancer and were receiving different treatment, the results from the reliability testing seems to be transferable.

A factor that is important for improving a study's reliability and validity is representativeness. The patients in this study were recruited from three university

hospitals at four locations (e.g., OUS-Rikshospitalet, OUS-Ullevål, St. Olav University Hospital, Haukeland University Hospital), and from three of the five Regional Health Authorities (i.e., helseregioner) in Norway. This approach was used to increase the representativeness of the sample and reduce the risk of selection bias. The gender and age distribution in this sample were not significantly different from the total distribution of lung cancer surgery patients in Norway (113). A large and varied sample size increases the validity of a study (93). In addition, larger sample sizes insure a more representative sample (116). The sample (n=264) in this study was larger than in previous studies of symptoms and QOL in lung cancer patients prior to and following lung cancer surgery. In the previous studies the sample sizes range from 45 to 173 patients (14, 16-19).

Validity is the degree to which an instrument measures what it is intended to measure and that it is useful for its intended purpose (116). Reliability and validity are not independent qualities of an instrument, an unreliable instrument cannot be valid (93). Content validity refers to whether an instrument measures the intended topic (116). All three of the instruments used in this study (i.e., MSAS, EORTC QOL-LC13, SCQ) have established content validity (90, 100, 105).

Other factors that are important for an instrument's quality, especially in a longitudinal study, is its sensitivity (i.e., ability to distinguish between two groups) and responsiveness (i.e., ability of a scale to detect changes) to change (116). In this study, significant differences were found in symptom ratings, as well as in the scores for the three dyspnea items from the EORTC QOL-LC13 scale over time. Therefore, the instruments appear to be sensitive to change. The symptom and QOL scores showed changes over time, which indicates the instrument's responsiveness to

changes in the patients' experience with symptoms. Comorbidity measure was used at the preoperative and 5 months assessments. However, changes in comorbidity were not evaluated.

Only data from the 3 item dyspnea scale from the EORTC QOL-LC13 (i.e., SOB at rest, SOB walking, SOB climbing stairs) were used in this thesis. This choice may be a limitation because it is recommended that the EORTC QOL-LC13 should be used with the core EORTC QOL to perform a valid assessment of a person's QOL (106). However, in this thesis the scale was used to provide additional information on patients' dyspnea experience. The manual for the EORTC QOL-LC13 states that the 3 dyspnea items form a reliable scale for measuring dyspnea (106).

6.2 General discussions

The patients in this study experienced a high number of symptoms before and after lung cancer surgery. The mean number of symptoms was 9 preoperatively, 13 at one month, and 11 at five months. Previous research found that cancer patients experience multiple co-occurring symptoms. In a review of 18 studies of patients with various cancer diagnoses using multiple symptoms scales (67), 40% to 61% of patients experienced more than one symptom, and 22% to 30% of patients experienced more than five concurrent symptoms.

This high number of symptoms affects patients' lives in several ways. The occurrence of multiple symptoms is associated with decreased functional status and QOL (67). In addition, symptoms may slow the rehabilitation process (69). Multiple co-occurring symptoms may form symptom clusters. A symptom cluster is three or more concurrent symptoms that are related to each other (e.g., pain, fatigue, sleeplessness, depression) (118). The co-occurrence of several symptoms appears

to create a synergistic effect in that the negative effect of multiple symptoms on patients' morbidity and on their QOL is greater than the simple sum of its parts (119).

An updated literature review revealed no new research in multiple symptoms in patients who underwent surgery for lung cancer. Therefore, the comparison of our results will be done with the literature that was published at the time the manuscripts were written. The number of symptoms reported by patients in this study was higher than in previous studies of surgically treated lung cancer patients (14, 16-19). However, a direct comparison of the results is difficult, because the majority of the previous studies had a main focus on QOL and only reported a limited number of symptoms (16-18). In addition, different instruments were used across the studies. Three of the previous studies (16-18) assessed the severity of 14 symptoms using the EORTC QLQ-C30 and LC13, one study measured the severity of 11 symptoms using the Symptom Distress Scale (14), and the last study measured the severity of 6 symptoms using the Lung Cancer Symptom Scale (19).

One interesting finding, in the study, is that different symptoms had the highest occurrence rates, as well as frequency, severity, and distress ratings at five months after surgery (Table 4). These findings are consistent with the results of a study of breast cancer patients receiving CTX (63). However, they contrast with the findings from a study of different groups of cancer patient, that found that the symptoms with the highest severity and distress ratings were also the most prevalent (120). While both these studies used the MSAS, the reason for these differences is not evident. Of note, some of the symptoms that were rated as very severe or distressing in the present study were only experienced by a few patients, like "I don't look like myself" (i.e. 13 patients) or problems with urination (i.e. 33). That different symptom is

experienced as distressing, severe and occurring support the need for assessing of multiple dimensions of symptoms. Additional research is needed to determine what factors contribute to patients' perception of symptoms severity and distress.

At five months, the majority of patients reported symptom severity scores for the most severe symptoms that ranged between moderate and severe. The distress scores for the most distressing symptoms were rated between a little bit and somewhat distressing. However, it should be noted that between 5% and 10% of the patients reported high severity distress scores. These patients warrant more comprehensive assessment and follow-up care Symptoms like pain, SOB, and lack of energy are treatable (25, 121-124). Early interventions can decrease severity and distress associated with these symptoms (124).

6.2.1 Symptoms at the different assessments

The total number of symptoms increased significantly from the preoperative ($\bar{x}$ =9.1 SD=7.0) to the 1 month ($\bar{x}$ =12.8, SD=6.7, p<.001) assessment. At 5 months after surgery, the number of symptoms was lower than at 1 month but significantly higher ($\bar{x}$=11.0, SD=6.9, p<.001) than at the preoperative assessment.

6.2.1.1. Preoperative symptoms

In the present study, the first data assessment were done before surgery, which is an advantage since a previous study reported that candidates for resection for lung cancer had a worse preoperative QOL compared with the general population (71). The most frequently reported symptoms, that were reported by more than 45% of the patients preoperatively, were: cough, lack of energy, feeling drowsy, SOB, worrying, difficulty sleeping, and dry mouth (Paper 1).

The most frequently reported symptoms in previous studies were: cough, pain, dyspnea, fatigue, and insomnia (14, 16-18). However, because the previous studies assessed different symptoms is it difficult to compare the results.

The three studies that assessed symptoms using the EORTC QLQ-C30 and LC13 (16-18) all reported that cough and dyspnea were two of the most common symptoms. In addition, two of these studies reported that pain and fatigue was common symptoms. Why previous studies reported different symptoms is difficult to explain. However, all of these symptoms had high occurrence rates in our sample. While, the samples in two of the previous studies were quite similar to our sample (17, 18), the last study included only patients over 70 years (16). However, none of these studies reported worrying as a frequent symptom, even though the EORTC QLQ-C30 scale assesses this symptom. The reason for this difference is not readily apparent. However, it may be that the symptom was reported as a part of EORTC QLQ-C30 functional scales (i.e., physical, role, emotional, social and cognitive functioning) (18).

