# SYMPTOM CLUSTERS AND THEIR INFLUENCES ON THE FUNCTIONAL STATUS IN ADVANCED LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY

**THIDARAT KHAMBOON**

**A THESIS SUBMITTED IN PARTIAL FULFILLMENT**
**OF THE REQUIREMENTS FOR**
**THE DEGREE OF DOCTOR OF PHILOSOPHY (NURSING)**
**FACULTY OF GRADUATE STUDIES**
**MAHIDOL UNIVERSITY**
**2014**

Thesis
entitled

# SYMPTOM CLUSTERS AND THEIR INFLUENCES ON THE FUNCTIONAL STATUS IN ADVANCED LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY

THIDARAT KHAMBOON
.....
Miss Thidarat Khamboon
Candidate

K. Pongthavornkamol
.....
Assoc. Prof. Kanaungnit
Pongthavornkamol,
Ph.D. (Nursing)
Major advisor

Karin Olson
.....
Prof. Karin Olson,
Ph.D. (Educational Psychology)
Co-advisor

Doungrut Wattanakitkrileart
.....
Asst. Prof. Doungrut Wattanakitkrileart,
D.N.S.
Co-advisor

Chukiat Viwatwongkasem
.....
Assoc. Prof. Chukiat Viwatwongkasem,
Ph.D. (Statistics)
Co-advisor

W. Lausoontornsiri
.....
Mr. Wirote Lausoontornsiri,
M.D.
Co-advisor

B. Mahaisavariya
.....
Prof. Banchong Mahaisavariya,
M.D., Dip Thai Board of Orthopedics
Dean
Faculty of Graduate Studies
Mahidol University

Yajai Sitthimongkol
.....
Assoc. Prof. Yajai Sitthimongkol,
Ph.D. (Nursing)
Program Director
Doctor of Philosophy in Nursing
Faculty of Nursing
Mahidol University

Thesis
entitled

# SYMPTOM CLUSTERS AND THEIR INFLUENCES ON THE FUNCTIONAL STATUS IN ADVANCED LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY

was submitted to the Faculty of Graduate Studies, Mahidol University
for the degree of Doctor of Philosophy (Nursing)
on
December 24, 2014

THIDARAT KHAMBOON
.....
Miss Thidarat Khamboon
Candidate

.....
Assoc. Prof. Sureeporn Thanasilp,
D.N.S.
Member

Somchit Hanucharurnkul
.....
Emeritus Prof. Somchit Hanucharurnkul,
Ph.D. (Nursing)
Chair

Chukiat Viwatwongkasem
.....
Assoc. Prof. Chukiat Viwatwongkasem,
Ph.D. (Statistics)
Member

K. Pongthavornkamol
.....
Assoc. Prof. Kanaungnit
Pongthavornkamol,
Ph.D. (Nursing)
Member

.....
Mr. Wirote Lausoontornsiri,
M.D.
Member

Karin Olson
.....
Prof. Karin Olson,
Ph.D. (Educational Psychology)
Member

Doungrut Wattanakitkrileart
.....
Asst. Prof. Doungrut Wattanakitkrileart,
D.N.S.
Member

.....
Prof. Winit Phuapraditt,
M.D., M.P.H.
Dean
Faculty of Medicine, Ramathibodi
Hospital
Mahidol University

B. Mahaisavariya
.....
Prof. Banchong Mahaisavariya,
M.D., Dip Thai Board of Orthopedics
Dean
Faculty of Graduate Studies
Mahidol University

Fongcum Tilokskulchai
.....
Assoc. Prof. Fongcum Tilokskulchai,
Ph.D. (Nursing)
Dean
Faculty of Nursing
Mahidol University

# ACKNOWLEDGEMENTS

The achievement of this dissertation would not have been possible by a single effort of me. I would like to express my sincere appreciation and gratitude to those who always supported me throughout my doctoral studies. My most earnest acknowledgement express to my major advisor, Assoc. Prof. Dr. Kanaungnit Pongthavornkamol for her generosity, guidance, valuable counsel, kindly support, encouragement, and providing endless consultant throughout the coursework and in dissertation process. My words cannot express all of my grateful to her.

I would like to express my deep gratitude to Prof. Dr. Karin Olson, my co-advisor at University of Alberta, Canada for her thoughtful suggesting, valuable guidance, comments, and enthusiastic work with me on developing dissertation proposal during my study in Canada. I would like to extend my sincere thanks and appreciation to the members of my dissertation committee, Asst. Prof. Dr. Doungrut Wattanakitkrileart, Dr. Wirote Lausoontornsiri, Dr. Nopadol Soparattanapaisarn for their valuable and creative suggestions and Assoc. Prof. Dr. Chukiat Viwatwongkasem for his intellectual guidance in data analysis. I am also especially grateful to Prof. Emeritus Dr.Somchit Hanucharurnkul, chair of my dissertation defense for her supporting, guiding, and Assoc. Prof. Dr. Sureeporn Thanasilp my external examiner, for her time to read my study thoroughly, particularly her valuable comments. They have generously given their time and expertise to better my work.

My thanks also go to the head and staff nurses at the Chemotherapy and Blood Transfusion Unit of Siriraj Hospital and the National Cancer Institute of Thailand for their supporting and for serving as a resource person and consultant for my research.

My deepest gratitude goes to my wonderful family, my parents for their greatest love and support. I wish to thank all my friends, and Ph.D. nursing students' batch 9, my doctoral classmates, for their experience and information sharing, friendship, and support.

Finally, I wish to my best wishes, and sincere appreciation to all cancer patients and their families who participated in this study for their willingness to share information. Without their cooperation, this study could not have been successful. It is my sincere hope that they, and other cancer patients in the future, benefit from my research.

Thidarat Khamboon

SYMPTOM CLUSTERS AND THEIR INFLUENCES ON THE FUNCTIONAL STATUS IN ADVANCED LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY

THIDARAT KHAMBOON 5237818 NRNS/D

Ph.D. (NURSING)

THESIS ADVISORY COMMITTEE: KANAUNGNIT PONGTHAVORNKAMOL, Ph.D., KARIN OLSON, Ph.D., CHUKIAT VIWATWONGASEM, Ph.D., DOUNGRUT WATTANAKITKRILEART, Ph.D., WIROTE LAUSOONTORNSIRI, M.D.

ABSTRACT

This study explores symptom experiences, symptom clusters, and their influences on the functional status, as well as to determine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experiences differed in their functional status. The theory of Unpleasant Symptom was used to guide this study. Three hundred patients with advanced lung cancer receiving chemotherapy at a super-tertiary care university hospital in Bangkok and the National Cancer Institute of Thailand were purposively selected. Three questionnaires were used: a demographic questionnaire, the Memorial Symptom Assessment Scale (MSAS), and the Inventory of Functional Status-Cancer (IFS-CA). Descriptive statistics were used to describe symptom experiences. Factor analysis and multiple regressions were used to identify symptom clusters and their synergistic effects on the functional status of the patients. Cluster analysis and independent sample t-test were used to determine whether patients in different subgroups differed in their functional status.

The results showed that the patients with advanced lung cancer experienced multiple symptoms concurrently with an average of 13.95 symptoms. Lack of appetite was rated as the most prevalent symptom. Problems with urination was rated as the most frequent symptom. Lack of appetite was rated as the most severe symptom, and constipation was rated as the most distressing symptom. Symptom clusters existed differently across symptom dimensions. Five symptom clusters existing in both symptom severity and distress dimensions explained 42.53% and 43.69% of variance in symptom severity and symptom distress dimensions, respectively. The factor scores of all five symptom clusters of symptom severity and symptom distress together significantly explained 12.6% and 10.3% of the variance in the functional status, respectively ($P<0.05$). The ‘Respiratory-related sleep disturbance symptoms cluster’ was the strongest key cluster affecting the functional status in symptom severity. The ‘Anorexia-related symptoms cluster’ was the strongest key cluster affecting the functional status in symptom distress. Patients in the ‘high-symptom burden group’ had greater symptom prevalence, severity, and distress, but poorer functional status compared to the ‘low-symptom burden group’.

The implications of this study can help nurses and other health care providers better understand multiple symptom experiences in advanced lung cancer patients receiving chemotherapy and plan to target specific symptom management interventions to each subgroup which can reduce symptoms. Future research needs to consider the use of a longitudinal design to identify symptom patterns and testing an intervention program developed for managing symptom clusters experienced by advanced lung cancer patients receiving chemotherapy.

KEY WORDS: SYMPTOM EXPERIENCE / SYMPTOM CLUSTER / FUNCTIONAL STATUS / LUNG CANCER / CHEMOTHERAPY

188 pages

กลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด
SYMPTOM CLUSTERS AND THEIR INFLUENCES ON THE FUNCTIONAL STATUS IN ADVANCED LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY

ธิดารัตน์ คำบุญ 5237818 NRNS/D

ปร.ด. (การพยาบาล)

คณะกรรมการที่ปรึกษาวิทยานิพนธ์: คนึงนิจ พงศ์ถาวรกมล, Ph.D., KARIN OLSON, Ph.D., ชูเกียรติ วิวัฒน์วงศ์เกษม, Ph.D., ดวงรัตน์ วัฒนกิจไกรเลิศ, Ph.D., วิโรจน์ เหล่าสุนทรศิริ, M.D.

บทคัดย่อ

การวิจัยนี้มีวัตถุประสงค์เพื่อศึกษาประสบการณ์การมีอาการ โครงสร้างของกลุ่มอาการ และอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรม รวมทั้งศึกษาว่าผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัดที่ถูกจำแนกอยู่ต่างกลุ่มกันมีการปฏิบัติกิจกรรมแตกต่างกันหรือไม่ โดยใช้กรอบแนวคิดอาการที่ไม่พึงประสงค์ของเลนซ์และคณะ (Lenz, 1997) กลุ่มตัวอย่างเป็นผู้ป่วยมะเร็งปอดระยะลุกลามจำนวน 300 คน ที่มารับยาเคมีบำบัดที่โรงพยาบาลมหาวิทยาลัยระดับตติยภูมิ 1 แห่งในกรุงเทพมหานครและสถาบันมะเร็งแห่งชาติ ประเทศไทย และมีคุณสมบัติตามเกณฑ์ที่กำหนด เครื่องมือที่ใช้ได้แก่ แบบบันทึกข้อมูลส่วนบุคคล แบบประเมินอาการจากโรคและการรักษา และแบบสอบถามเพื่อประเมินการปฏิบัติกิจกรรม วิเคราะห์ข้อมูลโดยใช้สถิติบรรยายการศึกษาประสบการณ์การมีอาการ สถิติการวิเคราะห์ปัจจัยและการวิเคราะห์ความถดถอยเชิงพหุในการศึกษาองค์ประกอบของกลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรม จำแนกกลุ่มตัวอย่างด้วยเทคนิคการวิเคราะห์กลุ่ม และทดสอบความแตกต่างค่าเฉลี่ยการปฏิบัติกิจกรรมของกลุ่มตัวอย่างที่ถูกจำแนกอยู่ต่างกลุ่มกัน

ผลการศึกษาพบว่าผู้ป่วยมะเร็งปอดระยะลุกลามเกิดอาการหลายอาการร่วมกันโดยเฉลี่ย 13.92 อาการ อาการไม่อยากอาหารพบมากที่สุด อาการมีปัญหาเวลาปัสสาวะพบมีความถี่ในการเกิดบ่อยครั้งที่สุด อาการไม่อยากอาหารมีความรุนแรงมากที่สุด และอาการท้องผูกเป็นอาการที่ทุกข์ทรมานมากที่สุด กลุ่มอาการในมิติความรุนแรงและมิติความทุกข์ทรมานมีความแตกต่างกัน ในการวิเคราะห์จัดกลุ่มอาการทั้งในมิติความรุนแรงและมิติความทุกข์ทรมานสามารถจำแนกได้ 5 กลุ่มโดยอธิบายความแปรปรวนของอาการทั้งหมดได้ร้อยละ 42.53 ในมิติความรุนแรง และ ร้อยละ 43.69 ในมิติความทุกข์ทรมาน ทั้งกลุ่มอาการในมิติความรุนแรงและมิติความทุกข์ทรมานมีอิทธิพลต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลาม กลุ่มอาการสามารถอธิบายความแปรปรวนของการปฏิบัติกิจกรรมทั้งหมดอย่างมีนัยสำคัญทางสถิติได้ร้อยละ 12.6 ในมิติด้านความรุนแรง และ ร้อยละ 10.3 ในมิติด้านความทุกข์ทรมาน ($P<0.05$) กลุ่มอาการด้านการหายใจที่เกี่ยวข้องการนอนหลับ มีอิทธิพลต่อการปฏิบัติกิจกรรมมากที่สุดในมิติความรุนแรง กลุ่มอาการเบื่ออาหารที่เกี่ยวข้องกับอาการอื่นๆ มีอิทธิพลต่อการปฏิบัติกิจกรรมมากที่สุดในมิติความทุกข์ทรมาน ผู้ป่วยที่ถูกจำแนกอยู่ในกลุ่ม ความรุนแรงอาการสูง พบว่ามีจำนวนอาการที่เผชิญ ความรุนแรงของอาการและความทุกข์ทรมานจากอาการมากกว่า และมีคะแนนการปฏิบัติกิจกรรมน้อยกว่า เมื่อเปรียบเทียบกับผู้ป่วยที่อยู่ในกลุ่ม ความรุนแรงอาการต่ำ

ผลการศึกษาเป็นประโยชน์ต่อพยาบาลและบุคลากรทีมสุขภาพอื่นๆ ให้มีความเข้าใจแบบแผนของกลุ่มอาการที่เกิดขึ้นในผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด และนำไปใช้ในการวางแผนพัฒนาโปรแกรมการจัดการ ที่เฉพาะเจาะจงกับแต่ละกลุ่มอาการ เพื่อลดความรุนแรงของอาการ สำหรับงานวิจัยต่อไปในอนาคตควรมุ่งไปยังการศึกษาประสบการณ์การเผชิญอาการในระยะยาว รวมทั้งพัฒนาโปรแกรมและทดสอบประสิทธิผลของโปรแกรมในการจัดการกับกลุ่มอาการในผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับเคมีบำบัดต่อไป

188 หน้า

# CONTENTS


| | Page |
|---|---|
| **ACKNOWLEDGEMENTS** | **iii** |
| **ABSTRACT (ENGLISH)** | **iv** |
| **ABSTRACT (THAI)** | **v** |
| **LIST OF TABLES** | **ix** |
| **LIST OF FIGURES** | **xii** |
| **CHAPTER I INTRODUCTION** | |
| Background and Significance of the Study | 1 |
| Research Questions | 5 |
| Proposes of this Study | 6 |
| Conceptual Framework | 6 |
| Research Framework | 10 |
| Scope of the Study | 11 |
| Definition of Terms | 12 |
| Expected Outcomes and Benefits | 14 |
| **CHAPTER II LITERATURE REVIEW** | **16** |
| Lung Cancer and Treatments | 17 |
| Symptom Associated with Chemotherapy in Advanced Lung Cancer Patients | 21 |
| Symptom Experiences Based on Theory of Unpleasant Symptoms | 29 |
| Performance Outcome: Functional Status | 45 |
| Gaps in Knowledge | 54 |
| **CHAPTER III MATERIALS AND METHODS** | **58** |
| Research Desigh | 58 |
| Population and Samplings | 58 |
| Settings | 59 |
| Instruments | 60 |

# CONTENTS (cont.)


| | Page |
|---|---|
| Protection of Human Rights | 63 |
| Data Collection Procedures | 64 |
| Data Analysis | 65 |
| **CHAPTER IV RESULTS** | **69** |
| Demographic and Clinical Characteristics of the Participants | 69 |
| Symptom Experiences and Symptom Cluster a cross Dimension | 72 |
| Functional Status and the Influence of Symptom Cluster on the Functional Status Symptom Cluster across Dimension | 83 |
| Determine Lung Cancer Patients with Different Groups by Symptoms Experience and Functional Status | 96 |
| Summary of the Results in this Chapter | 97 |
| **CHAPTER V DISCUSSION** | **99** |
| Participants' Characteristics | 99 |
| Symptom Experiences of Advanced Lung Cancer Patients Receiving Chemotherapy | 100 |
| Symptom Clusters based on Symptom Severity Dimension | 106 |
| Symptom Clusters based on Symptom Distress Dimension | 110 |
| Symptom Clusters across Symptom Dimensions | 113 |
| Functional Status among Advanced Lung Cancer Receiving Chemotherapy | 114 |
| The Influences of Symptoms Cluster on Functional status in Advanced Lung Cancer Receiving Chemotherapy | 116 |
| Patient Subgroup Differences in Symptoms experience and Functional Status | 121 |
| Strengths and Limitations of the Study | 123 |

# CONTENTS (cont.)


| | | Page |
|---|---|---|
| **CHAPTER VI CONCLUSIONS** | | **126** |
| Summary of the Study | | 126 |
| Implications to Nursing Practice | | 129 |
| Implication to Nursing Science | | 130 |
| Recommendations for Future Research | | 130 |
| **REFERENCES** | | **132** |
| **APPENDICES** | | **149** |
| Appendix A | Documentary Proof for Ethical Clearance on Human Rights | 150 |
| Appendix B | Participant Information and Consent Form | 158 |
| Appendix C | Instruments | 163 |
| Appendix D | Additional Results | 185 |
| **BIOGRAPHY** | | **188** |

# LIST OF TABLES


| Table | | Page |
|---|---|---|
| 2.1 | The number system for lung cancer staging | 20 |
| 3.1 | Reliability tests of the MSAS in a pilot study and the main study | 62 |
| 3.2 | Reliability tests of the IFS-CA in a pilot study and the main study | 63 |
| 4.1 | Demographic characteristics of the participants | 70 |
| 4.2 | Clinical characteristics of the participants | 71 |
| 4.3 | Descriptions of symptom prevalence | 73 |
| 4.4 | Descriptions of symptom frequency | 74 |
| 4.5 | Descriptions of symptom severity | 75 |
| 4.6 | Descriptions of symptom distress | 76 |
| 4.7 | Exploratory factor analysis of symptom severity | 78 |
| 4.8 | Exploratory factor analysis of symptom distress | 79 |
| 4.9 | The similarities and dissimilarities clustering of symptoms across | 81 |
| 4.10 | Functional scores categorized by groups of activities | 84 |
| 4.11 | Summary of multiple regression analysis of symptom clusters of symptom severity affecting functional status analyzed by using factor scores | |
| 4.12 | Models of multiple regression of Emotional-elimination discomfort symptoms cluster affecting functional status analyzed by using symptom severity scores | 85 |
| 4.13 | Models of multiple regression of Anorexia-related symptoms cluster affecting functional status analyzed by using symptom severity scores | 86 |

# LIST OF TABLES (cont.)


| Table | | Page |
|---|---|---|
| 4.14 | Models of multiple regression of Treatment-related gastrointestinal and other symptoms cluster of symptom severity affecting on functional status by using symptom severity scores | 87 |
| 4.15 | Models of multiple regression of Neuropsychological and body image symptoms cluster affecting on functional status by using symptom severity scores | 87 |
| 4.16 | Models of multiple regression of Respiratory and sleep disturbance symptoms cluster affecting on functional status by using symptom severity scores | 88 |
| 4.17 | Summary of multiple regression analysis of symptom clusters of symptom distress affecting on functional status by using factor score | 89 |
| 4.18 | Models of multiple regression of Emotional-elimination discomfort symptoms cluster affecting on functional status by using symptom distress score | 90 |
| 4.19 | Models of multiple regression of Body image symptoms cluster affecting on functional status by using symptom distress score | 91 |
| 4.20 | Models of multiple regression of Anorexia-related symptoms cluster affecting on functional status by using symptom distress score | 92 |
| 4.21 | Models of multiple regression of Treatment-related gastrointestinal and other symptoms cluster affecting on functional status by using symptom distress score | 92 |
| 4.22 | Models of multiple regression of Treatment-related neurological and other symptoms cluster and functional scores affecting on functional status by using symptom distress score | 93 |

# LIST OF TABLES (cont.)


| Table | | Page |
|---|---|---|
| 4.23 | The comparison of symptom clusters across symptom dimensions between symptoms clusters of symptom severity and symptom distress affecting on functional status. | 94 |
| 4.24 | The comparisons of mean symptom experience scores and functional status by patient subgroup | 97 |

# LIST OF FIGURES


| Figure | | Page |
|---|---|---|
| 1.1 | The conceptual framework of this study: Theory of Unpleasant Symptom | 8 |
| 1.2 | The research framework of this study guided by the Theory of Unpleasant Symptoms | 11 |

# CHAPTER I
# INTRODUCTION

## Background and Significance of the Study

Lung cancer is a common malignant disease globally including Thailand. Lung cancer is the second most common cancer found in Thai men (15.5%) and the fourth most common cancer that found in women (6.5%) (National Cancer Institute of Thailand, 2011). Most lung cancer patients are diagnosed when their cancer is already in advanced stage which accounts for low survival rate (Blackhall, Shepherd, & Albain, 2005; Porter, Keefe, Garst, McBride, & Baucom, 2008). Two major types of lung cancer are small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Roughly 75-80% of lung cancer patients are diagnosed with NSCLC while SCLC accounts for the remaining 20-25% of cases (DeVita Jr, Weinberg, DePinho, & Lawrence, 2008).

Chemotherapy is the principal treatments for lung cancer. The goal of chemotherapy is to destroy cancer cells along with micro-metastases in patients with lung cancer. However, chemotherapy causes side effects and toxicities, which have profound secondary effects on patients' emotional, social, physical and spiritual well-being (Fan, Filipczak, & Chow, 2007; Thompson & Subirana, 2005).

Patients with lung cancer frequently suffer from various symptoms resulting both from the primary disease itself, as well as from its treatment (Wang, Tsai, Chen, Lin, & Lin, 2008). There are several common signs and symptoms associated with lung cancer. The symptom distress of patients with cancer is rooted in the tumor and in the side effects of the treatment. Symptoms associated with lung cancer include cough, dyspnea (distress with breathing or breathing discomfort), hemoptysis (coughing up blood), and chest discomfort. Some individuals also have weight-loss or fatigue. Patients with lung cancer often seek medical attention for symptom distress, such as difficulty in breathing, increased sputum, or hemoptysis (Beckles, Spiro, Colice, & Rudd, 2003). "Difficulty in breathing" is one of the

symptoms that most troubles patients with lung cancer. This symptom is inextricably linked with fatigue and often occurs in tandem with coughing, chest pain, wheezing, and insomnia (Nowack, 1989; Ryan, 1987). Because their tumors involve the blood vessels to the lungs, patients with lung cancer often experience hemoptysis, metastasis to the bones causing pain, and metastasis to the brain and pressure on nerves causing neurogenic symptoms (Muers & Round, 1993). Consequently, emotional distress may be high (Beckles et al., 2003). Many previous studies have noted that lung cancer patients experience more symptom distress than patients with different sorts of cancer (Cooley, Short, & Moriarty, 2003; Tishelman et al., 2005).

Previous research revealed that lung cancer patients often experience several symptoms simultaneously (Chan, Richardson, & Richardson, 2005; Fox & Lyon, 2006; Henoch, Ploner, & Tishelman, 2009; Tishelman et al., 2005; Wang, Tsai, Chen, Lin, & Lin, 2008; Malangpoothong, Pongthavornkamol, Sriyuktasuth & Soparattanapaisarn, 2009). For example, Sarna (1993a) found that the symptoms of fatigue, pain, and sleepless tended to happen together in lung cancer patients.

The presence of numerous symptoms happening together, known as a symptom cluster, is concerning because simultaneous symptoms may impact each other and thus increase the overall level of symptom severity (Cleeland & Reyes-Gibby, 2002). Statistically, relationships among symptoms within a cluster are stronger than relationships with other symptoms that are not in a cluster (Kim, McGuire, Tulman, & Barsevick, 2005). Some authors describe symptom clusters as groups of stable symptoms that are relatively independent of other symptoms (Kim et al., 2005). The idea that symptoms are stable is interesting, but is incongruent with our clinical observations which suggest that the intensity of any given symptom may vary widely over the course of a shift, depending on treatment and state of disease, and that the relationships among symptoms change over time.

Theories about symptom clutters have been evolving. The theory of unpleasant symptoms (TOUS) has been used regularly in guiding symptom cluster research (Chan et al., 2005; Fox, Lyon, & Farace, 2007; Hoffman, Given, Eye, Gift, & Given, 2007). TOUS is particularly valuable as a middle-range theory because it highlights symptom experience and potential starategies for symptom management that are not addressed by more symptom-specific models (Lenz & Pugh, 2003). It

proposes an approach to integrate information about the complexity of the symptom experience (Cooley, 2000). In addition, TOUS goes beyound symptom specific concepts and theories to stimulate considering about common factors that numerous impact more than one symptom (Lenz & Pugh, 2003). TOUS has three main reciprocal components: symptom appraisal, influential factors (may be physiologic, psychologic, or situational), and performance (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). According to the theory, symptom appraisal has four dimensions: intensity, timing, level of distress perceived, and quality. Performance is the consequence of the interaction between symptom appraisal and influential factors, and includes both functional and cognitive dimensions.

The impact of symptom clusters on patient outcomes has become a nursing concern and is consistent with the performance component of TOUS. Some authors have found synergistic effects between symptom clusters and functional status in oncology patients (Chen & Tseng, 2006; Dodd et al., 2001a), and have also noted that symptom clusters predicted morbidity in patients with lung cancer (Gift, Jablonski, Stommel, & Given, 2004). Several researchers have reported that cancer patients experience severe symptom distress caused by a composite of symptoms, which has a strong negative effect on patient physical functioning (Cooley, 2000; Gift, Stommel, Jablonski, & Given, 2003; Tishelman et al., 2005). Lung cancer patients are more severely limited in functional status when compared with other cancer patients (Margot Kurtz, Kurtz, Stommel, Given, & Given, 1999; Sarna, 1993). Gift and colleagues (2004) found that a cluster comprised fatigue, dyspnea, weakness, vomiting, and pain was significantly related to physical function and role restrictions in a group of patients with lung cancer.

There have been some studies of symptom clusters in Thai cancer patients (Suwisith et al., 2008; Phligbua et al., 2013) studied symptom clusters in Thai women with breast cancer and Chaiviboontham et al (2011) studied symptom clusters in a sample of Thai individuals with advanced cancer including cancers of the gastro-intestinal tract, the breast, the hepato-biliary system, and lungs. Pudthong and team (2014) studied symptom cluster in lung cancer patients. However, there has been no studies that focused solely on of symptom clusters and their impact on patient outcomes in Thai patients with lung cancer. The result of symptom clusters studies in

other cancers or in studies that used heterogeneous samples cannot be generalized to patients with lung cancer, since different types of cancer have different signs, symptoms, treatments, and outcomes.

Any study of symptom clusters is complicated by several issues. First, the concept of symptom cluster has been proposed and created from studies inside the setting of western culture, but there is some evidence that the meaning of symptoms is socially constructed and thus it is important to consider the impact that this might have on the meaning and management of symptom clusters in other contexts (Pongthavornkamol, 2000). More clarity is needed about the minimum number of symptoms constituting a cluster, and criteria to use to evaluate the relationship between and among the symptoms (Beck, 2004; Miaskowski, Aouizerat, Dodd, & Cooper, 2007; Xiao, 2010). Second, there is limited knowledge of the methodological decision for symptom cluster research that may have important implications for research findings. For examples, a variety of symptom assessment tools exist, enabling the assessment of variation in individual symptoms, common to specific diagnoses and treatments (Beck, 2004; Miaskowski, Dodd, & Lee, 2004). As Miaskowski and team (2004) noted, symptoms are multidimensional. The number and types of symptom clusters need to be compared based on whether the symptom clusters are determined using different ratings of symptom dimensions (Miaskowski, Dodd, & Lee, 2004). Therefore, determination of symptom clusters using different dimensions is needed. This study explored the clusters of symptom severity and symptom distress dimensions. Symptom prevalence or occurrence was inappropriate to support the method of analysis as its measuring scale is nominal and dichotomous. Symptom frequency, there were some symptoms that can persist for a long period of time and the pattern of their occurrences might not be observed for a short period of time. Symptom prevalence and symptom frequency were not selected to analyze in this study. In addition, qualitative research with a variety of patient populations is often valuable in describing the quality of the symptom experience. Therefore, the quality dimension was not explored in this study.

To date, one focus of symptom cluster research has been on cluster symptoms, usually through the administration of a comprehensive symptom inventory and subsequent factor analysis of the inventory (Gift et al., 2004). An equally valuable

approach for symptom cluster research would be to cluster patients based on the intensity of symptoms reported for an a priori identified symptom cluster. The approach may allow for the identification of subgroups of patients who experience multiple symptoms with greater or lesser severity and who may be at risk for poorer outcome. Grouping individuals based on their symptom experience has occurred in a few studies of oncology patients (Dodd, Cho, Cooper, & Miaskowski, 2010; Ferreira et al., 2008; Gwede, Small, Munster, Andrykowski, & Jacobsen, 2008; Pud et al., 2008). To date, no published study identifying distinct subgroups of lung cancer patients who differed on symptom experience during chemotherapy treatment. The finding can guide treatment/management of disease- or treatment related symptoms through interventions tailored to individuals in each group (Gwede et al., 2008). The result will allow clinicians to target specific symptom management interventions to each subgroup.

To fill the gaps of knowledge in this area as previously mentioned, this study aims to; 1) describe symptom experiences in all dimensions, 2) explore the existence of symptom clusters in severity and distress dimensions, 3) compare the similarity of symptom cluster classified by severity and distress 4) determine the influences of symptom cluster on the functional status, and 5) determine whether subgroups of advanced lung cancer patients with different symptom experiences differ in their functional status. The results of this study may help understanding the underlying mechanism of the symptoms. Moreover, an understanding of symptom clusters would also provide new avenues for interventions to minimize the impact of symptoms on health-related outcomes.

## Research questions

The research questions of this study addressed were:

1. What are the characteristics of symptoms experienced by patients with advanced lung cancer receiving chemotherapy?

2. What are the symptom clusters in severity and distress dimensions experienced by patients with advanced lung cancer receiving chemotherapy?

3. Do symptom clusters exist differently across symptom dimensions?

4. Do the symptom clusters influence the functional status in advanced lung cancer patients receiving chemotherapy?

5. Do subgroups of advanced lung cancer patients receiving chemotherapy with different symptoms experience differed in their functional status?

## Purposes of this Study

The aims of this study addressed are to:

1. To describe symptom experiences in advanced lung cancer patients receiving chemotherapy.

2. To explore the existence of symptom clusters in advanced lung cancer patients receiving chemotherapy.

3. To compare the similarity of symptom cluster classified by severity and distress

4. To determine the influences of symptom cluster on the functional status in advanced lung cancer patients receiving chemotherapy.

5. To determine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experience differed in their functional status.

## Conceptual Framework

The Theory of Unpleasant Symptoms (TOUS) was utilized as a conceptual framework to guide this study. This middle-range theory was developed by nurse researchers in 1995 (Lenz, Suppe, Gift, Pugh, & Milligan, 1995). The theory of unpleasant symptoms (TOUS) was intended to integrate existing knowledge about a variety of symptoms. The model is based on the premise that there are commonalities across different symptoms experienced by a variety of clinical populations in varied situations. The assumption behind the theory is that there are sufficient commonalities among symptoms to warrant a theory that is not limited to one symptom, but can explain and guide research about symptoms. For example, the theory of unpleasant symptoms attempts to achieve parsimony by proposing that some of the same factors

may influence the experience of a number of different symptoms; consequently, similar interventions may be effective in alleviating more than one symptom (Lenz et al., 1997). The purpose of the theory is to improve understanding of the symptom experience in various contexts and to provide information useful for designing effective means to prevent, ameliorate, or manage unpleasant symptoms and their negative effects.

Its publication and more general exposure also pointed out some weaknesses of the theory as well as some aspects that were unclear. As a result, the authors continued to work on refining it, and an updated, improved version was subsequently published (Lenz et al., 1997). The original model of the TOUS considered only isolated symptoms and did not describe interactive or feedback effects between the influencing factors, the symptoms in their various dimensions, and performance.

The revised version of the TOUS (Lenz et al., 1997) include multiple symptoms, interactive effects between symptoms; interaction between the influencing factors; the impact of influencing factors on the symptoms; reciprocal or feedback influences of performance, and feedback influences of symptoms on influencing factors. The TOUS comprised three main components: 1) the symptoms that the individual is experiencing. Each symptom has four dimensions: intensity (strength or severity of the symptom), timing (duration and frequency of occurrence), distress (level of distress perceived, degree of discomfort or bothersome), and quality (the patient's description of what the symptom feels like). 2) Factors influencing symptoms include physiological, psychological, and situational antecedents. The influencing factors that give rise to or affect the nature of the symptom experience. 3) Performance is the consequence of the symptom experience, which includes functional and cognitive activities.

The TOUS hypothesizes that when patients experience more than one symptom, the symptom experiences are related to one another. The relationship can be an interactive one, even multiplicative. The influencing factors are assumed to impact the nature of the symptom experience, which, in turn, impact performance. Three categories of influencing factors are hypothesized to influence one another, and to influence symptom experience. However, symptom experience can also change the

patient's psychological, physiological, or situational factor. The symptom experience can serve as a mediating variable between influencing factors and performance. Performance can also have a feedback effect on the physiologic, psychologic, and situational factors (Lenz & Pugh, 2003).

The overall structure of the theory, which is portrayed in Figure 1.1, asserts that three interrelated categories of factors (physiologic, psychologic, and situational) influence predisposition to and manifestation of a given symptom or multiple symptoms and the nature of the symptom experience. The symptom experience, in turn, affects the individual's performance, which encompasses cognitive, physical, and social functioning. The performance outcomes can feed back to influence the symptom experience itself as well as to modify the influencing factors. This model provides a theoretical framework for research on symptom clusters by indicating effects of concurrent symptoms (Xiao, 2010). A framework that highlights common elements and dimensions has potential to be useful in both nursing practice and research.

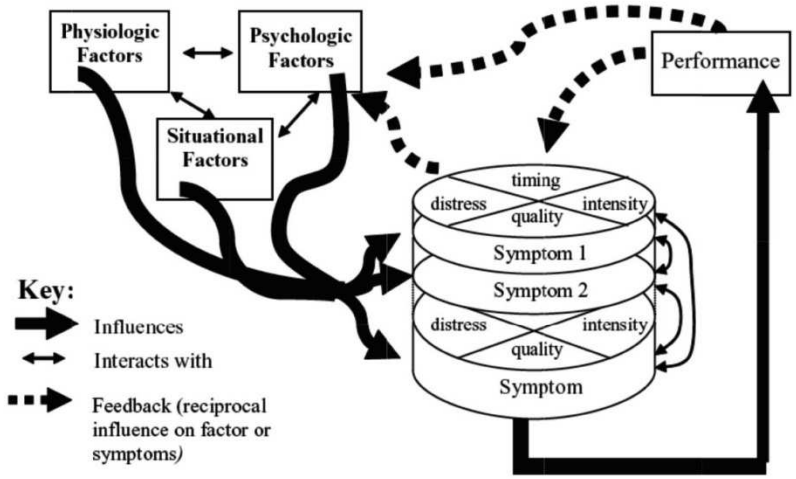



**Figure 1.1** Theory of Unpleasant symptoms (Lenz & Pugh, 2003)

### Critique of the Theory of Unpleasant Symptoms (TOUS)

The Theory of Unpleasant Symptom emphasizes the interplay among influential factors, symptoms, and performance outcomes. The aim of this theory is to enhance understanding of the symptom experience in different contexts, and the effect

of symptoms on patient outcomes (Lenz & Pugh, 2003). This model gives a hypothetical system to research on symptom clusters by demonstrating multiplicative impacts of numerous simultaneous symptoms (Xiao, 2010). The main changes in the update version of the TOUS include incorporation of multiple symptoms and a charity of interactive impacts including those among different symptoms. Symptoms may happen simultaneously and independently (Lenz et al., 1997). This proposition is compatible with the attribute concurrent of symptoms in a symptom cluster. Moreover, this theory provides a structure for beginning to determine the extent of overlapping among symptoms, and also the dimensions of symptoms or the characteristics of the symptoms in the TOUS (Lenz et al., 1997). Several clinicians have described it as having intuitive appeal because it is relatively straightforward, easy to understand and apply, and focused on relevant concerns (Lenz & Pugh, 2003).

The TOUS has been compared to the Symptom Management Model developed by Dodd and teams (2001). The symptom management model proposed three components; symptom experience, symptom management strategies, and outcomes. Symptom experience defines as a subjective experience indicating changes in the bio-psychosocial performing, feeling, or condition of a person (Dodd et al., 2001). Symptom experience comprises perception, evaluation, and response to symptoms. The symptom management model is offered as a conceptualization to guide selection of management strategies in contrast to a recently published theory of unpleasant symptoms that focuses more on explaining the symptom experience and how it affects function (Dodd et al., 2001b). In addition, the symptom management model does not include an evaluation of multiple symptoms or a depiction of the interactive relationships among symptoms. No illustration is providing of how multiple symptoms could interact.

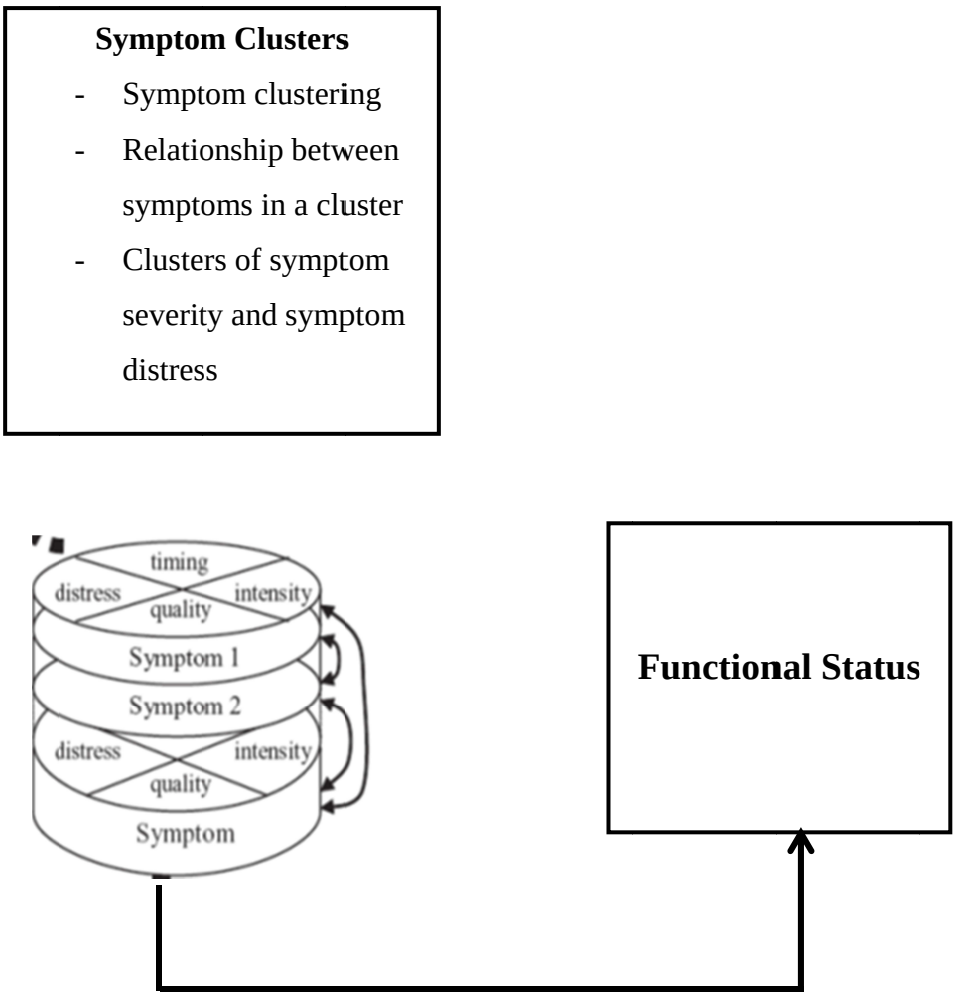
The Theory of Unpleasant Symptom is a parsimonious theory that considers the multiplicity of symptoms that occur simultaneously and interact. The TOUS represents to be a good fit to describe multiple symptom experience, relationships among symptoms as a symptom cluster, and their influence on the performance outcomes. It provided a useful framework for examining the relationships among symptoms (symptom clusters) and their influences on the functional status in advanced lung cancer patients receiving chemotherapy. This theory does not define

the meaning of symptom experience explicitly. However, both of the two theories are some commonality especially includes the part of symptoms experience. The meaning of symptom and symptom experience can be used interchangeably. Therefore, this study uses the meaning of symptom experience that has been defined by Dodd and team (2001) in the Symptom Management Model.

## Research framework of this study

Theory of Unpleasant Symptoms was used to guide formulation of the research questions, and selection of the study variables (Figure 2). This study aimed to explore symptom experiences more specifically on the symptom clusters derived from symptom experiences and their influences on functional status as a performance outcome in advanced lung cancer patients receiving chemotherapy. Lenz and team (1997) specified that the outcome or effect of symptom experience in the TOUS is performance. It represents the consequences of the symptom experience. Performance as conceptualized to include functional and cognitive activities. Functional performance includes physical activity, activities of daily living, social activities and interaction, and role performance including work and other role-related tasks. Cognitive activity includes a concentrating, thinking, and problem-solving (Lenz et al., 1997). The specification of performance as the key outcome of the model reflects a pragmatic orientation as well as a desire for relatively straightforward measurability.

