A CAUSAL MODEL FOR FATIGUE IN VIETNAMESE PERSONS WITH LUNG CANCER RECEIVING CHEMOTHERAPY

Mr. Long Nguyen Hoang

A Dissertation Submitted in Partial Fulfillment of the Requirements
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โมเดลเชิงสาเหตุของความเหนื่อยล้าในผู้ป่วยมะเร็งปอดชาวเวียดนามที่ได้รับเคมีบำบัด

นายลอง เหวียน ฮวาง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาพยาบาลศาสตรดุษฎีบัณฑิต
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By	Mr. Long Nguyen Hoang
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Thesis Advisor	Associate Professor Sureeporn Thanasilp, DNS, APN
Thesis Co-Advisor	Associate Professor Ratsiri Thato, PhD, RN

Accepted by the Faculty of Nursing, Chulalongkorn University in Partial Fulfillment of the Requirements for the Doctoral Degree

.....Dean of the Faculty of Nursing
(Associate Professor Sureeporn Thanasilp, DNS, APN)

THESIS COMMITTEE

.....Chairman
(Associate Professor Jintana Yunibhand, PhD, APN)
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(Associate Professor Sureeporn Thanasilp, DNS, APN)
.....Thesis Co-Advisor
(Associate Professor Ratsiri Thato, PhD, RN)
.....Examiner
(Associate Professor Siridej Sujiva, PhD)
.....Examiner
(Assistant Professor Sunida Preechawong, PhD, APN)
.....External Examiner
(Associate Professor Orasa Pankpakdee, DNS, APN)

ลอง เหวียน ฮวาง : โมเดลเชิงสาเหตุของความเหนื่อยล้าในผู้ป่วยมะเร็งปอดชาวเวียดนามที่ได้รับเคมีบำบัด (A CAUSAL MODEL FOR FATIGUE IN VIETNAMESE PERSONS WITH LUNG CANCER RECEIVING CHEMOTHERAPY) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ดร.สุรีพร ธนศิลป์, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: รศ. ดร.รัตน์ศิริ ทาโต, 260 หน้า.

การวิจัยภาคตัดขวางครั้งนี้มีวัตถุประสงค์เพื่อวิเคราะห์โมเดลเชิงสาเหตุ ของความหนื่อยล้าในผู้ป่วยมะเร็งปอดที่ได้รับเคมีบำบัด ในศูนย์มะเร็ง 6 แห่งในภาคเหนือของประเทศเวียดนาม โดยการใช้แนวคิดความเหนื่อยล้าของ Piper ร่วมกับการทบทวนวรรณกรรม กลุ่มตัวอย่างจำนวน 246 คน ถูกคัดเข้าสู่การวิจัยด้วยวิธีการเลือกตามความสะดวก เก็บข้อมูลโดยใช้แบบสอบถาม ได้แก่ Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACT-F), Insomnia Severity Index (ISI), Cancer Dyspnea Scale (CDS), Manchester Cough in Lung Cancer Scale (MCLCS), Depression Anxiety Stress Scale 21-Anxiety subscale (DASS 21-An), และ International Physical Activity Questionnaire-short from โดยมีค่าสัมประสิทธ์ ครอนบราคอัลฟา ของ FACT-F, ISI, CDS, MCLCS, DASS 21-An เท่ากับ 0.93, 0.90, 0.86, 0.86, และ 0.77 ตามลำดับ ในส่วนของภาวะโภชนาการ เก็บข้อมูลจากการคำนวนค่า Nutrition Risk Index จากข้อมูลในเวชระเบียน สถิติที่ใช้ในการทดสอบโมเดลสมมุติฐานด้วยโมเดลสมการเชิงโครงสร้าง

ผล การวิเคราะห์ พบว่าอาการนอนไม่หลับ อาการหายใจลำบาก อาการไอ ความวิตกกังวล ระยะของโรค กิจกรรมทางกาย และภาวะโภชนาการ สามารถทำนายความแปรปรวนของความเหนื่อยล้าได้ 42.9% ($\chi2$ = 51.556, df = 38, p = 0.070; $\chi2$/df = 1.357; GFI = 0.963; AGFI = 0.937; CFI = 0.974; RSMEA = 0.038) นอกจากนี้ยังพบความสัมพันธ์กันระหว่างตัวแปรอาการหายใจลำบาก อาการไอ การนอนไม่หลับ ความวิตกกังวล และสามารถร่วมกันทำนายความเหนื่อยล้า โดยพบว่า อาการหายใจลำบากมีอิทธิพลมากที่สุดต่อความเหนื่อยล้า (β = 0.397, p < 0.01) รองลงมาคืออาการไอ (β = 0.343, p < 0.01), การนอนไม่หลับ (β = 0.318, p < 0.01) และความวิตกกังวล (β = 0.115, p < 0.05) ในขณะที่พบว่า ระยะของโรคส่งผลทั้งทางตรงต่อความเหนื่อยล้า (β = 0.154, p < 0.05) และทางอ้อมผ่านกิจกรรมทางกายภาพ (β = 0.025, p < 0.05) ส่วนกิจกรรมทางกายและภาวะทางโภชนาการส่งผลเฉพาะทางตรงในด้านต่อความเหนื่อยล้า (β = -.148 และ -0.156, p < 0.01 ตามลำดับ)

โดยสรุป โมเดลเชิงสาเหตุของความเหนื่อยล้าในผู้ป่วยมะเร็งปอดที่ได้รับเคมีบำบัดสอด คล้องกับข้อมูลเชิงประจักษ์ ในการพัฒนารูปแบบการพยาบาลเพื่อควบคุมความเหนื่อยล้า พยาบาลชาวเวียดนามควรคำนึงถึงปัจจัยด้านการนอนไม่หลับ นอกจากนี้ยังพบว่า การบำบัดอาการไอ และอาการหายใจลำบากยังเป็นปัจจัยส่งเสริมในการจัดการอาการเหนื่อยล้าได้อีก ทางหนึ่ง ถึงแม้ว่ากิจกรรมทางกาย ภาวะทางโภชนาการ ความวิตกกังวลจะส่งผลต่ออาการเหนื่อยล้าไม่มาก แต่อย่างไรก็ตามการพยาบาลควรมุ่งเน้นถึงปัจจัยเหล่านี้ด้วย สำหรับพยาบาลชาวเวียดนามสิ่งสำคัญในการพัฒนารูปแบบการจัดการความเหนื่อยล้า แบบบูรณาการ คือการคำนึงการจัดการอาการนอนไม่หลับ อาการหายใจลำบาก ความวิตกกังวล และอาการไอ

สาขาวิชา พยาบาลศาสตร์ ลายมือชื่อนิสิต .....

ปีการศึกษา 2557 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

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LONG NGUYEN HOANG: A CAUSAL MODEL FOR FATIGUE IN VIETNAMESE PERSONS WITH LUNG CANCER RECEIVING CHEMOTHERAPY. ADVISOR: ASSOC. PROF. SUREEPORN THANASILP, DNS, APN, CO-ADVISOR: ASSOC. PROF. RATSIRI THATO, PhD, RN, 260 pp.

This cross-sectional study aimed to examine the causal model explaining fatigue in lung cancer patients during chemotherapy. The study was conducted in six oncology centers throughout the North of Vietnam. The hypothesized model was constructed based on the Piper's Integrative Fatigue Model and the review of literature. A convenience sample of 246 patients was interviewed by self-administered questionnaires, which were Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACT-F), Insomnia Severity Index (ISI), Cancer Dyspnea Scale (CDS), Manchester Cough in Lung Cancer Scale (MCLCS), Depression Stress Anxiety Scale 21-Anxiety subscale (DASS-21-An), and International Physical Activity Questionnaire-short form. Cronbach's alpha coefficients of FACT-F, ISI, CDS, MCLCS, and DASS-21-An found in this study were 0.93, 0.90, 0.86, 0.86, and 0.77, respectively. Nutrition status of patients was assessed by Nutrition Risk Index based on information in patients' medical records. Structural equation modeling was used to examine the hypothesized model in this study.

It was found that the final model (consisted of insomnia, dyspnea, cough, anxiety, stage of disease, physical activity, and nutrition status) explained 42.9% fatigue variance ($\chi 2 = 51.556$, df = 38, $p = 0.070$; $\chi 2/ df = 1.357$; GFI = 0.963; AGFI = 0.937; CFI = 0.974; RSMEA = 0.038). There were the interplays among dyspnea, cough, insomnia, and anxiety in determining fatigue. Among such factors, dyspnea had the largest total effect on fatigue ($\beta = 0.397$, $p < 0.01$), followed by cough ($\beta = 0.343$, $p < 0.01$), insomnia ($\beta = 0.318$, $p < 0.01$) and anxiety ($\beta = 0.115$, $p < 0.05$). Stage of disease influenced fatigue by its direct effect ($\beta = 0.154$, $p < 0.05$) and indirect effect via physical activity ($\beta = 0.025$, $p < 0.05$). Physical activity and nutrition status, however, had only direct and negative effects on fatigue ($\beta = -.148$ and -0.156, $p < 0.01$, respectively).

In conclusion, the model fits well to explain fatigue in lung cancer patients during chemotherapy. Vietnamese nurses should include insomnia in their fatigue control programs. In comparison to cough, dyspnea might be a better intervening factor to manage fatigue. Interventions focusing on physical activity, nutritional status, and anxiety may promise positive, although not too large, outcomes in reducing fatigue. Importantly, the interplay among insomnia, dyspnea, anxiety, and cough suggests that the development of comprehensive symptom management programs, which focus on those symptoms, could be a promising approach to control fatigue for Vietnamese nurses.

Field of Study: Nursing Science
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Student's Signature .....
Advisor's Signature .....
Co-Advisor's Signature .....

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INTRODUCTION

Background and significance of the study

Cancer is the new epidemic of modern world (WHO, 2008). Among malignant diseases, lung cancer has been remaining as the most popular for several decades (Ferlay et al., 2010). This disease results in 18.2% of the total mortality from cancer. Its survival rate is only nearly 9% in developing countries (Parkin, Bray, Ferlay, & Pisani, 2005). In Vietnam, there are 20,000 new cases and 17,000 deaths due to this disease annually (Phương, 2013). A national survey ranked lung cancer as the fourth and the seventh cause of death in male and female, respectively (T. T. N. Nguyen et al., 2011).

Chemotherapy is the most common treatment for lung cancer in Vietnam (Ngo, 2008). It would be used alone or combined with radiation to treat for all stages (Hansen, 2008). While surgery or radiation aims to remove or to kill tumor cells locally, chemotherapy is a systemic treatment, which spreads the drug throughout the body. Consequently, it causes various side effects, negatively influencing patients' life (Akin, Can, Aydiner, Ozdilli, & Durna, 2010; Matsuda, Yamaoka, & Tango, 2012). Chemotherapy is provided in cycles. A typical cycle lasts for 2 to 5 days, followed by several non-treatment days to allow the body recover. The recommended length is from 4 to 6 cycles (Soon, Stockler, Askie, & Boyer, 2009).

Lung cancer is the disease of symptoms (Soni et al., 2002). Nearly ninety percent of newly diagnosed patients suffered from two or more symptoms (J. K. Brown, Cooley, Chernecky, & Sarna, 2011). In average, each patient suffered from more than

ten symptoms, and most of them are at moderate level of severity (Liao et al., 2011). Noticeably, symptoms in lung cancer are significantly worsened during chemotherapy (Chen, Yu, & Yang, 2008; Genç & Tan, 2011). Among those symptoms, fatigue is a severe problem.

Fatigue is "a subjective, unpleasant symptom which incorporates total body feelings ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals' ability to function to their normal capacity" (Ream & Richardson, 1996, p. 527). Jacobs and Piper (1996) conceptualized fatigue as the subjective feeling of tiredness which can vary in unpleasantness, intensity and duration. The presence of either 1) a pathological physical or psychological condition, and 2) patients' consciousness and cognitive ability to evaluate feelings subjectively are antecedents of fatigue. Consequences of fatigue are impairments in both physical abilities (everyday activities) and mental abilities **(**irritability, impaired thought processes, inability to concentrate, inability to cope, forgetfulness, poor motivation, etc.) (Ream & Richardson, 1996). Cancer patients described that their fatigue is distinctively different from, and much more distressing than, the "ordinary" fatigue that they experienced before diagnose (Glaus, Crow, & Hammond, 1996). Ekfors and Petersson (2004), by qualitative approach, examined patients' experiences during treatment. Interestingly, the concept of fatigue described in lung cancer population appears to be similar to that in other cancer populations.

In comparison to other symptoms in lung cancer, fatigue is the most problematic one, in terms of all prevalence, intensity, and distress level (Okuyama et al., 2001; Sarna & Brecht, 1997; Simoff et al., 2013; Swanson, 2006; Yang et al., 2012). In Vietnam, 74.35% of lung cancer patients had fatigue before starting their treatments (Thanh,

2002). Nearly one in every two Vietnamese lung cancer patients on chemotherapy rated their fatigue from moderate to extremely severe intensity levels (T. M. Phuong, 2009; Toan, 2012).

Authors have highlighted the need to control fatigue during chemotherapy for cancer patients (Genç & Tan, 2011; Hanprasitkam, 2006). Nevertheless, the inefficient management of fatigue in lung cancer is evident. In particular, despite fierce efforts to control it, fatigue is still the most distressing among all symptoms in lung cancer patients on chemotherapy (Genç & Tan, 2011). In Vietnam, Toan (2012) reported that nearly half of lung cancer patients rated their fatigue during chemotherapy at moderate or extremely severe levels. Using a five-point Likert scale (0-4), T. M. Phuong (2009) revealed that 47.3% of Vietnamese lung tumor patients on chemotherapy reported fatigue score of 2 or 3. Two other studies used EORCT QLQ-30 to assessed quality of life during treatments among mix cancer sites samples, including lung cancer. In both studies, fatigue was the most severe one among all symptoms, with the severity score of 51/100 (Vu, Hanh, Giang, & Hoang, 2010) and 70/100 (N. T. T. Phuong, 2014).

Currently, a study was conducted to survey the effectiveness of supportive care for Vietnamese cancer patients (n = 202, 27.7% was lung cancer) (N. T. T. Phuong, 2014). The author compared fatigue scores (EORTC QLQ-30) before and after receiving supportive care. Fatigue intensity was statistically reduced from 70 to 62 ($t = 9.06$, $p < 0.05$). However, this change is still far from the desirable level. It is suggested that the difference of fatigue score assessed by EORTC QLQ-30 should be 14 to show a clinically meaningful improvement of the symptom (Maringwa et al., 2011). More importantly, the fatigue score after treatment ($\bar{x} = 62$) in Vietnamese population is still at severe level (King, 1996), which is nearly doubled than its reference mean value

recommended by EORTC workgroup ($\bar{x}$ = 34.6, SD = 27.8, n = 23,553) (N. W. Scott et al., 2008).

In conclusion, previous findings indicated a need for the enhancement of fatigue management in Vietnamese lung cancer patients on chemotherapy. Currently, no nursing interventions for this symptom in Vietnamese population have been found.

To manage fatigue in lung cancer, there is only one guideline from American College of Chest Physicians, which recommends the use of antidepressants, psychostimulants, and anxiolytics (Simoff et al., 2013). For cancer fatigue in general, the Vietnam Ministry of Health suggested only nutrition intervention to manage fatigue in cancer (Vietnam Ministry of Health, 2006). Worldwide, the most commonly recommended intervention for fatigue is exercise (walking, cycling, or swimming, ect.) (Mitchell, Beck, Hood, Moore, & Tanner, 2007). Other interventions are medications (erythropoietin, and darbepoetin, etc.), energy conservation, hypnosis, sleep hygiene, muscle relaxation, acupuncture, massage, ginseng, yoga, etc.

However, these interventions produce certain positive effects on fatigue but the results small (Campos, Hassan, Riechelmann, & Del Giglio, 2011; Finnegan-John, Molassiotis, Richardson, & Ream, 2013; Kirshbaum, 2010; Minton, Richardson, Sharpe, Hotopf, & Stone, 2008; Mitchell et al., 2007). It must be noted that most existing fatigue programs are not specific to any kind of cancer (Campos et al., 2011; Finnegan-John et al., 2013; Kirshbaum, 2010; Minton et al., 2008; Mitchell et al., 2007). Since they are not tailored to address particular characteristics of each cancer type, their effectiveness is small and inconsistent among trials (Jacobsen, Donovan, Vadaparampil, & Small, 2007). This shortcoming make the clinicians less confident about effectiveness of their intervention to be applied in their specific population of

interest. More importantly, those intervention may not be suitable to use in certain cancer type. In the situation of this study, such population is lung cancer.

In particular, although physical activity intervention is widely recommended, it requires a moderate intensity to be effective (Kirshbaum, 2010). Moderate intensity, however, stresses the respiratory and cardiovascular systems. In lung cancer, the tumorous lungs, whose functions may be already damaged, may not endure such requirements. The intervention indeed puts patients in a danger, the situation that oncology nurses must be highly cautious in designing their intervention to reduce fatigue (Mitchell et al., 2007). Additionally, dyspnea and cough are inevitable entities of lung cancer, which may be very important predictors of fatigue in this population. Such uniqueness should be took into account in designing intervention for lung cancer patients.

In conclusion, it is necessary to tailor the fatigue program in specification to each cancer type. The use of factors specifically contributing to fatigue in lung cancer could help to enhance the effectiveness of the interventions. Nevertheless, no framework, which suggests the factors that could be selected to manage fatigue in lung cancer population, is currently found, neither in Vietnam or worldwide. Several studies explored factors related to fatigue in lung cancer patients with chemotherapy. Found related factors of fatigue were stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea (Borthwick, Knowles, McNamara, Dea, & Stroner, 2003; Brant, 2008; D. J. Brown, McMillan, & Milroy, 2005; Chen et al., 2008; Molassiotis et al., 2011; Sarna & Brecht, 1997; Sarna et al., 2008; Sterzi et al., 2013; Wang, Tsai, Chen, Lin, & Lin, 2008). However, previous researchers only reported bidirectional associations between fatigue

and those factors in their single studies. Obviously, without examining those factors in the same model, no comprehensive picture toward how those determinants influence fatigue would be depicted. Therefore, a study of a causal model, which addresses these specific variables to lung cancer, is important and necessary.

Nursing care aims to optimize health and well-being (Fawcet, 2005). Fatigue is the most distressing symptom in lung cancer, which significantly affects patients' quality of life (M. Joyce, Schwartz, & Huhmann, 2008), mortality (Cheville et al., 2011b), functional status (Cella, Eton, Hensing, Masters, & Parasuraman, 2008), the utilization of healthcare service (Doyle, Lloyd, & Walker, 2008), hospital readmission (Borneman, Ferrell, Koczywas, & Cristea, 2008), and daily activities (A. Gift, A. Jablonski, M. Stommel, & C. W. Given, 2004).

Additionally, fatigue may also influence patients' family members. 64% of Vietnamese caregivers indicated that they were spending more than 10 hours for cancer patients (Green, Kinh, & Khue, 2006). It is clear that fatigue prohibits patients from doing normal works and lowers their quality of life (A. Gift et al., 2004). That makes patients more dependent, bringing more burdens to their family caregivers.

Moreover, medical treatments and nursing care for fatigue in Vietnamese population are limited. In Vietnam National guideline for supportive care, the treatment for fatigue is mainly relied on medications, such as methylphenidate or corticoids. Nutritional intervention is the only recommended nursing intervention for this symptom now (Vietnam Ministry of Health, 2006). Notably, it was indicated that although Vietnamese healthcare workers concerned about fatigue, nearly sixty percent of them confessed that they do not have enough information to design intervention for this symptom (Green et al., 2006).

Therefore, the study on causal model of fatigue in lung cancer patients with chemotherapy would offer valuable contribution to nursing care in Vietnam. The model would enable nurses in developing interventions to manage this symptom. Moreover, it should be noted that Vietnamese physicians appear to consider fatigue as the non-evitable symptom and thus pay less attention to it than to other symptoms (Duc et al., 2003; Thong & Duyen, 2010). Therefore, the initiation of intervention for fatigue would highlight nursing role in enhancing wellness of patients and their families.

Objectives of the study

1. To develop a causal model, consisted of stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea, for explaining fatigue in Vietnamese persons with lung cancer receiving chemotherapy.

2. To test the causal relationships among stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea, and fatigue in Vietnamese persons with lung cancer receiving chemotherapy.

Research questions

1. What are the relationships among stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, dyspnea, and fatigue in Vietnamese lung cancer patients receiving chemotherapy?

2. Does the hypothesized model explain fatigue in Vietnamese lung cancer patients receiving chemotherapy and does the model adequately fit with the data?

Conceptual framework of the study

This study uses the Integrated Fatigue Model (IFM) (Piper, 1993) as the theoretical framework to select the independent variables of the study.

Center of the IFM is the manifestations of fatigue, which is surrounded by 14 influencing patterns (Figure 1). Manifestations of fatigue include both subjective (perceptual) and objective (physiological, biochemical and metabolic, and behavioral) indicators. However, from the nursing perspective, Piper proposed that subjective aspect of fatigue is the key and central concern. Fatigue in the IFM is defined as the subjective feeling of tiredness which can vary in unpleasantness, intensity and duration (Jacobs & Piper, 1996). It consists of physical, emotional, affective, behavioral, and mental dimensions (Piper, 1993).

Among 14 factors in IFM, seven factors were included in the model of the current study. Those factors were selected because they are strongly supported by empirical evidence specific to lung cancer population. They were Changes in energy and energy substrate patterns (represented by nutritional status), Disease patterns (represented by stage of disease), Activity/rest patterns (represented by physical activity), Symptom patterns (represented by cough and dyspnea), Sleep/awake patterns (represented by insomnia), Psychological patterns (represented by anxiety), and Accumulation of metabolites (represented by number of cycles completed).

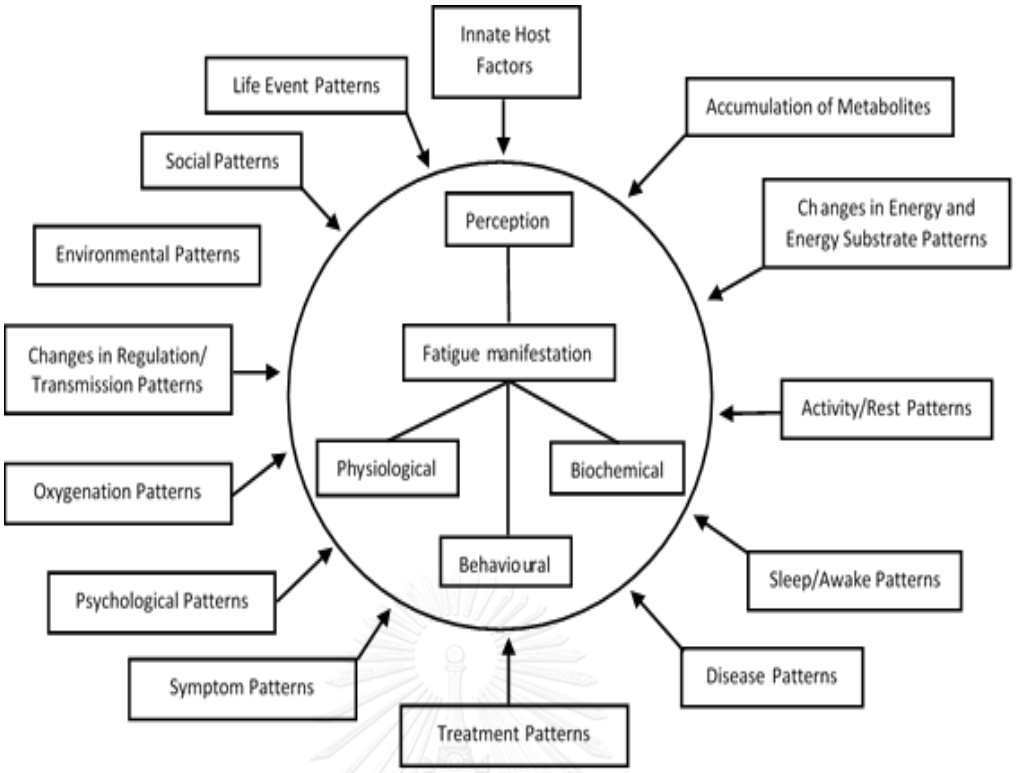


Figure 1 Piper's Integrated Fatigue Model

The IFM inherits the common idea from previous models, which proposed that fatigue results from the imbalance among energy production, energy transformation, and energy expenditure of the body. Any changes of those processes, which lead to the depletion of energy, would consequently result in fatigue.

In IFM, *Changes in energy production and substrate* may lead to fatigue. Energy production is the source of energy of the body. If the production of energy is inadequate, fatigue presents. In cancer, various factors such as nausea, vomiting, or mucosis limit patients' food intake. Whereas, the body requires a large amount of energy to deal with physical and psychological stress (Ferrell & Coyle, 2010). Those mechanisms lead to the poor nutritional status, indicating the body's energy insufficiency. Consequently, fatigue occurs.

Sleep-wake patterns also contribute to fatigue. According Piper, Olson, and Hagelin (2011) the remain of normal circadian rhythm is crucial to get rid of fatigue. The circadian rhythm of sleep and awake helps the body to restores its energy. If that circadian rhythm changes, fatigue occurs (Lee, Cho, Miaskowski, & Dodd, 2004). Insomnia indicates the poor quality of sleep, or the "quality" of the energy restoration period. Its severity also manifests the severity of change in circadian rhythm. Therefore, it could be hypothesized that insomnia causes fatigue.

The *Alterations in activity and rest patterns* would influence fatigue. Rest is necessary to restore body's energy. However, prolonged bedrest, unnecessary sedentariness or immobility may cause fatigue (Piper, 1992). It is assumed that the being sedentariness would reduce muscle oxidative capacity, leading to the higher demand of oxygen for activities. Moreover, muscle enzymes are depleted and nitrogen secretion is increased. Consequently, fatigue occurs. Guidelines for fatigue always recommend that patients should perform physical activity to lessen their fatigue (Hilarius et al., 2011; Portenoy & Itri, 1999). Therefore, it could be hypothesized that better physical activity will reduce fatigue.

Accumulation of metabolites is the important determinant of fatigue (Piper, 1993). Chemotherapy is a systemic treatment. The agents spread throughout the body, destroy both tumorous and healthy cells. A long with the course, more metabolites are accumulated within the body. Consequently, more fatigue occurs. The number of cycles that patients have completed may reflect the amount of metabolites augmented in the body. Therefore, it could be hypothesized that more cycles are completed, the more severe fatigue is.

Symptom Patterns can influence fatigue. Piper (1993) described that concurrent

symptoms would affect fatigue. Researchers widely accept the interactions among symptoms (Dodd et al., 2001; Lenz & Pugh, 2008). The patterns of interactions may depend on the nature of the symptoms. Cough and fatigue occupy fiercely respiratory muscles. It consumes a large amount of energy. Moreover, cough periods interrupt the normal respiratory pattern, leading to the lack of oxygenation – one source of body energy. Consequently, cough and dyspnea cause fatigue.

Piper (1993) acknowledges the idea of Selye toward the influence of stress to the body. According to the IFM, any usual response to stressors may influence fatigue. *Physiological factors,* which put the body in a stressful condition, would drain body's energy and cause fatigue. Therefore, it could by hypothesized that anxiety increases fatigue.

Although the IFM identifies comprehensively predictors of fatigue, it is somewhat limited in guiding the interplay among those determinants. Polit and Beck (2012) proposed that theory and prior findings would be used in combination to generate hypothesized explanations toward the underlying causes of the phenomenon. Previous authors (Hanprasitkam, 2006; Seo, Oh, & Seo, 2010) combined IFM and previous findings to build their hypothetical models. This study will used the same approach to generate the model. Particularly, the IFM and empirical evidence are used to explain the causative associations between determinants and fatigue. Relationships among determinants are hypothesized by empirical evidence.

In particular, dyspnea has found to be closely associated with insomnia in lung cancer patients on chemotherapy (Chen et al., 2008). Dyspnea spoils patients' sleep by making them unable to sleep or sleep with uncomfortable position. In addition, Dyspnea closely associates with cough, even up to five year after diagnosis with lung cancer

(Cheville et al., 2011a). In qualitative studies on experience of cough in lung cancer, patients strongly indicated that their cough triggers dyspnea and, makes them unable to lay down and sleep (Magasi et al., 2013; Molassiotis et al., 2011). The interactions among concurrent symptoms are also strongly supported by existing theories (Dodd et al., 2001; Lenz & Pugh, 2008). Thus, it could be hypothesized that there is the interplay among fatigue, dyspnea, cough, and insomnia.

In summary, this study used IFM as the theoretical framework select possible causative factors of fatigue, in combination with a review of empirical evidence. Eight independent variables were selected, which were particularly specific with lung cancer patients on chemotherapy. Those factors were stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea. To test the causative associations among such variables and fatigue, eight hypotheses were examined as followings.

Hypotheses and rationales

This study proposed eight hypotheses as followings:

Hypothesis 1

Statement: Insomnia has a positive and direct effect to fatigue.

Rationale: Theoretically, the function of sleep is to restore body energy (Sateia & Nowell, 2004). Thus, when sleep is disturbed or insufficient, it results in fatigue. Empirically, relationship coefficients between fatigue and insomnia were varied, from 0.27 (Sarna & Brecht, 1997), to 0.25 (Chen et al., 2008), 0.38 (Stone, Richards, A'Hern, & Hardy, 2000), 0.45 (Kuo & Ma, 2002), or 0.58 (Wang et al., 2008). Additionally, all frequency, intensity, and distress of fatigue associated with insomnia, regardless the

control of covariates such as age, sex, site and stage of cancer (Keehne-Miron, 2007).

Hypothesis 2

Statement: Anxiety has a positive and direct effect to fatigue.

Rationale: Theoretically, factors depleting energy of the body would result in fatigue (Piper, 1993; Ryden, 1977). Anxiety mobilizes the body to react with the stressful situation and thus consumes body's energy. The long lasting anxiety in cancer constantly drains the energy of the body (Henoch, Bergman, Gustafsson, Gaston-Johansson, & Danielson, 2007; L. S. Ryan, 1996; Salvo et al., 2012). Consequently, fatigue occurs. Literature review yielded pooled association coefficient between fatigue and anxiety was 0.46, and the OR was 1.19 (L. F. Brown & Kroenke, 2009). The mean effect size of anxiety on fatigue was large (1.11) (H. S. Oh & Seo, 2011). With regard to lung cancer, anxiety was related to fatigue in patients on chemotherapy ($r = 0.31$) (Liao et al., 2011), radiotherapy ($r = 0.62$) (Chan, Richardson, & Richardson, 2005), different treatments ($r = 0.46$) (Kuo & Ma, 2002), and in survivors (OR = 2.31) (R. Hung et al., 2011). The association between insomnia and fatigue was also supported by study on other cancer population ($r = 0.38$, $p < 0.01$) (Kim, 2006).

Hypothesis 3

Statement: Physical activity has a negative and direct effect to fatigue.

Rationale: Physical activity alters factors such as muscle mass, muscle strength, or proinflammatory cytokines and thus affects fatigue (Al-Majid & Gray, 2009). In particular, physical activity helps to prevent the loss of oxygen capacity, muscles' mass and endurance, and thus reduces fatigue (Piper, 1993). Empirically, physical activity predicted fatigue ($\beta = -0.327$, $p = 0.001$) (Luctkar-Flude, Groll, Woodend, & Tranmer, 2009). Lung cancer survivors, who were more physically active, were less likely to

have moderate/severe fatigue (OR = 0.29, P = 0.02) (R. Hung et al., 2011). A causal model showed that exercise explained nearly 70% variance of fatigue with mix cancer sample (Seo et al., 2010). The association between fatigue and physical activity was also found in breast cancer ($r = -0.56$, $p < 0.001$) (Haas, 2001). More importantly, physical activity appears to be the most widely recommended methods to relieve fatigue during treatments by systematic reviews (Finnegan-John et al., 2013; Jacobsen et al., 2007; Kuchinski, Reading, & Lash, 2009; Labourey, 2007).

Hypothesis 4

Statement: Nutritional status has a negative and direct effect to fatigue.

Rationale: Nutritional status indicates the energy resource of the body. In cancer, the limit nutrition intake and excessive energy consumption results in the energy deficit (Borthwick et al., 2003; Sarna & Brecht, 1997; Wang et al., 2008). Consequently, fatigue occurs (Piper, 1993). Empirically, the coefficient between fatigue and nutritional status was 0.54 in lung cancer (Xará, Amaral, & Parente, 2011). Other researchers found association between fatigue and nutritional status measurement (BMI) in heterogeneous cancer sample (RR= - 0.17; - 0.31; - 0.02) (Stone, Richards, et al., 2000). Interventions on nutrition also positively influences on fatigue during radiotherapy (Mortimer et al., 2010). In its guidelines, the Vietnam Ministry of Health also strongly highlighted the role of nutrition in managing cancer fatigue (Vietnam Ministry of Health, 2006).

Hypothesis 5

Statement: Cough has positive effects, both direct and indirect (through insomnia and dyspnea), to fatigue.

Rationale: Hypothetically, prolonged coughing may lead to the physical

exhaustion because respiratory muscles are occupied fiercely. It consumes a large amount of energy and thus results in fatigue (Piper, 1993; Ryden, 1977). Indirectly, cough causes sleep disturbance, making the patients cannot take enough rest. Cough may also triggers dyspnea. Sleep disturbance and dyspnea result in the exacerbation of fatigue (Molassiotis et al., 2011).

Empirically, the association between fatigue and cough were found to be 0.34 (Kuo & Ma, 2002). Cough was related with dyspnea with the coefficient of 0.45 (Sarna & Brecht, 1997) and 0.47 (Kuo & Ma, 2002). Notably, cluster analysis confirmed dyspnea, fatigue and cough constituted a symptom cluster, lasting up to five years (Cheville et al., 2011a). The interactions among fatigue, dyspnea, and cough were also described in qualitative studies in both Vietnamese and other populations (Green et al., 2006; Molassiotis et al., 2011). Additionally, the association between cough and insomnia is evident with $r = 0.31$ (Sarna & Brecht, 1997), or 0.281 (Henoch, Ploner, & Tishelman, 2009). Compared to healthy persons, lung cancer patients has significantly higher sleep disturbance related to cough ($z = -2.39$, $p < 0.05$) (Vena et al., 2006). Study on symptom cluster also found cough, fatigue and insomnia form a cluster of closely associated symptoms (Fodeh et al., 2013).

Hypothesis 6

Statement: Dyspnea has positive effects, both direct and indirect (through insomnia), to fatigue.

Rationale: Theoretically, dyspnea required fierce efforts from patients to breath. Consequently, it consumes a large amount of energy, especially for the respiratory muscles (E. G. Oh, Kim, Lee, & Kim, 2004). Moreover, the lack of oxygen intake - the energy resource - during the dyspnea period also exacerbates fatigue. In addition,

dyspnea spoils patients' sleep by making them unable to sleep or sleep with uncomfortable position. Consequently, insomnia occurs, contributing to the exacerbation of fatigue.

Empirically, the relationship coefficients between dyspnea and fatigue were varied with studies, such as 0.60 (Wang et al., 2008), 0.38 (Borthwick et al., 2003), or 0.45 (Henoch et al., 2009). Dyspnea at walking was the strongest predictor of fatigue even in ones with no active treatments (OR = 2.56, $p < 0.01$) (Okuyama et al., 2001). In lung cancer survivors, dyspnea is strongly associated with fatigue ($r = 0.52$, $p < 0.01$) (Devonish, 2010). Systematic review on factors related to fatigue in cancer reported the effect size of dyspnea on fatigue was 0.45 (H. S. Oh & Seo, 2011). It was evident that dyspnea was strongly associated with insomnia. The coefficients ranged from 0.35 (Sarna & Brecht, 1997), 0.51 (Chen et al., 2008), 0.62 (Wang et al., 2008), to 0.68 (Devonish, 2010). Studies on symptom cluster found fatigue, dyspnea, and cough were strongly interrelated with cluster coefficient of 0.615 (Kozachik, 2006).

Hypothesis 7

Statement: Stage of disease has a positive and direct effect to fatigue.

Rationale: Theoretically, advanced tumors and metastases consume dramatically energy of the body and thus directly exacerbate fatigue (Piper, 1993; Ryden, 1977). Empirically, stage is the factor that positively associated with fatigue in lung cancer with chemotherapy ($r = 0.149$, $p < 0.05$) (Hoffman, 2007). Studies on lung cancer patients on receiving radiotherapy (Borthwick et al., 2003), chemotherapy (Brant, 2008), or mix cancer sites during chemotherapy (Given, Given, Azzouz, Kozachik, & Stommel, 2001) found that patients with more advanced disease described higher level of fatigue than others.