In the last study that evaluated preoperative symptom distress (14), pain, fatigue, and insomnia were the most distressing symptoms. Two of the three symptoms were the same as in our study where; “I don’t look like myself”, difficulty sleeping, and pain were the three most distressing symptoms.

6.2.1.2 Symptoms at 1 month

The four symptoms with the highest occurrence rates at one month after surgery were SOB, lack of energy, pain, and feeling drowsy (Paper 2). SOB was the symptom that had the highest occurrence rate (85.5%) and its severity increased significantly from slight to moderate at one month. This symptom is reported to have

a significant impact on QOL (125) and warrants additional research. Only four studies have evaluated lung cancer symptoms 1 month after surgery, three with EORTC QLQ-C30 and LC13 (16-18), and one with Lung Cancer Symptom Scale (19). SOB, pain, and lack of energy were some of the most frequently reported symptoms 1 month after surgery, in all four studies (16-19).

The number of patients who reported pain after surgery was higher in the present study than in previous reports (17, 18). Pain warrants ongoing evaluation because higher levels of postoperative pain increase the risk for the development of persistent pain following thoracotomy (126). Consistent with previous studies of oncology patients (127) and of patients who had major surgery (128), fatigue was a common symptom. Feeling drowsy was a symptom frequently reported by patients in our study, but not measured in previous studies. The literature on this symptom is sparse, but in a review of symptoms in patients who underwent day surgery (129), feeling drowsy was reported as a frequent problem.

Of note, both in our study and previous studies, symptoms that might affect patients' nutritional status were common (i.e., lack of appetite (19), nausea (17, 18), vomiting (17)). More than 50% of the patients in our study reported lack of appetite at 1 month. Surgery, as well as CTX and radiotherapy, can have a negative impact on patients' nutritional status. In addition, weight loss is a poor prognostic sign in patients with lung cancer (130).

6.2.1.3 Symptoms at 5 months

The six most common physical symptoms reported 5 months after surgery were: pain, lack of energy, feeling drowsy, difficulty sleeping, SOB, cough. The most frequent psychological symptom was worrying (Paper 3). These symptoms were

reported by more than 45% of the patients. Five previous studies assessed lung cancer symptoms at 4 to 6 months after surgery, three assessed symptom severity with EORTC QLQ-C30 and LC13 (16-18), one assessed symptom distress with Symptom Distress Scale (14), and one assessed symptom severity with Lung Cancer Symptom Scale (19). However, in these five studies the findings were inconsistent.

In one study that assessed symptoms using EORTC QLQ-C30 and LC13 (18), all of the symptoms had returned to preoperative levels at 6 months after surgery. In another study that used the same instruments (16), all symptoms except thoracic pain had returned to preoperative levels after 6 months. However, in the third study that used the QLQ-C30 and LC13 (17), the severity of fatigue, dyspnea, and pain remained high at the 4 month assessment. The two studies that assessed symptoms using a symptom assessment scale (14, 19) found high levels of fatigue, dyspnea, and pain combined with a high level of cough. The reasons for these differences may be related to the specific symptoms that were assessed on each instrument and the symptom dimensions that were assessed.

SOB was the symptom with highest occurrence rate 5 months after surgery, as 79% of the patients reported this symptom (Paper 3). SOB was also a frequent, severe, and distressing symptom. This finding is consistent with findings from previous studies (17-19). SOB affects patients' physical and social functioning. It can lead to clinically significant depression and to a lack of physical activity (125, 131). In a previous study (125), >30% of lung cancer patients reported this symptom several years after surgery and it had a significant negative impact on their QOL.

One factor that may influence the occurrence and severity of SOB is smoking. Of note, 94% of the patients in this study were current or previous smokers. Another

factor that could influence SOB is pain (132, 133). In a study of COPD patients with dyspnea and pain (133), their two symptoms appeared to create a vicious cycle. Five months after surgery, 56% of the patients in the present study reported pain and 36% were still using analgesics' (Paper 3). The International Association for the Study of Pain (IASP) defines chronic pain after thoracotomy as pain that persists for at least 3 months after the surgical procedure (134). The finding that more than 50% of the patients reported pain after surgery in the present study is consistent with findings from previous studies (126, 135).

Three of the 7 symptoms reported 5 months after surgery are known to be interrelated: namely lack of energy, difficulty sleeping, and feeling drowsy (64). Few studies have explored the consequences of feeling drowsy in cancer patients. However, both lack of energy and difficulty sleeping are often documented to significantly impair patients' QOL and ability to function (127, 136). Previous studies in lung cancer patients have measured only lack of energy and difficulty sleeping. One study reported that lack of energy returned to pre-surgical levels 6 months after surgery (18). In the other two studies (17, 19), fatigue scores remained elevated for up to two years. Difficulty sleeping was reported in only one study (18), and was found to be a frequent problem preoperatively.

The severity of cough decreased over the first month then it increased from 1 month to 5 months (Paper 3). A previous study found the same pattern for cough. The authors hypothesized that patients suppressed cough shortly after surgery due to pain (18). Regardless of the cause, cough is a distressing symptom and has important implications for the QOL of lung cancer patients (137, 138).

Worrying was the most frequent psychological symptom in the present study. Forty-seven percent of the patients reported this symptom at 5 months (Paper 3). A previous study reported that 51% of patients experienced worrying to be at least "somewhat of a problem" and that high levels of preoperative worry were associated with a significantly higher number of symptoms even before treatment (139). Patients in this study reported other psychological symptoms like feeling nervous (40%) and feeling sad (37%). The high rates of psychological symptoms as measured here may be related to patients' cancer diagnosis (140). Previous studies found that psychological symptoms in lung cancer patients continued for up to a year and that these patients need psychological support (141, 142).

Of note, 43% of the patients reported problems with sexual interest preoperatively and at 5 months 47% of the patients reported this symptom. Problems with sexual interest was the most frequent, severe, and distressing symptom at 5 months. This symptom was not assessed in the previous studies of symptoms in surgically treated lung cancer patients (14, 16-19). However, in a previous study in lung cancer patients receiving different kind of cancer treatment (15), this symptom was described as severe. In a large study of causes and consequences of sexual changes after cancer, this symptom was described as distressing and causing relationship difficulties (143). Qualitative interviews with health professionals and patients revealed that they had different foci with regard to sexual problems (144). While patients wanted information, support, and practical strategies about how to live with intimate and sexual changes after treatment for cancer, health professionals focused on patients' fertility, contraception, menopausal status, or erectile status (144). This finding warrants additional research to determine how clinicians assess sexual problems in patients with cancer (144).

