TOWARDS UNDERSTANDING PATIENTS’ AND CAREGIVERS’ ASSESSMENTS OF SYMPTOMS AND QUALITY OF LIFE IN LUNG CANCER

Eva Broberger

Stockholm 2007
ABSTRACT
Towards understanding patients’ and caregivers’ assessments of symptoms and quality of life in lung cancer.
Eva Broberger, Department of Neurobiology, Care Science and Society

Lung cancer is associated with a wide range of symptoms arising from both disease progression and treatment side effects. Nurses caring for patients with lung cancer are thus challenged to help patients cope with a variety of problems. Individual perspectives, influences and experiences are of great importance to consider when interpreting patients’ and caregivers’ assessments of symptoms and quality of life.

The overall aim of this thesis is to gain better understanding of different aspects influencing assessments of patients’ symptom experiences and quality of life by patients with inoperable lung cancer and their professional and family caregivers. The focus is on perspectives, symptom characteristics, changes in patients’ internal standards and prioritizations over time, and measurement approaches. The specific aims are to 1) explore whether there may be discrepancies between patients’ and their professional and family caregivers’ assessments of symptom occurrence and symptom distress, 2) examine changes in internal standards of measurement in patients regarding physical function, fatigue and overall quality of life, 3) examine changes over time and in retrospect in what patients spontaneously report as most distressing, 4) examine to what extent a standardized cancer-specific questionnaire assesses those concerns patients spontaneously reported as most distressing and 5) examine relationships between symptom occurrence, intensity and distress.

The database for the four papers included in this thesis is comprised of prospective and retrospective symptom and quality of life assessments from sub-sets of patients participating in a longitudinal descriptive study of 400 patients diagnosed with inoperable lung cancer during the first year post-diagnosis.

The relationship between symptom occurrence and symptom distress was studied in different ways, with all approaches confirming that they are separate components of patients’ symptom experiences. Patients’ and caregivers’ dyadic assessments of patient’s symptom experience show that patients and caregivers were able to separate these two components although caregivers assigned most symptoms higher levels of intensity than patients themselves did. A symptom’s association with distress was neither consistently related to its current occurrence, nor to whether high intensity levels were reported for that symptom. Patients’ spontaneous reports of a wide variety of concerns perceived as currently causing most distress changed over time and in retrospect. The cancer-specific questionnaire did not always adequately assess patients’ priorities, changes over time, or the content and intensity of concerns reported as most distressing. Decisive support to demonstrate that changes in patients’ internal standards of measurement influenced their assessments of symptom experience and quality of life during the first six months following diagnosis was not found. In summary, findings stress the importance of considering perspectives, symptom characteristics, patients’ priorities and adaptive processes, as well as measurement approaches when planning for symptom interventions to prevent or alleviate problems for the individual patient.

Keywords: Lung cancer, symptom experience, quality of life, change, assessments
I. Broberger, E., Tishelman, C., von Essen, L.
Discrepancies and similarities in how patients with lung cancer and their professional and family caregivers assess symptom occurrence and symptom distress. *Journal of Pain Symptom Management*, 2005; 29 (6) 572-583

II. Broberger, E., Sprangers, M., Tishelman, C.

III. Broberger, E., Tishelman, C., von Essen, L., Doukkali, E., Sprangers, M.
Spontaneous reports of most distressing concerns in patients with inoperable LC: at present, in retrospect and in comparison with the EORTC-QLQ-C30+LC13. *Quality of Life Research*, published online, October 2007

IV. Broberger, E., Tishelman, C., von Essen, L., Sprangers, M.
Relationships between symptom occurrence, intensity and distress in patients with inoperable lung cancer. *Submitted for publication*
# CONTENTS

1 INTRODUCTION 1

2 RESEARCH AIMS 3

3 BACKGROUND 4

3.1 LUNG CANCER 4
  3.1.1 SYMPTOMATOLOGY 5
  3.1.2 IMPACT ON QUALITY OF LIFE 5

3.2 SYMPTOMS 6
  3.2.1 SYMPTOM EXPERIENCE 6
  3.2.2 SYMPTOM PERCEPTION 8

3.3 DISTRESS AS A BROADER CONCEPT 8

3.4 QUALITY OF LIFE 9

3.5 DISCREPANCIES AND SIMILARITIES BETWEEN PATIENTS’ AND THEIR CAREGIVERS’ ASSESSMENTS OF SYMPTOMS AND QUALITY OF LIFE 10

3.6 RESPONSE SHIFT 11

3.7 MEASUREMENT ISSUES 13
  3.7.1 MEASURING SYMPTOM EXPERIENCES AND QUALITY OF LIFE 13
  3.7.2 MEASURING CHANGE IN SYMPTOM EXPERIENCE AND QUALITY OF LIFE 14

4 DESIGN AND METHODS 16

4.1 DATA COLLECTION INSTRUMENTS 18
  4.1.1 FREELISTING (PAPERS III AND IV) 18
  4.1.2 THE SYMPTOM DISTRESS SCALE (SDS) (PAPER I) 19
  4.1.3 THURSTONE SCALE OF SYMPTOM DISTRESS – LUNG CANCER (TSSD-LC) (PAPERS I AND IV) 20
  4.1.4 THE EOR TC-QLQ-C30+LC13 (PAPERS II, III AND IV) 22
  4.1.5 THENTESTS (PAPERS II AND III) 23
  4.1.6 TRANSITION QUESTIONS (PAPER II) 23

4.2 SAMPLE RECRUITMENT 24

4.3 DESIGN OF STUDIES 24

4.4 DATA ANALYSIS 25

4.5 ETHICAL CONSIDERATIONS 26

5 PRESENTATION OF PAPERS 27

5.1 PAPER I: DISCREPANCIES AND SIMILARITIES IN HOW PATIENTS WITH LUNG CANCER AND THEIR PROFESSIONAL AND FAMILY CAREGIVERS ASSESS SYMPTOM OCCURRENCE AND SYMPTOM DISTRESS 27

  5.1.1 SAMPLE AND RECRUITMENT 27
  5.1.2 DATA COLLECTION AND ANALYSIS 28
  5.1.3 RESULTS 29
  5.1.4 SUMMARY AND DISCUSSION OF FINDINGS 31
5.2 PAPER II: DO INTERNAL STANDARDS OF QUALITY OF LIFE CHANGE IN LUNG CANCER PATIENTS? 31
5.2.1 SAMPLE AND RECRUITMENT 32
5.2.2 DATA COLLECTION AND ANALYSIS 32
5.2.3 RESULTS 33
5.2.4 SUMMARY AND DISCUSSION OF FINDINGS 34

5.3 PAPER III: SPONTANEOUS REPORTS OF MOST DISTRESSING CONCERNS IN PATIENTS WITH INOPERABLE LUNG CANCER: AT PRESENT, IN RETROSPECT AND IN COMPARISON WITH EORTC-QLQ-C30+LC13 35
5.3.1 SAMPLE AND RECRUITMENT 36
5.3.2 DATA COLLECTION AND ANALYSIS 36
5.3.3 RESULTS 37
5.3.4 SUMMARY AND DISCUSSION OF FINDINGS 38

5.4 PAPER IV: RELATIONSHIPS BETWEEN SYMPTOM OCCURRENCE, INTENSITY AND DISTRESS IN PATIENTS WITH INOPERABLE LUNG CANCER 39
5.4.1 SAMPLE AND RECRUITMENT 40
5.4.2 DATA COLLECTION AND ANALYSIS 40
5.4.3 RESULTS 41
5.4.4 SUMMARY AND DISCUSSION OF FINDINGS 42

6 DISCUSSION 45

6.1 ASPECTS INFLUENCING ASSESSMENTS OF SYMPTOMS AND QUALITY OF LIFE 45
6.1.1 THE PERSPECTIVES OF PATIENTS, NURSES AND FAMILY CAREGIVERS 45
6.1.2 INDIVIDUAL AND ENVIRONMENTAL FACTORS 47
6.1.3 SYMPTOM CHARACTERISTICS 47
6.1.4 RESPONSE SHIFT 48
6.1.5 MEASURING SYMPTOM EXPERIENCES AND QUALITY OF LIFE 49

6.2 METHODOLOGICAL CONSIDERATIONS 50
6.2.1 SAMPLE RECRUITMENT 50
6.2.2 ASSESSMENTS OF DISTRESS 51
6.2.3 DIFFERENCES IN TIME FRAMES AND RESPONSE OPTIONS 52
6.2.4 RETROSPECTIVE REPORTS 52
6.2.5 INDUCTIVE ANALYSIS 53

6.3 NURSING IMPLICATIONS 54
6.3.1 CLINICAL IMPLICATIONS 54
6.3.2 RESEARCH IMPLICATIONS 55

7 ACKNOWLEDGEMENTS 57

8 SAMMANFATTNING (IN SWEDISH) 59

9 REFERENCES 61
## LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>EORTC-QLQ-C30</td>
<td>European Organization for Research and Treatment in Cancer Quality of Life Questionnaire Core Questionnaire (30 items)</td>
</tr>
<tr>
<td>Exp</td>
<td>Expectations</td>
</tr>
<tr>
<td>FC</td>
<td>Family Caregiver</td>
</tr>
<tr>
<td>HCS</td>
<td>Health Care System</td>
</tr>
<tr>
<td>LC13</td>
<td>European Organization for Research and Treatment in Cancer Quality of Life Lung Cancer Module (13 items)</td>
</tr>
<tr>
<td>NCCN</td>
<td>U.S. National Comprehensive Cancer Network</td>
</tr>
<tr>
<td>NSCLC</td>
<td>Non-Small Cell Lung Cancer</td>
</tr>
<tr>
<td>PFC</td>
<td>Patient-Family Caregiver</td>
</tr>
<tr>
<td>PN</td>
<td>Patient-Nurse</td>
</tr>
<tr>
<td>RT</td>
<td>Radiotherapy</td>
</tr>
<tr>
<td>SCLC</td>
<td>Small Cell Lung Cancer</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SDS</td>
<td>Symptom Distress Scale</td>
</tr>
<tr>
<td>T1</td>
<td>Time point close to diagnosis and before initiation of treatment</td>
</tr>
<tr>
<td>T2</td>
<td>Time point two weeks after T1</td>
</tr>
<tr>
<td>T3</td>
<td>Time point one month after T1</td>
</tr>
<tr>
<td>T4</td>
<td>Time point three months after T1</td>
</tr>
<tr>
<td>T5</td>
<td>Time point six months after T1</td>
</tr>
<tr>
<td>T6</td>
<td>Time point one year after T1</td>
</tr>
<tr>
<td>TSSD-LC</td>
<td>Thurstone Scale of Symptom Distress-Lung Cancer</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
1 INTRODUCTION

Lung cancer is associated with a wide range of symptoms arising from both disease progression and treatment-related side effects. As patients with advanced lung cancer are expected to have a limited survival time, skilled professional interventions are needed to prevent and alleviate symptoms. Nurses caring for patients with lung cancer are challenged to help patients cope with a wide variety of problems and symptoms. Moreover, as home care becomes increasingly common, with family and significant others having greater responsibility both as informal caregivers and as advocates for their family member, it is imperative for professional caregivers to understand how family caregivers view patients’ symptom experiences in order to help patients to achieve effective symptom management. An especially challenging question is then to what extent caregivers - both professionals such as nurses, and family caregivers - can provide an adequate account of the multidimensional nature of symptom experiences in patients with lung cancer.

My interest in the issues addressed in this thesis began when I collected data as a research nurse for a longitudinal descriptive project investigating patterns of symptom experiences in 400 patients newly diagnosed with inoperable lung cancer. In my encounters with these patients, I was struck by how they responded to the symptom and quality of life questionnaires. From my perspective, both as a cancer nurse specialist and as a healthy person, I felt that patients often diminished their symptoms or concerns and overestimated their health and quality of life. Moreover, the interviews were most often conducted in the patients’ homes. Family caregivers were present many times, and commented on how patients assessed their symptoms and functional status, finding patient assessments to be overly positive. My experiences while collecting data opened my eyes for the differences in perspectives between patients and professional and family caregivers, as well as between sick and healthy persons. I also became interested in how patients and their professional and family caregivers reason when assessing different aspects of patients’ symptoms and quality of life during disease trajectory.

We humans are often unaware of our body, taking it for granted until it is injured or affected by disease. At that time, we become aware of what we earlier took for granted. To counterbalance dualism, that is the idea that body and soul are separate dimensions, within nursing science the concept of embodiment is often used. This concept emanates from the idea that we live and experience the world through our bodies, especially through perception, emotion, language, movement in space, time and sexuality [1, 2]. This view of humans allows us to access to what ordinarily is taken for granted in everyday living. Embodiment also means being situated in the world, and being affected by personal relationships and social, cultural, political and historic forces [2]. These specific, individual contexts have to be interpreted to be understood as our experiences may or may not be similar to what others experience. Individual perspectives on symptom experiences and perceived quality of life may thus be influenced by both past and present experiences as well as by fears and expectations for the future [3].

With this background from nursing, I entered this project with the assumption that individual perspectives, influences and experiences are of great importance to consider.
when interpreting patients’ and caregivers’ assessments of symptoms and quality of life in lung cancer as a basis for effective symptom management. In this thesis I have therefore attempted to gain an understanding of different aspects influencing how patients with inoperable lung cancer and their caregivers assess patients’ symptom experiences and quality of life during disease trajectory. I have also attempted to discuss how patients’ concerns, symptoms, prioritizations and change over time can be assessed. All studies included in this thesis derive from the longitudinal project on patients with inoperable lung cancer, mentioned above, although the studies in this thesis were designed to answer the research questions of my interest. Other researchers collaborating in the longitudinal project have directed their interest towards other issues [3-7].
2 RESEARCH AIMS

The overall aim of this thesis is to gain better understanding of different aspects influencing assessments of patients’ symptom experiences and quality of life by patients with inoperable lung cancer and their caregivers.

The specific aims are:

- To explore whether there may be different patterns in discrepancies and similarities between patients’ and their caregivers’ assessments of symptom occurrence and symptom distress (paper I).

- To examine changes in internal standards of measurement in patients regarding fatigue, global health/quality of life and physical function (paper II).

- To examine changes over time in what patients spontaneously report as most distressing (paper III).

- To examine to what extent the standardized EORTC-QLQ-C30+LC13 questionnaires assess those issues patients spontaneously report as most distressing (paper III).

- To examine the relationships between symptom occurrence, symptom intensity and symptom distress from the perspective of patients (paper IV).

Specific research questions/hypotheses are presented with each specific paper in sections 5.1-5.4.
3 BACKGROUND

In the following background section, an orientation to lung cancer and its consequences is first presented. This is followed by a presentation of definitions and earlier research on central theoretical concepts of importance for this thesis, mainly focusing on aspects of symptom experiences, quality of life, patient-caregiver assessments, response shift and measurement issues.

3.1 LUNG CANCER

Globally lung cancer is the leading cause of malignant deaths. In 2005, the incidence of lung cancer was 3,308 cases, 1,810 men and 1,498 women, representing 6.5% of the cancer incidence in Sweden [8]. During the last decade there has been a tendency towards an increasing incidence among women and a decreasing incidence in lung cancer among men. The relative 5-year survival is 10% for men and 15% for women [9].

Lung cancer is one of the few cancers with specific, known carcinogens identified. Smoking, first-hand as well as second-hand is the single major risk factor [10] with 87% of all lung cancers related to smoking [11]. Other factors known to increase individual susceptibility to lung cancer include various occupational exposures (e.g. radon and asbestos), diet and gender [10].

Histopathologically, lung cancer can be divided into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Approximately 80% of all lung cancer diagnoses are NSCLC with three major subtypes: adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Adenocarcinoma represents about 40% of all lung cancers and is the most common form of lung cancer among women and in non-smoking individuals of both sexes. Squamous cell carcinoma represents 30-35% of all lung cancers and is the most common type of lung cancer among men. SCLC originates in hormonal cells in the lung and rapidly proliferates. Subtypes of SCLC include oat cell carcinoma, intermediate cell type and combined oat cell carcinoma [10, 12].

The extent of the lung cancer disease is classified according to the TNM clinical classification based on tumor size (T), regional lymph nodes (N) and distant metastases (M), where stage I represents a tumor less than 3 cm without invasion outside the lung. In stages II and III, the tumor is spread to regional lymph nodes and in stage IV to organs outside the lung [13]. The most common locations for metastases are the lungs, the central nerve system, liver, bone and adrenal glands. Patients are generally diagnosed with advanced stage cancer (i.e. Stage III and IV) [10]. In a study of all 364 patients diagnosed with lung cancer in a Swedish county, 80% of patients were reported as diagnosed in stage III or IV [14].

Treatment modalities vary depending on classification and stage. The most common treatments are surgery, radiotherapy and chemotherapy. For early stages of NSCLC, the primary treatment is surgery. For advanced stages of NSCLC, a combination of chemotherapy and radiotherapy aims at local tumor control and preventing metastases. For both extensive and limited SCLC, chemotherapy has been the cornerstone of
treatment. Many combinations of chemotherapeutic agents are currently used. Standard treatment for limited disease includes chemotherapy plus thoracic radiation given either sequentially, concurrently or alternating between therapies [10, 12]. All these treatment modalities are associated with a variety of potentially severe and serious side effects for patients [10, 12].