The theory asserts that the experience of symptoms can have an impact on the individual's ability to function. The symptoms can occur together and simultaneously. Each symptom could vary in duration or timing, intensity or severity, distress, and quality. Moreover, multiple symptoms can occur together as a result of a single event, or one symptom can precede another (Lenz et al., 1997). Similarly, advanced lung cancer patients receiving chemotherapy who experienced more numerous or more severe symptoms tend to have lower functional status. The research framework of this study is illustrated in Figure 1.2




**Key:**

→ Influences

↔ Interacts with

**Figure 1.2** The research framework of this study guided by the Theory of Unpleasant Symptoms (Lenz et al., 1997)

## Scope of the Study

This study focuses on symptom clusters and their effects on functional status in advanced lung cancer patients receiving chemotherapy. The populations under study were patients with advanced lung cancer receiving chemotherapy attending at the Chemotherapy and Blood Transfusion Unit of the Out-Patient

Department of Siriraj Hospital in Bangkok and the National Cancer Institute of Thailand as most patients with lung cancer usually access cancer treatment. The study was conducted during May, 2013 to March, 2014.

## Definitions of Terms

**Symptoms experiences:**

*Conceptual definition:* The interplay of an individual's perception of the symptoms or the meaning given to the symptoms and the physiological, cognitive, emotional, or behavioral response to symptoms (The University of California, San Francisco School of Nursing Symptom Management Group, 1994; Dodd et al, 2001b).

*Operational definition:* The perceived of the changes in biopsychosocial functions, sensation or cognition reported by advanced lung cancer patients receiving chemotherapy. In this study using The Memorial Symptom Assessment Scale (MSAS) as assessment to capturing occurrence of symptoms, symptom intensity, symptom frequency, and symptom distress during the past 7 days (Portenoy et al., 1994)

**Symptom prevalence:**

*Conceptual definition:* The changes in an individual in the way person usually feels or behaves, as noticed by that individual. It is conscious cognitive interpretationbbof information gathered by the senses in the context of a particular environment or situation (Dodd, et al., 2001b).

*Operational definition:* The prevalence of symptoms perceived and interpreted by advanced lung cancer patients receiving chemotherapy in the study. The prevalence of symptoms can either occur or not occur. Total numbers of symptoms was summed and used as the empirical referent for the occurrence of symptoms.

**Symptoms frequency:**

*Conceptual definition:* Intermittence of symptom occurrence. The duration of a persistent symptom, a combination of frequency and duration, or the number of times the symptom occurs within a given timeframe (Lenz et al., 1997)

*Operational definition:* The evaluation of advanced lung cancer patients receiving chemotherapy in the study is achieved by assessing how often each symptom occurs within 7 days. The frequency of symptoms was assessed by using MSAS on a 4-point Likert scale from 1 (rarely) to 4 (almost constantly).

**Symptom severity:**

*Conceptual definition:* The dimension that quantifies the degree, strength, severity, or amount of the symptom being experienced (Lenz et al., 1997).

*Operational definition:* The severity of symptoms perceived and interpreted by advanced lung cancer patients receiving chemotherapy in the study. The symptom severity was assessed by using a 5-point response scale from 1(slight) to 4 (very severe) for each symptom listed in The MSAS.

**Symptom distress:**

*Conceptual definition:* Physical or mental anguish or suffering that results from the experience of symptom occurrence and/or the perceptions of feeling stress(Rhodes, Watson, Johnson, Madsen, & Beck, 1987) or distress is the degree to which the individual is bothered by the symptoms (Lenz et al., 1997)

*Operational definition:* Symptom distress is the extent of physical or mental suffering attributed to the symptom experienced by advanced lung cancer patients receiving chemotherapy. Symptom distress was evaluated by using MSAS scaled on a 5-point response scale from 1 (not at all) to 5 (very much).

**Symptom cluster:**

*Conceptual definition:* Symptom cluster refers to two or more concurrent symptoms that are related to one another that occur together, and independent of other symptom clusters. Relationships among symptoms within a cluster should be stronger

than relationships among symptoms across different clusters, and are independent of other symptom clusters or combinations (Kim et al., 2005).

*Operational definition:* Two or more symptoms of frequent and distressing symptom experienced by advanced lung cancer patients receiving chemotherapy in the study that are related to each other and analyzed by using the statistical method of factor analysis.

**Functional status:**

*Conceptual definition:* The individuals' actual performance of activities and tasks associated with their current life roles (Richmond et.al, 2004). Functional status as a multidimensional concept that encompasses continuation of usual household and family, social and community, personal care, and occupational activities following diagnosis of cancer (Tulman, Fawcett, & McEvoy, 1991) .

*Operational definition*: The actual performance of activities and tasks associated with the current life roles of advanced lung cancer patients receiving chemotherapy is measured by using the Inventory Functional Status-Cancer (IFS-CA) developed by Tulman and team (1991). Functional status encompasses the continuation of usual household and family, social and community, personal care, and occupational activities following diagnosis of cancer (Tulman et al., 1991). Using this instrument, individuals are rated from 1 (not at all) to 4 (fully) for household, family, social, and community activities; and 1 (never) to 4 (all of the time) for personal care and occupational activities.

## Expected Outcomes and Benefits

1. The findings obtained from this study may provide health care providers for a better understanding about multiple symptom experiences and their influence on functional status in advanced lung cancer patients receiving chemotherapy.

2. The research findings may provide a scientific basis and new directions for clinical assessment and intervention in advanced lung cancer patients receiving chemotherapy.

3. The finding can be used as a guide for the development of a nursing intervention program in order to more effective symptom management, reduced medication use and enhanced functional status for patients with lung cancer, symptom clustering, in advanced lung cancer patients receiving chemotherapy is needed.

4. The knowledge from this study may be used to guide further research on symptom clusters in order to help advanced lung cancer patients receiving chemotherapy manage effectively with their multiple symptom experiences.

# CHAPTER II

# LITERATURE REVIEW

This study aimed to explore symptom experience, the existence of symptom clusters and their influences on functional status of patients with advanced lung cancer receiving chemotherapy. The review has been organized under the three major concepts of the theory of unpleasant symptoms: symptom/multiple symptoms, and performance outcome (functional status). The review of the literature has presented as follows:

1. Lung cancer and treatments
2. Symptoms associated with chemotherapy in advanced lung cancer patients receiving treatment
    - 2.1 Common symptoms in Lung
    - 2.2 Symptoms associated with chemotherapy treatment in patients with lung cancer
    - 2.3 Symptom assessment
        - 2.3.1 Symptom assessment scales
        - 2.3.2 Symptom measurement issues
3. Symptom experiences based on Theory of unpleasant symptoms (Lenz et al., 1997)
    - 3.1 Symptom dimensions :
        - 3.1.1 Symptom frequency
        - 3.1.2 Symptom severity
        - 3.1.3 Symptom distress
    - 3.2 Multiple symptom experiences as symptom clusters
    - 3.3 Clustering of symptom cluster : approaches to the study of symptom clusters
    - 3.4 Clustering of symptom clusters in lung cancer
4. Performance outcome : Functional status
5. Gaps in knowledge

## Lung Cancer and Treatments

Lung cancer refers to a disease characterized by uncontrolled cell growth in tissues of the lung. Lung cancer begins when cells in the lung change and grow uncontrollably to form a mass called a tumor (or a lesion or nodule). A tumor can be benign (noncancerous) or malignant (cancerous). A cancerous tumor is a collection of a large number of cancer cells that have the ability to spread to other parts of the body in a process (Horn, Pao & Johnson, 2012).

Lung cancer is the major cause of death among cancers. The five-year survival rate for lung cancer cases is less that 15%. In Thailand over the period 1998-2000, lung was the second common cancer in males after liver cancer while it was the fourth common cancer after cervical cancer, breast cancer and liver cancer in females (Martin, 2009).

### Types of Lung Cancer

There are two major types of lung cancer, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

1) Non-small cell lung cancer (NSCLC). These are grouped together because they behave in a similar way and respond to treatment in a different way to small cell lung cancer. Non-small cell lung cancer accounts for about 75-80 percent of lung cancers (DeVita Jr et al., 2008). There are 3 major subtypes of NSCLC.

1.1) Adenocarcinoma develops from the cells that line the airways. It develops from a particular type of cell that produces mucus (phlegm). It is often found in the outer areas of the lungs.

1.2) Squamous cell carcinoma (which is also called epidermoid carcinoma) is the most common type of lung cancer. It develops from the cells that line the airways and it is often found near the center of the lung in one of the main airways (the left or right bronchus). This type of cancer is often due to smoking.

1.3) Large cell carcinomas is a fast-growing form that grows near the surface of the lung.

2) Small-cell lung carcinoma (SCLC). It is also called oat cell carcinoma. Small cell LC tends to start in the larger breathing tubes and progresses rapidly becoming quite large.

In Thailand, adenocarcinoma was the most common type of lung cancer especially in females followed by squamous cell carcinoma and small cell lung carcinoma. For males, squamous cell carcinoma was found more common than adenocarcinoma (Martin, 2009).

**Stage of Lung Cancer**

Staging is based on diagnostic evaluations. Staging involves evaluation of a cancer's size and its penetration into surrounding tissue as well as the presence or absence of metastases in the lymph nodes or other organs. Accurate staging of the disease is an important part of the management as it provides estimation of patient's prognosis and identifies treatment strategies. The American Joint Committee on Cancer (AJCC) as well as the International Union Against Cancer (UICC) recommend TNM staging, which is a two-step procedure. Their TNM system, which they now develop jointly, first classifies cancer by several factors, T for tumor, N for nodes, M for metastasis, and then groups these TNM factors into overall stages. As in each edition of the TNM staging system, that used from 2010 January 1 ($7^{th}$ edition) made significant changes to the schema that is used for non-small cell lung carcinoma, small-cell lung carcinoma and broncho-pulmonarycarcinoid tumors (Detterbeck, Boffa, & Tanoue, 2009). The 2009 TNM system for lung cancer has been revised and follows the tumors staging system below (Mirsadraee, Oswal, Alizadeh, Caulo, & van Beek, 2012).

**Tumor**

T1 = the tumor is 3 cm or less at its widest point.

T1a = the cancer measures 2 cm or less across.

T1b = the cancer measures more than 2 cm but is no bigger than 3 cm across.

T2 = the tumor is more than 3cm but no bigger than 7 cm across. It may affect the main airway (bronchus) or the membrane covering the lung (pleura) or the lung may have partially collapsed.

T2a = the cancer is over 3 cm but no bigger than 5 cm across.

T2b =the cancer is over 5 cm but no bigger than 7 cm across.

T3 = the tumor measures over 7 cm. The lung has completely collapsed, or there are two or more tumors in the same lobe of the lung, or the tumor has spread to one of the following: the chest wall, the muscle separating the chest and the abdomen (diaphragm), the covering membrane in the middle of the chest (mediastinal pleura), the phrenic nerve , the outer covering of the heart (pericardium), the main airway (bronchus) near where it divides to go into each lung.

T4 = The tumor is any size that has spread to the central area of the chest (mediastinum), the heart, a major blood vessel, the windpipe (trachea), the nerve that controls the voicebox, the gullet (oesophagus), a spinal bone, or the main bronchus where it divides or there is another tumor in a different lobe in the same lung.

**Lymph nodes**

There are different groups of lymph nodes in the lungs. The doctors will look closely to see which, if any, are affected. The following is a guide to the lymph node.

**Staging:**

N0 = There is no cancer in the lymph nodes.

N1 = There are cancer cells in the nearby lymph nodes in the same side of the chest as the cancer.

N2 = There are cancer cells in lymph nodes in the centre of the chest (still on the same side), or in the nodes under the place in the chest where the windpipe (trachea) divides into the left and right bronchus.

N3 = There are cancer cells in lymph nodes on the opposite side of the chest, or in the nodes at the top of the lungs, or by the collarbone on either side of the chest.

**Metastases**

M0 = The cancer has not spread to anywhere else in the body.

M1 = The cancer has spread to the opposite lung; the person has fluid around the lungs (malignant pleural effusion) or heart (malignant pericardial effusion), which contains cancer cells (M1a); or the cancer has spread to other parts of the body (M1b).

**Table 2.1 The number system for lung cancer staging**

| Stage | Tumor | Lymph nodes | Metastases |
|---|---|---|---|
| Stage 1A | T1a or T1b | N0 | M0 |
| Stage 1B | T2a | N0 | M0 |
| Stage 2A | T1a or T1b or T2a | N1 | M0 |
| | T2b | N0 | M0 |
| Stage 1A | T1a or T1b | N0 | M0 |
| Stage 1B | T2a | N0 | M0 |
| Stage 2A | T1a or T1b or T2a | N1 | M0 |
| | T2b | N0 | M0 |
| Stage 2B | T2b | N1 | M0 |
| | T3 | N0 | M0 |
| Stage 3A | Any T between T1a and T2b | N2 | M0 |
| | T3 | N1 or N2 | M0 |
| | T4 | N0 or N1 | M0 |
| Stage 3B | T4 | N2 | M0 |
| | Any T between T1a and T4 | N3 | M0 |
| Stage 4 | Any T | Any N | M1a or M1b |

**Treatments of Lung Cancer**

Treatments for lung cancer can involve surgical removal of the cancer, chemotherapy, or radiation therapy, as well as combinations of these treatments. They can each be used alone or together. The decision about which treatments will be appropriate for a given individual must take into account the location and extent of the tumor as well as the overall health status of the patient (Bircan et al., 2003).

Non-small cell lung cancer (NSCLC) can be treated with surgery, chemotherapy, radiotherapy or a combination of these, depending on the stage when the cancer is diagnosed. Surgery is the only treatment modality that can consistently cure a small number of patients with early NSCLC, although radiation therapy can be curative in some limited circumstances. Chemotherapy may contribute in an adjuvant or neoadjuvant role, but it is used mostly as a palliative therapy for advanced disease.

Small cell lung cancer (SCLC) is more chemo sensitive and can be cured in a minority of patients with chemotherapy and radiation therapy. Chemotherapy is usually the main treatment (Earle, 2004).

Surgery: Surgical removal of the tumor is generally performed for limited-stage (stage I or sometimes stage II) NSCLC and is the treatment of choice for cancer that has not spread beyond the lung. Surgery is less often performed with SCLC than with NSCLC because these tumors are less likely to be localized to one area that can be removed.

Radiation: Radiation therapy is delivered to a very specific region of the diseased lung, with the goal of a minimal radiation dose given to normal tissue (Collins, Haines, Perkel, & Enck, 2007). Radiation therapy may be employed as a treatment for both NSCLC and SCLC. It can have unpleasant side effects, including fatigue and lack of energy. Radiation therapy can irritate the skin in the area that is treated, but this irritation generally improves with time after treatment has ended.

Chemotherapy: Both NSCLC and SCLC may be treated with chemotherapy. Chemotherapy refers to the administration of drugs that stop the growth of cancer cells by killing them or preventing them from dividing. Chemotherapy may be given alone, as an adjuvant to surgical therapy, or in combination with radiotherapy. Unfortunately, the drugs used in chemotherapy also kill normally dividing cells in the body, resulting in unpleasant side effects.

## Symptoms Associated with Chemotherapy in Advanced Lung Cancer Patients Receiving Treatment

The definitions of symptoms are mostly related to individual perceptions of the changes of physical, psychological and cognitive state associated with disease (Dodd et al., 2001b; Lenz et al., 1997; Rhodes & Watson, 1987). A symptom may be defined as “A morbid phenomenon or departure from the normal in structure, function, or sensation, experienced by the patient and indicative of disease” (Pugh, 2000). Rhodes and Watson (1987) define symptoms as “the perceived indicators of change in normal functioning as experienced by patients.” Symptoms are viewed and explained differently depending on their conceptual foundation. Dodd and team (2001) defined

symptoms as subjective experiences or the changes in bio-psychosocial function, sensation or cognition. Symptom experience is defined as the interplay of an individual's perception of the symptoms or the meaning given to the symptoms and the physiological, cognitive, emotional, or behavioral response to symptoms. Lenz and team (1997) stated that symptoms are unpleasant. The key attributes of unpleasant symptoms include severity, timing, level of distress perceived and quality. This team also addressed the idea that symptoms can occur alone or in isolation from one another. In conclusion, a symptom is a sensation or perception of change related to health function experienced by an individual.

**Common Symptoms in Lung Cancer Patients**

Patients with lung cancer often suffer from numerous symptoms resulting both from the primary disease itself, as well as from its treatment (Wang et al., 2008). The majority of patients are diagnosed when their lung cancer is at a relatively advanced stage (Molassiotis et al., 2010).Several studies have focused on patients with lung cancer to show how these patients have most common and severe symptoms. Fatigue is a frequent symptom in lung cancer patients, with nearly 85% of patients experiencing this symptom (Hollen, Gralla, Kris, & Potanovich, 1993). Pain, or dyspnea, affects 63%-88% of lung cancer patients cared for by palliative care services (Potter & Higginson, 2004). The National Institutes of Health held a State-of the-Science Conference on symptom management, they listed the most common cancer symptoms as pain, depression, and fatigue (Wang et al., 2008).These symptoms have been studied in isolation, despite the fact that they often occur simultaneously and their interaction may exacerbate the severity of each (Dodd, Miaskowski, & Lee, 2004; Ross & Alexander, 2001). Cooley (2003) reviewed many studied of lung cancer patients suggested that the most common symptoms in newly diagnosed lung cancer patients included fatigue, pain, loss of appetite, insomnia, hemoptysis, and chest pain, disruptions in outlook, functional decline, weight loss, coughing, bowel disruption as well as dyspnea and anorexia. She found that most patients with lung cancer suffer multiple symptoms during most of the illness trajectory and treatment phases (Cooley, Short, & Moriarty, 2003; Sarna & Brecht, 1997).

Most patients with lung cancer experience multiple symptoms; symptoms may differ at various points in the illness trajectory, and among various treatments. Furthermore, some of these symptoms may tend to cluster together (Krech, Davis, Walsh, & Curtis, 1992). Sarna and Brecht (1997) found common serious symptoms associated with lung cancer including fatigue and functional decline, weight loss, pain, insomnia, difficulties in concentration, cough, dyspnea, bowel disruption, and central nervous system effects and neurologic parasthesias (Sarna & Brecht, 1997).

**Symptoms Associated with Chemotherapy Treatment in Patients with Lung Cancer**

Chemotherapy is the principal treatment for lung cancer (Kuo & Ma, 2002). Treatment can be to cure, control, or alleviate symptom distress. However, chemotherapy causes side effects and toxicities that may affect patients physically, emotionally, and socially and may increase their symptom distress. Patients often attempt to reduce the severity of symptom distress, thus minimizing its effects (Fan et al., 2007; Daly et al., 2007). Patients, with advanced lung cancer and more comorbidity at the time of diagnosis, who are treated with chemotherapy, are most likely to have multiple symptoms (Gift et al., 2004). Some of these symptoms may tend to cluster together.

Several studies have focused on patients with lung cancer to show how these patients have side effects from chemotherapy. The common physical symptoms experienced by lung cancer patients undergoing treatment were lack of energy, coughing, pain, lack of appetite, and nausea, and their psychological symptoms were feeling nervous, difficulty sleeping, feeling sad, and worrying (Akin, Can, Aydiner, Ozdilli, & Durna, 2010). The results of the study by Kuo and team (2002) and the reviewed show that approximately 60% of chemotherapy patients are given gemcitabine, navelbine, and cisplatin and, consequently, nausea and vomiting are the most common typical physical symptom distresses encounterd in patients undergoing chemotherapy (Kuo & Ma, 2002). In addition, Bircan and team (2003) study the effects of chemotherapy in lung cancer patients. They reported alopecia, sore mouth, nausea and vomiting score were increased with chemotherapy. Taken together, these

studies suggest that most patients with lung cancer experience multiple symptoms. Furthermore, some of these symptoms may tend to cluster together.

**Symptom Assessment**

Better assessment is a prelude to successful symptom treatment. Symptom assessment is challenging because of the evolving course of cancer, and complex interrelationship between disease stage and symptoms (Kirkova et al., 2006). Currently, symptom detection for research purposes relies on chart review, elicitation by a survey or questionnaire, or spontaneous reporting. Chart reviews typically underestimate symptom prevalence, because symptoms are often unrecorded, and thus, chart reviews are not useful assessment methods in the clinical management of individuals with cancer-related symptoms (Kroenke, 2001). There is evidence that in a general population, structured surveys can produce "over-endorsement bias," a tendency for patients to select large numbers of symptoms from a checklist making it difficult for clinicians to prioritize the most distressing concerns (Okuyama et al., 2003; Wang et al., 2004). Yet in the cancer arena, hesitancy to report symptoms is common. Therefore, significant concerns about over reporting do not seem to apply to this population. The third method of symptom detection through volunteered, spontaneous reporting may be optimal in a general population but is not practical in cancer settings. The very label used to describe these reports, "chief complaint," indicates some of the perceptions patients and clinicians hold about these remarks.

**Symptom Assessment Scales**

Currently, several instruments have been designed to specifically measure symptom clusters, such as the Edmonton Symptom Assessment Scale (ESAS), the M.D. Anderson Symptom Inventory (MDASI), the Rotterdam Symptom Checklist (RSC), the Symptom Distress Scale (SDS), the Memorial Symptom Assessment Scale (MSAS), and others (Paice, 2004).

The Edmonton Symptom Assessment Scale (ESAS) consists of nine visual analog scales (using a 10-cm line) that measure pain, activity, nausea, depression, anxiety, drowsiness, lack of appetite, well-being, and shortness of breath (Bruera, Kuehn, Miller, Selmser, & Macmillan, 1991). A tenth symptom can be added to individualize the scale. The ESAS Distress score is a sum of the nine symptoms.

The ESAS was found to be valid and reliable in a population of cancer inpatients and outpatients within the Veteran's administration, although test–retest was better at 2 days than at 1 week. Furthermore, patients required more explanation regarding the use of the ESAS than the MSAS or FACT. The authors of this study found that the visual analog format was more difficult to use that categorical scale (Chang, Hwang, & Feuerman, 2000). To remedy some of these limitations, ESAS is currently a combination of visual analog scales supplemented with numeric rating scales. In addition, The ESAS was used to compare palliative care symptom control across institutions. However, the authors noted that one obstacle to the use of the ESAS as a quality tool was inconsistent documentation of the symptoms within the patients' charts (Dudgeon, Harlos, & Clinch, 1999).

The M.D. Anderson Symptom Inventory (MDASI) is a multi-symptom patient-reported outcome (PRO) measure for clinical and research use. The MDASI is a list of 13 symptoms rated on an 11-point scale (0 –10), with 0 indicating "not present" and 10 meaning "as bad as you can imagine" (Charles S Cleeland et al., 2000). The MDASI's 13 core symptom items include those found to have the highest frequency and/or severity in patients with various cancers and treatment types. The MDASI has several advantages over other symptom-assessment scales in that it applies broadly across cancer types and treatments, is easy for patients to complete, includes items related to symptom interference with daily life, and it is easily translated into other languages. Cleeland and colleagues (2000) developed this tool specifically to incorporate new technologies in health care. Using interactive voice response (IVR), patients can be called via the telephone at predetermined times to answer the MDASI using the keys on their touchtone telephone. The information is then communicated to health care professionals, with alerts or prompts for action if a particular symptom is rated as severe. Several intriguing outcomes of this system may include not only improved clinical management of cancer-related symptoms but also a unique strategy for data collection during multicenter clinical trials, or even providing information for quality-improvement efforts within institutions.

The Rotterdam Symptom Checklist (RSC) is a 31-item scale specifically designed to measure symptoms experienced by patients undergoing cancer clinical trials (De Haes, Van Knippenberg, & Neijt, 1990). Patients are asked to rate

symptoms that bothered them using the following descriptors: “not at all, “a little, “quite a bit,” and “very much. As with other instruments employing verbal descriptors, these cues may be difficult for some patients to use, and the length of the tool can be cumbersome for very ill people. Furthermore, the RSC measures distress alone without determining the severity of these symptoms (Paice, 2004).

The Symptom Distress Scale (SDS) is a 13-item tool that measures the frequency, intensity, and distress associated with 11 symptoms, providing a valid measure of global symptom distress in people with cancer (McCorkle & Young, 1978). One possible limitation of this tool is the small number of symptoms measured (Kukull, McCorkle, & Driever, 1986; Peruselli, Camporesi, Colombo, Mazzon, & Paci, 1993).

The Memorial Symptom Assessment Scale (MSAS) measures the prevalence, severity, and distress associated with 32 physical and psychologic symptoms experienced during the prior week (Portenoy, Thaler, Kornblith, McCarthy Lepore, Friedlander-Klar, Kiyasu et al., 1994). Each symptom frequency is rated as occurring “rarely, “occasionally, “frequently, and “almost constantly. Severity is measured as “mild, “moderate, “severe, and “very severe. Symptom related distress is rated using a 5-point Likert scale: “not at all, “a little bit, “somewhat, “quite a bit, and “very much”. Each symptom score is an average of the three dimensions. The tool consists of physical (MSAS-PHYS) and psychologic (MSAS-PSYCH) subscales, as well as a Global Distress Index (MSAS-GDI). The total MSAS (TMSAS) score is the average of the symptom scores for all 32 symptoms. According to the authors, the total MSAS appears to provide information about overall symptom distress, yet the Global Distress Index may be more clinically meaningful because of the high correlation between this measure and quality of life and clinical status (Portenoy, Thaler, Kornblith, McCarthy Lepore, Friedlander-Klar, Kiyasu, et al., 1994). The MSAS has demonstrated validity and reliability in a cancer in- and outpatient population (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000b). Recently, the MSAS was used in a study of seriously ill cancer and noncancer patients, providing preliminary evidence for construct validity and demonstrating the feasibility of the use of this tool in patients near end of life (Tranmer et al., 2003).

Each of the above instruments measures different symptoms, although there is a core set of symptoms that are captured by each tool. The ESAS measures severity of each symptom, the MDASI measures severity and functional impairment, and the MSAS evaluates frequency, severity, and the degree to which each symptom causes distress. The choice of instrument depends on the purpose, including research, clinical practice, or targeted symptoms (Kirkova et al., 2006). Since a symptom cluster is based on the symptoms and scaling used in a particular assessment tool, the number and type of symptoms in an instrument plays a significant role in identifying clusters. A balance must be struck between comprehensiveness and patient compliance with assessment, especially in clinical practice. When too many symptoms are included in an instrument, it overtaxes ill patients and reduces compliance; when too few symptoms are included, important symptoms are overlooked. In addition, symptom assessment instruments should be comprehensive, accurate, and reliable (Kirkova et al., 2006).

In the case of a symptom cluster, the easiest approach is to measure one dimension on multiple symptoms. This unidimensional approach to the measurement of multiple symptoms has the advantage of simplicity and low response burden. However, the disadvantage of this approach is that other critical dimensions of the symptom cluster may not be assessed. It must be noted, however, that research has not established the critical dimensions of a symptom cluster that are essential to measure. A thorough and sound measure of symptom clusters would be multidimensional for multiple symptoms. The researcher could minimize the response burden by including the symptoms that are most appropriate for a given clinical context (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006). The MSAS is a validated multidimensional symptom assessment instrument that captures patient rated severity, frequency, and distress associated with 32 highly prevalent symptoms. Since its introduction, the MSAS has found applications in various studies of patients with cancer such as ovarian carcinoma, breast cancer, head and neck carcinoma, and lung cancer (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000a). The MSAS was used to measure the symptoms experienced in this study.

## Symptom Measurement Issues

The aspects that should be considered when assessing symptoms include not only the prevalence but also the location, temporal factors (such as onset, periodicity, and duration), severity (including intensity as well as the effect of this severity on overall distress and suffering), and outcomes (including relief, patient satisfaction, and cost) (Ivanova et al., 2005; Yun et al., 2006). This information is required in order to determine treatment approaches, but many assessment instruments do not include this information. Practicality must be considered when selecting an appropriate tool to measure symptoms. The ease of completion is particularly important in a cancer population, because they often experience many symptoms. Tools must be validated, but must also be brief, with large print, and should include clear instructions. Because symptoms are subjective, the patient is the optimal source of information. However, cognitive impairment resulting from dementia, delirium, or other factors may limit the ability of the patient to respond. When patients are unable to respond, family members are often enlisted as proxies, yet studies suggest that caregivers typically report higher pain and disability. Aids to communication include communication boards and assistive devices for the hearing impaired, as well as education of patients, families and professionals to overcome fears, biases, and lack of knowledge (Yun et al., 2006). When clinical trials that include patient self-report in the application of treatment guidelines are conducted in patients with diverse linguistic backgrounds, cultural differences can confound the accuracy and cross-similarity of the PROs (patient reported outcomes), thus complicating the interpretation of the trial results and the application of the clinical guidelines. Knowing the degree to which symptom ratings might vary as a function of language or nationality is therefore important for both the clinical trials and the treatment of symptoms and requires empirical evidence of the effects of language on the performance of a symptom measure (Bowden & Fox-Rushby, 2003).

Wang and team (2010) studied the impact of cultural and linguistic factors on symptom reporting by patients with cancer. They analyzed M.D. Anderson Symptom Inventory (MDASI) symptom and interference ratings from cancer patients in five countries—the United States, China, Japan, Russia, and Korea and found that the variance of the random effects for country were between 20% and

50% of the inter subject variance. These results give some reassurance that symptom data obtained using various language versions of the MDASI, and can be pooled to analyze multinational clinical research. Moreover, the results of this study indicate that national and linguistic (country) variations in patient responses to the MDASI are small relative to individual patient-related factors. It is important to note that the MDASI includes only symptom severity and does not provide any of the other information noted above for good symptom assessment such as timing, distress, and quality. The MSAS will be chosen to use in this study, because it includes the aspects of symptom missing in the MDASI, and is thus more consistent with symptom experience as defined in the conceptual framework.

## Symptom Experiences Based on Theory of Unpleasant Symptoms

Lenz and colleagues (1997) defined symptoms as the perception-based definition that assumes awareness by the individual and that the nature of a symptom can be truly known and described only by the individual experiencing it. Symptom experiences are multidimensional which can occur as separate entities or concurrently as a symptom cluster (Lenz et al., 1997). Concurrent symptoms are likely to result in an experience that is multiplicative rather than additive. The theory of unpleasant symptoms (TOUS) asserts that symptoms can occur either in isolation—one at a time—or in combination with other symptoms. In some situations, one symptom may precede and possibly give rise to another. In the TOUS, symptoms are conceptualized as manifesting multiple variable and measurable dimensions. It is asserted that all symptoms vary in intensity or severity, degree of associated distress, timing, and quality. These dimensions are also related to one another.

### Symptom Dimensions

#### Symptom frequency

Symptom frequency refers to the time dimension which an intermittent symptom occurs, the duration of a persistent symptom, or a combination of frequency and duration (Lenz et al., 1997). The time dimension includes the way symptoms vary in duration and frequency. First they vary in duration, the length of

time they continue. Secondly, intermittent symptoms vary in the frequency with which they occur; they can also vary in their regularity and periodicity.

Several studies focused on the frequency of symptom in lung cancer patients. Hoffman and team (2007) examined the most frequently occurring symptoms in newly diagnosed people with lung cancer undergoing chemotherapy. The findings parallel the guiding principles of the TOUS in that newly diagnosed people with lung cancer undergoing chemotherapy experience multiple symptoms simultaneously rather than symptoms in isolation. Fatigue, pain, nausea, constipation, insomnia, and poor appetite were the most frequently reported symptoms experienced by at least 50% of the sample. The top five symptoms for men were, from most frequent to less frequent, fatigue, pain, nausea, cough, and insomnia; for women, fatigue, pain, poor appetite, constipation, and insomnia (Hoffman, Given, Eye, Gift, & Given, 2007).

**Symptom severity or Symptom intensity**

Symptom severity is the dimension that quantifies the degree, strength, or severity of the symptom (Lenz et al., 1997). The symptoms severity reported by lung cancer patients varied from study to study. Cooley and team (2003) reported in the study of 117 newly diagnosed people receiving treatments for lung cancer that more than one-third of the patient reporting insomnia. Vainio and colleagues (1996) identified that the incidence and severity of dyspnea were highest in the lung cancer population, as compared with other patients with advanced cancer (Vainio & Auvinen, 1996). Wang and colleague (2008) explored the phenomenon of symptom distress in lung cancer patients. The top five most-severe symptoms were fatigue, sleep disturbance, lack of appetite, shortness of breath, and general distress.

**Symptom distress**

Symptom distress refers to the degree to which the individual experiencing the symptom is bothered by it (Lenz et al., 1997). The degree of distress experienced with a symptom is related to its intensity; however, it can also be moderated by other considerations. Distress can be influenced by the degree of focused attention that the individual directs toward the symptom. Several studies gave noted that adults with lung cancer experience more symptom distress than patients with other types of cancer (Cooley, Short, & Moriarty, 2003; Degner & Sloan, 1995;

Tishelman et al., 2005). Patients with advanced disease reported more distress than those with early-stage disease (Degner & Sloan, 1995). Cooley and team (2000) studied in 117 patients to describe which symptoms are most distressing, describe the prevalence of symptoms in adults receiving treatment for lung cancer. The results found fatigue and pain were the most distressing symptoms.

**Quality of symptom**

The quality of the symptom dimension refers to the nature of the symptom or the way in which it is manifested or experienced, that is, what it feels like to have the symptom (Lenz et al., 1997). By including this dimension, the TOUS acknowledges that in addition to reflecting characteristics that are common across all symptoms, each symptom has unique aspects and characteristics. The descriptors that best characterize each symptom are highly specific. Describing and measuring the quality of specific symptoms (and symptom clusters) depends on the patient's ability to articulate what he or she is experiencing. Individuals differ in the descriptors that they use and also in their ability to communicate. Qualitative research with a variety of patient populations is often valuable in describing the quality of the symptom experience. Therefore, the quality dimension will not explore in this study.

**Multiple Symptoms Experience as Symptom Clusters**

Lung cancer patients often experience multiple symptoms related to the disease itself and its treatment, and those symptoms can independently predict changes in patient function, treatment failures, and post-therapeutic outcomes (Fan et al., 2007; Fox and Lyon, 2006). Symptoms can exist alone, but most often multiple symptoms occur concurrently and commonalities exist (Lenz et al., 1997; Dodd et al., 2001). There is increasing interest in studying symptom clusters in patients with cancer as patients often experience several symptoms simultaneously (Dodd et al., 2001; Gift et al., 2003; Given et al., 2002; Cooley et al., 2002). Part of the symptom experienced by patients with lung cancer may be the result of the simultaneous occurrence of symptoms, also known as "clustering" of symptoms. Although the term of symptom clusters is not used in the TOUS, the conceptualization of multiple symptoms can occur concurrently is similar to the concept of symptom clusters (Lenz et al., 1997).

## The Concept of Symptom Cluster

Dodd and colleagues (2001a) defined the term "symptom cluster," as three or more concurrent symptoms that are related to each other but are not required sharing the same etiology. Kim et al (2005) refined the definition of a symptom cluster by Dodd and colleagues as follows: a symptom cluster as a stable group of two or more concurrent symptoms that are related to one another and independent of other symptom clusters. Relationships among symptoms within a cluster should be stronger than relationships among symptoms across different clusters, and are independent of other symptom clusters or combinations. Miaskowski et al (2004) have suggested that symptoms can be related to one another through a common etiology, by sharing common variance, or by producing different outcomes than individual symptoms alone.

Although most researchers agree that symptoms in a cluster are correlated with each other and coexistent (Barsevick, 2007; Dodd et al., 2001a; Kim et al., 2005), there is still disagreement about some essential elements in the definition of symptom clusters. Different researchers have different understandings of the relationship between symptoms in a cluster. Some have identified the relationship by the correlation between and among symptoms (Gaston-Johansson et al., 1999; Gift et al., 2003). Others have measured the relationship based on the effect of symptoms on outcomes (Fox et al., 2007). The TOUS asserts that symptoms can occur either in isolation—one at a time—or in combination with other symptoms. In some situations, one symptom may precede and possibly give rise to another (Lenz & Pugh, 2003). Clarifying the meaning of relationships between and among symptoms in a cluster will be necessary to define the concept of symptom clusters.

Another discrepancy in the definition of symptom clusters is the minimum number of symptoms constituting a cluster. Many data-based studies have shown that two symptoms in a cluster (Chen and Lin, 2007; Chow et al., 2007; Walke et al., 2007), while others have supported at least three symptoms in a cluster (Bender et al., 2005; Chan et al., 2005). Therefore, the definition of a symptom cluster requires refinement. In particularly, clarifying the meaning of relationships between and among symptoms in a cluster is necessary to define the concept of symptom clusters.

Recognizing and understanding the scientific basis for symptom clusters could help in several ways. A cluster could provide the basis for identifying or diagnosing a syndrome or condition related to cancer or its treatment and help identify subgroups of individuals with different of unique symptom profiles. Furthermore, a symptom cluster also could guide the search for a common etiology or mechanism underlying a group of symptoms and could provide a basis for understanding how multiple symptoms are related to one another (Barsevick, 2007).

In summary, although clinicians long have noted that symptoms in cancer may occur together, research related to the clustering of symptoms is still in its infancy. Many previous studies commonly determined symptom experiences and clusters by focusing on only one dimension, usually severity or distress. In this study, the multidimensional instrument was used for symptom assessment because clusters are multidimensional in nature. This approach influenced the choice of the TOUS as the conceptual framework for this study. A second conceptual issue is related to the number of symptoms in a symptom cluster. Symptom clusters were originally defined as three or more concurrent symptoms that were related to one another (Dodd et al., 2001a). Kim et al. (2005) suggested however that a cluster could include two or more symptoms. This matter warrants investigation within and across cancer diagnoses, cancer treatments, and stages of disease (Miaskowski et al., 2007). Symptom cluster determination is influenced by the instrument used to assess symptoms. There is growing awareness that different populations may require slightly different assessment instruments, usually a basic symptom assessment scale, with the additional of symptoms specific to a given population. On one hand, it would be easier to compare results across populations if all researchers used the same instrument. On the other hand, this approach may inadvertently exclude symptoms that are very important in the care of individuals with a particular type of cancer.

**Symptom cluster mechanisms**

Cancer patients may experience multiple concurrent symptoms, or symptom clusters. Symptom clusters are variously defined as three or more concurrent symptoms that are related to each other, (Dodd et al., 2001) or two or more symptoms related to each other that occur together (Kim et al., 2005). Symptom

clusters are composed of stable groups of symptoms, are relatively independent of other clusters, and may reveal specific underlying dimensions of symptoms. Relationships among symptoms within a cluster should be stronger than relationships among symptoms across different clusters. Symptoms in a cluster may or may not share a common etiology (Kim et al., 2005). Whether the definition accepted is two or three or more symptoms, key to the concept is that the symptoms occur in groups and are related to one another (Wang, Tsai, Chen, Lin, & Lin, 2008).

The exact reasons of why symptoms form clusters are little known. The explanation to purely physiological mechanisms and causes of symptom are complicated and perhaps unclear (Suwisith et al., 2008). Possible reasons behind the clustering of symptoms have been suggested such as shared etiology, symptom interactions, and symptoms stimulation of other symptoms (Armstrong et al., 2004; Cleeland et al., 2003; Lee et al., 2004; Kim et al., 2005). This is because mechanisms underlying the symptoms are multidimensional.

As the information on symptom cluster is insufficient, this concept has recently become prominent in symptom-related concepts and research. Kim and her team (2005), on their concept analysis on symptom clusters, identified five critical attributes of symptom clusters which are concurrence, relationships, underlying dimensions, stability and common etiology. The attribute of concurrence and relationships seems similar to described by Dodd and her team (2001). Underlying dimensions refers to clusters of symptoms. Stability refers to pattern of clustering and should not change either across subjects on times. Common etiology is the psychological or biological mechanisms that cause the combinations of symptoms. Parker et al. (2005) proposed the Symptom Interactional Framework to explain the phenomena of symptom pair and clusters. Symptom pairs or symptom clusters are defined as the concurrent occurring of two or more symptoms. Symptom interactions are defined as occurring when two or more symptoms coexist, precipitate or synergize each other or trigger the development of other symptoms. The mechanisms underlying symptom pairs and clusters are defined as alterations in an optimally functioning process. This framework provides the structure of mechanisms underlying the formation of symptom pairs and clusters with shared etiology, shared mechanisms, and symptom interactions. This also raises another issue on whether it is important to

define symptom clusters as having more than two symptoms in order to constitute in a cluster or not.

Additional research is needed to determine if symptom clusters in oncology patients share a common etiology. These studies are challenging to conduct because many of the most prevalent symptoms that oncology patients report (i.e., pain, fatigue, depression, sleep disturbances) can occur as a result of the patients' cancer diagnosis, their treatment regimen, or interactions between the cancer, the treatment, and the patients' underlying comorbidities (Miaskowski et al., 2007).

**Clustering of Symptom Cluster: Approaches to the Study of Symptom Clusters** Symptom cluster research is relatively new. Studies conducted so used either a "most common symptom" approach or an "all possible symptom" approach.

**Most Common Symptom Approach.** There are five different strategies used within this group of studies. In the first approach the investigators choose common symptoms before empirical analysis, presumably on the basis of clinical observations, and then calculate correlations among the symptoms. Generally the clusters of interest are comprised of two to three symptoms. This approach has been used by many research groups (Chan et al., 2005; Dodd et al., 2001a; Fox and Lyon, 2007; Hoffman et al., 2007; So et al., 2009). For example, Fox and Lyon (2007) explored the relationship between pain, fatigue, and depression in patients with ovarian cancer, and found fatigue and depression were grouped as a cluster because these two symptoms were correlated significantly with each other. The majority of these studies further supported symptom clusters by showing the influence of these clusters on patient outcomes, such as QOL and functional status.