6.2.1.4 Summary of the symptoms

The patients in this study experienced a high symptom burden over time. Both before and after surgery, symptoms like lack of energy and SOB had high occurrence rates, as well as high severity, frequency, and distress scores. However, pain was a symptom that increased the first month after surgery and remained quite high at five months. In contrast, the occurrence of cough was high at all three assessments. However, cough was not among the most frequent, severe, or distressing symptoms at five months. Psychological symptoms like worrying, feeling sad, or feeling nervous were common preoperatively, and their occurrence rates remained relatively high at one and five months after surgery. These differences suggest the need for detailed symptom assessments of patients before and after surgery in order to be able to implement effective symptom management interventions.

6.2.2 Demographic and clinical characteristics that influence symptom burden

Demographic and clinical characteristics had differential effects on patients' symptom experiences. The analyses in Paper 2 and 3 gave different results in terms of which characteristics influenced patients' symptom experience. These differences may be because various characteristics differ in their contributions over time. In paper 2, which assessed changes in symptoms from the preoperative period to one month after surgery, we found that the only characteristic that was associated with a higher number of postoperative symptoms was the number of preoperative symptoms reported by the patient. This finding was a bit unexpected because previous studies of lung cancer patients reported that demographic characteristics (i.e., age, gender, living situation) and clinical characteristics (i.e., preoperative FEV1, comorbidity, stage of cancer, extent of surgery, postoperative complications) were

associated with QOL and symptom scores reported 1 month after surgery (55, 86, 125).

However, the multilevel growth model that assessed the trajectories of symptoms showed that age, comorbidities, receipt of adjuvant CTX, and gender influenced the change in the occurrence and severity of symptoms to a different extent. The possible reasons for these differences are discussed under each demographic and clinical characteristic.

6.2.2.1 Age

As previously mentioned, one of the initial purposes of this study was to evaluate symptom burden in surgically treated elderly lung cancer patients. We hypothesized that elderly patients would experience more symptoms than younger patients. In the initial analyses few age-related differences were found between older and younger patients. When age differences were identified, older patients reported lower symptom occurrence rates and lower severity and distress ratings (Paper 1 and 3).

Preoperatively, when 32 symptoms were assessed, older patients reported lower occurrence rate for feeling drowsy; a lower severity score for feeling nervous; and a lower distress rating for lack of energy (Paper 1). In the second paper, when we evaluated for changes in symptom occurrence rates and severity ratings, from the preoperative period to 1 month after surgery, no age-related differences were found. In the third paper, when we analyzed the trajectories of symptom occurrence rates and severity ratings from before through five months after lung cancer surgery; age influenced the occurrence rates for pain and feeling drowsy, and demonstrated a

cross level interaction (i.e., influenced the change in symptoms over time) with the severity of SOB when climbing stairs.

A limited number of studies have evaluated the associations between age and the occurrence, severity, and distress of symptoms (117). To our knowledge, the one study that focused on age differences in symptoms of lung cancer patients evaluated symptom distress in newly diagnosed lung cancer patients (145). The study reported that older patients experience less symptom distress than younger patients. One reason why older patients report fewer symptoms may be that they are referred to the thoracic surgeon earlier than younger patients (140). Another explanation may be that older persons experience a "response shift" in symptom perceptions. A "response shift" is a change in a person's internal standard, in values, or in the conceptualization of experiences that are catalyzed by a change in their health status (146). Older patients may have experienced symptoms from other medical conditions for a long time which may have resulted in a reconceptualization of their symptoms (147).

The results from other studies on age related differences in symptoms are inconsistent (117, 145, 148-150). In a study of oncology patients undergoing radiation therapy (RT) (149), sleep disturbance, pain, and distress were significantly less prevalent among older patients compared to younger patients, while SOB was significantly more prevalent among older patients. In another study of multiple symptoms in patients newly diagnosed with gastrointestinal cancer (150), patients >70 years of age reported higher symptom distress scores compared to patients <70 years of age. In a study of patients with advanced cancer (148), younger patients reported higher pain severity scores and better appetite. In the last study of 593

oncology outpatients receiving active treatment for their lung cancer (117), older patients reported lower occurrence rates as well as lower symptom severity, frequency, and distress ratings. The reasons for the inconsistent findings regarding age-related differences in symptoms are not readily apparent. One possible explanation may be that different samples had different levels of comorbidity.

6.2.2.2 Comorbid conditions and preoperative symptoms

In paper 2, the only characteristic that was associated with a higher number of postoperative symptoms was the number of preoperative symptoms reported by the patient. That the number of preoperative symptoms influenced symptom occurrence at 1 month is consistent with previous research (14, 18). Comorbid conditions did not have a significant influence on the total number of symptoms at 1 month (Paper 2). However, a higher level of comorbidity (i.e., higher SCQ scores) influenced the occurrence and severity of several symptoms when analyzed using a multilevel growth model (Paper 3). The reason for this difference may be that the number of preoperative symptoms was highly correlated with the level of comorbidity. When number of preoperative symptoms was removed from the general linear model, the SCQ scores showed a significant correlation with the number of symptoms at the 1 month assessment.

The SCQ score prior to surgery influenced the occurrence rates for six of the seven symptoms (i.e., pain, lack of energy, feeling drowsy, difficulty sleeping, SOB, worrying) in the multilevel growth models that analyzed changes in symptoms from before to five months after surgery. This finding is consistent with previous reports (63, 88). In the present study, no significant differences were found in the number of comorbid conditions between older and younger patients. The number of

comorbidities that patients experienced varied; 15% had no comorbidities, 23% had 1, 26% had 2, and 37% had 3 or more comorbid conditions. The most common comorbid conditions were: back/neck pain (46%), hypertension (34%), and COPD (32%). While it is not clear which comorbid condition had the greatest influence on the occurrence of each symptom, the findings regarding the negative impact of comorbid conditions on patients' symptom experience suggest that these patients warrant detailed assessments and more aggressive symptom management interventions.

6.2.2.3 Gender

Gender had little impact on patients' symptom experience in the present study. It did not influence the total number of symptoms 1 month after surgery. However, it did influence the occurrence of worrying and the severity of pain at 5 months (Paper 3). Being female was associated with a higher symptom burden for both the occurrence of worrying and the severity of pain. This finding differs from a previous report (19) where being male was associated with a higher overall symptom severity score at 4 months after lung cancer surgery. Data on the influence of gender on oncology patients' symptom experience are inconclusive (151). However, in two studies (139, 152), women reported higher occurrence rates for worrying in the preoperative period and higher pain intensity scores in the immediate postoperative period (153, 154). The reasons for these differences may be that women may have a lower pain threshold as well as sex-related differences in the effects of opioid analgesics (153).

6.2.2.4 Adjuvant chemotherapy (CTX)

Adjuvant CTX is usually given to patients 4 to 6 weeks after surgery (44). In this

study, an unexpected finding was that patients who received adjuvant CTX at 1 month had higher occurrence rates for five symptoms preoperatively. In contrast, the receipt of adjuvant CTX did not influence the occurrence rates for symptoms over time. This finding suggests that it was patients with more advanced disease who received adjuvant CTX. While receipt of adjuvant CTX was a significant predictor of symptom severity in a previous study (19), it did not influence symptom severity in our study (Paper 3). The association between the receipt of adjuvant CTX and an increased symptom burden prior to surgery is most likely explained by the fact that adjuvant CTX is primarily given to younger patients with more advanced disease (57).