3.1.1 Symptomatology

The development of a tumor in the lung is expected to take several years [15]. Symptoms and signs differ depending on tumor growth and invasion. In early stages of the disease, there are few symptoms and signs due to the lack of sensory nerve fibers in the lung parenchyma, while at time of diagnosis more than 90% of patients with lung cancer are said to experience symptoms [16]. Although the disease is often already spread at time of diagnosis, Beckles et al [17] found that only a minority of patients report tumor specific symptoms such as cough or site-specific pain while unspecific general symptoms like fatigue or weight loss are more commonly reported. Other commonly reported symptoms are dyspnea [6, 18-21], pain [18-20, 22], insomnia [18, 22], and appetite loss [18-20, 22]. As a majority of patients diagnosed with lung cancer are over 65 years old, it is likely that co-morbidities will be presented. In a study by Given et al [23] it was shown that 25% of patients with lung cancer who were 65 years or older had more than three co-morbidities as compared to 18% in patients in the same age group with cancer in other sites. The most commonly reported co-morbidities were high blood pressure, heart failure, chronic lung disease and arthritis of which all may cause symptoms.

3.1.2 Impact on quality of life

Beyond physical symptoms, lung cancer has been shown to have an impact on patients’ mental, emotional and social functioning [24]. Cancer is often said to symbolize life threats, social isolation, shame and blame, symbols that may be even more accentuated in lung cancer with smoking often a primary causal agent. In addition, the lack of effective curative treatment and poor prognosis might lead to feelings of powerlessness.

The profound impact of lung cancer on quality of life has been widely reported [25-27]. The experience of living with a potentially fatal disease may have both positive and negative influences on physical, mental, emotional, social and spiritual dimensions of daily living [28]. In an analysis of quality of life in patients with NSCLC, the most important aspects influencing patients’ quality of life were found to be physical function, encompassing both physical symptoms and functional status, emotional function and social function [24]. Because of limited survival time and multifaceted symptomatology patients with advanced lung cancer may experience more disruptions in quality of life as compared to other patients with cancer. For instance, Zabora et al found that patients with lung cancer had the highest level of psychological distress when compared to other patient groups with cancer [29].
3.2 SYMPTOMS

The word “symptom” can be traced to its Latin origin, *symthoma* and was first used in its present sense in the 1600s [30]. The term sign was differentiated from symptom in the 1800s, with signs described as alterations that can be ascertained by the senses of the observer and symptoms described as functional changes in the affected parts of the body [30]. In other words, a symptom was said to be a subjective perception (e.g. pain, fatigue and nausea) while a sign was described as something that can be objectively observable (e.g. through blood analyses, measures of blood pressure or radiology).

Several theories have been developed, in attempts to explain the occurrence of symptoms and their relationship to other factors. In their theory of self-regulation, the psychologists, Leventhal and Johnson’s [31] describe symptoms as concrete representations of disease experienced by an individual as a component of cognitive processing. Their theory differentiates between the occurrence of a concrete, objective symptom and the emotional response to that symptom. Rhodes and Watson [30] defined symptoms in two ways; either as subjective phenomena regarded by individuals as an indication of a condition departing from normal function, sensation or appearance or as perceived indicators of change in normal functioning as experienced by patients. In Lenz et al’s [32] middle-range nursing theory of unpleasant symptoms, symptoms are defined as patients’ experiences of perceived indicators of changes in normal functioning. Lenz et al conceptualised each symptom as a multidimensional experience that can be measured separately or in combination with other symptoms. These definitions share some common features, e.g. that symptoms are subjective and multidimensional experiences, depart from normal function and include an emotional response.

In summary, symptom is a term that can be defined and interpreted in a variety of ways depending on the perspective of the involved persons. Goodell and Nail [33] points out the importance of understanding how patients conceptualize the terms being used and that these terms are conceptualized from a lay perspective. According to Benner and Wrubel [34], the term symptom is more often used by health care professionals than by patients. In cancer care, health care professionals usually view symptoms as perceptible changes in the body or its functions, indicating disease progression or treatment side-effects, while as a rule, patients themselves do not use the term symptoms, they instead talk about changed sensations or perceptions and their consequences for daily life [4, 35]. I use the term symptom in its broadest meaning throughout this thesis to indicate patients’ subjective perceptions including those that also are directly observable by others, e.g. cough.

3.2.1 Symptom experience

Historically, there has been a lack of conceptual clarity with regard to the general concept of symptom experience and its specific components and consequently in how symptom assessments should be instrumentalized, interpreted and translated into clinical practice. Rhodes and colleagues [30, 36] define symptom experience as the
patient’s perception and response to the two specific components of symptom occurrence and symptom distress.

Rhodes at al [37] described perceived dimensions of symptom occurrence as including frequency, duration and intensity of symptoms. Frequency and duration refer to temporal aspects of symptom occurrence, with frequency referring to intermittent occurrence and duration to persistent occurrence. Intensity refers to the perceived severity or strength of a symptom and is the dimension most generally addressed and assessed in clinical practice [38].

In their seminal work, McCorkle and Young [39], defined symptom distress as “the degree of discomfort reported by the patient in relation to his/her perception of the symptoms being experienced”. Nearly a decade later, Rhodes and Watson [30] added a notion of suffering in their definition of symptom distress expressed as “the physical or mental upset, anguish or suffering that results from the experience of symptom occurrence and/or the perception of feeling states from a specific symptom” (p.243). Lobchuk [40] builds further on Rhodes et al. ’s work, in her description of symptom distress as a separate emotional outcome or negative emotion that arises in response to symptom occurrence.

At the time I began this research, distinctions between the two main components of symptom experience – occurrence and distress – were not often clarified and operationalized in research. Recent empirical research supports the theoretical distinction proposed by Rhodes et al [30, 36], indicating that the dimensions of frequency and intensity of symptoms are not equivalent with distress from symptoms [3, 26, 41-44]. This distinction has increasingly begun to be independently addressed by several nurse researchers in recent years, often from Sweden [3, 7, 35, 44-46].

In medical anthropology, symptoms are often seen as representing the meaning the disease holds for an individual [47]. In line with this, Tishelman et al [48] began to examine the relationship between symptom distress and individual meaning in 1991. Based on a concept analysis of symptom experience, Armstrong [38] suggest including a third component in addition to occurrence and distress, the individual’s perception of the meaning of symptoms as they occur and are expressed. According to Armstrong, this meaning may be situational and/or existential and may have profound effects on the individual’s quality of life. How patients perceive the impact of symptoms on daily life is termed situational meaning, while the term existential meaning is used, for example, to include sense of vulnerability and mortality, as a result of symptoms being reminders of the cancer disease.

Symptoms can be experienced differently, and assessed differently, depending on the situation. According to Benner and Wrubel [34], symptoms function as an empirical guide to diagnosis and treatment decisions in the onset of a disease, while in chronic illness, symptoms usually function as a signal for problems that may be familiar but persistent. The symptom(s) could then hold a meaning related to the implications for the person’s life and no longer function primarily as evidence of an underlying disease; it may instead give the patient permission to take needed rests, function as a sign of disruption or even raise feelings of strength and self-confidence.
In this thesis, I will focus on both components of symptom experience described above, symptom occurrence and symptom distress. Here, symptom occurrence has been studied with regard to frequency, intensity and/or severity of symptoms and symptom distress in terms of the subjective impact of symptoms for patients. I use the term symptomatology as a more general term without referring to a particular dimension. While meaning is an important component, I have not explicitly examined the meaning symptoms hold for the individual patient.

### 3.2.2 Symptom perception

Symptoms are part of the experience of living with a cancer disease and can be as previously mentioned experienced differently. According to Benner and Wrubel [34], the mind is the receiver and interpreter of impressions from the body. Thus, a symptom can be viewed as the mind’s subjective interpretation of the body’s disease experience. A central assumption is that a symptom is the outcome of a perceptual process. Van Wijk and Kolk [49] have developed a symptom perception model, aiming to enhance the comprehensibility of the complexity of symptoms. Perception is a process where individuals compile and interpret information received by the mind. This process is guided by four assumptions. The first assumption is that individuals are limited in the amount of information that can be processed in a given time, thus resulting in a selection of information. The second assumption is that potential information exists both within and outside the individual, resulting in a continuous competition between internal and external information. The third assumption is that information is selected dependent on the quality and quantity of internal and external stimuli. And the last assumption is that information is selected dependent on the cognitions and characteristics of the individual. These processes may operate simultaneously, although there may be individual differences in their relative distribution, depending on the clarity and intensity of the available information as well as on the strength of cognitive ability and personality traits. With the above in mind, the symptom perception model distinguishes six more or less chronological steps: internal somatic information, selection of information through attentional processes, detection of somatic sensations, attribution of sensations to somatic or psychological causes, selection as determined by situation, individual dispositions and earlier experiences, and output in terms of somatic or psychological distress and illness behavior. This model presumes that symptom perception involves both body and mind and that the experience of symptoms cannot be distinguished from the reporting of symptoms.

### 3.3 DISTRESS AS A BROADER CONCEPT

In this thesis, beyond symptom distress I use the general term distress to examine other concerns that may negatively affect quality of life in patients with inoperable lung cancer. This approach broadens the focus from symptom experiences to also include how patients perceive their disease and life situation in general.
According to Rhodes and Watson [30], distress may be due to a state of difficulty, a burden that may cause limitations in daily living for the individual or bring forth an action. Over ten years later, Haberman and Bush [50], illustrated how Rhodes and Watson distinguish between the concepts of “symptom distress” and “symptoms of distress” where the latter is a more global concept referring to physical, psychological, social, and immunological responses to disease and distress. Holland [51] argues that the term distress is relevant for a number of psychological responses as it is more objective and less stigmatising than other psychological terms often used such as anxiety and depression.

The U.S. National Comprehensive Cancer Network (NCCN) [52] defines cancer-related distress as an unpleasant emotional experience that is multifactorial in nature and causes difficulties for the individual in coping effectively with cancer, its physical symptoms and treatment. According to NCCN, distress extends along a continuum, ranging from normal feelings of vulnerability, sadness and fears to problems that can become disabling such as depression, anxiety and social isolation. This definition emphasizes the psychological response to physical distress, but excludes, for example the physical response to psychological distress, which I argue is essential to include in a nursing-relevant conceptualisation of distress. Left untreated, distress may contribute to poorer quality of life and lesser satisfaction with care [53], but also to poorer adherence to treatment and possibly decreased survival times [54, 55]. The NCCN [52] suggests that distress should be recognized, monitored, documented and treated promptly in all stages of disease.

### 3.4 QUALITY OF LIFE

Quality of life is a concept with a broad range of definitions. Quality of life is often associated with life satisfaction and well-being and might therefore mirror an individual’s life values. Today, there is on the other hand a relative consensus that quality of life is a subjective and multidimensional phenomenon, which includes a number of life aspects influencing the individual’s well-being [56].

Health-related quality of life is a related and more recent term based on the WHO definition of health as a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity (WHO 1948). Health-related quality of life focuses on the consequences of disease and treatment for the individual and can be regarded as part of an individuals’ total quality of life. According to Sjödén [57] this means that the patient should be free from physical and mental distress and with regard to disease and treatment maintain as good physical, mental and social functioning as is possible in daily life.

As quality of life generally is defined as a subjective phenomenon, individual patients may perceive the same illness, problem, symptom or treatment differently, indicating that certain life aspects of importance for one person may have little or no relevance for another person. According to Grant and Rivera [58] quality of life is dynamic in nature and therefore susceptible to changes in accordance with changes in e.g. health condition and life circumstances.
In health care sciences, the concepts of quality of life and health-related quality of life are often used synonymously [56]. In this thesis, I use the term quality of life to broaden the focus from consequences of disease and treatment. This is in an effort to avoid excluding other life circumstances that may influence an individual’s quality of life.

3.5 DISCREPANCIES AND SIMILARITIES BETWEEN PATIENTS’ AND THEIR CAREGIVERS’ ASSESSMENTS OF SYMPTOMS AND QUALITY OF LIFE

During the past decade, a number of studies have examined the level of agreement between patients and their professional and family caregiver ratings of patients’ symptom experiences and quality of life [59-69]. Reviews of this research show that professional caregivers perceive cancer patients to experience more symptomatology than patients report themselves, especially concerning psychological symptoms [67, 70]. It has also been shown that health care professionals tend to rate chronically ill patients as having lower levels of functioning and health than patients report themselves [67], something I experienced on a personal level, as noted in the introduction section. Moreover, patients with lung cancer have reported lower levels of emotional distress than has been reflected in assessments by their nurses and doctors [71].

Research concerning patient versus family caregiver perceptions of patients’ symptom experiences and quality of life generally show better agreement [67, 72]. The levels of agreement between patients with cancer and their family caregivers have been shown to be better with regard to patients’ global physical or health perceptions than on an individual symptom basis, where the range in agreement level is wider [67, 72]. Higher levels of agreement between patients and both professional and family caregivers have been demonstrated for symptoms that are more concrete and observable (e.g. breathing, mobility and cough) and require less interpretation by the observer than for symptoms that are more subjective in nature (e.g. mood, fatigue and pain) [67, 72].

A number of factors related to both patients and caregivers have been discussed as influential on patterns of discrepancies. As Wennman-Larsen et al [73] point out, there is little research developing theoretical explanations that might contribute to the understanding of professional and family caregivers’ estimations of patients’ symptom experiences and quality of life. Professional caregivers’ attitudes to cancer have been shown to be strongly influenced by their professional experiences of the disease [74, 75]. Professional caregivers’ knowledge of the cancer disease, treatment side effects and prognosis as well as the fact that they often encounter the most seriously ill patients may influence their perception of patient’s symptom experiences and quality of life [70]. Moreover, working in cancer care has been reported to be highly stressful [76-79]. High levels of stress in cancer care may negatively influence professional caregivers’ ability to assess patient’s distress adequately, as has been found concerning medical students [80]. The relationship between workload and nurses’ ability to assess patients’ symptoms and distress appears to be less investigated as I have been unable to find research addressing this issue.
Discrepancies between patients and their family caregivers’ assessments have been related to the family member’s perception of caregiver burden. Caring for a seriously ill family member can be highly burdensome. It has been reported that agreement on psychosocial functioning is negatively affected by family caregiver burden [60, 67, 81, 82]. Such burden may lead to a family caregiver’s underestimation of patient’s functioning. It has been demonstrated that for severely impaired patients, the family caregivers’ assessments of patients’ psychosocial functioning were more associated with the level of the family caregiver’s own distress and caregiver burden than with patient’s psychosocial health [83, 84]. In general, the greater the contact and involvement with the patient are the better the agreement becomes [67, 82, 84-86].

Greater involvement can be expected to increase knowledge about patient’s symptoms and needs. On the other hand, involvement may also distort the family caregiver’s perception of the patient. In a recent study on patients with lung cancer, Wennman-Larsen et al [73] found that family caregivers’ lower ratings of lung cancer patients’ emotional functioning and global quality of life as compared to patients’ own ratings were related to family caregivers’ reports of lack of family support and own health problems. Moreover, moderate agreement on emotional functioning was found to be related to caregiver esteem.

Patients may have numerous reasons for moderating what they report about their symptom experiences and quality of life, e.g. to avoid burdening others or as a result of an effort to cope with their situation. Cancer patients may also have previous negative experiences during their disease trajectory as references, thus leading to a more positive assessment when judging a new situation [82]. A number of studies have shown that seriously ill patients report similar or better levels of quality of life as compared to less sick or healthy individuals [87-92]. In addition, several Swedish studies have found that reported levels of quality of life in patients with cancer did not differ from that of non-cancer populations [93, 94]. One possible explanation for this seeming paradox may be that along with a changing health, individuals may also change their perceptions and definitions of quality of life. Finally, there is evidence to suggest that patient ratings of symptom experiences and quality of life may be the result of changes related to adaptation to the disease [95, 96]. In the area of quality of life research, patients’ adaptive processes have been related to the phenomenon of response shift [95, 97-100].

### 3.6 RESPONSE SHIFT

Discrepancies between patient and caregiver assessments may reflect response shift in how patients subjectively calibrate, conceptualize, or value and prioritize symptoms and quality of life aspects in comparison with their caregivers [67, 96, 101, 102]. Considering response shift may lead to a deeper understanding of the process of adaptation and may enhance the role that caregiver assessments can play in nursing care and research.

Although response shift has increasingly been applied to quality of life research, the concept has its origin in research on educational training interventions and organizational change [96]. Response shift includes three interrelated phenomena referring to changes in the meaning of a target construct as a result of a change in
internal standards (recalibration), a change in values or priorities (reprioritization), or a change in the definition of the target construct (reconceptualization) [96, 98].

Recalibration can be illustrated by a situation in which a woman with lung cancer may perceive herself as exhausted at the time of diagnosis, but several months later during treatment feels that her fatigue level has further worsened. From her new perspective, she may look back at the time of diagnosis and perceive that she had not been exhausted then, but merely tired. Her internal standard of measurement for the target construct, fatigue has thus changed as a result of her experiences.