A second strategy used in this approach is based on the identification of concurrent multiple symptoms. Here the researcher does not need any statistical analyses, but defines a cluster based on the co-occurrence of selected related symptoms (Liu et al., 2009; Reyes-Gibby et al., 2006; Wilmoth et al., 2009). Thee studies further identified the synergistic effect of multiple concurrent symptoms on patient outcomes. Compared with patients who reported no pain, fatigue or insomnia, those reporting two or three symptoms had a higher risk of lower functional status (Given et al., 2001a). Patients with more symptoms also experienced more severe

symptoms than those who reported only one or no symptom (Given et al., 2001b; Liu et al., 2009). However, as this method identifies a cluster only by the concurrent characteristic of selected symptoms, it is difficult to exclude the possibility that some unselected concurrent symptoms may be related to these selected symptoms, and thus should also be included in the cluster.

A third strategy for identifying symptom clusters based on most common symptoms is based mediation effects. Baron and Kenny (1986) defined a mediating variable as a variable that explained the relationships between independent and dependent variables; moderating variables, on the other hand, were defined as variables that could change the impact of independent variables on dependent variables. The proponents of this third strategy for identifying symptom clusters were interested in symptoms as mediators. Barsevick and team (2006) conducted a secondary analysis of data obtained in a randomized trial of a fatigue intervention. They found that in the control group, functional status mediated the relationship between fatigue and depression, but this finding was not supported in the experimental group. However, it is difficult to assume the causal relationships of any mediation model, especially when there is not a strong theoretical framework to guide analyses (Polit and Beck, 2004).

The fourth strategy focuses on exploring interaction effects within symptom clusters. Dodd and team (2001a) determine the effect of the symptom cluster of pain, fatigue, and sleep insufficiency on functional status during three cycles of chemotherapy in 93 patients with cancer. The authors did not find significant interactions among any of the independent variables in the regression model. On the other hand, Hoffman and teams (2007) examine the relationships among pain, fatigue, insomnia, and gender while controlling for age, co-morbidities, and stage of cancer in patients newly diagnosed with lung cancer. A model containing all main effects (two-way interactions of pain and fatigue, pain and insomnia, and insomnia and gender; and the three-way interaction of pain, fatigue, and insomnia, along with three covariates (age, co morbidities, and stage of cancer) was a good fit to the data. Parameter estimates indicated that a statistically significant effect from the model was the three-way interaction of pain, fatigue, and insomnia. The main reason for the inconsistency could come from the different dependent variables in these models; Hoffman and

colleagues (2007) used gender as the dependent variable while Dodd and colleagues (2001) were interested in the impact of symptom clusters on functional status.

The fifth strategy focuses on identifying subgroups of patients with similar symptom experience based on a specific symptom cluster. This method clusters patients together instead of symptoms. Miaskowski and colleague (2006) studied patients with cancer, and identified four subgroups of patients using cluster analysis: high fatigue and low pain, low fatigue and high pain, all symptoms low, and all symptoms high. This study further found that the subgroup of patients who reported low levels of all symptoms reported the best functional status and QOL. Although several distinct subgroups of patients with similar symptom experience were identified in these studies, the differences in most demographic and clinical characteristics among these subgroups have not yet been demonstrated (Dodd et al., 2010; Miaskowski et al., 2006; Pud et al., 2008).

A limitation of the “most common symptom” approach is that important symptoms that are less common may be missed.

**All Possible Symptom Approach**

The second way of identifying symptoms clusters in cancer patients is called the all-possible symptom approach. Any potential symptoms that cancer patients experience are considered in cluster identification, and symptom clusters are only determined after statistical analyses.

**Analytic strategies**

Different approaches have been used to study all possible symptom clusters (Fox, Lyon, & Farace, 2007; Miaskowski et al., 2007; Xiao, 2010). Different methods may yield different sets of clusters, and results may vary depending on the statistical analysis technique used. Approaches used to date include correlations (Chen & Lin, 2007; Chow, Fan, Hadi, & Filipczak, 2007), factor analysis or principal component analysis (Chen & Lin; Chen & Tseng, 2006; Wang et al., 2008; Suwisith et al., 2008; Chaiviboontham et al., 2011; Phligbua et al., 2012), cluster analysis (Bender, Ergyn, Rosenzweig, Cohen, & Sereika, 2005; Walsh & Rybicki, 2006) , and structural equation modeling (SEM) (Hayduk, Olson, Quan, Cree, & Cui, 2010; Olson et al., 2008). The analytical methods most commonly used are cluster analysis and factor analysis. Both cluster analysis and factor analysis are exploratory techniques that are

intended to reveal the underlying structure of data. Although factor analysis tends to be used with group variables and cluster analysis tends to be used with groups of individual variables, the two methods can be used interchangeable. The choice of method, however, depends upon the study objectives, underlying assumptions and method of symptom assessment.

1) Factor analysis and Cluster analysis

A number of analytic approaches have been used to examine symptom clusters; however, “best” practice with regard to analysis has not been established. The most common approach to grouping symptoms is factor analysis, which examines the relationships among a number of variables (e.g., symptoms severities) based on the matrix of correlation coefficients between the variables (Thompson, 2004). Factor analysis is used to predict a set of latent factors that are responsible for covariance among a group of symptoms. Symptoms due to this latent factor would covary more strongly with each other than they would with symptoms that are affected by a different latent factor. This covariance can be examined using a general factor model or principle components analysis. A benefit of the principle component analysis is that it can yield principle component scores, which reduces several items to a single weighted score for use in other parametric analyses such as test of group differences. However, the limitation of factor analysis in investigating symptom cluster is that each symptom can only load on one factor. In addition, factor analysis does not provide the kind of information required to establish causal relationships.

Cluster analysis is another procedure that can be used to define a symptom cluster. It is used to “discover” underlying groups of individuals who are similar in their symptom experience or symptom profile (Woods, Mitchell, & Lentz, 1999). There is an inherent appeal for the use of cluster analysis in the study of symptom clusters. Whereas factor analysis groups symptoms into similar groupings (factors), cluster analysis groups individuals into mutually exclusive subsets of individuals with similar profiles of symptoms (Blashfield & Aldenderfer, 1978). Cluster analysis could be useful clinically to identify subgroups of individuals who have a distinctive profile of symptoms allowing clinicians to target specific interventions to each subgroup. Grouping individuals based on their symptom

experience has occurred in a few studies of oncology patients (Dodd, Cho, Cooper, & Miaskowski, 2010; Gwede, Small, Munster, Andrykowski, & Jacobsen, 2008; Maliski, Kwan, Elashoff, & Litwin, 2008; Miaskowski et al., 2006; Pud et al., 2008).

Factor analysis and cluster analysis can be used to discover the underlying structure of symptoms or the underlying groupings of patients with similar symptom profiles. Factor analysis is well known for its use in the construction of psychometrically sound scales. A scale is typically constructed around the latent factors discovered in the analyses. For instance, symptoms could factor into two scales comprised of somatic and psychological factors. These scales could be used in parametric analyses to examine correlates (antecedents or consequences).

Both factor analysis and cluster analysis methods are exploratory and descriptive, examining the underlying structure of a group of symptoms (factor analysis) or the clustering of individuals with similar symptom patterns (cluster analysis). Factor analysis is based on the covariance (correlation) between symptoms. Alternatively, cluster analysis may classify symptoms with similar response patterns, but there is no theoretical (conceptual) basis to interpret the cluster, as can be suggested by factor analysis. Cluster formation simply depends on mathematical rules as the method of classification, in contrast to factor analysis, which has developed from a substantial statistical base (Aldenderfer & Blashfield, 1984). When multiple symptoms occur concurrently, a combination of mechanisms may be responsible for the resultant symptom
experience.

2) Path models and Structural equation modeling (SEM)

It is possible that one symptom could influence another symptom through its relationship to a third symptom or factor. Path models allow for the examination of both direct and indirect relationships among variables such as a group of symptoms. Path analysis models and structural equation modeling could be used to examine direct and indirect effects of variables (Cohen, 2003). Investigating causal connections among symptoms offers another possibility to examine symptom clusters.

Structural equation modeling (SEM) was used to identify the causal connection among symptoms in palliative patients who had various types of

cancer (Olson et al., 2008). This method enables researchers to identify subsets of variables that are argued to collectively represent a higher order construct that is not or cannot be measured directly, for example, a complex symptom cluster. Such constructs are called latent variables and, if well represented by a subset of measured variables, can be evaluated by means of equations. This approach permits the examination of the relation of the latent variable to other variables (either independent or outcome variables) of interest. In addition to evaluating higher order constructs, a significant advantage of structural equation modeling is the ability to assess simultaneously the relationships between multiple variables, mediators, and outcome variables (Kim & Abraham, 2008).

Olson et al (2008) conducted a longitudinal study for patients receiving palliative care. Structural equation modeling (SEM) was used to identify the causal connection among symptoms. As required by SEM, an initial model of exogenous variables, pain, anxiety, nausea, shortness of breath and drowsiness, and endogenous variables, appetite, tiredness (fatigue), depression and well-being, was built before data analyses. The model fit was acceptable. Several causal relationships were reported: drowsiness displayed consistent effects on appetite, tiredness and well-being; anxiety's effect on well-being changed over time. The structural equation modeling provides a way to test hypotheses about causal relationships; Olson and colleagues have published two papers demonstrating this point (Hayduk et al., 2010; Olson et al., 2008). Although this model explained part of causal connections, some limitations might blur the relationship. For instance, the initial model was not based on published studies, but on researchers' clinical experience.

3) Qualitative approaches

The third approach for studying symptom clusters is qualitative. There is one qualitative study of symptom cluster in lung cancer. Semi-structured interviews were conducted with patients and their primary caregivers at four time points: At the beginning of treatment and then subsequently at three, six, and twelve months. Interpretative Phenomenological Analysis was employed in the data analysis. Findings indicate that a cluster of interacting respiratory symptoms play a central role in patients' symptom experiences within the lung cancer population. The interviews also suggest that symptoms such as cough which are under-represented in

research within this population may play an important role in patients' symptom experiences (Molassiotis, Lowe, Blackhall, & Lorigan, 2010).

4) Hybrid approaches

The fourth approach uses a combination of instruments and statistical methods. Henoch and team (2009) explored the existence of symptom clusters among a homogenous group of patients with inoperable lung cancer close to diagnosis using different assessment and various statistical methods in a large cohort of lung cancer patients. The samples included patients newly diagnosed with lung cancer. Data were gathered using various questionnaires, including the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, the EORTC LC13, and the Symptom Distress Scale. Items in the instruments were adapted to increase their correspondence. Symptom clusters were analyzed with Pearson correlations, cluster analysis, factor analysis. The authors consistently identified three clusters across instruments and analyses: first, a pain cluster consisting of pain, nausea, bowel issues, appetite loss, and fatigue; second, a mood cluster consisting of mood, outlook, concentration, and insomnia; and third, a respiratory cluster consisting of breathing and cough.

Interestingly, fatigue and appetite loss were closely related to more than one cluster in several analyses. A second important point is that the authors found consistent symptom clusters for a large cohort of patients with lung cancer at a comparable point in their cancer trajectory, across different measurement tools and statistical methods. The finding is contradictory to the finding of Chen and team (2011), who reviewed literature reporting empirically determined symptom clusters in lung cancer patients. They excluded studies examining the presence of predetermined clusters, and reported on five studies published between 1997 and 2009 (Gift et al., 2004; Henoch, Ploner, & Tishelman, 2009; Sarna & Brecht, 1997; Wang et al., 2008; Wang et al., 2006). They showed that the authors of these five studies reported significantly diverse findings with regards to composition of symptom cluster in lung cancer patients. The number of symptoms in a cluster ranged from 2 to 11. The only cluster that was consistently identified in two studies was composed of nausea and vomiting symptoms. Respiratory clusters identified in two studies were also comparable, containing both dyspnea and cough, among other symptoms. Methodological

disparities, including differences in sample population characteristics, assessment tools and analytical methods, were evident in the five studies reviewed. The authors noted that when data were analyzed using the same statistical method, different symptom assessment tool yielded significantly contrasting symptom clusters, but when different analyses employing varied analytical methods were used to analyze data collected using the same instrument, similar symptom clusters were obtained. This finding may suggest that the statistical methods used plays a lesser role in the determination of results that do the tools used for data collection (Chen et al., 2011).

## Clustering of Symptom Clusters in Lung Cancer

### Symptom clusters in lung cancer using the "Most Common Symptom Approach."

There are 2 studies that used tested proposed clusters using correlational analysis (strategy 1). First, Chan and colleagues (2005) assessed the existence of a symptom cluster involving breathlessness, fatigue and anxiety in patients with advanced lung cancer undergoing palliative radiation. The researchers measured the intensity of anxiety, breathlessness and fatigue at 3 points in time: 1 day prior to palliative radiotherapy (RT) (baseline, T0), and at week 3 (T1) and week 6 (T2) after the commencement of the RT. They found that the correlations between the 3 symptoms were moderately strong at T1 and T2, and that the proposed symptom cluster had high internal consistency all three time points. These data support the notion that the symptoms—breathlessness, fatigue, and anxiety—may be viewed as a symptom cluster. Second, Fox and Lyon (2006) explored the relationship between pain, fatigue, and depression in 51 patients with lung cancer, and found fatigue and depression were correlated significantly with each other. Both of these studies showed a significant relationship between their respective symptom clusters and quality of life.

A second group of authors studied interaction effects within symptom clusters (strategy 4). The interaction effect postulates that "the differing effect of one independent variable on the dependent variable depends on the particular level of another independent variable" (Cozby, 1997). Hoffman and team (2007) examined the relationships among pain, fatigue, insomnia, and gender while controlling for age, co morbidities, and stage of cancer in 80 patients newly diagnosed

with lung cancer within 56 days of receiving chemotherapy. Multinomial log-linear modeling was performed to explain the relationships among pain, fatigue, insomnia, and gender. A model containing all main effects showed two-way interactions among pain and fatigue, pain and insomnia, and insomnia and gender, and a three-way interaction among pain, fatigue, and insomnia, along with three covariates. Parameter estimates indicated that the three-way interaction among pain, fatigue, and insomnia was statistically significant (Hoffman et al., 2007).

**Symptom clusters in lung cancer using the "All Possible Symptom Approach"**

Sarna and Brecht (1997) were the first authors to study cluster symptoms in lung cancer patients. The primary endpoint of their study was to explore the structure of symptom distress in women with advanced lung cancer receiving palliative treatment. To identify symptom combinations, the authors used principal component analysis with varimax rotation. Their results showed symptoms clustered in 4 groups. These clusters were emotional and physical suffering, gastrointestinal distress, respiratory distress, and malaise.

Gift and colleagues have conducted several studies of symptom clusters using the "All Possible Symptoms" approach. Gift and team (2003) identify a cluster of symptoms at 3 and 6 months after diagnosis in newly diagnosed with lung cancer patients by used an exploratory factor analysis. They found that the symptoms of fatigue, nausea, weakness, appetite loss, weight loss, altered taste, and vomiting formed a cluster. In a later study, Gift and colleagues (2004) surveyed another sample of newly diagnosed patients with lung cancer. Using factor analysis to find and extract clusters, they again found one cluster comprised of the same symptoms as their earlier study: nausea, fatigue, weakness, appetite loss, weight loss, altered taste, and vomiting. Patients receiving chemotherapy experienced more symptoms in that cluster. In addition, the results found that the number and severity of symptoms in a cluster was significantly related to physical function. Wang and team (2008) explore the symptom clusters and relationships to symptom interference with daily life in Taiwan lung cancer patients. The top five most-severe symptoms were fatigue, sleep disturbance, lack of appetite, shortness of breath, and general distress.

Factor analysis generated a two-factor solution (general and gastrointestinal symptoms) for symptom severity items.

There was the study of symptom clusters have been conducted with Thai individuals with advanced lung cancer by Pudthong and colleague (2011). Participants were Thai patients with advanced lung cancer. The result found that lung cancer patients experienced multiple symptoms, averaged 14.65 symptoms. Coughing was reported the most common symptom. Seven symptom clusters were identified. The factors were labeled as: body image symptom cluster, neuropsychological symptom cluster, sleep alteration symptom cluster, digestive impairment symptom cluster, dermatologic and dizziness symptom cluster, bowel-emotional dysfunction symptom cluster, and pain related discomfort symptoms cluster. The other study was published by Chaiviboonthom et al (2011). Subjects were 240 Thai patients with various advanced cancer. The results found that four symptom clusters were identified: pain, sickness-behavior and psychological; anorexia-cachexia; gastro-intestinal and elimination; and, “cutaneous and other.”

Within the “All Possible Symptoms” approach, it is possible to investigate changes over time. Wang and team (2006) conducted a longitudinal study of advanced lung cancer patients undergoing chemoradiation therapy (CXRT). Four symptom cluster patterns appeared during CXRT: steady increase which included pain and sore throat; early increase which included nausea and vomiting; early/late increase which included fatigue, lack of appetite, drowsiness, sleep disturbance, dry mouth, and distress; and minimal change which included sadness, difficulty remembering, and others. Although other longitudinal studies have been conducted to identify symptom cluster changes (Chow et al., 2007; Gleason et al., 2007; Jarden et al., 2009; Kim et al., 2009a, 2008; Molassiotis et al., 2010), the study by Wang and colleagues (2006) is the only study comparing symptom cluster based on the symptom severity changes over time. The underlying mechanism and clinical meanings of the results from this method are still unclear.

## Performance outcome: Functional status

The outcome concept in the TOUS is performance. It represents the consequences of the symptom experience. Performance is conceptualized to include functional and cognitive activities. The concept of performance has several possible dimensions: physical activity and impairment; functional role performance, including activities of daily living; cognition, including comprehension, learning, concentration, and problem solving; and social interaction (Lenz et al., 1997). Quite simply, the theory asserts that the experience of symptoms can have an impact on the individual's ability to function, with function including motor skills, social behaviors, and cognition. The specification of performance as the key outcome of the model reflects a pragmatic orientation as well as a desire for relatively straightforward measurability.

Several research groups have examined the impact of symptom clusters on various outcomes including quality of life, mortality, and functional status. For example, Fox and Lyon (2006) explored the prevalence and intensity of depression, fatigue, and pain in survivors of lung cancer, and examined the relationship of symptoms in a cluster to quality of life (QOL) of lung cancer patients. The results found that the cluster had a negative relationship with QOL. Mortality is another common health outcome. For example, in a longitudinal study to identify symptom clusters in patients with lung cancer, Gift and team (2003) found that symptom clusters were stable over the course of lung cancer and that the severities were an independent of these cluster symptoms predictor of death.

The Oncology Nursing Society work on evidence-based outcomes has identified the return of physical function as an important outcome for cancer (Given, Given, Sikorskii, & Hadar, 2007). Several researchers have reported that cancer patients experience severe symptom distress caused by a combination of symptoms, which has a strong negative impact on patient physical functioning (Cooley, 2000; Gift, Stommel, Jablonski, & Given, 2003; Tishelman et al., 2005). In addition, several studies have focused on patients with lung cancer found these patients have severe symptoms that had a strong negative impact on patient physical functioning (Cooley, 2000; Gift, Stommel, Jablonski, & Given, 2003; Tishelman et al., 2005). In this study, functional status was selected as a performance outcome.

**Concepts of Functional Status**

The Oncology Nursing Society work on evidence-based outcomes has identified the return of functional status as an important outcome for cancer (Oncology Nursing Society, 2006). Functional status is a significant component of quality of life and plays an important role in assessing the patients when they are first diagnosed with lung cancer, monitoring responses of the patients to medical treatments, and predicting prognosis, survival rates, and progression of the disease (Kurtz, Kurtz, Stommel, Given, & Given, 2000).

The concept of functional status has been defined in various ways both within the discipline of nursing and by other health-care disciplines. Functional status refers to individuals' actual performance of activities and tasks associated with their current life roles (Richmond, 2004). Wang (2004) defined functional status as activities performed by people in the normal course of their lives to meet basic needs, fulfill usual roles, and maintain their health and well-being. The levels of performance correspond to normal expectations of individuals according to their nature, structure, and conditions.

Tulman and Fawcett (1991) defined functional status as a multidimensional concept that encompasses continuation of usual household and family, social and community, personal care, and occupational activities following diagnosis of cancer. Tulman and Fawcett (1991) was designed The Inventory of Functional Status-Cancer (IFS-CA) which is a self-report instrument that was directly derived from the role function mode of the Roy Adaptation Model of Nursing. In keeping with the Roy Adaptation Model role function mode, functional status is defined as a multidimensional concept that encompasses performance of and feelings about various activities associated with primary, secondary, and tertiary roles. The Roy Adaptation Model takes 3 categories of roles primary, secondary, and tertiary into account. Performance of primary role behaviors is represented by the personal care activities dimension of functional status, such as bathing, dressing, eating, exercising, relaxing, resting, and sleeping. Performance of secondary role behaviors is represented by the dimensions of household and family, activities and occupational activities, such as cleaning, cooking, doing dishes, shopping, caring for spouse and children, amount of job responsibilities, and hours worked. Performance of tertiary role behaviors are

represented by the dimension of social and community activities such as participation in community and religious organizations, socializing with friends and relatives, and time spent on hobbies.

There is a plethora of articles in the literature regarding functional status in various populations; however, it has only been analyzed conceptually in one nursing publication by Leidy in 1994. Functional status is an individual's ability to perform normal daily activities required to meet basic needs, fulfill usual roles, and maintain health and well-being. From the analytical framework of functional status of Leidy (1994), the constructs of functional status are abilities and activities necessary to human life. Activities people choose to perform are based on their personal preferences and their capacities.

Leidy (1994) suggests that there are four dimensions of functional status that should be distinguished in assessing outcomes: functional capacity, performance, reserve, and capacity utilization. Functional capacity is an individual's maximum potential to perform activities. These activities people do in the normal course of their lives to meet basic needs, fulfill usual roles, and maintain their health and well-being level. Functional performance refers to the day-to-day corporeal activities people do in the normal course of their lives. These activities are the outcome of individual choice, subject to limits imposed by capacity. Functional reserve is the difference between capacity and performance and refers to latent or dormant abilities that can be called upon in times of perceived need. Finally, functional capacity utilization is the extent to which capacity is called upon in the selected level of performance. This dimension of functional status accounts for the common observation that two patients with the same apparent capacity can display different levels of performance. Both functional reserve and functional capacity utilization add clarity to the understanding of functional status. The terms ‘functional ability’ and ‘functional capacity’ are often used interchangeably with functional status (Leidy, 1994).

Based on the critical attributes identified, it is clear that functional status can be best differentiated from functional ability or functional capacity as the ‘‘actually performed versus ability to perform.’’ Although Leidy (1994) suggested that functional status should include both performance and capacity, in most instances functional status was used to indicate performance only (Wang, 2004). Functional

status can be influenced by biological or physiological impairment, symptoms, mood, and other factors. It is also likely to be influenced by health perceptions. In the proposed study my operational definition of functional status is focused on actual performance.

**The Measurement of Functional Status**

Functional status assessment originated in rehabilitation practice for the purpose of determining capacity in relation to expected performance. Assessment scales developed to operationalize functional status were used primarily to assess activity performance of daily living to determine disability and facilitate clinical management.

Functional status measurement defined as ‘‘any systematic attempt to measure the level at which a person is functioning in a variety of areas, such as physical health, quality of self-maintenance, quality of role activity, intellectual status, social activity, attitude toward the world and toward self, and emotional status’’ (Moinpour, McCorkle, & Saunders, 1992). Functional status assessment is carried out through professional observation, testing, and/or self-report by the patient or a proxy. Hundreds of specialized instruments have been developed to assist practice in such areas as geriatrics, psychiatry, and nursing practice. Functional status measures can be further grouped into those that are generic and those that are designed for specific conditions. Generic measures are designed to assess functional status regardless of an individual’s impairment or disability. Condition specific measures are designed to be sensitive to the specific impairment or disability of interest (Cohen & Marino, 2000). Some functional status instruments are generic, such as;

1) The SF-36 Health Survey includes one multi-item scale measuring each of the eight health concepts and includes a single-item measure of health transition or change. The SF-36 can also be divided into two aggregate summary measures the Physical Component Summary (PCS) and the Mental Component Summary (MCS) (Ware Jr & Hays, 1988). The SF-36 Health Survey items and scales were constructed using the Likert method of summated ratings. Answers to each question are scored (some items need to be recoded). These scores are then summed to produce raw scale scores for each health concept which are then

transformed to a 0 – 100 scale. Scoring algorithms can then be applied to produce the PCS and MCS scores (These two summary scores have the major advantage of being norm based. They also have reduced floor and ceiling effects.) (Ware Jr & Sherbourne, 1992).

2) The Katz Index of Independence in Activities of Daily Living, commonly referred to as the Katz ADL, is the instrument to assess functional status as a measurement of the client's ability to perform activities of daily living independently. The Index ranks adequacy of performance in the six functions of bathing, dressing, toileting, transferring, continence, and feeding. Clients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicate moderate impairment, and 2 or less indicates severe functional impairment. It does not assess more advanced activities of daily living. Katz developed another scale for instrumental activities of daily living such as heavy housework, shopping, managing finances and telephoning. Although the Katz ADL Index is sensitive to changes in declining health status, it is limited in its ability to measure small increments of change seen in the rehabilitation of older adults (Katz, Downs, Cash, & Grotz, 1970).

3) The Barthel Index consists of 10 items that measure a person's daily function specifically the activities of daily living and mobility. The assessment can be used to determine a baseline level of functioning and can be used to monitor improvement in activities of daily living over time. The items are weighted according to a scheme developed by the authors. A score of 0, 5, 10 or 15 is assigned to each level; overall scores range from 0 to 100. The scores are intended to reflect the amount of time and assistance a patient requires. "The person receives a score based on whether they have received help while doing the task. The scores for each of the items are summed to create a total score. The higher the score mean the more "independent" the person. Independence means that the person needs no assistance at any part of the task. If a person does about 50% independently then the "middle" score would apply. The advantage of the instrument is its simplicity (Shah, Vanclay, & Cooper, 1989; Van der Putten, Hobart, Freeman, & Thompson, 1999).

4) Functional Independence Measure (FIM). The FIM is an 18-item, 7-level scale developed to uniformly assess severity of patient disability and

medical rehabilitation functional outcome. The FIM's assessment of degree of disability depends on the patient's score in 18 categories, focusing on motor and cognitive function. Each category or item is rated on a 7-point scale (1 = <25% independence; total assistance required, 7 = 100% independence) (Chumney et al., 2010).

5) The Lawton Instrumental Activities of Daily Living (IADL) is an appropriate instrument to assess independent living skills (Lawton & Brody, 1969). These skills are considered more complex than the basic activities of daily living as measured by the Katz Index of ADLs. The instrument is most useful for identifying how a person is functioning at the present time, and to identify improvement or deterioration over time. There are eight domains of function measured with the Lawton IADL scale. Women are scored on all 8 areas of function; historically, for men, the areas of food preparation, housekeeping, laundering are excluded. Clients are scored according to their highest level of functioning in that category. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women, and 0 through 5 for men (Lawton & Brody, 1970; Self-maintenance, 1969). The Lawton IADL is an easy to administer assessment instrument that provides self-reported information about functional skills necessary to live in the community. Administration time is 10-15 minutes. Specific deficits identified can assist nurses and other disciplines in planning for safe discharge.

6) Functional status questionnaire (FSQ) is a 34 item questionnaire that covers the following domains related to activities of daily living: basic and intermediate activities; mental health; work performance; social activity; and quality of interaction, as well as some non-categorized items. The Functional Status Questionnaire can be used as a self-administered functional assessment for a patient seen in primary are. It provides information on the patient's physical, psychological, social and role functions. It can be used both to screen initially for problems and to monitor the patient over time (Jette, 1980).

7) Sickness Impact Profile (SIP) is a behaviorally based self-report measure used to evaluate the impact of disease on both physical and emotional functioning. Patients are asked to respond to the items as they are on that day. It contains 136 items that are divided into 12 categories. In addition to category scores

and the overall score, the instrument can be used to calculate a physical and a psychosocial dimension score. It is intended for use in measuring the outcomes of care in health surveys, in program planning, in policy formation and it is also used in monitoring patient progress. It is known as a valid and reliable measure of functional status (Jette, 1980).

The specific functional assessments are disease-specific, such as*;*

1) Edmonton Functional Assessment Tool (EFAT) is a tool to evaluate functional performance of patients with advanced cancer over time and to document the degrees of functional performance of patients throughout the terminal phase. It assesses the status of 10 functions, mainly; communication, pain, mental status, dyspnea, sitting or standing balance, mobility, walk or wheelchair locomotion, activities of daily living, fatigue and motivation. These are assessed by the Physical and Occupational Therapists and are quick, simple and don't require much training. Each item in the EFAT is evaluated by a 4 point rating scale from 0 to 3 (0 = functional independent performance; 3 = total loss of functional performance). A total possible score on the EFAT is 30. In addition to the EFAT a global performance status rating (PS) asks for an overall judgment of functional performance taking into account the 10 functions assessed by the EFAT (Kaasa, Loomis, Gillis, Bruera, & Hanson, 1997).

2) Karnofsky Performance Scale (KPS) is commonly used for assessing terminally ill patients, often used to determine appropriateness of hospice referral. The Karnofsky index was introduced in the 194Os, at the beginning of cancer chemotherapy (Karnofsky, 1949). It is rated on a scale of O-100, in steps of 10. It describes the patient’s ability to perform normal activity and do active work, and whether there is any need for assistance. At 100 all is well; at 0 the patient is dead. KPS has proved useful and has survived in both practical and scientific oncology.

3) ECOG Performance Status. A tool for doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient, and how to determine appropriate treatment and prognosis runs from 0 to 5, with 0 denoting perfect health and 5 death. Its advantage over the Karnofsky scale lies in its simplicity (Oken et al., 1982).

4) The Inventory of Functional Status-Cancer (IFS-CA) was developed to measure functional status in women with cancer. The questionnaire includes four subscales measuring the extent to which the woman continues her usual household and family, social and community, personal care, and occupational activities. The IFS-CA is a 39-item questionnaire. It consists of four subscales of household and family, social and community, personal care, and occupational functions, with a 4-point rating scale ranging from 1 (not at all) to 4 (fully) for household, family, social, and community activities; and 1 (never) to 4 (all of the time) for personal care and occupational activities (Portenoy, Thaler, Kornblith, McCarthy Lepore, Friedlander-Klar, Kiyasu et al., 1994).

Several issues surround the selection of an instrument to measure function. Issues to consider include the primary purpose of measurement, the match between the theoretical dimension of function (functional ability, functional status), the focus of the instrument, the unique requirements of the population of interest, and methodologic concerns (Richmond, 2004). For this study, the specific measurement is suitable for measuring functional status of lung cancer patients receiving chemotherapy which need the instruments that can detect important changes that occur over time in the disease. The Inventory of Functional Status-Cancer (IFS-CA) is selected for measuring functional status of lung cancer patients in this study. This instrument was designed to approach to measurement of functional status to the situation of serious illness. The IFS-CA was derived from role function mode of Roy's Adaptation Model of Nursing. The IFS-CA obtains a baseline of the patient's usual activities and compares current level of functioning in all areas to that baseline (Tulman et al., 1991). Furthermore, the instrument has been guided by an explicit conceptual model of nursing and, therefore, reflects a distinctive nursing perspective of functional status.

**Influences of Symptom Experiences on Functional Status**

Symptom clusters were found having synergistic effects on the functional status in oncology patients in general (Chen & Tseng, 2006; Dodd et al., 2001). There is preponderance of data that has demonstrated negative associations between functional status and the number or severity of symptom clusters (Ferreira et al., 2008;

Fox, Lyon, & Farace, 2007; Suwisith et al., 2008). Miaskowski et al (2006) found that patients who reported low levels of all four symptoms (pain, sleep disturbance, fatigue, and depression) reported the best functional status. This result was confirmed by Pud et al (2008) cross-sectional investigation and Dodd et al (2010) longitudinal research. A study further found that symptom clusters explained 17.4-19.8% of the variance in functional status (Suwisith et al., 2008).

There were studies on the influences of the symptom experiences on functional status in lung cancer patient.

Sarna (1994) conducted study that was to describe physical functional status in women with lung cancer. The typical subject had non-small cell limited disease, and was not currently receiving treatment. The most prevalent disruptions in physical function were reduced energy, difficulty with household chores, and interference with work. A third of the sample had serious limitations in three or more activities. Approximately 26% of the sample had severe limitations in moderate activities. Physical function was different by income category, with those with the lowest income having the poorest function.

Gift and team (2003) identify a cluster of symptoms at 3 and 6 months after diagnosis in lung cancer patients. The results found that the number of symptoms reported in the cluster of fatigue, dyspnea, weakness, vomiting, and pain was significantly related to physical function and role limitations in a group of patients with lung cancer. However, this study has limitations that the effect of age on functional limitations was not controlled for in this study. Increasing age typically is associated with greater numbers of comorbidities and declining functional status. To what extent functional limitations resulted as a natural consequence of aging as opposed to the symptom experience is unclear.

Gift, Jablonski, Stommel, & Given (2004) conducted research that aims were identify the number, type, and combination of symptoms experienced by patients with lung cancer and describe the relationships among symptoms reported, demographic variables, disease characteristics, and perceived level of functioning. The result found that the number of symptoms reported in the cluster of fatigue, dyspnea, weakness, vomiting, and pain was significantly related to physical function and role limitations in a group of patients with lung cancer.

Siefert (2010) examined the relationship of fatigue and pain with functional status and the pattern of the two symptoms' occurrence over time in individuals with cancer who were receiving chemotherapy. The results found that most frequently reported symptom; pain was rarely and almost exclusively reported by patients with lung cancer or lymphoma during their early treatments. Fatigue and functional status impairment were highly associated with each other and had similar relationships with the other variables. A significant difference existed in functional status when treatment number was controlled. The level of functional status differed significantly over time. The low number of comorbidities an also helps to explain the overall low level of functional status impairment.

There were very few studies on the effect of the symptom cluster on functional status in lung cancer patient (Gift, Jablonski, Stommel, & Given, 2004; Siefert, 2010). The results found that patients with lung cancer suffered from multiple symptoms that significantly related to functional status. However, some studies used a patient group with a range of different cancers (Dodd, Miaskowski, & Paul, 2001; Siefert, 2010). This can be problematic because cancer encompasses a diverse array of illnesses, each with particular difficulties patients face. In addition, most studies were conducted in western countries and thus do not provide information about whether difference attributable to culture could affect perceptions, evaluation, and response to symptoms.

## Gaps in Knowledge

### Gaps in Understanding about Symptom Cluster

There are several issues that need to be addressed in order to understand the impact of symptom clusters on functional status. These critical considerations are grouped as: conceptual issues and methodological problems (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006; Fox, Lyon, & Farace, 2007; Miaskowski et al., 2007; Xiao, 2010), there is still disagreement about some essential elements in the definition of symptom clusters. For instance, different researchers have different understandings of the relationship between symptoms in a cluster. Some have identified the relationship by the correlation between and among symptoms (Gift et al., 2003).

Others have measured the relationship based on the effect of symptoms on outcomes (Fox et al., 2007). In order to clarify the meaning of relationships between and among symptoms in a cluster, it will be necessary to define the concept of symptom clusters.

Another discrepancy in the definition of symptom clusters is the minimum number of symptoms constituting a cluster. Many data-based studies have since shown that two symptoms clustered have negative influences on patient's quality of life or functional status (Chen and Lin, 2007; Chow et al., 2007; Walke et al., 2007), while others have said that a cluster must include at least three symptoms (Bender, Erg n, Rosenzweig, Cohen, & Sereika, 2005; Dodd et al., 2001). Additionally, it is also not well understood whether all symptoms in a cluster should be presented at the same time (Kim et al., 2008; Molassiotis et al., 2010). These discrepancies reflect different understandings of the concept of symptom clusters. Variations in study designs, cluster identification methods, and characteristics of study samples could also contribute to these discrepancies. Determining the clinical and theoretical significance of symptom clusters might clarify these issues.

The second knowledge gap is related to methodological issues. Many previous studies commonly determined symptom experiences and cluster using only one dimension, usually focused on severity or distress. However, symptom experiences are multidimensional. So, determination of symptom clusters using different dimensions is needed. The number and types of symptom clusters need to be compared. The benefit could lead to better understanding on the different dimensions of symptom clusters between symptom severity and symptom distress (Miaskowski et al., 2007).

The third knowledge gap is grouping individuals based on their symptom experience has occurred in a few studies of oncology patients (Dodd, Cho, Cooper, & Miaskowski, 2010; Ferreira et al., 2008; Gwede, Small, Munster, Andrykowski, & Jacobsen, 2008; Pud et al., 2008). To date, no published study identifying distinct subgroups of lung cancer patients who differed on symptom experience during chemotherapy treatment. The finding can guide treatment/management of disease- or treatment related symptoms through interventions tailored to individuals in each group (Gwede et al., 2008). The result will allow clinicians to target specific symptom management interventions to each subgroup.

**The Gaps of Existing Knowledge about Symptom Cluster in Lung Cancer Patients**

Symptom cluster research is in its early stages, and many questions remain unanswered in this field. The literature search in the present review found 15 articles about symptom cluster in patients with lung cancer between 1997 and 2014 (Akin, Can, Aydiner, Ozdilli, & Durna, 2010; Brown, Cooley, Chernecky, & Sarna, 2011; Chan, Richardson, & Richardson, 2005; Chen et al., 2011; Fox & Lyon, 2006; Gift et al., 2004; Gift, Stommel, Jablonski, & Given, 2003; Henoch, Ploner, & Tishelman, 2009; Hoffman et al., 2007; Kuo & Ma, 2002; Molassiotis, Lowe, Blackhall, & Lorigan, 2010; Sarna & Brecht, 1997; Wang, Tsai, Chen, Lin, & Lin, 2008; Wang et al., 2006; Pudtong, 2011). The number of symptoms in a cluster ranged from 2 to 11. The only cluster that was consistently identified in two studies was composed of nausea and vomiting symptoms. Respiratory clusters identified in two studies were also comparable, containing both dyspnea and cough, among other symptoms. The majority of current symptom cluster research associated with lung cancer is cross-sectional in nature.

The literature review reveals gaps existing knowledge about symptom clusters in lung cancer patients which can be concluded that the evidence of symptom clusters and their influences on individual outcomes in lung cancer patients are not well documented and the studies have been recently undertaken. Symptoms are multidimensional. All of previous lung cancer studies determined symptom cluster using only severity or distress dimension. No study compare the similarity of symptom cluster classify by severity and distress dimension. In addition, no information has been found on symptom cluster of multidimensional and their influences on the functional status in Thai patient with advanced lung cancer. A clear understanding is needed of what effects the combinations of symptoms have on the patients' level of functioning. In addition, no published study identified distinct subgroups of advanced lung cancer patients who differ on symptom experience.

Therefore, studying symptom clusters and their effect on the functional status in advanced lung cancer patients receiving chemotherapy, as well as identifying distinct subgroups of advanced lung cancer patients who differ on symptom experience and functional status will fill these gaps of knowledge. To fill the gaps of

knowledge in this area as previously mentioned, this study aims to; 1) describe symptom experiences in all dimensions, 2) explore the existence of symptom clusters in severity and distress dimensions, 3) compare the similarity of symptom cluster classify by severity and distress 4) determine the influences of symptom cluster on the functional status, 5) determine whether subgroups of lung cancer patients with different symptom experiences differ in their functional status_Such knowledge can guide clinicians to treatment/management of disease- or treatment related symptoms through interventions tailored to individuals in each group which could improve patient outcomes (Gwede, et al., 2008; Miaskowski et al., 2006; Gwede et al., 2008; Pud et al., 2008).

# CHAPTER III
# METHODOLOGY

This chapter provided description of research methodology used in this study including research design, population and sample, setting, research instruments, ethical considerations, data collection procedures, and data analysis.

## Research Design

A cross-sectional descriptive design was used to investigate symptom clusters of advanced lung cancer patients receiving the course of chemotherapy.

## Population and Samplings

The target populations in this research were the patients with advanced lung cancer patients who were receiving chemotherapy at the Chemotherapy and Blood Transfusion Unit of the Out-Patient Department of Siriraj Hospital and the National Cancer Institute of Thailand.

### Sample

The patients with advanced lung cancer who met eligibility criteria were recruited to participate in the study using convenience sampling. The inclusion criteria were: 1) being an adult, i.e. 18 years of age or older, 2) being a newly diagnosed of lung cancer and receiving chemotherapy for lung cancer treatment, 3) receiving chemotherapy treatment at least 1 cycle. The period of this cycle is 1-4 weeks after the last chemotherapy, 4) willing to participate in the study. The exclusion criteria include: 1) having uncontrolled psychiatric diseases, 2) having brain metastasis resulting in poor cognitive functions, 3) being unable to answer the questionnaires or be interviewed due to poor health status.

**Sample size**

The optimal sample size in this study based on the statistical tests used to answer the research questions. This study used the factor analysis to identify symptom clusters. The number of subjects needed was usually assessed in relation to the number of variables being measured. The number of cases should always exceed the number of variables. In general, a ratio at least 10 subjects for each variable (item) is desirable to generalize from the sample to a wider population (Dixon, 2005; Hair, Anderson, Tatham & Black, 1995; Knapp, 1999). However, Hair and colleagues (2010) suggest that the minimum of at least five subjects per variable is acceptable, and the more acceptable size would have a ten-to-one ratio (Hair, Black, Babin, Anderson, & Tatham, 2010).

The numbers of symptoms being investigated in this study were 32 symptoms. The sample size of this study was therefore at least 160 cases. Ten percent of the total number of samples was needed as over-estimation to account for incomplete questionnaires, which is equal to 32 cases. In addition, 30 cases of patients with lung cancer were participated in a pilot study. At the initial recruitment, 330 participants were willing to participate in this study. Thus, the remaining participants, who consented in participating in this study, were 300. This number of participants was adequate to determine symptom cluster. Thus the participants from the Chemotherapy and Blood Transfusion Unit of the Out-Patient Department of Siriraj Hospital were 200 and from the National Cancer Institute of Thailand were 100. The samples of both setting were similar in terms of chemotherapy treatment protocol and service care.