Chronological age is not a strong predictor of toxicities or responsiveness to CTX. In fact, many older patients tolerate CTX better than their younger counterparts (23). However, patient's age is often considered when making a decision about adjuvant CTX. The Norwegian guidelines recommend that adjuvant CTX should not be given to patients >70 years of age (44). Recent studies found that patients who were ≥65 years of age benefited from adjuvant CTX after surgery (155, 156), and even patients at 75 years had the same clinical and pathological characteristics as younger patients (157). However, in those over 80 years of age, no additional survival benefit was realized (156). The presence of comorbid disease was prognostic in this retrospective study and may be a more relevant inclusion or exclusion criteria for treatment than chronologic age (84).

6.2.3 Consequences and treatment of a high symptom burden

The patients in this study had a high symptom burden at 5 months after surgery. This finding is important because the occurrence of multiple symptoms is

associated with decreased functional status and QOL (67) and will have a negative effect on patients' rehabilitation process (69). Lung cancer patients appear to have a larger number of unmet psychosocial and daily living needs than other cancer patients (30, 158). Many patients report that life after a lung cancer diagnosis is difficult and that their concerns are not being met (19, 140, 159). In addition, lung cancer patients experience added difficulties and stigma because of the close connection between the disease and smoking (160-162). Patients experience stigma to a different degree. Of note, higher levels of lung cancer stigma (LCS) were associated with higher levels of anxiety and depression, as well as poorer QOL (160, 161).

It is important to give these patients and their family members information at hospital discharge about how to manage their symptoms and when to seek care for unrelieved symptoms (9). Close follow-up and assistance with symptom management are extremely important. The Norwegian guideline for diagnosis, treatment, and follow-up of lung cancer patients recommends that patients should be seen at 1 month after surgery, then every 3 months until 9 months after surgery (44). However, based on the high symptom burden of lung cancer patients after surgery, these patients may need closer follow-up and more assistance with symptom management either in the hospital or in an outpatient clinic.

Cancer patients are vulnerable to an overall decrease in activity. An early intervention can prevent problems, as it is much easier to maintain strength and range of motion than to regain it (69). Rehabilitation can play a role in improving tolerance to treatment and adaption to disability (23). The European Respiratory Society (ERS) and the European Society of Thoracic Surgery (ESTS) clinical

guidelines on fitness for radical therapy in lung cancer patients (45) recommend early pre- and postoperative rehabilitation in operable lung cancer patients.

In the present study, 42% of the patients received physical therapy and/or inpatient rehabilitation. When total number of symptom was compared between that patients' who did and did not receive physiotherapy/rehabilitation, no differences were found. However, we lack knowledge about when the patients received physiotherapy, as well as how much and what type of physiotherapy they received. Both the Medical Research Council and the developers of the TSM noted that the intervention itself, as well as the timing and dose of the intervention are important considerations when evaluating an interventions effect (10, 24). A systematic review of exercise interventions for patients surgically treated for NSCLC concluded that even though the quality of the evidence has many limitations, it appears that an exercise intervention improved patients' cardiopulmonary exercise capacity, increases their muscle strength, and reduces fatigue, post-operative complications and hospital length

of stay (122). In a recent Norwegian study (123) , high-intensity training following lung cancer surgery improved peak oxygen uptake, muscular strength, total muscle mass, functional fitness, and QOL. Until further studies are done, referrals to physical therapy or rehabilitation programs need to be considered for all patients who undergo lung cancer surgery.

6.3 Theory of Symptom Management (TSM)

The initial purpose of this study was to develop an intervention to improve symptom management in surgically treated lung cancers patients. This plan was under consideration, because in a previous, small, qualitative study done by our

research group, patients described a postoperative period characterized by discomfort and lack of support from clinicians (12). However, when a literature review was done; lack of knowledge about surgically treated lung cancer patients' symptom experience was identified. This paucity of research made the development of a tailored and effective symptom management intervention difficult. The Medical Research Council (MRC) in United Kingdom clearly states that an intervention should be systematically developed based on previous evidence (24). It is also emphasized that if factors that caused and sustained the problem were not well understood, one needed to do some primary research to understand the phenomes of interest (24, 25).

Starting with the collection of data on patients' symptom experience is consistent with how knowledge development was done in previous studies of symptoms in other patient groups (e.g., COPD, diabetes) (10). First studies on patients' symptom experiences were done. Then symptom management interventions were developed and evaluated, first in terms of efficacy and then in terms of clinical effectiveness.

The TSM was used as the theoretical framework for this study, because this theory describes how to assess symptoms and how to develop interventions to relieve patients' symptom burden. The theory was useful in clarifying the characteristics that may influence the patients' symptom experience (i.e. personal, environmental, health &illness), and how both the frequency and severity of a symptom influences the level of distress associated with a symptom. In addition, the theory explains how different types of interventions (symptom management

strategies) can change patients' symptom experiences as well as associated outcomes (symptom outcomes).

The main focus in this study was on the symptom experience dimension of the TSM. However, in addition to the data collection on patients' symptom experience, we explored the relationships between symptom experience and some demographic and clinical characteristics in the three domains of nursing science (i.e., person, environment, health & illness). Data were collected on how age and gender from the person domain affects patients' symptom experience. In addition, we evaluated how comorbidity, receipt of adjuvant CTX, and number of preoperative symptoms from the health & illness domain affected patients' symptom experience. We also collected some information on symptom management strategies (i.e. rehabilitation, physiotherapy) and symptom status outcome (i.e. patients employment status, SOB at rest, SOB when walking, SOB climbing stair) symptom.

In this study, we collected data about which symptoms had the highest occurrence rates as well as which symptom were the most severe, distressing, and frequent at different assessment points. This information is a good starting point to develop and test an intervention to relive symptoms in surgically treated lung cancer patients. The next step in our research group will be to develop and test symptom management interventions to ease patients' symptom status; either by making the symptom less frequent, less intense, or less distressing. The best way to develop and test interventions is by starting with a series of pilot studies, and moving on to exploratory studies and then to a definitive evaluation (24). This approach is called a pragmatic design (163). When these pilot testes are done, it is possible to design and conduct a randomized controlled trial; where on group of patients receives the

intervention and the other group receives either standard care or some type of alternative

control intervention. Then the effects of the intervention on patients' symptoms could be evaluated.

7.0 CONCLUSIONS AND CLINICAL IMPLICATIONS

This dissertation provides evidence that surgically treated lung cancer patients experience a high symptom burden. At 5 months, the number of symptoms was significantly higher than at the preoperative assessment. This high symptom burden in lung cancer patients before and after surgery requires that clinicians perform a comprehensive symptom assessment prior to surgery and at regular intervals after surgery. Psychological symptoms (e.g., worrying) were common, especially preoperatively, and warrant consideration because of their negative effects on postoperative outcomes (164). It is important that clinicians speak with patients about their concerns and initiate referrals to mental health professionals if warranted.