Reprioritization relates to a change in the respondent’s values. A patient diagnosed with lung cancer may attach less importance to physical function over time, but may discover that role and social functioning have become increasingly important. The relative importance of quality of life issues would thus have changed as a result of changes in health condition although the patient’s concept of quality of life might not have changed – the same issues could still constitute quality of life for that patient.

Reconceptualization involves a redefinition of the target construct, e.g. quality of life. A woman with lung cancer who has seen herself as an atheist might realize towards the end of her life that she gains comfort from a pastoral counselor. She may therefore now add spiritual issues to her perception of aspects important to her quality of life. Thus, the issues that constitute her conception of quality of life would have changed over time.

The original definition of response shift included the aspects recalibration and reconceptualization. Sprangers and Schwartz later added reprioritization as a third aspect when they developed a theoretical model addressing how response shift may affect perceived quality of life [96]. Their model has five interrelated components; catalysts, antecedents, mechanisms, response shifts and perceived quality of life. Catalysts refer to changes in health status resulting from the disease itself or from treatment. The antecedents refer to individual characteristics such as socio-demographic factors, personality, culture, environment, spiritual identity and expectations. Mechanisms encompass behavioral, cognitive and affective processes to accommodate changes in catalysts. Examples of such mechanisms include initiating social comparisons, using coping strategies, reordering goals or reframing expectations.

Changes in health status may prompt behavioral, cognitive and affective processes necessary to accommodate illness. These mechanisms have the potential to change individual standards, priorities or conceptualizations of quality of life. These response shift effects will thus influence perceived quality of life. The type of mechanisms that an individual will engage in as well as the magnitude and type of response shift will be dependant on individual characteristics. The antecedents are thus postulated to have both indirect and direct effects on potentiating response shift effects. Perceiving a sub-optimal quality of life may lead the individual to reinitiate established or new mechanisms. This feedback loop aims to maintain or improve perceived quality of life.
Response shift is hypothesized to be more likely to occur in patients who report either improvement or deterioration with regard to the target construct than in patients who remain stable over time [99, 103]. This is based on the expectation that those patients who report improvement or deterioration over time are also expected to re-evaluate the target construct, e.g. quality of life, as worse or as better than at previous occasion. Response shift is also hypothesized as more likely to occur in domains that are subjective in nature and therefore more susceptible to changes in patients’ internal standards [104], consequently making them difficult for “outsiders” to detect.

3.7 MEASUREMENT ISSUES

3.7.1 Measuring symptom experiences and quality of life

Multiple symptom measurement approaches ranging from single-question assessments to more complex multi-symptom measures can be used to evaluate symptom experiences in terms of a variety of dimensions. As symptoms are subjective in nature, it is commonly understood that patient self-reports are the most accurate approach to symptom assessments [32, 105]. Frequently used questionnaires measuring symptoms in cancer patients have a predefined set of questions and response alternatives, such as the Symptom Distress Scale (SDS) [39, 106], the Edmonton Symptom Assessment Scale (ESAS) [107, 108], the M.D. Anderson Symptom Inventory (MDAS) [109], The Memorial Symptom Assessment Scale (MSAS) [110], and the Rotterdam Symptom Checklist (RSCL) [111, 112]. The most widely used general scale is the 0 to 10 numeric scale for rating symptoms, where 0 indicates no symptom occurrence and 10 represents the worst possible symptom experience [113]. This scale was initially used for assessments of pain, but has been extended to be used for assessments of a number of cancer-related symptoms.

Instruments for measuring quality of life can be either generic or disease-specific [56]. Generic instruments such as the SF-36 [114] encompass several aspects of quality of life and can be used for comparisons across patient groups, whereas disease-specific instruments are developed for measuring quality of life in a particular group of patients and are best for capturing changes unique to the specific group studied, e.g. patients with a specific type of cancer. Among frequently used disease-specific quality of life instruments in cancer care, there are both core questionnaires, developed for measuring common concerns and problems in patients with cancer as well as disease-specific modules measuring aspects of relevance for specific cancer diseases or treatment regimens. This approach allows for a great deal of consistency and commonly used instruments in cancer care is the European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire 30-items (EORTC-QLQ-C30) [115] and the Functional Assessment of Cancer Therapy-General Scale (FACT-G) [116, 117]. Both these instruments can be complemented with different modules measuring specific disease-related aspects of quality of life.

Most quality of life questionnaires measure different aspects or dimensions of quality of life, such as physical, mental, emotional, social and cognitive functions [56]. Focus is generally on the occurrence of negative phenomena or limitations of different
functions, which may be relevant for clinicians’ intent on minimizing the negative consequences of disease and treatment [56]. From a research perspective this approach, which omits positive phenomena of importance for quality of life, such as joy, is more limited. For instance, the absence of depression cannot be interpreted as the presence of joy. Quality of life instruments have, like the standardized symptom assessment instruments been criticized for having predefined items, which include only certain aspects or dimensions of quality of life [56]. Thus, the respondents are unable to choose which domains should be included in their conceptualization of quality of life or to weigh the importance of different domains.

3.7.2 Measuring change in symptom experience and quality of life

Although there is support for the psychometric properties of the above-mentioned symptom and quality of life questionnaires, assessments of change over time derived from such scales do not distinguish objective change in symptom experiences or quality of life from change due to adaptation [96]. The use of questionnaires with predefined items in longitudinal studies is based on the assumption that the same symptoms and quality of life domains are relevant over time and that the meaning and importance of each symptom and quality of life domain remains constant over time. If individuals have adapted to deteriorating health, then instruments that account for the relative importance of different symptoms and quality of life domains may be needed to evaluate changes in the individual’s experiences [118]. Standardized measures may often not be sensitive enough to assess such change adequately, as they generally do not account for patients’ prioritizations.

One alternative to standardized instruments for assessing change in symptom experiences and quality of life over time are measures that incorporate individually generated content, allowing respondents to identify relevant areas and the importance of these areas. Examples of instruments measuring individual aspects of quality of life are the Quality of Life Index [119], the Patient-Generated Index [120] and the Schedule for the Evaluation of Individual Quality of Life (SEIQoL) [42]. A version of the latter instrument, SEIQoL-Direct Weighting has been used in several studies in patients with cancer [121]. These individual approaches, where patients are able to select the areas of importance for their quality of life, provide an opportunity to assess changes of selected areas as well as the importance the respondent assigns to each area [42, 118].

3.7.2.1 Measuring response shift

One means of studying recalibration response shift is a thentest approach, asking the patients to provide a renewed judgment about their earlier experiences [98]. This means that participants respond to the measurement twice at follow-up. They assess both how they perceive the relevant aspect of their experience to be at present, and are then asked to provide a renewed judgment (thentest) about their experience at baseline. By answering the follow-up measurements and the thentest in close proximity, it is assumed that the assessments will be completed with the same internal standard of measurement. The difference between the baseline assessment and the thentest assessment is said to provide an indication of the magnitude and direction of response.
shift. The comparison of the thentest and follow-up measurement can thus be considered as an indication of true change, corrected for response shift effects. This method has been widely used in assessing changes in internal standards and is probably the best-established approach [98], although its validity depends on the respondents’ recall of previous health conditions, and if cognitive dissonance and social desirability affect the measurements [122].

A variety of methods are described in literature for assessing changes in reprioritization and conceptualization, including individualized methods, preference-based methods, successive comparison approaches and qualitative methods [98]. Individualized methods attempt to make the concerns of the individual central to defining and measuring relevant quality of life domains. These methods integrate individual patient feedback in defining quality of life by identifying the relevant domains, anchors and relative importance weights, which are used to generate quality of life outcome scores. Preference-based methods assess the importance and value a patient explicitly places on a symptom or quality of life dimension. Successive comparison approaches involve judgments about the ordering or ranking of symptoms or quality of life issues. Sloan [123] points out that one manner by ranking is achieved by presenting the items in all possible subsets of two and asking the respondents to judge which item in the pair they prefer over the other, e.g. Thurstone scaling [123]. Qualitative methods for evaluating response shift can be accomplished through focus group discussions or semi-structured interviews, encouraging the respondents to delineate their experiences [98].
4 DESIGN AND METHODS

This thesis derives from a longitudinal descriptive study of patients with inoperable lung cancer (here referred to as the main project). The primary purpose of the main project was to describe patterns of symptom experiences in patients newly diagnosed with inoperable lung cancer both on and off treatment [3]. I begin by describing those aspects of the main project that are of relevance for the studies in this thesis.

Nine hundred and ten patients were invited to participate in the main project. In total 400 patients with inoperable lung cancer participated. They were consecutively recruited close to time of diagnosis (mean = 31 days, median = 23 days) through the lung medicine departments of two university hospitals in Stockholm from April 1998 - October 2002. These hospitals are the primary centers for non-surgical treatment of lung cancer in the Stockholm area. The sample in the main project has been the basis for recruiting patients for the studies in this thesis.

As shown in Table 1, 54 non-participants deceased before data collection or could not be reached for participation consent. Most non-participants declined without specified reason (n = 148) or said they were too tired to participate (n = 126) [3]. Despite the large number of non-participants, recruitment and participation in the main project is good compared to other non-treatment studies of lung cancer patients [41, 124, 125].

Table 1. Attrition and reasons for non-participation in the main project as reported by patients (N = 510).

<table>
<thead>
<tr>
<th>Reasons for attrition</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased before data collection</td>
<td>31</td>
</tr>
<tr>
<td>Could not be reached</td>
<td>23</td>
</tr>
<tr>
<td>No reason specified</td>
<td>148</td>
</tr>
<tr>
<td>Too tired to participate</td>
<td>126</td>
</tr>
<tr>
<td>Lack of time</td>
<td>50</td>
</tr>
<tr>
<td>Poor physical condition</td>
<td>41</td>
</tr>
<tr>
<td>Critical of the study</td>
<td>18</td>
</tr>
<tr>
<td>Cognitive problems</td>
<td>14</td>
</tr>
<tr>
<td>Other reasons</td>
<td>59</td>
</tr>
</tbody>
</table>

Table 2 shows demographic and clinical patient characteristics for the patients participating in the main project [3]. The sample had nearly equal numbers of men and women with men significantly older than women (p < 0.001). Men were also more likely to be married, whereas women more often were divorced or widowed. The study participants were younger (p < 0.001) and survived longer (mean survival, 320 days; p = 0.001) than non-participants (mean survival, 263 days). The study participants also differed from population data of patients newly diagnosed with inoperable lung cancer during the same period in the Stockholm-Gotland Cancer Registry. The cancer registry
population was older (mean age, 68.8 years) and did not live as long (mean survival, 178 days) [3].

Table 2. Demographical and clinical characteristics for patients in the main project [3].

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Women (%)</th>
<th>Men (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
<td>400</td>
<td>100</td>
<td>209</td>
<td>52</td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>64.5</td>
<td>62.6</td>
<td>66.2</td>
<td>0.001</td>
</tr>
<tr>
<td>SD</td>
<td>10.5</td>
<td>9.9</td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>63</td>
<td>60</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married or cohabiting</td>
<td>253</td>
<td>63</td>
<td>154</td>
<td>74</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>64</td>
<td>16</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Widow/widower</td>
<td>47</td>
<td>12</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Unmarried</td>
<td>32</td>
<td>8</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; High school</td>
<td>128</td>
<td>32</td>
<td>75</td>
<td>36</td>
</tr>
<tr>
<td>High school or equivalent (12 yrs)</td>
<td>75</td>
<td>19</td>
<td>44</td>
<td>31</td>
</tr>
<tr>
<td>&lt; High school (9 yrs)</td>
<td>185</td>
<td>46</td>
<td>88</td>
<td>97</td>
</tr>
<tr>
<td>Missing</td>
<td>12</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td><strong>Type of lung cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.059</td>
</tr>
<tr>
<td>SCLC</td>
<td>56</td>
<td>14</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>Non-SCLC</td>
<td>339</td>
<td>85</td>
<td>160</td>
<td>84</td>
</tr>
<tr>
<td>Missing</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.524</td>
</tr>
<tr>
<td>Stage I</td>
<td>11</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Stage II</td>
<td>20</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>35</td>
<td>9</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>78</td>
<td>19</td>
<td>35</td>
<td>18</td>
</tr>
<tr>
<td>Stage IV</td>
<td>164</td>
<td>41</td>
<td>83</td>
<td>44</td>
</tr>
<tr>
<td>Unclassified tumor</td>
<td>23</td>
<td>6</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Missing</td>
<td>69</td>
<td>17</td>
<td>35</td>
<td>18</td>
</tr>
<tr>
<td><strong>Treatment received</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.318</td>
</tr>
<tr>
<td>Chemotherapy (CT) alone</td>
<td>195</td>
<td>49</td>
<td>105</td>
<td>55</td>
</tr>
<tr>
<td>Radiotherapy (RT) alone</td>
<td>49</td>
<td>12</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Concomitant CT and RT</td>
<td>51</td>
<td>13</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>Both CT and RT</td>
<td>64</td>
<td>16</td>
<td>33</td>
<td>17</td>
</tr>
<tr>
<td>No treatment</td>
<td>41</td>
<td>10</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td><strong>Accrual</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.028</td>
</tr>
<tr>
<td>T1</td>
<td>245</td>
<td>61</td>
<td>103</td>
<td>54</td>
</tr>
<tr>
<td>T2</td>
<td>155</td>
<td>39</td>
<td>88</td>
<td>46</td>
</tr>
</tbody>
</table>

SD: standard deviation; SCLC: small cell lung carcinoma; T1: close to diagnosis and prior to treatment; T2: 2 weeks after T1 or after treatment start.
The staff at both lung medicine departments was asked to give patients a first information letter, with a copy also sent by the research team to the patients’ homes. Several days later, a research nurse contacted the patient to provide further information and to obtain informed consent for study participation [3].

In addition to providing basic demographic and medical/treatment information, all patients in the main project completed three self-report questionnaires and responded to an open-ended question at six time points: close to diagnosis and prior to initiation of treatment (T1), two weeks after T1 (T2), one month after T1 (T3), three months after T1 (T4), six months after T1 (T5) and one year after T1 (T6). Patients who were included in the study after initiation of treatment were entered at T2. The time points were selected to provide assessments both on and off treatment in order to capture changes that might occur during the process of treatment and disease progression [3].

All data were collected in presence of a research nurse at a venue determined by the patient e.g. the patient’s home, hospital clinic or hospital ward. Efforts were made for the same nurse to conduct all data collection with the same patient at all time points. During the data collection period, April 1998 to October 2003, a total of 10 research nurses collected data, with an equivalent of about three full-time positions at any time. During this time period, besides my work as lecturer and director of studies for the nursing program, I had the primary responsibility for data collection from 15 patients resulting in 60 data collection sessions. I also collected all data from the professional caregivers in paper I. Due to the emotionally stressful nature of interviewing so many seriously ill patients, often until death, and following the same patient during this period, the data collection team received supporting counseling every third week with a professional nurse-counselor, specialized in psychosocial oncology.

At the conclusion of each data collection session, patients were offered a gift certificate of 50 SEK, donated by the COOP, Sweden, a national federation of cooperative stores.

4.1 DATA COLLECTION INSTRUMENTS

The instruments were completed in the same order as described below at all time points. I have also indicated in which studies each instrument has been used.

4.1.1 Freelisting (papers III and IV)

This instrument was included in data collection from January 1999 with the recruitment of the 52nd patient. From this time point, all data collection began with a freelisting technique, derived from anthropological research [126, 127]. Freelisting is used to allow identification of relevant issues without imposing researchers’ assumptions and was used in the main project to provide a structure for asking the patients to state the concerns that they found most distressing at present. Patients were asked the question: “What do you perceive as most distressing for you at present”? They responded verbally in different ways, from single words to a few sentences with all responses
documented in writing by the interviewer, using direct quotes as much as possible, otherwise paraphrasing the content.

While one of the other data collection instruments, the Thurstone Scale of Symptom Distress – Lung Cancer (TSSD-LC) (see below), investigates ranking of association with distress from nine specific symptoms, it is theoretically possible that these symptoms do not represent the symptoms or concerns that are most distressing for the patient. This was something I and the other research nurses had noted when collected data, since patients often verbally described concerns that were not captured in the TSSD-LC or in the other structured questionnaires used for data collection. The freelisting technique provides an opportunity to examine the comprehensiveness of the items assessed in other questionnaires used and addresses individual concerns that may be related to other aspects of disease experiences, other than symptoms.