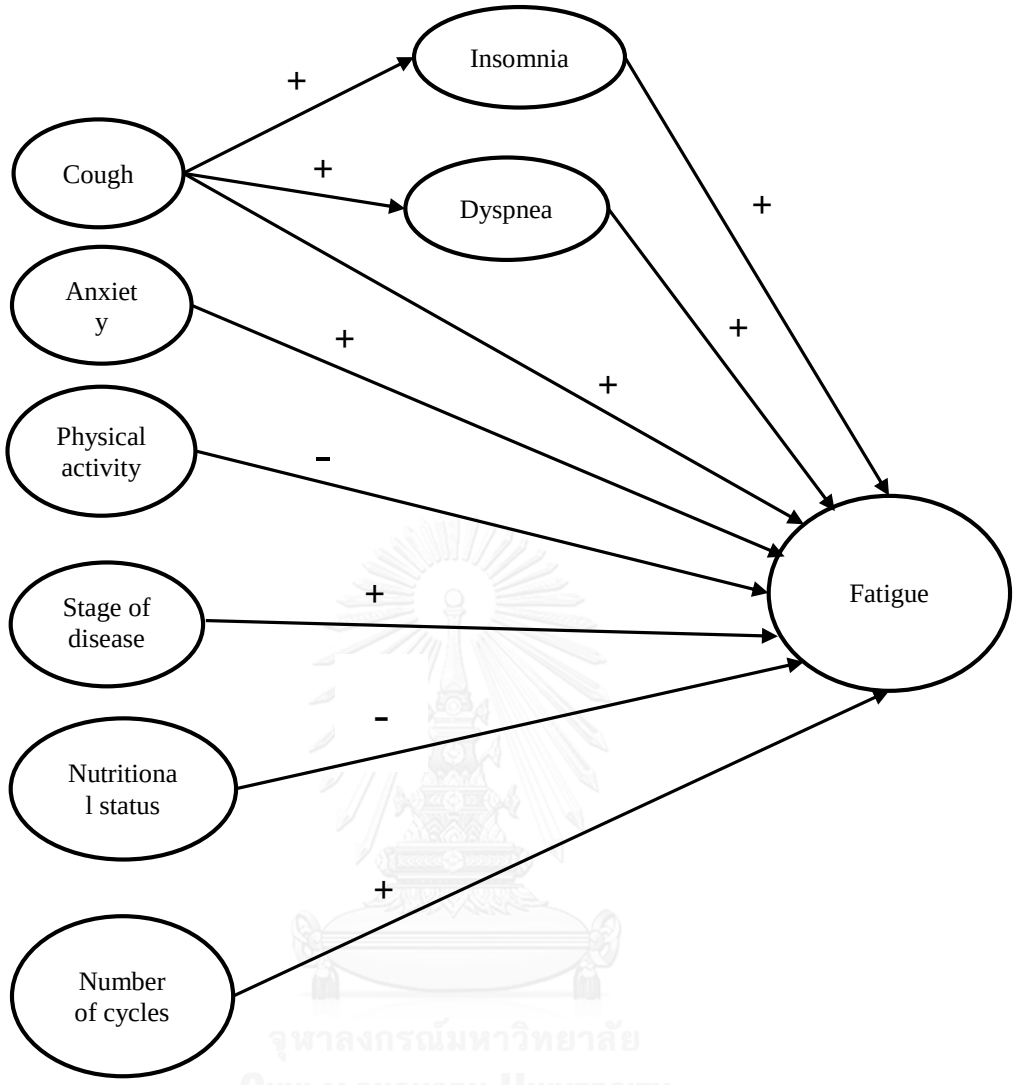


Figure 2 Theoretical framework of the study

Hypothesis 8

Statement: Number of cycles has a positive and direct effect to fatigue.

Rationale: Theoretically, the accumulation of metabolites within the body influences fatigue (Piper, 1993). Along with the chemotherapy course, more cells are destroyed and more metabolites are accumulated. Consequently, fatigue is more severe. Empirically, it was found that fatigue severity in lung cancer at commencement is

significantly higher than at the beginning of the chemotherapy course (Shallwani, 2010). Another study in two consecutive chemotherapy cycles showed an increase of fatigue in advanced lung cancer (Bozcuk et al., 2006). Using the Latent growth curve, Brant (2008) found that fatigue in lung cancer patients continuously increased over the six cycles.

Scope of the study

The study is a cross-sectional study to develop and test the causal model of fatigue in lung cancer patients receiving chemotherapy. Examining factors are stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea. The study will be conducted in Vietnamese population.

Operational definitions

Fatigue referred to perception of Vietnamese lung cancer patients receiving chemotherapy toward the subjective, persistent, and overwhelming feeling of tiredness or lack of energy, which is highly distressing and negatively interferes with patients' ability to function normally. Fatigue was measured by The Functional Assessment of Cancer Therapy-Fatigue subscale (FACT-F) (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997).

Insomnia referred to the perception toward the difficulties in falling asleep, staying asleep, and early awakening, leading to daytime impairments of the patients as reported

by Vietnamese lung cancer patients receiving chemotherapy. Insomnia was measured by the Insomnia Severity Index (Morin, 1993).

Cough referred to perception toward severity and influence of the violent expulsion of air from the lungs with a characteristic sound as reported by Vietnamese lung cancer patients receiving chemotherapy. Cough was measured by the Manchester Cough in Lung Cancer Scale (Molassiotis et al., 2012).

Anxiety referred to the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension as reported by Vietnamese lung cancer patients receiving chemotherapy. Anxiety will be measured by the Anxiety subscale of Depression, Anxiety, Stress Scale (DASS 21) (T. D. Tran, Tran, & Fisher, 2013).

Dyspnea referred to the subjective perception of breathing discomfort as reported by Vietnamese lung cancer patients receiving chemotherapy. Dyspnea was measured by the Cancer Dyspnea Scale (Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2000).

Nutritional Status referred to the state of nourishment, evaluated based on patient's weights and serum albumin, of Vietnamese lung cancer patients receiving chemotherapy. Nutritional status was measured by Nutritional Risk Index (Prendergast et al., 1989).

Physical Activity referred to levels of Vietnamese lung cancer patient's participation in activities (vigorous intensity activity, moderate intensity activity, and walking) during previous seven days. Physical activity was measured the International Physical Activity Questionnaire-Short Form (IPAQ-SF) (D. V. Tran, Lee, Au, Nguyen, & Hoang, 2013).

Number of Cycles referred to the number of cycles of the chemotherapy course that the Vietnamese patients with lung cancer receiving chemotherapy have completed. The number of cycles was obtained from patients' medical record.

Stage of Disease referred to the current stage of lung malignant disease of patients classified based on TNM system. The stage of disease will be obtained from patients' medical records, classified in to stage I, II, III, and IV.

Benefits of the study

This study examined a causal model explaining fatigue in Vietnamese lung cancer population. The hypothesized model consisted of factors, which are potentially modifiable. Therefore, the findings would help nurses and other healthcare workers having a comprehensive picture about determinants of fatigue. More importantly, the results would provide valuable information for those healthcare professionals, especially Vietnamese Nurse, in selecting suitable factors for their future fatigue control programs.

Besides fatigue, this study also provides a plenty of descriptions on dyspnea, cough, anxiety, physical activity, insomnia, and nutritional status of Vietnamese lung cancer patients. Such information is currently not widely reported in this country. Therefore, the findings of this study are not only identifying a hypothesized model explaining fatigue, but also providing useful information for Vietnamese researchers and clinicians toward current situation of those problems. The data could be the "hints" for further studies and clinical practitioners to develop their works concerning those issues.

This study also provided the measurements of fatigue, dyspnea, cough, insomnia,

anxiety in Vietnamese population. In particular, up to our knowledge, instruments in Vietnamese to measure these phenomena are rare. Obviously, the unavailability of standard measurements may hinder the advancement of research and practice on that phenomenon. This study translated and validated measurements of fatigue, dyspnea, cough, insomnia, and anxiety in Vietnamese population. Such questionnaires could be useful resources for Vietnamese researchers and clinicians. Equally important, the availability of internationally standardized instruments in Vietnamese would facilitate cross-cultural studies in the future.

CHAPTER II
LITERATURE REVIEW

The purpose of this study was to examine a causal model of fatigue in Vietnamese lung cancer patients on chemotherapy. This chapter presents the review of literature related to the study. Major issues addressed are 1) lung cancer in Vietnam, 2) the concept, theories, and measurements of fatigue in cancer, 3) the occurrence, consequence and management of fatigue in lung cancer, and 4) causative factors of fatigue in lung cancer patients on chemotherapy and their measurements.

Lung cancer in Vietnam

The incidence of cancer in Vietnam has been continuously increasing during the past decade (Vuong, Velasco-Garrido, Lai, & Busse, 2009). It is becoming a most problematic non-communicable disease this country. Among cancer, lung cancer is a highly common one, with 20,000 new cases annually. The majority of Vietnamese is diagnosed with lung cancer at the age over 40 (Bui, Le, & Nguyen, 2010a; Q. H. Nguyen, Vi, Lê, & Trần, 2010; Toan & Hiep, 2012). A study of Thang and Chuong (2012) reported that the most common age of lung cancer was 50-69 (67,9%), least prevalent (1,8%) was the group age of 30-39. The reported ratio of male/female was from 2.8/1 (Q. H. Nguyen et al., 2010) to 3.48/1 (Thang & Chuong, 2012).

Most cancer patients in Vietnam present to the hospital at advanced stages (65-80%) (Anh & Duc, 2002). Moreover, the North showed a significant higher incidence of lung cancer than the South. For example, the age-standardized rate of lung cancer (per 100 000) in males in the North was 38.8, whereas that incidence of the South was

24.6 (Anh & Duc, 2002). It is believed that the higher prevalence of smoking in the North than in the South is the main reason of the difference (Ngoan le, 2006; Ngoan, Fukumitsu, Kaneko, & Yoshimura, 2001).

Interestingly, in comparison to all other ASEAN states, the age-standardized DALYs lost per 100,000 from all cancers in Vietnam was the second ranked, only lower than Laos. With regard to lung cancer, Vietnam showed a highest mortality rate in comparison to its neighboring countries (21.5 per 100,000). That rate in other countries such as Singapore, Philippines or Cambodia were 21.2, 14.2, and 14.7, respectively (Kimman, Norman, Jan, Kingston, & Woodward, 2013).

According to the Vietnam Ministry of Health, the treatment and care for malignant diseases in Vietnam are limited ("National strategies for cancer control," 2009). Healthcare sectors in Vietnam are classified into national, provincial, district, and community level. Currently, only several national hospitals can provide systematic cancer treatments (N. C. Hung, Minh, Dung, & Thinh, 2008). Provincial hospitals offer simple tumor resection surgery for early stage patients. Most of patients (80%) then will be referred to the national hospital for further treatments. Community healthcare sectors are not allowed to offer any anti-tumorous treatments ("National strategies for cancer control," 2009).

Moreover, palliative care is not readily available to the vast majority of Vietnamese (Krakauer, Ngoc, Green, Van Kham, & Khue, 2007). Vietnamese patients are suffering from various distressing symptoms and fatigue is the most prevalent one (Green et al., 2006). The Ministry of Health explicitly stated that symptom relief is one of the five major goals in its national plan for cancer control ("National strategies for cancer control," 2009). A study of Tung (2010) demonstrated that, in comparison to all other

cancers, lung cancer showed a highest need for palliative care.

Fatigue in non-cancer population

Fatigue as the symptom in healthy population

Fatigue is a universal experience of human being. Every individual has fatigue in some moments in life. In general, most people experiencing fatigue do not see it as anything unusual. Healthy persons attribute fatigue to their daily prolonged activities or stimulation (Hotopf, 2004; Trendall, 2000). Trendall (2000) called fatigue in healthy person “acute fatigue” or “normal fatigue”. It is related to exertion, rapid in onset, and short in duration. (Trendall, 2000). Acute fatigue is “localized”, which patients are usually able to indicate the site where it occurs. Normally, fatigue present at limbs after activities and it reflects the decreased ability of the muscle to generate force (Yavuzsen et al., 2009).

Other characteristic of fatigue in healthy person its temporality. In particular, fatigue can be relieved by “lay” methods such as rest, good night’s sleep, food or water (Hotopf, 2004; Trendall, 2000). It is believed that acute fatigue is a protective function of the body. Being fatigued, “the body is forced to avoid further stress and thus allow recovery” (Trendall, 2000)

Fatigue as the syndrome in non-cancer population

In non-cancer population, fatigue may also occur as the syndrome. Chronic fatigue syndrome (CFS) is a condition of fatigue, which is severe disabling, lasting for at least six months (Vercoulen et al., 1997). Jones (2008) described that CFS is clinically unexplained, which is found in patients whose clinical examination and laboratory tests do not show any abnormality. Fatigue also is not the result of ongoing

exertion, is not substantially alleviated by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities.

It was described that CFS may result from the chronic ongoing infections, especially with virus. Some other authors proposed that immune alterations would be potential explanations of CFS after infection (Jones, 2008). From other point of view, several scholars believed that patient experiences certain symptoms and learns that physical activity aggravates these symptoms, especially fatigue. Patients then attribute fatigue to ongoing physical illness and thus tries to prevent fatigue by avoiding physical activity. Prolonged inactivity leads to physical deconditioning, and conversely, fatigue occurs as the consequences of progressively lower levels of physical activity. The circle is ongoing and the syndrome established (Vercoulen et al., 1997). However, those above explanations remain dramatic controversies, and the exact mechanism of CFS has not been established (Evering, van Weering, Groothuis-Oudshoorn, & Vollenbroek-Hutten, 2011).

Clear criteria have been proposed to diagnose the CFS. The presence of fatigue which is persistent or relapsing at least 6-months, is not alleviated by rest, and that causes substantial reduction in activities (more than 50% of the base line) is the first criteria. The fatigue is not attributed to medical or psychiatric conditions. Equally important, fatigue must be accompanied by at least 4 of 8 case defining symptoms The fatigue must be accompanied by at least 4 of 8 self-reported symptoms: (1) unusual post-exertion malaise, (2) unrefreshing sleep, (3) impaired short-term memory or concentration, (4) headaches of a new type, pattern, or severity, (5) muscle pain, (6) multi-joint pain without swelling or redness, (7) sore throat, and (8) tender cervical/axillary lymph nodes. (Patarca-Montero, 2004; Reeves et al., 2005)

Fatigue in cancer population

Definition of fatigue

Authors use several terms to describe fatigue as the symptom in cancer population. They are cancer related fatigue, cancer fatigue, or fatigue (Levy, 2008; Patarca-Montero, 2004; Stone, Richardson, et al., 2000). However, the descriptions of those terms appear to be similar. Ream and Richardson (1996) defined fatigue "a subjective, unpleasant symptom which incorporates total body feelings ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals' ability to function to their normal capacity.'' (p. 527). NCCN's Fatigue Guidelines Committee proposed "Cancer related fatigue is an unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (Hotopf, 2004). Irvine and colleagues (1994, p. 368) conceptualized cancer fatigue as a "(a) self-recognized phenomenon that is (b) subjective in nature and is (c) experienced as a feeling of weariness, tiredness, or lack of energy that varies in degree, frequency, and duration".

According to Aaronson et al. (1999), fatigue is "the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity." (p. 46). Scruggs (2009) proposed that "Fatigue is a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion that is not proportional to recent activity, is unrelieved by sleep and interferes with usual functioning." (p. 16). Tiesinga and colleagues (1996) found several definitions of fatigue in the literature, which are "an overwhelming, sustained sense of exhaustion and decreased capacity for physical and mental work", "unusual, abnormal or excessive whole body tiredness,

disproportionate to or unrelated to activity or exertion" (p. 54).

It is evident that fatigue, which occurs in cancer, demonstrated unique characteristics. Glaus et al. (1996) found that although fatigue in cancer and healthy person demonstrated similar dimensions (physical, affective and cognitive), their experiences are distinctively different. Cancer patients indicated fatigue as a "chronic, unpleasant, distressing, life- and activity-limiting tiredness throughout the day". Healthy persons, in contrast, described it as "a pleasant, acute, normal, regulating phenomenon which helped them to schedule their daily rhythm and which disappeared after a good night's sleep." (p. 93).

A qualitative study of Holley (2000) proposes that, in comparison to ordinary fatigue, fatigue in cancer is more rapid in onset, more energy draining, more intense, longer lasting, and often unexpected. According to Scott and colleagues (2011), other unique characteristic of fatigue in cancer is its overwhelming or "all-encompassing" feelings. In contrast, fatigue in healthy person is only localized at muscles or limbs.

In conclusion, the analysis of existing definitions of fatigue showed several identities of this concept. Fatigue is the subjective experience, characterized by the persistent and overwhelming feelings of tiredness or lack of energy. It is a highly distress symptom, which negatively interferes with patients' ability to function normally.

Pathophysiology of fatigue in lung cancer patients on chemotherapy

Up to date, the exact pathophysiological mechanisms of the associations between fatigue, cancer, and cancer treatments have not been affirmed. It is unclear to which extend fatigue is caused by the tumor and its effects, the treatment modalities, or

an interaction between the two (Andrews, Morrow, Hickok, Roscoe, & Stone, 2004). Currently, there are many hypotheses toward the etiologies of fatigue in cancer.

In particular, cancer and its treatment may lead to a defect in the mechanism for regeneration of adenosine triphosphate (ATP) in skeletal muscle. Consequently, the ability to perform mechanical work is reduced resulting in symptoms of fatigue. Other mechanism of fatigue is the serotonin dysregulation. The tumor and treatments increase brain serotonin (5-HT) level in specific brain regions, and/or an upregulation of a population of 5-HT receptors leading to reduced somatomotor drive, modified HPA function, and a sensation of reduced capacity to perform physical work. Cancer and its treatments also can cause a modification of hypothalamic–pituitary axis (HPA) function resulting in endocrine changes either causing or contributing to fatigue (Andrews et al., 2004; Narayanan & Koshy, 2009; Radbruch et al., 2008; J. L. Ryan et al., 2007).

High cytokine content have been found in patients undergoing chemotherapy or radiation treatment (Narayanan & Koshy, 2009). The increase of several proinflamatory cytokines is known to induce “sickness behavior”. Sickness behavior” includes symptoms such as fatigue, increased sleep, malaise, listlessness, inability to concentrate, subjective feelings of poor memory, fever, and decreased appetite (J. L. Ryan et al., 2007).

Another potential process by which cancer may cause fatigue is circadian rhythm disruption. Circadian rhythms are endogenous genetically- and physiologically-based patterns that are controlled by the body’s “biological clock.” Cancer patients suffer from various circadian changes in endocrine rhythms, metabolic processes, the immune system, and rest–activity patterns due to the tumor and its treatments. It is hypothesized that the change in circadian rhythm is an important factor causing fatigue

(Andrews et al., 2004; Narayanan & Koshy, 2009; Radbruch et al., 2008; J. L. Ryan et al., 2007).

It is also believed that the systemic effects of chemotherapy causing accumulation of metabolites as a result of normal tissue damage give rise to fatigue (Narayanan & Koshy, 2009). Equally important, many drugs with sedative properties regularly used in palliative care such as opioid analgesics, benzodiazepines, anti-depressants or anti-convulsants can add to the fatigue load (Radbruch et al., 2008).

In particular to lung cancer, there are also some mechanisms, which are specific to this population, may cause fatigue. Fatigue also may be due to Neuromuscular paraneoplastic syndromes such as Lambert-Eaton myasthenic syndrome (LEMS). The Lambert-Eaton myasthenic syndrome that is usually associated with small cell lung cancer. This syndrome manifested by fatigue, weakness of the proximal muscles of the pelvis, thighs, shoulders, and arms, and a weakening or absence of deep tendon reflexes. Other syndrome, paraneoplastic syndromes, which consisted of anorexia, cachexia, weight loss and fatigue, is also associated with lung cancer (Eaby-Sandy, 2011).

Theories of fatigue in cancer

Theories explaining fatigue

Several theoretical explanations of cancer related fatigue have been proposed. Mitchell (2010) classified them in four categories, which are 1) energy balance/energy analysis, 2) fatigue as a stress response, 3) neuroendocrine-based regulatory, and 4) hybrid models.

Energy balance/energy analysis models

Energy balance/energy analysis models describe that fatigue results from the

imbalance among energy intake, metabolism and expenditure. For example, Ryden (1977) proposed a conceptual framework of Energy expenditure. The model assumed that human body is an open system that needs energy from food, oxygen, and water to survive. The body continuously exchanges energy with environment. If the energy expenditure is excessively higher than the supply, fatigue occurs. Chronic illness, such as cancer, and its treatment consume a large amount of energy. However, the energy supply is limited and fatigue occurs as the result of the energy deficit. Although this model is an early theoretical explanation of fatigue, Payne (2004) argues that it is too simple. The model addresses fatigue merely in term of body energy balance and omits various other variables. Consequently, the model is not widely tested (Payne, 2004).

Fatigue as a stress response models

Stress response models consider fatigue as the response to stress (Mitchell, 2010). Aistars's (1987) (as cited in Payne (2004)) described stress as the primary cause of fatigue in patients with chronic conditions such as cancer. Other secondary causes are pain, infection, anemia, and emotional factors. It is hypothesized that multiple stressors trigger the stress response, causing the excessive use of body's energy. Consequently, the body suffers from fatigue. In comparison to Ryden (1977) model, Aistars's model is more detail and has been empirically tested. The linkage between fatigue and stress has been shown by several trials, which reported positive effects of stress-relieving strategies to fatigue.

Another model of the stress response model group is the Fatigue adaptation model (Olson, 2007). According to this model, tiredness, fatigue, and exhaustion are merely the different stages of the body adaptive conditions. If the body responds non-adaptively to tiredness, fatigue occurs. If an adaptive response at this phage can help

the body dealing with fatigue, the patient can move back to tiredness and, eventually, to no tiredness. In contrast, if adaptation is not effective, fatigue will progresses to exhaustion (Olson, 2007). Although this model is a new and fruitful perspective toward fatigue, it is still in its very infancy. Firstly, the model does not clearly differentiate fatigue, tiredness and exhaustion. In particular, all three concepts demonstrate in the same six dimensions (sleep quality, cognition, stamina, emotional reactivity, control over body processes, and social interaction). However, it is not clear to which extent the patient's condition could be classified as tiredness, fatigue or exhaustion. Moreover, the model merely focuses on the relationship between fatigue, tiredness and exhaustion, it does not address any factor that contributes to or influences fatigue. Therefore, the application of this model in real practice is still questionable.

Neuroendocrine-based regulatory models

This group consists of various hypothetical explanations toward fatigue. The common idea is that fatigue is the consequence of a dysfunction in neuroimmunoendocrine regulatory systems (Mitchell, 2010). Several scientists hypothesize that CRF is resulted from the dysregulation of 5-HT, a brain serotonin. 5-HT has numerous functions. It influences appetite, sleep, memory, learning, temperature regulation, mood, behavior, cardiovascular function, muscle contraction, endocrine regulation, and depression. Cancer and/or cancer treatment stimulate the release of 5-HT. The increase of 5-HT leads to reduced somatomotor drive, modified hypothalamic–pituitary–adrenal (HPA) axis function, and reduced capacity to perform physical work. Consequently, fatigue occurs (J. L. Ryan et al., 2007).

The impairment of hypothalamic–pituitary–adrenal (HPA) axis function is other hypothesis toward CRF. The HPA axis is the central regulatory system, which controls

the secretion of cortisol. Scientists assume that cancer and cancer treatment influence function of the HPA axis. Consequently, body endocrine is changed, resulting in fatigue (J. L. Ryan et al., 2007). The disruption of circadian rhythm is another theory of CRF. Circadian rhythms are genetic-endocrine-psychological circle patterns of the body. These 24-hour rhythms are sensitive to environmental and psychological factors. Cancer patients suffer from dramatic changes in body rhythms causing by genetic, psychosocial, environmental, behavioral, and tumorous factors. Hypothetically, the dysregulation of circadian rhythms leads to the occurrence of CRF (J. L. Ryan et al., 2007).

Argument to neuroendocrine-based regulatory fatigue models is that they heavily address fatigue by biological mechanism. Most models are developed by physicians (Mitchell, 2010) and appear to be more suitable for medical practice than for holistic nursing activities because they are limited in guiding non-pharmacological intervention for CRF. Lastly, J. L. Ryan et al. (2007) propose that these models still need further validation because existing findings yielded controversial evidence toward the credibility of them.

Hybrid models

The last group of CRF models is the hybrid model. This group explains CRF by the complex interactions among biological, psychological and functional factors (Mitchell, 2010). Al-Majid and Gray (2009) propose a Biobehavioral model to guide trials on exercise for CRF. The model describes that fatigue is influenced by biological factors (muscle mass, muscle strength, anemia, and proinflammatory cytokines) pyschobehavioral factors (psychological, distress, and sleep disturbances), and functioning factors (physical functioning, and functional capacity). Exercise

intervention alters those variables, resulting in the improvement of CRF.

Olson et al. (2008b) introduce the Edmonton fatigue framework. According to authors, cancer patients suffer from various stressors. Fatigue, tiredness, and exhaustion are body's abilities of adaptation to those stressors. Determinants of those abilities are muscle endurance, nutrition status, sleep quality, and cognitive function. In this model, no tiredness and ordinal tiredness are the adaptive response to stressors. In contrast, exhaustion is non-adaptive response. Fatigue is the state that moves between tiredness and exhaustion.

In general, although hybrid model group consists of only two models, they are somewhat more holistic than other groups. However, they show several limitations and narrowness in scopes. In particular, the biobehavioral model (Al-Majid & Gray, 2009) is built for only exercise intervention. It cannot guide other strategies, such as education or psychotherapy. The Edmonton fatigue framework (Olson et al., 2008b), on the other hand, is the model designed only for advanced cancer. Moreover, although the Edmonton fatigue framework allows nurses to generate hypothesis for clinical intervention, the model limits interventions to only four antecedents of CRF in advanced cancer, which are muscle endurance, nutrition status, sleep quality, and cognitive function.

The selection of theoretical guide

Among above theories, only the Integrated Fatigue Model (IFM) (Piper, 1993) has been used in studies examining causative factors of fatigue in cancer. Seo et al. (2010) and Hanprasitkam (2006) used this model in combination with empirical evidence to propose their hypothetical models.

The analysis of other fatigue models found their several shortcomings. Energy

analysis models of Ryden (1977) and Irvine et al. (1994) are not widely tested and their credibility has not been proven. Neuroimmuendocrine model merely focus on physical determinants of fatigue. It appears to neglect the fact that fatigue might be influenced by various physical and psychosocial factors (J. L. Ryan et al., 2007).

The Edmonton Fatigue Framework of Olson et al. (2008a) is immature in its concept development. In particular, the authors considered tiredness, fatigue and exhaustion as three stages response to stress, from adaptive to non-adaptive status. However, those three concepts have not been clearly differentiated. In addition, this model has not been tested (Payne, 2004). The behavioral model of Al-Majid and Gray (2009), on the other hand, is narrow in its scope. This theory targets to guide exercise intervention for fatigue rather than to explain how fatigue occurs.

Based on the analysis of existing models for fatigue in cancer, the IFM is selected as the theoretical guide for this study. Firstly, it is the most widely used and tested in studies on fatigue in cancer. Focusing systematically on multi-etiological factors of fatigue, IFM has been used to guide studies with causal modeling for this symptom. The model also allows generating hypotheses, which can be empirically tested. Other models do not show those unique qualifications.

The Integrated Fatigue Model

In 1987, Piper and colleagues proposed the IFM to explain fatigue in cancer. According to Piper (1993), fatigue is manifested by both subjective (perceptual) or objective (physiological, biochemical and metabolic, and behavioral) indicators. Objective manifestations of fatigue refer to the manifestations that can be observed objectively. Fatigue can be identified by physiological indicators such as the decrease

in hematocrit, blood glucose, thyroid, or oxygenation saturation levels. Biochemical and metabolic indicators of fatigue are the alteration in pH or electrolytes. Changes in physical appearance, affect, communication and activity patterns are examples of behavioral indicators of fatigue (Piper, 1993).

Subjective manifestations of fatigue refer to the subjective perception of the experiencing individual toward her fatigue. It includes physical, emotional, behavioral, and cognitive and mental component. Physical symptoms may include the expressions about feeling about physical exhaustion, tired arms, eyes, legs or the whole-body tiredness. Emotional dimension of subjective fatigue is the feeling of abnormal or unpleasant, for examples feeling impatient, irritable, disinterested, or lack motivation. Behaviorally, patients may perceived that it takes longer time or requires more effort to do things or even no longer able to do certain activities. In mental and cognitive dimension, patients may state that they feel difficulties in concentration, memories, or ability to think clearly.

Surrounding fatigue, there are 14 stressor patterns, which may cause or modulate fatigue. The *accumulation of various metabolites* ($NH4^+$, K^+, HP02, Pi, etc.) within the body may affect fatigue. *Changes in energy production and substrate* such as cachexia, anorexia, or fever may lead to fatigue. The *alterations in activity and rest patterns* would influence fatigue. Prolonged bedrest, unnecessary sedentariness or immobility are the examples of such alterations. *Physiological factors*, such as anxiety, motivation, and usual response to stressors may influence fatigue. *Environmental patterns* (e.g. temperature or humidity), *Life events* (e.g. pregnancy, parenting, or divorce), *Innate host factors* (e.g. age, sex, race, or genes), *Social patterns* (cultural belief or economic factors) may also influence fatigue.

Sleep-wake patterns also contribute to fatigue. Lack of restful sleep at night can lead to increased fatigue during the day. Other factors influencing fatigue are *Disease patterns, Treatment patterns, and Symptom patterns*. Moreover, any factors that may *change the ability to maintain adequate oxygen levels* can produce fatigue. Fluid and electrolytes imbalances, changes in neurohormone levels are examples of *Changes in regulation/transmission patterns* that can cause fatigue.

The selection of measurements for fatigue in cancer

The selection of instrument for fatigue in this study is based on two systematic reviews on measurements of fatigue in cancer (Minton & Stone, 2009; Seyidova-Khoshknabi, Davis, & Walsh, 2011). Based on psychometric properties and clinical feasibility of the instrument, the two reviews recommended totally six scales.

a) The Fatigue subscale of EORTC-QLQ-C30 consists of three items assessing physical and mental fatigue during last week. The scale has reasonable psychometric properties (reliability and convergent validity).

b) Fatigue Questionnaire (FQ) is an 11-item scale assessing fatigue physical and mental manifestations of fatigue. Its psychometric properties have been validated. However, it was originally developed for general practice setting and its main use was for the investigation of chronic fatigue syndrome in non-cancer population.

c) Functional Assessment of Cancer Therapy Fatigue (FACT-F) is a 13-item scale measuring intensity of fatigue. The instrument was first developed in a group of mixed cancer patients on treatment. FACT-F demonstrated good psychometric properties.

d) Cancer Fatigue Scale (CFS) consists of 15 items measuring intensity of

cancer fatigue in terms of physical and psychological manifestations. The scale was organically developed and tested in Japanese. The scale has good psychometric properties. However, its English version has not been validated.

e) Brief Fatigue Inventory (BFI) consists of nine items, rating on visual analog scale. It has reasonable psychometric properties but has had limited ongoing use. Moreover, the scale is used for screening purposes only.

f) Multidimensional Fatigue Symptom Inventory–Short Form (MFSI-SF) measures cognitive, physical, and affect domains of fatigue. The scale was validated in a heterogeneous population by cancer sites during chemotherapy and radiotherapy. It has favorable psychometric properties. However, this scale is burden to the respondents, especially advanced cancer, due to its length (30 items).

g) Besides above six scales, the Revised Piper Fatigue Scale (PFS) is also taken in the selection because of its close association with the theoretical guide of this study (IMF). This instrument assesses behavioral, affect meaning, sensory, and cognition aspects of fatigue. The PFS has good psychometric properties. However, the scale has some redundancy among items, difficult wording, and is somehow long (27 items).

The analysis of instruments for fatigue gives a favor to the FACT-F. The scale is relevant to the operational definition of fatigue, has good psychometric properties, reasonable length, and has been using widely in cancer populations. Thus, the FACT-F will be used in this study.

Occurrence and consequences of fatigue in lung cancer

Occurrence of fatigue in lung cancer

In fact, fatigue is the most prevalent symptom in lung tumor. Surveys showed

that nearly 90% of patients stated that they had fatigue during the past week (Lidstone et al., 2003) or in the past 24 hours (Swanson, 2006). More currently, a large study (n=1,213) found that nearly all lung cancer patients (98%) reported fatigue (S. Iyer, Taylor-Stokes, & Roughley, 2013). Another study investigated the change of symptoms during 52 weeks. Fatigue remained consistently as the most common symptom, whose prevalence ranged from 74.8% to 90.3% in all follow-up points (Koczywas et al., 2012). In Vietnam, a large cross sectional study found that fatigue is the most prevalent symptom in advanced cancer, including lung malignancy (Vu et al., 2010).

Fatigue is also the most severe symptom in lung cancer. In particular, 40% of advanced lung cancer reported moderate level and 22% reported severe level of fatigue (Swanson, 2006). According to R. Hung et al. (2011), 41% of early stage lung cancer had mild fatigue and 16.8% had moderate or severe fatigue. A study with Vietnamese lung cancer during concomitant chemoradiation therapy revealed that fatigue was the most problematic symptom with nearly 30% of the patients rated the score from severe to very severe (Toan, 2012). The severity score of fatigue was significantly higher than all other symptoms such as pain, dyspnea, cough, or appetite (S. Iyer et al., 2013).

It is also evident that fatigue is the most distress symptom in lung cancer (Degner & Sloan, 1995). Genç and Tan (2011) explored symptoms in lung cancer patients undergoing chemotherapy. Among 18 identified symptoms, fatigue was the most distress one. Similarly, Sarna and Brecht (1997) also found fatigue the most distress one among 13 identified symptoms in advanced lung cancer women. Notably, 10% of the respondents gave the maximum score of distress for this symptom.

Consequences of fatigue in lung cancer

There is convincing evidence toward the negative effects of fatigue to quality of

life of lung cancer patients. Bozcuk et al. (2006) examined quality of life in advanced lung cancer patients with chemotherapy. It was found that fatigue is an important predictor of quality of life (F = 7.92, P = .001). In other seven-year follow up longitudinal study with 447 lung cancer survivors, regression model indicated fatigue as one independent predictor of quality of life (Yang et al., 2012).

Fatigue also dramatically hinders daily life activities of lung cancer patients. According to Swanson (2006), fatigue significantly interfered with patients' walking ability (79%), general activity (77%) and normal work (78%), mood (70%), enjoyment of life (68%) and relations with others (56%). Other study pointed out that fatigue interfered with at least one daily life activity in nearly 90% of advanced lung cancer group (Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2002b).

Fatigue not only harms patients' physical health, it also spoils their mental health. Tishelman, Petersson, Degner, and Sprangers (2007) investigated 400 lung cancer patients and found that, along with pain and dyspnea, fatigue is the factor that most associated with patients' distress.

Additionally, many other negative influences of fatigue in lung cancer also have been reported. They are diminished survival (Cheville et al., 2011b; H. R. Scott et al., 2002), the increased utilization of healthcare service (Doyle et al., 2008), hospital readmission (Borneman et al., 2008) or early referral to supportive care specialist (Reyes-Gibby, Anderson, Shete, Bruera, & Yennurajalingam, 2012).

The existing interventions of fatigue

Fatigue in cancer is managed by various forms of intervention. However, currently, there is no specific programs to treat fatigue in lung cancer. Only one

guideline from American College of Chest Physicians recommended the use of antidepressants, psychostimulants, and anxiolytics to management of fatigue in lung cancer population (Simoff et al., 2013). Other programs are generic, and can be applied for various cancer populations.

In Vietnam, the guideline from the Ministry of Health suggested only one intervention to manage fatigue in cancer. It is nutrition enhancement (Vietnam Ministry of Health, 2006). Worldwide, the most commonly recommended intervention for fatigue is exercise. A review by Mitchell et al. (2007) identified various exercise modalities which have been used in the literature. They were walking, cycling, swimming, resistive exercise, or combined exercise. The frequency varied from two times per week to two times daily. Most programs were moderate in intensity and lasted from two weeks to one year.

Various complement therapy are also used to control fatigue. They are energy conservation and activity management, hypnosis, sleep hygiene, progressive muscle relaxation, acupuncture, massage, ginseng, yoga, and education for self-management behaviors. These interventions produce certain positive effects on fatigue but the results small. More importantly, previous trials employed such interventions showed inconsistent findings, and most of them were at high risk of bias (Campos et al., 2011; Finnegan-John et al., 2013; Kirshbaum, 2010; Mitchell et al., 2007).

With regard to medications, a meta-analysis of 10 studies by Minton et al. (2008) reported that erythropoietin effective in reduce fatigue in cancer patients on chemotherapy. The use of darbepoetin was also found effective in manage fatigue. In contrast, progestational steroids and paroxetine did not help to reduce this symptom.

It could be seen although various interventions have been tried worldwide to control fatigue, Vietnam is lacking of evidence to guide clinicians in designing their interventions. More importantly, the analysis of existing fatigue interventions showed that all programs are not specific to any kind of cancer. Therefore, such programs are not tailored to address particular characteristics of each cancer type. That could be the reason why when those interventions are tested in a mix cancer sample, their effectiveness is small and inconsistent among trials. This shortcoming make the clinicians less confident about effectiveness of their intervention when apply them in their specific population of interest. More importantly, those intervention may not be suitable to use in certain cancer type. In the situation of this study, such population is lung cancer.

In particular, although physical activity intervention is widely recommended, it requires a moderate intensity to be effective (Kirshbaum, 2010). Moderate intensity, however, makes the respiratory and cardiovascular systems work more intensively. In lung cancer, the tumorous lungs, whose functions may be already damaged, may not endure such requirements. It indeed puts patients in a danger, the situation that oncology nurses must be cautious in designing their intervention to reduce fatigue (Mitchell et al., 2007). Additionally, dyspnea and cough are inevitable entities of lung cancer, which may be very important predictors of fatigue in this population. Therefore, the management of fatigue in lung cancer may not be suitable without considering such symptoms in the program. Regretfully, previous trials tended to focus various rather than a specific cancer type and did not consider the uniqueness of each cancer population.

In conclusion, the analysis of existing fatigue interventions found that such program are developed and used for a mix cancer population. However, due to the unique characteristics of each cancer type, it is necessary to tailor the fatigue program in specification to that cancer. In lung cancer, the use of factors specifically contributing to fatigue could help to enhance the effectiveness of the interventions. Nevertheless, no framework, which suggests the factors that could be selected to manage fatigue in lung cancer population, is currently available. Such kind of framework could be a causal model explaining fatigue in this population. Several factors related to fatigue have been reported in the literature. However, currently, no study addresses a causal model for fatigue in lung cancer population has been found. Therefore, this study is an attempt to fill in that gap.