The findings from this study can be used to identify patients who are at higher risk for more severe symptoms before and after lung cancer surgery and to initiate more aggressive symptom management interventions. Patients with comorbidities and a higher number of preoperative symptoms need special attention because they tend to experience a higher number of postoperative symptoms.

The results in this study can be used to improve the information given to the patients about the normal course of postoperative recovery after lung surgery. More knowledge about which symptoms are expected after lung cancer surgery and how to cope with these symptoms can make the rehabilitation period easier for the patients. Even though it is recommended (45), less than 50% of the patients in this study received physical therapy or inpatient rehabilitation. The number of patients who worked decreased from 30% preoperatively to 9% at five months after surgery.

In summary, this clinical, interdisciplinary multi-center, study with 264 lung cancer patients provides important information on the symptom burden of these

patients who underwent lung cancer surgery. This information can be used to develop tailored symptom management interventions and that may significantly improve postoperative and survivorship outcome for this group for this group of patients.

8.0 FUTURE RESEARCH

Additional studies are needed to confirm the findings from this study. For example, future studies could evaluate if patient who undergo different types of surgical procedures (e.g., thoracotomy or VATS) have different symptom experiences. It would be interesting to see if other studies find similar patterns as in this study, namely that younger lung cancer patients experience a higher symptom burden than older patients. Future studies could evaluate for subgroups of patients which experience higher symptom burden, using statistical approaches like latent class analyses (165, 166). In addition, future studies could evaluate for the number and types of symptom cluster in these patients and whether the number and types of symptom cluster change over time. Additional research needs to focus on the etiology of the symptoms identified. In addition, it is important to develop and test symptom management interventions to improve symptom management in these patients. It is important that these interventions focus on multiple symptoms and that they help patients to cope with their symptom burden.

Future studies could focus on additional elements of the TSM. For example, studies could focus on the impact of symptom management strategies on the patients' symptom experience. Then it would be possible to evaluate how this intervention influences symptom outcomes. This change in symptom status can either be that the symptom is less frequent, less intense, or less distressing, or remains the same. The assessment should be longitudinal as symptom burden varies over time. In addition, one could evaluate whether changes in symptom status has an impact on a variety of symptom outcomes (e.g., QOL, return to work)

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APPENDIX

Appendix 1 **Reg.nr** ☐☐☐

2010 Lungeoperasjonsstudien

Rehabilitering etter lungeoperasjon

Pasientens navn: _____

2010 Lungeoperasjonsstudien **Reg.nr** ☐☐☐

CRF 1 **Inklusjon**

Sykehus: ☐ OUS - Rikshospitalet ☐ OUS - Ullevål ☐ St. Olav ☐ Haukeland

Skriv tydelig med store bokstaver (evt lim:

Fornavn :……

Etternavn : ……...

Adresse : ……...

Postnr : ..... **Sted:** ……

Telefonnummer: ☐☐☐☐☐☐☐☐

Fødselsdato: ☐☐ ☐☐ ☐☐☐☐
dag måned år

Kjønn: ☐ Mann ☐ Kvinne

Inklusjonskriterier			**Kontrollert:**		
1. Menn og kvinner over 18 år	☐ Ja	☐ Nei	Informert samtykke mottatt	☐ Ja	☐ Nei
2. Mistanke om lungekreft	☐ Ja	☐ Nei	Spørreskjema mottatt	☐ Ja	☐ Nei
3. Ingen kognitive forstyrrelser	☐ Ja	☐ Nei	Registrering nr. mottatt	☐ Ja	☐ Nei
4. Kunne lese og skrive norsk	☐ Ja	☐ Nei			

Fyll ut skjema, send melding til Trine på tlf: 91774995 for tildeling av registreringsnummer. Skriv dette øverst i høyre hjørne (også på spørreskjema). Samle alle skjemaene i en konvolutt og oppbevar på avtalt sted.

☐☐ ☐☐ ☐☐☐☐ ……
dag måned år signatur

CRF 2

Røyking : ☐ Ja ☐ Nei ,ikke lenger ☐ Nei

Fra år: ☐☐☐☐ Til år: ☐☐☐☐

Ca antall sigaretter pr dag (en sigarett tilsvarer ca 1 gram tobakk): ☐☐

Hvordan ble sykdommen oppdaget:

1. Pasienten hadde symptomer ☐ Ja ☐ Nei
2. Røntgen thorax tatt i utredning av annen sykdom ☐ Ja ☐ Nei
3. Screening ☐ Ja ☐ Nei

Kliniske funn og undersøkelser preoperativt:

Høyde: ☐☐☐ **cm**

Vekt: ☐☐☐ **kg**

FEV1: ☐, ☐☐ **liter**

FVC: ☐, ☐☐ **liter**

Medisiner preoperativt:

☐ Psykofarmaka Hvilke……..

☐ Smertestillende medikament: Hvilke……..

☐ Steroid inhalasjon (Pulmicort/ Flutide)

☐ Beta-2-agonist inhalasjon (Ventoline/ Bricanyl/ Oxis/ Serevent)

☐ Anticholinergica inhalasjon (Spiriva/ Atrovent /Ipraxa)

☐ Kombipreparat inhalasjon (Symbicort/ Seretid)

☐ Steroid tabletter (Prednisolon)

Tumortype:

☐ Adenokarsinom

☐ Plateepitelkarsinom

☐ Storcellet

☐ Ikke småcellet

☐ Annet……

TNM klassifikasjon (fra patolog):

T: ☐

N: ☐

M: ☐

Operasjonsdag: ☐☐. ☐☐. ☐☐☐☐

Operasjonstype:

☐ Lobektomi

☐ Bilobektomi

☐ Pneumonektomi (pulmektomi)

☐ Kilereseksjon/ Wedge

☐ Annet: ……

Postoperativt:

Antall døgn med dren: ☐☐ dager

Antibiotika skiftet: ☐ Ja ☐ Nei

Reoperajon: ☐ Ja ☐ Nei

CRP først fallt, deretter steget: ☐ Ja ☐ Nei

Andre komplikasjoner: ……

Pasienten overflyttet til annet sykehus postoperativt: ☐ Ja ☐ Nei

Sykehus pasienten ble overflyttet til: .....

Appendix 2

Inklusjon

Inklusjon: Nå dere skal inkludere pasienten finner dere først fram inklusjonsmappe. Ta med "informert samtykke" forteller deretter pasienten litt om studien. Det er viktig å sjekke om pasienten har hørt at det er mistanke om kreft før du gir pasienten arket med "Informert samtykke". Dersom pasienten ikke vil være med i studien noteres dette på ark. Det skal noteres kjønn, alder og evt. årsak – dersom pasienten oppgir dette. Dersom pasienten ikke oppgir årsak skal dere ikke spørre om dette.