4.1.2 The Symptom Distress Scale (SDS) (paper I)

The SDS is a well-known self-report measure commonly used in studies of symptoms in patients with lung cancer [128]. This scale, originally developed by McCorkle and Young [39] to measure distress from symptoms in adult cancer patients, does not attempt to discriminate between symptoms caused by the disease itself and those caused by treatment side effects. The instrument was later revised and expanded by McCorkle and Quint-Benoliel [106], in part to reflect the symptoms patients with lung cancer may experience. Although the definition of symptom distress used when developing the instrument was “the degree of discomfort from the specific symptom being experienced as perceived by the patients”, the SDS has been interpreted in this project as assessing symptom occurrence rather than symptom distress, as patients are primarily asked to rate intensity and frequency of symptoms. The Swedish VAS-version consists of 15 items explicitly measuring the intensity of 10 symptoms (appearance, appetite, concentration, fatigue, insomnia, mobility, mood, nausea, outlook and pain) and frequency of two symptoms (nausea and pain). Three symptoms (bowel function, breathing and cough) are ambiguously formulated to assess either intensity or severity. As shown in Figures 1a and b, each item was presented on a separate card asking the patient to assess their symptomatology at present. The items are scored by measuring the distance from the beginning of the scale to the mark made by the patient across the 10 centimeter VAS-line, thus yielding a score of 0-10 for each item with higher scores indicating greater symptomatology. The summated scores for all items can range from 0-150. In the main project, the Cronbach’s alpha varied across time points from 0.84 to 0.88[3], comparing well with a Swedish Likert version showing an alpha coefficient of 0.81 [129] and with previous English versions reporting alpha scores between 0.70 and 0.92[130]. In paper I, the Cronbach’s alpha coefficients varied from 0.85 to 0.92 for the different samples.
4.1.3 Thurstone Scale of Symptom Distress – Lung Cancer (TSSD-LC) (papers I and IV)

The TSSD-LC was developed and piloted for use in the main project in an attempt to increase stringency in measuring symptom distress. The instrument consists of pairwise comparisons of nine symptoms to rank the symptoms that patients with lung cancer perceive as associated with most distress, irrespective of current occurrence. Nine symptoms from the SDS previously identified as the most distressing by 37 lung cancer patients in Canada [18] and reconfirmed as appropriate in a Swedish pilot study [44] were included in the instrument: appearance, appetite, bowel function, breathing, cough, fatigue, insomnia, outlook and pain. The symptoms were arranged in pairs of every possible subset of two, yielding 36 pairs \( \frac{n(n-1)}{2} \). The number of symptoms selected for use in the TSSD-LC was restricted to nine in order to limit the number of symptom pairs presented to respondents. The Ross matrix of optimal ordering [131] was used to determine the order in which the paired symptoms were to be presented. This procedure ensures maximum spacing for the maximum number of items to avoid selection bias. Each symptom pair was presented on a separate card and patients were asked to select the symptom from each pair associated with most distress irrespective of current occurrence. Figure 2 shows an example of a symptom pair relevant for lung cancer patients.
An analysis method based on “Thurstone’s law of comparative judgment” [123] ranks which symptoms are perceived as associated with most distress, giving a score representing an average preference for each symptom, based on the standard normal distribution. TSSD-LC scores have an infinite range, but generally range from -3 to +3, while the percent preference for each symptom can range from zero to one hundred percent. The more respondents that select one symptom of a pair over the other symptom, the greater the association with distress for that symptom, and the higher its score becomes. Higher score values thus indicate more distress associated with that symptom.

![Figure 2. Example of an item included in the TSSD-LC.](image)

Two measures of reliability were applied to the TSSD-LC data. The internal consistency of each individual’s comparative judgments was identified by calculating the number of circular triads, indicating inconsistencies in each patient’s comparisons. Between 97% and 99% of the 400 patients participating in the main project were consistent in their preferences at each time point: those patients with ≥ 6 missing values were excluded from the analysis. Twenty-eight interviews with 16 patients (of a total of 1428 interviews with 400 patients), were excluded for this reason [3]. The Gulliksen and Tukey’s index of scalability which measures the extent to which TSSD-LC scores can account for response variability in each patient’s response was 0.95 - 0.98 across time points [3]. In paper I, no respondents were found to be inconsistent in their comparisons and the mean number of inconsistencies varied from 2.0 - 2.9 for the different samples. The Gulliksen and Tukey’s index was between 0.94 - 0.98 across samples. In paper IV, between 1 - 3% of participating patients were inconsistent in their responses at each time point and the Gulliksen and Tukey’s index varied from 0.97 - 0.98 across time points.

Kendall’s coefficient of agreement was used to measure the degree of consistency among patients’ ranking of symptoms. The closer the value is to 1, the closer the patients are to complete agreement about the relative distress from the different symptoms. In the main project Kendall’s coefficient ranged from 0.24 - 0.31 [3], indicating a low to moderate level of agreement among patients with respect to symptoms associated with most distress. In paper I, Kendall’s coefficient varied from 0.21 - 0.29 across samples and in paper IV it ranged from 0.24 - 0.28 across time points.
4.1.4 The EORTC-QLQ-C30+LC13 (papers II, III and IV)

The EORTC-QLQ-C30 was developed for assessing health related quality of life for cancer patients participating in clinical trials. The core questionnaire, C30 is designed to cover a range of health-related quality of life issues relevant to most cancer diagnoses [115]. It consists of 30 items and includes 9 multi-item scales: five functional scales (physical, role, emotional, cognitive and social functioning); one global health and quality of life scale, and three symptom scales (pain, fatigue, nausea/vomiting). Single items are included to assess symptoms (dyspnea, insomnia, appetite loss, constipation, and diarrhea) as well as the economic impact of the disease and its treatment. The lung cancer specific module, LC13 is a 13-item measure of lung cancer-related symptoms (cough, hemoptysis, dyspnea, and site-specific pain), treatment side effects (sore mouth, dysphagia, peripheral neuropathy, and alopecia) and pain medication. As shown in Figure 3a, each item has a 4-point response scale (not at all, a little, quite a bit, very much) with the exception of the two items measuring global health and quality of life, which have 7-point response scales (see Figure 3b). In accordance with the scoring instructions given by the EORTC Quality-of-Life Study Group, the scale scores are linearly transformed to 0-100 scores for analysis [115]. For the functional and global health and quality of life scales, a higher score indicates better functioning. For the symptom-oriented scales and items, a higher score corresponds to a higher level of symptomatology. High internal consistency, overall reliability and validity for the instrument have been demonstrated across languages and countries in numerous international trials with cancer patients, including patients with lung cancer in Sweden [132] and a Swedish population sample [93].

<table>
<thead>
<tr>
<th>During the past week</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Did you need to rest?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. Have you felt weak?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18. Were you tired?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

*Figure 3a. Example of items (= fatigue symptom scale) included in the EORTC-QLQ-C30.*

<table>
<thead>
<tr>
<th>29. How would you rate your overall health during the past week?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

Very poor

Excellent

<table>
<thead>
<tr>
<th>30. How would you rate your overall quality of life during the past week?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

Very poor

Excellent

*Figure 3b. The EORTC-QLQ-C30 global health and quality of life scale.*
4.1.5 Thentests (papers II and III)

Two thentests were developed for use in the studies included in this thesis and were used in sub-sets of the sample in the main project.

The thentest used in paper II was added to the set of data collection instruments in the main project from October 2000 (patient number 193). It consists of ten items from the EORTC-QLQ-C30: the three-item fatigue scale, the two items measuring global health and quality of life, and the five-item physical function scale. The domains fatigue and global health/quality of life were selected, as they are subjective in nature and thus were expected to be susceptible to changes in internal standards [98]. Physical function was chosen for validation purposes as it more objective in nature and is assessed by relatively concrete items, and consequently expected to be less susceptible to changes in internal standards. Before completion of the thentest, the research nurse first reminded the patients about the first time they completed the questionnaires. This was followed by the instruction: “We would like you to answer the following questions about how you now perceive your health was then, at the time of the first interview. Please note that you should make a new judgment of how you now perceive your health was then, and not try to remember how you answered then”.

The thentest used in paper III was added to the data set for the main project from August 2001 (patient number 265 at T5). It is based on the freelisting technique (see section 4.1.1) in which patients were asked to provide a renewed judgment about which concerns they now perceive had been most distressing at the time point for the first data collection session. The question posed for this purpose was: “From your perspective today, what do you now perceive was most distressing for you at… (referred to time point for the first data collection)? The patients responded verbally in different ways, from single words to a few sentences. The research nurse documented all response in writing by using direct quotes as much as possible, otherwise paraphrasing the content.

4.1.6 Transition questions (paper II)

Within the area quality of life research, transition refers to a direct change over time. Three questions based on Osoba et al’s [133] Subjective Significance Questionnaire investigated the extent to which patients perceive they have changed since baseline with respect to the domains fatigue, overall quality of life and physical function. In accordance with Guyatt et al’s [134] recommendations, these transition questions were used to define groups of patients who have changed or remained stable over time with regard to these three domains. The instruction to the transition questions was: “We would like to know if there have been any changes in your condition since the first interview”. As illustrated in Figure 4, the questions were formulated as follows: “Compared to then, my fatigue (alternatively, overall quality of life or physical condition) today is…” Patients responded on a 7-point response scale ranging from much worse (1) to much better (7).
Compared to then, my fatigue today is….

1 2 3 4 5 6 7
Much worse Moderately worse A little worse About the same A little better Moderately better Much better

Figure 4. Example of a transition question.

4.2 SAMPLE RECRUITMENT

All patients who were included for the studies in this thesis were recruited from the main project. Table 3 gives an overview of the number and characteristics of patients included for the different papers. A more detailed description of the study populations will be presented in the presentation of papers in section 5.1-5.4.

Table 3. Patient characteristics for the samples in papers I-IV.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Paper I (PN)</th>
<th>Paper II</th>
<th>Paper III</th>
<th>Paper IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 33</td>
<td>N = 52</td>
<td>N = 115</td>
<td>N = 399</td>
</tr>
<tr>
<td>Number</td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>Female</td>
<td>12 26</td>
<td>26 50</td>
<td>56 49</td>
<td>43 191</td>
</tr>
<tr>
<td>Male</td>
<td>21 64</td>
<td>26 50</td>
<td>59 51</td>
<td>26 208</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/common-law</td>
<td>24 73</td>
<td>48 92</td>
<td>76 66</td>
<td>32 70</td>
</tr>
<tr>
<td>Single/divorced/widowed</td>
<td>7 21</td>
<td>4 8</td>
<td>39 34</td>
<td>14 30</td>
</tr>
<tr>
<td>Missing</td>
<td>2 6</td>
<td></td>
<td></td>
<td>4 1</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>13 39</td>
<td>23 44</td>
<td>47 41</td>
<td>15 33</td>
</tr>
<tr>
<td>High school</td>
<td>11 33</td>
<td>19 37</td>
<td>41 36</td>
<td>16 35</td>
</tr>
<tr>
<td>College/university</td>
<td>8 24</td>
<td>8 15</td>
<td>27 23</td>
<td>15 33</td>
</tr>
<tr>
<td>Missing</td>
<td>1 3</td>
<td>2 4</td>
<td></td>
<td>1 11</td>
</tr>
<tr>
<td>Age Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>62 (10)</td>
<td>61 (9)</td>
<td>61 (8)</td>
<td>61 (10)</td>
</tr>
<tr>
<td>Male</td>
<td>65 (9)</td>
<td>64 (9)</td>
<td>67 (11)</td>
<td>70 (12)</td>
</tr>
</tbody>
</table>

PN = patients from patient-nurse sample; PFC = patients from patient-family caregiver sample

4.3 DESIGN OF STUDIES

This thesis comprises one explorative dyadic cross-sectional study (paper I), two explorative longitudinal and retrospective studies (papers II and III) and one explorative longitudinal study (paper IV). Table 4 summarizes the characteristics of these studies.

In paper I, two dyadic samples of patients and caregivers participated.
Table 4. Characteristics of studies included in thesis.

<table>
<thead>
<tr>
<th>Design</th>
<th>No. of participants</th>
<th>Age (Mean)</th>
<th>Time points</th>
<th>Questionnaires/assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Explorative Dyadic Cross-sectional</td>
<td>33 patients 29 nurses 52 patients 54 FC</td>
<td>64 41 63 56</td>
<td>T2, T3, or T4 T2, T3, or T4 T2, T3, T4, T5, or T6</td>
<td>SDS TSSD-LC</td>
</tr>
<tr>
<td>II. Explorative Longitudinal Retrospective</td>
<td>115 patients</td>
<td>64</td>
<td>T1/T2,T4, and T5</td>
<td>EORTC-QLQ-C30+LC13 Thentest Transition questions</td>
</tr>
<tr>
<td>III. Explorative Longitudinal Retrospective</td>
<td>46 patients</td>
<td>66</td>
<td>T1/T2 and T5</td>
<td>EORTC-QLQ-C30+LC13 Freelisting Freelisting thentest</td>
</tr>
<tr>
<td>IV. Explorative Longitudinal</td>
<td>399 patients</td>
<td>65</td>
<td>T1/T2, T4, T5</td>
<td>TSSD-LC EORTC-QLQ-C30+LC13 Freelisting</td>
</tr>
<tr>
<td>FC = Family Caregiver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.4 DATA ANALYSIS

Descriptive statistics were used in all papers to describe the sample, symptom occurrence, distress associated with symptoms, and quality of life domains, with means, standard deviations and/or median presented, where appropriate. Table 5 gives an overview of statistical methods used in papers I – IV.

A more detailed description over statistical analyses for papers I-IV as well as for the inductive analysis for paper III is found with the presentation of papers in sections 5.1–5.4.

Table 5. Statistical methods used in papers I – IV.

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Statistical method</th>
<th>Paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of agreement</td>
<td>Intra-class correlation</td>
<td>I</td>
</tr>
<tr>
<td>Mean differences between two dependent measures</td>
<td>Dependent t-tests</td>
<td>I, II</td>
</tr>
<tr>
<td>Differences in mean between two independent groups</td>
<td>Independent t-tests</td>
<td>III, IV</td>
</tr>
<tr>
<td>Relations between groups</td>
<td>Chi-square tests</td>
<td>IV</td>
</tr>
<tr>
<td>Magnitude in differences, effect size</td>
<td>Cohen’s d</td>
<td>I, II</td>
</tr>
<tr>
<td>Correlations between measures (ordinal data)</td>
<td>Spearman rank correlation</td>
<td>I, IV</td>
</tr>
<tr>
<td>Correlation between measures (continuous data)</td>
<td>Pearson product moment correlation</td>
<td>II</td>
</tr>
</tbody>
</table>
4.5 ETHICAL CONSIDERATIONS

All studies were conducted in accordance with the World Medical Association Declaration of Helsinki [135] as well as in accordance with Swedish laws and regulations [136, 137]. All participants received oral and written information and consented verbally to participation. They were also informed about their rights to withdraw from the study at any time without having to give a reason. They also received written information about how their data were treated with confidentiality. All data collected for this thesis have been kept in a locked archive.

Ethical issues concerning autonomy and risk of causing participants emotional injury through questionnaires were considered. Integrity may be at risk of being encroached when questions are posed that can be perceived as sensitive or too private. One way of managing this risk was that data collection was conducted at a venue determined by the patient and/or family caregiver. Most interviews were conducted in the patient’s home, with the research nurse thus having to adapt to the patient’s environment, rather than the patient having to adapt for the research nurse’s comfort. Another potential risk is that questions may raise emotions that can be difficult to manage. Therefore, efforts were made for the same research nurse to collect data from the same patient at all time points. This approach involved a possibility for the research nurse to answer further questions and to refer the patient to relevant authority. Great consideration has been taken to participants’ wishes to withdraw during data collection, due to either psychological distress or lack of energy.

In research on severely ill patients, there might be a conflict between good research praxis and good nursing care. These issues are discussed in literature, and according to Addington-Hall [138], the researcher has to be sensitive to the patients in their vulnerable situation, to avoid causing them further burden and to give them the possibility to consider whether they wish to participate in research. Earlier research [139, 140] in terminally ill patients has shown that patients perceived their participation in research as valuable and as a positive and even therapeutic experience. Within the main project, several patients and family caregivers expressed the value of having a continuously contact and for sharing their experiences.

The Research Ethics Committee at Karolinska Insitutet has approved all studies (KI dnr 97-258, appendices 990503, 010220, 010731,021212 and KI dnr 98-318.
5 PRESENTATION OF PAPERS

In this section, the papers are presented with aim(s), research questions, sample(s), data collection and analysis, and results with the main findings summarized and discussed.

5.1 PAPER I: DISCREPANCIES AND SIMILARITIES IN HOW PATIENTS WITH LUNG CANCER AND THEIR PROFESSIONAL AND FAMILY CAREGIVERS ASSESS SYMPTOM OCCURRENCE AND SYMPTOM DISTRESS

The aim of this study was to explore the hypothesis that there may be different patterns in discrepancies and similarities between patients’ and their caregivers’ assessments of symptom occurrence and symptom distress. Prior research, clinical experience and experience from data collection in the main project led me to question whether these components of symptom experience are viewed differently by patients, nurses and family caregivers. The specific research questions addressed were: (1) what are the patterns of discrepancies and agreement between patients and their nurses/family caregivers in how they perceive symptom occurrence and symptom distress and (2) is there agreement between patients’ and their nurses/family caregivers’ ranking order of symptom occurrence and symptom distress? The research questions were examined in two dyadic samples of patient – caregivers: one sample consisting of patients and nurses and one sample consisting of patients and family caregivers.

5.1.1 Sample and recruitment

For the patient - nurse sample 33 patients undergoing radiation treatment were consecutively included from June 1998 - October 2002. Inclusion criteria were having received radiation therapy for at least five consecutive days and that data collection should coincide with one of the time points (T2 – T6) for data collection in the main project. All patients who met the inclusion criteria agreed to participate. Patients were equally distributed between the two radiotherapy departments and received a variety of full dose, concomitant and palliative treatment regimens. At time for data collection, they had received radiation treatment daily for an average of twelve days. There was a statistical significant overrepresentation of male patients (64%) as opposed to the main project with 52 % male participants.