The following section is the review of literature on factors contributing to fatigue in lung cancer population. The outcome is to select suitable variables for construction of a hypothesized causative model of fatigue in lung cancer.

Correlates of fatigue in lung cancer patients receiving chemotherapy

Sarna and Brecht (1997) conducted a study with 61 advanced lung cancer women. Among the sample, 66.7% of them were receiving chemotherapy. The Symptom Distress Scale was used. Fatigue was significantly associated with nausea severity ($r = 0.4$), nausea frequency ($r = 0.33$), dyspnea ($r = 0.37$), and insomnia ($r = 0.27$). No associations were found between faitgue and pain intensity, pain frequency, and lack of appetite. In addition, insomnia was corrlated with dyspnea ($r = 0.35$), and cough ($r = 0.31$). Cough and dyspnea were also moderately associated ($r = 0.45$).

Wang et al. (2008) implemented a cross-sectional study in lung cancer

population. 108 patients, of which 67% were receiving chemotherapy, were recruited. The M. D. Anderson Symptom Inventory was used to measure symptoms. Fatigue was associated with pain (r = 0.59), sleep disturbance (r = 0.58), dyspnea (r = 0.60), difficulty remembering (r = 0.62), lack of appetite (r = 0.67), drownsiness (r = 0.62), dry mouth (r = 0.57), sadness (r = 0.66), and numbness (r = 0.39). Sleep disturbance was related to dyspnea (r = 0.62), and pain (r = 0.48).

A study of Keehne-Miron (2007) examined the association between fatigue, pain, and insomnia in 671 cancer patients. 21% of the sample were lung cancer patients. Symptoms were assessed by Symptom Experience Scale. Findings showed that the frequencies of pain and fatigue were associated ($\beta = 0.27$, SE = 0.4, $t = 6.75$, $p < 0.01$). Notably, insomnia remained as the significant predictor of fatigue regardless the control of age, gender, or comorbidity ($\beta = .18$, SE = .04, $t = 4.32$, $p < .01$).

Chen et al. (2008) investigated sleep disturbance and quality of life in lung cancer patients during chemotherpy. 115 patients were approached in their fourth cycle. The Pittsburg Sleep Quality Index and the EORTC QOL-30 were employed. Other measurements included Dyspnea Severity Index, Brief Pain Inventory, and Hospital Anxiety and Depression Scale. Fatigue showed significant associations with sleep disturbance (r = 0.25), dyspnea (r = 0.39), and depression (r = 0.33) but a non-significant relationship with pain. Sleep disturbance showed significant correlation with pain (r = 0.39), depression (r = 0.57), and dyspnea (r = 0.51).

Cheville et al. (2011a) conducted a large scale study on lung cancer patients (n = 2405), of whom 54.3% received chemotherapy. Patients' symptoms were assessed by the Lung Cancer Symptom Scale. Factor analysis was used to explore symptom clusters existing in this population. Data indicated that fatigue, cough, and dyspnea constituted

a cluster with the factor loadings of 0.68, 0.5, and 0.67, respectively.

Henoch, Bergman, and Danielson (2008) used a qualitative approach to study experience with dyspnea in 20 lung cancer patients. Patients clearly idenfity that fatigue is a immediate impact of dyspnea. Molassiotis et al. (2011) conducted a qualitative study to explore experience with cough in lung cancer. Twenty among 26 participants were treated with chemotherapy. Patients described that night cough caused sleep disturbance, making the patients cannot take enough rest. Some patients were awake all night. Cough may also trigger dyspnea. Sleep disturbance and dyspnea result in the exacerbation of fatigue. Additionally, prolonged coughing itself leads to the feeling of physical exhaustion.

Kuo and Ma (2002) recruited 73 lung cancer patients on treatments, who were currently receiving either chemotherapy or radiotherapy, to study the correlation of symptom distresses and coping strategies. The Symptom Distress Scale was used as the symptom measurement. Fatigue was associated with loss of appetite (r = 0.6), pain (r = 0.24), insomnia (r = 0.45), dyspnea (r = 0.43), cough (r = 0.34), numbness (r = 0.31), increased sputum (r = 0.41), vomiting (r = 0.24), difficulty swallowing (r = 0.3), anxiety (r = 0.46), depression (r = 0.48), confusion (r = 0.49). Insomnia was related to anxiety (r = 0.47). Cough and dyspnea were also associated (r = 0.47).

Luctkar-Flude et al. (2009) studied fatigue in 440 patients, of whom 10% had lung cancer. Memorial Symptom Assessment Scale (MSAS) and Physical Activity Scale for the Elderly (PASE) were used at baseline (during treatment), three months, and six months afterwards. It was found that physical activity and fatigue were negatively associated at all three assessment points (r = - 0.39, - 0.40, and - 0.43, respectively). At different assessments, regression analysis found that physical activity

explained 5% to 32% of the variance of fatigue.

Liao et al. (2011) implemented a study with 152 lung cancer patients who either receiving chemotherapy or non-treatment (16.4%). Symptom Severity Scale and Hospital Anxiety and Depression Scale were used. Data indicated that fatigue was related to depression (r = 0.42), and anxiety (r = 0.31). Anxiety and insomnia were also associated (r = 0.36).

Brant (2008) studied symptom trajectories during chemotherapy in 108 cancer patients. A group of lung cancer (46.6%), colorectal (26.3%), and lymphoma (27.1%) was recruited. Patients rated their symptoms on an electronic device. Severity of each symptom was scored on a 0-10 scale. Data indicated that patients with more advanced disease showed more intense fatigue.

Xará et al. (2011) investigated 56 lung cancer patients whore receiving chemotherapy, radiotherapy or none treatment. The Scored Patient Generated Subjective Global Assessment and the EORTC-QLQ 30 were used to measure nutritional status and quality of life of patients. It was found that patients, who were classified as undernourished, had more fatigue (r = 0.54), nausea and vomiting (r = 0.52), pain (r = 0.36), appetite loss (r = 0.7), constipation (r = 0.56), and lower quality of life (r = - 0.42). Non-significant associations were found between nutritional status and insomnia and dyspnea.

Stone, Richards, et al. (2000) studied prevalence, intensity and correlates of fatigue in 227 cancer patients. The lung cancer group accounted for 19% of the sample and all of them were receiving chemotherapy. Fatigue Severity Scale, the Hospital Anxiety and Depression Scale and EORTC-QLQ30 were employed. Data showed that anxiety and depression significantly associated with fatigue, r = 0.41 and 0.67,

respectively. Fatigue was also related to nutritional measurements including BMI (r = - 0.17), mid arm muscle circumstance (r = - 0.4). Others found correlates of fatigue were nausea and vomiting (r = 0.47), pain (0.57), dyspnea (r = 0.59), insomnia (r = 0.38). Multivariate analysis showed that 56% of the variance in fatigue scores could be explained by the combination of dyspnea, psychological distress, pain, and the stage of diseases.

In summary, the review of 13 studies related to lung cancer during chemotherapy found 20 correlates of fatigue. According to the Integrated Fatigue Model those factors could be classified into different patterns. Ten factors, which are under the Symptom patterns, are *nausea* (supported by 2 studies, r = 0.4 - 0.47), *dyspnea* (supported by 6 studies, r = 0.37 – 0.6), *pain* (rejected by 2 studies, supported by 4 studies, r = 0.24 – 0.59), *cough* (supported by four studies, r = 0.34), *lack of appetite* (rejected by 1 study, supported by 1 studies, r = 0.6 – 0.67), *dry mouth* (supported by 1 study, r = 0.57), *numbness* (supported by two studies, r = 0.31 and 0.39), *increased sputum* (supported by 1 study, r = 0.41), *vomiting* (supported by 2 studies, r = 0.24 and 0.47), and *difficulty swallowing* (supported by 1 study, r = 0.3).

Six factors, which are under the Psychological patterns, were *anxiety* (supported by 2 studies, r = 0.31 and 0.46), *depression* (supported by 3 studies, r = 0.33 – 0.42), *difficulty in remembering* (supported by 1 study, r = 0.62), *drownsiness* (supported by 1 study, r = 0.62), *sadness* (supported by 1 study, r = 0.66), *confusion* (supported by 1 study, r = 0.49). One factor, which is under the Changes in energy and energy substrate patterns, is *nutritional status* (supported by three studies, r = 0.54). One factor, which is under Activity/rest patterns, is *physical activity* (supported by 1 study, r = - 0.39 to - 0.43). One factor, which is under the Sleep/awake patterns, is *insomnia* (supported by

6 studies, r = 0.25 – 0.58). Lastly, one factor, which is under the Disease patterns, is *stage of disease* (supported by 1 study).

The selection of variables for the hypothesized model

Among 20 corellates of fatigue that found in lung cancer patients on chemotherapy, this research studied seven variables. They are dyspnea, anxiety, insomnia, cough, nutritional status, physical activity, and stage of disease. The reasons to exclude other variables are as followings.

Numbness, increased sputum, and *sadness* were excluded because there would not be plausible causative mechanism between them and fatigue (Piper, 1993). Identified relationships between those factors and fatigue seem to reflect their concurrent presence, not a causative connection. *Difficulty in remembering, drownsiness*, and *confusion* will not be studied as well. Seemingly, these factors are manifestaions of fatigue rather its causative factors.

The current did not examine *difficulty swallowing, lack of appetite, dry mouth, vomiting*, and *nausea* in its model. These factors and fatigue are closely related because, partially, they are all severe side effects of a common etiology – the chemotherapy. More importantly, the causative associations between these factors and fatigue, if present, might be indirect via the alteration of nutritional status. Those symptoms prohibit food intake, causing under-nutrition status, and thus lead to fatigue. Interventions focusing on lack of appetite, vomiting, or nausea to reduce fatigue, indeed, are just means to enhance nutritional status. Therefore, since the model has included nutritional status as a direct causative factor of fatigue, difficulty swallowing, lack of appetite, dry mouth, vomiting, and nausea will not be studied.

The causal relationship from *pain* to fatigue appears to be indirect rather than direct. Authors described that there is no plausible explanation for this direct association (Beck, Dudley, & Barsevick, 2005; Piper, 1993). Studies on relationships between fatigue and pain in lung cancer also rejected the direct relationship between these two symptoms (Hoffman, 2007; Okuyama et al., 2001; Swanson, 2006). Seemingly, pain contributes to the occurrence of fatigue via insomnia and limited physical activity - the two important causes of fatigue. Since there would be no direct association from pain to fatigue, and insomnia and physical activity have been included in the model, pain will not be studied in the current study.

It was widely noted that fatigue and *depression* are closely related in cancer population. However, there is unclear about the nature of this relationship. Whether fatigue causes depression, depression causes fatigue, or the two simply share the same etiology still remain controversies. The idea that depresion causes fatigue came from some pieces of evidence that the use of antidepressant may reduce fatigue (Hickok, Morrow, McDonald, & Bellg, 1996; Kirshbaum, 2010). However, there is evidence apposing that causative association. Currently, the efficacy of antidepressants in alleviating fatigue has not been established (Cantarero-Villanueva et al., 2011). Importantly, the impacts of medication do not necessarily reflect a causative association from depression to fatigue. Probably, those two may share the same etiology, such as the increase in brain serotonin (5-HT) (J. L. Ryan et al., 2007). Longitudinal study found that fatigue increased while depression remained the same (Servaes, Verhagen, & Bleijenberg, 2002) or decreased over the treatment (J. L. Ryan et al., 2007).

More importantly, current measurements of fatigue and depression are overlapping in their items. Most of depresison scales consist of items assessing fatigue

or tiredness (Yavuzsen et al., 2009). Thus, the similarity in measurements would be another reason making fatigue and depression were closely statistically associated. For above reasons, although depression is related to fatigue in lung cancer receiving chemotherapy, depression will not be included in this study as the cause of fatigue.

Other six factors, including *anxiety*, *dyspnea*, *cough*, *insomnia*, *physical activity*, and *nutritional status* will be examined in this study. The associations between fatigue and *anxiety, dyspnea, cough, and insomnia* are strongly supported by empirical evidence and theory.

The relationship between *physical activity* and fatigue in lung cancer receiving chemotherapy is found in one study. However, physical activity is the most widely recommended intervention for cancer fatigue up to date. Its effectiveness has been found. Nevertheless, it is unclear about the degree that physical activity influence fatigue in lung cancer patients receiving chemotherapy.

Role of *nutritional status* is supported by three studies. In Vietnam, nutritional improvement is the only nursing intervention for fatigue recommended by the Ministry of Health (Vietnam Ministry of Health, 2006). However, it is currently unclear how nutritional status contributes to fatigue in this population.

With regards to *stage of disease*, despite not much evidence towards the relationship between it and fatigue is available, this variable will still be investigated. Both theories of fatigue and theories of symptoms in general support the influence of disease characteristic in determining symptom (Lenz & Pugh, 2008; Piper, 1993). Obviously, besides the treatment, the disease is the focal and inevitable factor that influences fatigue. Therefore, since this study does not focus on specific stages of lung cancer, the inclusion of this factor in the model is necessary.

Besides above seven variables, this study included the *number of cycles* of the chemotherapy course that patients have completed as other independent variable. Theoretically, it is thought that the accumulation of metabolites from treatment may influence fatigue (Piper, 1993). It was evident that severity of fatigue increases along with the number of the cycles of the chemotherapy course (Brant, 2008). Moreover, although two other studies did not investigate fatigue during the whole chemotherapy courses, they found the increase of fatigue between before and after treatments (Shallwani, 2010) and between two subsequent cycles (Bozcuk et al., 2006). This evidence enforces the belief that fatigue increase along with the number of chemotherapy cycles. Therefore, since chemotherapy is a focal factor that influences fatigue, the number of cycles will be included in the model of this study.

Existing evidence in lung cancer on chemotherapy did not report any correlates of fatigue belong to others seven patterns of the IFM. Therefore, those patterns are excluded from the hypothesized model until the availability of empirical findings.

However, it is apprehended that the variation in the *Treatment patterns* would have confounding influence to fatigue. Patients may be treated by chemotherapy or concurrent chemoradiation. Before receiving such treatments, patients may undergo lung resection surgery. Two studies with lung cancer of Brant (2008) (n = 118) and Liao et al. (2011) (n = 152) showed that there was no difference in fatigue between patients with chemotherapy and concurrent chemoradiation. However, it is unclear whether prior surgery would influence fatigue during treatment course or not. Therefore, confounding effects of *Treatment patterns* are controlled by excluding patients with surgery prior to the chemotherapy course.

Concepts and measurements of independent variables

Insomnia

Concept of insomnia

Insomnia is the perception or complaint of inadequate or poor-quality sleep (Parker & Parker, 2002). The term sleep disturbance is widely used to describe the characteristics of insomnia, such as sleep latency, frequent waking up at night, un-refreshing sleep, inefficiency sleep (Morin & Espie, 2004). In general, insomnia is not subjectively defined by the number of hours of sleep a person gets or how long it takes to fall asleep. Individuals vary normally in their need for, and their satisfaction with, sleep. Insomnia can be classified as short-term, intermittent, and chronic (Parker & Parker, 2002).

The international classification of sleep disorders defined insomnia as "A complaint of difficulty initiating sleep, difficulty maintaining sleep or waking up too early or sleep that is chronically nonrestorative or poor in quality" (cited in Bonnet, Burton, & Arand, 2014). Roberson (2011) described insomnia is "difficulty falling asleep *(sleep onset insomnia),* staying asleep *(sleep maintenance insomnia),* and nonrestorative *(or poor quality)* sleep for at least one month. In addition to these preceding subjective complaints, a person must also experience daytime dysfunction due to the loss of sleep." According to J. Savard and Morin (2001), "insomnia is a heterogeneous complaint that may involve difficulties falling asleep (initial or sleep onset insomnia), trouble staying asleep with prolonged nocturnal awakenings (middle or maintenance insomnia), early morning awakening with inability to resume sleep (terminal or late insomnia), or a complaint of nonrestorative sleep." (p. 896).

In this study, insomnia is defined as person's perception toward the difficulties in falling asleep, staying asleep, and early awakening and nonrestorative sleep.

Occurrence of insomnia in lung cancer

Insomnia is the common in lung cancer. In a study of Wang, Chang, and Lin (2010), 85% of patients reported sleep disturbance during the previous week. The prevalence of lung cancer patients having poor sleep (based on Pittsburgh Sleep Quality Index score) were 56.6% (long-term survivors) (Gooneratne et al., 2007) and 52% (during chemotherapy or radiotherapy) (Chen et al., 2008). A large cross sectional survey examined sleep in nearly one thousand cancer patients. Data showed that lung cancer patients reported more severe insomnia than gastrointestinal, genitourinary, gynecologic, and non-melanoma cancer individuals. In general, lung cancer patients had longer sleep latencies, more difficulty remaining asleep, and more sleep fragmentation than others did (Davidson, MacLean, Brundage, & Schulze, 2002; Induru & Walsh, 2013; Vena et al., 2006).

Measurements of insomnia

Numerous approaches to the assessment of sleep and insomnia are available (Carney & Edinger, 2010). Sleep can be measured objectively by polysomnogram (PSG), electroencephalogram (EEG), electrocardiogram (EKG), or electromyogram (EMG). Carney and Edinger (2010) classified subjective measurement of insomnia into several groups. They are global sleep questionnaires (e.g. Insomnia Severity Index, and Pittsburgh Sleep Quality Index), Cognitive Insomnia Questionnaires (e.g. The Dysfunctional Beliefs and Sleep Self-Efficacy Scale), Behavioral Insomnia Questionnaires (e.g. The Sleep Hygiene Practice Scale and Sleep-Related Behaviors Questionnaire), and Daytime Insomnia Symptom Questionnaires (Epworth Sleepiness

Scale). In general, the instruments of sleep and insomnia demonstrated good psychometric properties and have been using in various population.

The review of literature identified that the a) Insomnia Severity Index (M. H. Savard, Savard, Simard, & Ivers, 2005) and the Pittsburgh Sleep Quality Index (Buysse, Reynolds Iii, Monk, Berman, & Kupfer, 1989) have been validated and used in research for cancer patients. Researchers described that the two questionnaires are excellent tools to measure insomnia in clinical study (Morin, 2003). However, in comparison to the b) Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Index is briefer (ISI) (19 items vs 7 items). It takes 5 to 10 minutes to complete the PSQI. Respondents easy feels confused and there is a high risk to get missing data when use this instrument in cancer population (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004).

It is obvious that lung cancer patients are critically ill. Therefore, the use of a brief and feasible instrument would be prioritized. Thus, the Insomnia Severity Index was used to measure insomnia in this study.

Cough

Concept of cough

Fontana and Widdicombe (2007) defined that cough is "A violent expulsion of air from the lungs with a characteristic sound" (p. 307). The Thoracic Society Cough Guideline Group described cough as "a forced expulsive manoeuvre, usually against a closed glottis and which is associated with a characteristic sound." (Morice, McGarvey, & Pavord, 2006, p. i5). Cough is believed to process in three phases, including an initial inspiration, the closure of the glottis and a forced expiratory effort, and the opening of the glottis and vigorous expiration. Cough may occur as a single event or may include several or many expiratory efforts in a single episode (Fontana & Widdicombe, 2007).

In this study, cough is defined as perception toward severity and influence of the violent expulsion of air from the lungs with a characteristic sound as reported by Vietnamese lung cancer patients receiving chemotherapy.

Occurrence of cough in lung cancer

In general, cough is a reflex, which protects the airways by forcibly removing obstructive or harmful substances. However, in lung cancer, cough appears as a common and distressing symptom. Prevalence of cough is about 80% of patients with lung cancer. This symptom presents in all stages and types of lung cancer. It occur regardless the treatment modalities, e.g chemotherapy, radiation therapy, and palliative care therapy (Chernecky, Sarna, Waller, & Brecht, 2004). According to Kvale (2006), cough is present in more than 65% of patients at diagnose with lung cancer, and productive cough is present in only one-quarter of patients.

Various factors contribute to the occurrence of cough in lung cancer. They are cancer centrally located tumors, bleeding tumors, infection, COPD, smoking, anti-tumorous treatment (Harle, Blackhall, Smith, & Molassiotis, 2012). These factors trigger the receptors of nerve fibers, which are distributed throughout the ciliated epithelial cells of airways from the pharynx to the terminal bronchioles. The greatest concentration of cough receptors are located in the larynx, carina, and at the bifurcation of medium- to large-sized bronchi (Simpson & Amin, 2006).

Measurements of cough

Literature review identified three qualified scales assessing cough (Chung, 2006; Harle et al., 2012). They are Leicester Cough Questionnaire (LCQ), the Cough-specific Quality of Life Questionnaire (CQLQ), and the Manchester Cough in Lung Cancer Scale.

a) LCQ consists of 19 items. The scale examines three domains of cough, including physical, psychological and social on a seven-point Likert scale. b) CQLQ is a 28-item questionnaire. This scale measures cough in six domains, which are physical complaints, extreme physical complaints, psychosocial issues, emotional well-being, personal safety fears and functional abilities. **c)** MCLCS consists of 10 items measuring intensity of cough. This self-rated scale was developed for a specific use in lung cancer.

A review of Chung (2006) pointed out that the LCQ and CQLQ still require further validation and have been used mainly in non-cancer populations. MCLCS (Molassiotis et al., 2012) is developed for use lung cancer population. It is brief, clear, and demonstrates good psychometric quality. Therefore, the current study used this instrument to measure cough.

Dyspnea

Concept of dyspnea

Dyspnea is described as "a subjective experience of breathing discomfort" (Huhmann & Camporeale, 2012). The term dyspnea is used interchangeably with breathlessness, shortness of breath, breathing difficulty, and labored breathing in literature (Simon, Higginson, Booth, Harding, & Bausewein, 2011). Patho-physiologists explain that that dyspnea is caused by a discrepancy between the effort of the respiratory muscles necessary to get air into the lungs and the actual amount of air that was displaced (inhaled). Another mechanism for dyspnea is a disturbance of blood gas levels (De Peuter et al., 2004).

"Dyspnea is a subjective symptom with a sensory component of labored breathing and an affective reaction expressed as distress" (M. M. Joyce, 2009, p. v). American Thoracic Society (ATS) found many definitions of dyspnea in the literature,

including “difficult, labored, uncomfortable breathing”, “awareness of respiratory distress”, “the sensation of feeling breathless or experiencing air hunger”, and “an uncomfortable sensation of breathing” (American Thoracic Society, 1999). ATS also described dyspnea as “a term used to characterize a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity” (p. 322). In agreement, (Huhmann & Camporeale, 2012) also proposed dyspnea as “a subjective experience of breathing discomfort”.

In this study, dyspnea is defined as a subjective perception of breathing discomfort.

Occurrence of dyspnea in lung cancer

Dyspnea is a very prevalent symptom of lung cancer. Since the disease involves directly to the respiratory system, dyspnea, in fact, the inherent entity of lung cancer. A integrative review of Kathiresan, Clement, and Sankaranarayanan (2010) pointed out that the average prevalence reported by studies on dyspnea in lung cancer was 70.5%, with a range of 50%–87%. This indicates a high prevalence of the symptom. In general, the pooled score of symptom distress indicated that the distress associated with dyspnea.

In lung cancer, being dispneic is frightening to both patients and caregivers, making them anticipate about death (A. C. Williams, Grant, Tiep, Kim, & Hayter, 2012). Many factors can cause and exacerbate dyspnea. Lung tumor, obstruction of pulmonary tissue, anemia, hot weather, obesity, anxiety, and cancer treatments such as chemotherapy, biotherapy or radiotherapy are examples of those factors (Huhmann & Camporeale, 2012; A. C. Williams et al., 2012).

Measurements of dyspnea

Several instruments for dyspnea have been employed. In the summary of measurements of fatigue by Oncology Nursing Society, M. Joyce and Beck (2005) identified eleven instruments. The instruments varied, from a single Visual Analog Scale (measure dyspnea intensity) to the 164 item-scale as like the Pulmonary Function Status and Dyspnea Questionnaire. Questionnaires focused on various aspects of dyspnea. For example, the Cancer Dyspnea Scale assessed sense of effort, sense of anxiety, sense of discomfort of dyspnea; the Shortness of Breath Questionnaire evaluated the ADL related shortness of breath; the Modified Borg Scale measured degrees of perceived exertion. In general, existing instruments of dyspnea appear to be highly qualified in psychometric requirements. Those questionnaires would be used for dyspnea either in non-tumorous pulmonary diseases or in cancer.

Among instruments, only the **a)** Visual Analog Scale (VAS) and the **b)** Cancer Dyspnea Scale (CDS) were tested in lung cancer population (M. Joyce & Beck, 2005). While the VAS is a single-dimension (severity), the CDS evaluates multi-facets of dyspnea. Moreover, its psychometric properties in lung cancer population, including construct validity, convergent validity, internal consistency, and stability, have been reported. Researchers asserted that this is a qualified instrument to measure dyspnea in lung cancer (Henoch, Bergman, & Gaston-Johansson, 2006; Tanaka et al., 2000; Uronis et al., 2012). The CDS is also brief (12 items) and requires short time to complete (2 minutes). These characteristics make it very practically usable in clinical setting (Uronis et al., 2012).

For those above reasons, this study used the Cancer Dyspnea Scale (Tanaka et al., 2000) to measure dyspnea.

Physical Activity

Definition of physical activity

According to World Health Organization, physical activity consists of any muscle-skeletal movements, which consume body's energy. It may be activities related to work or leisure exercises (World Health Organization, 2010). The current study concerned about physical activity in terms of the levels that lung cancer patient's participate in activities (vigorous intensity activity, moderate intensity activity, and walking) during previous days.

Physical activity in lung cancer

A low level of physical mobility in lung cancer has been reported. Granger et al. (2014) conducted a prospective observational study with 50 lung cancer individuals staged I to III. Physical mobility was measured objectively as number of steps per day by an electrical device. Self-reported physical activity was also measured by the Physical Activity Scale for the Elderly. Data was collected at diagnosis, then 10 weeks and six months later and was compared to that of thirty-five healthy non-cancer persons. The result showed that individuals with NSCLC were less physically active than healthy individuals in both objective and subjective measure. One-third (30%) of the patients were classified as sedentary (performing 0 minutes of physical activity per week). In other study in lung cancer survivors, (R. Hung et al., 2011) found that only 24% of patients met the guideline for physical activities (engaging in at least 150 minutes per week of at least moderate intensity activity.

Measurement of physical activity

Three scales for PA used in cancer population have been found.

a) Physical activity behavior scale is a single question asking patients to classify

themselves as sedative, low to moderate, moderate to high, and high intensity physical active. This scale was used to measure physical activity of cancer patients undergoing chemotherapy (Midtgaard et al., 2009). However, no information related to its psychometric properties have been found. **b)** Seo et al. (2010) used three questions to measure physical activity in their study on a mix cancer group. The questions are about t intensity, frequency, and durations of exercise. However, scale is available in Korean and information related to its quality is limited. **c)** Godin Leisure-Time Exercise Questionnaire (GLTEQ) (Godin & Shephard, 1997) is a four-term scale, asking about frequency of exercise (mild, moderate, and intense) that patients performed. It has been used in patients following chemotherapy or bone transplantation (Courneya, Keats, & Turner, 2000), colorectal survivors (Courneya et al., 2003), breast and prostate survivors (Humpel & Iverson, 2010), and lung cancer patients on active treatment (Lin, Wu, Rau, & Lin, 2013). However, the GLTEQ consists of items asking about activities, which appear not to be suitable with Vietnamese context, for example playing golf, skiing, or basketball. Therefore, those above instruments are not suitable to use in this study.

The search for other existing instruments, which would be used in this study, found that the International Physical Activity Questionnaire-Short Form (IPAQ-SF) is the suitable one. Firstly, it measures physical activity in general, not with specific to any type of activities. Secondly, it evaluates physical activities in previous 7 days, not the habitual physical activity. Lastly, the questionnaire has been validated in Vietnamese population and its Vietnamese version shows acceptable psychometric properties (D. V. Tran et al., 2013).

Anxiety

Concept anxiety

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) defined anxiety as "The apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension." (American Psychiatric Association, 2005, p. 764). A concept analysis of Whitley (1992) described that anxiety is as a vague, uneasy feeling of discomfort or dread, stimulated by unknown or unspecific causes. Anxiety consists of both subjective responses and objective signs.

Anxiety is the universal human experience and the most basic of emotions. With regard to severity, anxiety could be classified into four levels: mild, moderate, severe and panic. Anxiety at the mild and moderate levels is constructive, which help the sufferers deal with the situation. However, at the severe and panic levels, anxiety is destructive. It diminished patients' physical and mental function, resulting in exhaustion (Townsend, 2009).

In this study anxiety is defined as an apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension.

Occurrence of anxiety in lung cancer

Among psychological problems of lung cancer, anxiety is a severe issue. Anxiety presented in 40% of advanced lung cancer patients and the prevalence is not different between in- and out-patient groups (Du-Quiton et al., 2010). In patients with early stage (IA or IB) lung cancer, anxiety was reported by nearly every one of five individual (19.7%) (R. Hung et al., 2011). In a study with heterogeneous lung cancer stage sample, 32.6% of patients demonstrated anxiety (HAD-A $\geq$ 8) (Pirl et al., 2008).

Anxiety is also a long lasting problem in lung cancer. (Feinstein et al., 2010) investigated in 342 long-term lung cancer survivors. It was found that 20.2% of the respondents report anxiety (HAD-A score ≥ 8). Some authors conducted a follow-up study over 12 months in lung cancer population. The data showed that in general, the level of anxiety was mild (HADS score was around five) did not change over time (Henoch et al., 2007)

In addition, anxiety in lung cancer is also characterized by its severity. (Genç & Tan, 2011) used Brief Symptom Inventory to examine lung cancer patients undergoing chemotherapy. The data showed that patients suffered from noticeable level of anxiety. While the maximum possible score was 10, the mean score of anxiety was 5.8 ± 2.38. In a large scale theory, Hopwood and Stephens (2000) demonstrated that thirty-four percent of lung malignant patients (334 of 974) self-reported anxiety, of whom 18% (171) were at the level of probable case and 17% (163) were at the level of borderline severity (HADS).

Measurements of anxiety

The measurements of anxiety consist of both objective and subjective methods. Clinicians could use electroencephalogram for recording central nervous system responses, and the electrocardiogram for cardiovascular system responses. Respiration rate and depth, stomach pH or stomach motility, and palmar sweating responses are also examples of objective assessment of anxiety (McDowell, 2006).

Subjectively, anxiety can be measured by self-rating or clinician rating scales. Several anxiety scales have been used in lung cancer population.

a) The anxiety items of general symptom questionnaires or self-developed item have been used in studies of Genç and Tan (2011) (Brief Symptom Inventory),

Kuo and Ma (2002) (Symptom Distress Scale) or Tsai, Wu, Chiu, and Chen (2010) (single self-developed item). The items mainly focus on intensity of anxiety. However, those measurements are not specific for anxiety and could not offer highly reliable and comprehensive information toward the patients' problem. **b)** State-Strait Anxiety Inventory (STAI) is a highly qualified questionnaire. It consists of two subscales measuring state anxiety (20 items) and strait anxiety (20 items). Researchers have used it to measure strait anxiety in lung cancer (Alacacıoğlu, Öztop, & Yılmaz, 2012; Smith et al., 2001). **c)** Anxiety subscale of the Hospital Anxiety and Depression scale is the most commonly used to measure anxiety in lung cancer. This subscale consists of seven items, measuring intensity of anxiety. Its excellent psychometric properties are widely reported (Ostroff et al., 2011; Pirl et al., 2008; Uronis et al., 2012; Vos, Putter, van Houwelingen, & de Haes, 2011). **d)** The Anxiety subscale of the Depression, Anxiety, and Stress Scale 21 (DASS-21) has also been used in lung cancer population (Sharp, Carsin, & Timmons, 2013). It consists of seven items and demonstrates good psychometric properties (Henry & Crawford, 2005; Norton, 2007; Szabó, 2010).

Although STAI, DASS 21-A, and HDAS-A are all qualified scales, the STAI is not prioritized because it is the longest one. Obviously, a small number of items would make other scales more practical than STAI in clinical setting. The DASS 21-A and HDAS-A are quite equivalent. However, the DASS 21-A has been validated in Vietnamese in both reliability and construct validity (T. D. Tran et al., 2013). Therefore, the DASS 21-A was selected.

Nutritional Status

Concept of nutritional status and nutritional status of lung cancer patients

Nutritional status is the state of nourishment of the body. Nutrition problem of lung cancer patients has been reported. Chermiti Ben Abdallah et al. (2013) examined nutritional status in 30 lung cancer patients before and during chemotherapy. The data was collected by Nutritional Risk Index. Before treatment, Nearly half (47%) of the sample was classified as malnutrition. During the treatment, malnutrition was noted in 77% of patients and 26.7% of the sample demonstrated severe malnutrition.

Measurements of nutritional status

Several scales were used to measure nutritional status in cancer.

a) Nutritional Risk Index (NRI) (Prendergast et al., 1989) combines albumin with present and usual weight to grade the level of malnutrition. Patients are categorized according to their NRI score as "well nourished", "mildly malnourished", "moderately malnourished", or "severely malnourished". **b)** Subjective Global Assessment (SGA) (Bauer, Capra, & Ferguson, 2002) is commonly used. To complete SGA, investigators use a standardized questionnaire obtaining patients' height and weight, appetite, intake, gastrointestinal symptoms. The examiner then conducts subjective assessment of fat loss, muscle wasting, edema and ascites, and existing medical conditions (e.g., infection, renal insufficiency). By SGA, patients are classified into well nourished, moderately malnourished, or severely malnourished. **c)** Malnutrition Universal Screening Tool (MUST) (Poulia et al., 2012) uses current BMI, unintentional weight loss and the presence of any acute disease effect that could compromise nutritional intake for >5 days to predict the risk of malnutrition. Patients are labeled as low, medium, and high risk of malnutrition.

The comparison among scales gives a favor to the NRI. Firstly, NRI could offer score at ratio level, which can be used to classified patients afterward. MUST,

however, produces score at ordinal level only. Moreover, the NRI measures current state of nourishment, whereas MUST is a careening tool, which predicts future malnutrition. The SGA is reliable but it is complicated and requires well-trained dietarian to perform. NRI is briefer and more applicable, which has been employed in lung cancer as well (Chermiti Ben Abdallah et al., 2013). For these above reasons, the NRI was used.

In the current study, nutritional status is defined as the state of nourishment, evaluated based on patient's weights and serum albumin.

Stage of disease

For the purpose of diagnosis, treatment, and prognosis, malignant diseases are classified into different stages by international criteria (Kameyama et al., 2009). The two most commonly encountered types of stage assessment are clinical staging (the stage determined using all information available prior to any treatment) and pathologic staging (determined after a resection has been carried out) (Detterbeck, Boffa, & Tanoue, 2009). Clinicians widely used the TNM classifications to differentiate the stage of malignant disease. In this system, T stands for Primary Tumor, N stands for Regional lymph nodes, and M stands for Distant Metastasis. Based on the description of each three components clinician identified the stage of the disease. For example, T component is classified into T1 (tumor size ≤ 3 cm), T2 (tumor size ≤ 7 cm), and T3 (tumor size > 7 cm) (Rami-Porta, Crowley, & Goldstraw, 2009).

Based on TNM descriptors, the 7th classification system of lung cancer categorized the disease into I to IV stages. Since classifying the stage of disease is not of the professional role of nurses, this study used the diagnosis of the physician as the

measurement of the variable. The stage of disease was obtained from patients' medical profiles.

In conclusion, a review of the literature showed that fatigue is a severe problem of lung cancer patients on chemotherapy, in both Vietnam and worldwide. However, it is currently under-managed. Evidence also suggested that fatigue management program should be tailored to address specific issues to lung cancer population. To develop such programs, it is necessary to have a framework pinpointed the possible intervention factors. Hence, there is a need to construct a causal model explaining fatigue on lung cancer patients on chemotherapy.

The concept of fatigue has been clearly defined, various theories and measurements for this concept are also available. Factors that could be found to be causative variables of fatigue in lung cancer on chemotherapy are stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea. The concept and measurements of these variables are also well-defined.

CHAPTER III
METHODOLOGY

Research design

This was a cross-sectional predictive study. The obvious advantage of this design is that it allows the investigation of a large number of interrelationships in a relatively short time (Polit & Beck, 2012). Moreover, unlike experimental studies, correlational research is seldom criticized because of its artificiality (Polit & Beck, 2012; Powers & Knapp, 2006). From above rationales, a cross-sectional predictive design was selected in this study.

Settings and time frame

Vietnam is divided into three main parts: the north, the centre, and the south. The country is in an S-shape with the approximated length is 1.700 km. For the feasibility of the study, data was collected in the North and the Centre. These two areas are selected because, since last decade, they demonstrated significant higher prevalence of lung cancer than the South (Ngoan le, Mizoue, & Yoshimura, 2002; Ngoan et al., 2001).

In the north and the centre, there are 5 national oncology centers and other 5 center/hospitals at provincial level offering treatments for cancer patients (National project on prevention and control of cancer from 2008 to 2010, 2008). Among them, two are in the centre and eight are in the north. Application packages were sent to all of those hospitals. Permissions from six hospitals were granted and data was collected from all those institutions. Among these six hospitals, one is in the centre (Nghe An

Oncology Hospital) and five are in the north (Bach Mai hospital, 103 Military Centre Hospital, 108 Hospital, National Lung Hospital, Thai Nguyen Centre Hospital).