## Settings

Data were collected at the National Cancer Institute of Thailand and the Chemotherapy and Blood Transfusion Unit of the Out-Patient Department of Siriraj Hospital, as most patients with lung cancer usually access cancer treatments in these places where treatment and care services were provided to cancer patients receiving chemotherapy, which includes making appointment with and teaching to the patients and their caregivers regarding chemotherapy treatment plan, potential side effects, and

ways to manage the symptom following up the patients' conditions; offering telephone consultation for patients and caregivers who could call for information during the service hour specified, and providing chemotherapy treatment to patients. Similarly, The National Cancer Institute of Thailand (NCI) is part of the Department of Medical Services under the Ministry of Public Health. NCI has approximately 30 beds for cancer patients receiving chemotherapy treatment. NCI provides chemotherapy treatment and care services to patients with cancer from Mondays to Fridays.

## Instruments

**1. Demographic and Medical Record Form (DMRF)** was used to obtain information about personal data and medical history. Personal data was included age, gender, education, marital status, religion, income and financial status, living arrangement, method of payment for medical expenses, and sources of support. Medical history was included the type of treatment received, and length of time since diagnosis with lung cancer, medications and other illnesses not related to lung cancer.

**2. The Memorial Symptoms Assessment Scale (MSAS)** was used to measure the symptoms experienced by the subjects. The instrument includes data regarding symptom occurrence, frequency or prevalence, severity or intensity and distress for 24 symptoms, and symptom prevalence, severity or intensity, and distress only for another 8 symptoms. In developing the MSAS, Portenoy and team (1994) omitted to investigate the frequency of eight symptoms (mouth sore, change in the way food taste, weight loss, hair loss, constipation, swelling of arms or legs, image change, and change in skin.) because these symptoms can persist for a long period of time and the pattern of their occurrences might not be observed or notice by the individual for a short period of time. This instrument was completed by the patient based on their experience in the previous 7 days (after they received chemotherapy for 7 days) and all symptoms were rated using a Likert scale. Occurrence is rated "yes" or "no". If the symptom was not present (no), a value of zero was assigned. For the symptoms answered "yes", patients were asked to rate symptoms based on severity using 4-point rating scale ranging from 1 (slight) to 4 (very severe), to rate frequency was using a 4-point rating scale ranging from 1 (rarely) to4 (almost constantly). The

scales of symptom distress is using a 5-point rating scale ranging from 0 (not at all) to 4 (very much) with 0.8, 1.6, 2.4, 3.2 and 4 as suggested by the original instrument (Poternoy et al, 1994). An additional 8 symptoms were evaluated using these same scales for prevalence, severity or intensity, and distress only. Validity of MSAS has been confirmed with the reporting of a strong correlation of MSAS with Functional Living Index for Cancer (FLIC) quality of life measurement and Karnofsky Performance Status Scale (KPS) (Portenoy et al., 1994). This instrument was translated into Thai using the back translation technique by Suwisith, et al (2008); the internal consistency for all items in the back translated MSAS was 0.96.

Reliability of this instrument was examined in 246 inpatients and outpatients with prostate, colon, breast or ovarian cancer. Three major subscales were defined as phychological (PHYCH), High prevalence physical (PHYS-H), and low prevalence physical (PHYS-L). The internal consistency for the psychological symptoms in this scale was 0.83, for the high frequency physical symptoms was 0.88, and for low frequency physical symptoms was 0.58 (Portenoy et al., 1994). The use of MSAS was reported in several studies but only a few studies reported their reliability testing. The internal consistency of the subscales of this instrument ranged from 0.78-0.87 and physical subscales were ranged from 0.82-0.85 (Lobchuk, 2003).

A Thai version of MSAS was translated by Suwisith (2007) and used in a symptom cluster study among Thai women with breast women with breast cancer. The reliability of translated MSAS was use one-day test-retest reliability in a pilot study of 29 women with breast cancer receiving treatment. The test-retest results were significantly a highly correlated (r= 0.82-0.88). Cronbach's alpha coefficient of MSAS in the main study (N=317) of each dimension was ranged from 0.89-0.93. Furthermore, the modified MSAS was used in 190 Thai women with cervical cancer undergoing treatment program Cronbach's alpha coefficient range from 0.78-0.91 (Sumdaengrit, 2010). Four symptoms from the literature review were added in this study including vaginal discharge, rectal irritation, headache, and fever.

In this study, the researcher conducts a pilot test for reliability of the Modified Memorial Symptom Assessment Scale (MSAS) in 30 Thai advanced lung cancer patients receiving chemotherapy. The Cronbach's alpha coefficients for pilot and main study were shown in Table 3.1

**Table 3.1 Reliability tests of the MSAS in a pilot study and the main study**

| Subscales | Cronbach's alpha | |
|---|---|---|
| | **Pilot study ( N = 30)** | **Main study ( N = 300)** |
| Symptom prevalence | .762 | .723 |
| Symptom frequency | .806 | .732 |
| Symptom severity | .834 | .791 |
| Symptom distress | .827 | .811 |
| **Total** | **.946** | **.934** |

**3. Functional status**: **The Inventory of Functional Status-Cancer (IFS-CA)** was used to determine functional status in this study. The tool was first developed aiming to assess functional status of women with breast cancer during and after receiving chemotherapy based on the Roy adaptation model role function response mode, which reflects activities associated with a person's primary, secondary, and tertiary roles (Tulman & Fawcett, 1991). The IFS-CA, a 39-item Questionnaire, consisted of four constructs of household and family (item number 1- 15), social and community (item number 16-21), personal care (item number 22-31), and occupational functions (item number 32-39 for participant still working only). Using this instrument, individuals must rate from 1 (not at all) to 4 (fully) for household, family, social, and community activities; and 1 (never) to 4 (all of the time) for personal care and occupational activities. A "not applicable" code, which was excluded from score calculations, was used for items not engaged in by a patient prior to diagnosis with lung cancer. There were eight items that were negative questions which were recoded backwardly when analyzed. They were the item number 22, 23, 25, 27,28,33,34 and 36. The total IFSCA score was finally computed. The higher score represented greater total functional status. A mean score was calculated for each subscale and for the total score based on the number of relevant items. Mean total score; 1-1.99 = very limited functional activities, 2-2.99 = partially limited, 3-3.99 = moderate or less limited, 4 = fully function or no limited functional activities.

The IFS-CA has been used in patients diagnosed with different types of cancer (Suwisith et al., 2008; Thanasilp & Kongsaktrakul, 2005; Tulman, Fawcett, & McEvoy, 1991). Reliability of IFS-CA was reported with internal consistency of 0.56-

0.92 and test-retest was 0.91 in the study of Tulman et al. (1991). The subscale coefficients ranged from .64 to .74 for the baseline administration of the IFS-CA were reported in the study of Samarel, Fawcette and Tulman (1997). Content validity was established at 98.5% (Tulman et al., 1991). This instrument was translated into Thai by Suwisith et al (2008); the internal consistency for all items in the back translated IFS-CA was 0.89. This instrument was used in Thai patients diagnosed with cancer (Suwisith et al., 2008; Thanasilp & Kongsaktrakul, 2005). Alpha Cronbach reliability of IFS-CA in Thai patients with breast and lung cancer was 0.92 in the study of Tanasilp and Kongsaktrakul (2005). In this study, the researcher conducted a pilot test for reliability of The Inventory of Functional Status-Cancer (IFS-CA) in 30 Thai advanced lung cancer patients. The Cronbach's alpha values for household and family, social and community, personal care, occupational and total functional subscales in a pilot and the main study were shown in Table 3.2

**Table 3.2 Reliability tests of the IFS-CA in a pilot study and the main study**

| Subscales | Cronbach's alpha | |
|---|---|---|
| | Pilot study ( N = 30) | Main study ( N = 300) |
| Household and family functions | .730 | .754 |
| Social and community functions | .835 | .729 |
| Personal functions | .538 | .519 |
| Occupational functions | .990 | .985 |
| **Total** | **.911** | **.880** |

## Protection of Human Rights

The study proposal was submitted to the Institutional Review Board (IRB) of Mahidol University, Siriraj hospital, and the National Cancer Institute of Thailand (NCI). After receiving a letter of approval from the committee, the researcher explained the study to the head nurse and staff nurses.

The researcher informed potential participants about the purpose and design of the study. Participants were not pressured or coerced to participate in this

study. All participants' confidentiality was protected by using code numbers on all data forms. Their names were not appearing on questionnaires. Confidentiality was protecting. Only the researcher (the doctoral student) and her advisor can access to these data. The participants were informed that at any point in the study they could withdraw with no effect on treatment or services they should receive and with no question to be asked.

## Data Collection Procedures

Following approval of the Institutional Review Board (IRB) of Siriraj Hospital and The National Cancer Institute of Thailand for obtaining permission of data collection, data collection procedures were performed as follow;

1. The researcher contacted the head nurse and staff nurses at the outpatient chemotherapy clinic to set up a time to provide information about the purpose of the study and data collection. Stuff nurses at the outpatient chemotherapy clinic to provided information about the study and data collection for patients and then the researcher met the patients and informed them of the study and gave them a chance to ask questions to clarify their doubts. If the patients agreed to participate in the study, the formal written consent form was subsequently obtained.

2. After an inform consent process, the researcher asked the participants to complete three questionnaires (Demographic Questionnaires 21 items, the MSAS 32 items, and IFS-CA 39 items). Information of Demographic and Medical Record Form was obtained from the participants (11 items) and medical record (10 items). The participants who were able to read and written, were given by the questionnaires and explanation of how to fill out the questionnaires in detail. The participants were provided a chance to ask question if they do not understand anything, and they were allowed to fill out the questionnaires freely, with the researcher waiting nearby in case they need help. The researcher herself conducted and interviewed all participants in the counseling room of the Chemotherapy and Blood Transfusion Unit.

## Data analysis

The process of data analysis was in accordance to the research questions and aims of this study. The SPSS statistical program version 17.0 was used to analyze the data. Statistical analytic methods used in this research study were as follows:

**Purpose 1:** To describe symptom experiences in advanced lung cancer patients receiving chemotherapy. The characteristics of symptom dimensions were analyzed by using descriptive data analysis.

**Purpose 2:** To explore the existence of symptom clusters in advanced lung cancer patients receiving chemotherapy. Factor analysis was used to identify the clusters of symptom severity and symptom distress dimension.

**Purpose 3:** To compare the similarity of symptom cluster classified by severity and distress

Symptom prevalence and symptom frequency were not selected to analyses in this study. Symptom prevalence or occurrence was little known as the scale measuring was nominal and dichotomous and inappropriate to support the method of analysis. Symptom frequency, there were some symptoms that can persist for a long period of time and the pattern of their occurrences might not be observed for a short period of time. Symptoms were mouth sore, change in the way food taste, weight loss, hair loss, constipation, swelling of arms or legs, image change, and change in skin. The different numbers of symptom investigated can affect reliability, method of analysis and results of the study. Portenoy et al (1994) omitted to investigate the frequency of these symptoms in their study. Investigating symptom frequency within a day or a week was cautious for these symptoms and should be excluded in the analysis process.

The statistical method used to analyze this research purpose was exploratory factor analysis with principal components (rotated component matrix with varimax rotation). Factor analysis was used to uncover the latent structure or factor of a cluster of variables; namely symptom clusters. The testing of normal distribution for symptom scores revealed deviated distributions in nine symptoms. These symptoms were difficulty concentrating, feeling nervous, diarrhea, feeling sad, sweats, problem with sexual interest activity, difficulty swallowing, mouth sores, and swelling of arms or legs. These symptoms were also reported as having low

prevalence (< 30 %). In order to have a manageable number of symptoms for factor analysis, 23 symptoms with > 30% prevalence were selected (Phligbua, 2012; Pudtong, 2011). Nine symptoms, difficulty concentrating, feeling nervous, diarrhea, feeling sad, sweats, problem with sexual interest activity, difficulty swallowing, mouth sores, and swelling of arms or legs, were excluded from the factor analysis.

The application of factor analysis was performed with four major steps. They were testing of assumptions, extracting factors and rotation, testing clustering and naming the factors.

2.1 Testing of assumptions; According to Hairs et al., (1995).

2.1.1 Interval or near interval data. There were no categorical variables used to analyze with factor analysis in the current study. Both symptom severity and symptom distress scores were interval data.

2.1.2 Multicollinearity. Mulitcolinearity means the conditions that two or more independent variables were highly correlated and cause difficulty in determining their separate effects on the dependent variables. The Bartlett's test of sphericity was another statistical test for correlations among variables (Hair et al., 1995). It was used to evaluate whether a correlation matrix is suitable for factor analysis. It tests the null hypothesis that the original correlation matrix is an identity matrix (no correlation between the variables). Significant Bartlett's test means that there are correlations that at least some variables and factors can be formed. The Bartlett's test in the current study rejected the null hypothesis both in the dimension of symptom severity ($\chi^2$ = 1036.352, df = 253, P<0.000) and in the dimension of symptom distress ($\chi^2$ = 1145.489, df =253, P<0.000). This means the correlations among symptom variables were identified and they were capable to form factors.

2.1.3 The variables having too high intercorrelations may indicate a multicollinearity problem. Kaiser-Meyer-Olkin (KMO) statistics was then used to examine multicollinearity in the factor analysis of this study. KMO measure is based on the principle of if variables share common factors, and then partial correlations between pairs of variables should be small when the effects of other variables are controlled. The value of KMO varies from 0 to 1.0. The numbers of sample should be adequate if the value of overall KMO is equal to .60 or higher to proceed with factor analysis. In this study, the value of KMO for symptom severity

scores was .731. The value of KMO for symptom distress scores was .753. Generally, the KMO equaled .90 or over can be interpreted as remarkable significance for sample adequacy (Hair, et al, 1995). Therefore, the problem of multicolinearity did not exist in this study.

2.2 Extracting factors: Forcing Eigen values greater than 1.2 with varimax rotation technique to identify symptom cluster were used in this study. Eigen values are helpful in deciding how many factors should be used in the analysis, the scree plot was interpreted to aid in factor retention decision making.

2.3 Naming the factor extracted. When a factor solution was obtained in which variables had a significant loading on a factor, some meaning was assigned to the pattern of factor loadings. Kim and colleagues (2009) suggested that the name of symptom cluster should base on the most the symptoms presented within the cluster. The name lists of symptom clusters in this study were then based on the sets of symptoms having high factor loading scores.

**Purpose 4:** To determine the influences of symptom cluster on the functional status in advanced lung cancer patients receiving chemotherapy. Multiple regression analysis was used.

According to Hair et al (2010), there were three main assumptions about the relationships between the dependent and independent variables in using multiple regressions: linearity of relationships, independence of the error term, and the absence of multicollinearity. Independence of the error term or homoscedasticity of residuals assumes that each predicted value is independent (Hair, et al., 1995). The Durbin-Watson statistic test (d) was used to examine this assumption. Generally, the value of d is ranged from 0 to 4 and the values ranged from 1.5 to 2.5 indicate good independence of observations. Multicollinearity is the intercorrelation of independent variables and is against using multiple regressions. To assess multivariate multicollinearity of the data in this study, tolerance or VIF was the statistic used to examine. If VIF is greater than 10 and/or tolerance is less than .20, a problem with multicollinearity is indicated. From the analysis, a proportion of the variance in functional status was explained by a set of factor scores at a significant level. To evaluate the influence of symptom clusters on the functional status, the factor scores were used as independent variable, whereas functional status scores were

used as dependent variable. Next, to determine the influence of symptoms in each cluster on functional status, symptoms scores were used instead of factor score. The analysis was done in each cluster. The results from this process helped the researcher identify the key symptoms of each cluster influencing the functional status. This led to identify which clusters and symptoms produce the most effect on functional status of the patients with lung cancer.

**Purpose 5:** To determine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experience differed in their functional status. Cluster analysis was used to determine whether distinct subgroups of advanced lung cancer patients experiencing differing levels of symptom burden. Symptom burden group were the different burden of symptom prevalence, symptom severity and symptom distress experienced by advanced lung cancer patients receiving chemotherapy. It was felt that using all of symptom prevalence score, symptom severity score, and symptom distress score allow a better characterization of the variability in individual symptoms and overall symptom burden. They provided the best description of the data. Symptom frequency was also a significant dimension of symptom experience. However, symptom frequency was not evaluated in eight symptoms. This study was cross-sectional design. Some symptoms could persist and were difficult to evaluate their frequency within a short-time frame. It was not provided the good characterization of the variability in individual symptoms and overall symptom burden. Therefore, it was not used to determine subgroups of advanced lung cancer.

A combination approach using a hierarchical approach followed by a nonhierarchical approach was used for analysis in this study. A hierarchical approach was used to select the number of clusters and profile cluster centers that serve as initial cluster seeds in the nonhierarchical procedure. For final clustering solution, a nonhierarchical method then clusters all observations using the seed points to provide more accurate cluster memberships. In addition, independent sample t-test was used to examine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experience differed in their functional status.

# CHAPTER IV
# RESULTS

This chapter presents the results from the data analysis of this study. They compose of four major parts. The first part presents demographic and clinical characteristics of the sample. The second part presents symptoms experience and symptom cluster across dimension. The third part presents functional status and the influence of symptom cluster on the functional status. The fourth part presents patient subgroup differences in symptoms experience and functional status.

## Part 1: Demographic and Clinical Characteristics of the Participants

### Demographic Characteristics of the Participants

Three hundred patients with advanced lung cancer receiving chemotherapy were consented to participate in this study. The final participants, who consented in participating in this study, were 300. Most of participants were males, married, and older adults. The majority had primary school education, retired and government service with household income less than 5,000 baths per month but sufficient and saving expense. Health services were covered by government welfare. Most of them live with their family and spouse was main caregiver. The demographic characteristics of participants (N=300) were summarized in Table 4.1

**Table 4.1 Demographic characteristics of the participants (N=300)**

| Characteristics | | N | % | Characteristics | N | % |
|---|---|---|---|---|---|---|
| **Sex** | | | | **Financial status** | | |
| Male | | 167 | 55.7 | Sufficient and saving | 203 | 67.7 |
| Female | | 133 | 44.3 | Sufficient and no saving | 63 | 21.0 |
| **Age (years)** | | | | Insufficient and no debt | 20 | 6.7 |
| Range | 29-86 | | | Insufficient and debt | 14 | 4.7 |
| Mean | 61.39 | | | **Methods of payment** | | |
| SD | 10.26 | | | Government welfare | 173 | 57.7 |
| **Marital status** | | | | Universal health care coverage ( Gold Card) | 88 | 29.3 |
| Single | | 42 | 14 | Social coverage | 17 | 5.7 |
| Married/ partnered | | 224 | 74.7 | Others ( Private Health Insurance) | 6 | 2.0 |
| Widowed/separated/divorced | | 34 | 11.3 | **Living arrangements** | | |
| **Level of education** | | | | Living alone | 6 | 2.0 |
| Primary School | | 136 | 45.3 | With family | 287 | 95.7 |
| Secondary School | | 17 | 5.7 | With relative | 4 | 1.3 |
| High School | | 21 | 7.0 | With friend | 3 | 1.0 |
| Diploma/ Certificate | | 12 | 4.0 | **Having caregiver** | | |
| Bachelor degree | | 102 | 34.0 | No | 9 | 3.0 |
| Postgraduate | | 12 | 4.0 | Yes | 291 | 97.0 |
| **Occupation** | | | | **Person who most provide support as caregivers** | | |
| Government service | | 62 | 20.7 | | | |
| Business person | | 55 | 18.3 | | | |
| Company/ labor | | 34 | 11.3 | | | |
| Housewife | | 20 | 6.7 | | | |
| Farmer | | 22 | 7.3 | | | |
| Not working / Unemployed | | 45 | 15.0 | Spouse | 135 | 45.0 |
| Others ( Retired) | | 62 | 20.7 | Mother or father | 16 | 5.3 |
| | | | | Daughter/ son | 96 | 32.0 |
| | | | | Others : relative, friend | 53 | 17.7 |

**Table 4.1 Demographic characteristics of the participants (N=300) (cont.)**

| Characteristics | N | % | Characteristics | N | % |
|---|---|---|---|---|---|
| **Income (baht/ month)** | | | | | |
| Range | 700-200,000 | | | | |
| Mean | 28054.66 | | | | |
| SD | 31755.77 | | | | |
| Less than 5,000 | 103 | 34.3 | | | |
| 5,001-10,000 | 53 | 17.7 | | | |
| 10,001-20,000 | 58 | 19.3 | | | |
| 20,001-30,000 | 23 | 7.7 | | | |
| 30,001-40,000 | 12 | 4.0 | | | |
| 40,001-50,000 | 21 | 7.0 | | | |
| More than 50,000 | 30 | 10.0 | | | |

**Clinical Characteristics of the Participants**

Most of the participants were diagnosed with NSCLC stage IV. Participants were currently undergoing chemotherapy with various treatment regimens. The majority treatment regimens received were carboplatin and gemcitabine. Data on the patient's comorbid conditions was present in 94% of the participants, Hypertension was found the most. The study clinical characteristics are summarized in Table 4.2.

**Table 4.2 Clinical characteristics of the participants**

| Characteristics | N | % | Characteristics | N | % |
|---|---|---|---|---|---|
| **Type of Lung cancer** | | | **Stage of Lung cancer** | | |
| NSCLC | 292 | 97.3 | III | 54 | 18.0 |
| SCLL | 8 | 2.7 | IV | 246 | 82.0 |

**Table 4.2 Clinical characteristics of the participants (cont.)**

| Characteristics | N | % | Characteristics | N | % |
|---|---|---|---|---|---|
| **Chemotherapy regimens** | | | **Co-morbidity** | | |
| Carboplatin and Gemcitabine | 179 | 59.7 | None | 18 | 6 |
| Paclitaxel and Carboplatin (Anzatax) | 75 | 25.0 | Yes | 282 | 94 |
| | | | One co-morbidity | 208 | 69.3 |
| Alimta | 19 | 6.3 | Hypertension | 141 | 47.0 |
| Doxetaxol or Taxotere | 12 | 4.0 | Diabetes | 38 | 12.7 |
| Etoposide and Cisplatin | 2 | 0.7 | Heart disease | 6 | 2.0 |
| Etoposide and Carboplatin | 7 | 2.3 | BPH | 8 | 2.7 |
| Cisplatin and Vinerebine | 6 | 2.0 | Dyslipidemia | 4 | 1.3 |
| **Number of cycles received** | | | COPD | 2 | 0.7 |
| 1 | 164 | 54.7 | Gout | 2 | 0.7 |
| 2 | 79 | 26.3 | Two co-morbidities | 41 | 13.7 |
| 3 | 40 | 13.3 | Three co-morbidities | 30 | 10.0 |
| 4 | 12 | 4.0 | Four co-morbidities | 3 | 1.0 |
| 5 | 5 | 1.7 | | | |

## Part 2: Symptom Experience and Symptom Cluster across Dimension

### 2.1 Symptom Experiences in Advanced Lung Cancer Patients Receiving Chemotherapy

#### 2.1.1 Symptom Prevalence

The participants in this study reported 3 to 26 symptoms, with a mean of 13.95 symptoms (SD = 4.66). The five most prevalence symptoms were lack of appetite (81.7%), followed by lack of energy (78%), constipation (70.3%), dry mouth (66.7%), and change in the way food (62.7%). The study symptom prevalence was summarized in Table 4.3.

**Table 4.3 Descriptions of symptom prevalence by rank**

| Symptom experience | N | Prevalence (%) | Symptom experience | N | Prevalence (%) |
|---|---|---|---|---|---|
| 1. Lack of appetite | 245 | 81.7 | 17. Numbness/ tingling in hand/ feet | 143 | 47.7 |
| 2. Lack of energy | 234 | 78.0 | | | |
| 3. Constipation | 211 | 70.3 | 18. Feeling irritable | 141 | 47.0 |
| 4. Dry mouth | 200 | 66.7 | 19. Weight loss | 139 | 46.3 |
| 5. Change in the way food taste | 188 | 62.7 | 20. Itching | 123 | 41.0 |
| | | | 21. Worrying | 115 | 38.3 |
| 6. Shortness of breath | 186 | 62.0 | 22. Vomiting | 97 | 32.3 |
| 7. Problem with urination | 183 | 61.0 | 23. Change in skin | 97 | 32.3 |
| 8. I don't look like myself | 181 | 60.3 | 24. Difficulty concentrating | 88 | 29.3 |
| 9. Cough | 176 | 58.7 | 25. Feeling nervous | 75 | 25.0 |
| 10. Pain | 170 | 56.7 | 26. Problems with sexual interest or activity | 75 | 25.0 |
| 11. Difficulty sleeping | 165 | 55.0 | 27. Mouth sores | 74 | 24.7 |
| 12. Feeling drowsy | 156 | 52.0 | 28. Diarrhea | 36 | 12.0 |
| 13. Hair loss | 156 | 52.0 | 29. Feeling sad | 33 | 11.0 |
| 14. Nausea | 151 | 50.3 | 30. Sweats | 22 | 7.3 |
| 15. Dizziness | 147 | 49.0 | 31. Swelling of arms of legs | 18 | 6.0 |
| 16. Feeling bloated | 146 | 48.7 | 32. Difficulty swallowing | 13 | 4.3 |

### 2.1.2 Symptom Frequency

Of the participants who had symptoms, the mean symptom frequency scores raged from 1.58-2.84 in possible score 1-4. The five most frequency symptoms were problem with urination (mean = 2.84, SD = 0.57), followed by lack of appetite (mean = 2.80, SD = 0.88), numbness/tingling in hands/feet (mean = 2.73,

SD = 1.00), lack of energy (mean= 2.58, SD = 0.96), and feeling nervous (mean = 2.52, SD = 0.83). The symptom least frequently occurred was diarrhea (mean = 1.58, SD = 0.91). See Table 4.4 for more details.

**Table 4.4 Descriptions of symptom frequency by rank**

| Symptom experience | N | Mean | SD | Symptom experience | N | Mean | SD |
|---|---|---|---|---|---|---|---|
| 1. Problem with urination | 183 | 2.84 | 0.57 | 13. Difficulty swallowing | 13 | 2.23 | 0.60 |
| 2. Lack of appetite | 245 | 2.80 | 0.88 | 14. Cough | 176 | 2.16 | 0.85 |
| 3. Numbness/tingling in hands/feet | 143 | 2.73 | 1.00 | 15. Dizziness | 147 | 2.12 | 0.85 |
| | | | | 16. Sweats | 22 | 2.05 | 0.79 |
| 4. Lack of energy | 234 | 2.58 | 0.96 | 17. Feeling irritable | 141 | 2.02 | 0.76 |
| 5. Feeling nervous | 75 | 2.52 | 0.83 | 18. Nausea | 151 | 2.00 | 0.93 |
| 6. Difficulty sleeping | 165 | 2.45 | 0.89 | 19. Difficulty Concentrating | 88 | 1.97 | 0.76 |
| 7. Pain | 170 | 2.42 | 0.92 | | | | |
| 8. Dry mouth | 200 | 2.42 | 0.93 | 20. Itching | 123 | 1.97 | 0.90 |
| 9. Feeling bloated | 146 | 2.42 | 0.83 | 21. Feeling sad | 33 | 1.88 | 1.02 |
| 10. Feeling drowsy | 156 | 2.32 | 0.94 | 22. Vomiting | 97 | 1.86 | 0.94 |
| 11. Shortness of breath | 186 | 2.30 | 0.67 | 23. Problems with sexual interest or activity | 75 | 1.59 | 0.72 |
| 12. Worrying | 115 | 2.24 | 0.80 | | | | |
| | | | | 24. Diarrhea | 36 | 1.58 | 0.91 |

### 2.1.3 Symptom Severity

The mean symptom severity scores raged from 1.40-2.56 in possible score 1-4. The five most severe symptoms were lack of appetite (mean = 2.56, SD = 0.75), followed by difficulty swallowing (mean = 2.54, SD =0.66), hair loss (mean = 2.52, SD = 1.17), constipation (mean = 2.48, SD = 0.80), and change in the way food tastes (mean = 2.40, SD = 0.68) respectively (See Table 4.5 for more details).

**Table 4.5 Descriptions of symptom severity by rank**

| Symptom experience | N | Mean | SD | Symptom experience | N | Mean | SD |
|---|---|---|---|---|---|---|---|
| 1. Lack of appetite | 245 | 2.56 | 0.75 | 17. Vomiting | 97 | 1.99 | 0.84 |
| 2. Difficulty swallowing | 13 | 2.54 | 0.66 | 18. Problem with urination | 183 | 1.98 | 0.70 |
| 3. Hair loss | 156 | 2.52 | 1.17 | | | | |
| 4. Constipation | 211 | 2.48 | 0.80 | 19. Numbness/ tingling in hands/feet | 143 | 1.93 | 0.86 |
| 5. Change in the way food tastes | 188 | 2.40 | 0.68 | | | | |
| 6. Lack of energy | 234 | 2.34 | 0.70 | 20. Weight loss | 139 | 1.92 | 0.86 |
| 7. Pain | 170 | 2.28 | 0.79 | 21. Cough | 176 | 1.90 | 0.76 |
| 8. Feeling nervous | 75 | 2.28 | 0.83 | 22. Feeling drowsy | 156 | 1.90 | 0.75 |
| 9. Difficulty sleeping | 165 | 2.25 | 0.81 | 23. Dry mouth | 200 | 1.88 | 0.74 |
| 10. Worrying | 115 | 2.23 | 0.75 | 24. Swelling of arms or legs | 18 | 1.83 | 1.10 |
| 11. Feeling bloated | 146 | 2.17 | 0.80 | | | | |
| 12. Shortness of breath | 186 | 2.16 | 0.60 | 25. Feeling sad | 33 | 1.82 | 0.95 |
| 13. Dizziness | 147 | 2.08 | 0.78 | 26. Itching | 123 | 1.77 | 0.83 |
| 14. Nausea | 151 | 2.07 | 0.85 | 27. Mouth sore | 74 | 1.69 | 0.68 |
| 15. I don't look like myself | 181 | 2.07 | 0.95 | 28. Difficulty Concentrating | 88 | 1.60 | 0.69 |
| 16. Sweats | 22 | 2.00 | 0.82 | 29. Feeling irritable | 141 | 1.57 | 0.72 |
| | | | | 30. Changes in skin | 97 | 1.54 | 0.65 |
| | | | | 31. Diarrhea | 36 | 1.50 | 0.70 |
| | | | | 32. Problems with sexual interest | 75 | 1.40 | 0.62 |

### 2.1.4 Symptom Distress

The mean symptom distress scores ranged from 0.94-2.70 in possible score 1-4. The five most distress symptoms were constipation (mean = 2.70, SD = 0.83), followed by lack of appetite (mean = 2.68, SD = 0.68), pain (mean = 2.56, SD = 0.80), feeling nervous (mean = 2.49, SD = 0.83), and worrying (mean = 2.41, SD = 0.80) respectively. The least severe symptom was problems with sexual interest (mean = 0.94, SD = 0.58) as shown in Table 4.6.

**Table 4.6 Descriptions of symptom distress by rank**

| Symptom experience | N | Mean | SD | Symptom experience | N | Mean | SD |
|---|---|---|---|---|---|---|---|
| 1. Constipation | 211 | 2.7 | 0.83 | 18. I don't look like myself | 181 | 1.99 | 1.08 |
| 2. Lack of appetite | 245 | 2.68 | 0.68 | | | | |
| 3. Pain | 170 | 2.56 | 0.80 | 19. Feeling sad | 33 | 1.94 | 1.02 |
| 4. Feeling nervous | 75 | 2.49 | 0.83 | 20. Itching | 123 | 1.93 | 0.83 |
| 5. Worrying | 115 | 2.41 | 0.80 | 21. Mouth sores | 74 | 1.78 | 0.63 |
| 6.Difficulty swallowing | 13 | 2.4 | 0.92 | 22. Numbness/ tingling in hands/feet | 143 | 1.68 | 0.84 |
| 7. Lack of energy | 234 | 2.38 | 0.80 | | | | |
| 8. Difficult sleeping | 165 | 2.38 | 0.87 | 23. Dry Mouth | 200 | 1.63 | 0.75 |
| | | | | 24. Diarrhea | 36 | 1.62 | 0.80 |
| 9. Feeling bloated | 146 | 2.36 | 0.81 | 25. Problem with urination | 183 | 1.58 | 0.85 |
| 10. Change in the way food tastes | 188 | 2.34 | 0.85 | 26. Feeling drowsy | 156 | 1.53 | 0.97 |
| 11. Shortness of breath | 186 | 2.31 | 0.69 | 27. Weight loss | 139 | 1.5 | 0.86 |
| | | | | 28. Feeling irritable | 141 | 1.49 | 0.82 |
| 12. Sweats | 22 | 2.29 | 1.03 | 29. Difficult concentrating | 88 | 1.35 | 0.71 |
| 13. Nausea | 151 | 2.24 | 0.89 | | | | |
| 14. Vomiting | 97 | 2.23 | 0.92 | 30. Swelling of arms of legs | 18 | 1.29 | 0.68 |
| 15. Dizziness | 147 | 2.13 | 0.82 | | | | |
| 16. Cough | 176 | 2.12 | 0.87 | 31. Change in skin | 97 | 1.25 | 0.63 |
| 17. Hair loss | 156 | 1.90 | 1.16 | 32. Problems with sexual interest or activity | 75 | 0.94 | 0.58 |

In summary, the most commonly reported symptom prevalence was lack of appetite, whereas the most frequent symptom was problem with urinary. Lack of appetite was rated as the most severe symptom whereas constipation was commonly reported to be the most distressing symptom.

### 2.2 Symptom Cluster across Dimension

A total of 23 symptoms with > 30% prevalence were selected to analyze for factor structures of both symptom severity and symptom distress. Difficulty concentrating, feeling nervous, diarrhea, feeling sad, sweats, problem with sexual interest activity, difficulty swallowing, mouth sores, and swelling of arms or legs, were excluded from the factor analysis. The criteria used for selecting symptoms in terms of symptom dimensions were described in Chapter III. The Bartlett's test of sphericity, and the Kaiser-Meyer-Olkin Measure of Sampling Adequacy (KMO) were used to examined the strength of the relationships among the variables (See detailed in Chapter III). The problem of multicolinearity did not exist in this study. Factor analyses with principal components analysis as extraction method and varimax rotation were performed to determine the number of symptom clusters.

**2.2.1 Symptom clusters of symptom severity.** With varimax rotation, five factors were extracted from the analysis, accounted for 42.53% of variance. These five clusters were labeled as: (See detailed in Table 4.7).

Cluster 1: 'Emotional-elimination discomfort symptoms cluster' had the most percentage of variance (10.16%) composed of feeling irritable, feeling bloated, problems with urination, constipation, feeling drowsy, dizziness, and changes in skin

Cluster 2: 'Anorexia-related symptoms cluster' consisted of three symptoms, dry mouth, and change in the way food tastes, and lack of appetite, which explained 8.70% of factor variance.

Cluster 3: 'Treatment-related gastrointestinal and other symptoms cluster' consisted of nausea, vomiting, and hair loss, which explained 8.63% of factor variance.

Cluster 4: 'Neurological and body image symptoms cluster' consisted of numbness/tingling in hands/feel, "I don't look like myself", pain, worrying, and weight loss, which explained 7.76% of factor variance.

Cluster 5: 'Respiratory and sleep disturbance symptoms cluster' consisted of shortness of breath, cough, and difficulty sleeping, which explained 7.28% of factor variance.

**Table 4.7 Exploratory factor analysis of symptom severity (N=300)**

| Symptoms | Factor Loading | | | | |
|---|---|---|---|---|---|
| | **1** | **2** | **3** | **4** | **5** |
| Feeling irritable | **0.632** | | | | |
| Feeling drowsy | **0.552** | | | | |
| Feeling bloated | **0.547** | | | | |
| Dizziness | **0.524** | | | | |
| Problems with urination | **0.475** | | | | |
| Constipation | **0.428** | | | | |
| Changes in skin | **0.411** | | | | |
| Dry mouth | | **0.665** | | | |
| Change in the way food tastes | | **0.653** | | | |
| Lack of appetite | | **0.612** | | | |
| Nausea | | | **0.749** | | |
| Vomiting | | | **0.722** | | |
| Hair loss | | | **0.450** | 0.423 | |
| Numbness/tingling in hands/ feet | | | | **0.571** | |
| “ I don’t look like myself ” | | | | **0.504** | |
| Pain | | | | **0.471** | |
| Worrying | | | | **0.457** | |
| Weight loss | | | | **0.432** | |
| Shortness of breath | | | | | **0.599** |
| Cough | | | | | **0.572** |
| Difficulty sleeping | | | | | **0.527** |
| **Variance explained** | **10.158** | **8.697** | **8.634** | **7.761** | **7.282** |
| **Total variance explained** | | | | | **42.532** |

**2.2.2 Symptom clusters of symptom distress.**

As shown in Table 4.8, five symptom clusters were extracted from the analysis, using Eigen value of 1.2 with varimax rotation, accounted for 43.69 % of variance. The detail of each factor was presented as the following: (See detailed in Table 4.8).

Cluster 1: 'Emotional-elimination discomfort symptoms cluster' had the most percentage of variance (10.54%), which composed of feeling irritable, feeling bloated, problems with urination, constipation, shortness of breath, and worrying.

Cluster 2: 'Body image symptoms cluster' consisted of 'I don't look like myself', hair lost, itching, and changes in skin, which explained 9.01% of factor variance.

Cluster 3: 'Anorexia-related symptoms cluster' consisted of lack of appetite, change in the way food tastes, dry mouth, and lack of energy, which explained 8.77 % of factor variance.

Cluster 4: 'Treatment-related gastrointestinal and other symptoms cluster' consisted of nausea, vomiting, and dizziness, which explained 8.40% of factor variance.

Cluster 5: 'Treatment-related neurological and other symptoms cluster' consisted of numbness/tingling in hands/feet, weight loss, and difficulty sleeping, which explained 6.97 % of factor variance.

**Table 4.8 Exploratory factor analysis of symptom distress (N=300)**

| Symptoms | Factor Loading | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| Feeling irritable | **0.589** | | | | |
| Feeling bloated | **0.570** | | | | |
| Problems with urination | **0.549** | | | | |
| Constipation | **0.523** | | | | |
| Shortness of breath | **0.519** | | | | |
| Worrying | **0.471** | | | | |

**Table 4.8 Exploratory factor analysis of symptom distress (N=300) (cont.)**

| Symptoms | Factor Loading | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| "I don't look like myself" | | **0.592** | | | |
| Hair loss | | **0.580** | | | |
| Itching | | **0.492** | | | |
| Changes in skin | | **0.457** | | | |
| Lack of appetite | | | **0.742** | | |
| Change in the way food tastes | | | **0.682** | | |
| Dry mouth | | | **0.566** | | |
| Lack of energy | | | **0.509** | | |
| Nausea | | | | **0.769** | |
| Vomiting | | | | **0.747** | |
| Dizziness | | | | **0.462** | |
| Numbness/tingling in hands/ feet | | | | | **0.656** |
| Weight loss | | | | | **0.554** |
| Difficulty sleeping | | | | | **0.405** |
| **Variance explained** | **10.541** | **9.010** | **8.765** | **8.397** | **6.974** |
| **Total variance explained** | | | | | **43.69** |

**2.2.3 The similarities and dissimilarities clustering of symptoms across dimension between symptom severity and symptom Distress.**

The results of this study showed that symptom clusters of symptom severity and those of symptom distress were not identical. Although the number of clusters was equal between symptom severity and symptom distress, they were different in terms of the characteristics of the clusters.

Five major clusters were extracted in the dimensions of both symptom severity and symptom distress. With regard to the overall detail in each of symptom clusters of both severity and distress dimensions, it is somewhat similar in terms of the number of items. Four clusters of symptom severity compare with

clusters of symptom severity. The result found that the 'Anorexia-related symptoms cluster' was existed almost similarly across symptom dimensions. The other three clusters found partially similar. The 'Respiratory and sleep disturbance symptoms cluster' in severity dimension cannot compare with the 'Body image symptoms cluster' in distress dimension. In symptom severity dimension, the 'Respiratory and sleep disturbance symptoms cluster' composed of shortness of breath, cough, and difficult sleeping which formed together as cluster, whereas all of these symptoms loaded in separate factor in distress dimension. In the same way, the 'Body image symptoms cluster' existed as cluster in distress dimension. Whereas, the 'Body image symptoms cluster complied with the 'Neurological symptom cluster' in the severity dimension. The differences between symptoms across symptom dimensions were feeling drowsy, pain and cough were existed only in the dimension of symptom severity. Lacks of energy, worrying and itching existed only in the dimension of symptom distress. Symptom clusters across symptom dimensions were compared in Table 4.9.