During the data collection period, each nurse at the two radiotherapy departments in Stockholm who had been responsible for treatment and primary nursing care for one of the included patients for at least four treatment sessions was asked to participate. All 29 eligible nurses, six men and 23 women, agreed to participate. Four nurses responded for two patients each and 25 nurses for one patient each. The nurses had long professional nursing experience (mean 13 years) with a mean of eight years working experience with radiotherapy. Nurses had been responsible for their corresponding patient between 4-24 days and reported knowing two patients very well, 26 patients well or fairly well and five patients not at all.
For the patient – family caregiver sample, family caregivers were consecutively included from May 2001 - August 2002 by asking the patients in the main project if they were willing to identify a family caregiver, who might be willing to participate in the study. Inclusion criteria were that both patients and family caregivers should be able to communicate in Swedish, data collection should coincide with one of the time points (T2 – T6) for data collection in the main project, and family caregivers should be over 18 years old and have a close and stable relation to the patient. When the research nurse got permission from the patient to contact a family caregiver, the family caregiver received an information letter, which was then followed by a telephone contact from the research nurse providing further information and a request for participation in the study. During the data collection period 72 patients were asked to identify a family caregiver and 68 patients allowed the research team to contact at least one family caregiver. Eight patients died before data could be collected, five family caregivers declined participation, and three family caregivers were not included due to logistical problems. Two patients recruited two family caregivers each, giving a total of 54 patient – family caregiver dyads. Forty-four family caregivers were spouses, nine were adult children and one was a sibling. None of the patients within these dyads were included in the patient – nurse dyads. The patient sample consisted of equal numbers of women and men, while there was a slight overrepresentation of women (56%) among family caregivers. Patients were older (mean 63 years) than their family caregivers (mean 56 years).

5.1.2 Data collection and analysis

In this paper, the SDS was used to assess symptom occurrence and the TSSD-LC to assess symptom distress. Patients responded to these questionnaires as part of data collection within the main project, while nurses and family caregivers were asked to respond to the questionnaires with regard to how they perceived the patient’s symptom experiences. Data from nurses and family caregivers were generally collected immediately after the data collection from patients. The longest interval was within a patient – nurse dyad with the nurse responding the day after the patient, but without contact with the patient during the interim period. Several research nurses collected data from patients, whereas I collected all data from nurses and all data from family caregivers was collected by the same research nurse.

Dependent t-tests were used to calculate differences in patients’ and caregivers mean ratings of symptom occurrence. Agreement at the individual level was analyzed with intra-class correlations. Spearman rank correlation was used to determine the correlations between patients and caregivers’ ranking order of symptom occurrence and symptom distress. For interpreting the strengths of agreement between patients and caregivers Cohen’s d was used with ≥0.81 interpreted as excellent agreement, 0.61-0.80 as good agreement, 0.41 – 0.60 as moderate agreement and ≤ 0.40 as fair to poor agreement.
5.1.3 Results

5.1.3.1 Discrepancies and agreement between patients with inoperable lung cancer and their primary nurses

Both patients and nurses reported fatigue and outlook as two of the three most intense symptoms, although nurses assigned these symptoms a significantly greater intensity than patients did. Nurses rated the intensity of eight symptoms significantly greater than patients with the largest differences in mean scores found for outlook, mood, and fatigue. Patients and nurses agreed that mobility was the least intense symptom for patients. The intra-class correlation between patients’ and nurses’ ratings of symptom intensity according to the SDS varied from 0.01 to 0.43, showing poor to moderate agreement. When patients’ and nurses’ summed SDS scores were compared within dyads, the differences ranged from –0.62 to +21.9 with a statistically significant mean difference of –18.3, showing that nurses tended to assess patients’ symptom occurrence as greater than patients did themselves. In total, within 23 dyads nurses assessed patients’ symptom occurrence as greater than patients did and within 10 dyads as less than patients did.

Patients and nurses were more in agreement about which symptoms would cause most distress. Both groups ranked breathing, pain, fatigue and cough as the symptoms most associated with distress and appearance as associated with least distress for patients. The greatest discrepancy in ranking order of symptoms between patients and nurses was found for outlook, which nurses ranked as being more associated with distress than patients did. The greatest discrepancies in mean score values were found for bowel function and outlook, with nurses reporting that outlook would be more associated with distress for patients than patients reported themselves. The contrary was shown for bowel function where patients associated this symptom with more distress than their nurses reported for patients.

Table 6 summarizes patients’ and nurses’ assessments of symptom occurrence and symptom distress for the nine symptoms included in both questionnaires (SDS and TSSD-LC).

Table 6. Symptom occurrence and symptom distress in patients as assessed by patients themselves compared to assessments from their nurses.

<table>
<thead>
<tr>
<th>Symptom occurrence (SDS)</th>
<th>Symptom distress (TSSD-LC)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Ranking</strong></td>
<td><strong>Mean score</strong></td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.1</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2.7</td>
</tr>
<tr>
<td>Outlook</td>
<td>2.7</td>
</tr>
<tr>
<td>Appetite</td>
<td>2.5</td>
</tr>
<tr>
<td>Appearance</td>
<td>2.5</td>
</tr>
<tr>
<td>Breathing</td>
<td>2.2</td>
</tr>
<tr>
<td>Cough</td>
<td>2.2</td>
</tr>
<tr>
<td>Pain</td>
<td>1.8</td>
</tr>
<tr>
<td>Bowel</td>
<td>1.5</td>
</tr>
</tbody>
</table>
5.1.3.2 Discrepancies and agreement between patients with inoperable lung cancer and their family caregivers

Both patients and their family caregivers reported fatigue, outlook and appearance as the most intense symptoms, although family caregivers assigned these symptoms greater intensity levels than patients did. Patients and family caregivers agreed that nausea was the least intense and the least frequent symptom for patients. The family caregivers otherwise rated the intensity of all symptoms as significantly greater than patients did with the largest differences in mean scores for cough, insomnia, mood and outlook. The intra-class correlation between patients’ and family caregivers’ rating of symptom intensity according to the SDS varied from 0.13 to 0.57, showing poor to moderate agreement. The mean difference in summated SDS scores varied within dyads from –74.9 to +25.8 with a mean difference of –17.5, indicating that family caregivers estimated patients’ symptom occurrence as greater than patients did themselves. Within 70% of dyads, the family caregivers rated patients’ symptom occurrence as greater than patients did.

Patients and their family caregivers both ranked breathing, pain, and fatigue as the three symptoms most associated with distress, and appearance as least associated with distress, irrespective of current occurrence. The greatest discrepancies in ranking order of symptoms between patients and family caregivers was found for outlook, which family caregivers ranked as causing more distress than patients did and for bowel function which family caregivers rated as less distressing than patients. For both of these symptoms the mean difference in score values was 0.61.

In table 7, patients’ and their family caregivers’ assessments of symptom occurrence and symptom distress for the nine symptoms included in both instruments (SDS and TSSD-LC) are summarized.

Table 7. Symptom occurrence and symptom distress in patients as assessed by patients themselves compared to assessments from their family caregivers.

<table>
<thead>
<tr>
<th>Symptom occurrence (SDS)</th>
<th>Symptom distress (TSSD-LC)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td><strong>Family caregivers</strong></td>
</tr>
<tr>
<td>Rating</td>
<td>Mean score</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.6</td>
</tr>
<tr>
<td>Outlook</td>
<td>3.4</td>
</tr>
<tr>
<td>Appearance</td>
<td>3.2</td>
</tr>
<tr>
<td>Appetite</td>
<td>2.8</td>
</tr>
<tr>
<td>Pain</td>
<td>2.8</td>
</tr>
<tr>
<td>Breathing</td>
<td>2.6</td>
</tr>
<tr>
<td>Cough</td>
<td>2.5</td>
</tr>
<tr>
<td>Bowel</td>
<td>2.1</td>
</tr>
<tr>
<td>Insomnia</td>
<td>2.1</td>
</tr>
</tbody>
</table>
5.1.4 Summary and discussion of findings

Both nurses and family caregivers rated symptom occurrence as greater than patients did themselves with statistically significant differences for most symptoms. The findings were more in agreement between patients and caregivers on the assessments of symptom distress (TSSD-LC) as compared to the SDS measure of symptom occurrence. These results support the hypothesis that there are greater discrepancies in how patients and nurses assess symptom occurrence compared to how they assess symptom distress. The hypothesis was not supported in assessments from patients and their family caregivers, although family caregivers provided different information than patients regarding both symptom occurrence and symptom distress.

Although caregivers provided different information than patients regarding symptom occurrence and symptom distress, patients, nurses and family caregivers were all able to differentiate between these two components of symptom experience. The greatest discrepancies between patients and caregivers were found for the less observable symptoms, such as fatigue, mood and outlook, which is in line with other research on patient–caregiver discrepancies [70, 72, 82, 141, 142].

By examining symptom occurrence and symptom distress, we attempted to gain an understanding of different symptom characteristics that may influence caregivers’ assessments of patients’ symptom experiences. This is of particular interest with regard to the more subjective symptoms that are less observable by others. Nurses and family caregivers seemed to be able to assess which symptoms patients perceive as most distressing, although they rated their intensity as greater than patients. Whereas it is assumed that it is optimal for patients and their caregivers to rate patients’ symptom experiences similarly, we argue that the patterns found in this study may be functional in effective symptom management. Caregivers’ ability to identify patients’ symptom distress along with their assessments of greater symptom occurrence may prompt them to notice and report as well as actively manage and alleviate patients’ symptoms, thus contributing to optimize patients’ quality of life. Agreement in assessments of symptom distress may be more important than agreement in assessments of symptom occurrence, as the pattern found in this study with caregivers rating symptom intensity greater than patients, might have positive consequences in leading to prophylactic symptom management. This is line with Watson’s [143] argument that it is more serious to miss those patients who are in need of effective symptom management that to pick up those with less symptom experiences.

5.2 PAPER II: DO INTERNAL STANDARDS OF QUALITY OF LIFE CHANGE IN LUNG CANCER PATIENTS?

Although professional and family caregivers in paper I seemed to be able to provide a reasonable account of which symptoms patients perceive as most distressing, they rated symptom occurrence as greater than patients did. A number of factors related to both patients and caregivers have been discussed as influential in these patterns of discrepancies.
Existing knowledge suggests that patients’ low ratings of symptom occurrence may be the result of patients’ successful adaptation to the disease, which has been related to the phenomenon response shift [70, 82]. One form of response shift involves changes in patients’ internal standards of measurement [96].

In this paper, changes in internal standards of measurement were examined with regard to assessments of fatigue, global health/quality of life and physical functioning at three and six months following a baseline assessment. It was expected that a change in internal standards of measurement would occur only in patients reporting improvement or deterioration in fatigue and/or global health/quality life. Consequently, no changes were expected to be found in patients who remained stable over time or in relation to physical functioning. The specific research questions addressed were to what extent there are indications of change in internal standards of measurements, and to what extent there is agreement between an external measure of change (transition question) and change scores?

5.2.1 Sample and recruitment

One hundred twenty-six patients were consecutively included between October 2000 and June 2003. Inclusion was based on accessibility for data collection at three months (T4) and/or six months (T5) from baseline (T1/T2). At the three months follow-up, 11 patients were excluded for the following reasons: three patients declined participation due to fatigue and/or disease progression, four patients could not be reached within the required time frame and four patients were excluded due to incomplete data sets. One hundred and fifteen patients thus participated at three months follow-up. At six months follow-up, 28 of these patients had died, four patients declined participation due to fatigue and/or disease progression, and five patients had incomplete data sets, with a total of 89 patients remaining of the original 126 patients.

5.2.2 Data collection and analysis

For this study, patients’ responses to the EORTC-QLQ-C30 domains of physical function, fatigue and global health/quality of life at baseline (T1/T2), 3 months follow-up (T4) and six months follow-up (T5) were used. At three and six months follow-up patients also responded to comparable items in a thentest and to the three transition questions measuring how patients perceive that their condition had changed over time with regard to the examined domains. The transition questions were used to form mutually exclusive patient groups for each domain. These groups were based on responses indicating deterioration (transition scores, 1-2), stability (transition scores, 3-5) or improvement (transition scores, 6-7) with regard to physical function, fatigue and global health/quality of life.

Dependent t-tests were used to test mean differences between the thentest and baseline scores as indication for changes in internal standards of measurement. T-tests were also used to examine changes over time as indicated by follow-up EORTC-QLQ-C30 scores minus thentest scores. For examining agreement between transition scores and
EORTC-QLQ-C30 change scores, Pearson Product Moment Correlation coefficients were calculated. The equality of correlations between transition scores and EORTC-QLQ-C30 measures of change were tested with a Chi-square test. To examine the clinical significance of the results, effect sizes were calculated by dividing the EORTC-QLQ-C30 mean change scores by the standard deviation of baseline [144]. For interpreting the strengths of clinical significance, Cohen’s guidelines [144] were used and an effect size of 0.2 was considered small, 0.5 moderate and 0.8 as large.

Because of the relatively large number of statistical tests in relation to (sub)-sample sizes, a significance level of 0.01 was adopted for those instances where change was expected to occur, and a level of 0.05 for those instances where a change was unexpected to occur.

5.2.3 Results

5.2.3.1 Indications of change in internal standards of measurement

A statistically significant change in internal standards was found in the entire sample for global health/quality of life at three and six months after baseline but not for fatigue and physical functioning. However, further analyses according to the hypotheses of expected and unexpected changes in internal standards of measurement with regard to the examined domains and patients’ reports of changed or stable condition over time show a more detailed picture. With regard to fatigue, expected change in internal standards was seen in patients who reported that their fatigue had deteriorated at 3 months follow-up and in patients reporting improvement after 6 months, but not in patients reporting improvement after 3 months or deterioration after 6 months. With regard to global health/quality of life, expected change was seen in patients reporting improvement after 3 and/or 6 months, but not in patients reporting deterioration over time. Unexpected changes were found in patients reporting stable global health/quality of life after 3 months. Although no changes were expected to occur with regard to physical function, unexpected changes were seen in patients who reported improved physical functioning after both three and six months. In Table 8, results are summarized according to expectations about change.

Table 8. Outcomes according to expectations about change.

<table>
<thead>
<tr>
<th></th>
<th>Reported deterioration</th>
<th>Reported stable condition</th>
<th>Reported improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 months</td>
<td>6 months</td>
<td>3 months</td>
</tr>
<tr>
<td>Exp Outcome</td>
<td>Exp Outcome</td>
<td>Exp Outcome</td>
<td>Exp Outcome</td>
</tr>
<tr>
<td>Fatigue n</td>
<td>31 +</td>
<td>18 +</td>
<td>55 -</td>
</tr>
<tr>
<td>QL n</td>
<td>13 +</td>
<td>6 +</td>
<td>69 +</td>
</tr>
<tr>
<td>PF n</td>
<td>19 -</td>
<td>8 -</td>
<td>53 -</td>
</tr>
</tbody>
</table>

Exp = expectation

Shaded areas indicate results according to expectations about change.
Given these inconsistent results, it could not be concluded that changes in internal standards of measurement occurred in this group of patients with inoperable lung cancer. However, when examining the results in relation to our expectations, the follow-up minus thentest mean scores were more in agreement with transition ratings than were the follow-up minus baseline mean scores.

5.2.4 Summary and discussion of findings

Statistically significant changes in internal standards of measurement, as measured by thentest minus baseline mean EORTC-QLQ-C30 scores, were found in four out of the eight instances where they were expected and in three out of the ten instances in which they were unexpected.

As seven out of a total of 18 instances were not in accordance with expectations based on literature on response shift, we could not conclude that changes in internal standards of measurement occurred in this group of severely ill patients. One possible explanation for these inconsistent results may be that since these patients reported high levels of symptoms even at baseline they may have in part adapted to their symptoms before study entry. This explanation is supported by Corner et al’s [145] recent findings that symptoms in lung cancer start between two years and four months before patients’ diagnosis. Moreover, based on qualitative data from the patients included in this paper, Leveälahdi et al [4] also noted an extended process of adaptation to symptoms prior to diagnosis. A further analysis of why changes in internal standards did not occur when expected and why they occurred when not expected in this group of patients with inoperable lung cancer is however warranted.

With regard to fatigue, the unexpected results that no statistically significant changes in internal standards of measurement were found among patients who reported less fatigue after three months or among those who reported more fatigue after six months are surprising and difficult to explain as previous research suggest that fatigue is prone to changes in internal standards of measurement. However, a closer inspection of their EORTC-QLQ-C30 mean scores show that the 19 patients who reported improved fatigue level at three months follow-up, retrospectively judged their baseline fatigue level as worse than at baseline. The reverse pattern was shown in the 18 patients who reported deterioration after six months and retrospectively judged their baseline level of fatigue as better than they did at baseline. These patterns indicate that some change in internal standards of measurement in the expected direction might have occurred. The small sample sizes and the large standard deviations may in part explain why these changes did not reach statistical significance.