This study was conducted from 5/2014 to 7/2015:

- 5/2014: Dissertation proposal approval
- 5/2014 – 8/2014: Instrument translation and content validity checking
- 8/2014 – 10/2014: IRB approval
- 11/2014: Research assistant training
- 12/2014 – 3/2015: Data collection
- 3/2015 – 7/2015: Data analysis and final report

Population and sample

Population

Subjects of this study were Vietnamese lung cancer patients who are receiving chemotherapy.

Sample

Selection Criteria: Participants were recruited in accordance to inclusion criteria, which are: 1) diagnosed with primary lung cancer, 2) are able to read and verbally communicate in Vietnamese, 3) hospitalized for chemotherapy treatment, and 4) have completed at least one cycle of the chemotherapy course. Exclusion criteria was 1) having prior lung resection surgery.

Sampling Technique: Participants was selected using convenience sampling method (Thompson, 1992). All patients who met the selection criteria and available at the time the data collection taken place were recruited in the study.

To recruit participants, under the permission of hospital's authorities,

researchers requested the Information Office of each hospital to provide the name list, contact number, and basic information (against the selection criteria) of all lung cancer patients who were receiving chemotherapy in that hospital. At inpatients units of each hospital, the researcher approach eligible participants and invited them to participate in the study. During the communication, patients, who belonged to minor Vietnamese group and could not communicate in Vietnamese, were excluded.

Sample Size: A common rule of thumb to calculate sample size for a study with Structural Equation Modeling is the so called N:q rule (Jackson, 2003). N is the number of needed subjects per one parameter (q). In general, the proportion is commonly set as 10:1. The ratio lower than 10:1 would lessen the credibility of the findings (Byrne, 2010; R. B. Kline, 2011). Therefore, this study used the ratio of 10:1.

Sample size for the pilot study: Before the main data collection taken place, a pilot study was conducted to examine the psychometric properties of instruments. CFA was employed to evaluate the construct validity of measurements. Hence sample size of the pilot study was estimated to satisfy the use of CFA. The suggested number of subjects per one item of the instrument varies from 2 (P. Kline, 1998) to from 5 to10 (DeVellis, 2012). Among questionnaires, FACT-F is the longest one (13 items). Using the ratio of 10:1, at least 130 respondents were needed for the pilot study. The final sample of the pilot study consisted of 136 patients who met the same criteria as in the main study.

Sample size of the main study: The hypothesized model of this study consisted of 22 parameters. Therefore, at least 220 subjects should be recruited. To compensate the potential missing data, 10% more was added to the sample size. Finally, 246 patients were obtained in the study.

Instrument translation and psychometric testing

Instruments (MCLCS, DASS-21 Anxiety Subscale, CDS, and ISI) were translated from English to Vietnamese by back-translation technique (Maneesriwongul & Dixon, 2004). In the translation process, firstly, two bilingual Vietnamese (one is a nurse and one is an English teacher) translated instruments from English to Vietnamese. In the second step, two other bilingual Vietnamese two English teachers) translated the instruments back to English. A British teacher who was teaching English for Vietnamese undergraduate students was then consulted about the semantic equivalence between English original and translated instruments. Comments were sent back to the translators for modification. The process was run until the semantic equivalence between back and original questionnaires was assured. The FACT-F has already been translated into Vietnamese by its copyright holder following their standardized procedure. Therefore, this instrument was used for validation step without any prior translation or modification. Psychometric properties of all instruments were examined in a pilot study. Content validity was judged by five Vietnamese experts. The acceptable level of item and total CVI is 0.8. Construct validity was validated by confirmatory factor analysis (CFA). With regard to reliability, Cronbach's alpha coefficients were used.

Pilot study

The pilot study was conducted in December 2014 to examine psychometric properties of instruments. Three among six hospitals of the main study (Thai Nguyen Centre Hospital, National Lung Hospital, and Bach Mai Hospital) were selected for the pilot study. To examine construct validity of instrument by CFA, at least 130

participants were needed for the pilot study. Participants were recruited using the same selection criteria and were excluded thereafter from the sample frame of the main study. The final sample of the pilot study consisted of 136 patients. The mean age of the piloted sample was 60.31 ± 6.6 years (range: 45 – 74 years) with the majority was female (72.1%). The main duration of being diagnosed with lung cancer was 4.9 ± 1.7 months (range: 1 – 11 months).

Figure 3 Number of subjects by hospitals

	BMH	**TNCH**	**NLH**	**NAH**	**103MH**	**108MH**	**Total**
Pilot study	40	34	62	0	0	0	136
Main study	40	20	52	98	21	15	246
Total	80	54	114	98	21	15	

BMH: Bach Mai Hospital TNCH: Thai Nguyen Centre Hospital

NLH: National Lung Hospital NAH: Nghe An Oncology Hospital

103MH: 103 Military Hospital 108MH: 108 Military Hospital

Measurements

Measurement of Fatigue

The Functional Assessment of Cancer Therapy-Fatigue subscale (FACT-F) (Yellen et al., 1997) was used to measure fatigue in this study.

Description: The FACT-F consists of 13 items measuring intensity of fatigue. The time frame assessed is previous 7 days. Each item is rated on a 5-point Likert scale, ranging from 0 (not at all) to 4 (very much so). The scale has been translated into Japanese and Brazilian and the translations also demonstrate good

psychometric properties in the target languages.

Psychometric Properties: According to its authors, the Cronbach's alpha of the FACT-F ranged from 0.93 to 0.95 (Yellen et al., 1997). In other study, the internal-consistency coefficient calculated from 470 cancer patients was of 0.94. The coefficient between items and the total score varied from 0.52 to 0.82 (Van Belle et al., 2005). It also demonstrates a good test–retest reliability with the coefficient of 0.90 (3-7 day interval) (Yellen et al., 1997).

Data indicated that Fatigue subscale FACT-F has strong association with POMS Fatigue (r = - 0.83), Piper Fatigue Scales (r = - 0.77), and with POMS vigor (r = 0.61) (Yellen et al., 1997). The scale also could discriminate the level of Performance Status assessed by ECOG performance status. It also showed strong association (r = 0.76) with measurement of quality of life (SF-36) (Ishikawa et al., 2010).

In the current study, the content validity index (CVI) of the whole scale was 0.98 with item-CVI ranging from 0.8 to 1.0. The Cronbach's alpha coefficient of FACT-F was 0.93 in a pilot and 0.94 in main study. CFA analysis found that 13 items formed a single factor ($\chi^2 = 62.22$, $p > 0.05$, df = 56, $\chi^2/df = 1.1$, CFI = 0.99, GFI = 0.93, AGFI = 0.89, RMSEA = 0.029, SRMR = 0.04). Standardized regression weights of items ranged from 0.36 (item 8) to 0.94 (item 3), most of items had loadings more than 0.7.

Scoring and interpretation: The total score is the sum of individual score of 13 items. The possible scores range from 0 to 52. To interpret the level of fatigue, this study categorized total fatigue score into four levels:

Total FACT-F core	Interpretation
0	No fatigue
1 – 17	Mild fatigue
18 – 35	Moderate fatigue
36 – 52	Severe fatigue

Measurement of Insomnia

The Insomnia Severity Index (ISI) (Morin, 2003) was used to measure insomnia in this study.

Description: ISI consists of 7 items, divided into two subscales, measuring the severity of sleep difficulties and the impact of sleep difficulties. Patients answer the questions by rating on the 5-point scale (0-4).

Psychometric Properties: ISI has been widely tested in various populations (Morin, 2003). M. H. Savard et al. (2005) conducted a large-scale study to validate ISI in cancer (n = 1670). For reliability, overall Cronbach's alpha was of 0.90 and item total correlations ranging from 0.65 to 0.78 depended on the tested cancer group. Baseline score and scores measured at 1 month, 2 month, and 3 month afterward were associated with the coefficients of 0.83, 0.77, and 0.73 ($p < 0.05$).

Factors analysis confirmed that ISI consists of two factors (severity of sleep difficulties and the impact of sleep difficulties or insomnia interference). For convergent validity, the ISI showed associations with quality of life (M. H. Savard et al., 2005), sleep onset latency, time in bed, early morning awakening, and sleep efficiency (assessed by dairy) (Bastien, Vallieres, & Morin, 2001).

In the current study, the CVI of ISI was 1.0. Cronbach's alpha coefficient

of whole ISI was 0.94 in the pilot and 0.90 main study. The reliability coefficients of insomnia severity subscale were 0.91 (pilot study) and 0.89 (main study) and those of the insomnia interference were 0.91 and 0.88, respectively. In pilot study, CFA analysis found that 7 items of ISI formed two factors ($\chi^2 = 12.33$, $p > 0.05$, $df = 13$, $\chi^2/df = 0.95$, CFI = 1.00, GFI = 0.98, AGFI = 0.95, RMSEA = 0.00, SRMR = 0.02). Factor loadings of items of the first dimension (insomnia severity) ranged from 0.826 to 0.863, and of the second dimension (insomnia interference) was 0.799 to 0.903.

Scoring and interpretation: The total score is calculated by summing the seven items. Possible scores range from 0 to 28. A higher score indicates a greater insomnia severity. According to Bastien et al. (2001) the total ISI score can be categorized into four levels:

Total ISI core	**Interpretation**
0 – 7	No clinically significant insomnia
8 – 14	Sub-threshold insomnia
15 – 21	Moderate insomnia
22 – 28	Severe insomnia

Measurement of Cough:

The Manchester Cough in Lung Cancer Scale (MCLCS) (Molassiotis et al., 2012) was used to measure cough in this study.

Description: The MCLCS was developed for lung cancer population. This 10-item, unidimensional scale measures patients experience with cough in terms of its frequency, intensity, and bothersomeness.

Psychometric Properties: For reliability, the Cronbach's alpha was 0.86. Items also showed high item to total correlations, ranging from 0.40 to 0.76 ($P < 0.001$).

The test-retest (after a week) reliability was examined by Spearman's rho correlation coefficient (0.76, P < 0.001). The Intra-Class Coefficient of average measure was 0.83 (95% confidence interval 0.74 - 0.90).

Face validity of the scale was validated by 18 patients and 25 healthcare professionals. The Principal Components Analysis showed all items clustered around a single factor, suggesting a unidimensional scale (Molassiotis et al., 2012). The correlation between MCLCS and the VAS for cough in lung cancer patients on treatment were 0.66 - 0.68 (Burnham, Buffin, Blackhall, Smith, & Harle, 2013).

In the current study, the CVI of the MCLCS was 0.96 with the item-CVI ranged from 0.8 to 1.0. Cronbach's alpha coefficient of MCLCS was 0.91 in pilot and 0.89 in main study. In the pilot study, CFA analysis found that 10 items formed a single factor ($\chi^2 = 34.55$, $p > 0.05$, $df = 31$, $\chi^2/df = 1.11$, CFI = 0.99, GFI = 0.95, AGFI = 0.91, RMSEA = 0.029, SRMR = 0.03). Standardized regression weights of items ranged from 0.42 (item 8) to 0.86 (item 10).

Scoring and interpretation: The score of item 8 is reversed before calculating the total score. The total score is the sum-score of all 10 items. Possible range is 1 to 50. One indicates no cough and higher score indicates more severe cough. To interpret the level of cough, this study categorized MLCLCS score into four levels:

Total MLCLCS core	**Interpretation**
1	No cough
2 – 17	Mild cough
18 – 34	Moderate cough
35 – 50	Severe cough

Measurement of Physical Activity

The International Physical Activity Questionnaire-Short Form (Lovibond & Lovibond, 1995) was used to measured physical activity in this study.

IPAQ-SF is a self-reported questionnaire that records duration of different levels of physical activity. It consists of 8 items. The questionnaire is structured to capture physical activity in 4 generic dimensions of physical activity, namely vigorous, moderate, walking and sitting.

Psychometric Properties: The test-retest reliability after one week ranged from 0.32 to 0.88 (Craig et al., 2003). In Vietnamese population, test retest reliability of IPAQ-SF was evaluated by three consecutive assessments (day 1, day 9, and day 12). Results showed good reliability of IPAQ-SF with all ICC (for moderate, high, and low level) > 0.80 ($P < 0.05$) (D. V. Tran et al., 2013).

For validity, the IPAQ-SF showed a significant association with accelerometer ($N = 781$, $\rho = 0.30$, 95% CI 0.23– 0.36) (Craig et al., 2003). In validation study of IPAQ-SF in Vietnamese, patients' physical activity was measured by IPAQ-SF and also recorded in seven days by the PA log - book. The correlation coefficient between IPAQ-SF with PA log was 0.46, suggesting acceptable criterion validity of the instrument. (D. V. Tran et al., 2013)

Scoring and interpretation:

Scores are computed into MET-minutes/week.

- Walking MET-minutes/week = 3.3 * walking minutes * walking days
- Moderate MET-minutes/week = 4.0 * moderate-intensity activity minutes * moderate days
- Vigorous MET-minutes/week = 8.0 * vigorous-intensity activity minutes *

vigorous-intensity days

- Total physical activity MET-minutes/week = sum of Walking + Moderate + Vigorous METminutes/week scores.

The total MET-minutes/week can be used as a continuous variable representing physical activity. According to IPAQs guideline, participants can also be classified into three categories: low, moderate, and high level of PA.

Category 1 Low:

Those individuals who not meet criteria for categories 2 or 3 are considered to have a ‘low’ physical activity level.

Category 2 Moderate:

The pattern of activity to be classified as ‘moderate’ is either of the following criteria:

a) 3 or more days of vigorous-intensity activity of at least 20 minutes per day

OR

b) 5 or more days of moderate-intensity activity and/or walking of at least 30 minutes per day

OR

c) 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum Total physical activity of at least 600 MET-minutes/week.

Individuals meeting at least one of the above criteria would be defined as accumulating a minimum level of activity and therefore be classified as ‘moderate’.

Category 3 High

A separate category labeled ‘high’ can be computed to describe higher levels of

participation.

The two criteria for classification as ‘high’ are:

a) vigorous-intensity activity on at least 3 days achieving a minimum Total physical activity of at least 1500 MET-minutes/week

OR

b) 7 or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a minimum Total physical activity of at least 3000 MET-minutes/week.

Measurement of Dyspnea

The Cancer Dyspnea Scale (CDC) (Tanaka et al., 2000) was used to measure dyspnea in this study.

Description: The CDS consists of 12-items, divided in to three subscales, which are ‘sense of effort’ (physical dyspnea or dysfunction of ventilation with organic cause(s) worsened on exertion) ‘sense of anxiety’ (affected or amplified by psychological status), and ‘sense of discomfort’ (unpleasant and unrelaxed feeling at rest as well). Patients respond by rating in the 5-point scale from “not at all” (1) to “very much” (5). The scale takes about 2 minutes to complete (Tanaka et al., 2000).

Psychometric Properties: Factor analysis has confirmed CDS three subscales. The mean value of inter-subscale correlation coefficients was 0.48. Cronbach’s alpha of total scale was 0.86 and of subscales were 0.83 (sense of effort), 0.81 (sense of anxiety), and 0.94 (sense of discomfort). Test–retest coefficients (7-day interval) between sense of efforts, sense of anxiety, and sense of discomfort and the total score were 0.71, 0.69, and 0.58, respectively (Tanaka et al., 2000).

In lung cancer, the Cronbach's alpha of sense of effort, sense of anxiety, and sense of discomfort subscales were 0.84, 0.08, and 0.84, respectively. The CDS also significantly related to VAS (r = 0.82), Borg's scale (r = 0.87), HADS (r = 0.57), physical status (r = 0.44), SpO2 (r = 0.29) (Uronis et al., 2012).

In the current study, the scale CVI of CDS was 1.0. The Cronbach's alpha coefficient of CDS was 0.83 in pilot and 0.86 in main study. With regards to subscale, the coefficients of the sense of effort subscale were 0.71 (pilot study) and 0.86 (main study), of the sense of anxiety subscale were 0.74 (pilot study) and 0.74 (main study), and of the sense of discomfort were 0.81 (pilot study) and 0.70 (main study) In the pilot study, CFA analysis found that 12 items formed 3 factors ($\chi^2 = 47.54$, $p > 0.05$, df = 48, $\chi^2/df = 0.99$, CFI = 1, GFI = 0.94, AGFI = 0.91, RMSEA = 0.00, SRMR = 0.05). Factor loadings of items of three factors ranged from 0.51 – 0.80 (sense of discomfort), 0.47 – 0.67 (sense of anxiety), and 0.66 – 0.78 (sense of effort).

Scoring and interpretation: Score for sense of effort subscale is calculated by the formula (items 4 + 6 + 8 + 10 + 12) – 5, producing the possible range from 0 to 20. Score for sense of anxiety is obtained by formula (items 5 + 7 + 9 + 11) – 4, producing the possible range from 0 to 16. And the formula for sense of discomfort subscale is 15 – (items 1 + 2 + 3), producing the possible range from 0 to12. The total dyspnea score is the sum of three subscale's scores. Higher score indicates higher level of dyspnea. The reason to compute subscale and total item scale as guided is to produce the score of 0, which represents "no dyspnea" (Tanaka et al., 2000). The scoring as guided by Tanaka et al (2000) is convenient because it does not require the recode of item 1, 2, and 3, which are negatively coded items. However, since those items are negative coding, their scores require conversion before conducting CFA to prevent

negative association among items and among factor score. Nevertheless, the inversion of the score makes the formula to calculate the sense of discomfort subscale's score not appropriate. For such reason, the current study use the same patterns as used by Tanaka et al. (2000) to sum the score of sense of effort and sense of anxiety subscale to calculate score of sense of discomfort subscale. In particular, the score is calculated by the formula: (items 1 + 2 + 3) – 3. This calculation also produces the total score ranging from 0 to 40.

To interpret the level of dyspnea, the total CDS score was categorized into four levels:

Total MLCLCS core	Interpretation
0	No dyspnea
1 – 13	Mild dyspnea
14 – 27	Moderate dyspnea
28 – 40	Severe dyspnea

Measurement of Anxiety

The Anxiety subscale of the Depression Anxiety Stress Scale – 21 was used in the current study to measure anxiety.

Description*:* The Anxiety subscale is one of three subscales of the Depression Anxiety Stress Scales 21 (DASS-21) (Lovibond & Lovibond, 1995). The DASS - 21 is the measurement assessing Depression, Anxiety, and Stress. The Anxiety subscale consisted of 7 items. The items assess symptoms of autonomic arousal, skeletal musculature effects, situational anxiety and subjective experience of anxious affect. It is a self-report questionnaire, in which participants rate the frequency or

severity of experiencing such symptoms over the previous week. Frequency/severity ratings are made on a series of 4-point scales (0 = did not apply to me at all, 3 = applied to me very much, or most of the time) (Norton, 2007).

Psychometric Properties: Henry and Crawford (2005) validated the DASS-21 in a sample of 1,794 general adult UK population. Cronbach's alpha of the anxiety subscale was found to be 0.82. The internal consistency coefficients were found to be from 0.78 to 0.81 (Norton, 2007) or 0.79 (Szabó, 2010) in other studies.

The construct validity of the Anxiety subscale of DASS-21 was widely confirmed in various studies. It was reported that sevens item of the Anxiety subscale formed a single factor (Henry & Crawford, 2005; Norton, 2007; Szabó, 2010).

T. D. Tran et al. (2013) conducted a study to validate the DASS-21 in Vietnamese. The cronbach's alpha of the DASS 21 – Anxiety subscale was found to be 0.77. Exploratory Factor Analysis was performed to test the construct validity of the instrument. 21 items of the DASS 21 constitute 3 factors. Seven items of the Anxiety subscale fit to one single factor, suggesting that they form an independent subscale. The loading factors of items ranged from 0.46 to 0.7. Correlation coefficients between DASS21-D and DASS21-A were 0.65, and DASS21-S and DASS21-A was 0.72. In comparison to the women without depression and anxiety, the patients with depression and anxiety (assessed by the Structured Clinical Interviews for DSM IV Axis 1 Diagnoses (SCID) modules for depression (mild, moderate, and severe Major Depression or Dysthymia) and anxiety (Generalised Anxiety Disorder and Panic Disorder) showed higher score in Anxiety subscale of DASS-21, suggestion the discriminant validity of the instrument.

In the current study, the total CVI of the Anxiety Subscale DASS-21 was

0.97 and item-CVI ranged from 0.8 to 1.0. The Cronbach's alpha coefficient of DASS-21 Anxiety was 0.78 in pilot and 0.77 in main study. In the pilot study, CFA analysis found that 7 items formed a single factor (χ^2 = 13.71, p > 0.05, df = 11, χ^2/df = 1.25, CFI = 0.99, GFI = 0.97, AGFI = 0.93, RMSEA = 0.04, SRMR = 0.04). Standardized regression weights ranged from 0.35 to 0.78.

Scoring and interpretation: The anxiety score is obtained by summing score of all seven items, ranging from 0 to 21. Higher score indicates more intense fatigue. For the convenient interpretation of score, the total DASS-21 anxiety score was categorized into four levels:

Total DASS-21 Anxiety core	Interpretation
0	No anxiety
1 – 7	Mild anxiety
8 – 14	Moderate anxiety
15 – 21	Severe anxiety

Measurement of Nutritional Status

The Nutritional Risk Index (NRI) (Prendergast et al., 1989) was used to measure nutritional status.

Description: The NRI was originally developed and tested in postoperative population, including ones with lung cancer (The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group, 1991). It has been used as an index of malnutrition, which combines albumin with weight in a single formula. NRI is calculated as follows: NRI = (1.519 x serum albumin concentrations, g/L) + 41.7 x (present weight/usual weight x 100).

The usual weight is defined as the weight during 6 months or more before admission. The present weight is determined by objective measurement (Andreoli, De Lorenzo, Cadeddu, Iacopino, & Grande, 2011). In this study, patient's current weight is measured by weighing scales in the day that patient was interviewed. Usual weight is obtained by asking the patient about her weight during six months before admission. Serum albumin reported in the most current blood test (no longer than 2 weeks before the data collection day) was collected from patients' medical records.

Psychometric Properties: Test-retest coefficient of NRI ranged from 0.74 to 0.82. The index showed significant associations with Kcal intake, dietary protein intake, BMI, and hemoglobin (Prendergast et al., 1989). NRI is also relevant to the results of other nutritional measurements such as Generated Subjective Global Assessment, Malnutrition Universal Screening Tool, or Nutritional Risk Screening 2002 (Poulia et al., 2012). Testing in colorectal cancer, with PG-SGA as the reference, the sensitivity of NRI was found to be 95.2% (Tu, Chien, & Chou, 2012).

Scoring and interpretation: NRI score is calculated by the above formula. Patients are categorized according to their NRI score into four levels

NRI core	**Interpretation**
> 100	Well nourished
97.5 - 100	Mildly malnourished
83.5 - 97.5	Moderately malnourished
< 83.5	Severely malnourished

Stage of Disease: stage of disease in this study was determined based on physician diagnosis, and is classified into four stages: I, II, III, and IV. Information

toward stage of disease was obtained in patients' medical records.

Protection of human subjects

This study was conducted with the approval of the IRB of the Hanoi School Public Health (IORG0003239), decision number 282/2014/YTCC-HD3. Informed consent was obtained before the data collection taken places. Patients had all rights to refuse participation in the study at any time or not to answer any questions without explanation. No invasive procedures were conducted. No potential physical and psychological harms to the patients were identified.

Data collection

Data was collected by the principal researcher and three research assistants from 12/2014 to 3/2015. The research assistants were nurse educators at the Division of Nursing, Faculty of Health Sciences, Thang Long University, Ha Noi, Vietnam.

Before the data collection took place, three research assistants were trained about the objectives, design, instruments, ethical issues and data collection steps of the current study. They were required to attend two data collection sessions, which conducted by only the principal researcher, before fully involving in the process. The responsibilities of research assistants were a) support the principal researcher in preparing data collection packages, b) contact with the patients to make appointment for data collection, c) facilitate the principal researcher while he working with patients, deliver consent form, questionnaires, pen to the respondents, d) collect questionnaires from the patients and re-check them to make sure no items were left blank before terminating the interview.

Before the data collection taken place in certain hospital, the researcher obtained list of all lung cancer patients who were currently receiving chemotherapy in that hospital. The list was then screened to select patients who preliminarily met selection criteria.

Based on the chemotherapy schedules of each patient, the researcher knew the exact day that they would receive the next cycle. The researcher/research assistant contacted the patient, set the appointment with him/her to collect data.

In the day of data collection, the researcher and a research assistant went to patients' room and invited potential subjects to participate in the study. If the patient agreed, the consent form would then be obtained.

Questionnaires and pen were then delivered to patients. The researcher explained how to answer the instruments and allowed patients to have enough time to respond to questionnaires. The researcher was available around the participant to offer explanation or clarification of the instruments if needed.

After the respondent finished all questionnaires, the investigator checked all pages to scan for missing data. After checking, the investigator verbally thanked to the respondent and terminated the data collection procedure for that patient.

Data analysis

SPSS Statistics version 20 and SPSS AMOS version 20 were used for analyzing data in this study. Descriptive statistics were used to describe characteristics of the sample and variables of interests. Measurement models of each latent variable were examined by confirmatory factor analysis. Structural Equation Modeling was employed to evaluate the directional and in-directional associations among variables. The

goodness of fit statistics were used to examine how well the hypothesized model fits the data. The current study used Maximum Likelihood (ML) as the estimation method (Stevens, 2009).

With regard to fit indices, Meyers, Gams, and Guarino (2006) asserted that at least three indices should be used to evaluate the fit of the model: one is absolute, one is relative and one is parsimonious index. According to Hair, Black, Babin, and Anderson (2009) the reported of Chi-square and the degree of freedom, the CFI or TLI, and the RMSEA will usually provide sufficient unique information to evaluate the model. Vieira (2011) recommended the use of chi-square test, normed chi - square test, RMSEA, GFI, AGFI, and NNFI, and CFI. Based on previous recommendations, the current study employed Chi-square, normed Chi-square, GFI, AGFI, CFI and RMSEA to examine the goodness-of-fit of the data.

Table 1 Fit indices and cut-off points

Fit Indices	**Cut-offs**
$\chi 2$	$p > 0.05$
$\chi 2/df$	< 2
CFI	> 0.9
GFI	> 0.9
AGFI	> 0.9
RMSEA	< 0.08

To conclude whether an indirect effect is significant or not, the estimation of its confidence interval and p-value is necessary. This study used bootstrapping with the bias-corrected method to estimate the interval confidence of indirect effect. According

to G. W. Cheung and Lau (2008), the number of samples was commonly set up 500 to 1000. In the current study, the number of bootstrapped samples was set at 500.

CHAPTER IV
RESULTS

The current study aims to examine the model explaining causal associations among stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, dyspnea, and fatigue. This chapter presents the main findings of the study. Results will be outlined into four parts, which are 1) the characteristics of the sample, 2) descriptive statistics of the studied variables, 3) measurement models of latent variables and, lastly 4) full structural regression model.

Description of sample characteristics and studied variables

As showed in the table 2, the sample was aged at late adult (mean age = 60.79 ± 6.59). The majority (72.8%) of the sample was male. Approximately one-third of the sample finished their college/bachelor (26.8%) and postgraduate studies (6.5%). Patients with high school degree accounted for the biggest prevalence (34.6%).

Table 2 Demographic characteristics of the sample (n = 246)

	Min - max	**Mean ± SD**	**n (%)**
Age	47 - 79	60.79 ±6.59	
≤ 55			44 *(17.9)*
56 - 60			81 *(32.9)*
61 – 65			69 *(28)*
66 - 70			30 *(12.2)*
≥ 71			22 *(8.9)*

	Min - max	Mean ± SD	n (%)
Gender			
Female			67 *(27.2)*
Male			179 *(72.8)*
Education level			
Primary			40 *(16.3)*
Secondary			39 *(15.9)*
High School			85 *(34.6)*
College/Bachelor			66 *(26.8)*
Postgraduate			16 *(6.5)*
Working condition			
Working			110 *(44.7)*
Not Working			136 *(55.3)*
Time from diagnosis with lung CA (month)	1 - 26	5.44 ±3.97	
Height (cm)	145 - 190	163.05 ±6.96	
Albumin (g/DL)	26.5 - 52.1	39.03 ±5.49	
Current Weight (kg)	36 - 85	54.5 ±7.86	
Usual Weight (kg)	38 - 85	56.9 ±8.35	

Notably, more than half of the sample was not working (55.3%) at the time the data collection taken place. The duration of being diagnosed with lung cancer among the sample varied from 1 to 26 months. The mean of such duration was 5.44 ± 3.97 months. The average serum albumin concentration was 39.03 ± 5.49 g/DL, with the range from 26.5 to 52.1 (g/DL). The ranges of current weight and usual weight among the participants were quite similar, which were 36-85 and 35-85, respectively. The mean of usual weight (56.8 ± 8.35) was mildly higher than current weight (54.5 ± 7.86).

As can be seen in the table 3, patients experienced fatigue with a wide range (0-49). The mean score of fatigue was 27.69 ± 11.12. With regard to stage of disease, the most prevalent group was stage III (37.8%), followed by stage IV (35%). Patients with stage I accounted for a smallest proportion of the sample (8.5%). The mean of nutrition risk index was quite high (99.33 ± 9.11), and nearly half (49.2%) of the sample was classified as well-nourished. Remarkably, there were 5.7% of patients were severely malnourished. The proportions of patients with moderate and mild malnutrition were 32.5% and 12.6%, respectively.

The mean of MET-minutes/week of the sample was 1424.9 ± 1278.83. Nearly one-third of participants was categorized as low physically active. The prevalence of high and moderate physical activity levels was quite similar, which were 36.1% and 35.4% respectively.

Participants showed a high level of insomnia, with the mean total score of 13.46 ± 5.73. The range of score was quite wide, from 0 to 27. Using the cut-off point of 8 to categorized case and non-case, most of patients (84.5%) had significant insomnia. The majority of sample was classified as moderate insomnia (43.1%). Anxiety score was not too high, with the mean of 6.26 ± 3.7 and the range of 0 – 15. While most of patients had mild anxiety (64.7%), only 4 (1.6%) was categorized with severe anxiety. It could be noted that all of patients have some degree of cough (table 3), with the score ranged from 11 to 42. The mean score of cough was 23.89 ± 7.9. Most patients had moderate cough (67.5%), followed by mild cough (22%). With regard to dyspnea, the mean of total score was 11.97 ± 6.93, and the score ranged from 0 to 29. Interestingly, nearly 98% of patients had mild or moderate dyspnea.

Table 3 Description of studied variables (n=246)

	Min - max	Mean ± SD	n *(%)*
Fatigue (possible score: 0 – 52)	0 - 49	27.69 ±11.12	
No fatigue			1 *(0.4)*
Mild fatigue			43 *(17.5)*
Moderate fatigue			140 *(56.9)*
Severe fatigue			62 *(25.2)*
Stage of disease			
I			21 *(8.5)*
II			46 *(18.7)*
III			93 *(37.8)*
IV			86 *(35.0)*
Number of Chemotherapy Cycles completed	1 - 8	2.55 ±1.42	
Nutritional Risk Index	76.8 - 119.17	99.33 ±9.11	
Nutritional Status Classification			
Severely-malnourished			14 *(5.7)*
Moderately-malnourished			80 *(32.5)*
Mildly-malnourished			31 *(12.6)*
Well-nourished			121 *(49.2)*
Physical Activity (PA)			
Total MET-minutes/week	0 - 4800	1424.90 ± 1279.83	
Low PA level			70 *(28.5)*
Moderate PA level			87 *(35.4)*
High PA level			89 *(36.1)*
Insomnia (possible score: 0 - 28)	0 - 27	13.46 ± 5.73	
No clinically significant insomnia			38 *(15.4)*
Sub-threshold insomnia			90 *(36.6)*
Moderate insomnia			106 *(43.1)*
Severe insomnia			12 *(4.9)*

	Min - max	Mean ± SD	n *(%)*
Insomnia Interference	0 - 12	4.94 ± 2.91	
Insomnia Severity	0 - 16	8.52 ± 3.44	
Anxiety (possible score: 0 – 21)	0 - 15	6.26 ± 3.7	
No anxiety			7 *(2.8)*
Mild anxiety			159 *(64.7)*
Moderate anxiety			76 *(30.9)*
Severe anxiety			4 *(1.6)*
Cough (possible score: 1 - 50)	11 - 42	23.89 ± 7.9	
Mild cough			54 *(22)*
Moderate cough			166 *(67.5)*
Severe cough			26 *(10.5)*
Dyspnea (possible score: 0 - 40)	0 - 29	11.97 ± 6.93	
No dyspnea			1 *(0.4)*
Mild dyspnea			139 *(56.5)*
Moderate dyspnea			100 *(40.7)*
Severe dyspnea			6 *(2.4)*
Dyspnea Effort	0 - 13	5.01 ± 3.11	
Dyspnea Anxiety	0 - 13	3.39 ± 2.59	
Dyspnea Discomfort	0 – 10	3.58 ± 2.73	

Structural Equation Modeling assumption testing

Normality

Univariate normality

Skewness and kurtosis values are important indicators of normal distribution. According to West, Finch, and Curran (1995), the skewness and kurtosis values of 3 and 21, respectively, represent a highly non-normality. The skewness value of 2 and kurtosis value of 7 indicate a moderate departure from normal distribution.

Table 4 Skewness and Kurtosis values of studied variables (n = 246)

Variable	Skewness	Critical value	Kurtosis	Critical value
Fatigue	-.306	-1.962	-.341	-1.091
Cough	.169	1.084	-.625	-2.000
Anxiety	.541	3.466	-.423	-1.353
Insomnia severity	-.452	-2.896	.013	.043
Insomnia interference	.127	.813	-.743	-2.378
Dyspnea Discomfort	.300	1.921	-.801	-2.565
Dyspnea Anxiety	.798	5.108	.508	1.627
Dyspnea Effort	.392	2.511	-.627	-2.007
Nutrition Status	-.107	-.683	-.318	-1.017
Stage of Disease	-.606	-3.883	-.554	-1.772
Physical Activity	.870	5.569	-.035	-.113
Number of completed cycles	.976	6.252	.678	2.171
Multivariate			**7.511**	**3.213**

In the current study, the skewness values of variables range from -0.606 to 0.976. The kurtosis values are varied from -0.801 to 0.678 (Table 4). These values demonstrate that data does not remarkably depart from normal distribution. Importantly, it is evidence that the Maximum Likelihood still works well as long as measured variables were not severely non-normal (the skewness exceeds 2 and the kurtosis exceeds 7) (Stevens, 2009). It could be concluded that there is efficient evidence about the reasonable satisfaction of the univariate normality assumption.

Multivariate normality

Multivariate normality assumption requires that observations among all combinations of variables are normally distributed (Meyers et al., 2006). The

multivariate normality can be detected by the Mardia's test (R. B. Kline, 2011). The test estimates multivariate kurtosis and its critical ratio (C.R) – the most important factor to evaluate multinormality .The value of Kurtosis C.R is higher than 5 represents a non-normal distribution of variables (Byrne, 2010). In the current study, Mardia's test was run in AMOS to examine multivariate kurtosis and its critical ratio. As shown in table 4, Kurtosis value was 7.511 and C.R was 3.513. Thus, it could be concluded that the assumption of multivariate normality was not violated.

Multicollinearity

Multicollinearity refers to the interrelatedness of the independence variables. It is believed that the high correlations among variables would make the evaluation of statistical results problematic (Munro, 2005). According to R. B. Kline (2011), three common ways can be used to examined multicollinearity among variables. First, calculate a squared multiple correlation between each variable and all the rest. The observation that R-square > .90 for a particular variable analyzed as the criterion suggests extreme multivariate collinearity. Second, tolerance statistic (indicates the proportion of total standardized variance that is not explained by all the other variables) can be calculated by the formula $1 - R^{2.}$ Tolerance values < .10 may indicate extreme multivariate collinearity. Lastly, the variance inflation factor (VIF) (formula: $1/(1 - R^2)$). The VIF exceed 10 indicates multivariate collinearity (Meyers et al., 2006). Munro (2005) also suggested that the high correlations (> 0.85) among variables imply multicollinearity. In the current study, correlation coefficients, tolerance and VIF were used to examine multivariate collinearity.

It was showed that correlation coefficients among variables ranged from -0.218 to 0.421 (Table 6). None of them exceeded the value of 0.85. The tolerance of variables

ranged from 0.552 to 0.975, which were very close to 1.0. Additionally, the VIF varied from 1.025 to 1.810, which were much less than 10 (Table 5). Therefore, it could be concluded that there was no evidence toward multivariate collinearity found.