Dersom pasienten vil være med i studien skal han og du underskrive på "Informert samtykke". Der det står rolle i studien skal dere skrive prosjektmedarbeider. Etter dere begge har underskrevet tas kopi av informert samtykke og levere dette til pasienten sammen med spørreskjema. Det er viktig å gjøre pasienten oppmerksom på at på side 9 i spørreskjema (der en spør om smerte)- at dersom vedkommende ikke har smerter så skal han hoppe til side 12 i skjema. Sykepleier må nå fylle ut første side i CRF skjema (CRF 1). Det kan enten skrive for hånd eller ta en merkelapp med pasientopplysninger. Etterpå sender sykepleier en tekstmelding eller ringe til meg for å få inklusjonsnummer og skrive dette på alle dokumentene. Skriv opp hva dere har gjort på inklusjons sjekklisten.

Dersom dere lurer på noe må dere gjerne ringe meg enten på telefon nummer: 91774995 eller mobil 91173965.

Samtale ved inklusjon (Viktig å finne et sted som man kan være i fred, jeg sitter meg alltid ned). Bør bare ta med samtykket når du går inn første gangen og ikke de andre papirene.

Hei mitt navn ……. Årsaken til at jeg kommer og snakker med deg nå er at vi holder på med en studie (på avdelingen/ sykehuset). Bakgrunnen for studien er at vi vet lite om hvordan pasienter som blir operert i lungene har det etter operasjonen. Dette gjør det vanskelig å forberede pasientene på hva som venter etter operasjonen. Dersom det er noe mange er plaget med kan vi kanskje gjøre noe for å forebygge dette.

For å finne ut mer om hvordan pasientene har det har vi startet opp en studie som vi nå ber deg om å delta i. Studien innebærer for deg at du må svare på noen spørreskjema i tiden etter operasjonen. For å finne ut hvilke plager som du har hatt lenge og hvilke som evt. kommer etter operasjonen må du fylle ut første spørreskjema før operasjonen. Du trenger ikke gjøre det med en gang, men må gjøre det i løp av dagen. Her er litt informasjon om studien (levere samtykket) som du kan lese før du bestemmer deg for om du vil delta. Deltagelse i studien er frivillig og du vil få samme behandling selv om du ikke deltar.

Til slutt: Takk for hjelpen og lykke til med operasjonen.

Vanlige spørsmål:

- Tidsbruk til utfylling av spørreskjema? Dette er ca ½ time, varierer litt fra pasient til pasient.

- Hvor mange spørreskjema må besvares? Til sammen 5, ett før operasjon. Deretter etter 1,5,9 og 12 måneder. Grunnen til mellomrommet mellom 1 og 5 måneder er at en del pasienter får cellegift da.
- Hva skal spørreskjema brukes til? Resultatene vil bli publisert i nasjonale og internasjonale tidsskrift. Det er en sykepleier som skal ta doktorgrad på resultatene (noen pasienter synes det er veldig spennende)
- Hvem er med i studien? Oslo Universitetssykehus – Rikshospitalet og Ullevål og St Olavs hospital er med i studien. Studien er finansiert av kreftforeningen.

Forespørsel om deltakelse i forskningsprosjektet

"Rehabilitering etter lungeoperasjon"

Bakgrunn og hensikt
Dette er en forespørsel til deg som skal opereres med mistanke om lungekreft, om å delta i en studie for å få mer kunnskap om hvordan du opplever det første året etter operasjon. Studien vil kartlegge hvilke symptomer og plager pasienten kan oppleve, hvordan symptomer opptrer sammen og hvordan symptomene forandrer seg over tid. Studien vil også kartlegge hvilken støtte pasienten får etter operasjonen. Ved å få mer kunnskap om dette håper vi å kunne tilby bedre støtte og behandling til pasienter etter lungekreftoperasjon. Studien gjennomføres av Senter for Pasientmedvirkning og Sykepleieforskning ved Oslo Universitetssykehus, i samarbeid med Hjerte-, lunge og karklinikken ved OUS, Lungeavdelingen ved Haukeland Universitetssykehus samt Thoraxkirurgisk avdeling ved St Olavs Hospital.

Hva innebærer studien?
Alle som deltar i studien vil bli bedt om å fylle ut spørreskjema for å kartlegge ulike symptomer som smerte, tung pust, hoste tretthet (fatigue), søvnforstyrrelser, ernæringsproblemer, livskvalitet, angst og depresjon. Du vil også bli spurt om evt. andre sykdommer, helsetilstand, funksjonsstatus og hvilken sosial støtte du har fått etter operasjonen. For å kartlegge evt. endringer av symptomer over tid ønsker vi å følge deg i et år. Dette innbærer at du først fyller ut spørreskjema rett før operasjonen, deretter vil du få tilsendt skjema etter en, fem, ni og tolv måneder. Vi vil evt. ringe deg og minne deg på utfylling av skjemaene. Dersom du trenger hjelp til utfylling av skjema vil undertegnede være tilgjengelig på telefon. Det vil ta i underkant av en time og fylle ut spørreskjemaene.

Noen av de som samtykker i å delta studien vil bli forespurt om å bli intervjuet muntlig om hvordan de opplevde det å bli overflyttet til lokalsykehus og om hvordan det har vært og komme hjem. Intervjuene vil enten bli gjort hjemme hos deg eller hvis du ønsker det på et sykehus i nærheten av der du bor. Intervjuene vil bli tatt opp på bånd og deretter bli skrevet ut. Det er fult mulig å si nei til deltagelse i denne delen av prosjektet selv om du deltar i resten av studien.

Mulige fordeler og ulemper
Studien medfører ingen kostnader og det er ingen risiko forbundet med studien. Du vil kanskje oppleve det som slitsomt eller belastende å svare på noen av spørsmålene i spørreskjemaet. Vi vil bistå deg med hjelp til utfylling av skjemaer dersom du ønsker det, og du kan bruke så lang tid du ønsker på utfyllingen.

Hva skjer med informasjonen om deg?
Informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. Evt. lydbånd som er tatt opp vil bli slettet etter intervjuet er skrevet ut. En kode, som vil være unik for hver deltager i studien, vil knytte deltagerne til opplysninger. Listen som sammenkobler koden og personnummer, oppbevares innelåst i et skap, fysisk atskilt fra svarene på spørreskjemaene. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Vi regner med at studien i si helhet vil avsluttes i 2014, og at listen med koder vil slettes senest 5 år etter studien er avsluttet.

Som en del av studien ønsker vi informasjon om din sykdom, tilleggssykdommer og medisiner du står på fra din journal på sykehuset. Du vil ha rett til å ha innsyn i hvilke opplysninger som er registrert,

samt til å kreve retting av feilaktige opplysninger. Vi ønsker også å registrere opplysninger om alder, kjønn, diagnose og operasjonstype på dersom du sier nei til å delta i studien.