**Table 4.9 The similarities and dissimilarities clustering of symptoms across clustering of symptoms across dimension between symptom severity and symptom distress**

| Factor Structure | Symptom Severity | Symptom Distress | Comparison |
|---|---|---|---|
| **Number of Cluster** | 5 | 5 | Identical |
| | **Emotional-elimination discomfort symptoms cluster** ( 7 symptoms)<br>1) Feeling irritable<br>2) Feeling bloated<br>3) Problems with urination<br>4) Constipation<br>5) Feeling drowsy<br>6) Dizziness<br>7) Changes in skin | **Emotional-elimination discomfort symptoms cluster** (6 Symptoms)<br>1) Feeling irritable<br>2) Feeling bloated<br>3) Problems with urination<br>4) Constipation<br>5) Shortness of breath<br>6) Worrying | **Partially Similar** |

**Table 4.9 The similarities and dissimilarities clustering of symptoms across clustering of symptoms across dimension between symptom severity and symptom distress (cont.)**

| Factor Structure | Symptom Severity | Symptom Distress | Comparison |
|---|---|---|---|
| | **Anorexia-related symptoms cluster** (3 symptoms) 1) Dry mouth 2) Change in the way food tastes 3) Lack of appetite | **Anorexia-related symptoms cluster** (4 symptoms) 1) Dry mouth 2) Change in the way food tastes 3) Lack of appetite 4) Lack of energy | **Almost Similar** |
| | **Treatment-related gastrointestinal and other symptoms cluster** (3 Symptoms) 1) Nausea 2) Vomiting 3) Hair loss | **Treatment-related gastrointestinal and other symptoms cluster** (3 Symptoms) 1) Nausea 2) Vomiting 3) Dizziness | **Partially Similar** |
| | **Neurological and body image symptoms cluster** (5 Symptoms) 1) Numbness/tingling in hands/ feet 2) Weight loss 3) I don't look like myself 4) Pain 5) Worrying | **Treatment-related neurological and other symptoms cluster** (3 symptoms) 1) Numbness/tingling in hands/ feet 2) Weight loss 3) Difficulty sleeping | **Partially Similar** |

## Part 3: Functional Status and the Influence of Symptom Cluster on the Functional Status

### 3.1 Characteristics of functional status of the advanced lung cancer patients receiving chemotherapy.

The functional mean scores was ranged from 1.08-3.98 on scale of 1-4. The mean of total functional scores was 2.03 (SD = 0.36). Most participants have partially limited their functional activities. The activities mostly performed were personal care activities. The activities mostly limited were the occupational functions (See table 4.10).

**Table 4.10 Functional scores categorized by groups of activities**

| Groups of functional activities | N | Mean | SD |
|---|---|---|---|
| Household and family | 300 | 1.562 | 0.52 |
| Social and communication | 300 | 1.674 | 0.53 |
| Personal care | 300 | 2.562 | 0.30 |
| Occupational functions | 42 | 0.392 | 0.98 |
| **Total functions** | **300** | **2.031** | **0.36** |

* 1-1.99 = very limited functional activities, 2-2.99 = partially limited,
3-3.99 = moderate or less limited, 4 = fully function or no limited functional activities

### 3.2 The influences of symptom clusters on the functional status in advanced lung cancer patients receiving chemotherapy.

Multiple regression analysis with enter method was used to determine the effects of symptoms within the clusters on functional status of patients with advanced lung cancer. To evaluate the regression assumptions, normality, linearity, homoscedasticity, and independence of residuals were tested. All assumptions were met. The analyses were composed of two parts; 1) factor scores of symptom severity and symptom distress were examined for their significant associations with functional status. 2) symptoms scores in each cluster of symptom severity and symptom distress were used instead of factor scores. The analysis was done in each cluster.

**3.2.1 The influences of symptom clusters of symptom severity dimension on functional status analyzed by using factor scores.** Independent variables were factor scores and the dependent variable was functional status score. A problem with multicollinearity and autocorrelation problem were not indicated (Durbin Watson score = 1.773). The results have shown that five symptom clusters together explained 12.6% of the variance in the functional status ($R^2$ = .126, F = 8.507, df = 5, p = .000) (see Table 4.13). Only 'Anorexia-related symptoms cluster' and 'Respiratory and sleep disturbance symptoms cluster' were found to have statistically significant relationship with functional status (P<0.05). The cluster explaining the greatest proportion of the variance in the functional status was 'Respiratory- related sleep disturbance symptoms cluster' (Cluster 5), as shown in Table 4.11.

**Table 4.11 Summary of multiple regression analysis of symptom clusters of symptom severity affecting functional status analyzed by using factor scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .694 | .009 | | 75.863 | .000 |
| Cluster 1: Emotional-elimination discomfort symptoms cluster | .000 | .009 | .002 | .035 | .972 |
| Cluster 2: Anorexia-related symptoms cluster | -.035 | .009 | -.208 | -3.819 | .000 |
| Cluster 3: Treatment-related gastrointestinal and other symptoms cluster | -.006 | .009 | -.035 | -.637 | .525 |
| Cluster 4: Neurological and body image symptoms cluster | .000 | .009 | .002 | .032 | .974 |
| Cluster 5: Respiratory-related sleep disturbance symptoms cluster | -.048 | .009 | -.289 | -5.248 | .000 |
| $R^2$ | .126 | .009 | -.286 | -5.248 | .000 |
| Adjust $R^2$ | .112 | | | | |
| F Change | 8.507 | | | | |
| P | .000 | | | | |

**3.2.2 The influences of symptom clusters on functional status analyzed by using symptom severity scores.** Independent variables were symptom severity scores in each cluster and the dependent variable was functional score.

**3.2.2.1 Emotional-elimination discomfort symptoms cluster (Cluster 1)**. A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.062-1.172, tolerance = 0.942-0.853, Durbin Watson = 1.734). All independent variables were entered simultaneously. They all together explained 5.4% of the variance in functional status ($R^2$ = .054, F = 2.813, df = 6, p = .011) (See Table 4.12). Only change in skin was found to have statistically significant relationship with functional status (P<0.05) (See Table 4.12)

**Table 4.12 Models of multiple regression of Emotional-elimination discomfort symptoms cluster affecting functional status analyzed by using symptom severity scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .716 | .020 | | 36.248 | .000 |
| Feeling irritable | -.005 | .011 | -.029 | -.473 | .637 |
| Feeling bloated | -.015 | .008 | -.108 | -1.760 | .079 |
| Problems with urination | -.009 | .009 | -.062 | -1.048 | .295 |
| Constipation | .000 | .008 | -.004 | -.069 | .945 |
| Dizziness | -.009 | .009 | -.065 | -1.052 | .294 |
| Changes in skin | .040 | .012 | .190 | 3.254 | .001 |
| $R^2$ | .054 | | | | |
| Adjust $R^2$ | .035 | | | | |
| F Change | 2.813 | | | | |
| P | .011 | | | | |

**3.2.2.2 Anorexia-related symptoms cluster and functional scorers (Cluster 2).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.128-1.190, tolerance = 0.840-0.886, Durbin Watson score = 1.694). All independent variables were together explained 8.8% of the variance in functional status ($R^2$ = .081, F = 8.694, df = 3, p = .000) (see Table 4.15). Only dry mouth and lack of appetite were found to have statistically significant

relationship with functional status (P<0.05). The significant symptom explaining the greatest proportion of the variance in functional status in this cluster was lack of appetite (See Table 4.13).

**Table 4.13 Models of multiple regression of Anorexia-related symptoms cluster affecting functional status analyzed by using symptom severity scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .777 | .021 | | 36.901 | .000 |
| Lack of appetite | -.030 | .009 | -.212 | -3.539 | .000 |
| Change in the way food tastes | .012 | .008 | .089 | 1.456 | .146 |
| Dry mouth | -.028 | .009 | -.178 | -3.016 | .003 |
| $R^2$ | .081 | | | | |
| Adjust $R^2$ | .072 | | | | |
| F Change | 8.694 | | | | |
| P | .000 | | | | |

**3.2.2.3 Treatment-related gastrointestinal and other symptoms cluster and functional scores (Cluster 3).** To assess multivariate multicollinearity of the data, a problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.090-01.352, tolerance = 0.740-0.917, Durbin Watson score =1.708). It was not having autocorrelation problem. All independent variables together explained 0.9% of the variance in functional status ($R^2$ = .009, F = .878, df = 3, p = .453) (see Table 4.14). No symptom in this cluster was statistically significant relationship with functional status (P<0.05).

**Table 4.14 Models of multiple regression of Treatment-related gastrointestinal and other symptoms cluster of symptom severity affecting on functional status by using symptom severity scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .693 | .015 | | 47.093 | .000 |
| Nausea | -.003 | .009 | -.023 | -.345 | .730 |
| Vomiting | -.011 | .011 | -.067 | -.999 | .319 |
| Hair loss | .008 | .007 | .076 | 1.256 | .210 |
| $R^2$ | .009 | | | | |
| Adjust $R^2$ | -.001 | | | | |
| F Change | .878 | | | | |
| P | .453 | | | | |

**3.2.2.4 Neuropsychological and body image symptoms cluster and functional scores (Cluster 4).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.034-1.196, tolerance = 0.836-0.966, Durbin Watson score = 1.712). All independent variables were together explained 1.2% of the variance in functional status ($R^2$ =. 012, F = .698, df = 5, p = .626). No symptom in this cluster was statistically significant relationship with functional status (P<0.05) (see Table 4.15).

**Table 4.15 Models of multiple regression of Neuropsychological and body image symptoms cluster affecting on functional status by using symptom severity scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .716 | .018 | | 39.458 | .000 |
| Numbness/tingling in hands/feet | -.005 | .009 | -.032 | -.549 | .584 |
| "I don't look like myself" | .005 | .008 | .038 | .599 | .550 |

**Table 4.15 Models of multiple regression of Neuropsychological and body image symptoms cluster on functional status by using symptom severity scores (N=300) (cont.)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Pain | -.011 | .008 | -.085 | -1.359 | .175 |
| Worrying | -.006 | .008 | -.041 | -.675 | .500 |
| Weight loss | -.004 | .009 | -.027 | -.465 | .642 |
| $R^2$ | .012 | | | | |
| Adjust $R^2$ | -.005 | | | | |
| F Change | .698 | | | | |
| P | .626 | | | | |

#### 3.2.2.5 Respiratory and sleep disturbance

**symptoms cluster (Cluster 5).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.067-1.094, tolerance = 0.914-0.937, Durbin Watson score = 1.737). All independent variables together explained 6.1% of the variance in functional status ($R^2$ = .061, F = 6.405, df = 3, p = .000). Shortness of breath was statistically significant relationship with functional status (P<0.05) (See Table 4.16).

**Table 4.16 Models of multiple regression of Respiratory and sleep disturbance symptoms cluster affecting on functional status by using symptom severity scores (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .754 | .018 | | 42.736 | .000 |
| Shortness of breath | -.029 | .009 | -.195 | -3.306 | .001 |
| Cough | -.017 | .009 | -.110 | -1.886 | .060 |
| Difficulty sleeping | .000 | .008 | -.005 | -.094 | .925 |
| $R^2$ | .061 | | | | |
| Adjust $R^2$ | .051 | | | | |
| F Change | 6.405 | | | | |
| P | .000 | | | | |

**3.2.3 The influences of symptom clusters of symptom distress dimension on functional status analyzed by using factor scores.**

Independent variables were factor scores and the dependent variable was functional score. A problem with multicollinearity and autocorrelation problem were not indicated (Durnin Watson score = 1.767). All independent variables together explained 10.3% of the variance in the functional status ($R^2$ = .103, F = 6.761, df = 5, p = .000). Only 'Body image symptoms cluster, 'Anorexia- related fatigue symptoms' were found to have statistically significant relationship with functional status (P<0.05). The cluster explaining the greatest proportion of the variance in the functional status was Anorexia- related fatigue symptoms cluster (Cluster 2) (See in Table 4.17

**Table 4.17 Summary of multiple regression analysis of symptom clusters of symptom distress affecting on functional status by using factor score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .302 | .004 | | 74.873 | .000 |
| Factor1: Emotional-elimination discomfort symptom cluster | -.007 | .004 | -.096 | -1.743 | .082 |
| Factor 2: Body image symptoms cluster | .009 | .004 | .130 | 2.349 | .019 |
| Factor 3: Anorexia-related symptoms cluster | -.018 | .004 | -.250 | -4.517 | .000 |
| Factor 4: Treatment-related gastrointestinal and other symptom cluster | -.004 | .004 | -.055 | -1.000 | .318 |
| Factor 5: Treatment-related neurological symptoms cluster | -.008 | .004 | -.108 | -1.959 | .051 |
| $R^2$ | .103 | | | | |
| Adjust $R^2$ | .088 | | | | |
| F Change | 7.549 | | | | |
| P | .000 | | | | |

**3.2.4 The influences of symptom clusters on functional status analyzed by using symptom distress scores.**

Independent variables were symptom distress scores in each cluster and the dependent variable was functional score. Enter regression analysis was performed the contributions of the selected symptoms on the functional status.

**3.2.4.1 Emotional-elimination discomfort symptoms cluster (Cluster 1)**. A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.081-1.241, tolerance = 0.806-0.925, Durbin Watson score was 1.720). All independent variables all together explained 5.3% of the variance in functional status ($R^2$ = .053, F = 2.740, df = 6, p = .013). Shortness of breath was statistically significant relationship with functional status (P<0.05) (See Table 4.18).

**Table 4.18 Models of multiple regression of Emotional-elimination discomfort symptoms cluster affecting on functional status by using symptom distress score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .324 | .009 | | 37.708 | .000 |
| Feeling irritable | .005 | .005 | .065 | 1.031 | .304 |
| Feeling bloated | -.002 | .003 | -.038 | -.603 | .547 |
| Problems with urination | .000 | .004 | -.006 | -.108 | .914 |
| Constipation | .000 | .003 | -.013 | -.214 | .831 |
| Shortness of breath | -.012 | .004 | -.203 | -3.362 | .001 |
| Worrying | -.004 | .004 | -.068 | -1.106 | .270 |
| $R^2$ | .053 | | | | |
| Adjust $R^2$ | .034 | | | | |
| F Change | 2.740 | | | | |
| P | .007 | | | | |

**3.2.4.2 Body image symptoms cluster and functional scores.** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.097-1.184, tolerance = 0.845-0.912, Durbin Watson score was

1.699). All independent variables all together explained 5.3% of the variance in functional status ($R^2$ = .015, F = 1.139, df = 4, p = .000) (see Table 4.19). Change in skin was statistically significant relationship with functional status (P<0.05) (see Table 4.19).

**Table 4.19 Models of multiple regression of Body image symptoms cluster affecting on functional status by using symptom distress score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .300 | .007 | | 45.216 | .000 |
| I don't like myself | -.001 | .004 | -.021 | -.340 | .734 |
| Hair loss | .000 | .003 | -.017 | -.268 | .789 |
| Itching | -.001 | .004 | -.020 | -.324 | .746 |
| Change in skin | .014 | .006 | .129 | 2.125 | .034 |
| $R^2$ | .015 | | | | |
| Adjust $R^2$ | .002 | | | | |
| F Change | 1.139 | | | | |
| P | .000 | | | | |

### 3.2.4.3 Anorexia-related symptoms cluster

**(Cluster 3).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.156-1.315, tolerance = 0.761-0.865, Durbin Watson score was 1.757). All independent variables together explained 8.1% of the variance in functional status ($R^2$ = .081, F = 6.493, df = 4, p = .000) (see Table 4.22). Lack of energy was statistically significant relationship with functional status (P<0.05) (see Table 4.20).

**Table 4.20 Models of multiple regression of Anorexia-related symptoms cluster affecting on functional status by using symptom distress score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .345 | .010 | | 35.068 | .000 |
| Lack of appetite | -.007 | .004 | -.120 | -1.892 | .059 |
| Change in the way food tastes | .001 | .004 | .014 | .218 | .828 |
| Dry mouth | -.006 | .004 | -.079 | -1.315 | .190 |
| Lack of energy | -.012 | .004 | -.194 | -3.233 | .001 |
| $R^2$ | .081 | | | | |
| Adjust $R^2$ | .068 | | | | |
| F Change | 6.493 | | | | |
| P | .000 | | | | |

**3.2.4.4 Treatment-related gastrointestinal and other symptoms cluster and functional scores (Cluster 4).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.107-1.541, tolerance = 0.649-0.903, Durbin Watson score was 1.667). All independent variables together explained 1.5% of the variance in functional status ($R^2$ = .015, F = 1.468, df = 3, p = .223). Dizziness was statistically significant relationship with functional status (P<0.05) (See Table 4.21).

**Table 4.21 Models of multiple regression of Treatment-related gastrointestinal and other symptoms cluster affecting on functional status by using symptom distress score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .309 | .006 | | 49.336 | .000 |
| Nausea | .002 | .004 | .035 | .495 | .621 |
| Vomiting | -.002 | .004 | -.040 | -.585 | .559 |

**Table 4.21 Models of multiple regression of Treatment-related gastrointestinal and other symptoms cluster affecting on functional status by using symptom distress score (N=300) (cont.)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Dizziness | -.007 | .004 | -.120 | -1.977 | .049 |
| $R^2$ | .015 | | | | |
| Adjust $R^2$ | .005 | | | | |
| F Change | 1.468 | | | | |
| P | .223 | | | | |

**3.2.4.5 Treatment-related neurological and other symptoms cluster and functional scores (Cluster 5).** A problem with multicollinearity and autocorrelation problem were not indicated (VIF = 1.024-1.031, tolerance = 0.970-0.976, Durbin Watson score was 1.709). All independent variables together explained 1.1% of the variance in functional status ($R^2$ = .011, F = 1.074, df = 3, p = .360). No variable was statistically significant relationship between the set of symptoms in this cluster and the functional status ($P<0.05$) (See Table 4.22).

**Table 4.22 Models of multiple regression of Treatment-related neurological and other symptoms cluster and functional scores affecting on functional status by using symptom distress score (N=300)**

| Model | B | SE | Beta | t | sig |
|---|---|---|---|---|---|
| Constant | .311 | .007 | | 44.578 | .000 |
| Numbness/tingling in hands/feet | -.005 | .004 | -.070 | -1.191 | .235 |
| Weight loss | .000 | .005 | -.007 | -.116 | .908 |
| Difficult sleeping | -.004 | .003 | -.067 | -1.149 | .252 |
| $R^2$ | .011 | | | | |
| Adjust $R^2$ | .001 | | | | |
| F Change | 1.074 | | | | |
| P | .360 | | | | |

**3.2.5 The Comparisons of Symptom Clusters across Symptom Dimensions between Symptoms Clusters of Symptom Severity and Symptom Distress Affecting on Functional Status.**

Across symptom dimensions, the key cluster of symptom severity was found different to those of symptom distress. The key cluster of symptom severity was 'Respiratory-related sleep alteration symptom cluster'. The key predictor in this cluster was shortness of breath. The key cluster of symptom distress was 'Anorexia-related symptoms cluster'. The key predictor in this cluster was lack of energy. In addition, symptom clusters derived from ratings of severity score (12.6%) rather than distress score (10.3%) provided a more synergic effect of functional status (Details are summarized in Table 4.23).

**Table 4.23 The comparisons of symptom clusters across symptom dimensions between symptoms clusters of symptom severity and symptom distress affecting on functional status**

| Topics | Symptom Severity | Symptom Distress |
|---|---|---|
| **Clusters** | Cluster 1:<br>Emotional-elimination discomfort symptoms cluster<br>Cluster 2:<br>Anorexia-related symptoms cluster<br>Cluster 3:<br>Treatment-related gastrointestinal and other symptoms cluster<br>Cluster 4:<br>Neurological and body image symptoms cluster<br>Cluster 5:<br>Respiratory and sleep disturbance symptoms cluster<br>(12.6%) | Cluster 1:<br>Emotional-elimination discomfort symptoms cluster<br>Cluster 2:<br>Anorexia-related symptoms cluster<br>Cluster 3:<br>Treatment-related gastrointestinal and other symptoms cluster<br>Cluster 4:<br>Treatment-related neurological, and other symptoms cluster<br>Cluster 5:<br>Body image symptoms cluster<br>(10.3%) |
| **Key clusters** | **Factor 5:**<br>Respiratory and sleep disturbance symptoms cluster | **Factor 3:**<br>Anorexia- related symptoms cluster |

**Table 4.23 The comparisons of symptom clusters across symptom dimensions between symptoms clusters of symptom severity and symptom distress affecting on functional status (cont.)**

| Topics | Symptom Severity | Symptom Distress |
|---|---|---|
| **Clusters 1** | **Emotional-elimination discomfort symptoms cluster** | **Emotional-elimination discomfort symptoms cluster** |
| **Key Predictors** | - Feeling irritable<br>- Feeling drowsy<br>- Feeling bloated<br>- Dizziness<br>- Problems with urination<br>- Constipation<br>- Changes in skin<br>(5.4%) | - Feeling irritable<br>- Feeling bloated<br>- Problems with urination<br>- Constipation<br>- Shortness of breath<br>- Worrying<br>(5.3%) |
| **Cluster 2** | **Anorexia-related symptoms cluster** | **Anorexia-related symptoms cluster** |
| **Key Predictors** | - Dry mouth<br>- Change in the way food tastes<br>- Lack of appetite *<br>(8.1%) | - Lack of appetite<br>- Change in the way food tastes<br>- Dry mouth<br>- Lack of energy *<br>(8.1%) |
| **Cluster 3** | **Treatment-related gastrointestinal and other symptoms cluster** | **Treatment-related gastrointestinal and other symptoms cluster** |
| **Key Predictors** | - Nausea<br>- Vomiting<br>- Hair loss<br>(0.9%) | - Nausea<br>- Vomiting<br>- Dizziness<br>(1.5%) |

**Table 4.23 The comparisons of symptom clusters across symptom dimensions between symptoms clusters of symptom severity and symptom distress affecting on functional status (cont.)**

| Topics | Symptom Severity | Symptom Distress |
|---|---|---|
| **Cluster 4** | **Neurological and body image symptoms cluster** | **Treatment-related neurological and other symptoms cluster** |
| **Key Predictors** | - Numbness/tingling in hands/ feet<br>- "I don't look like myself "<br>- Pain<br>- Worrying<br>- Weight loss<br>(1.2%) | - Numbness/tingling in hands/ feet<br>- Weight loss<br>- Difficulty sleeping<br>(1.1%) |
| **Cluster 5** | **Respiratory and sleep disturbance symptoms cluster** | **Body image symptoms cluster** |
| **Key Predictors** | - Shortness of breath *<br>- Cough<br>- Difficulty sleeping<br>(6.1%) | - "I don't look like myself"<br>- Hair loss<br>- Itching<br>- Changes in skin*<br>(1.5%) |

*= Key symptoms

## Part 4: Determine Lung Cancer Patients with Different Groups by Symptoms Experience and Functional Status

Cluster analysis was used to determine lung cancer patients with different groups by different of symptoms experience. A combination approach using a hierarchical approach followed by a nonhierarchical approach was used analysis in this study. In the hierarchical cluster analysis, two, three, four, and five patient cluster solutions were extracted. The results indicated that the two clusters solution provided the best description of the data. Moreover, the three to five cluster solutions resulted in groups that contained a small number of patients. As a result, the two-cluster solution provided the best description of the data and was chosen because it provided

better group separation and more parsimonious interpretation. This solution labeled as a 'high-symptom burden group' (cluster 1, n= 139) and a 'low-symptom burden group' (cluster 2, n= 161). The results indicated that there were significant differences between the two subgroups of patients' symptom experience scores. Patients who were categorized in the 'high-symptom burden group' had significantly ($p< 0.05$) greater mean symptom prevalence, symptom frequency, and symptom severity scores compared to patients in the 'low-symptom burden group' (See table 4.24).

Independent sample t-test was used to examine the differences between the two subgroups of advanced lung cancer patients on functional status. Significant differences in functional status score were found between the two subgroups of advanced lung cancer patients. Patients who were categorized in the 'high-symptom burden group' were significantly ($p< 0.05$) more likely to have mean functional status score lower than the 'low-symptom burden group' (See table 4.24).

**Table 4.24 The comparisons of mean symptom experience scores and functional status by patient subgroup**

| Symptom Experience | High-symptom burden (N = 139 ) | | Low-symptom burden (N = 161) | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Symptom Prevalence | 17.86 | 2.90 | 10.57 | 2.94 | 0.00* |
| Symptom Severity | 39.69 | 9.26 | 20.56 | 6.44 | 0.00* |
| Symptom Distress | 39.96 | 10.39 | 20.10 | 6.66 | 0.00* |
| Functional Status | 1.99 | 0.281 | 2.071 | 0.405 | 0.03* |

* $p < 0.05$ based on group comparisons by independent t-test

## Summary of the Results in this Chapter

1. Lack of appetite was rated as the most prevalent symptom. Problem with urination was rated as the most frequent symptom. Lack of appetite was rated as the most severe symptom and constipation was rated as the most distressing symptom.

2. Five major clusters were extracted in both the dimensions of symptom severity and symptom distress. Symptom clusters of symptom severity and those of symptom distress were not identical. The ‘Anorexia-related symptoms cluster’ was existed almost similarly across symptom dimensions.

3. The functional mean score was 2.03 on 1-4 scale. Participants were partially limited functional status. The personal care activity was mostly maintained. The activity mostly limited was the occupational functions.

4. The factor scores of all five symptom clusters of symptom severity together significantly explained 12.6% of the variances in the functional ($P<0.05$). Only ‘Anorexia-related symptoms cluster’ and ‘Respiratory-related sleep disturbance symptom cluster’ were statistically significant predictors of functional status. The cluster explaining the greatest proportion of the variance in the functional status was ‘Respiratory-related sleep disturbance symptom cluster’. The key predictor in this cluster was shortness of breath.

5. The factor scores of all five symptom clusters of symptom distress together statistically significant explained 10.3% of the variances in the functional ($P<0.05$). Only ‘Body image symptoms cluster’ and ‘Anorexia-related symptoms cluster’ were statistically significant predictors of functional status. The cluster explaining the greatest proportion of the variance in the functional status was ‘Anorexia-related symptoms cluster’. The key predictor in this cluster was lack of energy.

6. Patients who were categorized in the ‘high-symptom burden group’ had significantly ($p< 0.05$) greater mean symptom prevalence, symptom severity, and symptom distress scores, but lower mean functional status score than patients in the ‘low-symptom burden group’.

# CHAPTER V
# DISCUSSION

This chapter provides discussions in relation to the results of this study. The discussion focused on interpretation of the main findings and examines the clinical significance and implications of the results as well as the need for the future research. Strengths and limitations of this study were also provided.

## Participants' Characteristics

An average age of the participants in this study was 61.39, which were older adults. Most of participants were male, and married. This finding were consistent with several previous studies both Thai studies (Malangpoothon, Pongthavorndamol, Sriyuktasuth, & Soparattanapaisarn, 2009; Pudtong et al., 2014) and aboard studies (Akin, Can, Aydiner, Ozdilli, & Durna, 2010; Molassiotis, Lowe, Blackhall, & Lorigan, 2010). The majority had retired and living with their family caregivers (97%). For the health care costs, most participants were supported by government welfare (57.7%) which was consistent with the previous Thai study of lung cancer patients (Pudtong et al., 2014; Malangpoothong et al., 2009).

Most of the participants were diagnosed with NSCLC stage IV. This result was consistent with the literature research found that most lung cancer patients were diagnosed when their cancer was already in advanced stage (Keefe, Garst, McBride, & Baucom, 2008). Participants were currently undergoing chemotherapy with various treatment regimens. Hypertension was found the most comorbid. This finding was similar to the previous studies both Thai studies (Malangpoothong et al., 2009; Pudtong et al., 2014)and aboard studies ( Hoffman, 2007).

## Symptom Experiences of Advanced Lung Cancer Patients Receiving Chemotherapy

The findings from this study showed that the symptoms experienced by advanced lung cancer patients receiving chemotherapy were complex and multidimensional. They experienced a variety of symptoms. In this study, of the 32 symptoms assessed, patients with lung cancer (N = 300) reported an average of 13.95 symptoms, with the ranges between 3 to 26 symptoms during the disease and treatment phases. In addition, participants experienced and weighted their symptoms differently across symptom dimensions. This result was congruent with the study by Pudthong and colleagues (2014) who found that patients with lung cancer experienced 2 - 32 symptoms with a mean of 14.65 symptoms. Lutz et al., (2001) found that 79% of patients reported three or more symptoms. The findings also revealed that they weighted the significance of their symptoms unequally.

### Symptom Prevalence

The top five prevalent symptoms were lack of appetite (81.7%), lack of energy (78%), constipation (70.3%), dry mouth (66.7%), and change in the way food taste (62.7%) respectively. These finding were consistent with previous studies both Thai (Malangpoothong et al., 2009; Pudthong et al., 2014) and aboard studies (Akin, et al., 2010; Chan, et al., 2005). It was interesting to recognize that although the studies were conducted in different countries and at different points in time, the symptoms prevalence experienced by the lung cancer patients were similar.

Lack of appetite was rated as the most prevalent symptom and also was rated as the top five in all symptom dimensions. Symptom experiences were subjective by nature and people evaluated and gave meanings to the occurrence of perceived symptom. In addition, the associations among components of symptom experiences were bidirectional. Therefore, the symptoms reported as high prevalence and frequency might be perceived and interpreted as more severe and distressful (Dodd et al., 2001). Lack of appetite may be resulted from chemotherapy which causes the taste buds to lose its function. They may have numbness of their tongue and lose the ability to smell food; as a result, the sense of eating declines. This finding corresponds

with previous studies (Lutz et al., 2001; Malangpoothong et al., 2009; Pudtong et al., 2014).

In addition**,** lack of energy or fatigue was rated as the second rank of prevalent symptom. These results relevant with several previous studies reported that lack of energy was found in about more than 40 % to 100% of patients with lung cancer (Malangpoothong et al., 2009; Pudtong et al., 2014; Hoffman, 2007). Lack of energy may be resulted from the tumor necrosis factor (TNF) which stimulates the body to use more protein. Moreover, cancer patients were confronted with pathology of the disease and long-term treatments; as a result they develop stress. A long period of stress makes the body use reserved energy; consequently, lack of energy occurs.

Interestingly, participants were reported constipation as the top five of all symptom dimensions (the third rank of prevalent symptoms, the fourth rank of severe symptom, and the first rank of distressing symptom). This finding corresponds with previous studies by Pudthong and team (2014) found 55.8% of patients with lung cancer reported constipation. For Western study, Hoffman and team reported constipation was found in about 53% (the fourth rank of prevalent symptoms) of patients with lung cancer. Constipation may be resulted from cancer disease itself, and the effects of opioids, nacrotic, and chemotherapy (Woolery et al., 2008). Among patients with cancer, the prevalence of constipation may be as high as 60% and increases to 87% in such patients taking opioids to reduce their pain (Wirz & Klaschik, 2005). In addition, 81.7% of the participants experienced lack of appetite, change in the way food taste, dry mouth resulting in inadequate consumption of vegetables and fruits, a low residue diet, including inadequate fluid intake. This may cause them to experienced constipation.

Dry mouth was also reported as the fourth rank of prevalent symptom. Interestingly, this symptom was not rated as severe symptom and distressing symptoms. From patient's interviewed, patients reported that when they experienced dry mouth, they just plenty drank more fluids. They did not feel bothered by this symptom. Dry mouth may be resulted from chemotherapy and vomiting-reducing medications. This finding was congruent with the previous studies which found that 49-69% of patients with lung cancer who received chemotherapy experienced dry

mouth (Gift et al., 2004; Malangpoothong, et al., 2009; Pudtong et al., 2014) which consequently caused lack of appetite and changes in food taste.

A change in food taste is a common symptom in patients with cancer and resulted from both cancer and chemotherapy. In this study, about 62.7 % of patients with lung cancer were reported this symptom as the fifth rank of top five prevalent symptoms. The patients were more sensitive to bitter taste, spicy and detecting salty but have difficulty detecting sweet tastes. It leads to lack of appetite, weight loss, and malnutrition (Cunningham, 2004). These finding were consistent with previous studies which reported a change in food taste was reported 35% to 48.9% in patients with lung cancer (Gift, Stommel, Jablonski, & Given, 2003; Malangpoothong et al., 2009; Pudtong et al., 2014).

**Symptom Frequency**

The top five frequent symptom were problem with urination (mean = 2.84), followed by lack of appetite (mean = 2.80), numbness/tingling in hands/feet (mean = 2.73), lack of energy (mean= 2.58), and feeling nervous (mean= 2.52).

Problem with urinary was rates as the most frequent symptom. For chemotherapy treatment, there were many different chemotherapy drugs with the potential for many different side effects. The kidneys work to excrete the powerful chemotherapy drugs as they move through the body. In the process, some kidney and bladder cells can become irritated. Symptoms of bladder irritation include increased urinary frequency (HealthLine & Team, 2014). In addition, it was possible that advice from nurses about to drink plenty more of fluids to flush the medication from the system and to keep the system functioning properly. These finding were consistent with previous studies both in patients with lung cancer (Gift et al., 2004; Malangpoothong et al., 2009).

Lack of appetite and lack of energy were also rated as the top five frequent symptoms. These findings were consistent with previous studies both in patients with lung cancer ( Hoffman et al., 2007; Malangpoothong et al., 2009; Pudtong et al., 2014) and breast cancers (Phligbua et al., 2013).

Numbness/tingling in hands/feet were rated at the third rank of frequent symptom. Chemotherapy drugs may cause problems with nervous. Some chemo

drugs such as carboplatin and paclitaxel can cause numbness, or tingling in the hands and feet (peripheral neuropathy)(Macmilian, n.d.). Patients may also fine it hard to fasten buttons or do other fiddly tasks (HealthLine & Team, 2014). This finding was consistent with the previous studies both in patients with lung cancer (Malangpoothong et al., 2009).

In addition, this study found feeling nervous was rated as the top five frequent symptoms and also the top five distressing symptom. Nervous is feeling excited and worried, or showing anxiety. A patient may become more anxious as cancer spreads or treatment becomes more intense. The patients were feeling nervous about cancer that is not responding to treatment, or they cannot receive chemotherapy in the next time. Moreover, tumors in the lungs may create physical problems that cause anxiety and nervous (HealthLine & Team, 2014).

**Symptom Severity**

The top five severe symptoms were lack of appetite (mean = 2.56), followed by difficulty swallowing (mean = 2.54), hair loss (mean = 2.52), constipation (mean = 2.48), and change in the way food tastes (mean = 2.40), respectively. These findings were consistent with previous studies in lung cancer patients (Malangpoothong et al., 2009; Pudtong et al., 2014; Wang, 2008). Lack of appetite and constipation were also rated as top five prevalent symptoms, and distressing symptoms. Hair loss was rated as the third rank of severe symptoms, but it was not reported as prevalent symptom, and distressing symptom. In this study, 59.7% of advanced lung cancer patient receiving carboplatin and gemcitabine. Gemcitabine and carboplatin were less common side effects of hair loss. Hair may thin but unlikely to lose all the hair (Chemocare, n.d.; Macmillian, n.d.). It was almost always temporary and hair will grow back after chemotherapy ends. In addition, most of patients in this study are more than 60 years old. They always just stay at home. Therefore, they were rated hair loss as symptom severity but not distressful. These findings were consistent with a previous study in patients with lung cancer by Pudthong and team (2014) which also found that hair loss was rated as the third rank of severe symptom, but it was not rated as distressing symptom. However, the result was different from a study in breast

cancer which found that patients with breast cancer were rated hair loss as the most severe symptom and also distressing symptom (Suwisith et al., 2008).

Interestingly**,** in this study and the previous Thai studies in both lung cancer (Malangpoothong et al., 2009; Pudtong et al., 2014) and other types of cancers (Chaiviboontham, Viwatwongkasem, Hanucharurnkul, & McCorkle, 2011; Phligbua et al., 2013; Suwisith et al., 2008) found cancer patients experienced problem with sexual interest of activity approximately 0-25%. The symptom was not rated as the top five of all symptom dimensions. Inconsistent with a western study by Gift and team (2004) who found elderly lung cancer patients experienced lack of sexual interest 31%, but they were rated this symptom as the most severity symptom. This incongruent result may be caused by cultural difference. Unlike Western, a Thai person is not comfortable to even discuss this issue openly because they think that it's private and very personal issue. Therefore, they may be afraid to talk with others about this symptom.

**Symptom Distress**

The top five distressing symptoms were constipation (mean = 2.70), lack of appetite (mean = 2.68), pain (mean = 2.56), feeling nervous (mean = 2.49), and worrying (mean = 2.41) respectively. Constipation was rated as the most distressing symptom and also rated as top five symptoms of all dimension. This finding was consistent with previous studies in breast cancer (Phligbua, 2012; Suwisith et al., 2008). Constipation is a major source of distress for patients with cancer. It can be secondary to disease squealed, side effects of treatment, or preexisting conditions. If constipation is not managed proactively, patients can experience increased discomfort and negative consequences, such as feeling bloated, anorexia, nausea, bowel impaction, or bowel perforation, all of which can be life threatening and have an impact on quality of life (Myra Woolery et al., 2008). Lack of appetite was also rated as the top five distressing symptoms and all symptom dimensions. The findings also confirmed by previous studies (Malangpoothong et al., 2009; Pudthong et al., 2014).

Approximately, 56.7% of patients in this study experienced pain and also reported this symptom as the third rank of the top five distressing symptom. Pain is resulted from various factors. About 70-90% of cancer patients developed pain when

the disease was in an advanced stage (Thammakumpee, 2004). Patients with lung cancer often appeared at late or advanced stages of the disease, and thus pain can also be a problem for patients (Claessens et al., 2000). Moreover, pain may be caused by chemotherapy. Short and long term consequences of chemotherapy treatment can involve pain in this study. The result was similarly found in lung cancer and general advanced cancer. This results relevant with previous studies found that pain was the distressful symptom ( Sarna et al., 1993; Pudthong et al., 2014).

Feeling nervous (mean = 2.49), and worrying (mean = 2.41) were also rated as the top five distressing symptom. The diagnosis of cancer and side effects of medications cause the patients exact a psychological and emotional toll. Patients may have anxiety, stress, and worry (HealthLine & Team, 2014). Moreover, patients also worry about becoming a burden to family members (Kuo & Ma, 2002). Congruently, the findings from previous studies which found that the most serious disruptions in women with advanced lung cancer were worry about ability to care for self, and worry about cancer progression (Sarna, 1993). If this psychological distressing symptom cannot be solved, other symptoms, such as depression, sleeping difficulty, and constipation can occur (Gobel, 2004).

In conclusion, advanced lung cancer patients undergoing chemotherapy commonly experienced multiple symptoms rather than a single symptom. This study's findings supported the theory of unpleasant symptom by Lenz and colleagues (1997) in the way that symptom experiences are multidimensional. Two or more symptoms occurring together were likely to catalyze each other.

In addition, the results of this study showed that the perceptions of symptoms were different among the dimensions of prevalence, frequency, severity, and distress. This finding confirmed the previous studies both in the lung cancer (Malangpoothong et al., 2009; Pudtong et al., 2014;Wang et al., 2008) and breast cancers (Phligbua et al., 2013; Suwisith et al., 2008) which found the symptoms that occurred most may not be the ones that the patients perceived in dimension of symptom prevalence, frequency, severity, and distress. The symptoms reporting most symptom prevalence were not necessarily to be the most symptom frequency, severity, or distress. In this study, lack of energy and dry mouth were rates as top five symptoms prevalence, but were not rated as top five severe symptoms. Problem with

urinary and numbness/tingling in hand/feet were rated as the top five frequent symptoms but were not reported as the top five in other symptom dimension.

Difficulty swallowing, hair loss, and change in food taste were rated as the top five most severe symptom but were not reported as top five most distressing symptom. Whereas pain, feeling nervous, and worrying were not reported as prevalent symptom and severe symptom but were rated as the top five most distressing symptom. Furthermore, the symptoms commonly existed in the top five ranks across symptom dimensions were lack of appetite and constipation.

## Symptom Clusters based on Symptom Severity Dimension in Lung Cancer Patients Receiving Chemotherapy

The findings from this study confirmed previous studies (Chaiviboontham, Viwatwongkasem, Hanucharurnkul, & McCorkle, 2011; Gift et al., 2004; Pudtong et al., 2014; Wang et al., 2008) that symptom clusters existed in patients with lung cancer receiving chemotherapy. Using principal component analysis with varimax rotation, five symptom clusters accounted for 42.53% of variance in all symptoms extracted in the dimensions of symptom severity. The name of the symptom cluster was assigned or given based on the majority of the symptoms within the cluster. The clusters were labeled as:

**1. Emotional-elimination discomfort symptom cluster** consisted of feeling irritable, feeling bloated, problems with urination, constipation, feeling drowsy, dizziness, and changes in skin. This cluster has not been reported in previous studies.

There were seven previous studies that examined symptom cluster in lung cancer by using severity score (Chan et al., 2005; Fox & Lyon, 2006; Gift et al., 2004; Gift et al., 2003; Hoffman, 2007; Wang et al., 2008) which used the different instruments, design, statistical method, and participant's characteristics. Three of seven studies identified symptom cluster by using the most common symptom approach which focused on a few symptoms empirically considered clinically important (Chan et al., 2005; Fox & Lyon, 2006; Hoffman et al., 2007). Those studies

were more likely selected different symptoms having associations to each other and determined the relationship between symptoms in a cluster. Rather, this current study identified symptom cluster by using all-possible symptom approach which any potential symptoms that patients experience are considered in cluster identification.

The findings from the current study revealed that the symptoms in each cluster seem to be aggregated with their similar types of symptoms. The other three studies using the same symptom approach with this study, but using different measurement and patient's condition. Wang et al (2008) examine symptoms cluster in lung cancer patients using MD Anderson Symptom Inventory measurement (MDASI). The MDASI is a list of 13 symptoms includes general activity, mood, and work, relations with other people, walking, and enjoyment of life. On MDASI, only two symptoms (i.e., feeling sad and distress) evaluate emotional status, while on the MSAS, four symptoms (feeling sad, worrying, feeling nervous, feeling irritable) evaluate emotional status. In addition, MSAS contained of items to measure eliminate function (problem with urinary, diarrhea, and constipation), whereas MDASI is not.