With regard to global health/quality of life, in accordance with expectations, changes in internal standards of measurement were found neither after three or six months for those patients reporting deterioration. The small sample sizes of 13 and six patients respectively with widely varying scores may thus explain these unexpected findings. The unexpected changes in internal standards of measurement that occurred in the relatively large group of 69 patients who at three months follow-up reported their
global health/quality of life had remained stable since baseline are difficult to explain. It can be noted that the retrospective baseline assessments for this group showed poorer global health/quality of life in comparison with their baseline assessments. However, a similar pattern has been shown in a less severe ill group of patients with early-stage breast cancer [100] and despite the differences in disease severity, both patient groups may have been overly positive in their baseline assessments.

There might be at least two possible explanations for the unexpected changes that were found for those 30 patients reporting improved physical function after three months and for those 28 patients reporting improvement after six months may be explained in two ways, although there is no documentation about this found in the literature. First, as their retrospective baseline assessments showed poorer physical function than their baseline assessments, they may have been overly positive in their assessments at baseline in an effort to minimize their problems with strenuous activities. Second, they may have adjusted their retrospective baseline assessments to the worse in an effort to feel that their physical function had not further deteriorated.

There are a number of methodological considerations that have been taken into account when considering whether internal standards of measurement occurred in this group of patients with inoperable lung cancer. These considerations are related to patients’ loss to follow-up, small sample sizes and retrospective reports and will be further discussed under methodological considerations in the discussion section (section 6.2).

In conclusion, this study did not provide decisive support for the hypothesis that a change in internal standards of measurement occurred in this group of patients with inoperable lung cancer. This raises questions about how to investigate response shift in longitudinal studies of patients with advanced stages of cancer diseases.

5.3 PAPER III: SPONTANEOUS REPORTS OF MOST DISTRESSING CONCERNS IN PATIENTS WITH INOPERABLE LUNG CANCER: AT PRESENT, IN RETROSPECT AND IN COMPARISON WITH EORTC-QLQ-C30+LC13

The inconsistent findings in paper II raised questions about how best to investigate changes in symptom experiences and quality of life in patients diagnosed with advanced stages of disease. While it is expected that patients recently diagnosed with inoperable lung cancer will experience distress, their values and priorities concerning symptom and quality of life issues may change during disease trajectory. Distress is, as earlier mentioned, often examined indirectly via occurrence in standardized questionnaires, which may be problematic in several ways. First, the predefined items may not include those issues that are most distressing for the individual patient. Second, the components of occurrence and distress may be conceptualized differently by patients [3, 44, 146]. And third, assessments of change over time using standardized instruments assume to measure changes in health condition but not change due to adaptation [96]. One alternative to standardized instruments is measures that incorporate individually-generated content, allowing the respondents to identify...
relevant areas and their importance. This approach provides both an opportunity to assess change in selected areas and to assign the importance of these areas [42, 147].

The first aim of this paper was therefore to examine what patients with inoperable lung cancer spontaneously report as most distressing and how these concerns change over time and in retrospect. The second aim was to examine how these spontaneously reported concerns compare with the areas included in the EORTC-QLQ-C30+LC13 questionnaires, with regard to content and intensity level.

5.3.1 Sample and recruitment

This study is based on data from a subset of patients who responded to the freelisting question about their most distressing concerns at baseline (T1/T2), six months follow-up (T5) and in retrospect at follow-up, as well as to the EORTC-QLQ-C30+LC13 at baseline and six months follow-up. Of the 105 patients from the main project who were asked to complete the freelisting thentest, 46 patients had full data sets at both baseline and six months follow-up and thus comprised the sample for this paper. This sample differed from the total sample in the main project, in that patients were statistically significantly older (mean, 66 years), had a higher education level and were more likely to be married or co-habiting.

5.3.2 Data collection and analysis

At baseline, patients were first asked to state the concerns they found most distressing at present (freelisting). Later in the interview, they then completed the EORTC-QLQ-C30+LC13 questionnaires. At six months follow-up, the same data collection procedure was conducted with the addition of the freelisting thentest, which was the final instrument in the data collection procedure.

To analyze the concerns patients spontaneously reported as most distressing, all freelisting statements within the main project were initially inductively coded by two members of the research team. Based on similarity in content and discussion with the entire research team, 17 categories were formulated and defined, and each code was sorted into one category only. Seven members of the research team then informally validated the categorizations by each person coding a number of freelisting statements, with discrepancies discussed and categories modified for increased clarity. The relationships between categories were then further discussed, and as a result 15 categories were grouped into three dimensions: Bodily distress, Distress from living with lung cancer and Iatrogenic distress, reflecting different aspects of distress. The remaining two categories consisted of statements about co-morbidities, and statements about not experiencing anything as most distressing. With another member of the research team, I classified all statements reported by patients for this paper, into the afore-mentioned 17 categories. We classified all statements independently and the few disagreements that arose were discussed until consensus was reached. Table 9 shows the categories within each dimension.
Table 9. Freelisting categorization.

<table>
<thead>
<tr>
<th>Bodily distress</th>
<th>Dyspnea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Cough</td>
</tr>
<tr>
<td></td>
<td>Digestive and gastrointestinal problems</td>
</tr>
<tr>
<td></td>
<td>Other somatic problems</td>
</tr>
<tr>
<td>Distress from living with lung cancer</td>
<td>Limitations in daily life</td>
</tr>
<tr>
<td></td>
<td>Concerns about the future</td>
</tr>
<tr>
<td></td>
<td>Sleep disturbances</td>
</tr>
<tr>
<td></td>
<td>Relationships</td>
</tr>
<tr>
<td></td>
<td>Disease as a whole</td>
</tr>
<tr>
<td></td>
<td>Financial problems</td>
</tr>
<tr>
<td></td>
<td>Emotional problems</td>
</tr>
<tr>
<td>Iatrogenic distress</td>
<td>Health care system (HCS)- related problems</td>
</tr>
<tr>
<td></td>
<td>Treatment-related problems</td>
</tr>
</tbody>
</table>

For examining the extent of agreement over time at the individual level as well as between prospective and retrospective freelisting reports, cross tables were used. For examining agreement between freelisting reports and EORTC-QLQ-C30 or LC13 ratings, each freelisting statement was considered as to whether it was also assessed by any item in the EORTC-QLQ-C30 + LC13 questionnaires. Independent t-tests were conducted to examine possible differences between those patients who had stated a concern as most distressing in freelisting and those who had not stated that concern as most distressing with regard to the mean score on the corresponding EORTC-QLQ-C30 or LC13 item.

5.3.3 Results

5.3.3.1 Spontaneous reports of most distressing concerns

Patients spontaneously reported a wide variety of concerns as most distressing. The concerns reported as currently causing most distress at baseline were primarily related to bodily concerns such as fatigue, pain and dyspnea with these along with a wider variety of concerns reported as most distressing at six months follow-up. In addition, concerns related to the health care system, such as long waiting times for information and treatment start were commonly reported at baseline, while at six months follow-up concerns categorized as other somatic problem were frequently reported. These somatic concerns included a variety of problems such as musculoskeletal problems, mucus secretions, sweating, hoarseness, alopecia and neuropathy. In the retrospective baseline reports at six months follow-up, in addition to pain and fatigue, concerns categorized as related to the disease as a whole were most frequently reported. These concerns mainly referred to their new life situation with lung cancer.
At the individual level, there was relatively low agreement over time as well as between present and retrospective reports of most distressing concerns. For example, at baseline statements related to the disease as a whole were reported as most distressing by six patients and in retrospect by 18 patients, while four of the patients stated this concern as most distressing in both their reports.

5.3.3.2 Relation between freelisting reports and EORTC-QLQ-C30+LC13 ratings

Across time points, between 56 – 62% of the concerns were found to be assessed by an item included in the standardized questionnaires. For seven of the freelisting categories, items included in the EORTC-QLQ-C30+LC13 did not specifically assess most of the concerns spontaneously reported as most distressing by these patients. These concerns were categorized as related to other somatic problems, concerns for the future, relationships, the disease as a whole, emotional problems, treatment-related problems or as problems related to the health care system.

In freelisting, pain, dyspnea and fatigue were among the most frequently reported concerns as causing most distress at all time points, but their intensity levels varied and were not always reflected in comparable EORTC-QLQ-C30+LC13 items. A majority of patients rated the intensity of these symptoms as “a little” or “quite a bit”. The highest intensity ratings were shown for pain at six months follow-up with a third of patients rating its intensity as “very much”.

5.3.4 Summary and discussion of findings

In summary, findings showed that patients perceived a variety of concerns as causing most distress and that these concerns changed over time and in retrospect. We also find that items included in the EORTC-QLQ-C30+LC13 assessed slightly over half of the concerns spontaneously reported as most distressing. Finally, findings supported previous research indicating that intensity and distress are distinct components of symptom experience.

The concerns spontaneously reported as currently causing most distress at baseline and at six months follow-up were primarily related to bodily distress, while in the retrospective baseline reports, concerns related to most distress from living with cancer were more common. This may indicate a change in perspective over time, demonstrating that patients are more attentive to bodily concerns in the present, while reflecting on the past they perhaps adopt a wider perspective integrating their entire life situation. It may also indicate that when deteriorating health results in considerable distress that is not effectively managed, patients may instead shift focus and prioritize aspects of life showing improvement. Sharpe et al [148] suggest that shifting focus from one area to another could support adaptation when the first area is not improving, a phenomena they found in patients with metastasized cancer. Carver and Scheier [149] have described this shift as scaling back goals in an effort to minimize deteriorating health.
The low agreement at the individual level over time and between present and retrospective baseline reports indicates a shift in concerns reported as most distressing. Such shift may be caused by factors related to deteriorating health, treatment side effects or disease progression. It may also reflect changes in values and priorities, suggesting a reprioritization response shift. Reprioritization response shift is said to occur as part of adjustment to illness and changing life situation when an individual change his/her values and prioritizations in order to accommodate to changing circumstances [150]. For the severely ill patients in this paper, this might well have been the case in an effort to accommodate to deteriorating health.

In line with results from paper I and from different data within the main project [3], this study confirms that the different dimensions of intensity and distress are not equivalent in these patients with inoperable lung cancer. Of the spontaneously reported concerns at all time points, pain, fatigue and dyspnea were among the most frequently reported as causing most distress, but their reported intensity level varied in comparable EORTC-QLQ-C30+LC13 items. These findings are also in line with Strömgren et al [43] who in their study of patients in palliative care found that patients’ prioritizations regarding fatigue, physical function, social function and activity were weekly associated with their intensity levels. Tishelman et al [3] suggest that from the perspective of patients, distress may be related to both past and current experiences as well as to future fears and expectations for the future. Therefore, considering what patients prioritize and find most distressing provides an important complement to assessments of occurrence and intensity in effective symptom management. For this purpose, in addition to standardized questionnaires individualized measures may have the potential to provide further detailed information about patients’ concerns, priorities and changes over time.

5.4 PAPER IV: RELATIONSHIPS BETWEEN SYMPTOM OCCURRENCE, INTENSITY AND DISTRESS IN PATIENTS WITH INOPERABLE LUNG CANCER

Results in study I and III, supported previous research indicating that symptom occurrence and symptom distress are perceived differently by patients with lung cancer and hitherto, there has been a lack of longitudinal studies examining the individual patient’s symptom experiences during disease trajectory. The overall aim of this study was therefore to provide an empirical basis to ensure that patients’ perspectives of their symptom experiences are considered in future interventions. This study was designed to both help understand more about the relationships between symptom occurrence, symptom intensity and symptom distress as well as how the association with distress from a symptom changes over time in relation to changes in relation to symptom intensity. Based on paper I and other data from the main project [3, 7], the following hypotheses were formulated:

1. If a symptom is reported as having the strongest association with distress by an individual (rank 1 on TSSD-LC), it will not necessarily also be reported as occurring by the same individual.
2. Therefore, the intensity level of a symptom reported by patients as highly associated with distress (rank 1-3 on the TSSD-LC) will not differ from the level of intensity reported for the same symptom by patients who do not highly associate that symptom with distress.

3. It is therefore also expected that when reported intensity for a specific symptom changes over time, no corresponding change in association with distress will necessarily be found.

4. But when a symptom is currently experienced as distressing, the situation will differ. Therefore:

   a) if an existing symptom is reported as currently causing most distress for an individual (on freelisting), it will also be reported as more intense than is the case for those individuals not reporting the symptom as currently causing most distress

   b) when an existing symptom is reported as currently causing most distress (on freelisting), it will also be more highly associated with distress than is the case for those individuals not reporting the symptom as currently causing most distress.

5.4.1 Sample and recruitment

A total of 399 patients from the main project were included in this study. Inclusion criterion was completed data set comprising the TSSD-LC and the EORTC-QLQ-C30+LC13 at baseline (T1/T2) (n = 399), three months follow-up (T4) (n = 274) and six months follow-up (T5) (n = 200). One of the 400 patients included in the main project had an incomplete data set at baseline.

5.4.2 Data collection and analysis

The database for this study consists of the TSSD-LC, the EORTC-QLQ-C30+LC13 and the freelisting question. Relationships between symptom occurrence, intensity and distress were examined for six symptoms: cough, dyspnea, fatigue, insomnia, pain and outlook. These symptoms were chosen for strategic and pragmatic reasons. Paper I as well as previous studies within the main project [3, 7] have shown that these symptoms represent different levels of association with distress. They are also commonly reported as occurring in patients with lung cancer [3, 18, 22, 29, 151, 152] and they are all included in the TSSD-LC and EORTC-QLQ-C30+LC13 with comparable data generated from the freelisting question.

Symptom occurrence is here used to indicate the reported existence of a symptom (EORTC-QLQ-C30+LC13) while symptom intensity refers to severity of a symptom (EORTC-QLQ-C30+LC13). Symptom distress is defined in two distinct ways, referring to both association with distress (TSSD-LC) and existing distress (freelisting).
Independent t-tests were used to examine differences in EORTC-QLQ-C30+LC13 mean scores between subgroups. Chi-square tests were used to test statistically significant differences between subgroups with regard to symptom occurrence and association with distress. Changes over time in symptom intensity in relation to changes in ranking order of association with distress were examined using Spearman rank correlation.

### 5.4.3 Results

#### 5.4.3.1 Relationships between symptom occurrence, intensity and distress

It was first hypothesized that the symptom most strongly associated with distress for an individual would not necessarily be reported as occurring by the same person. At baseline and at three months follow-up, the only statistically significant relationship between a symptom being ranked as having the strongest association with distress and its reported occurrence was found for outlook. At six months follow-up no statistically significant relationships were found for any of the symptoms. It is noteworthy that at all time points, approximately 40% of those patients who associated pain with most distress reported no occurrence of pain in comparable EORTC-QLQ-C30 item.

In the second hypothesis it was expected that the intensity level of the symptoms reported as highly associated with distress would not differ from the level of intensity reported for the same symptoms by patients who do not highly associate the same symptoms with distress. At baseline a statistically significant difference between these groups was found in mean symptom intensity for insomnia and outlook and at three months follow-up for dyspnea, fatigue and outlook, while at six months follow-up a significant difference remained for only outlook. It is notable that between subgroups no statistically significant differences in mean intensity levels were found for pain at any time point.

#### 5.4.3.2 Changes over time

It was further hypothesized that when a symptom’s intensity changes over time, no corresponding change in the ranking order of association with distress would necessarily be found. The only statistically significant correlation across all three time points between reports of stable or changed intensity level and analogous change in association with distress was found for outlook. In addition, between 3 and 6 months follow-up a significant correlation was found with regard to cough. Interestingly, in situations in which an increase in symptom intensity was reported for a symptom between baseline and 3 months follow-up, 52 – 67% of patients maintained the same ranking order of association with distress or ranked the same symptom as less associated with distress. A similar pattern was found between 3 and 6 months follow-up with 44 – 72% of patients maintaining the same ranking order of association with distress or associating the symptom with less distress.
5.4.3.3 Relationship between association with distress, occurrence, intensity and current distress

It was assumed that when a symptom was reported as actually experienced and currently causing most distress, it would also be reported as more intense and more highly associated with distress than for those patients not reporting the same symptom as currently causing most distress. Although relatively few patients reported each symptom examined as currently causing most distress, their reported intensity levels were statistically significantly higher than for those patients not reporting the same symptom as currently causing most distress. This pattern was consistent for all symptoms at all three time points with the exception for insomnia at 3 months follow-up and for fatigue at 6 months follow-up.

Finally, it was assumed that when an existing symptom was reported as currently causing most distress, its association with distress would be higher than in the case for those individuals not reporting the symptom as currently causing most distress. At baseline, a statistically significant relationship between current distress and association with distress was found for dyspnea, cough, insomnia and outlook. Three months later, outlook was the only symptom found to have statistically significant relationship between association with distress and most distress at present. At six months follow-up this relationship for outlook maintained with the addition of insomnia.