Oslo Universitetssykehus ved administrerende direktør er dataansvarlig for studien. Studien er godkjent av Regional Etisk Komité Sør-Øst Norge og Personvernombudet ved Oslo Universitetssykehus, avdeling Rikshospitalet. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien uten at dette vil få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Du kan kreve at innsamlet data blir slettet. Data som allerede er analysert og publisert kan ikke trekkes tilbake.

Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte sykepleier og doktorgradsstipendiat Trine Oksholm (trine.oksholm@rr-research.no, tlf: 23075437, eller mobil: 91173965), eller prosjektleder Tone Rustøen (tone.rustoen@rr-research.no, tlf: 23075462).

Med vennlig hilsen

Tone Rustøen (sykepleier og professor)	Johny Kongerud (seksjonsoverlege og forsker)	Trine Oksholm (sykepleier og stipendiat)

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

Registreringsnummer □□□

Oslo universitetssykehus

ST. OLAVS HOSPITAL
UNIVERSITETSSYKEHUSET I TRONDHEIM

Lungeopererte

"Vi vil vite hvordan du har det"

Spørreskjema til deltagere i studien

Dette er første spørreskjema til deg som har samtykket i å delta studien i studien. Du kan oppleve at noen av spørsmålene overlapper hverandre. Grunnen til dette er at vi bruker standardiserte skjemaer som gjør det mulig å sammenligne resultatene fra denne studien med andre studier. Vi ber deg svare på alle spørsmålene selv om du synes noen av dem ikke passer helt til deg.

Mange takk

Baseline

Registreringsnummer ☐☐☐

SYMPTOMLISTE (MSAS)

Veiledning: Vi har listet opp 32 symptomer nedenfor. Les hvert av dem nøye. Hvis du har hatt symptomet i løpet av siste uken, la oss få vite hvor ofte du hadde det, hvor kraftig det var det meste av tiden, og hvor mye det plaget eller bekymret deg, ved å sette ett kryss i den ruten du synes passer best. Hvis du IKKE HAR HATT symptomet, sett ett kryss i den ruten merket HAR IKKE HATT symptomet.

I løpet av den siste uken: **Har du hatt noen av de følgende symptomene?**	**Har ikke hatt symptomet**	**Hvis JA: Hvor ofte hadde du symptomet?**				**Hvis JA: Hvor kraftig var symptomet, det meste av tiden?**				**Hvis JA: Hvor mye plaget eller bekymret symptomet deg?**				
		Sjelden	Av og til	Ofte	Nesten hele tiden	Svakt	Moderat	Kraftig	Svært kraftig	Ikke i det hele tatt	Litt	En del	Ganske mye	Svært mye
Vanskelig å konsentrere seg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Smerter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Har lite energi	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hoste	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Føler meg nervøs	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Tørr i munnen	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kvalme	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Søvnig, mye trøtt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nummen / prikker i hender / føtter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Søvnvansker	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Luft i magen / oppblåst	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Problemer med vannlating	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaster opp	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kortpustet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Diaré	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Føler meg trist	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Svette	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Bekymrer meg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Problemer med seksuallyst / aktivitet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

SYMPTOMLISTE (MSAS) - del 2

I løpet av den siste uken: **Har du hatt noen av de følgende symptomene?**	**Har ikke hatt symptomet**	**Hvis JA: Hvor ofte hadde du symptomet?**				**Hvis JA: Hvor kraftig var symptomet, det meste av tiden?**				**Hvis JA: Hvor mye plaget eller bekymret symptomet deg?**				
		Sjelden	Av og til	Ofte	Nesten hele tiden	Svakt	Moderat	Kraftig	Svært kraftig	Ikke i det hele tatt	Litt	En del	Ganske mye	Svært mye
Kløe	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Manglende matlyst	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Svimmel / ør	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Vanskelig å svelge	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Føler meg irritabel	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sår i munnen	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Maten smaker annerledes	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Vekttap	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Mistet håret	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Treg mage / forstoppelse	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Hoven i armer og ben	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
"Jeg ser ikke ut som meg selv lengre"	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐
Forandringer i huden	☐					☐	☐	☐	☐	☐	☐	☐	☐	☐

Hvis du har hatt noen andre symptomer i løpet av den siste uken, vennligst skriv de opp nedenfor, og angi hvor mye det plaget eller bekymret deg.		Ikke i det hele tatt	Litt	En del	Ganske mye	Svært mye
Annet:		☐	☐	☐	☐	☐
Annet:		☐	☐	☐	☐	☐
Annet:		☐	☐	☐	☐	☐

Livskvalitetsskjema (EORTC)

Vi er interessert i forhold vedrørende deg og din helse. Vær vennlig å besvare hvert spørsmål ved å sette et kryss x i den boksen som best beskriver din tilstand. Det er ingen "riktige" eller "gale" svar.

	Ikke i det hele tatt	Litt	En del	Svært mye
1. Har du vanskeligheter med å utføre anstrengende aktiviteter, slik som å bære en tung handlekurv eller en koffert?	☐	☐	☐	☐
2. Har du vanskeligheter med å gå en lang tur?	☐	☐	☐	☐
3. Har du vanskeligheter med å gå en kort tur utendørs?	☐	☐	☐	☐
4. Er du nødt til å ligge til sengs eller sitte i en stol i løpet av dagen?	☐	☐	☐	☐
5. Trenger du hjelp til å spise, kle på deg, vaske deg eller gå på toalettet?	☐	☐	☐	☐

I løpet av den siste uka:	Ikke i det hele tatt	Litt	En del	Svært mye
6. Har du hatt redusert evne til å arbeide eller utføre andre daglige aktiviteter?	☐	☐	☐	☐
7. Har du hatt redusert evne til å utføre dine hobbyer eller andre fritidsaktiviteter?	☐	☐	☐	☐
8. Har du vært tung i pusten?	☐	☐	☐	☐
9. Har du hatt smerter?	☐	☐	☐	☐
10. Har du hatt behov for å hvile?	☐	☐	☐	☐
11. Har du hatt søvnproblemer?	☐	☐	☐	☐
12. Har du følt deg slapp?	☐	☐	☐	☐
13. Har du hatt dårlig matlyst?	☐	☐	☐	☐
14. Har du vært kvalm?	☐	☐	☐	☐

I løpet av den siste uka:	**Ikke i det hele tatt**	**Litt**	**En del**	**Svært mye**
15. Har du kastet opp?	☐	☐	☐	☐
16. Har du hatt treg mage?	☐	☐	☐	☐
17. Har du hatt løs mage?	☐	☐	☐	☐
18. Har du følt deg trett?	☐	☐	☐	☐
19. Har smerter påvirket dine daglige aktiviteter?	☐	☐	☐	☐
20. Har du hatt problemer med å konsentrere deg, f.eks. med å lese en avis eller se på TV?	☐	☐	☐	☐
21. Har du følt deg anspent?	☐	☐	☐	☐
22. Har du vært engstelig?	☐	☐	☐	☐
23. Har du følt deg irritabel?	☐	☐	☐	☐
24. Har du følt deg deprimert?	☐	☐	☐	☐
25. Har du hatt problemer med å huske ting?	☐	☐	☐	☐
26. Har din fysiske tilstand eller medisinske behandling påvirket ditt familieliv?	☐	☐	☐	☐
27. Har din fysiske tilstand eller medisinske behandling påvirket dine sosiale aktiviteter?	☐	☐	☐	☐
28. Har din fysiske tilstand eller medisinske behandling gitt deg økonomiske problemer?	☐	☐	☐	☐

Som svar på de neste spørsmålene, sett et kryss i den ruten som best beskriver din tilstand.