Therefore, the absence of emotional clinical cluster in previous study might be because they were not evaluated as they should be. Obviously, numbers and types of symptoms of each instrument used to evaluate symptoms take significant roles in identifying symptom clustering. Additionally, cluster type and composition depends on the population's characteristic, disease stage, assessment method, instrument, timeframe, and statistical method (Kim et al., 2009; Kirkova, Walsh, Aktas, & Davis, 2010)

**2. Anorexia-related symptoms cluster** consisted of lack of appetite, change in the way food tastes, and dry mouth. The findings were consistent with previous studies. Gift and colleague (2004) reported a single large cluster label as 'general symptom cluster' which contained the symptoms of lack of appetite and altered taste. Wang and team (2008) examined the cross-sectional study in lung cancer patients which found that appetite and dry mouth were formed together as 'general symptom cluster'. Further, previous Thai study examining symptom cluster in lung cancer patients reported lack of appetite and change in food taste were crusted together as a part of 'digestive impairment symptom cluster (Pudtong et al., 2014).

**3. Treatment-related gastrointestinal and other symptoms cluster** consisted of nausea, vomiting, and hair loss. This finding consistent with previous lung cancer studies reported nausea and vomiting were formed together with different sets of 'general symptom cluster' (Gift, et al., 2004), and 'gastrointestinal symptom cluster' (Wang et al., 2008). Further, nausea and vomiting have been found formed together in other types of cancer studies (Chen & Tseng, 2006; Walsh & Rybicki, 2006). Suwisith et al., (2008) examined symptom cluster in breast cancer reported nausea and vomiting clustered as a part of 'gastrointestinal symptom cluster'. The result in current study was supported previous study that nausea and vomiting clustered consistently (Kirkova et al., 2010).

**4. Neurological and body image symptoms cluster** consisted of numbness/tingling in hands/feet, 'I don't look like myself', pain, worrying, and weight loss. These cluster was consistent with previous Thai study (Chaiviboontham et al., 2011). The finding reaffirmed the findings of longitudinal study in a large heterogeneous group of patients with cancer by Molassiotis and colleagues (2010) who reported some initial link between the hand/foot cluster (numbness/tingling in hands/feet) and body image cluster( I don't look like myself).

Furthermore, the findings of this study revealed 'numbness/tingling in hands/feet, 'I don't look like myself', pain, worrying, and weight loss symptoms all loaded on one factor, whereas other previous studies found these symptom loaded in separate factors with their own distinct names. Example, Suwisith and colleague (2008) reported worrying and 'I don't look like myself' formed together as a part of 'emotions related symptoms cluster', whereas pain and numbness/tingling formed together as a part of 'pain related discomfort symptom cluster' in breast cancer study. Phligbua and colleague (2013) reported 'I don't look like myself' and worrying were formed together as a part of 'psychologically-related self-image symptom cluster'.

**5. Respiratory and sleep disturbance symptoms cluster** consisted of shortness of breath, cough and difficulty sleeping. Respiratory symptoms are central to patients symptom experiences in lung cancer populations because they also interact in various complex ways both with each other and with a variety of non-respiratory

symptoms such sleep disturbance (Cooley, 2000; Molassiotis et al., 2010). This cluster have not been reported as symptom cluster in breast cancer (Phligbua et al., 2013; Suwisith et al., 2008). This finding was consistent with previous lung cancer studies (Chan et al., 2005; Fox & Lyon, 2006; Hoffman et al., 2007).

Chaiviboonthum et al., (2011) reported shortness of breath and sleeping difficulty were formed together in advance heterogeneous group of Thai patients with cancer. Wang and colleague (2006) found cough and shortness of breath formed together as symptom cluster. Cough plays a central role with the respiratory symptom cluster. Cough can trigger breathlessness (and vice versa), persistent cough could lead to fatigue and perhaps low oxygen saturation from breathlessness can further deplete energy levels, providing a physiological link to each other (Molassiotis et al., 2010). Pudthong and team (2014) reported coughing and sleeping difficulty were formed together as a part of 'sleep alteration symptom cluster'. One qualitative study in the exploration of respiratory distress symptom cluster in lung cancer reported respiratory distress symptom cluster, encompassing cough, breathlessness and fatigue, which co-occur and influence each other. Unresolved coughing carried strong implications for patients' breathlessness, sleep disturbance, and fatigue (Molassiotis et al., 2010).

While it was acknowledged that symptom clusters were different in each study based on the scales used to assess symptoms and the particular timing of assessment, sample and sample size, they all contain 'core' symptoms (of cough and breathlessness). This result reaffirmed by the study of Kirkova and colleague (2011) who reviewed articles on cancer symptom which reported 'dyspnea (breathlessness) consistently clusters with cough (Sarna & Brecht, 1997; Walsh & Rybicki, 2006) and also cluster with insomnia problem (Sarna & Brecht, 1997). Therefore, this was an important symptom that was responsible for significant morbidity and impairment in a number of quality of life areas (Sarna et al., 2004), and its appropriate management was of paramount importance during the short survival span of lung cancer patients.

In conclusion, the findings obtained from this study confirmed those of the previous studies that symptom clusters based on symptom severity dimension existed in patients with advanced lung cancer receiving chemotherapy. The comparison of the specific symptom clusters identified in this study to previous studies revealed some similarities as well as some differences.

Differences in the composition of the clusters may be related to differences in the instruments used to assess the symptoms, the number of symptoms, analytical methods, and sample's conditions might cause the differences in the patterns of symptom clusters (Kim et al., 2009). Interestingly, dyspnea (breathlessness) consistently clusters with cough (Sarna & Brecht, 1997; Walsh & Rybicki, 2006) and also cluster with insomnia problem (Sarna & Brecht, 1997). In addition, nausea also crusted consistently with vomiting. Findings from this study and comparisons across studies suggest that the number and specific symptoms, as well as the rating scales that are included on a multidimensional questionnaire, need to be considered in future studies of symptom clusters.

## Symptom Clusters based on Symptom Distress Dimension in Lung Cancer Patients Receiving Chemotherapy

The findings from this study confirmed those from previous studies in that symptom clusters using distress score existed in patients with advanced lung cancer receiving chemotherapy. Using principal component analysis with varimax rotation, five symptom clusters which were identified accounted for 43.70% of variance in all symptoms was extracted in symptom distress. The name of the symptom cluster was based on the majority of the symptoms within the cluster. The clusters were labeled as:

**1. Emotional-elimination discomfort symptoms cluster** consisted of feeling irritable, feeling bloated, problems with urination, constipation, shortness of breath, and worrying. The findings of this study revealed that all symptoms loaded on one factor, whereas previous studies found these symptoms loaded in separate factors with their own distinct names. Molassiotis and team (2010) examined the qualitative research in the exploration of respiratory distress symptom cluster in lung cancer indicated that breathlessness tended to provoke emotional symptom (Molassiotis et al., 2010). In addition, the study of symptom cluster in Thai breast cancer reported feeling irritable, worrying, shortness of breath, and feeling bloated formed together as a part of 'emotions and pain related discomfort symptom cluster' (Suwisith et al., 2008),

problems with urinary, feeling bloated, and constipation formed together as a part of ‘discomfort symptoms cluster’ (Phligbua et al., 2013).

**2. Body image symptoms cluster** consisted of ‘I don’t look like myself’, hair loss, itching, changes in skin. This cluster tends to be associated with treatment and disease progression. The findings of this study revealed all symptoms loaded on one factor, whereas other previous studies found these symptoms loaded in separate factors with their own distinct names. Pudtong and colleague (2014) reported ‘I don’t look like myself’, and hair loss clustered together as a part of ‘body image symptom cluster’, while ‘itching and change in skin’ formed together as a part of ‘dermatologic and dizziness symptom cluster’.

**3. Anorexia-related symptoms cluster** consisted of lack of appetite, change in the way food tastes, dry mouth, and lack of energy. In the population of patients with advanced cancer, the most common cluster, anorexia-cachexia, also has been found in many studies (Cheung, Le, & Zimmermann, 2009; Jimenez et al., 2011; Miaskowski, Aouizerat, Dodd, & Cooper, 2007; Walsh & Rybicki, 2006). Lack of appetite was one of the factors that caused lack of energy in cancer patients because the body had inadequate nutrients to repair cells. This result of current study was consistent with previous studies both in lung cancer and other types of cancers (Gift et al., 2004; Henoch, Ploner, & Tishelman, 2009; Wang et al., 2008). In advance heterogeneous cancer study, Walsh and Rybicki (2006) reported fatigue, anorexia, lack of energy, dry mouth, and taste changes formed together as a part of ‘fatigue-anorexia-cachexia cluster’.

**4**. **Treatment-related gastrointestinal and other symptoms cluster** consisted of nausea, vomiting, and dizziness. ‘A cancer treatment-related symptom cluster’ refer to a group of three or more symptoms occurring together that arise or worsen during treatment (Honea, Brant, & Beck, 2007). This result of current study was consistent with previous studies by Hird et al., (2010) reported nausea, vomiting, and dizziness formed together as a part of symptom cluster in patients with brain metastasis receiving radiotherapy. In addition, treatment-related symptom clusters,

particularly GI symptoms (such as nausea, and vomiting) were reported as common adverse effects of chemotherapy in several studies both in lung cancer (Gift et al., 2004; Wang, et al., 2008), and in other types of cancer groups of oncology patients (Chaiviboontham et al., 2011; Chen & Tseng, 2006; Suwisith et al., 2008). The findings also confirmed by Chen et al., (2011) and Kirkova et al., (2011) which reviewed articles cancer symptom cluster reported nausea and vomiting clustered consistently across instruments and analyses.

**5. Treatment-related neurological and other symptoms cluster** consisted of numbness/tingling in hands/feet, weight loss, and difficulty sleeping. Group of these symptoms occurring together that arise or worsen during treatment. Chemotherapy drugs may cause problems with nervous such as carboplatin and paclitaxel can cause numbness, or tingling in the hands and feet (peripheral neuropathy)(Macmilian, n.d.). Patients may also fine it hard to fasten buttons or do other fiddly tasks (HealthLine & Team, 2014). In lung cancer, weight loss was associated with increased symptom distress (Sarna, Lindsey, Brecht, Dean, & McCorkle, 1994). Sarna and colleague (1993) found factors associated with weight loss in lung cancer were treatment with chemotherapy.

In conclusion, the findings from this study confirmed previous studies that symptom clusters based on symptom distress dimension existed in patients with advanced lung cancer receiving chemotherapy. A comparison of the specific symptom clusters identified in this study to previous reported some similarities as well as some distinct differences.

It was not surprising that inconsistent results were found across these studies in terms of the number of clusters identified (Kim et al., 2009). The differences in the specific symptoms within a cluster may be due to whether severity or distress ratings were used in the factor analyses. In addition, the instruments used to evaluate symptom clusters varied across these studies. Varieties of analytic procedures (e.g., factor analysis, cluster analysis, multiple dimensional scaling), and the number as well as the specific symptoms on the symptom inventories were used to identify symptom clusters with both heterogeneous and homogeneous samples of patients in terms of their cancer diagnoses. This also confirmed by previous studies which the

structures of symptom clustering were various even in homogenous sample (Kim et al., 2009; Pudtong et al., 2014; Suwisith et al., 2008).

## Symptom Clusters across Symptom Dimensions

The results of this study showed that symptom clusters of symptom severity and symptom distress were not identical. Although the number of clusters was equal between symptom severity and symptom distress, they were different in terms of the characteristics of the clusters (see Table 4.9). Cluster composition depends on multiple factor such as symptom dimension (Kirkova & Walsh, 2007). The differences in the specific symptoms within a cluster may be due to whether severity or distress ratings were used in the factor analyses (Chen & Lin, 2007; & Gift et al., 2004). The results of this study revealed some similarities, as well as some partially similar. For instance, the 'Anorexia-related symptoms cluster' existed almost similarly across symptom dimensions. In symptom severity dimension, the 'Respiratory and sleep disturbance symptoms cluster' composed of shortness of breath, cough, and difficult sleeping which formed together as cluster, whereas all of these symptoms loaded in separate factor in distress dimension. This can be explained with the homogeneity of this cluster in that the dimension of symptom dimension was not strong enough. Symptoms in this cluster then can aggregate with other symptoms in distress dimension. This result was consistent with previous study by Kim and team (2009) who evaluated for differences in symptom clusters in a homogeneous sample of oncology patients under receiving Radiotherapy using both the occurrence and severity dimensions of the MSAS. The results showed that although the specific symptoms within each cluster were not identical, there were three very similar symptom clusters were identified regardless of whether occurrence or severity dimensions were used. In addition, Suwisith and team (2008) reported that symptom clusters of symptom severity and those of symptom distress in patients with breast cancer were not identical. They were different in terms of the number of factors existed. However, the characteristics of the clusters were almost similar.

The different existence of symptom clusters between symptom severity and symptom distress might be discussed with their conceptual differences. Symptoms

themselves are unstable by nature as various factors can influence how an individual perceives and interprets them. Symptom severity is the dimension that quantifies the degree, strength, or severity of the symptom (Lenz et al., 1997) which involves human interpretation and the meaning given to the perceived symptom (Dodd et al, 2001a), whereas symptom distress refers to the degree to which the individual experiencing the symptom is bothered by it (Lenz et al., 1997). This finding was consistent with a study of Goddell and Nail (2005) who operationalized the concept of symptom distress using a literature synthesis and confirmed that symptom distress distinct from symptom intensity. However, these two symptom dimensions, to some degree, might overlap and share some similar processes of participants' interpretation. Therefore, it might be possible for the similarity of symptom clusters across symptom dimensions.

## Functional Status among Advanced Lung Cancer Receiving Chemotherapy

From the results, the functional mean scores was ranged from 1.08-3.98 on scale of 1-4. The mean of total functional score was 2.03(SD=0.36). Participants were partially limitation on functional status. The partially limited functional activities might be from their self-care behaviors in relations to prevent possible infections from any outdoor activities, limited their activities by family's member, and not from the symptoms. However, Tanaka and colleagues (2002), who studied impact of symptoms on daily life activities in patients with advanced lung cancer, found that symptoms rated as low severity (1 to 3 on a 0–10-point numerical scale) were severe enough to interfere with at least one daily life activity).

Comparing with previous study by Suwisith and colleague (2007) found the functional scores of Thai breast cancer patients undergoing chemotherapy were ranged from 1.34-3.55. The mean of total functional scores was 2.465 (SD=0.52). Naewjumpa and colleague (2014) reported the functional scores of Thai breast cancer patients receiving chemotherapy were ranged from 1.38-2.97. The mean of total functional scores was 2.12 (SD=0.39). These findings indicated that advanced lung cancer patients were more severely limited in functional status than breast cancer patients. This study also confirmed the previous findings that adults with lung cancer

are more severely limited in functional status when compared with other cancer patients ( Kurtz, Kurtz, Stommel, Given, & Given, 1999; Sarna, 1993)

Further, the result showed that personal care activities were mostly maintained. This result was consistent with previous studies (Kongsaktrakul, 2004; Naewjumpa et al., 2014; Suwisith et al., 2008). This findings was possible that patients also maintained their daily living by limiting their unnecessary functional activities to take their sick roles (Suwisith et al., 2008).

The activity mostly limited was the occupational functions. This result was consistent with previous studies in lung cancer patients (Kongsaktrakul, 2004; Sarna, 1994). In contrast with the finding of breast cancer , the researchers reported breast cancer patients can maintain their work during treatment (Naewjumpa et al., 2014; Suwisith et al., 2008). These results might be discussed with several reasons. For example, mostly participants in this study were elderly with an average age of 61.39 years and retired already (20.7%). In this study, the majority of participants' occupations were retired (20.7%), and unemployed (15.0%). A group of cancers who suffer from impaired health as a result of their illness, and this impairment sometimes leads to a decreased ability to work, or even disability. Employment and impaired work ability has most commonly been found to be associated with cancer type, type of treatment, and physical workload. Cancer has a negative impact on employment patterns with studies estimating between 10% and 38% of employees do not return to work following treatment for cancer. Some people find that they can't work at all and their families don't allow them to do any work. Some people choose to take some time off from work during treatment for cancer (Taskila & Lindbohm, 2007).

Further, side effects of treatment such as nausea and fatigue may have an influence on daily work routines. Cancer-related fatigue is very common among people being treated for cancer. In this study, lack of energy was rated as the most top five symptom prevalence (78%; the second rank) and symptom frequency (the fourth rank). Cancer-related fatigue can present significant challenges for workers: affecting their physical functioning, and causing emotional distress. Of patients who were employed, 75% changed their employment status as a result of fatigue (Taskila & Lindbohm, 2007).

In addition, participants in this study were advanced lung cancer who experienced with respiratory problem which associated with fatigue and functional decline (Sarna et al., 2004). This can be effects on colleagues and family. Inability to work during treatment or return to work after cancer treatment, frequent or prolonged work absenteeism, or problems with work performance may have substantial economic impact on participant's family. From the interview, some of patients in this study reported they quitted or reduced their own job during the period of cancer treatment and their family members work more. Changes in work also may have substantial impact on self-esteem, quality of life, and social or family roles (Steiner, Cavender, Main, & Bradley, 2004). Patients may need to take time off during their treatment or reduction in working hours or working days. Although colleagues and workplaces can offer a lot of potential support to employees diagnosed with cancer, taking a lot of time off can make individuals feel out of touch with what's going on at their workplace and they can lose confidence in their ability to do their job well. The impact of cancer and its treatment on work is very interesting and should be study in the future.

## The Influences of Symptom Clusters on the Functional status in Advanced Lung Cancer Receiving Chemotherapy

The results from this study partially supported the proposition of the conceptual framework for the study. The Theory of unpleasant symptoms asserts that the experience of symptoms can have an impact on the individual's ability to function. The symptoms can occur together and simultaneously. The results of this study showed that not all symptom clusters having statistically significant influence on functional status.

The detailed were as follows:

1. For severity dimension, the factor scores of all five symptom clusters of symptom severity together statistically significant explained 12.6% of the variances in the functional status ($P<0.05$). Only 'Anorexia symptoms cluster' and 'Respiratory and sleep disturbance symptom cluster' were statistically significant predictors of functional status.

1.1 The ‘Anorexia symptoms cluster’ ; lack of appetite were form together with dry mouth, and change in the way food taste as cluster, which all together statistically significant explained 8.1% of the variance in the functional status. Lack of energy was the statistically significant symptom explaining the greatest proportion of the variance in functional status in this cluster. This finding was consistent with a previous study by Suwisith and colleague (2008) which found that lack of appetite was the key predictors of ‘GI- related fatigue symptom cluster’ influencing the functional status in Thai breast cancer patients. In addition, these results was also consistent with previous studies which found that lack of appetite had a negative relationship with functional status in Thai advanced lung cancer patients (Malangpoothong et al., 2009) and breast cancer patients (Naewjumpa et al., 2014).

Not all symptoms in this cluster having statistically significant influence on the functional status. Although, only dry mouth and lacks of appetite were significant predictors of functional status, while change in the way food taste did not contribute significantly to regression. Just because a variable is not contributing a statistically significant degree of prediction in the model is not a reason to presume that the symptom itself is a poor predictor (Meyers, Gamst, Guarino 2013).

According to TOUS, multiple symptoms can occur together as a result of a single event, or one symptom can precede another (Lenz et al., 1997). In this cluster, change in the way food taste symptom jointly with dry mouth and lacks of appetite significant predicted functional status. Apparently, it is possible that change in the way food taste symptom may have indirect effect on functional status through other two symptoms within a cluster.

Consistent with several studies in lung cancer revealed that dry mouth resulted from chemotherapy which consequently caused lack of appetite and changes in food taste (Gift, et al., 2004; Malangpoothong, et al., 2009; Pudthong et al., 2014). Change in food taste was a common symptom in lung cancer patients which leads to lack of appetite and malnutrition (Cunningham, 2004; Malangpoothong et al., 2009; Pudtong et al., 2014).

Multiple regression and factor analysis have been used to interpret the multivariate relationship between independent and dependent variable, but these analytic approaches have limitation. The factor model is confined to

representing only direct effect between the factor and symptoms variables (Olson, Hayduk, and Thomas, 2014). Other analytic approaches that could be taken to identify symptom cluster such as structural equation models (SEM) is recommended. SEM permits more detailed representations by tracing the routed of causal impact (both direct and indirect) of interest to both the investigator and the clinician. In addition a study by Olson and colleague (2014) found that SEM permits investigating and testing of a greater variety of potential causal interconnections among symptoms. SEM incorporated and tested specific clinically anticipated causal relationships among the symptoms and changes in those symptoms over time.

1.2 The 'Respiratory and sleep disturbance symptom cluster' was the strongest predictor of the functional status. In this cluster, cough, shortness of breath, and difficulty sleeping form together as cluster, which they jointly explained 6.1% of the variance in the functional status. Only shortness of breath negatively predicted functional status. In particular, shortness of breath in relationship to physical function was commonly reported in the settings of advanced lung cancer.

A decrease in functional status in advanced lung cancer patients is resulted from the imbalance of oxygen supply and demand, which evokes a degree of respiratory failure. The patients cannot perform their activities as usual, move more slowly than usual, have to stay home, and cannot go to work. As a result, they feel worthless because they cause troubles to their family members (Lai, Chan, & Lopez, 2007). This result corresponds with the study by Tanaka and colleagues (2002) found that 55%of advanced lung cancer patients experienced shortness of breath which disturb on daily activity. The more severe the shortness of breath had a limited to perform activities and their functional status can be very low. Gift and colleague (2004) also found that shortness of breath was significantly related to physical function and role limitations in patients with lung cancer.

In this cluster, cough and difficult sleep were not significantly related to functional status. However, they were jointly with shortness of breathless significant predicted functional status. The study by Malangpoothong and colleague (2009) found that shortness of breath and difficult sleeping had a negative relationship with functional status in Thai lung cancer patients. When the patients sleep, all muscles are relax and the body's organs rest in order to regain their strength. When the patients

cannot sleep and have a difficult in sleeping, they cannot maintain their daily activities as usual because they need to sleep during the day time (Mills & Graci, 2004). Naewjumpa and colleague (2014) reported shortness of breast, coughing, and sleeplessness was negative relationship with functional status in Thai breast cancer patients.

Cough can trigger breathlessness (and vice versa), persistent cough could lead to fatigue and perhaps low oxygen saturation from breathlessness can further deplete energy levels, providing a physiological link to each other. Unresolved coughing carried strong implications for patients' breathlessness, sleep disturbance, and fatigue (Molassiotis et al., 2010), lead to they cannot maintain their daily activities. Apparently, it is possible that cough and difficult sleep have indirect effect on functional status through shortness of breath. Other analytic approaches that could be taken direct and indirect effect between symptoms such as structural equation models (SEM) is recommended.

2. For distress dimension, the factor scores of all five symptom clusters of symptom distress dimension together statistically significant explained 10.3% % of the variances in the functional ($P<0.05$). Only 'Anorexia-related symptoms cluster' and 'Body image symptom cluster' were statistically significant predictors of functional status.

2.1 The cluster explaining the greatest proportion of the variance in the functional status was the cluster of 'Anorexia-related symptoms cluster' ; lack of appetite, change in the way food tastes, dry mouth, and lack of energy were all together explained 8.1% of the variance in the functional status. Only lack of energy was negative significant predictors of functional status. The possible explanation is that lack of energy can cause the patients not to be able to perform their activities as usual (Cunningham, 2004). Lack of energy causes the patients to have discomfort, boredom, and a decrease in self-care ability (Tanaka et al., 2002). Lack of energy and functional status impairment were highly associated with each other and had similar relationships with the other variables (Siefert, 2010). This finding was consistent with a previous Thai study by Suwisith and colleague (2008) found that lack of appetite, and lack of energy had negative relationship with the functional status, and also was the strongest predictor of the functional status in Thai breast cancer patients. Lack of energy can predict a change in functional status about 7.3% (Dodd et al., 2001b).

Although, other symptoms (lack of appetite, change in the way food tastes, dry mouth) in this cluster did not contribute statically significant to regression, all these symptoms were jointly with lack of energy significant predictors of functional status. Apparently, it is possible that these symptoms may have indirect effect on functional status through lack of energy. Structural equation models (SEM) is recommended for testing specific clinically anticipated causal relationships among the symptoms in a cluster.

2.2 The 'Body image symptom cluster'; "I don't look like myself", hair loss, itching, changes in skin were all together explained 1.5% of the variance in the functional status. Only change in skin was significant predictor of functional status. The result was consistent with a previous study which found that hair loss, skin changes, and image changes formed together as symptoms cluster and have synergistic effect on functional status in Thai breast cancer patients (Suwisith et al., 2008). Although, other symptoms in this cluster did not contribute significantly to regression, all these symptoms were jointly with change in skin statistically significant predicted functional status. Apparently, it is possible that these symptoms may be having indirect effect on functional status through change in skin. Structural equation models (SEM) is recommended for testing specific clinically anticipated causal relationships among the symptoms.

In conclusion, the results of this study partially supported the conceptual model of the study. Only 'Anorexia symptoms cluster' and 'Respiratory and sleep disturbance symptom cluster' of severity dimension, and 'Anorexia-related symptoms cluster' and 'Body image symptom cluster' of distress dimension were statistically significant predictors of functional status. Structural equation models (SEM) is recommended for testing specific clinically anticipated causal relationships among the symptoms. The key cluster and the key predictors of symptom severity and symptom distress were found different. For severity dimension, the cluster of 'Respiratory and sleep disturbance symptom cluster' was the strongest predictor of functional status. The strongest symptom predictor of functional status in this cluster was shortness of breath. For distress dimension, the cluster of 'Anorexia-related symptoms cluster' was the strongest predictor of functional status. The strongest symptom predictor of functional status in this cluster was lack of energy. In addition, symptom clusters

derived from ratings of severity score rather than distress score provided a more effect on functional status of advanced lung cancer receiving chemotherapy.

## Patient Subgroup Differences in Symptoms experience and Functional Status

The result of the current study demonstrated that two distinctly different subgroups of patients with advanced lung cancer receiving chemotherapy were identified using a cluster analysis. These patients subgroups, characterized as 'high-symptom burden group' and 'low-symptom burden group'. Patients in the 'high-symptom burden group' had a greater symptom prevalence, symptom severity and symptom distress compared to the 'low-symptom burden group'. In addition, patients in the 'high-symptom burden group' were significantly more likely to have greater mean of functional status than the 'low-symptom burden group'. The 'high symptom burden group' was associated with poorer in functional status compared to the 'low-symptom burden group'. Therefore, these findings suggest that greater symptom burden is associated with greater deleterious effects on the functional status in advanced lung cancer patients. This current study confirmed and extended previous researches (Dodd et al., 2010; Finnegan et al., 2009; Gwede et al., 2008; Miaskowski et al., 2006; Pud et al., 2008) that patient subgroups with distinctly differing burden of symptom experience could be identified and these subgroups associated with differences in outcome.

This current study consistent with various previous studies which identification of subgroups of oncology patients who reported similar experiences. Gwede et al., (2008) identified distinct subgroup of breast cancer patients. The results reported that the 'high-symptom burden group' had a greater prevalence compared to the 'low-symptom burden group', and was associated with poorer quality of life compared to the low-symptom burden group. Finnegan et al (2009) identified subgroups of adult survivors of childhood cancers differed in frequency, severity, and distress ratings for eight symptoms (lack of energy, worry, pain, difficulty sleeping, feeling irritable, feeling nervous, difficulty concentrating, and feeling sad). The results found that distinctly different three subgroups of patients characterized as 'high

symptom subgroup' (high frequency, severity, and distress ratings for all symptoms), 'moderate symptom subgroup' (moderate frequency, severity, and distress ratings for all symptoms), and 'low symptom subgroup' (low frequency, severity, and distress ratings for all symptoms), differed in QOL outcomes. High symptom subgroup had the lowest mean QOL scores.

The other studies (Miaskowski et al., 2006; Pud et al., 2008; Dodd et al., 2010) used predetermined symptoms (i.e., pain, fatigue, sleep disturbance, and depression) which were identified as highly prevalent symptoms during active cancer therapy. Miaskowski et al (2006) identified distinct subgroup of various types of cancer patients who experience symptoms difference on severity score. The results found that distinctly different three subgroups of patients characterized as ' low levels of all four symptoms', 'high fatigue and low pain', 'low fatigue and high pain', and 'high levels of all four symptoms'. Patients who reported high levels of all four symptoms reported the worst functional (performance) status and QOL. Pud and team (2008) identified distinct subgroup of oncology outpatients. Four distinct patient subgroups based on symptom severity scores were identified: low levels of all four symptoms; high fatigue and low pain; moderate fatigue and high pain; and high levels of all four symptoms. Patients who reported high levels of all four symptoms had significantly poorer functional status and QOL. Dodd and team (2010) was explored the most prevalent symptoms of pain, fatigue, sleep disturbance and depression in breast cancer patients in a longitudinal design. The result found that based on symptom severity scores at T1 (the week before cycle two) and T2 (end of cancer treatment), four patient subgroups were identified: all low, mild, moderate, and all high. At T3 (end of the study approximately one year after the start of chemotherapy), three subgroups were identified: mild, moderate, and all high. Subgroups with high severity levels of all four symptoms had poorer functional status and QOL at each time point than other subgroups. Group membership changed over time.

The findings from this current study were consistent with those from the previous studies which reported that patient with in subgroups with high symptom burden levels had poorer functional status. The identification of subgroups of patients who have similar symptom experiences may help identify low, and high-risk groups of patients who may warrant different types, different doses, or more targeted symptom

management interventions which can improve patient outcomes (Miaskowski et al., 2006; Gwede et al., 2008; Pud et al., 2008). Thus, further research is needed to identify subgroups early and to identify factors amenable to intervention. For example, future research could include social support or coping measures to determine if the observed subgroup differences are associated with differences in support or coping styles. If identified factors are amenable to change before, during, or after the course of treatment, then the deleterious impact on outcome may be reduced or eliminated.

Summary of the results in this chapter, the finding from this study partially supported TOUS in that patients experience more than one symptom, the symptom experiences are relate to one another. The symptoms vary in severity and distress dimension. However, not all symptoms cluster influence on functional status. It's depending on the key predictor symptoms within the cluster and other factors that influence the symptoms and performance. Therefore, further research of symptom cluster still need.

## Strengths and Limitations of the Study

### Strengths

With insufficient research on symptom cluster and their influences on functional status in advanced lung cancer patients receiving chemotherapy, especially in Thailand. This study provides the evidence that will add to the growing body of knowledge about the symptom clusters and their influences on functional status in advanced lung cancer patients. Knowing which symptom cluster facilitated to understanding the underlying mechanism of symptoms, development of more effective symptom assessment and better cancer management strategies that are targeted at all symptoms within each cluster. The strengths of this study need to be addressed.

The strength of this study was its use of a sample with homogeneous clinical characteristics that were, advanced lung cancer patients receiving chemotherapy. Designs_of the study captured the whole series from symptom occurrences to their effects on individual outcomes. This study provides the understanding symptom experiences in all dimensions of prevalence, frequency,

severity, and distress symptom. There is a lack of study focusing on symptom clusters with different dimensions in advanced lung cancer. Most previous studies evaluated only one symptom when explored symptom clusters.

This is the first study to explored symptom clusters in Thai advance lung cancer across symptom dimensions. The finding of this study expanded the knowledge in terms of its existence in dimensions of severity and distress. The results of this study showed that symptom clusters of severity and distress were not identical. Participants rated symptoms to be highly severity but they may not be the most distress. The clusters with the highest variance explained in all symptoms were not necessary to be found the key cluster. Further, the symptoms with high factor loading scores in each cluster were not necessarily the key predictors in each cluster. This result could lead to better understanding on the different dimensions of symptom clusters between symptom severity and distress. By addressing an understudied problem, this study provides essential information for investigators who are moving toward evaluating multiple symptom clusters. Moreover, the results provided a basis for developing novel strategies to manage multiple symptoms in lung cancer and improve functional status.

In addition, this is the first study that was designed explicitly to determine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experiences differed in their functional status. The results may help to identify low and high-risk groups of patients, which can guide health care providers to treatment/management of disease or treatment related symptoms through interventions tailored to individuals in each group which could improve patient outcomes. Identification of patient subgroups with higher symptom burden may be useful in targeting the neediest individuals for intervention.

**Limitations**

The limitations were related to methodology and method of analysis. The generalization of the results from this study may be limited by the use of a convenience sample and random was not practical for this descriptive study. Also, a study using cross-sectional design limited the data to only one data point. This study, therefore, was unable to demonstrate a pattern of symptom experiences over time. In

addition, data regarding symptoms using the MSAS were assessed from the participants with advanced lung cancer coming to the hospital for receiving next cycle of chemotherapy when the symptoms were generally relieved. Time of assessment this may confound the study findings. Given the limitations of this study, the results should be generalized with caution.

# CHAPTER VI
# CONCLUSION

This chapter provides information on the summary of the study, conclusions, implications of findings and recommendations for future research.

## Summary of the Study

Symptom cluster exploration is an increasingly active field of research. A careful examination of symptom clusters may help both in understanding the underlying mechanism of these symptoms and in developing more effective treatments, and also provide new avenues for interventions to minimize the impact of symptoms on health related outcomes. This study aimed to: 1) describe symptom experiences in all dimensions, 2) explore the existence of symptom clusters in severity and distress dimensions, 3) compare the similarity of symptom cluster classified by severity and distress 4) determine the influences of symptom cluster on the functional status, and 5) determine whether subgroups of advanced lung cancer patients receiving chemotherapy with different symptom experience differed in their functional status. The Theory of Unpleasant Symptoms was used as the conceptual framework to guide the study.

Participants in this study were 300 patients with lung cancer receiving chemotherapy during October, 2013 to March, 2014. Most of participants were males, married, Buddhist, older adults. The majority had primary school education, retired and government service with household income less than 5,000 baths per month but sufficient and saving expense. Health services were covered by government welfare. Most of them live with their family which spouse was main caregiver. Most of the participants were diagnosed with NSCLC stage IV. Participants were currently undergoing chemotherapy with various treatment regimens. The majority treatment regimens received were carboplatin and gemcitabine. Data on the patient’s comorbid

conditions was presented in 94% of the participants, hypertension was found the most. The findings obtained from this study were as follows:

1. Patients with advanced lung cancer reported an average of 13.95 symptoms, with the ranges 3 to 26 symptoms during the disease and treatment phases. Lack of appetite was rated as the most prevalent symptom. Problem with urination was rated as the most frequent symptom. Lack of appetite was rated as the most severe symptom and constipation was rated as the most distressing symptom. The symptoms commonly existed in high top five ranks across symptom dimensions were lack of appetite and constipation.

2. Five symptom clusters were identified accounted for 42.53% of variance in all symptoms was extracted in the dimensions of symptom severity.

Cluster 1: 'Emotional-elimination discomfort symptom cluster' had the most percentage of variance (10.16%) composed of feeling irritable, feeling bloated, problems with urination, constipation, feeling drowsy, dizziness, and changes in skin.

Cluster 2: 'Anorexia-related symptoms cluster' consisted of three symptoms, dry mouth, and change in the way food tastes, and lack of appetite, which explained 8.70% of factor variance.

Cluster 3: 'Treatment-related gastrointestinal and other symptoms cluster' consisted of nausea, vomiting, and hair loss, which explained 8.63% of factor variance.

Cluster 4: 'Neurological and body image symptoms cluster' consisted of numbness/tingling in hands/feel, "I don't look like myself", pain, worrying, and weight loss , which explained 7.76% of factor variance.

Cluster 5: 'Respiratory and sleep disturbance symptoms cluster' consisted of shortness of breath, cough, and difficulty sleeping, which explained 7.28% of factor variance.

3. Symptom clusters of symptom severity and those of symptom distress were different in terms of characteristics of the clusters. Five symptom clusters were identified with 43.69 % variance in all symptoms.

Cluster 1: 'Emotional-elimination discomfort symptoms cluster' had the most percentage of variance (10.54%), which composed of feeling irritable, feeling bloated, problems with urination, constipation, shortness of breath, and worrying.

Cluster 2: ‘Body image symptoms cluster’ consisted of ‘I don't look like myself’, hair lost, itching, changes in skin, which explained 9.01% of factor variance.

Cluster 3: ‘Anorexia-related symptoms cluster’ consisted of lack of appetite, change in the way food tastes, dry mouth, and lack of energy, which explained 8.77 % of factor variance.

Cluster 4: ‘Treatment-related gastrointestinal and other symptoms cluster’ consisted of nausea, vomiting, and dizziness, which explained 8.40% of factor variance.

Cluster 5: ‘Treatment-related neurological_and other symptoms cluster’ consisted of numbness/tingling in hands/feet, weight loss, and difficulty sleeping, which explained 6.97 % of factor variance.

4. The functional mean score was 2.03 on 1-4 scale. Participants were partially limited functional status. Personal care activities were mostly maintained. The activity mostly limited was the occupational functions.

5. The factor scores of all five symptom clusters of symptom severity together significantly explained 12.6% of the variances in the functional ($P<0.05$). Only Respiratory-related sleep alteration symptom cluster’ and ‘Anorexia symptoms cluster’ were statistically significant predictors of functional status.

‘Respiratory-related sleep alteration symptom cluster’ was the cluster explaining the greatest proportion of the variance (10.3%) in the functional status. Shortness of breath was the key predictor of the functional status.

‘Anorexia symptoms cluster’ composed of lack of appetite, dry mouth, change in the way food taste as cluster, which all together explained 8.1% of the variance in the functional status. Lack of energy was the significant symptom explaining the greatest proportion of the variance in functional status in this cluster.

6. The factor scores of all five symptom clusters of symptom distress together statistically significant explained 10.3% of the variances in the functional ($P<0.05$). Only ‘Anorexia-related symptoms cluster’ and ‘Body image symptom cluster’ were statistically significant predictors of functional status.

‘Anorexia-related symptoms cluster’ was the cluster explaining the greatest proportion of the variance (8.1%) in the functional status. Lack of energy was the key predictor of the functional status.

‘Body image symptom cluster’ consisted of “I don’t look like myself”, hair loss, itching, and changes in skin, which all together explained (1.5%) of the variances in the functional ($P<0.05$). A change in skin was the key predictor of the functional status.

7. Patients in the ‘high-symptom burden group’ have greater symptoms prevalence, symptom severity, and symptom distress compared to the ‘low-symptom burden group’.

8. Patients in the ‘high-symptom burden group’ were associated with poorer in functional status compared to the ‘low-symptom burden group’.

## Implications to Nursing Practice

The findings of this study have provided evidence that advanced lung cancer receiving chemotherapy experienced multiple symptoms differently across symptom dimensions during treatment. The results also found that the presence of multiple symptoms influenced patient’s perceptions of their functional limitations. Nurses must assess the simultaneous occurrence of symptoms and beware of the potential for symptoms to cluster, possibly resulting in effect on functional status. Nurses should select assessments that identify multiple symptoms and define their co-occurrence. The regular use of multidimensional and comprehensive symptom assessment tools is suggested for assessment of prevalence, frequency, severity, and distress of the symptoms. It is also recommended to monitor symptoms before, during and after treatment.

Nurse practitioners should pursue strategies and guidelines that focus on the management of clusters of symptoms rather than single symptoms. To achieve this, nurses must begin to document the pattern of symptom severity, symptom distress and how symptoms vary, both in occurrence and patient response, to the intervention strategies. Interventions should be designed to address clusters, rather than isolated symptoms, to match the experiences of advanced lung cancer patients receiving chemotherapy.

In addition, intervention targeting the key symptom clusters and key predictors might reduce the impact of symptom cluster on functional status. Nurses

may begin by reviewing evidence-based strategies for each symptom and then consider how each symptom-specific strategy and existing recommended overlapping strategies might be effective for the management of an entire cluster of symptoms. In this way, each symptom can be examined as well as overall symptom burden; however, the focus is directed to performance outcomes critical to cancer care effectiveness.

## Implications to Nursing Science

The findings obtained from this study confirmed that advanced lung cancer patients undergoing chemotherapy experienced multiple symptoms rather than a single symptom. The symptoms are also multidimensional. The results of this study support the proposed by Lenz and team (1997) that several concurrent symptoms occur as a symptom cluster. This study helps in expanding the conceptual knowledge on the existence of symptom clusters that the clustering was differently across symptom dimensions.

## Recommendations for Future Research

Future research studies are recommended in order to fill the knowledge gaps of the current study and to expand more knowledge on the concept of symptom clusters.

1. Future studies need to consider the use of a longitudinal design to identify symptom patterns that might change over time, along the disease and treatment trajectory.

2. Future studies focusing specifically on the key cluster and the key symptoms affecting functional status of advanced lung cancer receiving chemotherapy is recommended.

3. The further symptom cluster approach such as Structural equation models (SEM) is recommend for tested specific clinically anticipated causal relationships among the symptoms. Including, the interaction effect model to predict the synergistic effect of symptom cluster on functional status is recommended.

4. The methods and effects of intervention for symptom clusters require extra examination. The testing of interventions to relieve the cluster of symptom is need.

# REFERENCES

Adams, M., Kerby, I., Rocker, I., Evans, A., Johansen, K., & Franks, C. (1989). A comparison of the toxicity and efficacy of cisplatin and carboplatin in advanced ovarian cancer. *Acta Oncologica, 28*(1), 57-60.

Akechi, T., Okamura, H., Nishiwaki, Y., & Uchitomi, Y. (2001). Psychiatric disorders and associated and predictive factors in patients with unresectable nonsmall cell lung carcinoma. *Cancer, 92*(10), 2609-2622.

Akin, S., Can, G., Aydiner, A., Ozdilli, K., & Durna, Z. (2010). Quality of life, symptom experience and distress of lung cancer patients undergoing chemotherapy. *European Journal of Oncology Nursing, 14*(5), 400-409.

Aldenderfer, M. S., & Blashfield, R. (1984). *Cluster analysis.* Beverley Hills, CA: Sage.

Allard, P., Dionne, A., & Potvin, D. (1994). Factors associated with length of survival among 1081 terminally ill cancer patients. *Journal of palliative care, 11*(3), 20-24.

Alley, E., Green, R., & Schuchter, L. (2002). Cutaneous toxicities of cancer therapy. *Current opinion in Oncology, 14*(2), 212-216.

Armstrong, T. S. (2003). Symptoms experience: a concept analysis. *Oncology Nursing Forum 30*, 601-606.