Table 5 Collinearity statistics

Variables	**Collinearity Statistics**	
	Tolerance	**VIF**
Anxiety	.866	1.154
Cough	.851	1.175
Dyspnea Effort	.585	1.711
Dyspnea Anxiety	.553	1.807
Dyspnea Discomfort	.655	1.527
Insomnia Interference	.552	1.810
Insomnia Severity	.597	1.674
Physical Activity	.924	1.082
Nutrition Status	.975	1.025
Number of completed cycles	.937	1.068
Stage of Disease	.915	1.093

Table 6 Correlations among variables (n = 246)

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Stage of Disease (1)	1								
Number of completed Cycles (2)	.175**	1							
Nutrition Status (3)	-.048	-.043	1						
Physical Activity (4)	-.170**	.028	.034	1					
Insomnia (5)	.131*	.143*	-.114	-.018	1				
Anxiety (6)	.077	.111	-.009	.018	.198**	1			
Cough (7)	.056	.125	.005	.079	.247**	.075	1		
Dyspnea (8)	.083	.106	-.082	.055	.269**	.186**	.325**	1	
Fatigue (9)	.262**	.224**	-.218**	-.154*	.460**	.261**	.329**	.400**	1

**. Correlation is significant at the 0.01 level (2-tailed); *. Correlation is significant at the 0.05 level (2-tailed).

Table 7 Covariance among variables (n = 246)

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
SD (1)	.882	.233	-.410	-203.948	.286	.420	.267	.419	.180	.240	.123	2.740
NC (2)	.233	2.011	-.555	50.712	.566	.595	.584	1.408	.453	.390	.198	3.531
NS (3)	-.410	-.555	83.020	400.046	-2.622	-3.356	-.296	.329	-2.429	-1.603	-1.170	-22.140
PA (4)	-203.948	50.712	400.046	1637974.286	-161.217	27.087	84.375	804.871	-83.787	68.946	501.484	-2189.853
IS (5)	.286	.566	-2.622	-161.217	11.842	6.275	2.159	5.282	1.934	1.940	1.031	15.706
II (6)	.420	.595	-3.356	27.087	6.275	8.478	2.040	5.981	2.503	1.871	1.404	13.635
An (7)	.267	.584	-.296	84.375	2.159	2.040	13.714	2.195	2.177	2.649	-.043	10.768
Co (8)	.419	1.408	.329	804.871	5.282	5.981	2.195	63.117	6.862	5.703	5.342	29.114
DE (9)	.180	.453	-2.429	-83.787	1.934	2.503	2.177	6.862	9.673	4.658	4.028	12.941
DA (10)	.240	.390	-1.603	68.946	1.940	1.871	2.649	5.703	4.658	6.687	3.441	11.679
DD (11)	.123	.198	-1.170	501.484	1.031	1.404	-.043	5.342	4.028	3.441	7.437	6.244
Fa (12)	2.740	3.531	-22.140	-2189.853	15.706	13.635	10.768	29.114	12.941	11.679	6.244	123.741

SD: Stage of Disease; NC: Number of completed Cycles; NS: Nutrition Status; PA: Physical Activity; IS: Insomnia Severity; II: Insomnia Interference; DE: Dyspnea Effort; DA: Dyspnea Anxiety; DD: Dyspnea Discomfort; An: Anxiety; Co: Cough; Fa: Fatigue

Linearity

The assumption of linearity requires that the associations among variables must be in a linear pattern. Because correlation represent only the linear association between variables, nonlinear effects will not be represented in the correlation values. This omission results in an underestimation of the actual strength of the relationship. According to Hair et al. (2009), linearity can be examined by simple regression analysis to assess residuals. The residuals reflect the unexplained portion of the dependent variable. Thus, any nonlinear portion of the relationship will show up in the residuals. In this study, normal P-P plots of regression standardized residuals showed linear association among variables (Appendix E). Thus, it could be concluded that the assumption of linearity was met.

Homoscedasticity

Homoscedasticity refers to the assumptions that the dependent variables exhibit equal level of variance across the range of predictor variables. Homoscedasticity is desirable because the variance of the dependent variable being explained in the dependence relationship should not be concentrated in only a limited range of the value. This assumption could be tested by the graphical test of equal variance dispersion. According to Hair et al. (2009), the test of homoscedasticity for two metric variables is best examined graphically. The homoscedastic data will show an equal distribution of residual across the central line. In the current study, the residual scatter plots show no violations of the homoscedasticity assumption (Appendix E).

Model testing

Measurement model of latent variables

FACT-F measurement model

Previous The FACT-F is a single dimensional scale, consisting of 13 items. Confirmatory factor analysis found that the initial model did not fit well to the empirical data ($\chi 2 = 142.569$, df = 65, $p < 0.05$; $\chi 2/ df = 2.193$; GFI = 0.908; AGFI = 0.871; CFI = 0.961; RSMEA = 0.070). Model adjustment was then taken place by allowing the covariation among residuals of observed indicators. The final model showed good fit to the data ($\chi 2 = 68.026$, df = 56, $p > 0.05$; $\chi 2/ df = 1.215$; GFI = 0.958; AGFI = 0.932; CFI = 0.994; RSMEA = 0.030). Standardized regression weights of items ranged from 0.534 (item 8) to 0.898 (item 4).

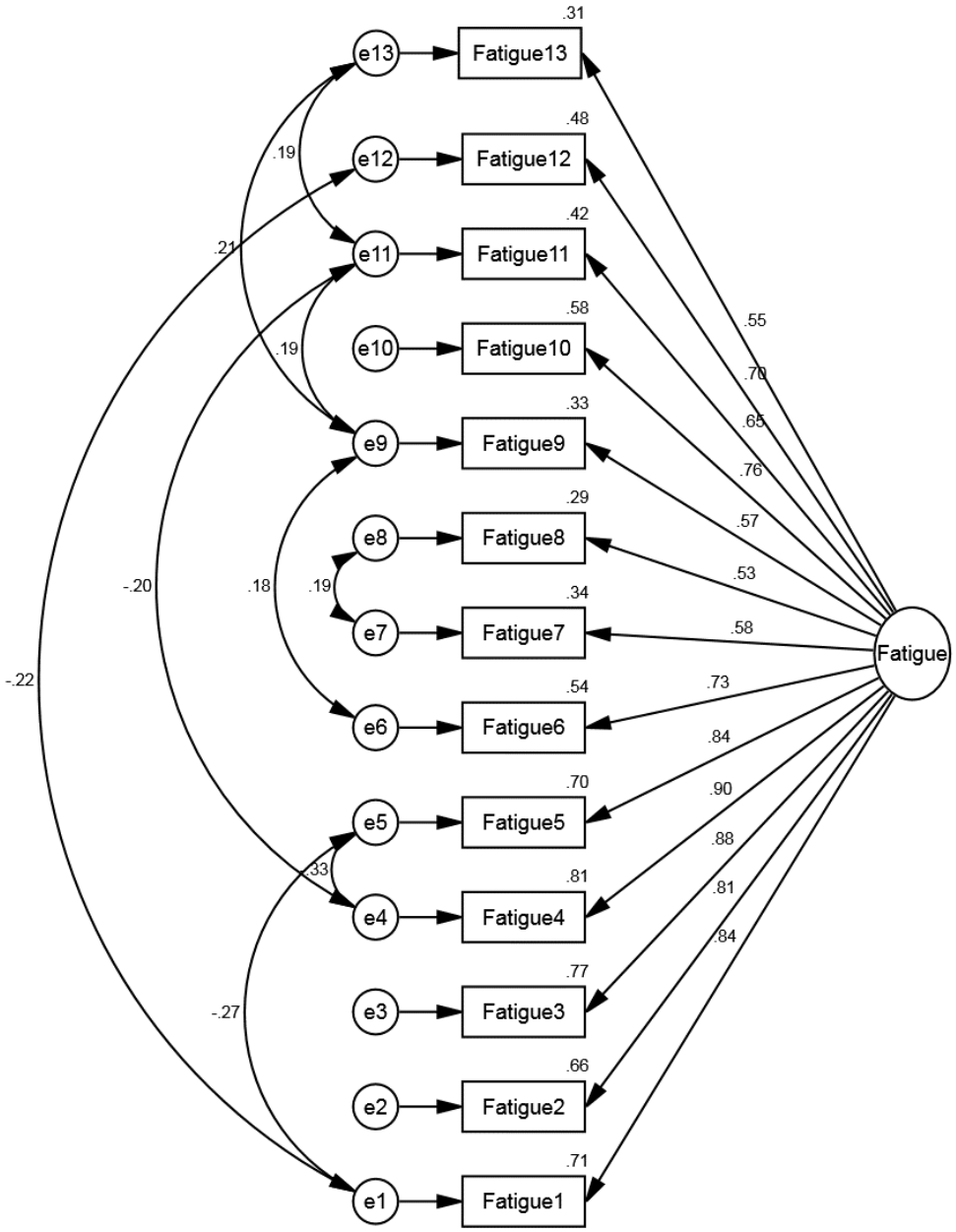


Figure 4 FACT - F measurement model

Insomnia Severity Index measurement model

The Insomnia Severity Index (ISI) consisted of 7 items, divided into two subscales. The subscales are insomnia severity (item 1, 2, 3, and 4) and insomnia interference (item 5, 6, and 7). CFA found that the initial model did not fit well to the

empirical data ($\chi 2$ = 57.716, df = 13, $p < 0.05$; $\chi 2$/ df = 4.44; GFI = 0.939; AGFI = 0.868; CFI = 0.966; RSMEA = 0.118). Model adjustment was then taken place by allowing the covariation among residuals of observed indicators. The final model showed good fit to the data ($\chi 2$ = 7.935, df = 9, $p > 0.05$; $\chi 2$/ df =0.882; GFI = 0.991; AGFI = 0.973; CFI = 1.00; RSMEA = 0.000). Standardized regression weights of items ranged from 0.776 (item 4) to 0.882 (item 6).

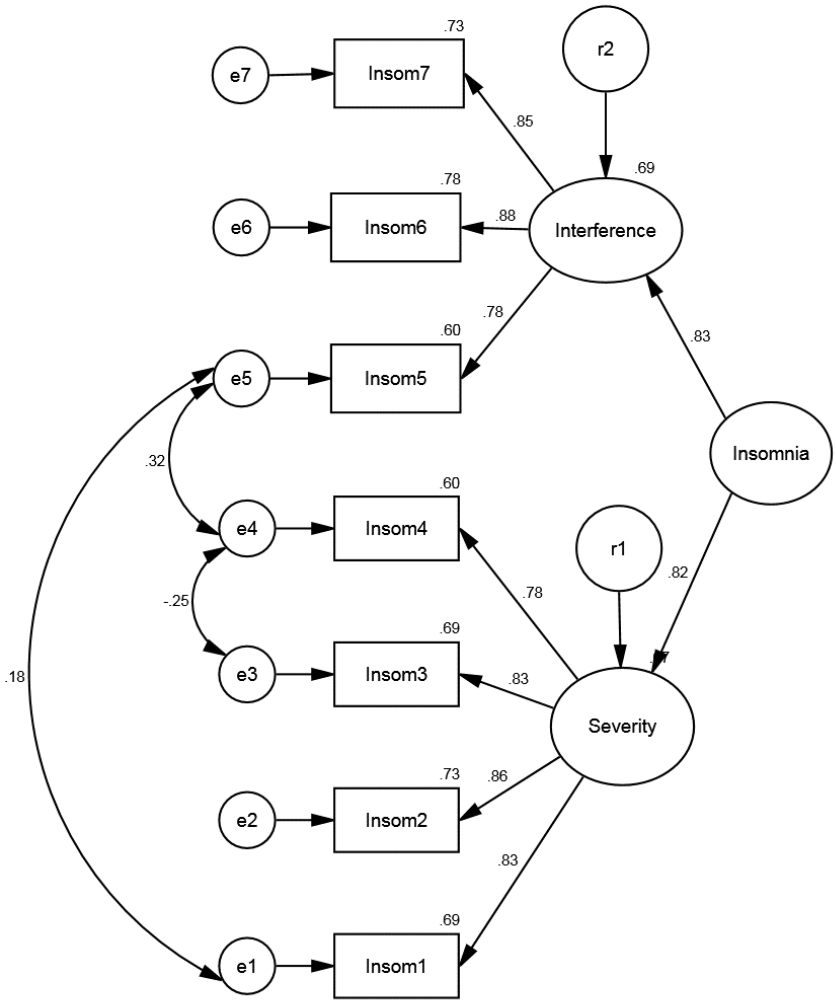


Figure 5 ISI measurement model

Manchester Cough in Lung Cancer Scale measurement model

The Manchester Cough in Lung Cancer Scale consisted of 10 items. Such items constituted a single factor. CFA found that the initial model did not fit well to the empirical data ($\chi 2 = 75.262$, df = 35, $p < 0.05$; $\chi 2/df = 2.1$; GFI = 0.947; AGFI = 0.916; CFI = 0.967; RSMEA = 0.069). Model adjustment was then taken place by allowing the covariation among residuals of observed indicators. The final model showed good fit to the data ($\chi 2 = 46.146$, df = 32, $p > 0.05$; $\chi 2/df = 1.442$; GFI = 0.967; AGFI = 0.943; CFI = 0.988; RSMEA = 0.042). Standardized regression weights of items were ranged from 0.399 (item 1) to 0.842 (item 5).

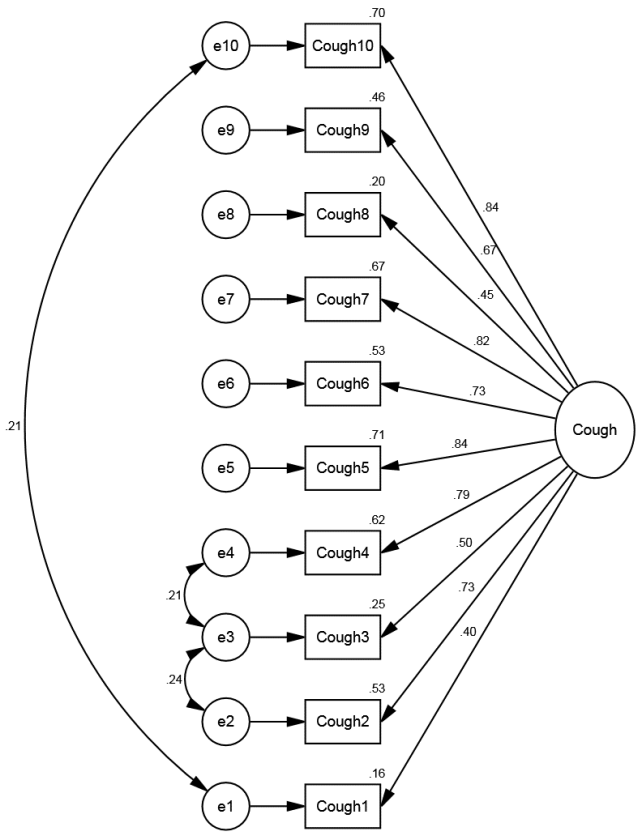


Figure 6 MCLCS measurement model

Cancer Dyspnea Scale measurement model

The Cancer Dyspnea Scale consisted of 12 items. There are three subscales: sense of effort, sense of discomfort, and sense of anxiety. CFA found that the initial model did not fit well to the empirical data ($\chi 2 = 80.894$, df = 51, $p < 0.05$; $\chi 2/$ df = 1.586; GFI = 0.950; AGFI = 0.924; CFI = 0.968; RSMEA = 0.049). Model adjustment was then taken place by allowing the covariation among residuals of observed indicators. The final model showed good fit to the data ($\chi 2 = 62.860$, df = 50, $p > 0.05$; $\chi 2/$ df = 1.257; GFI = 0.960; AGFI = 0.938; CFI = 0.986; RSMEA = 0.032). Standardized regression weights of items ranged from 0.472 (item 4) to 0.904 (item 3).

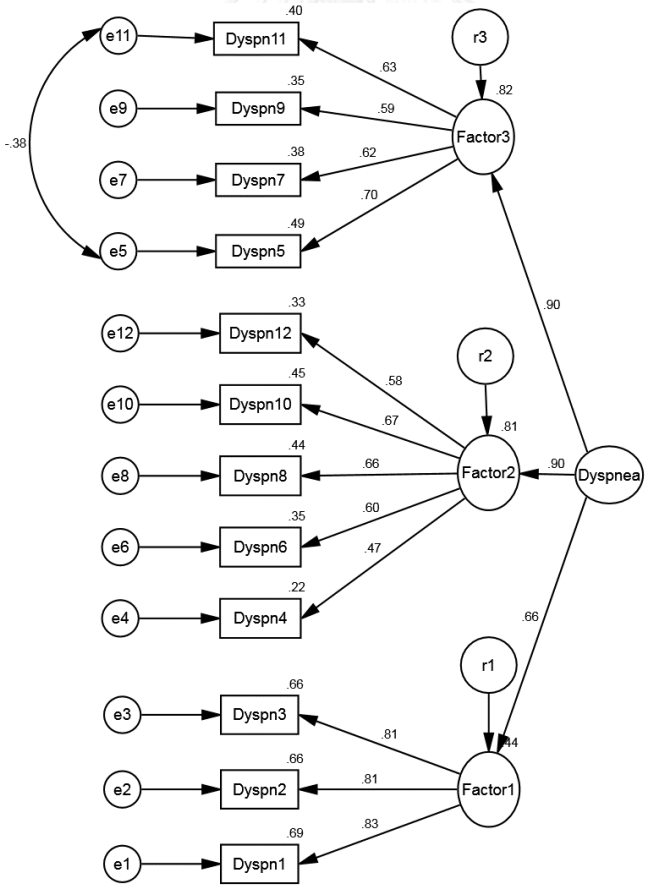


Figure 7 CDS measurement model

Anxiety Subscale – Depression Anxiety and Stress Scale - 21

The Anxiety subscale of Depression Anxiety and Stress Scale – 21 consisted of 7 items. These seven items formed a single scale. CFA found that the initial model did not fit well to the empirical data ($\chi 2 = 64.643$, df = 14, $p < 0.05$; $\chi 2/df = 4.617$; GFI = 0.924; AGFI = 0.849; CFI = 0.860; RSMEA = 0.112). Model adjustment was then taken place by allowing the covariation among residuals of observed indicators. The final model showed good fit to the data ($\chi 2 = 18.532$, df = 12, $p > 0.05$; $\chi 2/df = 1.529$; GFI = 0.979; AGFI = 0.951; CFI = 0.982; RSMEA = 0.046). Standardized regression weights of items ranged from 0.396 (item 2) to 0.705 (item 4).

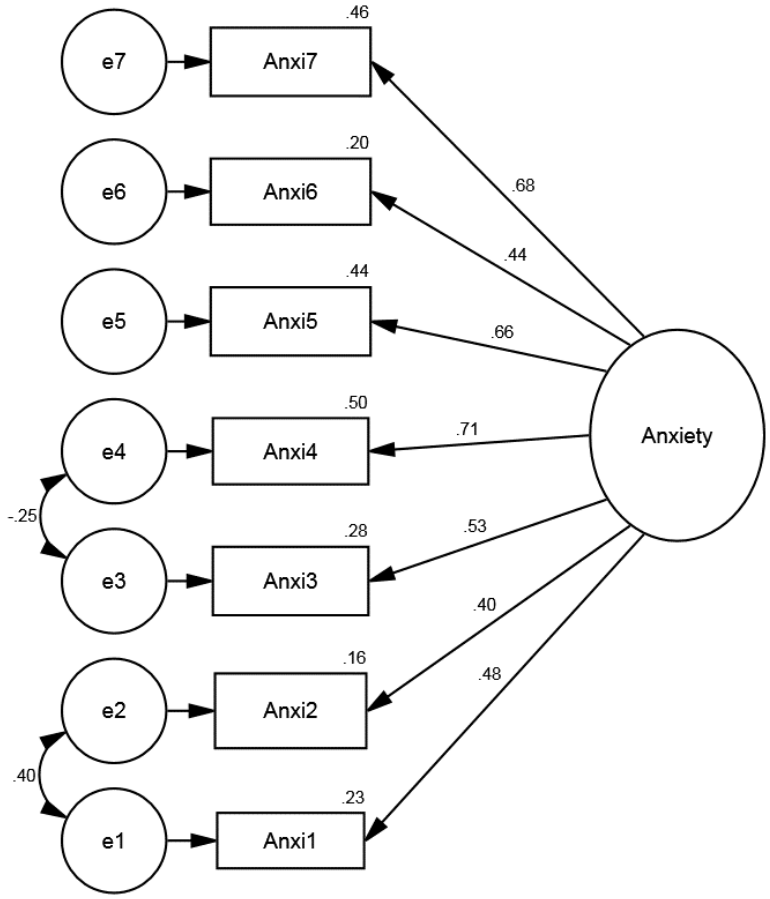


Figure 8 DASS - 21 Anxiety measurement model

Structural model

Model identification

The identification of the model is critical to test the model fit in SEM as well as its parameters. When the number of covariances exceeds the number of parameters being estimated, the model is over-identified. If the number of covariances equals to the number of estimated parameters, the model is just-identified. Lastly, the model is under-identified if the number of parameters is higher than the number of covariances. SEM requires the model to be over-identified (Munro, 2005).

A convinience way to assess the identification of the model is calculating its degree of freedom. The model degree of freedom is equal to adjusted degree of freedom minus the number of parameter in the model. If the model degree of freedom is possitive, the model is over-identified. Adjusted degree of freedom is produced based on the number of manifest variables [p*(p+1)/2] (Munro, 2005). The hypothesized model of the current study consisted of 9 variables. Thus, the adjusted degree of freedom was 45 [9*(9+1)/2]. There are 22 free parameters in the model. The model degree of freedom thus was 23 (45 minus 23). In conclusion, the hypothesized model is overidentification, allowing the perform of SEM.

CFA found that the FACT-F, MCLCS, DASS-21 Anxiety are uni-dimensional scales. According to Raykov and Marcoulides (2006) the model with unidimensional scale assessing latent variable is not identified. To solve this problem, some authors set the error variance of uni-dimensional latent variable equal to zero (Little, Cunningham, & Shahar, 2002). Unlike path analysis, structural regression takes measurement errors into the estimation of the model. Hence, unlike observed indicators, it may not be suitable to set the variance of the latent variable to zero, which mean the measurement

is perfectly reliable. Other option is to use first-order measurement model in the structural model (L. J. Williams & O'Boyle Jr, 2008). This means, every single observed variables are treated as indicators of the latent variable. However, this approach requires a large sample because the sample size is calculated based on the number of parameter under estimating. Therefore, this method is not suitable with this study. Bollen (1989), as cited in L. J. Williams and O'Boyle Jr (2008), suggested the method of total aggregation with reliability correction to deal with uni-dimensional latent variable. This method helps the hypothesized model identified but allow the consideration of measurement errors. In this method, the internal consistency coefficient of the instruments is priori determined. The variance of measurement error then is calculated by subtract 1 with the cronbach's alpha coefficient.

In the pilot study, it was found that the Cronbach's alpha of FACT-F, MCLSC, and DASS-21 Anxiety were 0.93, 0.91 and 0.78, respectively. Therefore, variances of measurement errors of such scales were set at 0.07, 0.09, and 0.22, consecutively.

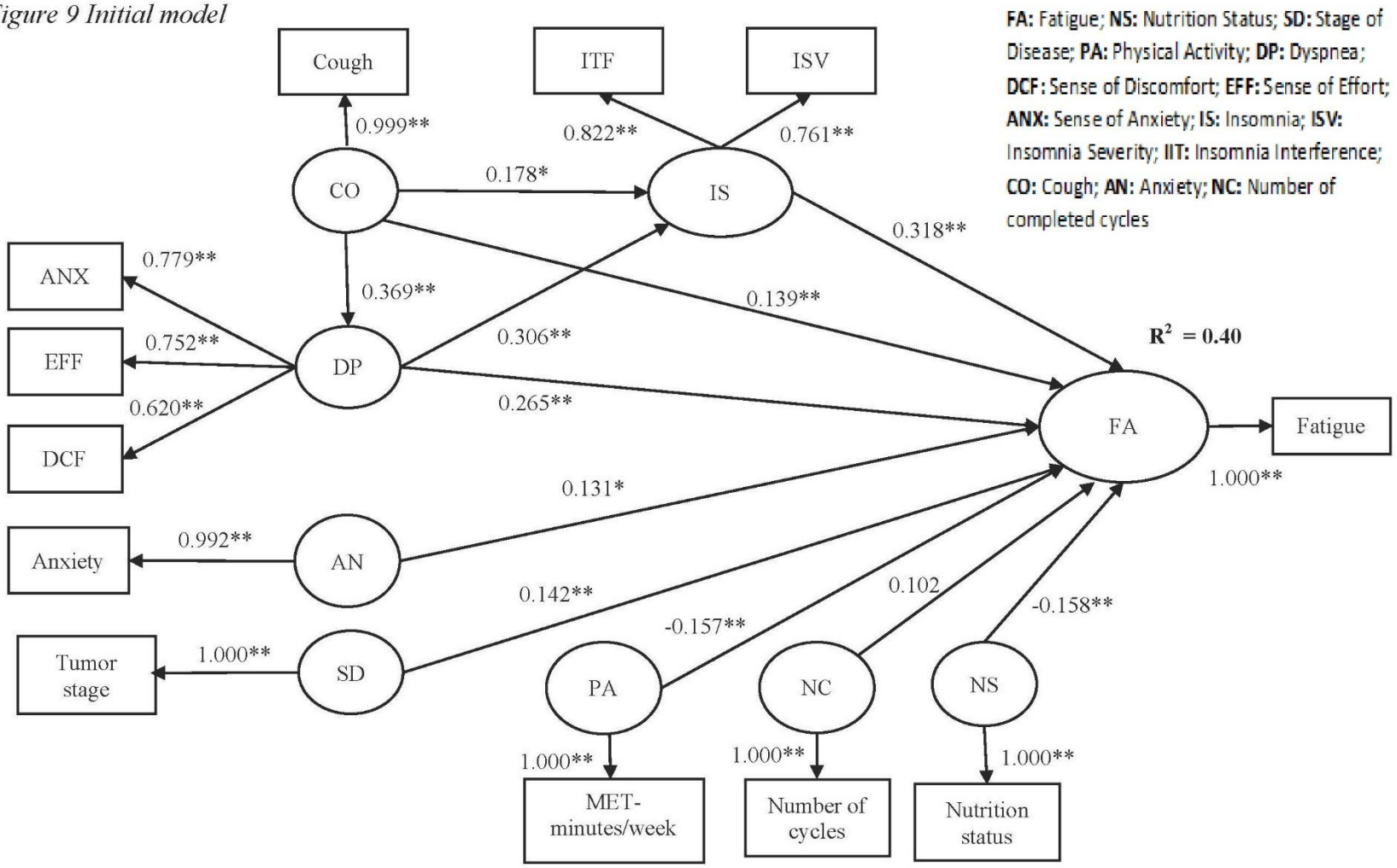
Model testing

Model 1: Initial model

The hypothesized model in this study consisted of 9 variables. Among them three were endogenous and six were exogenous variables.

It was found that the initial model did not fit well to the empirical data ($\chi 2 = 88.431$, df = 50, p = 0.001; $\chi 2$/ df = 1.77; GFI = 0.942; AGFI = 0.910; CFI = 0.926; RSMEA = 0.056). The model explained 40.4% of the variance of fatigue. Despite several fit indices were at the acceptable level, the chi-square test was non-significant. Therefore, model modification was necessary.

Figure 9 Initial model



Model 2: Drop the direct path from number of completed chemotherapy cycles to fatigue

The examination of regression weights among variables in the model revealed that the association between fatigue and number of completed chemotherapy cycles (β = 0.102, p = 0.05). Therefore, the model was modified by dropping the direct path between these variables. The examining model hence consisted of three endogenous and five exogenous variables.

Model testing yielded the results as follow: $\chi 2$ = 72.462, df = 40, p = 0.001; $\chi 2$/ df = 1.812; GFI = 0.950; AGFI = 0.918; CFI = 0.937; RSMEA = 0.058. All regression weights were significant. The model explained 40.7% of the variance of fatigue. As can be seen, although several fit indices improved, the model still appeared not to fit well to the empirical data. Therefore, the further modification was needed.

Model 3: Adding the path from dyspnea to anxiety

At this step, modification indices (MIs) were examined to identify several re-specifications of the model that could be taken. MIs, which are approximately equal to (or higher) 10 and par change of at least 0.1 should be considered for modification. Nevertheless, since the MIs are truly statistical estimation, any model adjustments need theoretical or empirical base to make its justified (Byrne, 2010). In considering the MI and the meaningfulness of possible model modification, the causal association from dyspnea to anxiety was added (MI = 12.492, Par change = 0.395), meaning that the more patients were dyspnea, the more anxious they were.

The examining model hence consisted of four endogenous and four exogenous variables.

Model testing yielded the results as follow: $\chi 2 = 58.462$, df = 39, p = 0.022; $\chi 2/$ df = 1.506; GFI = 0.959; AGFI = 0.931; CFI = 0.962; RSMEA = 0.045. All regression weights were significant. The model explained 42.4% of the variance of fatigue. As can be seen, although several fit indices improved, the model still appeared not to fit well to the empirical data because the Chi-square was still significant. Therefore, the further modification was needed.

Model 4 (Final model): Adding path from stage of disease to physical activity

The analysis of MIs and its substantive meaningfulness pointed out that a causal association should be added from stage of disease to physical activity (MI = 6.814, Par change = -223.384). The path suggested that patients with more severe the disease would demonstrated less physical activity.

The examining model hence consisted of five endogenous and six exogenous variables.

Model testing yielded the results as follow: $\chi 2 = 51.556$, df = 38, p = 0.070; $\chi 2/$ df = 1.357; GFI = 0.963; AGFI = 0.937; CFI = 0.974; RSMEA = 0.038. The model explained 42.9% of the variance of fatigue. At this step, the model fit well to the empirical data.

According to Byrne (2010), there is no firm rule for the researcher to know when to stop re-specification her model. Hence, "the researcher's best yardsticks include (a) a thorough knowledge of the substantive theory, (b) an adequate assessment of statistical criteria based on information pooled from various indices of fit, and (c) a watchful eye on parsimony. In this regard, the SEM researcher must walk a fine line between incorporating a sufficient number of parameters to yield a model that adequately represents the data, and falling prey to the temptation of incorporating too

many parameters in a zealous attempt to attain the best-fitting model statistically." (page. 192 - 193). In the current model, the fit statistics were all at the acceptable threshold. Moreover, the MIs suggest non-clinical relevant associations among variables. Importantly, the proposed modification helped improve model fit but the model, at this step, appeared to be parsimonious with initial hypothesized model. Therefore, the model was accepted at this stage and no further modifications were proposed.

Table 8 Fit indices comparison

Fit indices	Initial model	Final model
$\chi 2$	88.431	51.556
p value	< 0.05	> 0.05
df	50	38
$\chi 2$/ df	1.769	1.357
GFI	0.942	0.963
AGFI	0.910	0.937
CFI	0.926	0.974
RMSEA	0.056	0.038
Explained Variance	40.4%	42.9%

Hypothesis testing

Hypothesis 1: Insomnia has a positive and direct effect to Fatigue

The result shows that the standardized total effect from Insomnia to Fatigue is 0.318 (Table 10). The effect is statistically significant ($p < 0.01$). All of the effect is direct. The above-zero standardized regression weight represented a positive impact.

Therefore, it is concluded that the hypothesis toward the positive and direct effect from Insomnia to Fatigue is supported by empirical data in the current study.

Hypothesis 2: Anxiety has a positive and direct effect to Fatigue

The result shows that the standardized total effect from Anxiety to Fatigue is 0.115. It should be noted that the regression estimation yielded a significant p-value (0.031) of the coefficient between anxiety and fatigue (table 9). In contrast, the result from bootstrap revealed this effect is non-statistically significant, suggesting that the coefficient is indeed not different from zero. However, the p value from bias corrected bootstrap is only marginally non-significant ($p = 0.056$) (appendix. F). Therefore, it may be concluded that the association between anxiety and fatigue is significant. The above-zero standardized regression weight represented a positive impact.

Therefore, it is concluded that the hypothesis toward the positive and direct effect from Anxiety to Fatigue is supported in the current study.

Hypothesis 3: Physical activity has a negative and direct effect to Fatigue.

The result shows that the standardized total effect from Physical Activity to Fatigue is - 0.148. The effect is statistically significant ($p < 0.01$). All of the effect is direct (Table 10). The below-zero standardized regression weight represented a negative impact.

Therefore, it is concluded that the hypothesis toward the negative and direct effect from Physical activity to Fatigue is supported in the current study.

Hypothesis 4: Nutrition Status has a negative and direct effect to Fatigue.

The result shows that the standardized total effect from Nutrition Status to Fatigue is - 0.156 (table 10). The effect is statistically significant ($p < 0.01$). All of the effect is direct. The below-zero standardized regression weight represented a negative impact.

Therefore, it is concluded that the hypothesis toward the positive and direct

effect from Nutrition Status to Fatigue is supported in the current study.

Hypothesis 5: Cough has positive effects, both direct and indirect (through insomnia and dyspnea), to Fatigue.

The result showed that the standardized total effect from Cough to Fatigue is 0.343. The effect is statistically significant ($p < 0.01$). The direct effect is 0.143 ($p < 0.01$) and indirect effect is 0.200 ($p < 0.01$) (table 10). The above-zero standardized regression weight represented a positive impact.

Therefore, it is concluded that the hypothesis toward the positive and direct effect from Cough to Fatigue is supported in the current study.

Hypothesis 6: Dyspnea has positive effects, both direct and indirect (through insomnia), to Fatigue.

The result showed that the standardized total effect from Dyspnea to Fatigue is 0.397. The effect is statistically significant ($p < 0.01$). The direct effect is 0.266 ($p < 0.01$) and indirect effect is 0.131 ($p < 0.01$) (table 10). The above-zero standardized regression weights represented a positive impact. Dyspnea had a significant impact on Insomnia ($\beta = 0.317$, $p < 0.01$) and Anxiety ($\beta = 0.269$, $p < 0.01$). This suggested that the indirect impact of Dyspnea on Fatigue is not only via Insomnia but also via Anxiety.

Therefore, it is concluded that the hypothesis toward the positive, direct effect, and indirect effect (via Insomnia) from Dyspnea to Fatigue is supported in the current study but needs to be added up. In particular, Dyspnea also has a positive indirect impact on Fatigue via Anxiety.

Hypothesis 7: Stage of disease has a positive and direct effect to Fatigue.

The result showed that the standardized total effect from Stage of disease to Fatigue is 0.179. The effect is statistically significant ($p < 0.05$). The above-zero

standardized regression weight represented a positive impact. Notably, besides having the direct effect of 0.154 ($p < 0,05$), stage of disease also had the direct effect to Physical Activity ($\beta = -0.170$, $p < 0.01$) resulting in the indirect effect to Fatigue via Physical activity ($\beta = 0.025$, $p < 0.05$) (table 10).

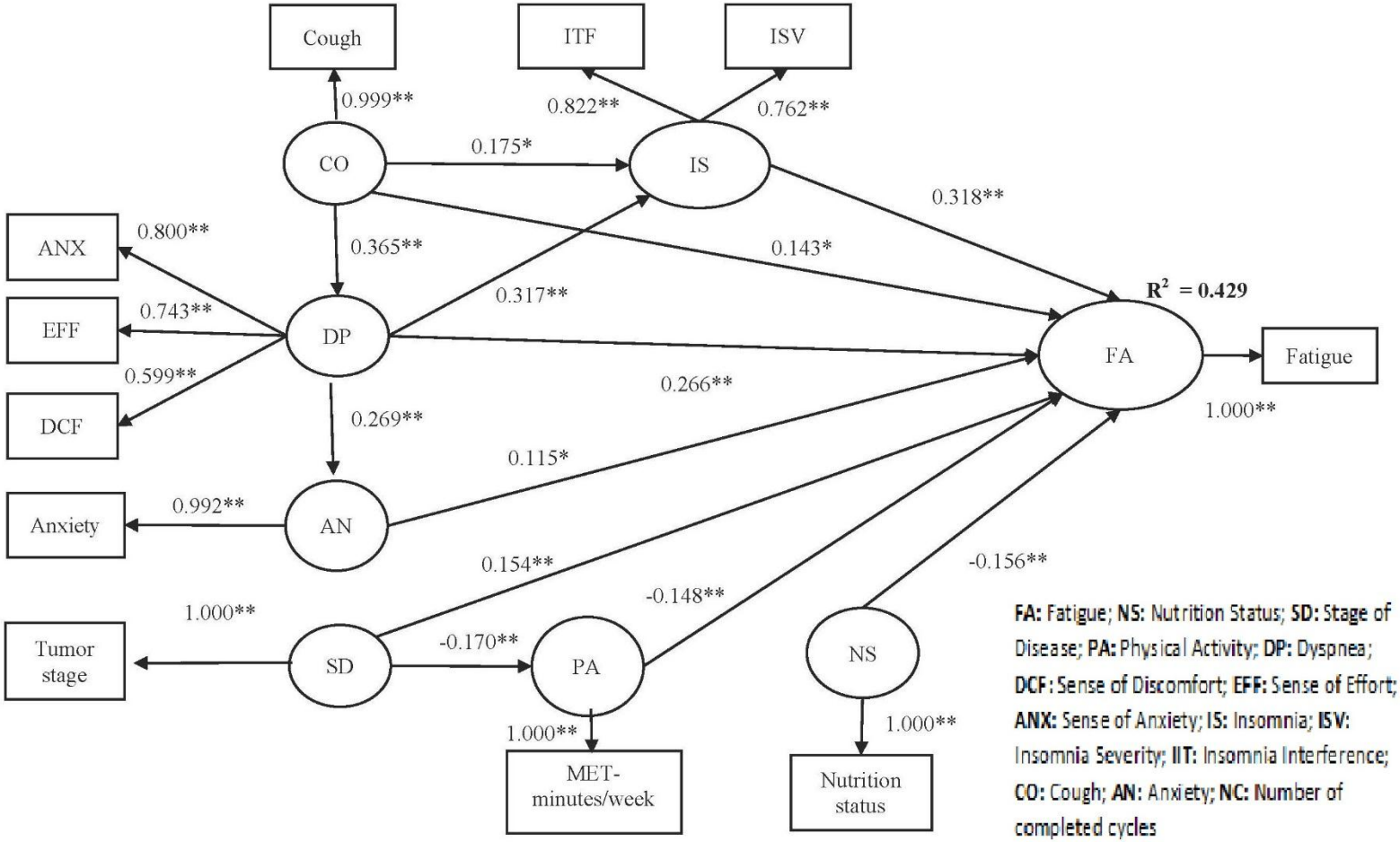
Therefore, it is concluded that the hypothesis toward the positive, direct effect from Stage of Disease to Fatigue is supported in the current study. However, the hypothesis should be revised. In particular, Stage of Disease also has indirect effect to Fatigue via Physical Activity.

Hypothesis 8: Number of completed cycles has a positive and direct effect to Fatigue.