29. Hvordan har din helse vært i løpet av den siste uka?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Svært dårlig						**Helt utmerket**

30. Hvordan har livskvaliteten din vært i løpet av den siste uka?

☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Svært dårlig						**Helt utmerket**

EORTC QLQ - LC13

Endel pasienter opplever av og til at har noen av følgende symptomer eller problemer. Vær vennlig å angi i hvilken grad du har hatt disse symptomene eller problemene i løpet av den siste uka.

I løpet av den siste uka:	**Ikke I det hele tatt**	**Litt**	**Endel**	**Svært mye**
31. Hvor mye har du hostet ?	☐	☐	☐	☐
32. Har du hostet blod ?	☐	☐	☐	☐
33. Har du vært tungpustet i hvile ?	☐	☐	☐	☐
34. Har du vært tungpustet når du har gått ?	☐	☐	☐	☐
35. Har du vært tungpustet når du har gått i trapper ?	☐	☐	☐	☐
36. Har du vært sår i munnen eller på tungen ?	☐	☐	☐	☐
37. Har du hatt svelgproblemer ?	☐	☐	☐	☐
38. Har du hatt prikkinget (stikninger) i hendene eller i bena ?	☐	☐	☐	☐
39. Har du hatt håravfall ?	☐	☐	☐	☐
40. Har du hatt smerter i brystet ?	☐	☐	☐	☐
41. Har du hatt smerter i arm eller skulder ?	☐	☐	☐	☐
42. Har du hatt smerter i andre deler av kroppen ?	☐	☐	☐	☐
Hvis ja, hvor har du hatt vondt ? _____				
43. Har du brukt smertestillende medisiner ?				
1. Nei ☐ **2. Ja** ☐				
Hvis Ja, hvor mye har det hjulpet ?	☐	☐	☐	☐

TILLEGGSSYKDOMMER (SCQ-18)

Det følgende er en liste over vanlige medisinske problemer. Sett ett kryss for hvert problem om hvorvidt du har problemet nå (ja eller nei).
Hvis du HAR problemet, så svar på spørsmålene om behandling og aktiviteter til høyre.
Hvis du IKKE HAR problemet, gå videre til neste problem.

	Har du problemet?		**HVIS JA: Får du behandling for det?**		**HVIS JA: Begrenser det dine aktiviteter?**	
1. Hjertesykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
2. Høyt blodtrykk	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
3. Andre lungesykd. (KOLS)	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
4. Diabetes	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
5. Magesår/magesykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
6. Tarmsykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
7. Nyresykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
8. Leversykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
9. Anemi eller annen blodsykdom	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
10. Hodepine	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
11. Depresjon	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
12. Slitasjegikt/artrose	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
13. Rygg/nakkesmerter	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
14. Leddgikt/revmatoid artritt	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
15. Sykdom i bindevev eller muskulatur	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
16. Hudlidelser	☐ Ja	☐ Nei	☐ Ja	☐ Nei	☐ Ja	☐ Nei
17. Andre medisinske problemer (angi)						
			☐ Ja	☐ Nei	☐ Ja	☐ Nei
			☐ Ja	☐ Nei	☐ Ja	☐ Nei
			☐ Ja	☐ Nei	☐ Ja	☐ Nei

Appendix 5

Rehabilitering etter lungeoperasjon

Kjære deltager i studien

Nå har det gått 1 måned siden du ble med i denne studien og fylte ut spørreskjema på sykehuset før lungeoperasjonen. Hensikten med studien er å få mer kunnskap om hvordan pasientene har det i tiden etter de operert. Som avtalt sender vi deg nå spørreskjema til utfylling samt en frankert konvolutt som du kan bruke til å sende skjemaene tilbake til oss. Vi håper du kan fylle det ut så snart som mulig. Dersom du glemmer å sende skjema tilbake vil vi sende et deg et påminningsbrev om et par uker. Deltagelse i studien er frivillig.

Dersom du har spørsmål om selve studien eller det er noe uklart med spørsmålene kan du ringe sykepleier og stipendiat Trine Oksholm ved Senter for pasientmedvirkning og sykepleieforskning på mobiltelefon: 917 74 995 eller eventuelt e-post: trine.oksholm@oslo-universitetssykehus.no.

Med vennlig hilsen

Tone Rustøen	Johny Kongerud	Trine Oksholm
(sykepleier og professor)	(seksjonsoverlege og forsker)	(sykepleier og stipendiat)

Oslo universitetssykehus

Hei.

Skal du opereres i lungen?

Da inviterer vi deg til å delta i en studie.

Studien undersøker hvordan pasienter som er operert i lungene har det etter operasjonen. Denne kunnskapen kan komme pasientene til gode på lengre sikt.

Bakgrunn for studien

Vi vet lite om hvordan pasienter som er operert i lungene har det i månedene etter at de er operert. For å få vite mer om dette har vi startet opp en studie. Hensikten med studien er å få mer kunnskap slik at helsepersonell bedre kan informere pasientene om hvilke problemer som kan oppstå etter operasjonen. Studien gjennomføres i samarbeid mellom Oslo Universitetssykehus, Rikshospitalet og Ullevål og St Olavs hospital i Trondheim.

Hva innebærer studien?

Alle som deltar i studien vil bli bedt om å fylle ut spørreskjema om ulike symptomer, livskvalitet og sosial støtte. For å kartlegge evt. endringer av symptomer over tid ønsker vi å følge deg i et år. For å vite hvilke symptomer og plager du evt. har fra før ber vi deg om å fylle ut spørreskjema før operasjonen. Skjema trengs ikke å fylles ut med en gang, bare du er ferdig før du skal opereres. De andre skjemaene vil du få tilsendt i posten etter en, fem, ni og tolv måneder. Dersom du trenger hjelp til utfylling av skjema kan vi hjelpe deg med dette. Det tar vanligvis i underkant av en halv time og fylle ut spørreskjemaet.

Hvordan er det mulig å delta?

Du har mulighet til å bli med i studien når du innlegges på sykehus før operasjonen. En sykepleier vil komme og spørre deg om du kan tenke deg å delta. Deltagelse i studien er frivillig. Dersom du sier nei vil det ikke påvirke behandlingen du får.

Har du spørsmål vedrørende studien, kan du kontakte meg:

Trine Oksholm
sykepleier og stipendiat
E-post: trine.oksholm@rikshospitalet.no
Telefon : 91774995.