Barsevick, A., Dudley, W., Beck, S., Sweeney, C., Whitmer, K., & Nail, L. (2004). A randomized clinical trial of energy conservation for patients with cancer related fatigue. *Cancer, 100*(6), 1302-1310.

Barsevick, A. M. (2007). The elusive concept of the symptom cluster. *Oncology Nursing Forum, 34*, 971-980.

Barsevick, A. M., Whitmer, K., Nail, L. M., Beck, S. L., & Dudley, W. N. (2006). Symptom cluster research: conceptual, design, measurement, and analysis issues. *Journal of Pain and Symptom Management, 31*(1), 85-95.

Beck, S. L. (2004). Abstract: Symptom Clusters: Impediments and Suggestions for Solutions. *JNCI Monographs, 2004*(32), 137.

Beck, S. L., Dudley, W. N., & Barsevick, A. (2005). Pain, sleep disturbance, and fatigue in patients with cancer: using a mediation model to test a symptom cluster. Paper presented at the Oncology Nursing Forum.

Beckles, M. A., Spiro, S. G., Colice, G. L., & Rudd, R. M. (2003). Initial Evaluation of the Patient With Lung Cancer. *Chest, 123*(1 suppl), 97S-104S.

Bender, C. M., Ergÿn, F. S., Rosenzweig, M. Q., Cohen, S. M., & Sereika, S. M. (2005). Symptom clusters in breast cancer across 3 phases of the disease. *Cancer Nursing, 28*(3), 219-225.

Bircan, A., Berktaş, M. B., Bayız, H., Başay, N., Bircan, S., & Berkoğlu, M. (2003). Effects of chemotherapy on quality of life for patients with lung cancer. *Turkish Respiratory Journal, 4*(2), 61-66.

Black, J. M., & Matassarin-Jacobs, E. (1993). *Luckmann and Sorensen's medical-surgical nursing: a psychophysiologic approach*: WB Saunders Company.

Blackhall, F. H., Shepherd, F. A., & Albain, K. S. (2005). Improving survival and reducing toxicity with chemotherapy in advanced non-small cell lung cancer: a realistic goal? *Treatments in Respiratory Medicine, 4*(2), 71-84.

Brown, J. K., Cooley, M. E., Chernecky, C., & Sarna, L. (2011). A Symptom Cluster and Sentinel Symptom Experienced by Women With Lung Cancer. *Oncoogy Nursing Forum 38*(6), 425-435.

Bruera, E., Kuehn, N., Miller, M. J., Selmser, P., & Macmillan, K. (1991). The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of alliative care patients. *Journal of palliative care, 7*(2), 6.

Chaiviboontham, S., Viwatwongkasem, C., Hanucharurnkul, S., & McCorkle, R. (2011). Symptom Clusters in Thais with Advanced Cancer. *Pacific Rim International Journal of Nursing Research, 15*(4), 265-277.

Chan, C., Richardson, A., & Richardson, J. (2005). A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer. *European journal of oncology nursing: the official journal of European Oncology Nursing Society, 9*(4), 325.

Chang, V. T., Hwang, S. S., Feuerman, M., Kasimis, B. S., & Thaler, H. T. (2000). The Memorial Symptom Assessment Scale Short Form (MSAS-SF). *Cancer, 89*(5), 1162-1171.

Chemocare. (n.d.). Retrieved July 6, 2014, from http://cheocare.com/chemotherapy/drug-info/gemcitabine.aspx.

Chen, M. L., & Lin, C. C. (2007). Cancer symptom clusters: a validation study. *Journal of Pain and Symptom Management, 34*(6), 590-599.

Chen, M. L., & Tseng, H. C. (2006). Symptom clusters in cancer patients. *Supportive Care in Cancer, 14*(8), 825-830.

Cheung, W., Le, L., & Zimmermann, C. (2009). Symptom clusters in patients with advanced cancers. *Supportive Care in Cancer, 17*(9), 1223-1230.

Chumney, D., Nollinger, K., Shesko, K., Skop, K., Spencer, M., & Newton, R. A. (2010). Ability of Functional Independence Measure to accurately predict functional outcome of stroke-specific population: systematic review. *Journal of rehabilitation research and development, 47*(1), 17.

Cimprich, & Bernadine. (1985). Symptom management: constipation. *Cancer nursing, 8*, 39-43.

Claessens, M. T., Lynn, J., Zhong, Z., Desbiens, N. A., Phillips, R. S., Wu, A. W., et al. (2000). Dying with lung cancer or chronic obstructive pulmonary disease: insights from SUPPORT. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Journal of the American Geriatrics Society, 48*(5 Suppl), S146-153.

Cleeland, C. S., Mendoza, T. R., Wang, X. S., Chou, C., Harle, M. T., Morrissey, M., et al. (2000). Assessing symptom distress in cancer patients. *Cancer, 89*(7), 1634-1646.

Cleeland, C. S., & Reyes-Gibby, C. C. (2002). When is it justified to treat symptoms? Measuring symptom burden. *Oncology, 16*(9), 64-70.

Cohen, M. E., & Marino, R. J. (2000). The tools of disability outcomes research functional status measures. *Archives of physical medicine and rehabilitation, 81*, S21-S29.

Collins, L. G., Haines, C., Perkel, R., & Enck, R. E. (2007). Lung cancer: diagnosis and management. *American family physician, 75*(1), 56.

Cooley, M. E. (2000). Symptoms in Adults with Lung Cancer:: A Systematic Research Review. *Journal of pain and symptom management, 19*(2), 137-153.

Cooley, M. E., Short, T. H., & Moriarty, H. J. (2003). Symptom prevalence, distress, and change over time in adults receiving treatment for lung cancer. *Psycho Oncology, 12*(7), 694-708.

Cunningham, R. S. (2004). The anorexia-cachexia syndrome. In C.H. Yabro, M.H. Frogge & M. Goodman (Eds.), *Cancer Symptom Management* (3 ed., pp. 137-167). Canada: John and Bartlett Publishers.

Deesomchok, A., Dechayonbancha, N., & Thongprasert, S. (2005). Lung cancer in Maharaj Nakorn Chiang Mai Hospital: Comparison of the clinical manifestations between the young and old age groups. *Journal of the Medical Association of Thailand., 88*(9), 1236-1241.

De Haes, J., Van Knippenberg, F., & Neijt, J. (1990). Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *British Journal of Cancer, 62*(6), 1034.

Degner, L. F., & Sloan, J. A. (1995). Symptom distress in newly diagnosed ambulatory cancer patients and as a predictor of survival in lung cancer. *Journal of Pain and symptom management, 10*(6), 423-431.

Detterbeck, F. C., Boffa, D. J., & Tanoue, L. T. (2009). The new lung cancer staging system. *CHEST Journal, 136*(1), 260-271.

DeVita Jr, V., Weinberg, R., DePinho, R., & Lawrence, T. (2008). *Rosenberg SA (ed). Cancer. Principles & practice of oncology 8th edition*: New York: Lippincott Williams & Wilkins.

Dodd, Janson, S., Facione, N., Faucett, J., Froelicher, E., Humphreys, J., et al. (2001b). Advancing the science of symptom management. *Journal of Advanced Nursing, 33*(5), 668-676.

Dodd, Miaskowski, C., & Paul, S. (2001a). Symptom clusters and their effect on the functional status of patients with cancer. *Oncology Nursing Forum, 28*(3), 465-470.

Dodd, M. J., Cho, M. H., Cooper, B. A., & Miaskowski, C. (2010). The effect of symptom clusters on functional status and quality of life in women with breast cancer. *European Journal of Oncology Nursing, 14*(2), 101-110.

Doorenbos, A., Given, B., Given, C., & Verbitsky, N. (2006). Physical Functioning: Effect of Behavioral Intervention for Symptoms Among Individuals With Cancer. *Nursing Research May/June, 55*(3), 161-171.

Dudgeon, D. J., Harlos, M., & Clinch, J. J. (1999). The Edmonton Symptom Assessment Scale (ESAS) as an audit tool. *Journal of palliative care, 15*(3), 14.

Elliott, L., Molseed, L. L., & McCallum, P. D. (2006). *The clinical guide to oncology nutrition*. Chicago: American Dietetic Association.

Fan, G., Filipczak, L., & Chow, E. (2007). Symptom clusters in cancer patients: a review of the literature. *Current Oncology*, *14*(5), 173-179.

Ferreira, K. A. S. L., Kimura, M., Teixeira, M. J., Mendoza, T. R., da N brega, J. C. M., Graziani, S. R., et al. (2008). Impact of cancer-related symptom synergisms on health-related quality of life and performance status. *Journal of Pain and Symptom Management*, *35*(6), 604-616.

Finnegan, L., Campbell, R. T., Ferrans, C. E., Wilbur, J., Wilkie, D. J., & Shaver, J. (2009). Symptom Cluster Experience Profiles in Adult Survivors of Childhood Cancers. *Journal of Pain and Symptom Management, 38*(2), 258-269.

Fox, S., & Lyon, D. (2006). Symptom clusters and quality of life in survivors of lung cancer. *Oncology nursing forum, 33*(5), 931-936.

Fox, S. W., Lyon, D., & Farace, E. (2007). Symptom Clusters in Patients With High Grade Glioma. *Journal of Nursing Scholarship, 39*(1), 61-67.

Gaston Johansson, F., Fall Dickson, J. M., & Bakos, A. B. (1999). Fatigue, Pain, and Depression in Pre Autotransplant Breast Cancer Patients. *Cancer Practice, 7*(5), 240-247.

Genç, F., & Tan, M. (2011). Symptoms of patients with lung cancer undergoing chemotherapy and coping strategies. *Cancer nursing, 34*(6), 503-509.

Gift, A., Jablonski, A., Stommel, M., & Given, C. W. (2004). Symptom clusters in elderly patients with lung cancer. *Oncology Nursing Forum*, *31*(2), 203-212.

Gift, A., Stommel, M., Jablonski, A., & Given, W. (2003). A cluster of symptoms over time in patients with lung cancer. *Nursing research, 52*(6), 393-400.

Given, B. A., Given, C.W., Sikorskii, A., Hadar, N. (2007). Symptom clusters and physical functions for patients receiving chemotherapy. *oncology Nursing 23*(2), 121-126.

Given, C. W., Given, B., Azzouz, F., Stommel, M., & Kozachik, S. (2000). Comparison of changes in physical functioning of elderly patients with new diagnoses of cancer. *Medical Care, 38*(5), 482-493.

Glaus, A., Boehme, C., Thürlimann, B., Ruhstaller, T., Schmitz, S. H., Morant, R., et al. (2006). Fatigue and menopausal symptoms in women with breast cancer undergoing hormonal cancer treatment. *Annals of oncology, 17*(5), 801-806.

Gobel, B. H. (2004). Anxiety In C. H. Yarbro, M. H. Frogge & G. Michelle (Eds.), *Cancer symptom management* ( 3 ed., pp. 651-664). Canada: Jones & Bartlett Learning.

Green, C. P. (1986). Changes in responsibility in women's families after the diagnosis of cancer. *Health care for women international, 7*(3), 221-239.

Gwede, C. K., Small, B. J., Munster, P. N., Andrykowski, M. A., & Jacobsen, P. B. (2008). Exploring the differential experience of breast cancer treatment-related symptoms: a cluster analytic approach. *Supportive Care in Cancer, 16*(8), 925-933.

Hair, J.F., Anderson, R.E., Tatham, R.L., & Black, W.C. (1995). *Multivariate Data Analysis*. 4th edition, Prentice Hall: Englewood.

Hair, J., Black, W., Babin, B., & Anderson, R. (2010). *Multivariate data analysis*. 7th edition, NJ: Prentice hall Upper Saddle River.

Hayduk, L., Olson, K., Quan, H., Cree, M., & Cui, Y. (2010). Temporal changes in the causal foundations of palliative care symptoms. *Quality of Life Research, 19*(3), 299-306.

Hayduk, L., Olson, K., Quan, H., Cree, M., & Cui, Y. (2010). Evidence confirming and clarifying the changing causal foundations of palliative care symptom restructuring. *Quality of Life Research 19*(3), 299-306.

HealthLine, & Team. (2014). The side effects of chemotherapy on the body. Retrieved March 5, 2014, from http://www.healthline.com/health/cancer/effects-on-body

Henoch, I., Ploner, A., & Tishelman, C. (2009). Increasing stringency in symptom cluster research: a methodological exploration of symptom clusters in patients with inoperable lung cancer. *Oncology Nursing Forum, 36*(6), 282-292.

Hoffman, A. (2007). *Fatigue, self-efficacy, and physical functional status in persons with lung cancer*. Michigan State University, United States -- Michigan.

Hoffman, A., Given, B., Eye, A., Gift, A., & Given, C. (2007). Relationships among pain, fatigue, insomnia, and gender in persons with lung cancer. *34*, 785-792.

Hollen, P. J., Gralla, R. J., Kris, M. G., Cox, C., Belani, C. P., Grunberg, S. M., et al. (1994). Measurement of quality of life in patients with lung cancer in multicenter trials of new therapies. Psychometric assessment of the Lung Cancer Symptom Scale. *Cancer, 73*(8), 2087-2098.

Honea, N., Brant, J., & Beck, S. L. (2007). *Treatment-related symptom clusters.* Paper presented at the Seminars in oncology nursing.

Hopwood, P., & Stephens, R. J. (2000). Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. *Journal of Clinical Oncology, 18*(4), 893-893.

Horn, L., Pao, W., & Johnson, D.H. (2012). Neoplasms of the Lung. In 18th (Ed.), *Harrison's principles of internal medicine*: McGraw-Hill.

Jette, A. M. (1980). Functional Status Index: reliability of a chronic disease evaluation instrument. *Archives of physical medicine and rehabilitation, 61*(9), 395.

Jimenez, A., Madero, R., Alonso, A., Martinez-Mar n, V., Vilches, Y., Martinez, B., et al. (2011). Symptom Clusters in Advanced Cancer. *Journal of Pain and Symptom Management*.

Joyce, M., Schwartz, S., & Huhmann, M. (2008). *Supportive care in lung cancer*. Paper presented at the Seminars in Oncology Nursing.

Kaasa, S., Mastekaasa, A., & Thorud, E. (1988). Toxicity, physical function and everyday activity reported by patients with inoperable non-small cell lung cancer in a randomized trial (chemotherapy versus radiotherapy). *Acta Oncologica, 27*(4), 343-349.

Kaasa, T., Loomis, J., Gillis, K., Bruera, E., & Hanson, J. (1997). The Edmonton Functional Assessment Tool: preliminary development and evaluation for use in palliative care. *Journal of pain and symptom management, 13*(1), 10-19.

Karnofsky, D. A. (1949). The clinical evaluation of chemotherapeutic agents in cancer. *Evaluation of chemotherapeutic agents*.

Katz, S., Downs, T. D., Cash, H. R., & Grotz, R. C. (1970). Progress in development of the index of ADL. *The Gerontologist, 10*(1 Part 1), 20-30.

Kenne Sarenmalm, E., hl n, J., Od n, A., & Gaston Johansson, F. (2008). Experience and predictors of symptoms, distress and health related quality of life over time in postmenopausal women with recurrent breast cancer. *Psycho Oncology, 17*(5), 497-505.

Kenne Sarenmalm, E., Öhlén, J., Odén, A., & Gaston-Johansson, F. (2008). Experience and predictors of symptoms, distress and health-related quality of life over time in postmenopausal women with recurrent breast cancer. *Psycho-Oncology, 17*(5), 497-505.

Kim, E., Jahan, T., Aouizerat, B. E., Dodd, M. J., Cooper, B. A., Paul, S. M., et al. (2009).

Differences in symptom clusters identified using occurrence rates versus symptom severity ratings in patients at the end of radiation therapy. *Cancer Nursing, 32*(6), 429.

Kim, H., Barsevick, A., & Tulman, L. (2009). Predictors of the Intensity of Cluster Symptoms in Patients With Breast Cancer. *Journal of nursing scholarship: an official publication of Sigma Theta Tau International Honor Society of Nursing/Sigma Theta Tau, 41*(2), 158-165.

Kim, H. J., McGuire, D. B., Tulman, L., & Barsevick, A. M. (2005). Symptom clusters: concept analysis and clinical implications for cancer nursing. *Cancer Nursing, 28*(4), 270-282.

Kirkova, J., Davis, M. P., Walsh, D., Tiernan, E., O'Leary, N., LeGrand, S. B., et al. (2006). Cancer symptom assessment instruments: a systematic review. *Journal of Clinical Oncology, 24*(9), 1459-1473.

Kirkova J, Walsh D. (2007). Cancer symptom clusters—a dynamic construct. *Supportive Care in Cancer*.;15(9):1011-3.

Kirkova, J., Walsh, D., Aktas, A., & Davis, M. P. (2010). Cancer symptom clusters: old concept but new data. *American Journal of Hospice and Palliative Medicine, 27*(4), 282-288.

Knapp, T.R. (1999). The over emphasis on power analysis. In F. Downs.(Ed). *Reading in Research Methodology,* 2nd edition, pp.13-15. Lippincott: Philadelphia.

Kongsaktrakul, P. (2004). *Relationships between types of cancer, fatigue experience, fatigue management strategies, family support and functional status of cancer patients receiving chemotherapy.* Unpublished master's thesis, Chulalongkorn University, Thailand.

Krech, R. L., Davis, J., Walsh, D., & Curtis, E. B. (1992). Symptoms of lung cancer. *Palliative medicine, 6*(4), 309.

Kukull, W. A., McCorkle, R., & Driever, M. (1986). Symptom distress, psychosocial variables, and survival from lung cancer. *Journal of Psychosocial Oncology, 4*(1-2), 91-104.

Kuo, T., & Ma, F. (2002). Symptom distresses and coping strategies in patients with non-small cell lung cancer. *Cancer nursing, 25*(4), 309-317.

Kurtz, M. E., Kurtz, J., Stommel, M., Given, C., & Given, B. (1999). The influence of symptoms, age, comorbidity and cancer site on physical functioning and mental health of geriatric women patients. *Women & health, 29*(3), 1-12.

Kurtz, M. E., Kurtz, J., Stommel, M., Given, C. W., & Given, B. A. (2000). Symptomatology and loss of physical functioning among geriatric patients with lung cancer. *Journal of pain and symptom management, 19*(4), 249-256.

Lai, Y., Chan, C. W., & Lopez, V. (2007). Perceptions of dyspnea and helpful interventions during the advanced stage of lung cancer: Chinese patients' perspectives. *Cancer Nursing, 30*(2), E1-E8.

Lawton, M., & Brody, E. M. (1970). Assessment of Older People: Self-Maintaining and Instrumental Activities of Daily Living. *Nursing research, 19*(3), 278.

Leidy, N. K. (1994). Functional status and the forward progress of merry-go-rounds: toward a coherent analytical framework. Nursing research, 43(4), 196-202.

Lenz, E. R., & Pugh, L. C. (2003). The theory of unpleasant symptoms *Middle range theory for nursing* (pp. 69-90). New York: Springer.

Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: an update. *Advances in Nursing Science, 19*(3), 14.

Lewis, F. M., Ellison, E. S., & Woods, N. F. (1985). *The impact of breast cancer on the family*. Paper presented at the Seminars in Oncology Nursing.

Lobchuk, M. M. (2003). The memorial symptom assessment scale: modified for use in understanding family caregivers' perceptions of cancer patients' symptom experiences. *Journal of Pain and Symptom Management, 26*(1), 644-654.

Lutz, S., Norrell, R., Bertucio, C., Kachnic, L., Johnson, C., Arthur, D., et al. (2001). Symptom frequency and severity in patients with metastatic or locally recurrent lung cancer: a prospective study using the Lung Cancer Symptom Scale in a community hospital. *Journal of palliative medicine, 4*(2), 157-165.

Macmilian. (n.d.). Chemotherapy. Retrieved July 6, 2014, from http://www.macmillian.org.uk/Canereinformation/Cancertreatment/Treatmenttypes/Chemotherapy/Individualdrugs/Paclitaxel.aspx

Malangpoothong R, Pongthavorndamol K, Sriyuktasuth A, & Soparattanapaisarn, N. (2009). Symptom experiences, management strategies and functional status in advanced lung cancer patients receiving chemotherapy. *Journal of Nursing Science, 27*(2), 69-78.

Malangpoothong, R., Pongthavornkamol, K., Sriyuktasuth, A., & Soparattanapaisarn, N. (2009). Symptom Experiences, Management Strategies and Functional Status in Advanced Lung Cancer Patients Receiving Chemotherapy. *Journal of nursing science, 27*(2), 69-78.

Maliski, S. L., Kwan, L., Elashoff, D., & Litwin, M. S. (2008). *Symptom clusters related to treatment for prostate cancer*. Paper presented at the Oncology Nursing Forum.

Mantovani, G. (2010). Randomised phase III clinical trial of 5 different arms of treatment on 332 patients with cancer cachexia. *Eur Rev Med Pharmacol Sci, 14*(4), 292-301.

McCorkle, R., & Quint-Benoliel, J. (1983). Symptom distress, current concerns and mood disturbance after diagnosis of life-threatening disease. *Social science & medicine, 17*(7), 431-438.

McCorkle, R., & Young, K. (1978). Development of a symptom distress scale. *Cancer Nursing, 1*(5), 373-378.

McShane, R., & McLane, A. (1985). Constipation. Consensual and empirical validation. *The Nursing clinics of North America, 20*(4), 801-808.

Miaskowski, C., Aouizerat, B. E., Dodd, M., & Cooper, B. (2007). Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer. *JNCI Monographs,* 37, 39-46.

Miaskowski, C., Cooper, B. A., Paul, S. M., Dodd, M., Lee, K., Aouizerat, B. E., et al. (2006). Subgroups of patients with cancer with different symptom experiences and quality-of-life outcomes: a cluster analysis. *Oncology Nursing Forum. 33*, 79-89.

Mills, M., & Graci, G. M. (2004). Sleep disturbances. In C. H. Yarbro, M. H. Frogge & M. Goodman (Eds.), *Cancer symptom management* (3 ed., Vol. 1, pp. 111-134). Canada: Jones & Bartlett Learning.

Milstein, D., Sapir, D., Cohen, Y., & Robinson, E. (1987). Prognostic factors in patients with lung cancer. *Israel journal of medical sciences, 24*(9-10), 588-592.

Mirsadraee, S., Oswal, D., Alizadeh, Y., Caulo, A., & van Beek, E. J. (2012). The 7th lung cancer TNM classification and staging system: Review of the changes and implications. *World Journal of Radiology, 4*(4), 128.

Molassiotis, A., Lowe, M., Blackhall, F., & Lorigan, P. (2010). A qualitative exploration of a respiratory distress symptom cluster in lung cancer: Cough, breathlessness and fatigue. *Lung Cancer*.

Mor, V., Guadagnoli, E., & Wool, M. S. (1987). An examination of the concrete service needs of advanced cancer patients. *Journal of Psychosocial Oncology, 5*(1), 1-17.

Mor, V., Masterson-Allen, S., Houts, P., & Siegel, K. (1992). The changing needs of patients with cancer at home. A longitudinal view. *Cancer, 69*(3), 829-838.

Muers, M., & Round, C. (1993). Palliation of symptoms in non-small cell lung cancer: a study by the Yorkshire Regional Cancer Organisation Thoracic Group. *Thorax, 48*(4), 339-343.

Munro, B. H. (2005). *Statistical Methods for Health Care Research* (5th ed.) Philadelphia: Lippincott Williams & Wilkins.

Meyers L., Gamst G., Guarino AJ. Applied Multivariate Research Design and Interpretation. (2013). Multiple Regression: Statistical Methods Using IBM SPSS: SAGE. p. 1104.

Naewjumpa, C., Saneha, C., Puwarawuttipanit, W., & Soparattanapaisarnhai, N. (2014). Symptom Experiences, Symptom Management Strategies, and Functional Status in Outpatient with Breast Cancer Stage IV Receiving Chemotherapy. *Thai Journal of Nursing Council 29*(1), 15-28.

Nowack, K. M. (1989). Coping style, cognitive hardiness, and health status. *Journal of Behavioral Medicine, 12*(2), 145-158.

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the Number of Classes in Latent Class Analysis and Growth Mixture Modeling: A Monte Carlo Simulation Study. Structural Equation Modeling: *A Multidisciplinary Journal*, 14(4), 535-569.

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T., et al. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American journal of clinical oncology, 5*(6), 649-656.

Okuyama, T., Wang, X. S., Akechi, T., Mendoza, T. R., Hosaka, T., Cleeland, C. S., et al. (2003). Japanese version of the MD Anderson Symptom Inventory: a validation study. *Journal of Pain and Symptom Management, 26*(6), 1093-1104.

Olson, K., Hayduk, L., Cree, M., Cui, Y., Quan, H., Hanson, J., et al. (2008). The changing causal foundations of cancer-related symptom clustering during the final month of palliative care: a longitudinal study. *BMC Medical Research Methodology, 8*(1), 36.

Paice, J. A. (2004). Assessment of symptom clusters in people with cancer. *JNCI Monographs, 2004*(32), 98-102.

Peruselli, C., Camporesi, E., Colombo, A. M., Mazzon, G., & Paci, E. (1993). Quality-of-life assessment in a home care program for advanced cancer patients: a study using the Symptom Distress Scale. *Journal of Pain and Symptom Management, 8*(5), 306-311.

Phligbua, W. (2012). *Symptom clusters and quality of life in women with breast cancer receiving adjuvant chemotherapy.* Unpublished Dissertation, Mahidol University, Thailand.

Phligbua, W., Pongthavornkamol, K., Knobf, T. M., Junda, T., Viwatwongkasem, C., & Srimuninnimit, V. (2013). Symptom clusters and quality of life in women with breast cancer receiving adjuvant chemotherapy. Pasific Rim International Thai Journal of Nursing Research, 17 (3), 249-267.

Piper, B., Lindsey, A. M., & , & Dodd, M. J. (1987). Fatigue mechanisms in cancer patients: Developing nursing theory. *Oncology Nursing Forum, 14*(6), 17-23.

Pongthavornkamol, K. (2000). *Coping with side effects and wmotional distress among Thai cancer patients receiving radiation therapy.* Unpublished Dissertation, Rochester University.

Portenoy R, Thaler H, Kornblith A, McCarthy Lepore J, Friedlander-Klar H, Coyle N, et al. Symptom prevalence, characteristics and distress in a cancer population. Quality of Life Research. 1994;3(3):183-189.

Portenoy, R., Thaler, H., Kornblith, A., McCarthy Lepore, J., Friedlander-Klar, H., Kiyasu, E., et al. (1994). The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer, 30*(9), 1326-1336.

Potter, J., & Higginson, I. J. (2004). Pain experienced by lung cancer patients: a review of prevalence, causes and pathophysiology. *Lung Cancer, 43*(3), 247-257.

Pud, D., Ben Ami, S., Cooper, B. A., Aouizerat, B. E., Cohen, D., Radiano, R., et al. (2008). The symptom experience of oncology outpatients has a different impact on quality-of-life outcomes. *Journal of Pain and Symptom Management, 35*(2), 162-170.

Pudtong N, & Aungsuroch Y, J. C. (2014). Symptom clusters in Thai patients with advanced lung cancer. *J Health Res, 28*(3).

Rhodes, V., Watson, P., Johnson, M., Madsen, R., & Beck, N. (1987). Patterns of nausea, vomiting, and distress in patients receiving antineoplastic drug protocols. *Oncology nursing 14*(4), 35.

Ryan, L. S. (1987). *Lung cancer: psychosocial implications.* Paper presented at the Seminars in Oncology Nursing.

Sarna, L. (1993). Correlates of symptom distress in women with lung cancer. *Cancer Practice, 1*(1), 21-28.

Sarna, L. (1994). Functional status in women with lung cancer. *Cancer nursing, 17*(2), 87-93.

Sarna, L., & Brecht, M. L. (1997). Dimensions of symptom distress in women with advanced lung cancer: a factor analysis. *Heart & lung: the journal of critical care, 26*(1), 23-30.

Sarna, L., Evangelista, L., Tashkin, D., Padilla, G., Holmes, C., Brecht, M. L., et al. (2004). Impact of respiratory symptoms and pulmonary function on quality of life of long-term survivors of non-small cell lung cancer. *CHEST Journal, 125*(2), 439-445.

Sarna, L., Lindsey, A., Dean, H., Brecht, M., & McCorkle, R. (1993). *Nutritional intake, weight change, symptom distress, and functional status over time in adults with lung cancer.* Paper presented at the Oncology Nursing Forum.

Sarna, L., Lindsey, A. M., Brecht, M. L., Dean, H., & McCorkle, R. (1994). Weight change and lung cancer: relationships with symptom distress, functional status, and smoking. *Research in nursing & health, 17*(5), 371-379.

Shah, S., Vanclay, F., & Cooper, B. (1989). Improving the sensitivity of the Barthel Index for stroke rehabilitation. *Journal of clinical epidemiology, 42*(8), 703-709.

Siefert, M. L. (2010). Fatigue, Pain, and Functional Status During Outpatient Chemotherapy. *Onclology Nursing Forum, 37*(2), 114-123.

Smith, S. (2001). Evidence-based management of constipation in the oncology patient. *European journal of oncology nursing, 5*(1), 18-25.

Steiner, J. F., Cavender, T. A., Main, D. S., & Bradley, C. J. (2004). Assessing the impact of cancer on work outcomes. *Cancer, 101*(8), 1703-1711.

Stuck, A. E., Walthert, J. M., Nikolaus, T., Büla, C. J., Hohmann, C., & Beck, J. C. (1999). Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Social Science & Medicine, 48*(4), 445-469.

Sumdaengrit, B., Hanucharurnkul, S., Dodd, M, Sarikapan W., Vorapongsathon, T., & Pongthavornkamol, K. (2010). Symptom experience and self-care among Thai woman with cervical cancer. *Pasific Rim International Thai Journal of Nursing Research 14*(3), 203-218.

Suwisith, N., Hanucharurnkul, S., Dodd, M., Vorapongsathorn, T., Pongthavorakamol, K., & Asavametha, N. (2008). Symptom Clusters and Functional Status of Women with Breast Cancer. *Thai Journal of Nursing Research, 12*(3), 153-165.

Tabachnick, Barbara G & Fidell, Linda S, (author.) (2013). Using multivariate statistics (6th edition). Boston Pearson.

Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2002). Impact of Dyspnea, Pain, and Fatigue on Daily Life Activities in Ambulatory Patients with Advanced Lung Cancer. *Journal of pain and symptom management, 23*(5), 417-423.

Taskila, T., & Lindbohm, M. (2007). Factors affecting cancer survivors' employment and work ability. *Acta Oncologica, 46*(4), 446-451.

Thammakumpee, K. (2004a). Clinical manifestation and survival of patients with non-small cell lung cancer. *Journal of the Medical Association of Thailand, 87*(5 ), 503-507.

Thammakumpee, K. (2004b). Clinical manifestation and survival of patients with non-small cell lung cancer. *Journal of the Medical Association of Thailand, 87*(5), 503-507.

Thanasilp, S., & Kongsaktrakul, P. (2005). Factors predicting quality of life of patients with cancer undergoing chemotherapy. *Thai Journal of Nursing Research, 9*(4), 306-315.

Thompson, E., & Subirana, M. (2005). Non-invasive interventions for improving well-being and quality of life in patients with lung cancer--a systematic review of the evidence. *Lung Cancer, 50*(2), 163-176.

Tishelman, C., Degner, L., Rudman, A., Bertilsson, K., Bond, R., Broberger, E., et al. (2005). Symptoms in patients with lung carcinoma. *Cancer, 104*(9), 2013-2021.

Tranmer, J. E., Heyland, D., Dudgeon, D., Groll, D., Squires-Graham, M., & Coulson, K. (2003). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the memorial symptom assessment scale. *Journal of Pain and Symptom Management, 25*(5), 420-429.

Trask, P. C., & Griffith, K. A. (2004). The identification of empirically derived cancer patient subgroups using psychosocial variables. *Journal of Psychosomatic Research, 57*(3), 287-295.

Tulman, L., Fawcett, J., & McEvoy, M. (1991). Development of the inventory of functional status-cancer. *Cancer Nursing, 14*(5), 254-260.

Tulman, L., Fawcett, J., & McEvoy, M. D. (1991). Development of the inventory of functional status-cancer. *Cancer Nursing, 14*(5), 254.

Vainio, A., & Auvinen, A. (1996). Prevalence of symptoms among patients with advanced cancer: an international collaborative study. *Journal of Pain and symptom management, 12*(1), 3-10.

Van der Putten, J., Hobart, J., Freeman, J., & Thompson, A. (1999). Measuring change in disability after inpatient rehabilitation: comparison of the responsiveness of the Barthel Index and the Functional Independence Measure. *Journal of Neurology, Neurosurgery & Psychiatry, 66*(4), 480-484.

Walke, L. M., Byers, A. L., Gallo, W. T., Endrass, J., & Fried, T. R. (2007). The association of symptoms with health outcomes in chronically ill adults. *Journal of Pain and Symptom Management, 33*(1), 58-66.

Walsh, D., & Rybicki, L. (2006). Symptom clustering in advanced cancer. *Supportive Care in Cancer, 14*(8), 831-836.

Wang, S., Tsai, C., Chen, B., Lin, C., & Lin, C. (2008). Symptom clusters and relationships to symptom interference with daily life in Taiwanese lung cancer patients. *Journal of pain and symptom management, 35*(3), 258-266.

Wang, X. S., Fairclough, D. L., Liao, Z., Komaki, R., Chang, J. Y., Mobley, G. M., et al. (2006). Longitudinal Study of the Relationship Between Chemoradiation Therapy for Non–Small-Cell Lung Cancer and Patient Symptoms. *Journal of clinical oncology, 24*(27), 4485.

Ware Jr, J. E., & Hays, R. D. (1988). Methods for measuring patient satisfaction with specific medical encounters. *Medical Care, 26*(4), 393-402.

Ware Jr, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, 473-483.

Wirz, S., & Klaschik, E. (2005). Management of constipation in palliative care patients undergoing opioid therapy: Is polyethylene glycol an option? *American Journal of Hospice and Palliative Medicine, 22*(5), 375-381.

Wisnivesky, J. P., Bonomi, M., Henschke, C., Iannuzzi, M., & McGinn, T. (2005). Radiation therapy for the treatment of unresected stage I-II non-small cell lung cancer. *CHEST Journal, 128*(3), 1461-1467.

Woolery, M., Bisanz, A., Lyons, H. F., Gaido, L., Yenulevich, M., & Fulton, S. (2008). Putting evidence into practice: Evidence-based interventions for the prevention and management of constipation in patients with cancer. *Clinical Journal of ONcology Nursing, 12*(2), 317-337.

Woolery, M., Bisanz, A., Lyons, H. F., Gaido, L., Yenulevich, M., Fulton, S., et al. (2008). Putting Evidence Into Practice®: Evidence-Based Interventions for the Prevention and Management of Constipation in Patients With Cancer. *Clinical Journal of ONcology Nursing, 12*(2), 317-337.

Wright, P. S., & Thomas, S. L. (1995). Constipation and diarrhea: The neglected symptoms. *Seminars in Oncology Nursing, 11*(4), 289-297.

Xiao, C. (2010). The state of science in the study of cancer symptom clusters. *European Journal of Oncology Nursing, 14*(5), 417-434.

# APPENDICES

# APPENDIX A
# LETTER PERMISSION

## The Inventory of Functional Status-Cancer (IFSCA)

## A request to obtain permission to use The IFS-CA

---

**From:** Thidarat Khamboon [mailto:thidarat111@gmail.com]
**Sent:** Monday, April 29, 2013 12:20 PM
**To:** Tulman, Lorraine tulman@nursing.upenn.edu
**Subject:** A request to obtain permission to use The IFS-CA

Mon, Apr 29, 2013 at 11:19 PM

Dear Dr. Tulman

My name is Thidarat Khamboon, a doctoral candidate in a doctor of philosophy (nursing) at Mahidol University, Bangkok, Thailand. I am developing my dissertation under the supervision of Assoc. Prof. Dr. Kanuangnit Pongthavornkamol of Mahidol University and Prof. Dr. Karin Olson of The University of Alberta, Canada. I am interested in using the Inventory of Functional Status-Cancer to conduct my research.

I plan to conduct a crossectional descriptive study about symptom experience and functional status in patients with lung cancer receiving adjuvant chemotherapy. Your instrument is an appropriate one to be used in conducting my research. This instrument was translated into Thai by Suwisith and colleague already. For this reason, I am writing to you to request you and your colleagues' permission to use the IFS-CA. Looking forward to hearing from you.

Sincerely, Thidarat Khamboon

**Tulman, Lorraine** tulman@nursing.upenn.edu

Tue, Apr 30, 2013 at 1:12 AM

To: Thidarat Khamboon thidarat111@gmail.com

Dear Ms. Thidarat,

You have my permission to use the IFS-CA in your work. I would like an abstract of your findings. Best of luck!

Lorraine Tulman, DNSc, RN, FAAN

# LETTER PERMISSION

## The Memorial Symptom Assessment Scale (MSAS)

**A request to obtain permission to use MSAS**

---

**Thidarat Khamboon** <thidarat111@gmail.com> Mon, Apr 29, 2013 at 1:17 PM
To: RPorteno@chpnet.org
Cc: thidarat khamboon <thidarat111@gmail.com>, "Assoc. Prof. Dr. Kanaungnit" <nskpt@mahidol.ac.th>

Dear Dr. Portenoy

Please let me start by introducing myself to you. My name is Thidarat Khamboon, a doctoral candidate at Mahidol University, Bangkok, Thailand (with international and collaborative links through our Foreign University Program). I am developing my dissertation under the supervision of Assoc. Prof. Kanaungnit Pongthavornkamol of Mahidol University and Prof. Dr. Karin Olson of The University of Alberta, Canada. I am interested in using the Memorial Symptom Assessment Scale (MSAS) to conduct my research.

I plan to conduct a crossectional descriptive study about symptom experience and functional status in patients with lung cancer receiving adjuvant chemotherapy. Your instrument is an appropriate one to be used in conducting my research. This instrument was translated into Thai by Suwisith and colleague already. For this reason, I am writing to you to request you and your colleagues' permission to use the IFS-CA. Looking forward to hearing from you.

Sincerely,
Thidarat Khamboon

**Russell Portenoy, MD** <RPorteno@chpnet.org> Mon, Apr 29, 2013 at 8:35 PM
To: Thidarat Khamboon <thidarat111@gmail.com>
Cc: "Assoc. Prof. Dr. Kanaungnit" <nskpt@mahidol.ac.th>

The MSAS is in the public domain and may be used as you wish.

Best of luck with your research.

R. Portenoy MD

https://mail.google.com/mail/Mui=2&ik=a161be960f&view=pt&search=inbox&th=13e547... 30-Apr-13

# LETTTER PERMISSION

## Documentary Proof of Ethical Clearance on Human Rights

2 ถนนพรานนก บางกอกน้อย
กรุงเทพฯ 10700

**คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล**
**เอกสารรับรองโครงการวิจัย**

หมายเลข Si 466/201

**ชื่อโครงการภาษาไทย** : กลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด

**รหัสโครงการ** : 427/2556(EC4)

**หัวหน้าโครงการ / หน่วยงานที่สังกัด** : นางสาวธิดารัตน์ คำบุญ
คณะพยาบาลศาสตร์ มหาวิทยาลัยมหิด

**สถานที่ทำวิจัย** : คณะแพทยศาสตร์ศิริราชพยาบาล

**เอกสารที่รับรอง** :

1. แบบขอรับการพิจารณาจากคณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล
2. โครงการวิจัย
3. เอกสารชี้แจงผู้เข้าร่วมการวิจัย / อาสาสมัคร
4. แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา
5. แบบบันทึกอาการ
6. แบบประเมินการปฏิบัติกิจกรรมของผู้ป่วย IFS-CA
7. ประวัติผู้วิจัย

**วันที่รับรอง** : 15 สิงหาคม 2556

**วันหมดอายุ** : 14 สิงหาคม 2557

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ดำเนินการให้การรับร
โครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในคนที่เป็นสากล ได้แก่ Declaration of Helsinki, the Belmont Report, CIO
Guidelines และ the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

ลงนาม .....
(ศาสตราจารย์ แพทย์หญิงชารุพิมพ์ สูงสว่าง)
ประธานคณะกรรมการจริยธรรมการวิจัยในคน

20 ส.ค. 2556
วันที่

ลงนาม .....
(ศาสตราจารย์คลินิก นายแพทย์อุดม คชินทร)
คณบดี คณะแพทยศาสตร์ศิริราชพยาบาล

21 ส.ค. 2556
วันที่

2 PRANNOK Rd. BANGKOKNOI
BANGKOK 10700

Tel. +66 2419 [illegible]
Fax. +66 2411 [illegible]

**Siriraj Institutional Review Board**

**Certificate of Approval**

COA no. Si 466/2013

**Protocol Title** : Symptom clusters and their influences on the functional status in advanced lung cancer patients receiving chemotherapy

**Protocol number** : 427/2556(EC4)

**Principal Investigator/Affiliation** : Miss Thidarat Khamboon
Faculty of Nursing, Mahidol University

**Research site** : Faculty of Medicine Siriraj Hospital

**Approval includes :**

1. SIRB Submission Form
2. Proposal
3. Participant Information Sheet
4. The Demographic and Medical Record Form (DMRF)
5. Memorial Symptom Assessment Scale (MSAS)
6. Assessment Form for Activity of IFS-CA Patient
7. Principle Investigator's curriculum vitae

**Approval date** : August 15, 2013

**Expired date** : August 14, 2014

This is to certify that Siriraj Institutional Review Board is in full Compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Jarupim Soongswang — 20 AUG 2013

(Prof. Jarupim Soongswang, M.D.) — date

Chairperson

Udom K — 21 AUG 2013

(Clin. Prof. Udom Kachintorn, M.D.) — date

Dean of Faculty of Medicine Siriraj Hospital

**เอกสารรับรอง**

**จาก**

**คณะกรรมการจริยธรรมการวิจัยในคน สถาบันมะเร็งแห่งชาติ**

**เลขที่ 022 / 2556**

| | |
|---|---|
| **ชื่อโครงการ** | กลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด |
| **ชื่อหัวหน้าโครงการ** | นางสาวธิดารัตน์ คำบุญ |
| **หน่วยงานที่สังกัด** | มหาวิทยาลัยมหิดล |
| **รหัสโครงการ** | 29_2013T_OUT317 |
| **สถานที่ทำวิจัย** | สถาบันมะเร็งแห่งชาติ |
| **เอกสารที่รับรอง** | 1. โครงร่างวิจัย ภาษาไทย<br>2. เอกสารชี้แจงข้อมูลโครงการวิจัย<br>3. เอกสารแสดงความยินยอมการเข้าร่วมในโครงการวิจัย<br>4. แบบสอบถาม |
| **วันที่รับรอง** | 15 สิงหาคม 2556 |

คณะกรรมการจริยธรรมการวิจัยในคน สถาบันมะเร็งแห่งชาติ ได้พิจารณาและมีมติ รับรองเอกสารดังที่ระบุไว้ข้างต้น โดยยึดหลักการจริยธรรมแห่งคำประกาศเฮลซิงกิ และการปฏิบัติการวิจัยทางคลินิกที่ดี

ลงชื่อ.....