5.4.4 Summary and discussion of findings

These results support earlier findings from papers I and III, and other studies emanating from the main project [3, 7] in demonstrating that the dimensions of symptom occurrence, intensity and distress are not equivalent, from the perspective of these patients with lung cancer. Other striking findings were that 1) the strongest relationships between symptom intensity and association with distress were found close to diagnosis, 2) no relationship between intensity and association with distress was found for pain 3) whereas for outlook, association with distress was related to reported intensity regardless of time point in disease trajectory, and 4) despite reported increased intensity for a particular symptom over time, a relatively large proportion of patients associated the same symptom with an equal or lesser degree of distress than was the case 3 months earlier.
In this paper, symptom distress was examined with respect to two aspects, association with distress and currently existing distress. The relationship between symptom occurrence, intensity and distress was found to differ between these two aspects of distress. As expected, currently existing distress was more related to intensity than association with distress. Relationships between intensity and association with distress were found for more symptoms close to diagnosis than three and six months later. Cooley et al [22] have earlier described a similar temporal pattern in patients undergoing treatment for lung cancer. Their study showed that patients’ symptom intensity was high at baseline, decreased after 3 months and further decreased for some symptoms while some symptoms’ intensity level increased after another three months. These temporal differences support Tishelman’ et al [3] argument that association with distress may be related to both past and current experiences as well as to fears and expectations for the future. Close to diagnosis, a currently existing and intense symptom may be related to association with distress, while later in disease trajectory both past experiences as well as fears and expectations might direct patients’ association with distress.

In this study, pain did not show the same pattern of temporality, as no relationship was found between intensity and distress during disease trajectory. It is noteworthy that the intensity level for pain was relatively low in comparison with other symptoms and that its intensity level decreased from baseline to 3 months follow-up and then increased again at 6 months follow-up to the same level as at baseline. This may be explained by pain being a frequent and feared symptom in patients with cancer [153] and may therefore be highly associated with distress throughout disease trajectory, irrespective of current occurrence. Moreover, in this group of severely ill patients, pain may function as a symbol for threats associated with distress and therefore being strongly associated with distress, even in times of low intensity levels.

On the other hand – outlook, which assessed patients’ worries for the future – was the only symptom for which a statistically significant relationship was found between intensity and association with distress at all investigated time points. Although relatively few patients ranked outlook as highly associated with distress, those who did also reported high intensity levels. This may illustrate that for those patients having fears and anxiety for the future, the entire life situation is strongly associated with this distress.

It was assumed that the association with distress would not change over time in accordance with changes in intensity levels. With the exception for outlook, this hypothesis was confirmed for all symptoms during the first three months, and partly confirmed at six months follow-up. A striking finding was that despite reporting increased intensity for a symptom over a time, there was a tendency for patients to associate the same symptom with equal or less distress than three months earlier. Gift et al [154] also noted a tendency for patients with lung cancer to maintain the same ranking order of symptom severity over time.
The differences in time frames and response options for the instruments used in this paper should be considered when interpreting the findings and consideration should also be given the manner in which patients ranking orders of distress on the TSSD-LC was interpreted. These methodological considerations will be further discussed in the discussion section of this thesis (section 6.2.)

In conclusion, this study confirmed earlier studies that the different dimensions of symptom experience, occurrence, intensity and distress are not equivalent in patients with lung cancer and extends earlier research by confirming that patients association with distress not consistently is related to the dimensions of occurrence and intensity.
6 DISCUSSION

The aim of this thesis was to gain better understanding of different aspects influencing how patients with inoperable lung cancer and their caregivers assess patients’ symptom experiences and quality of life. The findings in paper I showed that patients and caregivers were more in agreement about which symptoms patients associated with distress than about patients’ current symptom occurrence. Papers I, III and IV all confirmed that symptom occurrence and symptom distress are separate components of patients’ symptom experiences. There was no decisive support in paper II to demonstrate that recalibration response shift influenced patients’ assessments of their symptom experiences and quality of life during the first six months following diagnosis. The findings in paper III showed that patients perceive a variety of concerns as most distressing and that their concerns changed over time and in retrospect. It was also shown that patients concerns, priorities and changes over time not always were adequately assessed in the standardized cancer specific EORTC-QLQ-C30+LC13 questionnaires.

In the following discussion section, I will attempt to integrate results from the four papers in order to scrutinize how the different approaches contributed to gain a better understanding of some possible aspects influencing assessments of symptoms and quality of life in patients with inoperable lung cancer. These aspects include perspectives, individual and environmental factors, symptom characteristics and response shift. I will then discuss pros and cons of different measurement approaches assessing patients’ symptoms, concerns and priorities. Finally, I will discuss methodological considerations, starting with sample selection and limitations of measures followed by considerations concerning inductive data analyses.

6.1 ASPECTS INFLUENCING ASSESSMENTS OF SYMPTOMS AND QUALITY OF LIFE

6.1.1 The perspectives of patients, nurses and family caregivers

Patients and their professional and family caregivers sometimes assess aspects of symptoms and quality of life differently. Although both nurses and family caregivers seemed able to assess which symptoms are perceived as most distressing for patients, they rated symptoms occurrence as significantly greater than patients did themselves for a vast majority of symptoms. The greatest discrepancies were shown for symptoms that are less observable, such as outlook and mood.

An early theory by Dembo [155] points to the importance of the differences between the insider and outsider perspective. Referring this theory to the circumstance when a caregiver assesses a patients’ symptom experience, the caregiver – as compared to the patient – strongly emphasizes the disease and tends to identify the patient with his/her physical state. This discrepancy between outsider and insider perspectives is formulated in the “requirement of mourning” hypothesis [156], postulating that when a value that the caregiver regards as fundamental, e.g. physical health, is threatened, the caregiver
tries to safeguard his/her values by assuming that the patient is suffering even when he/she shows no such signs.

Patients and family caregivers may have conflicting beliefs about the disease and the illness experience as well as a lack of skills in how to manage these conflicts. In lung cancer with tobacco as primary causal agent, shame and blame may be factors contributing to such conflicting beliefs. Zhang and Siminoff [157, 158] have identified how family caregivers of patients with lung cancer are influenced by anger and blame towards the patient for causing the diagnosis which in turn, negatively influenced their perceptual understanding of patients’ symptom experiences, resulting in assessments biased by emotions and one-sided perspectives. Several recently conducted studies [159, 160] on patients with lung cancer have shown that the relationship between patients and spouses may develop negatively during the disease trajectory, thus hindering communication about patients illness experiences.

For interpreting assessments from caregivers, it is of importance to consider whether the caregiver can separate his/her own viewpoint from his/her perception of the patient’s viewpoint. The caregiver may assume that the patient’s thoughts and feelings are the same as his/her own thoughts and feelings, resulting in biased assessments. These assumptions are related to perspective-taking, which refers to ability of an observer to imagine placing one-self in another person’s shoes in order to understand another person’s thoughts and feelings [161, 162]. Pickard and Knight [163] have described at least three perspective-taking approaches for assessments of another person’s illness experiences. They assume that different prompts about perspective-taking result in varying levels of agreement between patient and caregiver assessments. First, the imagine-patient perspective requires the caregiver to make an inference about the patient experience that is not solely based on visible signs, to be aware of and able to differentiate between his/her own and patient’s viewpoint as well as being able to prevent his/her own viewpoint from influencing the assessment of the patient’s experience. Second, in the proxy-proxy or imagine-self perspective, the caregiver assesses the patient from his/her own perceptions of patient’s illness experiences, that is imagining how s/he hypothetically would react or feel if in the patient’s situation. In the third naturalistic or neutral perspective, the caregiver does not take on a specific perspective, so the assessments are based on the caregiver’s perceptions of patients’ experiences.

In clinical practice, the imagine-self perspective may be effective in providing additional information, expanding or clarifying the patient’s symptom experiences. For paper I, the professional and family caregivers were not prompted to take a specific perspective, since they were only asked to provide an assessment of the corresponding patient’s symptomatology. One might assume that for most family caregivers the assessments were provided from a imagine-self or neutral perspective, as described above.

Inspired by Pickard and Knight [163], Lobchuk et al [164] hypothesized that the interrater gap between patient self-assessments and caregiver assessment of patients’ symptom experiences would be reduced when caregivers were prompted to take the imagine-patient perspective. They therefore designed a study where the family caregivers were prompted to take on different perspectives. They found that the least
discrepancies between patients and caregivers occurred in the neutral perspective and
the greatest discrepancies in the imagine-self condition. Lobchuk and al [165] also
investigated how family caregivers feel and reason when assessing patients’ symptom
experiences based on different perspective-taking prompts and found that caregivers
assigned to the neutral condition reported similar thoughts and feelings as those
assigned to the imagine-patient perspective. Their assessments were generally based on
visual and verbal cues, information from clinic visits and imagining the patient’s
response, while those caregivers prompted to the imagine-self perspective primarily
based their assessments on how they themselves would feel and behave if they had
cancer. These results support Goodell and Nail’s [33] argument that it is important to
understand how patients and their caregivers interpret the concepts being used. This
suggests that professional caregivers planning and managing symptom alleviation need
to be aware of perceptual differences when considering their own judgments as well as
those of patients and/or family caregivers.

6.1.2 Individual and environmental factors

Although not examined in my papers, it is beneficial to consider the individual context
when discussing underlying aspects influencing patients’ and caregivers’ assessments
of symptom experiences and quality of life. The meaning attributed to different
symptoms and quality of life aspects, as well as how the individual patient responds
and copes is unique. This is influenced by an individual’s life history and the wider
culture in which illness is understood [34]. Gender, personality traits, health beliefs,
socio-economic status, environmental factors and coping strategies are all potent
influences on how symptoms are perceived and expressed by the individual patient
[166].

Such individual and environmental factors are included in a vast majority of theoretical
models describing symptom perception, symptom management, quality of life, coping
strategies and response shift. It is challenging for health professionals to consider these
multifaceted factors when assessing and interpreting distress from specific symptoms
for a specific patient, in order to effectively plan for symptom alleviation. For severely
ill patients, understanding the meaning symptom and problems hold for the individual
may thus contribute to reliable assessments as a basis for effective symptom
management, support and comfort.

6.1.3 Symptom characteristics

Perceptions of underlying symptom characteristics may influence assessments of
symptom experiences. As has been described in earlier research [3, 72] both patients
and caregivers seem to be able to differentiate between the components of symptom
occurrence and symptom distress (paper I), although they provided different
information about patients’ symptom experiences. Caregivers were able to assess which
symptoms would be most distressing to patients but rated patients’ symptom intensity
as greater than patients did, which were most evident in the case of professional
caregivers. In paper III, it was shown that most distress from a symptom was not always equivalent to high levels of intensity from that symptom. This pattern was also confirmed in paper IV, where patients’ association with symptom distress was not consistently related to symptom occurrence and intensity, although this varied by time and symptom.

These results point to the importance of considering how these two aspects of symptom experiences are understood and conceptualised. Consequently more stringency is needed in determining what symptom characteristic is the optimal focus for assessment, in order for interventions to be most appropriate. Literature on symptom theory suggests that by separately assessing underlying characteristics of symptoms (e.g. intensity, frequency and distress) researchers and clinicians may be more effective in designing, managing and evaluating interventions [167, 168]. In doing so, perceptual discrepancies between patients and professional caregivers on targeted symptom characteristics may be reduced.

From my clinical experience in cancer care, symptom intensity is generally more often addressed than symptom distress. As it is suggested that distress may reflect the meaning patients associate with different symptoms and concerns [38], and that perceived distress may be related to both past and current experiences as well as to fears and expectations for the future [3], addressing distress may provide a complement to assessments of symptom occurrence and intensity for effective management. Such an approach has the potential to ensure that patients’ perspectives of their symptom experiences are considered.

6.1.4 Response shift

It has been argued that changes in symptom experiences and quality of life that occur in seriously ill patients with life-threatening disease in part result from patients’ adaptation to their life situation. Patients may change their internal standards of measurement, prioritizations and conceptualisation of quality of life, including symptoms, and therefore make different assessments than they would have if they had not adapted to their life situation. According to Sprangers and Schwartz’ theoretical model [96] quality of life changes may result from an interaction between a change in health status, personality characteristics, behavioural, cognitive and affective processes, and response shift. This internal adaptation may explain the sometimes apparently paradoxical results of assessments of symptom experiences and quality of life in patients with inoperable lung cancer. In paper II, it was hypothesized that a change in internal standards of measure would occur in patients with inoperable lung cancer. The inconsistent findings provided no decisive support for this hypothesis, although some indications for changes in internal standards were shown with regard to fatigue and global health/quality of life. Because patients with inoperable lung cancer in most cases are diagnosed with advanced stages of disease and even at diagnosis show high levels of symptomatology [16], they may to some extent already have adapted to their symptoms, health condition and changed life situation prior to diagnosis. Thus, as a consequence have undergone a response shift. In paper III, it was found that patients’ prioritizations of what concerns they found most distressing changed over time and in retrospect. Such changes may be
due to health changes related to treatment or disease progression. They may also reflect changes in values and priorities, indicating a reprioritization response shift effect due to changing life circumstances.

Although not find here, patients’ adaptation to their symptom experiences and life situation may be one factor explaining the different assessments from patients and their professional and family caregivers. The fact that caregivers often rate patients’ symptom experiences and quality of life as worse than patients do, may thus reflect possible response shift effects in patients [67, 99, 102]. Response shift may also influence professional and family caregivers’ assessments of patients’ symptom experiences and quality of life, although to the best of my knowledge, this has not yet been empirically studied. Based on their encounters with severely ill patients, professional caregivers working in cancer may change their own internal standards, values and perceptions of what constitutes quality of life. Family members may also be prone to changes in internal standards, life values and conceptualisations, based on their perspective in a new life situation close to and emotionally involved with a family member with life threatening disease and perhaps newly situated as informal caregiver.

6.1.5 Measuring symptom experiences and quality of life

Major advances in instrument development related to symptom experiences and quality of life have been made over the past decades and a variety of reliable and valid instruments are available. Selection of an adequate instrument depends on several factors such as if the instrument is to be used for research or clinical purposes, characteristics of respondents and the construct of interest. As earlier mentioned, it is commonly understood that the optimal approach to symptom and quality of life assessment is through patient self-reports, allowing for consideration of the multiple dimensions of an individual’s perception of symptoms and quality of life aspects.

Multi-symptom instruments for measurement of cancer-related symptoms assess a variety of symptoms and have the advantages of having strong validity and reliability and usually taking less than 10 minutes to complete. Limitations regarding these instruments are that they require a basic level of cognitive functioning and are not designed for completion by proxies, such as professional and informal caregivers. The lack of consistent conceptual definition of symptom experiences is another problem resulting in a lack of clarity about which dimensions of the symptom experience are assessed. Many researchers [32, 169, 170] have argued that a multidimensional assessment of symptoms including frequency, duration intensity and distress is necessary to capture the complexity of symptoms. However, evaluations of the usefulness of such instruments with scales for the different dimensions usually presented side by side, are conflicting [110, 171], although Portenoy [110] suggests that symptom distress provides most information about quality of life and that frequency adds significant information.

Although not addressed in this thesis, symptom clusters defined as a stable group of at least two concurrent symptoms related to one another and independent of other symptom clusters [172] further complicates assessments and interpretations of...
symptom experiences. Symptom clusters broadens the focus from single symptoms to multiple concurrent symptoms and their interrelationships [173].

In this thesis, results indicate that standardized measures are not always comprised of relevant areas and dimensions to adequately assess patient’s problems, priorities and changes over time. While standardized questionnaires often are developed for evaluation of treatment and intervention outcomes of predefined groups of patients, in the clinical setting individualized measures may be useful for assessing and effectively managing distress in the individual patient. The addition of individualized measures allows for distinctions to be made between prioritized and non-prioritized concerns. In the clinical setting, after having identified prioritized areas, a further assessment focusing on frequency, intensity, distress, quality or character of the prioritized concerns may have the potential for providing further information for adequate alleviation.

6.2 METHODOLOGICAL CONSIDERATIONS

6.2.1 Sample recruitment

All study samples were recruited from the main project, a longitudinal study on 400 patients with inoperable lung cancer. This inclusion of patients for the studies in this thesis may raise questions about inclusion criteria. It is noteworthy that patient and caregiver recruitment for papers I, II and III was initiated after the main project began.

First, it should be noted that the sample in the main project represent the “healthiest” of this severely ill patient group as they were younger and had longer survival times than both non-participants and patients newly diagnosed with inoperable lung cancer during the same period in the same area, based on population data. Considering the well-known difficulties in recruiting patients with lung cancer for research, recruitment compared favorably with other studies on patients with lung cancer [124, 174, 175]. To gain representativeness in research on severely ill patients, it is recommended that participants are recruited from a variety of settings [176]. For the main project, patients were recruited through two different university hospitals where they received their diagnosis and thereby had access to university health care at low out-of-pocket costs. This implies that perceived symptomatology and concerns might be under-represented in comparison to many other patients with inoperable lung cancer.

Recruitment of patients and caregivers for paper I was associated with several difficulties due to some of the inclusion criteria. First, in the patient-nurse sample, inclusion criteria included that patients should have received radiation therapy for at least five consecutive days with data collection coinciding with one of the time points (T2 – T6) for data collection in the main project. Inclusion criteria for nurses were that they had been responsible for treatment and primary nursing care for the matched patient for at least four treatment sessions. The intention was that nurses should be matched to only one patient in an effort to reduce potential biasing influence on the agreement levels that could occur if a few nurses provided assessments for many patients. Recruitment closed when all 29 eligible nurses at the two radiotherapy departments had been matched to one patient, with four nurses matched to two patients.
each. In contrast to other research on patient-staff perceptions of symptom experiences in cancer care the dyadic sample was small, but consisted of independent assessments of the entire nurse population, with limited selection bias. This is a strength compared to earlier research.