The result showed that the regression weight from Number of completed cycles to Fatigue was non-significant**.** In other words, the current study did not observed any statistically significant association between these two variables.

Therefore, it is concluded that the hypothesis toward the positive and direct effect from Number of completed chemotherapy cycles to Fatigue is failed to affirm in the current study.

Figure 10 Final model



CHAPTER V
DISCUSSION

The objective of this study was to examine the causal model of fatigue in lung cancer patients during their chemotherapy courses. The independent variables included insomnia, cough, dyspnea, stage of disease, physical activity, number of completed cycles, nutrition status, and anxiety. This chapter is the discussion of the study's results. The main points, which will be presented, are characteristics of the studied subjects and variables, the causal model, the hypothesis testing, and limitations and application of the study.

Characteristics of the sample

The mean age of the sample was more than sixty years old (60.79 ± 6.59). This finding is similar to other studies (Shrividya Iyer, Roughley, Rider, & Taylor-Stokes, 2013; Magasi et al., 2013), in that most lung cancer patients were diagnosed at late adult age. This appears to reflect the nature of tumorous disease, which does not commonly occur at young age.

Notably, the majority (72.8%) of the sample was male. The high prevalence of lung cancer in Vietnamese male may associate to their smoking behavior – one of the most important causes of lung cancer. It was reported that smoking is highly prevalent in Vietnam. A nationwide study by Khue and Minh (2011) found that 56.7% of males aged from 25-44 years, and 59.5% of males aged from 45-64 years were smokers. This could be the reason why males were accounted for major proportion of this study sample.

The duration of being diagnosed with lung cancer ranged from 1 to 26 months, with the mean of 5.44 ± 3.97 months. This length of time appeared not to be long in comparison to the survival time reported by previous study. Bui, Le, and Nguyen (2010b) conducted a follow-up study on 122 lung cancer patients. It was found that the survival rate after five year was of 30.1 ± 7%. With regard to the stage of disease, which was classified as IA, IB, IIA, IIB, and IIIA, the length of survival time was 46 ± 7 months, 38.5 ± 5 months, 34.8 ± 5.7 months, 11.8 ± 1.8 months, and 12.1 ± 1.5 months. It can be said that the sample of the current study was at the beginning steps of the treatment as well as their lives with the cancer.

Characteristics of studied variables

With regard to stage of disease, 72.5% of the sample were at the late stage of the disease, with the most prevalent groups were stage III (37.8%), and stage IV (35%). Patients with stage I accounted for a smallest proportion of the sample (8.5%). These findings reflect the fact that the most patients were diagnosed at the advanced stages. Many patients came to hospital for treatments when the tumor had growth and spread widely (B. Đ. Nguyen, 2006). It was estimated that the prevalence of stage III and IV at diagnosis among Vietnamese cancer patients was ranged from 65% to 80%. The reason for this situation is the poor knowledge and awareness of the public and general practitioners at the community levels of the healthcare system (Anh & Duc, 2002).

In the current study, more than half (50.8%) of the sample and nearly half had malnutrition at some degree. About one-third (32.5%) of the sample was categorized as moderate malnourished and there were 5.7% of patients were severely malnourished. This prevalence of under-nutrition found in this study appeared to be higher than in

study by Xará et al. (2011), who reported that 7.1% of early staged lung cancer patients had malnutrition but such prevalence in advanced stage individuals was 45.2%. Similarly, other survey on 49 advanced lung cancer patients found that 22% of patients were well - nourished (PG-SGA rating A), 47% were at risk of malnutrition (B), and 31% of patients were malnourished (C) (Bortolon, Tartari, Nunes, da Silva, & Filho, 2009). It should be noted that the current study recruited patients at all stages. However, the prevalence of malnutrition found was still higher. In plain words, this study indicated that one in every two patients had malnutrition. The finding highlights the need for more effective management of patient's nutrition status in Vietnamese lung cancer population.

In the current study, nearly one-third of participants were categorized as low physically active. There was plenty of evidence showing the low level of physical activity not only in lung cancer but also in other cancer populations. For example, Granger et al. (2014) found that only 26% to 60% of lung cancer patients meet the WHO guideline for physical activity after diagnosis with the cancer. Midtgaard et al. (2009) surveyed physical activity in 451 Danish cancer patients who were undergoing chemotherapy. It was revealed that physical activity during chemotherapy of patients was remarkably declined in comparison to pre-treatment physical activity. In particular, the proportions of patients classified as sedentary increased from 7% (pre-treatment) to 30% (during treatment). In contrast, the prevalence of high physical activity (four hours/week) decreased from 12% to 2%.

The low level of physical activity among lung cancer population might not be a surprised finding. Any bodily movements require the involvement of cardiovascular, muscle skeletal, and, importantly, respiratory systems (Porth, 2006). In lung cancer, the

tumors directly harm the lungs, decreasing respiratory functions. Consequently, patients are not able to perform physical activity thoroughly. This could be the plausible explanation for the finding in this study.

Participants in current study showed a high level of insomnia, with the mean total score of 13.46 ± 5.73. Several patients even reported a quite high score of insomnia (score of 27). Notably, with the cut-off point of 8 to categorized case and non-case, most of patients (84.5%) had clinically significant insomnia. In the literature, sleep problems in lung cancer patients were commonly reported. Theoretically, tumor in the upper or lower respiratory system and the muscle weakness of advanced disease may lead to shortness of breath, sleep apnea, or hypoxia. These may disrupt the sleep regulatory mechanism and cause arousal. In addition, the cancer also alters various hormone levels and secondarily interferes with sleep homeostasis (Induru & Walsh, 2013).

It is important to note that, although the previous studies reported severe insomnia among cancer patients, the problem appears to be more problematic in the current study. Using Pittsburgh Sleep Quality Index to examine sleep in a sample with lung cancer, Chen et al. (2008) found that 52% were classified as poor sleepers during their chemotherapy. In other study with breast and prostate cancer patients, Humpel and Iverson (2010) reported that 30.1% of respondents were classified as poor sleepers. The current study found that more than 80% of the participants were classified as poor sleepers. This fact called for the urgent and appropriate management of sleep problems in lung cancer, especially in Vietnamese population. Further studies are needed to explore characteristics of sleep problem as well as its associated factor in particular to this population.

The mean of anxiety score was 6.26 ± 3.7 and the range of 0 – 15. Since there is no cut-off point for case and non-case in Vietnamese lung cancer or cancer population available, it is hard to categorize patients in different severity groups. However, a validation study of T. D. Tran et al. (2013) in Vietnamese community women suggested the cut-off point of 10 for DASS-21 anxiety subscale with the sensitivity and specificity of 0.79 and 0.67, respectively. Using this criterion, it could be seen that the mean anxiety score in this study is quite lower than the threshold. This suggested that anxiety might not be a severe problem in this studied sample. The finding is supported by previous study of Dean et al. (2010), who studied lung cancer patients on chemotherapy and reported that only fifteen percent of participants were classified as possible case for anxiety (HADS scores between 8 and 10) and 10% were cases for anxiety (HADS scores ≥ 11). Seemingly, the diagnosis of cancer could be a focal factor causing the patient anxious. However, participants in this study was diagnosed with the disease for a period of time (5.44 months), which may long enough for the patients lessen their anxiety and focus on treatment. This could be one of reasons why participants in this study were not severely anxious.

It could be noted that all patients in this study have some degree of cough, with the score ranged from 11 to 42. This finding is in line with other study in Vietnam, which asserted that one hundred percent patients had cough (even bloody cough) at diagnosis. It is one of the major symptoms bringing patients to hospitals (Cu, To, & Nguyen, 2000; T. M. P. Nguyen & Tran, 2010; Phạm, 2010). Finding of the current study, therefore, reflects the typical characteristics of Vietnamese lung cancer patients.

Participants in this study experienced fatigue with a wide range (0-49). The mean score of fatigue was 27.69 ± 11.12. It should be noted that the possible range of score

could be 0-52 when this study sample reported a score ranged from 0-49 with the mean of 27.69, suggesting that patients were suffered from remarkable fatigue intensity.

Previous studies, which used FACT-F scale also found high intense fatigue in cancer patients. Study of Humpel and Iverson (2010) found that the mean scores of fatigue (FACT-F) in a group of breast cancer (n = 32) and prostate cancer (n = 59) were 36.2 ± 11.0 and 39.8 ±10.4, respectively. Peddle-McIntyre, Bell, Fenton, McCargar, and Courneya (2012) recruited 15 lung cancer survivors to conduct an intervention study controlling fatigue and the baseline score of FACT-F was 45.6 ± 5.2. Lou, Yates, McCarthy, and Wang (2013) studied 271 Chinese cancer patients on chemotherapy and found the mean score of fatigue was 29.90 ± 10.73. These above findings strongly highlight the need to manage fatigue efficiently worldwide.

The causal model of fatigue in lung cancer patients on chemotherapy

After revision, final model in this study fit well to the empirical data ($\chi 2 = 51.556$, df = 38, p = 0.070; $\chi 2$/ df = 1.357; GFI = 0.963; AGFI = 0.937; CFI = 0.974; RSMEA = 0.038). However, the variance of fatigue that the model of current study accounted for was moderate (42.9%). This suggests that there could be other factors might be included in the causal model of this phenomenon. The current study relied the construction of its model on Piper Integrated Fatigue Model and empirical evidence. Therefore, since the current state of science identified only several variables that could be included in the model explaining fatigue in lung cancer patients on chemotherapy, this study examined only those factors, including insomnia, dyspnea, cough, anxiety, number of completed chemotherapy cycles, stage of disease, physical activity, and

nutrition status. The examination of other factors is, hence, recommended for future studies.

As stated before, this study model accounted for 42.9% of the variance of fatigue. Interestingly, the variance of fatigue explained by the current model was different from those in studies of Seo et al. (2010) and Hanprasitkam (2006). In particular, Seo et al. (2010) recruited 110 subjects with various types of cancer from in- and out-patient settings at a university hospital of South Korea. Studied predictors of fatigue in the model were physical distress, sleep-related, physiologic, psychological distress, physical performance, and exercise factors. It was found that only exercise directly effects and accounts for 70% of fatigue. Using path analysis, Hanprasitkam (2006) studied 159 Thai women with breast cancer to test the association between selected variables and fatigue. It was found that eight predictors (pain, nausea and vomiting, sleep disturbance, family support, friend support, Buddhist practices, anxiety, and depression) in the final model explained 80.4% of total variance in fatigue.

The disparity in explained variances of fatigue found among studies appears to be plausible because fatigue is influenced by various factors (Piper et al., 2011). Such factors might vary with diagnoses and situations. It could be seen that the target populations of three studies are different. This study focused on lung cancer subjects on chemotherapy, whereas Seo et al. (2010) and Hanprasitkam (2006) paid their attentions on a group of mix cancer sites and breast cancer, respectively. In addition, the determinants included in the three models were not the same. That could be the reason why findings were not similar. Therefore, the finding of this study appears to recommends the investigation of variables, which are specific to treatment and cancer types.

The modification of hypothesized model

The initial hypothesized model in this study yielded approximate fit indexes at the acceptable levels, but the Chi-square test was significant ($\chi 2 = 88.431$, df = 50, p = 0.001). R. B. Kline (2011) asserted that thresholds for approximate fit indexes are not golden rules and a significant Chi-square test should never be neglected. Proper attentions must be paid to this non-fit test because it might indicate a serious mis-specified model. Therefore, despite several fit indices were acceptable, the initial model was still considered as a not well-fit one.

To modify the model, review of the MIs reveals some evidence of misfit in the model. According to Byrne (2010), since in SEM the author is interested solely in the causal paths of the model, only a subset of indices related to the regression weights should be considered. "The reason for this statement is because in working with full SEMs, any misfit to components of the measurement model should be addressed when that portion of the model is tested for its validity" (page 177). Substantively meaningful causal associations among variables were taken into account, and the path from dyspnea to anxiety, and the path from disease severity to physical activity were added. The re-specification improved model fit and all indices were acceptable.

There modification of the hypothesized morel was supported by several previous findings:

With regard to the association between dyspnea and anxiety, there is evidence suggesting that dyspnea positively affects anxiety. Anxiety is the apprehensive anticipation of future danger (Callanan, 2000). Dyspnea, on the other hand, appears to be the inherent entity of lung cancer. From the patients' point of view, dyspnea is "a reminder of the lung cancer disease and of the serious consequences of being stricken

by a life-threatening disease" (Henoch, Bergman, & Danielson, 2008, p. 712). Hence, being dyspnea may triggers anxiety. This association was approved in qualitative studies of Henoch, Bergman, and Danielson (2008) and Lai, Chan, and Lopez (2007).

Several quantitative studies also reported the association between dyspnea and anxiety W. Y. Cheung, Le, and Zimmermann (2009) examined symptom cluster in 1,366 advanced cancer patients. The most common primary cancer sites in the sample were gastrointestinal (27%), lung (14%), and breast (11%). The association between dyspnea and anxiety was 0.28 ($p < 0.001$). Dudgeon and Lertzman (1998) studied symptoms in 100 patients with advanced lung, breast, prostate, colorectal, gynecological, stomach, bladder, and renal cancer. Some research used Visual Analog Scale to measure shortness of breath and anxiety. It was found that the correlation coefficient between these two symptoms was 0.29 ($p < 0.001$).

In lung cancer, Tanaka, Akechi, Okuyama, Nishiwaki, and Uchitomi (2002a) investigated factors related to dyspnea in advanced tumor patients ($n = 171$). Data indicated that anxiety (measured by Hospital Anxiety and Depression Scale) was associated with dyspnea ($r = 0.3$, $p < 0.01$). Similarly, Kuo and Ma (2002) obtained seventy-three patients with non-small cell lung cancer from two medical centers located in northern Taiwan. Participants were undergoing either chemotherapy or radiotherapy. The Symptom Distress Scale was used to investigate symptoms. It was found that tension-anxiety and difficulty with breathing were significantly associated with $r = 0.345$ ($p < 0.05$). However, interestingly, Feinstein et al. (2010) studied dyspnea 1,017 early stage lung cancer long term survivors. Authors used Baseline Dyspnea Index and Hospital Anxiety and Depression Scale to assess variables. The cutoff point of 8 was used to categorize patients into two groups, with and without significant anxiety. The

results showed that there was no difference in dyspnea score between case and non-case anxiety ($p = 0.65$).

Above findings suggested that, although there are inconsistences among studies toward the association between anxiety and dyspnea in lung cancer population, this relationship appears to be substantively meaningful and supported by empirical findings by both research in lung and other groups (Kuo & Ma, 2002; Tanaka et al., 2002a).

The association between stage of disease and physical activity, on the other hand, was added based on clinical soundness of this relationship. Stage of disease reflects the severity of the cancer. The more severe the disease is, the more it limits patients' physical activity due to the decline in physical health. Hence, it appears to be appropriate to propose that stage of disease negatively affects patients' physical activity.

Initially, number of completed chemotherapy cycles was included in the model based on the idea about accumulation of metabolites within the body. According to Piper (2011), the accumulation of metabolites in the body would worsen fatigue. Chemical agents are the administered into the body during chemotherapy courses. Hence, it was hypothesized that metabolites would gradually accumulate within the body in relevant to the finished cycles.

However, the data was analyzed, number of completed chemotherapy cycles was removed from the model due to its insignificant association with fatigue. There could be two possible explanations for this finding. Firstly, since current protocol for chemotherapy allows patients to take rest between two consecutive cycles. This off-time would help the body recover and eliminate harmful metabolites before new

chemical doses are administered. Hence, there may not be significant accumulation of those agents so that fatigue is worsened. Secondly, given the critical condition of lung cancer, patients who can follow more cycles would be the one who responds well to the treatment. Therefore, along with the number of chemotherapy cycles completed, patients' general condition would be improved. As the result, fatigue is lessened or, at least, does not get worse. These could be reasons why this study failed to observe significant association between number of completed chemotherapy cycles and fatigue.

In summary, the initial model was modified by removing number of completed chemotherapy cycles, adding causal paths from dyspnea to anxiety, and from stage of disease to physical activity. Both empirical and theoretical evidence suggested that these modifications were justified.

Hypothesis testing

It was affirmed in this study that anxiety positively and directly affects fatigue ($\beta = 0.115$, $p < 0.05$). This finding is contrast to what Seo et al. (2010) reported in their study. In particular, these authors failed to accept the causal relationship between anxiety and fatigue. From the empirical view, the methodological flaws in study of Seo et al. (2010) (as mentioned in previous paragraphs) may make its findings skeptical. More importantly, despite the exact mechanism of the causal relationship form anxiety to fatigue has not been clearly demonstrated, some theoretical hypotheses support this association. For example, from the energy balance viewpoint, factor, which depletes energy of the body, would result in fatigue (Ryden, 1977). Anxiety causes a stress condition, which mobilizes the body and prepares it to react with the situation. It consumes body's energy and consequently causes fatigue. Empirically, the association

between these two phenomena is supported by both descriptive study (R. Hung et al., 2011) and systematic reviews (L. F. Brown & Kroenke, 2009; H. S. Oh & Seo, 2011).

Nevertheless, it could be seen that the coefficient between anxiety and fatigue was quite small ($\beta = 0.115$, $p < 0.05$). This suggests that although the reduction of anxiety may provide positive outcomes in fatigue, the effectiveness of such intervention might not be high. However, it is strongly believed that this factor should not be neglected in the management of fatigue because this psychological problem is a very common and basic experience of human beings, which significantly influence one's well-being. Therefore, the combination of anxiety in an integrated fatigue-controlling program is recommended.

It was found that nutrition status negatively and directly affects fatigue. Nutrition was described as one of the modifiable influencing factors of fatigue (Kalman & Villani, 1997). The finding of this study supported the use of nutritional intervention as mean to control fatigue. Once nutrition status is enhanced, it would help to lessen fatigue. However, as many other problems in cancer, it is not easy to enhance nutrition status itself (Bozzetti, 2013).

According to Kalman and Villani (1997), nutritional intervention for fatigue in patients on chemotherapy should pay proper attentions on symptoms such as nausea, vomiting, loss of appetite or diarrhea. The management of these problems may help to prevent fatigue occurrence as well as to decrease its intensity. Additionally, the duration of nutritional intervention could also be important issues. It was asserted that "nutrition support for cancer patients is not considered appropriate when the expected duration is less than 5 days, or when, in a well-fed patient, the period of provided inadequate food intake is less than 10 days" (Nicolini et al., 2013).

It should be highlighted that the effect of nutrition status on fatigue found in this study was not high. More importantly, the NRI is calculated based on serum albumin and weights. One shortcoming of serum albumin is that it could rapidly change with metabolism, hormones, or underlying diseases (Fuhrman, 2002). There could be many other indicators of nutrition status (Barbosa-Silva, 2008), which were not studied in this research. Future studies focused on role of those factors in determining fatigue are recommended. The study of such indicators would offer more detailed understanding about the nature of their association with fatigue. Equally important, those findings would also help healthcare workers be more specific in designing their nutritional support programs.

With regard to physical activity, the hypothesis toward its negative and direct effect on fatigue was confirmed by the current study. The negative association between fatigue and physical activity was also found in other cancer population. For example a study with 47 breast cancer survivors found that (Schwartz Cancer Fatigue Scale) is significantly associated with physical activity (minutes per week). The coefficient was of - 0.23 ($p < 0.05$) (Winters-Stone, Bennett, Nail, & Schwartz, 2008). This means intervention aimed to make patients more physically active would help lessening fatigue. Physical activity indeed is one of the most widely recommended interventions for fatigue in cancer population (Albrecht & Taylor, 2012).

According to Al-Majid and Gray (2009), the interrelationship among biological factors including decreased skeletal muscle mass and strength, anemia, and increased levels of proinflammatory cytokines make patients fatigued. Hypothetically, physical activity attenuates the interrelationships as well as directly affects each biological variable, and, as the result, offering impacts on fatigue.

In the current study, physical activity referred to all bodily movements that consume energy. Its measurement, the International Physical Activity Questionnaire is also the general physical activity. The concept of physical activity in this study did not limit to leisure physical activity as mentioned in many previous studies (Labourey, 2007). Therefore, the finding of this study appeared not to support only the use of exercise in intervention design. Indeed, it suggested that enhancing patients' physical functioning, including exercise, should be considered as mean to reduce fatigue. Clinical trials can examine the effectiveness of such programs in the future.

Previous study has reported the factors that prohibit patients from exercising as much as they desired. Barriers were fatigue (74%), physical discomfort (nausea, pain) (45%), lacking an appropriate exercise opportunity (15%), lacking exercise partners (14%), uncertainty about own goals/lack of recommendations (14%), busy daily life (14%), and economic hindrances (3%) (Midtgaard et al., 2009). Therefore, nurses, who wish to enhance physical activities in patients, should consider those factors in their interventions.

This study observed the interplays among insomnia, dyspnea, cough, anxiety and fatigue. This finding is in agreement with assumptions of Lenz and Pugh (2008). These theorists strongly support the idea that concurrent symptoms are interactive. Previous descriptive studies also found these symptoms formed symptom clusters – a group of symptoms, which occur closely together (Cheville et al., 2011a; A. G. Gift, A. Jablonski, M. Stommel, & C. W. Given, 2004; Wang et al., 2008).

In the current study, cough and dyspnea significantly impacted fatigue with quite similar total effects (0.343 and 0.397). It suggested that either of them could be the selected factors for fatigue controlling program. However, this study recommended the

selection of dyspnea over cough. There are two reasons for that suggestion.

Firstly, data indicated that both dyspnea and cough had direct and indirect effects on fatigue. However, interestingly, those effects were not similar. In particular, the direct effect of cough was smaller than its indirect effect on fatigue (0.143 and 0.200, respectively). In contrast, the direct effect of dyspnea was higher than its indirect effect on fatigue (0.266 and 0.131, consecutively). Therefore, it assumed that the change of dyspnea would lead to better immediate improvement in fatigue.

Secondly, in comparison to cough, dyspnea appeared to be more distress and problematic. Study found that dyspnea is significantly affects patients life, making them more dependent (Henoch, Bergman, Gustafsson, Gaston-Johansson, & Danielson, 2008) or even negative perception of self (Lai et al., 2007). Patients asserted to suffer from pain rather than from dyspnea. The symptom even make some patients want to suicide (Lai et al., 2007). Cough, on the other hand, appears to be more "acceptable" and patients could be able to adapt to live harmoniously with the symptom (Molassiotis et al., 2011).

Finding of this study pointed out that insomnia would be, besides dyspnea, another factor of choice for the development of fatigue control programs. The total effect of insomnia on fatigue was the third-biggest one among effects of variables in this study (0.318, $p < 0.01$). Remarkably, effect is only direct. Interventions for insomnia are vastly available, both pharmacological and non-pharmacological approaches (Bain, 2006; Induru & Walsh, 2013). It was found that stimulus control, daytime sleep restriction, and combined approaches are the most effective intervention for insomnia in cancer. Sleep hygiene education alone may produce only modest outcomes in this group (Induru & Walsh, 2013). Nurses should consider these

interventions to control insomnia and as the result, improve patients' fatigue.

CONCLUSIONS

The current study examined a causal model of fatigue in lung cancer patients receiving chemotherapy. The hypothesized model consisted of stage of disease, number of completed chemotherapy cycles, nutrition status, physical activity, insomnia, anxiety, cough, and dyspnea. 246 patients from 6 oncology centers in Vietnam completed self-administered questionnaires.

The majority of the sample was male (72.8%) and the mean age was 60.79 ± 6.59 years. The most common education level was high school (34.6%). The mean duration of diagnosis time with lung cancer was 5.44 ± 3.96 months (range 1-26 months).

The mean score of fatigue was 27.69 ± 11.12 with the range from 0 to 49. The majority of the sample was at stage IV (35.0%) and III (37.8%). Patients had completed their chemotherapy from 1 to 8 cycles (mean = 2.55 ± 1.42). Notably, more than half (50.8%) of the sample had some degrees of malnutrition. Nearly one-third (28.5%) of subject was categorized at a low level of physical activity. The mean score of insomnia was 13.46 ± 5.73. Nearly half (48%) of the sample had moderate to severe insomnia. The mean scores of anxiety, cough, and dyspnea were 6.26 ± 3.7 (range 0-15), 23.89 ± 7.9 (range 11-42), and 11.97 ± 6.93 (range 0-29), respectively.

The initial model was found not to well fit to the empirical data. The model was modified by 1) removing the causal path from number of completed chemotherapy cycles to fatigue, 2) adding a causal path from dyspnea to anxiety, and 3) adding a causal path from stage of disease to physical activity. The final model then fit well to empirical data and explain 42.9% of fatigue variance ($\chi 2 = 51.556$, df = 38, p = 0.070;

$\chi 2$/ df = 1.357; GFI = 0.963; AGFI = 0.937; CFI = 0.974; RSMEA = 0.038). Among eight hypotheses of this study, seven were fully or partially supported by empirical data and one was failed to be accepted. In particular:

Empirical data supported the hypothesis that insomnia has a positive and direct effect to fatigue. The result showed that the total effect of insomnia to fatigue was 0.318 ($p < 0.01$).

Empirical data supported the hypothesis that anxiety has a positive and direct effect to fatigue. The result showed that the total effect of anxiety to fatigue is 0.115 (0.031).

Empirical data supported the hypothesis that physical activity has a negative and direct effect to fatigue. The result showed that the total effect of physical activity to fatigue is - 0.148 ($p < 0.01$).

Empirical data supported the hypothesis that nutrition status has a negative and direct effect to fatigue. The result showed that the total effect of nutrition status to fatigue is - 0.156 ($p < 0.01$).

Empirical data supported the hypothesis that cough has positive effects, both direct and indirect (through insomnia and dyspnea), to fatigue. The result showed that the total effect of cough to fatigue is 0.343 ($p < 0.01$). The direct effect is 0.143 ($p < 0.01$) and indirect effect is 0.200 ($p < 0.01$).

Empirical data partially supported the hypothesis that dyspnea has positive effects, both direct and indirect (through insomnia), to fatigue. The result showed that the total effect of dyspnea to fatigue is 0.397 ($p < 0.01$). The direct effect is 0.266 ($p < 0.01$) and indirect effect is 0.131 ($p < 0.01$). Dyspnea had a significant impact on and

anxiety ($\beta = 0.269$, $p < 0.01$), not only on insomnia ($\beta = 0.317$, $p < 0.01$) only as in the initial hypothesis.

Empirical data partially supported the hypothesis that stage of disease has a positive and direct effect to fatigue. The result showed that the total effect from stage of disease to fatigue is 0.179 ($p < 0.05$). Stage of disease did not only have direct effect 0.154 ($p < 0.05$), but also had the indirect effect (via physical activity) ($\beta = -0.170$, $p < 0.01$) in fatigue.

Empirical data did not support the hypothesis that number of completed cycles has a positive and direct effect to fatigue. The result showed that the regression weight from number of completed cycles to fatigue was non-significant.

RECOMMENDATIONS

Recommendations for nursing practices

Based on the findings, to lessen fatigue of lung cancer patients, it is suggested that Vietnamese nurses should develop interventions aimed at reducing dyspnea, insomnia, cough, and anxiety. In addition, programs help improving nutrition status and physical activity would also alleviate fatigue. Based on the effect size, insomnia and dyspnea appear to be factors of choice for future interventions.

The interplay found among cough, dyspnea, and fatigue suggested that Vietnamese nurses should consider to develop integrative program, which combines means to reduce these three symptoms simultaneously. It is believed that the comprehensive program may be more effective than separate interventions which focus on single symptom.

Recommendations for nursing education

Findings in this study could be used in nursing education. Firstly, the study pointed out the factors that Vietnamese nurses could use to develop fatigue interventions. Secondly, this study provided preliminary descriptive information on several common health problems of lung cancer population, which are fatigue, anxiety, physical activity, nutrition status, cough, dyspnea, and insomnia. Vietnamese nurse educators can integrate such information in their curriculum. Equally important, instructors can revise their curriculum, emphasize their teaching content on severe and important problems in Vietnamese lung cancer patients, such as fatigue, dyspnea, or insomnia. It is believed that the use of this study findings in nursing education would help student nurses be aware of, and concern to those problems in their future practices.

Recommendations for nursing research

Research design

This study was a cross-sectional research. The findings estimated the size effects of independent variables on fatigue. Thus, it may help nurses foresee the possible outcomes if a certain variable is selected for their interventions. However, due to the nature of its research design, the findings itself cannot be inferred as the approval of the causality among studied variables. Therefore, trials testing the real outcomes of interventions, which use the factors suggested from this study, are recommended.

Sample and sampling

In the current study, the convenient sampling method was used to recruit participants. It is assumed that the use of a convenience sample may influence the generalizability of the findings. Thus, other researchers are recommended to consider random technique in their study.

This study was conducted in the centre and the north of Vietnam. It is believed that the findings could represent more comprehensive picture about fatigue in Vietnamese lung cancer patients if the sample was larger and recruited throughout the country. Thus, future studies recruited patients from various centers nationwide are recommended.

In addition, it was found that the magnitude of the fatigue variance explained by this study's model was moderate. It suggested that other researchers could include other variables in the model to depict a more comprehensive picture about causality of fatigue in lung cancer population on chemotherapy.

Measurement and data collection

Up to our knowledge, this study was the first one which translated and examined psychometric properties of the instruments such as FACT-F, ISI, MCLCS or CDS. Future studies to further investigate other psychometric properties of those instruments in both lung cancer and other cancer population are recommended.

In the current study, several patients reported a zero score on fatigue, insomnia, and anxiety. The zero scores indicated that the patients did not experience those problems at the time the data collected. It is impossible to assure that those zero scores reflected the true experience of patients or due to any confounding factors. Nevertheless, during the data collection, it was noticed that social desirability could be the issue that future researchers should be cautious. Some participants, especially who were newly diagnosed with the disease and have just started their treatments, wished to look healthy. They appeared not want to express their problems, which may suggest the severity of the disease or the impacts of the treatment. Researchers in the future should consider to solve this issue in their studies.

Theoretical guide issues

The theoretical framework of this study was the Piper Integrated Cancer Fatigue Model Up to date, this model appears to be the most comprehensive model explaining fatigue in cancer population. The hypothetical associations between influencing factors and fatigue were supported in this study. It demonstrated that the model is valid to explain fatigue in lung cancer subjects on chemotherapy.

Nevertheless, the use of this model revealed some shortcomings. Firstly, although the model depicts various groups of factor modulating fatigue, some concepts were not clearly described. Therefore, the derivation of variables, especially latent variables from such concepts faces many difficulties. Secondly, IFM did not propose any interplays

among 14 influencing patterns of fatigue. Therefore, researchers, who wish to investigate interactions among determinant patterns, have to rely on very intensive synthesis of the literature.

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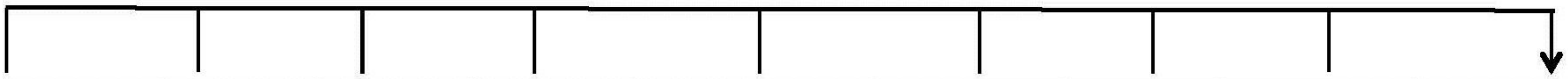
APPENDICES

APPENDIX A
THEORY SUBSTRACTION



Theoretical level	**Changes in energy and energy substrate patterns**	**Disease patterns**	**Activity/rest pattern**	**Symptoms patterns**		**Accumulation of metabolites**	**Sleep/awake patterns**	**Psychological patterns**	**Fatigue manifestations**
Variables	Nutritional status	Stage of disease	Physical activity	Dyspnea	Cough	Number of cycles completed	Insomnia	Anxiety	Fatigue
Empirical indicators	NRI	TNM classification	IPAQ-Sh	CDS	MCLCS	Number of cycles completed	ISI	DASS-21	FACT-F

NRI: Nutritional Risk Index; IPAQ-Sh: I International Physical Activity Questionnaire – Short form; CDS: Cancer Dyspnea Scale; MCLCS: Manchester Cough in Lung Cancer Scale; ISI: Insomnia Severity Index; DASS-21: Depression Anxiety Stress Scale -21; FACT-F: FACT-Fatigue Subscale

APPENDIX B
INSTRUMENTS

Date:_____

GENERAL INFORMATION

Code number:_____ **Hospital:**_____

Age:_____ **Time from diagnosis: _____months**

Gender: Male ☐ Female ☐

Stage: Stage I ☐ Stage II ☐ Stage III ☐ Stage IV ☐

Metastasis sites:_____

Treatment

Number of cycle completed:_____

Tumor removal surgery before: Yes ☐ No ☐

Additional notes on treatments:_____

Education		**Religion**	
Primary school	☐	Non-religion	☐
Secondary school	☐	Buddhism	☐
High school	☐	Christian	☐
Vocational school	☐	Others	☐
University and higher	☐		

Employment status Current worker ☐ Non-current worker ☐

Height: _____cm **Usual weight:** _____ kg **Current weight:** _____ kg

Current laboratory test

Hemoglobin	Albumin	Neutrophil

FATIGUE QUESTIONNAIRE (FACT – F)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

ADDITIONAL CONCERNS	**Not at all**	**A little bit**	**Some -what**	**Quite a bit**	**Very much**
I feel fatigued	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I feel listless ("washed out")	0	1	2	3	4
I feel tired	0	1	2	3	4
I have trouble starting things because I am tired	0	1	2	3	4
I have trouble finishing things because I am tired	0	1	2	3	4
I have energy	0	1	2	3	4
I am able to do my usual activities	0	1	2	3	4
I need to sleep during the day	0	1	2	3	4
I am too tired to eat	0	1	2	3	4
I need help doing my usual activities	0	1	2	3	4
I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
I have to limit my social activity because I am tired	0	1	2	3	4

FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT) LICENSING AGREEMENT

May 24, 2014

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INSOMNIA SEVERITY INDEX

For each question, please CIRCLE the number that best describes your answer.

Please rate the CURRENT (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia problem	None	Mild	Moderate	Severe	Very severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problem waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Much	Somewhat	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

RE: The permission for the use of Insomnia Severity Index

From: **Charles M. Morin** (cmorin@psy.ulaval.ca)
Sent: Monday, August 11, 2014 9:41:03 PM
To: Nguyen Hoang Long (long.51@hotmail.com)

Permission is granted to translate and use the ISI in your research. Good luck.

Charles M. Morin, Ph.D.

Professeur titulaire

Université Laval

École de Psychologie

2325, rue des Bibliothèques

Québec (Québec)

Canada G1V 0A6

Phone: 418-656-3275

FAX : 418-656-5152

THE MANCHESTER COUGH IN LUNG CANCER SCALE

This questionnaire asks you to describe your experience of cough in the past week.

Please answer question one and then read the instructions before completing the rest of the questionnaire.

	Never	Some of the time	Often	Most of the time	All of the time
1. In the past week how often have you coughed?	1	2	3	4	5

If you answered ‘‘Never’’ to question 1, please stop completing the questionnaire and return it to us.

If you indicated that you have experienced cough in the past week, then please complete the rest of the questionnaire.

For each question, please circle one option that best describes your experience over the past week.

	Never	Some of the time	Often	Most of the time	All of the time
2. Do you have difficulty breathing when you cough?	1	2	3	4	5
3. Do you have difficulty bringing up sputum (phlegm) when you cough?	1	2	3	4	5
4. Does your cough disturb your sleep?	1	2	3	4	5
5. Does your cough distress you?	1	2	3	4	5
6. Does coughing make you frustrated?	1	2	3	4	5
7. Do you worry that your cough means that your condition is getting worse?	1	2	3	4	5
8. Do you feel in control of your cough?	1	2	3	4	5

9. Does coughing interrupt your conversations or telephone calls?	1	2	3	4	5

In question 10, you should indicate how severe your cough has been in the past week.

	Very mild	Mild	Moderate	Severe	Very severe
10. Please rate how severe you think your cough is	1	2	3	4	5

RE: A request for the permission of using the MCLCS

From: **MOLASIOTIS, Alex [SN]** (alex.molasiotis@polyu.edu.hk)
Sent: Monday, September 15, 2014 12:50:50 PM
To: Nguyen Hoang Long (long.51@hotmail.com)
1 attachment
cough scale.pdf (444.6 KB)

Dear Nguyen

Thank you for your interest in using the cough scale I have developed. I give you my permission to use and translate the scale to Vietnamese, using forward/back translation, as explained below. Please let me have the translated instrument and any data about it in due course.

Best wishes

Alex

FORWARD/BACK TRANSLATION

The forward/back translation method requires, at a minimum, having one bilingual expert translate the English version of the document/tool to another language (forward translation) and having a second bilingual expert independently translate the tool that is in another language back into English (back translation) without any reference to the original teaching tool's wording. The original tool and back-translated version are then compared and if discrepancies are noted, the problematic terms or passages are retranslated and blindly back translated by another bilingual expert until no error of meaning is found.

Prof. Alex Molasiotis, RN, PhD

Angel S.P. Chan Lau Endowed Professor in Health & Longevity

Chair Professor of Nursing and Head of School

School of Nursing; &

THE CANCER DYSPNOEA SCALE

We would like to ask you about your breathlessness or difficulty in breathing. Please answer each question by circling only the numbers that best describes the breathing difficulty that you felt *during the past few days*. Base your response on your first impression.