(นายอนันต์ กรลักษณ์)

ประธานคณะกรรมการจริยธรรมการวิจัยในคน

สถาบันมะเร็งแห่งชาติ

ลงชื่อ.....

(นายธีรวุฒิ คูหะเปรมะ)

ผู้อำนวยการสถาบันมะเร็งแห่งชาติ

# Certificate of Approval
## From
## Ethics Committee of National Cancer Institute, Thailand
## EC COA 022/ 2013

| | |
|---|---|
| Protocol Title | Symptom clusters and their influences on the functional Status in advanced lung cancer patients receiving chemotherapy |
| Protocol Number | 29_2013T_OUT317 |
| Principal Investigator | Miss Thidarat Khambooon |
| Affiliation | Mahidol University |
| Research Site | National Cancer Institute |
| Document Approved | 1. Research Protocol<br>2. Participant Information Sheet<br>3. Informed Consent Form<br>4. Questionnaire |
| Date of Approval | August 15, 2013 |

The prior mentioned documents have been reviewed and approved by Ethics Committee, National Cancer Institute, Thailand, based on the Declaration of Helsinki and Good Clinical Practice

Anant Kalarak
.....
(Dr.Anant Kalarak)
Chairman, Ethics Committee

.....
(Dr. Thiravud Khuhaprema)
Director, National Cancer Institute

# APPENDIX B
# INFORMATION SHEET AND CONSENT FORM

**เอกสารชี้แจงผู้เข้าร่วมการวิจัย/อาสาสมัคร**

(Participant Information Sheet)

**ในเอกสารนี้อาจมีข้อความที่ท่านอ่านแล้วยังไม่เข้าใจ โปรดสอบถามหัวหน้าโครงการวิจัยหรือผู้แทนให้ช่วยอธิบายจนกว่าจะเข้าใจดี ท่านอาจจะขอเอกสารนี้กลับไปอ่านที่บ้านเพื่อปรึกษา หารือกับญาติพี่น้อง เพื่อนสนิท แพทย์ประจำตัวของท่าน หรือแพทย์ท่านอื่น เพื่อช่วยในการตัดสินใจเข้าร่วมการวิจัย**

**ชื่อโครงการวิจัย** กลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด

**ชื่อหัวหน้าโครงการวิจัย** นางสาว ธิดารัตน์ คำบุญ และผู้วิจัยร่วม 1) รองศาสตราจารย์ ดร. คนึงนิจ พงศ์ถาวรกมล 2) ผู้ช่วยศาสตราจารย์ ดร. ดวงรัตน์ วัฒนกิจไกรเลิศ 3) รองศาสตราจารย์ ดร. ชูเกียรติ วิวัฒน์วงศ์เกษม 4) นายแพทย์วิโรจน์ เหล่าสุนทรศิริ 5) ศาสตราจารย์ ดร. คาริน โอสัน

**สถานที่วิจัย** หน่วยเคมีบำบัดและให้เลือด ตึกผู้ป่วยนอกชั้น 7 โรงพยาบาลศิริราช คณะแพทย์ศาสตร์ศิริราชพยาบาล

**สถานที่ทำงานและหมายเลขโทรศัพท์ของหัวหน้าโครงการวิจัยที่ติดต่อได้ทั้งในและนอกเวลาราชการ** โครงการบัณฑิตศึกษาคณะพยาบาลศาสตร์ มหาวิทยาลัยมหิดล ถนนพรานนก เขตศิริราช แขวงบางกอกน้อย กรุงเทพมหานคร 10700

**โทรศัพท์(ติดต่อได้ทั้งในและนอกเวลาราชการ)** โทร 091-009-1246

**ผู้สนับสนุนทุนวิจัย** ไม่มี

**ระยะเวลาในการวิจัย** 1 ปี 3 เดือน

**ที่มาของโครงการวิจัย** โครงการนี้เป็นส่วนหนึ่งของการศึกษา: งานวิจัยปริญญาเอก

**วัตถุประสงค์ของโครงการวิจัย**

โครงการวิจัยนี้จัดทำขึ้นเพื่อศึกษาลักษณะของการเกิดกลุ่มอาการ ซึ่งหมายถึงอาการหลายๆอาการที่เกิดขึ้นร่วมกันที่พบในผู้ป่วยระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด และผลกระทบของกลุ่มอาการต่อการปฏิบัติกิจกรรมผู้ป่วย

ท่านได้รับเชิญให้เข้าร่วมการวิจัยนี้เนื่องจากได้รับทราบผลการวินิจฉัยโรคว่าป่วยเป็นมะเร็งปอดระยะลุกลามที่มีอายุมากกว่า 18 ปี อยู่ในระหว่างการรักษาด้วยยาเคมีบำบัด มีความสมัครใจที่จะเข้าร่วมการวิจัย ซึ่งการวิจัยครั้งนี้จัดทำขึ้นเพื่อช่วยในการประเมินและวางแผนจัดการอาการหลายๆอาการที่เกิดขึ้นร่วมกัน และช่วยทำให้มีความเข้าใจในกลุ่มอาการที่เกิดขึ้นร่วมกันและช่วยค้นหากลุ่มอาการที่มีผลต่อการปฏิบัติกิจกรรมในแต่ละวันของผู้ป่วย การวิจัยนี้จะมีผู้เข้าร่วมการวิจัยทั้งสิ้นประมาณ 372 คน เป็นผู้ป่วยที่ได้รับการรักษาที่ โรงพยาบาลศิริราชและสถาบันมะเร็ง

หากท่านตัดสินใจเข้าร่วมการวิจัยแล้ว จะมีขั้นตอนการวิจัยดังต่อไปนี้คือ

1. สิ่งที่ท่านจะได้รับแบบสอบถามจำนวน 3 ฉบับ เกี่ยวกับข้อมูลส่วนบุคคล อาการที่ปรากฏใน 1 สัปดาห์ที่ผ่านมา และการทำกิจกรรมในแต่ละวันในช่วง 1 สัปดาห์ที่ผ่านมา แบบสอบถามมีข้อคำถามประมาณ 23- 39 ข้อ

2. การตอบแบบบสอบถามจัดทำในสถานที่เป็นส่วนตัว ปราศจากการรบกวน ท่านสามารถตอบแบบสอบถามด้วยตนเอง หรือให้ผู้จัยอ่านข้อความให้ หากท่านมีความประสงค์จะกรอกข้อมูลที่บ้านหรือทางโทรศัพท์ ผู้วิจัยยินดีที่จะดำเนินการตามความประสงค์ของท่านโดยอธิบายวิธีตอบแบบสอบถามหรือแนบแบบสอบถาม ซองจดหมาย ที่อยู่และติดแสตมป์พร้อมส่งกลับมายังที่อยู่ของผู้วิจัย การตอบแบบสอบถามใช้เวลาประมาณ 15-30 นาที

3. ผู้วิจัยจะขอเก็บข้อมูลเกี่ยวกับการรักษามะเร็งปอดที่ท่านได้รับในปัจจุบันจากแฟ้มประวัติ โดยจะบันทึกในส่วนที่ 2 ของแบบบันทึกข้อมูลส่วนบุคคล

4. การเก็บข้อมูลจะทำเพียงครั้งเดียว

การวิจัยนี้ ท่านไม่มีความเสี่ยงที่อาจจะเกิดขึ้นเมื่อเข้าร่วมการวิจัย ไม่มีความเสี่ยงเนื่องจากเป็นการตอบแบบประเมิน ซึ่งเป็นข้อมูลที่ท่านมีประสบการณ์โดยตรงอยู่แล้ว และเป็นการเก็บข้อมูลเพียงครั้งเดียว ใช้ระยะเวลาสั้น ไม่มีการทดลองในบุคคล และหากพบว่าท่านกำลังมีอาการรุนแรงและทุกข์ทรมานในหลายอาการโดยมีได้รายงานให้แพทย์ผู้เกี่ยวข้องทราบ ผู้วิจัยจะให้คำแนะนำในการปรึกษาแพทย์ที่ทำการรักษาหรือประสานงานกับพยาบาลผู้เกี่ยวข้องในสถานที่เก็บข้อมูล

หากท่านไม่เข้าร่วมในโครงการวิจัยนี้ ท่านก็จะได้รับการตรวจเพื่อการวินิจฉัยและรักษาโรคของท่านตามวิธีการที่เป็นมาตรฐานตามปกติ หากมีข้อสงสัยที่จะสอบถามเกี่ยวข้องกับการวิจัย หรือหากเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัย ท่านสามารถติดต่อผู้วิจัยได้ที่หมายเลขโทรศัพท์ 091-009-1246

ประโยชน์ที่คาดว่าจะได้รับคือ สามารถค้นหากลุ่มอาการที่พบบ่อยในผู้ป่วยมะเร็งปอดและผลกระทบที่เกิดขึ้นต่อการปฏิบัติกิจกรรม สามารถนำไปเป็นข้อมูลเบื้องต้นเพื่อนำไปใช้ในการวางแผนการจัดการกับกลุ่มอาการที่เกิดขึ้นเหล่านั้นได้อย่างมีประสิทธิภาพ อันจะนำไปสู่การพัฒาคุณภาพชีวิตของผู้ป่วยมะเร็งปอดต่อไป

การวิจัยครั้งนี้ไม่มีค่าตอบแทนและไม่มีค่าใช้จ่ายใด และหากมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่จะเกี่ยวข้องกับการวิจัยนี้ ผู้วิจัยจะแจ้งให้ท่านทราบโดยรวดเร็วไม่ปิดบัง

ข้อมูลส่วนตัวของท่านจะถูกเก็บรักษาไว้เป็นความลับและจะไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลส่วนรวมโดยไม่สามารถระบุข้อมูลรายบุคคลได้ ข้อมูลของท่านเป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น ผู้ให้ทุนวิจัย ผู้กำกับดูแลการวิจัย สถาบันหรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ รวมถึงคณะกรรมการจริยธรรมการวิจัยในคน เป็นต้น โดยไม่ละเมิดสิทธิของท่านในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้

ท่านมีสิทธิ์ถอนตัวออกจากโครงการวิจัยเมื่อใดก็ได้ โดยไม่ต้องแจ้งให้ทราบล่วงหน้า และการไม่เข้าร่วมการวิจัยหรือถอนตัวออกจากโครงการนี้ จะไม่มีผลกระทบต่อการบริการและการรักษาที่ท่านสมควรจะได้รับตามมาตรฐานแต่ประการใด

หากท่านได้รับการปฏิบัติที่ไม่ตรงตามที่ระบุไว้ในเอกสารชี้แจงนี้ ท่านสามารถร้องเรียนไปยังประธานคณะกรรมการจริยธรรมการวิจัยในคนทราบได้ที่ สำนักงานคณะกรรมการจริยธรรมการวิจัยในคน อาคารเฉลิมพระเกียรติ ๘๐ พรรษา ๕ ธันวาคม ๒๕๕๐ ชั้น 2 โทร. 0 2419 2667-72 โทรสาร 0 2411 0162

ลงชื่อ..... ผู้ร่วมวิจัย/อาสาสมัคร

(.....)

วันที่.....

# หนังสือแสดงเจตนายินยอมเข้าร่วมการวิจัย

## (Consent Form)

วันที่..... เดือน..... พ.ศ.....

ข้าพเจ้า..... อายุ.....ปี อาศัยอยู่บ้านเลขที่.....ถนน.....แขวง/ตำบล..... เขต/อำเภอ.....จังหวัด.....รหัสไปรษณีย์..... โทรศัพท์ .....

ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยเรื่อง กลุ่มอาการและอิทธิพลของกลุ่มอาการต่อการปฏิบัติกิจกรรมของผู้ป่วยมะเร็งปอดระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัด

โดยข้าพเจ้าได้รับทราบรายละเอียดเกี่ยวกับที่มาและจุดมุ่งหมายในการทำวิจัย รายละเอียดขั้นตอนต่างๆ ที่จะต้องปฏิบัติหรือได้รับการปฏิบัติ ประโยชน์ที่คาดว่าจะได้รับของการวิจัย และความเสี่ยงที่อาจจะเกิดขึ้นจากการเข้าร่วมการวิจัย รวมทั้งแนวทางป้องกันและแก้ไขหากเกิดอันตรายขึ้น ค่าใช้จ่ายที่ข้าพเจ้าจะต้องรับผิดชอบจ่ายเอง โดยได้อ่านข้อความที่มีรายละเอียดอยู่ในเอกสารชี้แจงผู้เข้าร่วมการวิจัยโดยตลอด อีกทั้งยังได้รับคำอธิบายและตอบข้อสงสัยจากหัวหน้าโครงการวิจัยเป็นที่เรียบร้อยแล้ว

ข้าพเจ้าจึงสมัครใจเข้าร่วมในโครงการวิจัยนี้

หากข้าพเจ้ามีข้อข้องใจเกี่ยวกับขั้นตอนของการวิจัย หรือหากเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัยขึ้นกับข้าพเจ้า ข้าพเจ้าจะสามารถติดต่อกับ นางสาวธิดารัตน์ คำบุญ ที่โครงการบัณฑิตศึกษาคณะพยาบาลศาสตร์ มหาวิทยาลัยมหิดล โทรศัพท์ 091-009-1246

หากข้าพเจ้าได้รับการปฏิบัติไม่ตรงตามที่ระบุไว้ในเอกสารชี้แจงผู้เข้าร่วมการวิจัย ข้าพเจ้าสามารถติดต่อกับประธานคณะกรรมการจริยธรรมการวิจัยในคนได้ที่ สำนักงานคณะกรรมการจริยธรรมการวิจัยในคน อาคารเฉลิมพระเกียรติ ๘๐ พรรษา ๕ ธันวาคม ๒๕๕๐ ชั้น 2 โทร. 0 2419 2667-72 โทรสาร 0 2411 0162

ข้าพเจ้าได้ทราบถึงสิทธิ์ที่ข้าพเจ้าจะได้รับข้อมูลเพิ่มเติมทั้งทางด้านประโยชน์และโทษจากการเข้าร่วมการวิจัย และสามารถถอนตัวหรืองดเข้าร่วมการวิจัยได้ทุกเมื่อโดยไม่ต้องแจ้งล่วงหน้าหรือระบุเหตุผล โดยจะไม่มีผลกระทบต่อการบริการและการรักษาพยาบาลที่ข้าพเจ้าจะได้รับต่อไปในอนาคต และยินยอมให้ผู้วิจัยใช้ข้อมูลส่วนตัวของข้าพเจ้าที่ได้รับจากการวิจัย แต่จะไม่เผยแพร่ต่อสาธารณะเป็นรายบุคคล โดยจะนำเสนอเป็นข้อมูลโดยรวมจากการวิจัยเท่านั้น

ข้าพเจ้าได้เข้าใจข้อความในเอกสารชี้แจงผู้เข้าร่วมการวิจัย และหนังสือแสดง เจตนายินยอมนี้โดยตลอดแล้ว จึงลงลายมือชื่อไว้

ลงชื่อ..... ผู้ร่วมวิจัย/อาสาสมัครหรือผู้แทนโดยชอบธรรม/วันที่.....
(.....)

ลงชื่อ.....ผู้ให้ข้อมูลและขอความยินยอม/หัวหน้าโครงการวิจัย/วันที่.....
(.....)

ในกรณีผู้ร่วมวิจัย/อาสาสมัคร อ่านหนังสือไม่ออก มีพยานซึ่งไม่มีส่วนได้เสียอยู่ด้วยตลอดระยะเวลาที่มีการให้ข้อมูลและผู้ร่วมวิจัย/อาสาสมัครหรือผู้แทนโดยชอบธรรมให้ความยินยอมเข้าร่วมการวิจัย พยานขอยืนยันว่าข้อมูลในหนังสือแสดงเจตนายินยอมหรือข้อมูลที่ได้รับและเอกสารอื่นได้รับการอธิบายอย่างถูกต้อง และผู้ร่วมวิจัย/อาสาสมัครหรือผู้แทนโดยชอบธรรมแสดงว่าเข้าใจรายละเอียดต่างๆ พร้อมทั้งให้ความยินยอมโดยสมัครใจ จึงได้ลงลายมือชื่อไว้เป็นพยาน

ลงชื่อ..... พยาน/วันที่.....
(.....)

# APPENDIX C
# THE DEMOGRAPHIC AND MEDICAL RECORD FORM

## แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา

**รหัส**.....

**วันที่ประเมิน**.....

**ส่วนที่** 1: **ข้อมูลส่วนบุคคล**

**คำชี้แจง** กรุณาตอบแบบสอบถามเกี่ยวกับข้อมูลส่วนตัวของท่าน โดยทำเครื่องหมายกากบาท (X) หน้าข้อความ หรือเติมคำลงในช่องว่างที่ตรงกับข้อมูลตามความเป็นจริงของท่าน

1. เพศ

( ) ชาย ( ) หญิง

2. อายุ ..... ปี

3. สถานภาพสมรส

( ) โสด ( ) คู่ (แต่งงานหรืออยู่ด้วยกัน) ( ) หม้าย/ หย่า/ แยก

4. ศาสนา

( ) พุทธ ( ) คริสต์ ( ) อิสลาม ( ) อื่นๆ (โปรดระบุ).....

5. ระดับการศึกษา

( ) ไม่ได้เรียน ( ) ประถมศึกษา ( ) มัธยมศึกษาตอนต้น

( ) มัธยมศึกษาตอนปลาย/ ปวช. ( ) ประกาศนียบัตร / ปวส.

( ) ปริญญาตรีหรือเทียบเท่า ( ) สูงกว่าปริญญาตรี

( ) อื่น ๆ (โปรดระบุ).....

6. .....

( ) ..... ( ) .....

( ) ..... ( ) .....

( ) ..... ( ) .....

( ) ..... ( ) .....

7. .....

.....

8. .....

( ) ..... ( ) .....

( ) ..... ( ) .....

( ) .....

9. .....

( ) ..... ( ) .....

( ) ..... ( ) .....

( ) ..... ( ) .....

10. .....

( ) ..... ( ) .....

( ) …… ( ) ……

( ) ……

11. ……

( ) …… ( ) ……

……..

( ) ……..

( ) ……..

( ) ……..

( ) ……..

( ) ……..

**ส่วนที่** 2: ……..

1. ……

2. ……

3. …….

…… ……...

4. ……

5. ……

6. ……

……..……

7. ..……

8. ……..

( ) …… ( ) ……

9. ……..

10. ( ) …… ( ) ……

# DEMOGRAPHIC AND MEDICAL RECORD FORM

**Participant code**…….
**Date**…….

**Part I: Demographic**

1. Sex

( ) Male ( ) Female

2. Age…….

3. Marital status

( ) Single ( ) Married ( ) Widowed/ Divorced/Separated

4. Religion

( ) Buddhist ( ) Christian ( ) Islam

( ) Others (Please specify)…….

5. Level of education

( ) No formal education ( ) Primary school ( ) Secondary school

( ) High school ( ) Diploma/ Certificate ( ) Bachelor

( ) Postgraduate ( ) Others (Please specify)……

6. Occupation

( ) Government service ( ) Business person

( ) Company/ labor ( ) Housewife

( ) Student ( ) Farmer

( ) Nothing ( ) Others (Please specify)……

7. Income…… Baht/month

Family income……..Baht/month

8. …….

( ) …… ( ) ……

( ) …… ( ) ……

( ) …… ( ) ……

9. ……

( ) …… ( ) ……

( ) …… ( ) …… ( ) ……

( ) …… ( ) ……

10. ……

( ) …… ( ) ……

( ) …… ( ) ……

( ) ……

( ) ……

11. ……

( ) …….. ( ) ……

**……**

1. ..……

2. ……

3. ……

……...

4. ……

5. ……..……

6. ……

……

7. ……

……

8. ……

( ) …….. ( ) ……

9. ……..

( ) …….. ( ) ……

# แบบบันทึกอาการ

**รหัส**..... **วันที่**.....

**ส่วนที่** 1: ข้อความข้างล่างนี้เป็นรายการอาการจำนวน 32 อาการ กรุณาพิจารณาทีละอาการ **ในช่วง 1 สัปดาห์ที่ผ่านมา** ท่านมีอาการใดดังต่อไปนี้หรือไม่ หากท่าน**ไม่มี**อาการใด กรุณาใส่เครื่องหมาย กากบาท ( X ) ลงในช่อง "**ไม่มีอาการ**" แต่หากท่าน**มี**อาการใด กรุณาระบุความบ่อย ความรุนแรง และความรู้สึกทุกข์ทรมานจากอาการหรืออาการรบกวนการดำเนินชีวิตของท่านมากน้อยเพียงใด โดยการทำเครื่องหมาย**วงกลม**ตัวเลข ( O ) ตามความคิดเห็นของท่าน

| **ในช่วง 1 สัปดาห์ที่ผ่านมา** ท่านมีอาการดังต่อไปนี้หรือไม่ ? | **ไม่มีอาการ** | **ถ้ามี** ท่านเกิดอาการ**บ่อย**เพียงใด | | | | **ถ้ามี** อาการมัก**รุนแรง**มากเพียงใด | | | | **ถ้ามี** อาการดังกล่าวทำให้ท่าน**ทุกข์ทรมาน**หรือ**รบกวน**ท่านมากเพียงใด | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ตลอดเวลา | บ่อยมาก | บ่อยครั้ง | เป็นครั้งคราว | รุนแรงที่สุด | รุนแรงมาก | ปานกลาง | เล็กน้อย | ไม่เลย | เล็กน้อย | ปานกลาง | มาก | มากที่สุด |
| 1. ขาดสมาธิ หรือมีความลำบากในการรวบรวมสมาธิคิดช้าหลงลืม | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |
| 2. ปวด | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |
| 3. อ่อนเพลีย/เปลี้ย/ไม่มีแรง | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 0 | 1 | 2 | 3 | 4 |

| **ในช่วง** 1 **สัปดาห์ที่ผ่านมา** ท่านมีอาการดังต่อไปนี้หรือไม่ ? | ไม่มีอาการ | **ถ้ามี** ท่านเกิดอาการ**บ่อย**เพียงใด | | | | **ถ้ามี** อาการมัก**รุนแรง**มากเพียงใด | | | | **ถ้ามี** อาการดังกล่าวทำให้ท่าน**ทุกข์ทรมาน**หรือ**รบกวน**ท่านมากเพียงใด | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | น้อยที่สุด | น้อย | ปานกลาง | มาก | น้อยที่สุด | น้อย | ปานกลาง | มาก | น้อยที่สุด | น้อย | ปานกลาง | มาก | มากที่สุด |
| 4. ..... | | | | | | | | | | | | | | |
| 5. ..... | | | | | | | | | | | | | | |
| 6. ..... | | | | | | | | | | | | | | |
| 7. ..... | | | | | | | | | | | | | | |
| 8. ..... | | | | | | | | | | | | | | |
| 9. ..... | | | | | | | | | | | | | | |
| 10. ..... | | | | | | | | | | | | | | |
| 11. ..... | | | | | | | | | | | | | | |
| 12. ..... | | | | | | | | | | | | | | |
| 13. ..... | | | | | | | | | | | | | | |

| **ในช่วง** 1 **สัปดาห์ที่ผ่านมา** ท่านมีอาการดังต่อไปนี้หรือไม่ ? | ไม่มีอาการ | **ถ้ามี** ท่านเกิดอาการ**บ่อย**เพียงใด | | | | **ถ้ามี** อาการมัก**รุนแรง**มากเพียงใด | | | | **ถ้ามี** อาการดังกล่าวทำให้ท่าน**ทุกข์ทรมาน**หรือ**รบกวน**ท่านมากเพียงใด | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | น้อยที่สุด | น้อย | ปานกลาง | มาก | น้อยที่สุด | น้อย | ปานกลาง | มาก | น้อยที่สุด | น้อย | ปานกลาง | มาก | มากที่สุด |
| 14. ..... | | | | | | | | | | | | | | |
| 15. ..... | | | | | | | | | | | | | | |
| 16. ..... | | | | | | | | | | | | | | |
| 17. ..... | | | | | | | | | | | | | | |
| 18. ..... | | | | | | | | | | | | | | |
| 19. ..... | | | | | | | | | | | | | | |
| 20. ..... | | | | | | | | | | | | | | |
| 21. ..... | | | | | | | | | | | | | | |
| 22. ..... | | | | | | | | | | | | | | |
| 23. ..... | | | | | | | | | | | | | | |
| 24. ..... | | | | | | | | | | | | | | |

| **ในช่วง 1 สัปดาห์ที่ผ่านมา** ท่านมีอาการดังต่อไปนี้หรือไม่ ? | **ไม่มีอาการ** | **ถ้ามี** ท่านเกิดอาการ**บ่อย**เพียงใด | | | | **ถ้ามี** อาการมัก**รุนแรง**มากเพียงใด | | | | **ถ้ามี** อาการดังกล่าวทำให้ท่าน**ทุกข์ทรมาน**หรือ**รบกวน**ท่านมากเพียงใด | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | น้อยที่สุด | น้อย | มาก | มากที่สุด | น้อยที่สุด | น้อย | มาก | มากที่สุด | ไม่เลย | เล็กน้อย | ปานกลาง | มากจนทนไม่ได้ | มากที่สุด |
| 26. ..... | | | | | | | | | | | | | | |
| 27. ..... | | | | | | | | | | | | | | |
| 28..... | | | | | | | | | | | | | | |
| 29. ..... | | | | | | | | | | | | | | |
| 30. ..... | | | | | | | | | | | | | | |
| 31. ..... | | | | | | | | | | | | | | |
| 32. ..... | | | | | | | | | | | | | | |

# Memorial Symptom Assessment Scale (MSAS)

**Participant code…….** **Date……**

**Section 1**

**Instructions:** Instructions: We have listed 24 symptoms below. Read each one carefully. If you have had the symptom during this past week, let us know how OFTEN you had it, how SEVERE it was usually and how much it DISTRESSED or BOTHERED you by circling the appropriate number. If you DID NOT HAVE the symptom, make an "X" in the box marked "DID NOT HAVE."

| DURING THE PAST WEEK Did you have any of the following symptoms? | DID NOT HAVE | F YES How OFTEN did you have it? | | | | IF YES How SEVERE was it usually | | | | IF YES How much did it DISTRESS or BOTHER you? | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Rarely | occasionally | Frequently | Almost Constantly | Slight | Moderate | Severe | Very Severe | Not at all | A Little Bit | Somewhat | Very Much |
| Difficulty concentrating | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Pain | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Lack of energy | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Cough | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Feeling nervous | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Dry Mouth | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Nausea | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Feeling drowsy | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Numbness/ tingling in hands/feet | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Difficulty sleeping | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |

| DURING THE PAST WEEK Did you have any of the following symptoms ? | DID NOT HAVE | F YES How OFTEN did you have it? | | | | IF YES How SEVERE was it usually | | | | IF YES How much did it DISTRESS or BOTHER you? | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Rarely | occasionally | Frequently | Almost Constantly | Slight | Moderate | Severe | Very Severe | Not at all | A Little Bit | Somewhat | Very Much |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |
| …… | | | | | | | | | | | | | |

| DURING THE PAST WEEK Did you have any of the following symptoms? | DID NOT HAVE | F YES How OFTEN did you have it? | | | | IF YES How SEVERE was it usually | | | | IF YES How much did it DISTRESS or BOTHER you? | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Rarely | occasionally | Frequently | Almost Constantly | Slight | Moderate | Severe | Very Severe | Not at all | A Little Bit | Somewhat | Very Much |
| …… | | | | | | | | | | | | | |

**Section 2**

……..
……..
……..
……..

| DURING THE PAST WEEK Did you have any of the following symptoms? | DID NOT HAVE | IF YES How SEVERE was it usually | | | | IF YES How much did it DISTRESS or BOTHER you? | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Slight | Moderate | Severe | Very Severe | Not at all | A Little Bit | Somewhat | Very Much | Slight |
| …… | | | | | | | | | | |
| …… | | | | | | | | | | |
| …… | | | | | | | | | | |
| …… | | | | | | | | | | |
| …… | | | | | | | | | | |

| **Section 2** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| …….. | | | | | | | | | | |
| …….. | | | | | | | | | | |
| …….. | | | | | | | | | | |
| …….. | | | | | | | | | | |
| <u>DURING THE PAST WEEK</u> Did you have any of the following symptoms? | DID NOT HAVE | IF YES How SEVERE was it usually | | | | IF YES How much did it DISTRESS or BOTHER you? | | | | |
| | | Slight | Moderate | Severe | Very Severe | Not at all | A Little Bit | Somewhat | Very Much | Slight |
| …… | | | | | | | | | | |
| …… | | | | | | | | | | |
| …….. | | | | | | | | | | |
| ……. | | | | | | | | | | |
| ……. | | | | | | | | | | |
| ……. | | | | | | | | | | |

# แบบประเมินการปฏิบัติกิจกรรมของผู้ป่วย

**ส่วนที่ 1** โปรดทำเครื่องหมายถูก ( ✓ ) หน้าข้อความที่ตรงกับกิจกรรมที่ท่าน**เคยทำ**ก่อนป่วย และกรุณาระบุระดับการทำกิจกรรมดังกล่าวว่า **<u>ในช่วง 1 สัปดาห์ที่ผ่านมา</u>** ท่านได้ทำกิจกรรมนั้นมากน้อยเพียงใด โดยการทำเครื่องหมายวงกลมตัวเลข ( O ) ตามความคิดเห็นของท่าน หากกิจกรรมใด**ไม่เคย**ทำมาก่อนให้ทำเครื่องหมาย ( - ) และข้ามไปตอบข้อถัดไปโดยไม่ต้องตอบว่าปัจจุบันทำกิจกรรมนี้หรือไม่

| **รายการกิจกรรม** | **<u>เคยทำก่อนป่วยหรือไม่</u> ( ✓ = เคย ) ( - = ไม่เคย )** | **ฉันยังคงทำกิจกรรมนี้** | | | |
|---|---|---|---|---|---|
| | | **ไม่ได้ทำเลย** | **คงทำเล็กน้อย** | **ทำเป็นส่วนใหญ่** | **ทำเต็มที่เหมือนเดิม** |
| 1. ดูแล / เลี้ยงเด็กเล็ก | | 1 | 2 | 3 | 4 |
| 2. ดูแลสามี / ภรรยา | | 1 | 2 | 3 | 4 |
| 3. ดูแลญาติ | | 1 | 2 | 3 | 4 |
| 4. ทำความสะอาดบ้าน (กวาดบ้านถูบ้าน) | | 1 | 2 | 3 | 4 |
| 5.จัดบ้านให้เรียบร้อย (ทำเตียง เก็บข้าวของเป็นต้น) | | 1 | 2 | 3 | 4 |
| 6. ซักรีดเสื้อผ้า | | 1 | 2 | 3 | 4 |
| 7. ล้างจาน | | 1 | 2 | 3 | 4 |
| 8. ทำอาหาร | | 1 | 2 | 3 | 4 |
| 9. จัดการธุระของครอบครัว (เช่น จ่ายค่าน้ำ ค่าไฟ/ค่าโทรศัพท์/ไปธนาคาร เป็นต้น) | | 1 | 2 | 3 | 4 |
| 10. ไปซื้อของร้านขายของใกล้บ้าน / ไปร้านชำ / ไปตลาด | | 1 | 2 | 3 | 4 |
| 11. ไปซื้อของอื่นที่นอกเหนือไปจากของชำ/ ไปเดินห้างชอปปิ้ง | | 1 | 2 | 3 | 4 |

| **รายการกิจกรรม** | **<u>เคยทำก่อนป่วยหรือไม่</u> ( ✓ = เคย ) ( - = ไม่เคย )** | **ฉันยังคงทำกิจกรรมนี้** | | | |
|---|---|---|---|---|---|
| | | **ไม่ได้ทำเลย** | **คงทำเล็กน้อย** | **ทำเป็นส่วนใหญ่** | **ทำเต็มที่เหมือนเดิม** |
| ..... | | | | | |
| ..... | | | | | |
| ..... ..... | | | | | |
| ..... | | | | | |

**ส่วนที่ 2 .....**

| **รายการกิจกรรม** | **<u>เคยทำก่อนป่วยหรือไม่</u> ( ✓ = เคย ) ( - = ไม่เคย )** | **ฉันยังคงทำกิจกรรมนี้** | | | |
|---|---|---|---|---|---|
| | | **ไม่ได้ทำเลย** | **คงทำเล็กน้อย** | **ทำเป็นส่วนใหญ่** | **ทำเต็มที่เหมือนเดิม** |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |
| ..... | | | | | |

**ส่วนที่ 3 …….**

| กิจกรรม | ไม่เคย | บางครั้ง | เป็นส่วนใหญ่ | เป็นประจำ |
|---|---|---|---|---|
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |

**ส่วนที่ 4 ……..**

| กิจกรรม | ไม่เคย | บางครั้ง | เป็นส่วนใหญ่ | เป็นประจำ |
|---|---|---|---|---|
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |

## INVENTORY OF FUNCTIONAL STATUS - CANCER

PLEASE THINK ABOUT THE TIME SINCE YOU WERE DIAGNOSED WITH CANCER, AND THEN RESPOND TO THE FOLLOWING ITEMS.

**PART I.**

Please check all the usual household activities you did prior to your illness and then indicate to what extent you have continued doing these activities in the past week.

| **Prior to my illness, my usual activities included:** | I have continued doing this activity: | | | |
|---|---|---|---|---|
| | NOT AT ALL | JUST BEGINNING | PARTIALLY | FULLY |
| _____1. Care of children | 1 | 2 | 3 | 4 |
| _____2. Care of husband/wife | 1 | 2 | 3 | 4 |
| _____3. Care of other relatives | 1 | 2 | 3 | 4 |
| _____4. Cleaning the house | 1 | 2 | 3 | 4 |
| _____5. Tidying the house (making beds, picking up things, etc.) | 1 | 2 | 3 | 4 |
| _____6. Laundry | 1 | 2 | 3 | 4 |
| _____7. Doing dishes | 1 | 2 | 3 | 4 |
| _____8. Cooking | 1 | 2 | 3 | 4 |
| _____9. Household business (paying, bills, banking, etc.) | 1 | 2 | 3 | 4 |
| _____10. Grocery shopping | 1 | 2 | 3 | 4 |
| _____11. Shopping, other than groceries | 1 | 2 | 3 | 4 |
| _____12. Doing errands | 1 | 2 | 3 | 4 |
| _____13. Driving the car | 1 | 2 | 3 | 4 |
| _____14. Heavy housework, maintenance work, (seasonal cleaning, painting, etc. | 1 | 2 | 3 | 4 |
| _____15. Caring for pets | 1 | 2 | 3 | 4 |

Comments:

**PART II.**

……..

| **Prior to my illness, my usual activities included:** | I have continued doing this activity: | | | |
|---|---|---|---|---|
| | NOT AT ALL | JUST BEGINNING | PARTIALLY | FULLY |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |

Comments:

**PART III.**

……..

| **Prior to my illness, my usual activities included:** | I have continued doing this activity: | | | |
|---|---|---|---|---|
| | NEVER | SOME TIMES | MOST OF THE TIME | ALL OF THE TIME |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |

……..

**PART IV.**

……..

| **Prior to my illness, my usual activities included:** | I have continued doing this activity: | | | |
|---|---|---|---|---|
| | NEVER | SOME TIMES | MOST OF THE TIME | ALL OF THE TIME |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |
| …… | | | | |

Comments:

# APPENDIX D
# ADDITIONAL ANSLYSIS

**Table D1 Characteristic of Functional Level of the Sample in This Study (N=300)**

| Group of Functional status activities | Functional activities | N | % | Mean | S.D. |
|---|---|---|---|---|---|
| **Household and family** | Care of children | 16 | 5.3 | 1.81 | 0.66 |
| | Care of husband/wife | 13 | 4.3 | 1.69 | 0.95 |
| | Care of other relative | 7 | 2.3 | 1.43 | 0.53 |
| | Cleaning the house | 269 | 89.7 | 1.58 | 0.67 |
| | Tidying the house | 268 | 89.3 | 1.63 | 0.70 |
| | Laundry | 233 | 86.9 | 1.55 | 0.67 |
| | Doing dishes | 257 | 85.7 | 1.63 | 0.68 |
| | Cooking | 253 | 84.3 | 1.61 | 0.68 |
| | Household business | 72 | 24.0 | 1.71 | 0.88 |
| | Grocery shopping | 284 | 94.790.111. | 1.62 | 0.72 |
| | Shopping, other than groceries | 271 | 0 | 1.60 | 0.71 |
| | Doing errands | 33 | 80.3 | 1.18 | 0.39 |
| | Driving the car | 241 | 89.3 | 1.60 | 0.80 |
| | Heavy housework | 268 | | 1.08 | 0.41 |

**Table D1 Characteristic of Functional Level of the Sample in This Study (N=300) (cont.)**

| Group of Functional status activities | Functional activities | N | % | Mean | S.D. |
|---|---|---|---|---|---|
| **Social and community** | Caring for pets | 25 | 8.3 | 2.16 | 1.18 |
| | Community service organization | 140 | 46.7 | 1.26 | 0.45 |
| | Religious organization | 294 | 98.0 | 1.50 | 0.75 |
| | Socializing with friends | 293 | 97.7 | 1.53 | 0.69 |
| | Socializing with relative | 290 | 96.7 | 1.60 | 0.76 |
| | Social clubs | 293 | 97.7 | 1.38 | 0.62 |
| | Hobbies | 296 | 98.7 | 2.50 | 0.78 |
| **Personal care** | Rest or sleep during the day | 300 | 100 | 2.25 | 0.79 |
| | Spend most of the day in my pajamas/nightgown/bathrobe | 300 | 100 | 3.63 | 0.58 |
| | Walk as must as usually did before | 300 | 100 | 1.92 | 0.81 |
| | Sleep less at night | 300 | 100 | 2.86 | 0.70 |
| | Exercise as much as usually did before | 300 | 100 | 1.38 | 0.68 |
| | Have difficulty bathing/showering | 300 | 100 | 3.98 | 0.18 |
| | Having difficulty dressing myself | 300 | 100 | 3.98 | 0.18 |
| | Eat as much as I usually did before | 300 | 100 | 1.65 | 0.80 |
| | Eat the same types of food as usually did before | 300 | 100 | 1.66 | 0.96 |
| | Spend as much time relaxing as usually did before | 300 | 100 | 2.32 | 0.66 |

**Table D1 Characteristic of Functional Level of the Sample in This Study (N=300) (cont.)**

| Group of Functional status activities | Functional activities | N | % | Mean | S.D. |
|---|---|---|---|---|---|
| **Occupational functions** | Accomplishing as much as usual | 42 | 14 | 3.02 | 0.68 |
| | Acting irritably to ward my work associate | 42 | 14 | 3.88 | 0.40 |
| | Working fewer hours | 42 | 14 | 2.81 | 0.67 |
| | Doing my job as carefully and accurately as usual | 42 | 14 | 3.10 | 0.62 |
| | Working for only short periods of time and taking frequent breaks | 42 | 14 | 2.90 | 0.58 |
| | Having as much enthusiasm for job | 42 | 14 | 1.88 | 0.63 |
| | Carrying out my usual job responsibility | 42 | 14 | 3.26 | 0.54 |
| | Participating professional/union activities | 42 | 14 | 1.57 | 0.77 |

* 1-1.99=very limited functional activities, 2-2.99=partially limited, 3-3.99=moderate or less limited, 4=fully function or no limited functional activities

# BIOGRAPHY


| | |
|---|---|
| **NAME** | Miss Thidarat Khamboon |
| **DATE OF BIRTH** | 26 July 1978 |
| **PLACE OF BIRTH** | Lampang, Thailand |
| **INSTITUTIONS ATTENDED** | Mahidol University, 1996-1999<br>Bachelor of Science (Nursing)<br>Chulalongkorn University, 2002-2003<br>Master of Science (Nursing Education)<br>Mahidol University, 2009-2014<br>Doctor of Philosophy (Nursing) |
| **HOME ADDRESS** | 202/1 Mu 3, Bann Phung Village, Soi 2,<br>Sala sub district, Koakha district,<br>Lampang province, Thailand, 52130<br>Tel. 091-0091246<br>E-mail: 111thidarat@gmail.com |
| **EMPLOYMENT ADDRESS** | Faculty of Nursing, Naresuan University,<br>9, Tapho sub district, Muang district,<br>Pitsanulok province |