The recruitment procedure for the patient – family caregivers was associated with fewer problems although data collection was planned to coincide with data collection for the main project. The decision to consecutively recruit a minimum of 50 dyads was based on a review article [177] on proxy-ratings recommending ≥ 50 dyads to obtain methodological quality, a limit that is commonly used in other patient-proxy research [67, 70]. During a period of 16 months in 2001-2002, 72 patients were asked to identify a family member willing to participate which resulted in 54 participating dyads of patient-family caregivers, mainly spousal dyads. Attrition was mainly due to patients’ death and to patient or caregiver decline, suggesting that the “healthiest” patients and family caregivers with relatively low levels of burden may have been those who participated.

Patients’ loss to follow-up is a well acknowledge problem in longitudinal studies on severely ill patients with cancer, usually due to death or declining health, resulting in findings biased to the healthiest patients. This problem was managed in different ways. In papers II and IV, we accepted a level of attrition, whereas in paper III, we only analyzed data from those patients with complete data sets at both time points. Both approaches have their limitations. Although the participating patients with inoperable lung cancer were in poor health when entering study II, the loss of the most severely ill patients may in part explain the relatively high levels of quality of life scores in this patient group. For paper III, data was only analyzed for the 46 patients who had complete data sets at baseline (T1/T2) and at 6 months follow-up (T5). This approach was considered appropriate, as it allowed for longitudinal analyses at an individual level without considering attrition or imputing data, but limited the number and power of subgroup analyses.

6.2.2 Assessments of distress

Distress was measured with regard to two different aspects, association with distress and existing distress. Association with distress as measured by TSSD-LC referred to patients’ perceptions of whether a symptom is related to distress, irrespective of current symptom occurrence, while existing distress as measured by freelisting referred to a currently existing concern perceived as causing most distress at present. One might assume that patients may have had difficulties in distinguishing between these two aspects of distress. However, when both aspects were analysed in relation to symptom occurrence and intensity (paper IV) they were found to differ. Existing distress was highly related to intensity, while the relationship between intensity level and association with distress was less consistent, indicating that patients were able to distinguish between these two aspects of distress.
6.2.3 Differences in time frames and response options

The instruments differ with respect to both time frames and response options. The freelisting and the SDS request an assessment of current experiences, the EORTC-QLQ-C30+LC13 questionnaires request assessments of experiences during the past week, whereas the TSSD-LC asks what patients would find most distressing, regardless of current occurrence. The TSSD-LC is thus designed to address both the present and the hypothetical, based on a meaning-centred approach, assuming that distress can be caused by present situation, past experiences and fears and expectations for the future.

Differences in response options might have also influenced comparisons between the different dimensions of symptom experiences. Freelisting allows the respondent to identify relevant concerns themselves, minimizing imposition of researcher assumptions. The SDS and the EORTC-QLQ-C30+LC13 allow for individual assessments of predefined symptoms and concerns on a VAS-scale and (most often) a four-response Likert-scale respectively. It is well known that respondents may interpret VAS anchors differently for different items as well as over time, with a risk for mean values that would not be entirely comparable for different items or for the same item over time[178, 179] . This problem exists in much research using subjective self-report scale and but becomes more evident in the use of VAS-scales. The ranking of symptom distress on the TSSD-LC is based on a forced-choice comparison between pairs of symptoms, which might raise questions of reliability. Despite the severe illness of participating patients, they were able to conduct the 36 comparisons with few inconsistencies. Thus, these data compare favourable with other studies in less ill cancer populations using the Thurstone scaling for other purposes [180, 181]. Despite the forced-choice format, the index of scalability was high, suggesting that results reflect a viable dimension. The low to moderate Kendall coefficients of agreement between respondents indicate that participants responded according to individual preferences.

6.2.4 Retrospective reports

Retrospective reports have limitations that should be considered when interpreting their outcomes. These limitations are primarily related to interpreting differences between prospective and retrospective reports. In addition to random errors, differences found may be attributed to difficulties remembering the past, recall bias, social desirability and effort justification [98, 100, 182]. There are several ways to decrease these biases, which were considered in papers II and III, to increase the reliability and validity of the retrospective assessments. First, keeping the time frame as short as possible reduces the possibility of memory difficulties [183, 184]. Research on recall of baseline functioning suggests that patient’s ratings are affected consistently by recall bias throughout a period of 6 months to 5 years [185, 186], whereas other research suggests that recall bias does not occur within 6 weeks to 4 months from baseline [103, 187, 188]. We took this into consideration by referring to a salient and significant time point close to receiving the lung cancer diagnosis within a time span of three to six months, which also was the first time point the interviewer had met the patient. Second, giving respondents the possibility to report that they cannot recall helps avoid educated or wild
guesses. As we were present during all interviews, we were able to give patients the option to report they could not recall and discuss this with them. Third, asking specific rather than general questions may reduce recall bias. Considerable research has found that specific questions are more reliable than general questions [189]. A limited number of specific questions were posed in both studies. Despite these attempts, effort justification and social desirability may have affected the results, in that patients undergoing treatment and nursing interventions may have felt inclined to retrospectively diminish their assessments of their baseline condition to justify their invested efforts or to please their caregivers. This might be more evident in paper II, which used standardized instruments with standardized response alternatives, than in paper III using freelist.

Transition scores correlate change over time as assessed by standardized questionnaires with a patient’s direct overall evaluation regarding the extent to which they have improved, remained stable, or deteriorated. Transition scores have been criticized for their self-reported nature as such ratings are subject to the same biases as retrospective assessments, e.g. thentests [134]. Transition scores may also reflect patient’s current health status rather than the extent to which their health condition has changed since baseline [134]. In paper II, transition questions were used to form mutually exclusive sub-groups of patients according to changes in health condition over time. These groupings were determined according to patients’ responses on the 7-point response scale ranging from much worse to much better. We interpreted stable condition as ranging from ‘a little worse (3)’ to ‘a little better (5)’. As we suspected that this grouping of stable condition may have been too broad, stable sub-groups were reformed to only include patients who had responded ‘about the same (4)’ which did not alter the results significantly. Since the transition questions were responded to immediately after the thentest, awareness of a difference between follow-up and thentest assessments might have led patients to the conclusion that their health condition had changed over time, which in turn may have led to transition ratings correlating significantly higher with follow-up minus thentest mean scores than with the baseline minus follow-up mean scores.

### 6.2.5 Inductive analysis

The analysis of concerns reported as causing most distress was based on categorization of the content of patients’ spontaneous freelist statements (papers III and IV). Coding and categorizations were discussed within the research group with the team members with different previous knowledge and experiences, and finally validated by tests of inter-coder reliability. This procedure resulted in a coding guide for categorization of each patient’s statements. Although different procedures for coding and categorization are described in methodological literature, Graneheim and Lundman [190] state that one relevant method for validating content into categories is by using dialogue within the research group to achieve concordance. Although other categories might have been used instead, the members of the research team have independently considered the ones used in this analysis procedure appropriate. As patients’ statements could consist of single words, single sentences or short narratives written verbatim when possible and otherwise paraphrased, they were sometimes difficult to interpret.
Patients may have used different wordings or expressions over time to describe the same concern, resulting in the same concern possibly being categorized differently over time.

Descriptive statistics were used to present the inductive data from freelisting reports, by presenting the number of statements within each category and dimension. It is argued that the use of numbers enhances inductive data [191]. Presenting data as fully as possible enables the reader to judge whether the researcher has relied on rare events to the exclusion of more common events that may contradict findings and conclusions.

6.3 NURSING IMPLICATIONS

6.3.1 Clinical implications

This thesis adds to an understanding of some aspects influencing patient and caregiver assessments of symptoms and quality of life in patients with inoperable lung cancer. Although findings are based on severely ill patients with lung cancer, they may have wider relevance in the field of cancer nursing. The clinical implications addressed here are directed to nurses, but are relevant for all health care professionals involved in improving patients’ symptoms and quality of life.

Evidence-based nursing aims to promote effectiveness and improve quality. In order to enhance nursing practice and patient outcomes, cancer nursing is challenged to continually evaluate nursing strategies, retain effective interventions, develop new ones and refine those needing improvement [192]. Nurses within cancer care play a key role in maintaining and improving patients’ well-being and quality of life in all stages of the disease by understanding their experiences and influencing factors and outcomes.

Assessment is one key to the recognition and management of patients’ symptoms and concerns. To be able to interpret patients’ and their caregivers’ assessments, nurses need increased awareness of underlying factors influencing such assessments. This thesis points to the importance of being aware of the perspective from which assessments are provided, and what underlying symptom characteristics both patients and professional and family caregivers address when assessing the patient’s symptoms. It has been argued that when patient’s and caregiver’s assessments are at odds, the patient should have the final word. Based on this thesis, I argue that there is no unbiased “golden standard”, but rather that the different perspectives together contribute to clarify the complexity of patients’ symptom experiences. With this in mind, nurses are even more challenged to be aware of these different perspectives.

Findings from this thesis along with earlier findings[3, 7, 35, 44-46] show the importance of nurses being able to discriminate between the components of symptom distress and symptom occurrence, as well as their underlying dimensions. Perceived symptom distress is not always related to high levels of symptom intensity. Symptoms showing low levels of intensity might be perceived as causing high levels of distress and vice versa. Therefore, nurses should be aware of these perceptual differences and able to consider patients’ prioritisations and needs as a prerequisite for providing effective symptom alleviation. From the perspective of patients, it may be far more
serious to miss those symptoms causing much distress than to pick up those that might be more intensive but cause less distress.

For the patients participating in this thesis, association with distress was not always related to symptom occurrence and symptom intensity. From the perspectives of patients, association with distress may be related to both past and current experiences and to fears and expectations for the future as well as to the meaning different symptoms hold for an individual [3]. This challenges nurses to, early in the disease trajectory, identify those symptoms that are most feared by the individual patient. In accordance with WHO’s definition of palliative care [193], symptom prevention should be as prioritized as symptom management. Nurses, participating in preventive symptom interventions might thus contribute to improve patients’ quality of life.

Standardized questionnaires for assessments of patient’s symptoms, concerns and changes over time may not always be sensitive enough to recognize individual concerns and priorities. In clinical practice, an alternative is individualized measures that allow for a first identification of the individual patient’s unique priorities. This may then be followed by more in-depth assessment of prioritized areas, e.g. in terms of frequency, intensity, distress, quality or character of the prioritized concerns, which may have the potential for providing further information for symptom prevention and management.

Patients’ adaptation to their symptoms and their life situation in living with cancer might influence how their assessments are carried out and should be considered when planning for and evaluating nursing interventions. It is important for nurses to be aware that patients may undergo different response shifts. When interpreting change over time, nurses ought to consider if response shifts might have occurred and integrate this awareness with existing knowledge on coping.

6.3.2 Research implications

This thesis contributed to the theoretical basis for understanding factors influencing assessments and interpretation of the multidimensionality of symptom experiences and quality of life in lung cancer. Future research is recommended to focus on expanding this theoretical basis and on implementing and evaluating nursing interventions for symptom prevention and symptom management.

To improve symptom alleviation and quality of life in patients with lung cancer further research needs to focus on:

- Delineating the cues professional and family caregivers use when assessing a patient’s symptom experience and quality of life
- Examining how different symptoms are conceptualised by patients
- Symptom clusters and their predictors and interrelationships
- Development of individualized measures incorporating assessments of symptom clusters
• Intervention research to determine if assessment of both symptom occurrence and distress may lead to improved symptom control than only assessment of symptom occurrence or standard care.

• Intervention research aiming to prevent symptom distress through early assessment of symptoms that may be strongly associated with distress for the individual.
This thesis was carried out at the former Department of Nursing and at the Division of Nursing, Department of Neurobiology, Care Sciences and Society.

I would like to express my sincere gratitude to everyone who has contributed to this thesis by sharing their experiences and knowledge with me and by encouraging and supporting me when completing this work.

My special thanks to:

All the patients and their families for generously sharing your thoughts and experiences.

All the nurses at the departments of radiotherapy at the Karolinska University Hospital for your contributions to data collection.

Professor Carol Tishelman, my main supervisor, for your friendship, great support, encouragement, knowledge, guidance through the research process, constructive criticism and for believing in my capacity.

Professor Louise von Essen, my co-supervisor, for your encouragement, knowledge and for your questions helping me to understand my own thoughts and writings, especially in the early phases of my doctoral studies.

Professor Mirjam Sprangers, my co-supervisor during the later phase of my doctoral studies, for sharing your profound knowledge with me, for inspiring discussion and for pushing me through the process of finalizing the papers.

The “lung cancer group”, Agneta Wennman-Larsen, Ann Rudman, Carina Lund-Hagelin, Eva Doukkali, Ewa Stenvall, Helena Leveälahti, Kristina Bertilsson and Sonja Sönnert-Husa for sharing your experiences during data collection and afterwards. Malin Lövgren, who joined the project later, and Britt-Marie Bernhardsson, and Ylva Orrevall, who joined the “symptom group” for stimulating and constructive methodological discussions. And Sara Runesdotter for invaluable help and guidance in the field of statistics.

Associate professor Stefan Eriksson, former head of the Department of Nursing and Professor Åke Seiger, head of the Department of Neurobiology, Care Sciences and Society for believing in my capacity and for providing good research conditions.

All fellow PhD students at the Division of Nursing and the Research and Development Unit, Stockholm Sjukhem Foundation for fruitful and constructive discussions in the area of nursing.

My colleagues within the “Cancer Nursing Unit” at the Division of Nursing for your engagement and encouragement.

My colleagues and dear friends, Eva-Lisa Lundgren, Lilian Pohlkamp Turac, Marie Iwarzon, Monica Ekdahl, Barbro Mendel and Gunilla Lilja for sharing the joy in life and for inspiring and providing me with valuable advice and support.
My mother Ingrid and in memory of my father Ove for your love and support throughout life.

My family, Hannes, Sebastian and Pontus for giving me the greatest pleasure in life and to Staffan for sharing your experiences with me and for your true love, support and encouragement.

The research in this thesis was supported by the Swedish Cancer Society, the Swedish Heart-Lung Foundation, the Swedish Research Council, the Swedish Foundation for Health Care Sciences and Allergy Research and the Research Board for Health Care Sciences at Karolinska Institutet.
8 SAMMANFATTNING (IN SWEDISH)

Mot en förståelse för patienters och vårdares bedömningar av symtom och livskvalitet vid lungcancer

Eva Broberger, Institutionen för Neurobiologi, Vårdvetenskap och Samhälle

Lungcancer är förknippad med ett stortantal olika symtom orsakade av såväl sjukdomens fortskridande som behandlingsrelaterade biverkningar. Detta innebär att sjukskötterskor som vårdar patienter med lungcancer ställs inför utmaningen att underlätta för patienter att hantera ett antal olika problem. Vid tolkning av patienters och vårdares bedömningar av symtom och livskvalitet är det viktigt att ta hänsyn till individuella perspektiv, bakomliggande faktorer och erfarenheter.

Det övergripande syftet ned denna avhandling var att få en ytterligare förståelse för olika aspekter som kan påverka de bedömningar av symtom och livskvalitet som görs av patienter med inoperabel lungcancer och deras professionella och informella vårdare. Fokus var på symtomkaraktäristika, förändringar över tid avseende patientens interna mätnormer och prioriteringar samt mätmetoder. Specifika syften var att 1) undersöka om det förekommer skillnader mellan patienters och vårdares bedömningar avseende symtom förekomst och symtombesvär, 2) undersöka patienters förändringar i interna mätnormer med avseende på fysisk förmåga, orkeslöshet och övergripande livskvalitet, 3) prospektivt och retrospektivt undersöka förändringar över tid angående vilka problem som patienter spontant anger som mest besvärande, 4) undersöka i vilken utsträckning dessa spontant angivna problem kan bedömas via ett standardiserat cancerspecifikt frågeformulär och 5) undersöka relationen mellan symtoms förekomst, intensitet och besvär.

Databasen för de i avhandlingen ingående studierna bestod av prospektiva och retrospektiva bedömningar av symtom och livskvalitet från subgrupper av 400 patienter med inoperable lungcancer som under ett år från diagnos deltog i en longitudinal beskrivande studie avseende symtomupplevelser.

9 REFERENCES

35. Lindqvist, O., Att leva med kroppsliga förändringar vid obotlig cancersjukdom med fokus på prostatacancer; doctoral thesis in Department fo Nursing and Department of Radiation Sciences - Oncology. 2007, Umeå University: Umeå.
93. Michelson, H., Long term health-related quality of life among women with high-risk breast cancer receiving adjuvant high-dose chemotherapy: a comparison with the normal population, in Department of Oncology-Pathology. 2002, Karolinska institutet: Stockholm.
113. Rutledge DN; McGuire, C., Evidence-based symptom management, in Cancer symptom management, C.F. Yarbro, MH; Goodman, C, Editor. 2004, Jones and Bartlett: Boston, MA.