	Not at all	A little	Some-what	Consider-ably	Very much
Can you inhale easily?	1	2	3	4	5
Can you exhale easily?	1	2	3	4	5
Can you breathe slowly?	1	2	3	4	5
Do you feel short of breath?	1	2	3	4	5
Do you feel breathing difficulty accompanied by palpitations and sweating?	1	2	3	4	5
Do you feel as if you are panting?	1	2	3	4	5
Do you feel such breathing difficulty that you don't know what to do about it?	1	2	3	4	5
Do you feel your breath is shallow?	1	2	3	4	5
Do you feel your breathing may stop?	1	2	3	4	5
Do you feel your airway has become narrower?	1	2	3	4	5
Do you feel as if you are drowning?	1	2	3	4	5
Do you feel as if something is stuckin your airway?	1	2	3	4	5

From: **Yosuke Uchitomi** uchitomi@md.okayama-u.ac.jp
Subject: RE: A permission to use the Cancer Dyspnea Scale
Date: August 8, 2014 at 12:32 PM
To: Nguyen Hoang Long long.51@hotmail.com, uchitomi@okayama-u.ac.jp
Cc: uchitomi@md.okayama-u.ac.jp

Dear Ms. Nguyen Hoang Long, R.N, M.N.S

Thank you for your interest. I permit you to translate into Vietnamese.
Look forward to seeing your paper.
My best regards,
Yosuke, Uchitomi, MD, PhD,

Email: uchitomi@md.okayama-u.ac.jp
Department of Neuropsychiatry,
Okayama University Graduate School of Medicine,
Dentistry, and Pharmaceutical Sciences(^^)(^_^)(^^)(^_^)

DASS21 (Anxiety) *Name:*

Date:

Please read each statement and circle a number 0, 1, 2 or 3 that indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all

1 Applied to me to some degree, or some of the time

2 Applied to me to a considerable degree, or a good part of time

3 Applied to me very much, or most of the time

1	I was aware of dryness of my mouth	0	1	2	3
2	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
3	I experienced trembling (eg, in the hands)	0	1	2	3
4	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
5	I felt I was close to panic	0	1	2	3
6	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
7	I felt scared without any good reason	0	1	2	3

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

_____ **days per week**

☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

_____ **hours per day** _____ **minutes per day**

☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week**

☐

No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day** _____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day** _____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

APPENDIX C

PATIENT INFORMATION SHEET, CONSENT FORM AND IRB APPROVAL

PARTICIPANT INFORMATION SHEET

1. Title of study: A CAUSAL MODEL FOR FATIGUE IN VIETNAMESE PERSONS WITH LUNG CANCER RECEIVING CHEMOTHERAPY

2. Researcher name: Nguyen Hoang Long, RN, M.N.S

3. Title: Lecturer, Faculty of Health Science Thang Long University, Ha Noi, Vietnam
PhD Student, Faculty of Nursing Chulalongkorn University, Bangkok, Thailand

As the persons who have been working with individuals with lung cancer, we understand that fatigue is one of your severe health problem. In order to relieve fatigue, we would like to examine the factors that may cause or exacerbate this symptom. That is the reason why we would like to conduct this study.

We would like to invite you to participate in this study. We do believe that information given by you is very valuable. It will facilitate healthcare workers in reducing this distressing symptom. Please understand that your participation is the help for us as well as for individuals who have the same disease like yours in the future. However, before you decide whether you want to take part, please use several minutes to read the following short paragraphs. We would like to explain more about the study.

Who are invited to participate in this study?

We would like to individuals who have lung tumor and receiving chemotherapy. 242 participants will be recruited.

What do the participants do in this study?

We would like to ask participants to answer several questionnaires (by paper and pencil) about your symptom (fatigue, anxiety, insomnia, cough, and dyspnea) and other health problems (physical mobility and nutritional status). It takes about 20 minutes to complete all the questionnaires. After you finish answering, we would like

to check the complement of the questionnaires. The researcher may consult you about items that you leave blank. We also will obtain information related to your disease from your medical record after being permitted by you and your physician.

What are the potential risks for the participants?

We assume there are no risks to your health during participating in this study.

Do the invited persons have to involve in the study?

Your participation is definitely voluntary. Please feel freely to refuse participating if you wish to. Either you participate or not, your normal healthcare procedures will not be affected.

Can the participant stop involving in the study?

You have all rights to stop answering at any time without prejudice. You also do not have to explain the reason of the leaving.

How the information given by the participants will be used?

All questionnaires will be kept confidentially by the researchers. No information related to your personal identification is disclosed during data analysis and result report. Information is used for the purpose of this study only.

Who can the participants contact with if necessary?

Please do not feel hesitate to contact the researcher any time you wish to.

Name: Nguyen Hoang Long, RN, M.N.S

Postal mail: Department of Nursing, Faculty of Health Science, Thang Long University, Hoang Mai district, Ha Noi, Vietnam

Phone (office): 04-3-858-7347 *Email:* long.51@hotmail.com

One copy of this form will be given to you

CONSENT FORM

Research title: A CAUSAL MODEL FOR FATIGUE IN VIETNAMESE PERSONS WITH LUNG CANCER RECEIVING CHEMOTHERAPY

Code number: _____

Declaration by Participant

I have read through the Participant Information Sheet (or the researcher has read it to me). I have had an opportunity to ask questions about information provided and I am satisfied with the answers I have received. I understand the purposes, procedures and risks of the research.

I freely agree to participate in this research and accept the procedure as described in the information sheet. I know that I am free to withdraw at any time during the project without affecting my future health care.

I am willing to participate in this study under the above conditions.

Name of participant:_____ *Please sign:*_____

Location:_____ Date: _____

Name of witness:_____ *Please sign*:_____

Location:_____ Date: _____

Declaration by Researcher

I have given an explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of researcher:_____ Signature:_____

Location:_____ Date: _____

MINISTRY OF HEALTH
HANOI SCHOOL OF PUBLIC HEALTH

No.: 282/2014/YTCC-HD3
Subject: Ethical Approval

SOCIALIST REPUBLIC OF VIETNAM
Independence – Freedom - Happiness

Ha Noi, October 02, 2014

DECISION
On Ethical approval for research involving human subject participation

THE CHAIR OF THE ETHICAL REVIEW BOARD FOR BIOMEDICAL RESEARCH
HANOI SCHOOL OF PUBLIC HEALTH

- Based on Decision No. 201/QD-YTCC by the Dean of Hanoi School of Public Health on Establishment of The Institutional Ethical Review Board of Hanoi School of Public Health; 12 April 2012 ;
- Based on decision No. 202/QĐ-YTCC by the Dean of Hanoi School of Public Health on the Issuing Regulation of the Insitutional Ethical Review Board of Hanoi School of Public Health; 12 April 2012;
- After reviewing research ethics application No. **014-282/DD-YTCC** submitted by Nguyen Hoang Long – Faculty of Nursing- Thang Long University on 28 September, 2014.

DECIDED

Article 1. Grant ethical approval for ethnographic study project:

- Project Title: **A causal model for fatigue in Vietnamese persons with lung cancer receiving chemotherapy**
- Principal Investigator : **Nguyen Hoang Long-** Faculty of Nursing- Thang Long University; PhD candidate- Faculty of Nursing- Chulalongkorn University- Thailand.
- Supervisor**:** Associate Prof. Dr. Sureeporn Thanasilp- Faculty of Nursing- Chulalongkorn University- Thailand
- Research site: 10 hospitals in Northern of Vietnam.
- Project time: from 16/05/2014 to 30/10/2016
- Data collection time: from 10/10/2014 to 30/05/2015
- Review process: exempt review

Article 2. This decision is effective from **02/10/2014.**

Article 3. Principle Investigator should notify the Institutional Ethical Review Board of Hanoi School of Public Health (IRB of HSPH) immediately of any adverse effects arising from this study (e.g. unexpected adverse outcomes, unexpected community/subject risk factors or complaints, etc.). Active research projects are subject to random audit by the IRB of HSPH.

CHAIR OF
INSTITUTIONAL ETHICAL REVIEW BOARD
(Signature and full name)

Do Mai Hoa

SECRETARY
(Signature and full name)

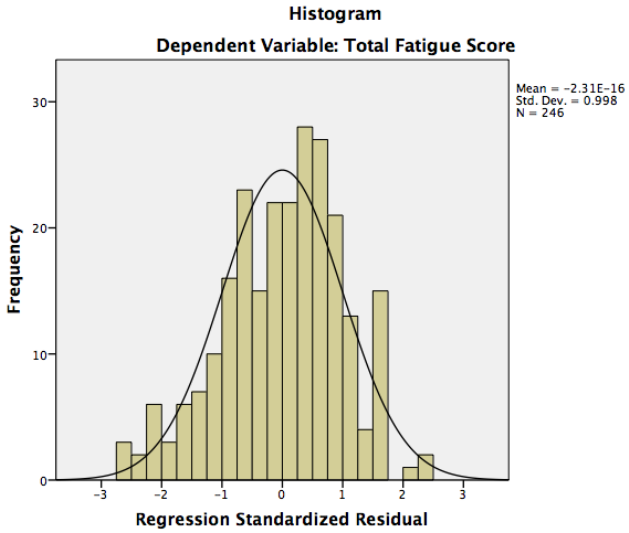
Nguyen Thi Minh Thanh

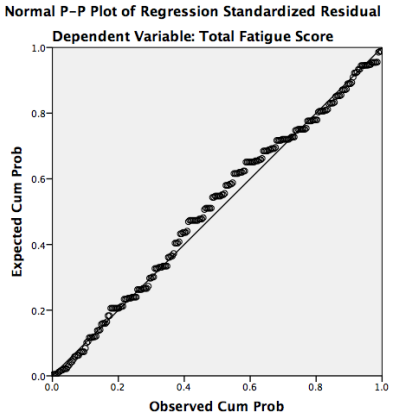
APPENDIX D

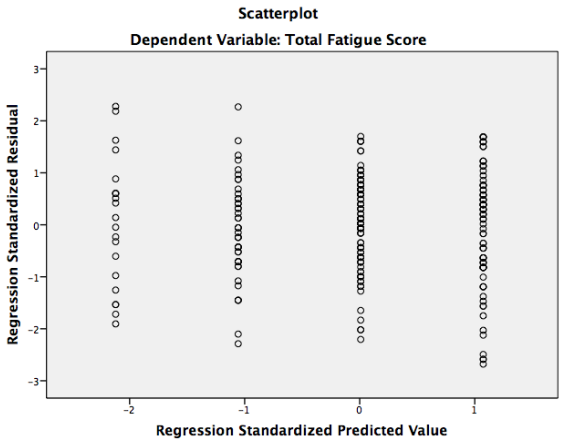
ASSUMPTION TESTING

(Linearity and Homoscedasticity)

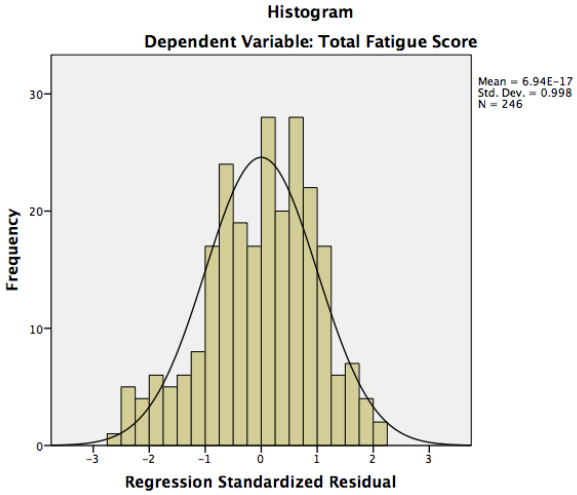
Fatigue vs Severity

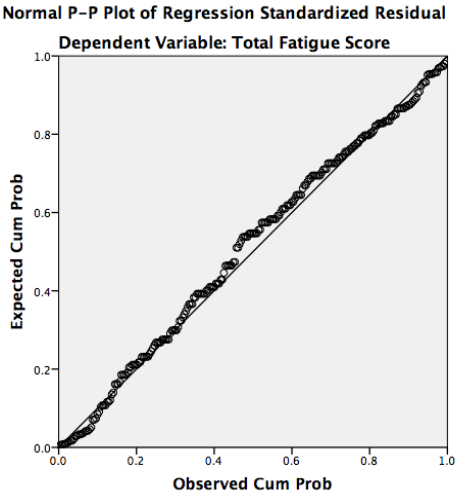


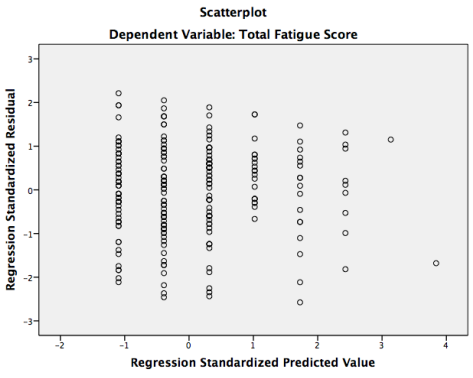




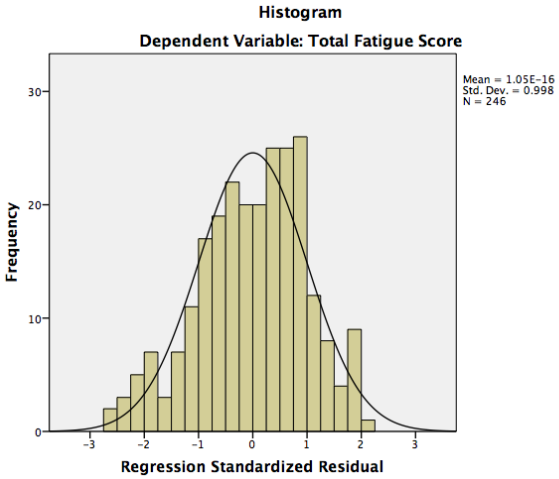
Fatigue vs Number of completed chemotherapy cycles

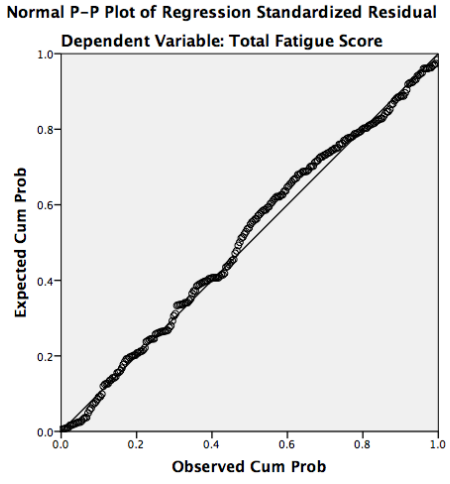


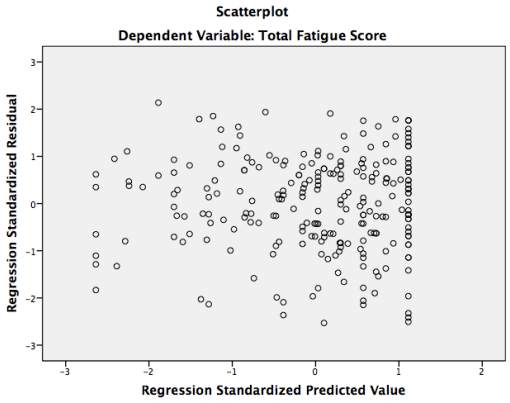




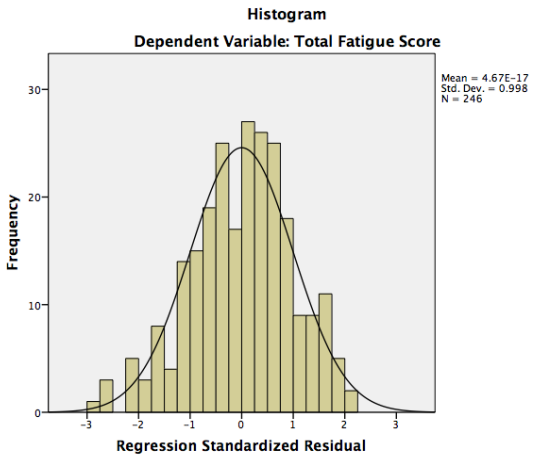
Fatigue vs Physical activity

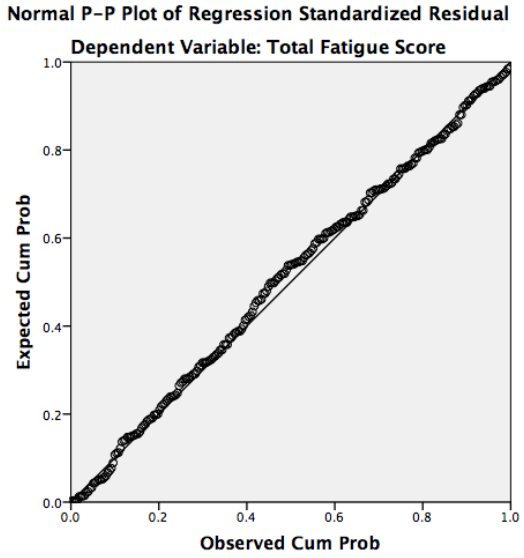


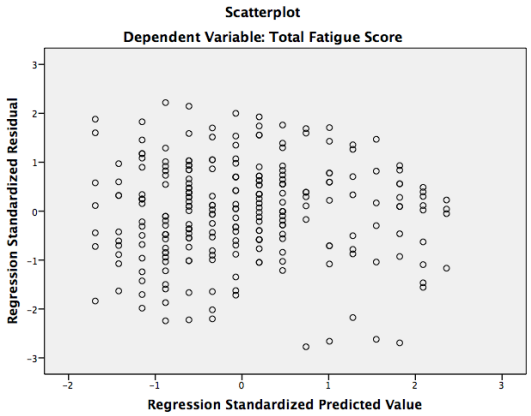




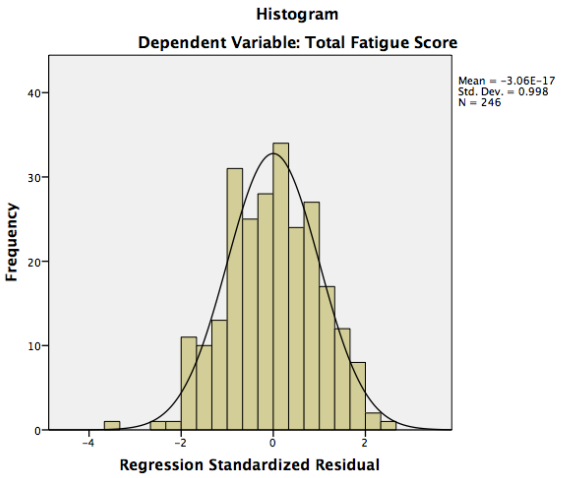
Fatigue vs Anxiety

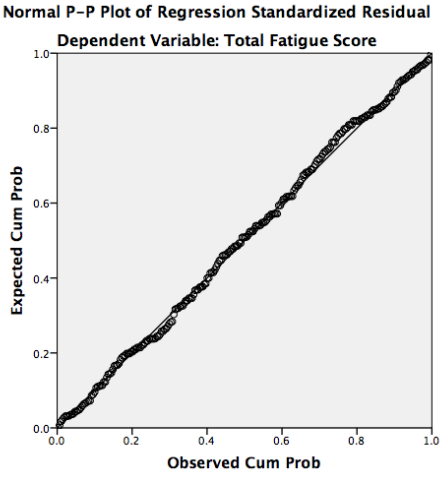


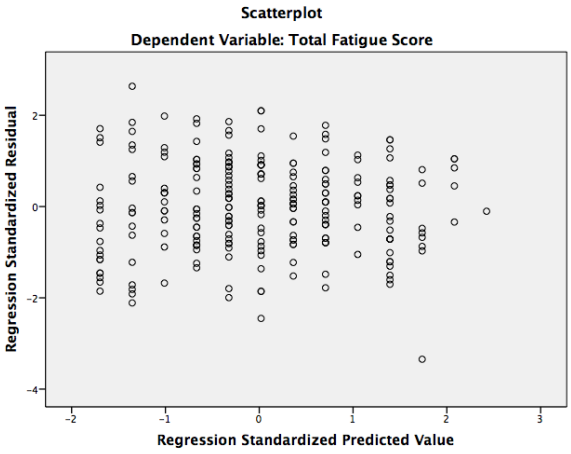




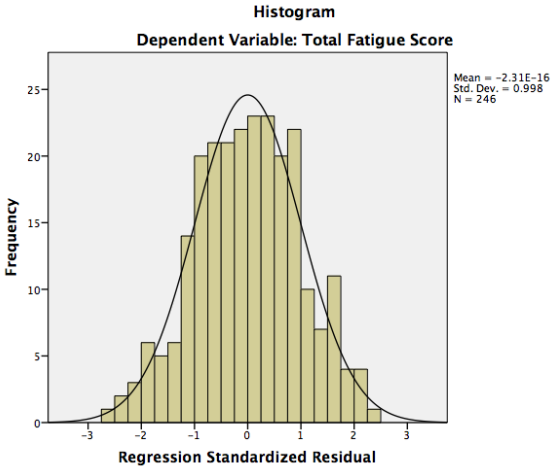
Fatigue vs Insomnia Interference

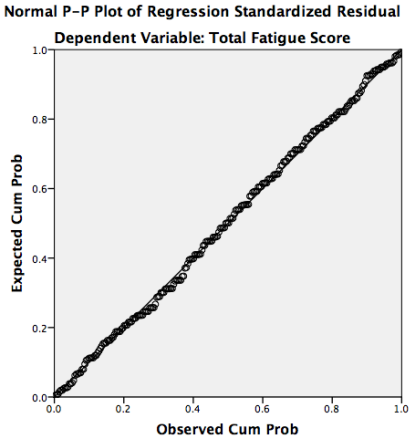


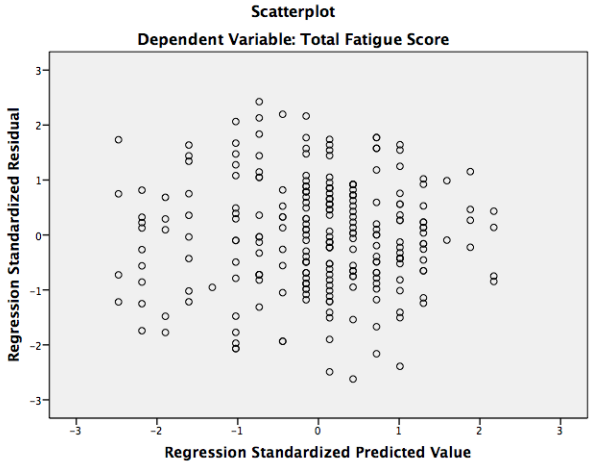




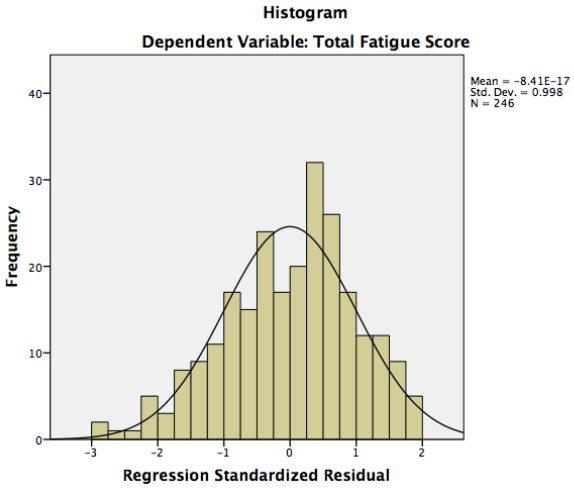
Fatigue vs Insomnia Severity

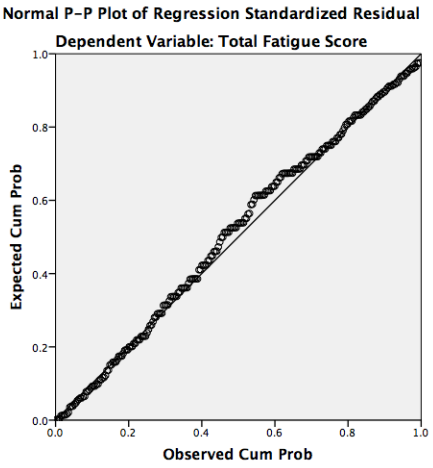


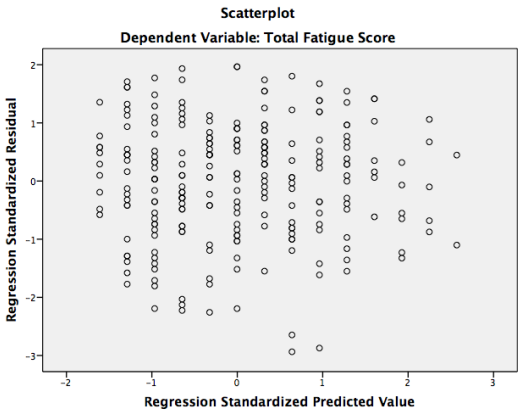




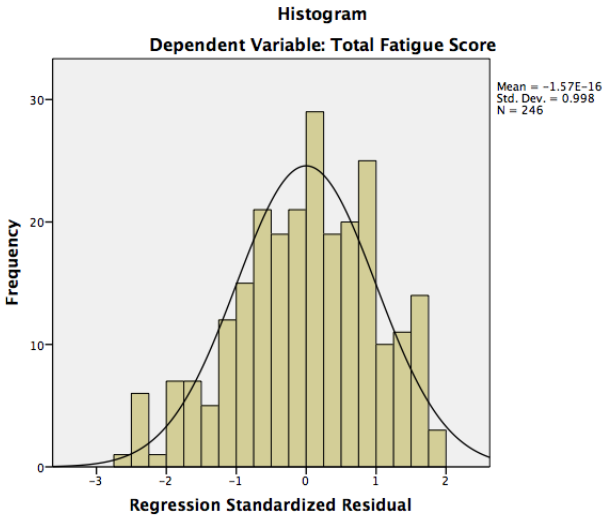
Fatigue vs Dyspnea Sense of Effort

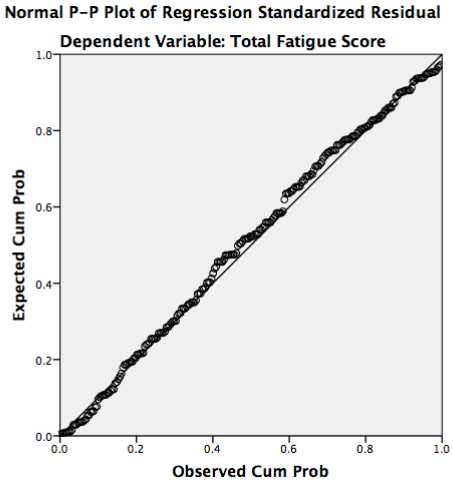


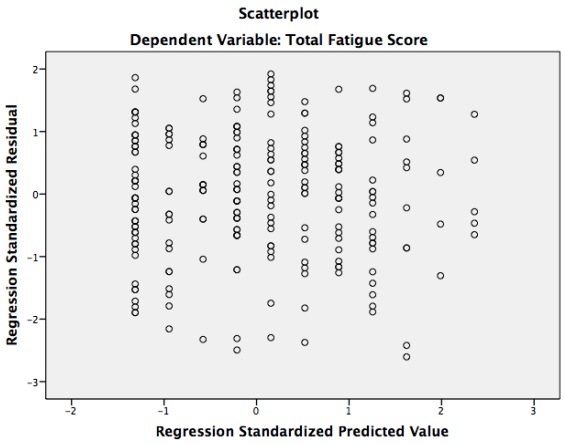




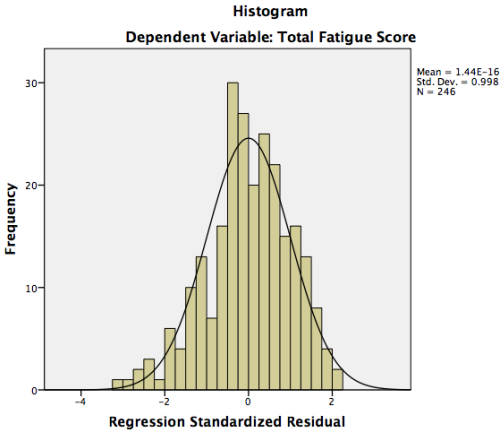
Fatigue vs Dyspnea Sense of Discomfort

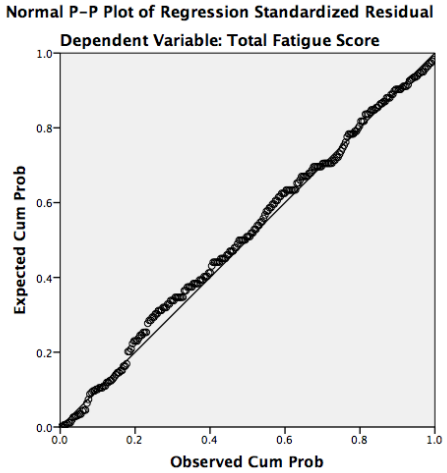


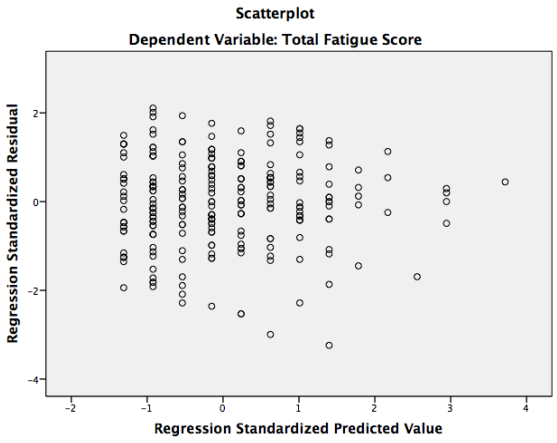




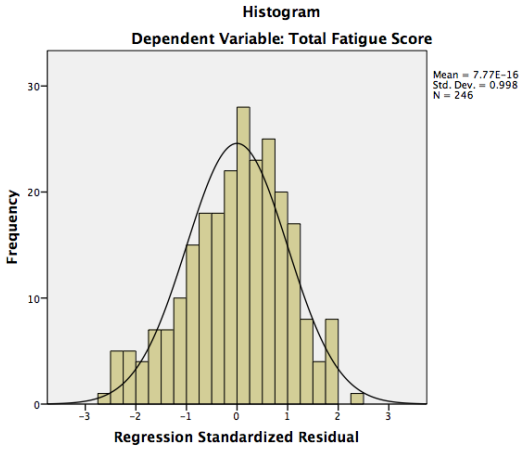
Fatigue vs Dyspnea Sense of Anxiety

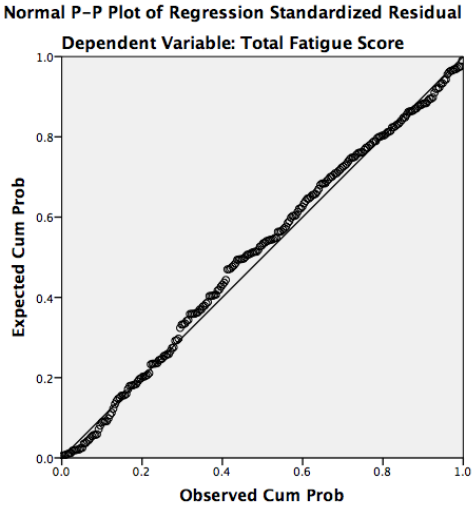


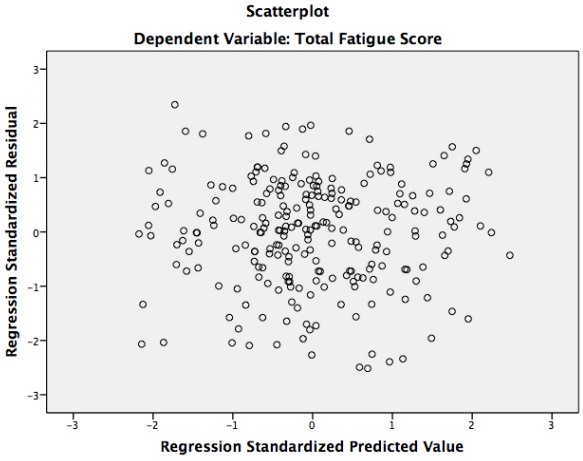




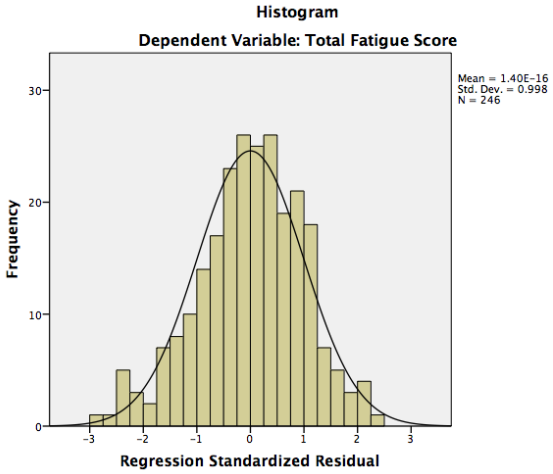
Fatigue vs Nutrition Status

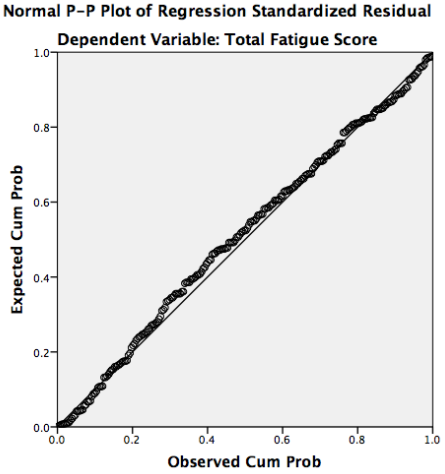


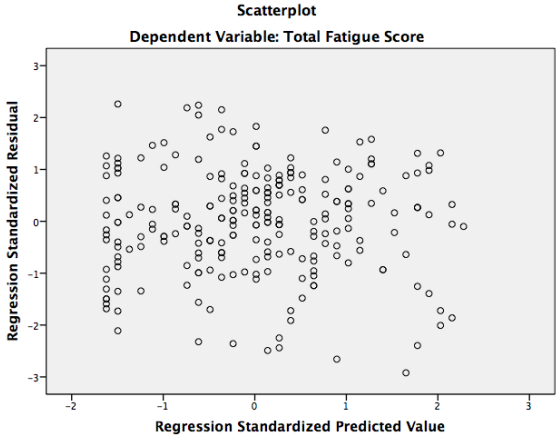




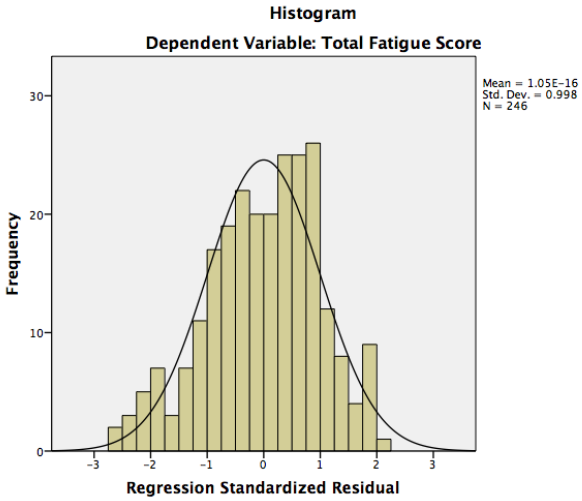
Fatigue and Cough

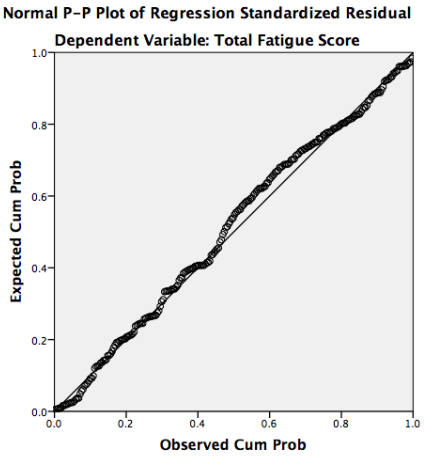


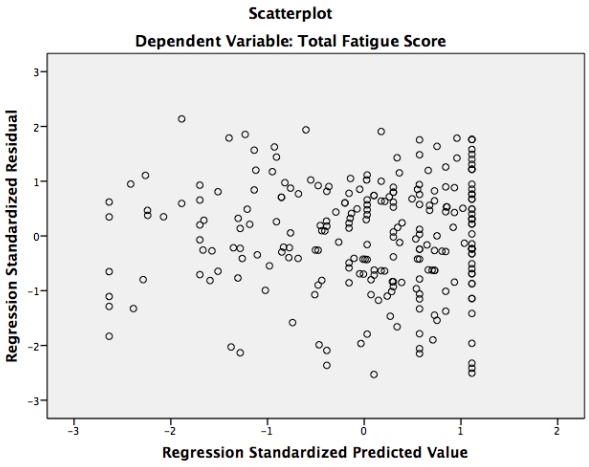




Fatigue vs Physical Activity







APPENDIX E
STRUCTURAL REGRESSION MODELS

Initial model

Group number 1 (Group number 1)

Notes for Group (Group number 1)

The model is recursive.

Sample size = 246

Variable Summary (Group number 1)

Your model contains the following variables (Group number 1)

Observed, endogenous variables

DyspneaEffort

DyspneaAnxiety

DyspneaDiscomfort

Insominfluence

Insomserverity

Anxietytotal

Coughtotal

TotalMET

Serverity

Nutritionscore

Fatiguescore

ChemoCyclecompleted

Unobserved, endogenous variables

Dyspnea

Insomnia

Fatigue

Unobserved, exogenous variables

r_dys_effort

r_dys_anxiety

r_dys_discomfort

r_insom_influence

r_insom_severity

Anxiety

r_anxiety_score

r_cough_score

Physicalactivity

r_MET

Severity

r_disease_severity

Nutrition

r_nutrition_score

r_fatigue_score

Cough

r_dyspnea

r_insomnia

r_fatigue

numberofcycles

r_chemocompleted

Variable counts (Group number 1)

Number of variables in your model:	36
Number of observed variables:	12
Number of unobserved variables:	24
Number of exogenous variables:	21
Number of endogenous variables:	15

Parameter Summary (Group number 1)

	Weights	Covariances	Variances	Means	Intercepts	Total
Fixed	24	0	7	0	0	31
Labeled	0	0	0	0	0	0

	Weights	Covariances	Variances	Means	Intercepts	Total
Unlabeled	14	0	14	0	0	28
Total	38	0	21	0	0	59

Assessment of normality (Group number 1)

Variable	min	max	skew	c.r.	kurtosis	c.r.
ChemoCyclecompleted	1.000	8.000	.976	6.252	.678	2.171
Fatiguescore	.000	49.000	-.306	-1.962	-.341	-1.091
Nutritionscore	76.806	119.165	-.107	-.683	-.318	-1.017
Serverity	1.000	4.000	-.606	-3.883	-.554	-1.772
TotalMET	.000	4800.000	.870	5.569	-.035	-.113
Coughtotal	11.000	42.000	.169	1.084	-.625	-2.000
Anxietytotal	.000	15.000	.541	3.466	-.423	-1.353
Insomserverity	.000	16.000	-.452	-2.896	.013	.043
Insominfluence	.000	12.000	.127	.813	-.743	-2.378
DyspneaDiscomfort	.000	10.000	.300	1.921	-.801	-2.565
DyspneaAnxiety	.000	13.000	.798	5.108	.508	1.627
DyspneaEffort	.000	13.000	.392	2.511	-.627	-2.007
Multivariate					7.511	3.213

Observations farthest from the centroid (Mahalanobis distance) (Group number 1)

Observation number	Mahalanobis d-squared	p1	p2
144	30.029	.003	.494
80	27.923	.006	.407
191	27.194	.007	.264
124	27.039	.008	.121
215	26.481	.009	.078
183	24.801	.016	.196
214	24.679	.016	.113

Observation number	Mahalanobis d-squared	p1	p2
143	24.543	.017	.063
141	24.093	.020	.058
122	24.009	.020	.030
70	23.714	.022	.023
113	22.968	.028	.046
99	22.901	.029	.026
136	22.519	.032	.029
217	22.216	.035	.029
198	21.959	.038	.027
226	21.782	.040	.021
222	21.735	.041	.012
62	20.773	.054	.074
243	20.734	.054	.049
172	20.616	.056	.039
129	20.284	.062	.054
188	20.275	.062	.034
22	20.240	.063	.022
152	20.071	.066	.021
148	19.870	.070	.023
244	19.623	.075	.029
203	19.462	.078	.029
145	19.444	.078	.019
121	19.410	.079	.012
45	19.128	.085	.019
190	19.023	.088	.017
216	18.621	.098	.041

Observation number	Mahalanobis d-squared	p1	p2
104	18.431	.103	.049
179	18.394	.104	.037
227	18.316	.106	.031
220	17.711	.125	.132
27	17.531	.131	.156
135	17.425	.134	.154
2	16.890	.154	.377
130	16.855	.155	.334
158	16.730	.160	.349
74	16.599	.165	.370
65	16.576	.166	.323
13	16.427	.172	.357
46	16.389	.174	.321
34	16.087	.187	.465
140	15.896	.196	.540
176	15.728	.204	.599
16	15.670	.207	.580
102	15.627	.209	.550
90	15.529	.214	.562
30	15.412	.220	.588
185	15.271	.227	.634
184	15.109	.236	.694
125	15.101	.236	.645
66	15.097	.236	.590
24	14.981	.242	.621
63	14.939	.245	.596

Observation number	Mahalanobis d-squared	p1	p2
28	14.937	.245	.539
150	14.865	.249	.538
9	14.751	.255	.572
64	14.748	.255	.516
187	14.554	.267	.616
131	14.549	.267	.564
101	14.475	.271	.568
245	14.409	.275	.566
171	14.295	.282	.605
230	14.207	.288	.622
5	14.177	.290	.592
173	14.175	.290	.538
78	14.120	.293	.530
181	14.096	.295	.495
236	14.075	.296	.458
218	13.750	.317	.681
195	13.734	.318	.643
178	13.641	.324	.669
212	13.521	.332	.716
234	13.499	.334	.686
209	13.460	.336	.668
117	13.430	.339	.644
242	13.411	.340	.610
8	13.363	.343	.600
58	13.338	.345	.570
235	13.321	.346	.532

Observation number	Mahalanobis d-squared	p1	p2
160	13.286	.349	.511
53	13.186	.356	.550
211	13.081	.363	.594
219	13.073	.364	.550
149	13.041	.366	.527
98	13.033	.367	.481
17	12.951	.373	.506
193	12.875	.378	.526
84	12.705	.391	.634
54	12.688	.392	.599
151	12.643	.396	.591
3	12.642	.396	.541
21	12.622	.397	.508
92	12.531	.404	.545
246	12.514	.405	.510

Models

Default model (Default model)

Notes for Model (Default model)

Computation of degrees of freedom (Default model)

Number of distinct sample moments:	78
Number of distinct parameters to be estimated:	28
Degrees of freedom (78 - 28):	50

Result (Default model)

Minimum was achieved

Chi-square = 88.431

Degrees of freedom = 50

Probability level = .001

Group number 1 (Group number 1 - Default model)

Estimates (Group number 1 - Default model)

Scalar Estimates (Group number 1 - Default model)

Maximum Likelihood Estimates

Regression Weights: (Group number 1 - Default model)

			Estimate	S.E.	C.R.	P	Label
Dyspnea	<---	Cough	.109	.021	5.109	***	
Insomnia	<---	Cough	.054	.023	2.335	.020	
Insomnia	<---	Dyspnea	.313	.091	3.429	***	
Fatigue	<---	Physicalactivity	-.001	.000	-3.080	.002	
Fatigue	<---	Severity	1.600	.575	2.785	.005	
Fatigue	<---	Anxiety	.376	.148	2.541	.011	
Fatigue	<---	Nutrition	-.183	.059	-3.096	.002	
Fatigue	<---	Cough	.185	.077	2.417	.016	
Fatigue	<---	Dyspnea	1.199	.320	3.748	***	
Fatigue	<---	Insomnia	1.405	.317	4.431	***	
Fatigue	<---	numberofcycles	.764	.380	2.008	.045	
DyspneaEffort	<---	Dyspnea	1.000				
DyspneaAnxiety	<---	Dyspnea	.861	.092	9.316	***	
DyspneaDiscomfort	<---	Dyspnea	.722	.087	8.294	***	
Insominfluence	<---	Insomnia	1.000				
Insomserverity	<---	Insomnia	1.094	.150	7.315	***	
Anxietytotal	<---	Anxiety	1.000				
TotalMET	<---	Physicalactivity	1.000				
Serverity	<---	Severity	1.000				
Nutritionscore	<---	Nutrition	1.000				
Fatiguescore	<---	Fatigue	1.000				
Coughtotal	<---	Cough	1.000				
ChemoCyclecompleted	<---	numberofcycles	1.000				

Standardized Regression Weights: (Group number 1 - Default model)

			Estimate
Dyspnea	<---	Cough	.369
Insomnia	<---	Cough	.178
Insomnia	<---	Dyspnea	.306
Fatigue	<---	Physicalactivity	-.157
Fatigue	<---	Severity	.142
Fatigue	<---	Anxiety	.131
Fatigue	<---	Nutrition	-.158
Fatigue	<---	Cough	.139
Fatigue	<---	Dyspnea	.265
Fatigue	<---	Insomnia	.318
Fatigue	<---	numberofcycles	.102
DyspneaEffort	<---	Dyspnea	.752
DyspneaAnxiety	<---	Dyspnea	.779
DyspneaDiscomfort	<---	Dyspnea	.620
Insominfluence	<---	Insomnia	.822
Insomserverity	<---	Insomnia	.761
Anxietytotal	<---	Anxiety	.992
TotalMET	<---	Physicalactivity	1.000
Serverity	<---	Severity	1.000
Nutritionscore	<---	Nutrition	1.000
Fatiguescore	<---	Fatigue	1.000
Coughtotal	<---	Cough	.999
ChemoCyclecompleted	<---	numberofcycles	1.000

Variances: (Group number 1 - Default model)

	Estimate	S.E.	C.R.	P	Label
Anxiety	13.438	1.234	10.890	***	

	Estimate	S.E.	C.R.	P	Label
Physicalactivity	1631315.854	147390.677	11.068	***	
Severity	.878	.079	11.068	***	
Nutrition	82.683	7.470	11.068	***	
Cough	62.770	5.679	11.052	***	
numberofcycles	2.003	.181	11.068	***	
r_dyspnea	4.712	.809	5.827	***	
r_insomnia	4.768	.887	5.378	***	
r_fatigue	66.510	6.531	10.184	***	
r_anxiety_score	.220				
r_cough_score	.090				
r_MET	.000				
r_disease_severity	.000				
r_nutrition_score	.000				
r_fatigue_score	.070				
r_chemocompleted	.000				
r_dys_effort	4.181	.610	6.859	***	
r_dys_anxiety	2.615	.423	6.177	***	
r_dys_discomfort	4.561	.497	9.180	***	
r_insom_influence	2.733	.746	3.663	***	
r_insom_severity	4.956	.954	5.192	***	

Squared Multiple Correlations: (Group number 1 - Default model)

	Estimate
Dyspnea	.136
Insomnia	.165
Fatigue	.404
ChemoCyclecompleted	1.000

	Estimate
Fatiguescore	.999
Nutritionscore	1.000
Serverity	1.000
TotalMET	1.000
Coughtotal	.999
Anxietytotal	.984
Insomserverity	.580
Insominfluence	.676
DyspneaDiscomfort	.384
DyspneaAnxiety	.607
DyspneaEffort	.566

Matrices (Group number 1 - Default model)

Total Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.109	.000	.000	.000	.000	.000	.000
Insomnia	.000	.088	.000	.000	.000	.000	.313	.000
Fatigue	.764	.439	-.183	1.600	-.001	.376	1.639	1.405
ChemoCyclecompleted	1.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.764	.439	-.183	1.600	-.001	.376	1.639	1.405
Nutritionscore	.000	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000	.000
Coughtotal	.000	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	1.000	.000	.000
Insomserverity	.000	.096	.000	.000	.000	.000	.342	1.094

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Insominfluence	.000	.088	.000	.000	.000	.000	.313	1.000
DyspneaDiscomfort	.000	.079	.000	.000	.000	.000	.722	.000
DyspneaAnxiety	.000	.094	.000	.000	.000	.000	.861	.000
DyspneaEffort	.000	.109	.000	.000	.000	.000	1.000	.000

Standardized Total Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.369	.000	.000	.000	.000	.000	.000
Insomnia	.000	.290	.000	.000	.000	.000	.306	.000
Fatigue	.102	.329	-.158	.142	-.157	.131	.362	.318
ChemoCyclecompleted	1.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.102	.329	-.158	.142	-.157	.131	.362	.318
Nutritionscore	.000	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000	.000
Coughtotal	.000	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.992	.000	.000
Insomserverity	.000	.221	.000	.000	.000	.000	.233	.761
Insominfluence	.000	.239	.000	.000	.000	.000	.251	.822
DyspneaDiscomfort	.000	.229	.000	.000	.000	.000	.620	.000
DyspneaAnxiety	.000	.287	.000	.000	.000	.000	.779	.000
DyspneaEffort	.000	.277	.000	.000	.000	.000	.752	.000

Direct Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.109	.000	.000	.000	.000	.000	.000

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Insomnia	.000	.054	.000	.000	.000	.000	.313	.000
Fatigue	.764	.185	-.183	1.600	-.001	.376	1.199	1.405
ChemoCyclecompleted	1.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.000	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000	.000
Coughtotal	.000	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	1.000	.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.000	1.094
Insominfluence	.000	.000	.000	.000	.000	.000	.000	1.000
DyspneaDiscomfort	.000	.000	.000	.000	.000	.000	.722	.000
DyspneaAnxiety	.000	.000	.000	.000	.000	.000	.861	.000
DyspneaEffort	.000	.000	.000	.000	.000	.000	1.000	.000

Standardized Direct Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.369	.000	.000	.000	.000	.000	.000
Insomnia	.000	.178	.000	.000	.000	.000	.306	.000
Fatigue	.102	.139	-.158	.142	-.157	.131	.265	.318
ChemoCyclecompleted	1.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.000	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000	.000

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Coughtotal	.000	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.992	.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.000	.761
Insominfluence	.000	.000	.000	.000	.000	.000	.000	.822
DyspneaDiscomfort	.000	.000	.000	.000	.000	.000	.620	.000
DyspneaAnxiety	.000	.000	.000	.000	.000	.000	.779	.000
DyspneaEffort	.000	.000	.000	.000	.000	.000	.752	.000

Indirect Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000	.000
Insomnia	.000	.034	.000	.000	.000	.000	.000	.000
Fatigue	.000	.253	.000	.000	.000	.000	.439	.000
ChemoCyclecompleted	.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.764	.439	-.183	1.600	-.001	.376	1.639	1.405
Nutritionscore	.000	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.000	.000	.000
Insomserverity	.000	.096	.000	.000	.000	.000	.342	.000
Insominfluence	.000	.088	.000	.000	.000	.000	.313	.000
DyspneaDiscomfort	.000	.079	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.000	.094	.000	.000	.000	.000	.000	.000
DyspneaEffort	.000	.109	.000	.000	.000	.000	.000	.000

Standardized Indirect Effects (Group number 1 - Default model)

	numberofcycles	Cough	Nutrition	Severity	Physicalactivity	Anxiety	Dyspnea	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000	.000
Insomnia	.000	.113	.000	.000	.000	.000	.000	.000
Fatigue	.000	.190	.000	.000	.000	.000	.097	.000
ChemoCyclecompleted	.000	.000	.000	.000	.000	.000	.000	.000
Fatiguescore	.102	.329	-.158	.142	-.157	.131	.362	.318
Nutritionscore	.000	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.000	.000	.000
Insomserverity	.000	.221	.000	.000	.000	.000	.233	.000
Insominfluence	.000	.239	.000	.000	.000	.000	.251	.000
DyspneaDiscomfort	.000	.229	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.000	.287	.000	.000	.000	.000	.000	.000
DyspneaEffort	.000	.277	.000	.000	.000	.000	.000	.000

Modification Indices (Group number 1 - Default model)

Covariances: (Group number 1 - Default model)

			M.I.	Par Change
Severity	<-->	numberofcycles	7.506	.232
Physicalactivity	<-->	Severity	7.057	-203.119
r_dyspnea	<-->	Anxiety	11.611	2.001
r_insomnia	<-->	Anxiety	5.049	1.351
r_chemocompleted	<-->	Severity	7.385	.228
r_disease_severity	<-->	numberofcycles	7.276	.225
r_disease_severity	<-->	Physicalactivity	6.841	-196.886
r_disease_severity	<-->	r_chemocompleted	7.155	.221

			M.I.	Par Change
r_MET	<-->	Severity	6.794	-195.545
r_MET	<-->	r_disease_severity	6.578	-189.328
r_anxiety_score	<-->	r_dyspnea	11.310	1.950
r_anxiety_score	<-->	r_insomnia	4.919	1.316
r_dys_discomfort	<-->	Physicalactivity	6.640	481.047
r_dys_discomfort	<-->	Anxiety	7.825	-1.511
r_dys_discomfort	<-->	r_MET	5.314	422.217
r_dys_discomfort	<-->	r_anxiety_score	6.621	-1.372
r_dys_anxiety	<-->	Anxiety	12.666	1.646
r_dys_anxiety	<-->	r_anxiety_score	11.464	1.546

Variances: (Group number 1 - Default model)

M.I.	Par Change

Regression Weights: (Group number 1 - Default model)

			M.I.	Par Change
Dyspnea	<---	Anxiety	11.611	.149
Insomnia	<---	Anxiety	5.049	.101
ChemoCyclecompleted	<---	Severity	7.385	.260
ChemoCyclecompleted	<---	Insomnia	5.790	.101
ChemoCyclecompleted	<---	Fatigue	4.258	.018
ChemoCyclecompleted	<---	Fatiguescore	4.253	.018
ChemoCyclecompleted	<---	Serverity	7.385	.260
ChemoCyclecompleted	<---	Insominfluence	5.250	.071
Nutritionscore	<---	Insominfluence	4.105	-.397
Serverity	<---	numberofcycles	7.276	.112
Serverity	<---	Physicalactivity	6.841	.000
Serverity	<---	Insomnia	4.865	.061

			M.I.	Par Change
Serverity	<---	Fatigue	4.257	.012
Serverity	<---	ChemoCyclecompleted	7.276	.112
Serverity	<---	Fatiguescore	4.251	.012
Serverity	<---	TotalMET	6.841	.000
Serverity	<---	Insominfluence	5.967	.050
TotalMET	<---	Severity	6.794	-222.721
TotalMET	<---	Serverity	6.794	-222.721
TotalMET	<---	DyspneaDiscomfort	4.176	60.115
Anxietytotal	<---	Dyspnea	12.523	.396
Anxietytotal	<---	Insomnia	10.658	.358
Anxietytotal	<---	Fatigue	5.038	.050
Anxietytotal	<---	Fatiguescore	5.032	.049
Anxietytotal	<---	Insomserverity	6.353	.171
Anxietytotal	<---	Insominfluence	8.949	.240
Anxietytotal	<---	DyspneaAnxiety	17.714	.380
Anxietytotal	<---	DyspneaEffort	8.503	.219
DyspneaDiscomfort	<---	Physicalactivity	6.640	.000
DyspneaDiscomfort	<---	Anxiety	7.825	-.112
DyspneaDiscomfort	<---	TotalMET	6.640	.000
DyspneaDiscomfort	<---	Anxietytotal	7.808	-.111
DyspneaAnxiety	<---	Anxiety	12.666	.123
DyspneaAnxiety	<---	Anxietytotal	12.652	.120

Minimization History (Default model)

Iteration		Negative eigenvalues	Condition #	Smallest eigenvalue	Diameter	F	NTries	Ratio
0	e	4		-.234	9999.000	591.039	0	9999.000
1	e	1		-.025	1.702	191.458	20	.628

Iteration		Negative eigenvalues	Condition #	Smallest eigenvalue	Diameter	F	NTries	Ratio
2	e	1		-.035	.628	105.726	4	.747
3	e	0	32.967		.371	90.589	6	.859
4	e	0	23.395		.194	88.488	1	1.010
5	e	0	24.743		.033	88.431	1	1.021
6	e	0	24.647		.001	88.431	1	1.001
7	e	0	24.652		.000	88.431	1	1.000

Model Fit Summary

CMIN

Model	NPAR	CMIN	DF	P	CMIN/DF
Default model	28	88.431	50	.001	1.769
Saturated model	78	.000	0		
Independence model	12	587.186	66	.000	8.897

RMR, GFI

Model	RMR	GFI	AGFI	PGFI
Default model	121.108	.942	.910	.604
Saturated model	.000	1.000		
Independence model	275.004	.646	.582	.547

Baseline Comparisons

Model	NFI Delta1	RFI rho1	IFI Delta2	TLI rho2	CFI
Default model	.849	.801	.928	.903	.926
Saturated model	1.000		1.000		1.000
Independence model	.000	.000	.000	.000	.000

Parsimony-Adjusted Measures

Model	PRATIO	PNFI	PCFI
Default model	.758	.643	.702
Saturated model	.000	.000	.000

Model	PRATIO	PNFI	PCFI
Independence model	1.000	.000	.000

NCP

Model	NCP	LO 90	HI 90
Default model	38.431	16.074	68.636
Saturated model	.000	.000	.000
Independence model	521.186	447.434	602.401

FMIN

Model	FMIN	F0	LO 90	HI 90
Default model	.361	.157	.066	.280
Saturated model	.000	.000	.000	.000
Independence model	2.397	2.127	1.826	2.459

RMSEA

Model	RMSEA	LO 90	HI 90	PCLOSE
Default model	.056	.036	.075	.286
Independence model	.180	.166	.193	.000

AIC

Model	AIC	BCC	BIC	CAIC
Default model	144.431	147.569	242.580	270.580
Saturated model	156.000	164.741	429.416	507.416
Independence model	611.186	612.530	653.250	665.250

ECVI

Model	ECVI	LO 90	HI 90	MECVI
Default model	.590	.498	.713	.602
Saturated model	.637	.637	.637	.672
Independence model	2.495	2.194	2.826	2.500

HOELTER

Model	HOELTER .05	HOELTER .01
Default model	188	211
Independence model	36	40

Execution time summary

Minimization:	.016
Miscellaneous:	.359
Bootstrap:	.000
Total:	.375

Final Model

Groups

Group number 1 (Group number 1)

Notes for Group (Group number 1)

The model is recursive.

Sample size = 246

Variable Summary (Group number 1)

Your model contains the following variables (Group number 1)

Observed, endogenous variables

DyspneaEffort

DyspneaAnxiety

DyspneaDiscomfort

Insominfluence

Insomserverity

Anxietytotal

Coughtotal

TotalMET

Serverity

Nutritionscore

Fatiguescore

Unobserved, endogenous variables

Dyspnea

Insomnia

Anxiety

Physicalactivity

Fatigue

Unobserved, exogenous variables

r_dys_effort

r_dys_anxiety

r_dys_discomfort

r_insom_influence

r_insom_severity

r_anxiety_score

r_cough_score

r_MET

Severity

r_disease_severity

Nutrition

r_nutrition_score

r_fatigue_score

Cough

r_dyspnea

r_insomnia

r_fatigue

r_anxiety

r_physical_activity

Variable counts (Group number 1)

Number of variables in your model:	35
Number of observed variables:	11
Number of unobserved variables:	24
Number of exogenous variables:	19
Number of endogenous variables:	16

Parameter Summary (Group number 1)

	Weights	Covariances	Variances	Means	Intercepts	Total
Fixed	24	0	6	0	0	30
Labeled	0	0	0	0	0	0
Unlabeled	15	0	13	0	0	28

	Weights	Covariances	Variances	Means	Intercepts	Total
Total	39	0	19	0	0	58

Assessment of normality (Group number 1)

Variable	min	max	skew	c.r.	kurtosis	c.r.
Fatiguescore	.000	49.000	-.306	-1.962	-.341	-1.091
Nutritionscore	76.806	119.165	-.107	-.683	-.318	-1.017
Serverity	1.000	4.000	-.606	-3.883	-.554	-1.772
TotalMET	.000	4800.000	.870	5.569	-.035	-.113
Coughtotal	11.000	42.000	.169	1.084	-.625	-2.000
Anxietytotal	.000	15.000	.541	3.466	-.423	-1.353
Insomserverity	.000	16.000	-.452	-2.896	.013	.043
Insominfluence	.000	12.000	.127	.813	-.743	-2.378
DyspneaDiscomfort	.000	10.000	.300	1.921	-.801	-2.565
DyspneaAnxiety	.000	13.000	.798	5.108	.508	1.627
DyspneaEffort	.000	13.000	.392	2.511	-.627	-2.007
Multivariate					5.643	2.617

Observations farthest from the centroid (Mahalanobis distance) (Group number 1)

Observation number	Mahalanobis d-squared	p1	p2
191	26.973	.005	.681
215	26.327	.006	.418
80	25.856	.007	.236
214	24.670	.010	.243
141	23.847	.013	.236
122	23.751	.014	.128
99	22.727	.019	.201
136	22.518	.021	.140
217	22.098	.024	.131

Observation number	Mahalanobis d-squared	p1	p2
222	21.641	.027	.139
113	21.582	.028	.085
124	21.080	.033	.109
183	20.774	.036	.107
143	20.773	.036	.061
62	20.634	.037	.045
152	20.038	.045	.089
243	19.602	.051	.130
188	19.326	.055	.143
121	19.291	.056	.100
145	19.275	.056	.065
70	19.207	.057	.047
45	19.123	.059	.035
190	18.968	.062	.032
172	18.782	.065	.032
179	18.335	.074	.068
104	18.335	.074	.044
148	18.307	.075	.030
198	18.223	.077	.023
22	17.919	.083	.038
129	17.621	.091	.061
216	17.509	.094	.056
135	17.358	.098	.059
158	16.588	.121	.285
227	16.507	.123	.265
130	16.409	.127	.256

Observation number	Mahalanobis d-squared	p1	p2
74	16.361	.128	.223
2	16.307	.130	.195
244	16.210	.134	.190
34	16.087	.138	.197
27	15.907	.145	.235
176	15.689	.153	.302
13	15.508	.160	.355
226	15.142	.176	.547
90	15.142	.176	.480
46	15.000	.183	.519
63	14.938	.185	.499
28	14.919	.186	.448
30	14.903	.187	.397
184	14.821	.191	.395
9	14.750	.194	.385
125	14.747	.194	.328
24	14.730	.195	.284
203	14.640	.200	.290
185	14.613	.201	.255
187	14.553	.204	.243
131	14.498	.207	.229
245	14.408	.211	.237
16	14.363	.214	.218
140	14.354	.214	.181
181	14.090	.228	.299
66	14.088	.228	.251

Observation number	Mahalanobis d-squared	p1	p2
230	13.959	.235	.290
101	13.899	.239	.282
64	13.772	.246	.324
173	13.729	.248	.304
102	13.502	.262	.432
220	13.455	.265	.416
209	13.437	.266	.375
236	13.423	.267	.333
212	13.416	.267	.289
171	13.372	.270	.273
160	13.239	.278	.326
53	13.162	.283	.337
195	13.118	.286	.322
149	13.034	.291	.339
98	12.997	.293	.319
17	12.946	.297	.311
211	12.922	.298	.283
218	12.910	.299	.247
178	12.760	.309	.317
84	12.670	.315	.342
3	12.606	.320	.347
123	12.412	.333	.472
92	12.395	.335	.434
234	12.340	.339	.433
77	12.329	.339	.392
40	12.172	.351	.487

Observation number	Mahalanobis d-squared	p1	p2
154	12.103	.356	.501
32	12.032	.361	.517
79	12.000	.364	.495
65	11.968	.366	.474
144	11.945	.368	.444
117	11.899	.371	.437
235	11.888	.372	.396
21	11.816	.378	.415
120	11.775	.381	.403
69	11.746	.383	.381
132	11.743	.383	.335
242	11.635	.392	.388
159	11.627	.392	.347

Models

Default model (Default model)

Notes for Model (Default model)

Computation of degrees of freedom (Default model)

Number of distinct sample moments:	66
Number of distinct parameters to be estimated:	28
Degrees of freedom (66 - 28):	38

Result (Default model)

Minimum was achieved

Chi-square = 51.556

Degrees of freedom = 38

Probability level = .070

Group number 1 (Group number 1 - Default model)

Estimates (Group number 1 - Default model)

Scalar Estimates (Group number 1 - Default model)

Maximum Likelihood Estimates

Regression Weights: (Group number 1 - Default model)

			Estimate	S.E.	C.R.	P	Label
Dyspnea	<---	Cough	.106	.021	5.058	***	
Insomnia	<---	Cough	.053	.023	2.309	.021	
Insomnia	<---	Dyspnea	.328	.092	3.584	***	
Anxiety	<---	Dyspnea	.427	.115	3.701	***	
Physicalactivity	<---	Severity	-231.347	85.822	-2.696	.007	
Fatigue	<---	Physicalactivity	-.001	.000	-2.912	.004	
Fatigue	<---	Severity	1.780	.587	3.031	.002	
Fatigue	<---	Anxiety	.339	.157	2.158	.031	
Fatigue	<---	Nutrition	-.186	.060	-3.123	.002	
Fatigue	<---	Cough	.196	.077	2.543	.011	
Fatigue	<---	Dyspnea	1.250	.338	3.695	***	
Fatigue	<---	Insomnia	1.447	.321	4.502	***	
DyspneaEffort	<---	Dyspnea	1.000				
DyspneaAnxiety	<---	Dyspnea	.895	.094	9.517	***	
DyspneaDiscomfort	<---	Dyspnea	.707	.087	8.125	***	
Insominfluence	<---	Insomnia	1.000				
Insomserverity	<---	Insomnia	1.096	.147	7.440	***	
Anxietytotal	<---	Anxiety	1.000				
TotalMET	<---	Physicalactivity	1.000				
Serverity	<---	Severity	1.000				
Nutritionscore	<---	Nutrition	1.000				
Fatiguescore	<---	Fatigue	1.000				
Coughtotal	<---	Cough	1.000				

Standardized Regression Weights: (Group number 1 - Default model)

			Estimate
Dyspnea	<---	Cough	.365
Insomnia	<---	Cough	.175

			Estimate
Insomnia	<---	Dyspnea	.317
Anxiety	<---	Dyspnea	.269
Physicalactivity	<---	Severity	-.170
Fatigue	<---	Physicalactivity	-.148
Fatigue	<---	Severity	.154
Fatigue	<---	Anxiety	.115
Fatigue	<---	Nutrition	-.156
Fatigue	<---	Cough	.143
Fatigue	<---	Dyspnea	.266
Fatigue	<---	Insomnia	.318
DyspneaEffort	<---	Dyspnea	.743
DyspneaAnxiety	<---	Dyspnea	.800
DyspneaDiscomfort	<---	Dyspnea	.599
Insominfluence	<---	Insomnia	.822
Insomserverity	<---	Insomnia	.762
Anxietytotal	<---	Anxiety	.992
TotalMET	<---	Physicalactivity	1.000
Serverity	<---	Severity	1.000
Nutritionscore	<---	Nutrition	1.000
Fatiguescore	<---	Fatigue	1.000
Coughtotal	<---	Cough	.999

Variances: (Group number 1 - Default model)

	Estimate	S.E.	C.R.	P	Label
Severity	.878	.079	11.068	***	
Nutrition	82.683	7.470	11.068	***	
Cough	62.770	5.679	11.052	***	

	Estimate	S.E.	C.R.	P	Label
r_dyspnea	4.609	.793	5.811	***	
r_insomnia	4.724	.872	5.417	***	
r_anxiety	12.468	1.169	10.661	***	
r_physical_activity	1584324.976	143145.014	11.068	***	
r_fatigue	67.301	6.628	10.155	***	
r_anxiety_score	.220				
r_cough_score	.090				
r_MET	.000				
r_disease_severity	.000				
r_nutrition_score	.000				
r_fatigue_score	.070				
r_dys_effort	4.317	.599	7.209	***	
r_dys_anxiety	2.397	.417	5.752	***	
r_dys_discomfort	4.747	.502	9.449	***	
r_insom_influence	2.742	.732	3.748	***	
r_insom_severity	4.945	.940	5.262	***	

Squared Multiple Correlations: (Group number 1 - Default model)

	Estimate
Dyspnea	.133
Physicalactivity	.029
Anxiety	.072
Insomnia	.172
Fatigue	.429
Fatiguescore	.999
Nutritionscore	1.000
Serverity	1.000

	Estimate
TotalMET	1.000
Coughtotal	.999
Anxietytotal	.984
Insomserverity	.581
Insominfluence	.675
DyspneaDiscomfort	.359
DyspneaAnxiety	.640
DyspneaEffort	.552

Matrices (Group number 1 - Default model)

Total Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.106	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-231.347	.000	.000	.000	.000
Anxiety	.045	.000	.000	.427	.000	.000	.000
Insomnia	.088	.000	.000	.328	.000	.000	.000
Fatigue	.471	-.186	2.070	1.870	-.001	.339	1.447
Fatiguescore	.471	-.186	2.070	1.870	-.001	.339	1.447
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-231.347	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.045	.000	.000	.427	.000	1.000	.000
Insomserverity	.096	.000	.000	.360	.000	.000	1.096
Insominfluence	.088	.000	.000	.328	.000	.000	1.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
DyspneaDiscomfort	.075	.000	.000	.707	.000	.000	.000
DyspneaAnxiety	.095	.000	.000	.895	.000	.000	.000
DyspneaEffort	.106	.000	.000	1.000	.000	.000	.000

Standardized Total Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.365	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.170	.000	.000	.000	.000
Anxiety	.098	.000	.000	.269	.000	.000	.000
Insomnia	.290	.000	.000	.317	.000	.000	.000
Fatigue	.344	-.156	.179	.397	-.148	.115	.318
Fatiguescore	.343	-.156	.179	.397	-.148	.115	.318
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-.170	.000	1.000	.000	.000
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.097	.000	.000	.267	.000	.992	.000
Insomserverity	.221	.000	.000	.242	.000	.000	.762
Insominfluence	.239	.000	.000	.261	.000	.000	.822
DyspneaDiscomfort	.219	.000	.000	.599	.000	.000	.000
DyspneaAnxiety	.292	.000	.000	.800	.000	.000	.000
DyspneaEffort	.271	.000	.000	.743	.000	.000	.000

Direct Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.106	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-231.347	.000	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Anxiety	.000	.000	.000	.427	.000	.000	.000
Insomnia	.053	.000	.000	.328	.000	.000	.000
Fatigue	.196	-.186	1.780	1.250	-.001	.339	1.447
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	1.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	1.096
Insominfluence	.000	.000	.000	.000	.000	.000	1.000
DyspneaDiscomfort	.000	.000	.000	.707	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.895	.000	.000	.000
DyspneaEffort	.000	.000	.000	1.000	.000	.000	.000

Standardized Direct Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.365	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.170	.000	.000	.000	.000
Anxiety	.000	.000	.000	.269	.000	.000	.000
Insomnia	.175	.000	.000	.317	.000	.000	.000
Fatigue	.143	-.156	.154	.266	-.148	.115	.318
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.992	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insomserverity	.000	.000	.000	.000	.000	.000	.762
Insominfluence	.000	.000	.000	.000	.000	.000	.822
DyspneaDiscomfort	.000	.000	.000	.599	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.800	.000	.000	.000
DyspneaEffort	.000	.000	.000	.743	.000	.000	.000

Indirect Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.045	.000	.000	.000	.000	.000	.000
Insomnia	.035	.000	.000	.000	.000	.000	.000
Fatigue	.275	.000	.290	.620	.000	.000	.000
Fatiguescore	.471	-.186	2.070	1.870	-.001	.339	1.447
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-231.347	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.045	.000	.000	.427	.000	.000	.000
Insomserverity	.096	.000	.000	.360	.000	.000	.000
Insominfluence	.088	.000	.000	.328	.000	.000	.000
DyspneaDiscomfort	.075	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.095	.000	.000	.000	.000	.000	.000
DyspneaEffort	.106	.000	.000	.000	.000	.000	.000

Standardized Indirect Effects (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.098	.000	.000	.000	.000	.000	.000
Insomnia	.116	.000	.000	.000	.000	.000	.000
Fatigue	.201	.000	.025	.132	.000	.000	.000
Fatiguescore	.343	-.156	.179	.397	-.148	.115	.318
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-.170	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.097	.000	.000	.267	.000	.000	.000
Insomserverity	.221	.000	.000	.242	.000	.000	.000
Insominfluence	.239	.000	.000	.261	.000	.000	.000
DyspneaDiscomfort	.219	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.292	.000	.000	.000	.000	.000	.000
DyspneaEffort	.271	.000	.000	.000	.000	.000	.000

Modification Indices (Group number 1 - Default model)

Covariances: (Group number 1 - Default model)

			M.I.	Par Change
r_insomnia	<-->	r_anxiety	4.059	1.172
r_insom_influence	<-->	r_disease_severity	4.039	.255
r_dys_discomfort	<-->	r_physical_activity	6.462	472.440
r_dys_discomfort	<-->	r_anxiety	12.636	-1.882
r_dys_discomfort	<-->	r_MET	5.274	419.603
r_dys_discomfort	<-->	r_anxiety_score	11.249	-1.754
r_dys_anxiety	<-->	r_anxiety	4.585	.941
r_dys_anxiety	<-->	r_anxiety_score	4.137	.884

Variances: (Group number 1 - Default model)

M.I. Par Change

Regression Weights: (Group number 1 - Default model)

			M.I.	Par Change
Nutritionscore	<---	Insominfluence	4.097	-.397
Serverity	<---	Insomnia	4.953	.061
Serverity	<---	Insominfluence	6.223	.050
TotalMET	<---	DyspneaDiscomfort	4.921	64.440
Anxietytotal	<---	DyspneaDiscomfort	6.415	-.211
DyspneaDiscomfort	<---	Physicalactivity	6.411	.000
DyspneaDiscomfort	<---	Anxiety	11.552	-.138
DyspneaDiscomfort	<---	TotalMET	6.411	.000
DyspneaDiscomfort	<---	Anxietytotal	11.563	-.136
DyspneaAnxiety	<---	Anxiety	4.219	.069
DyspneaAnxiety	<---	Anxietytotal	4.224	.068

Bootstrap (Group number 1 - Default model)

Bootstrap standard errors (Group number 1 - Default model)

Scalar Estimates (Group number 1 - Default model)

Regression Weights: (Group number 1 - Default model)

Parameter			SE	SE-SE	Mean	Bias	SE-Bias
Dyspnea	<---	Cough	.023	.001	.106	.000	.001
Insomnia	<---	Cough	.025	.001	.051	-.001	.001
Insomnia	<---	Dyspnea	.099	.003	.330	.001	.004
Anxiety	<---	Dyspnea	.136	.004	.424	-.003	.006
Physicalactivity	<---	Severity	83.866	2.652	-230.038	1.309	3.751
Fatigue	<---	Physicalactivity	.000	.000	-.001	.000	.000
Fatigue	<---	Severity	.685	.022	1.828	.048	.031
Fatigue	<---	Anxiety	.181	.006	.343	.004	.008
Fatigue	<---	Nutrition	.059	.002	-.185	.001	.003

Parameter			SE	SE-SE	Mean	Bias	SE-Bias
Fatigue	<---	Cough	.095	.003	.195	-.001	.004
Fatigue	<---	Dyspnea	.362	.011	1.229	-.022	.016
Fatigue	<---	Insomnia	.387	.012	1.460	.013	.017
DyspneaEffort	<---	Dyspnea	.000	.000	1.000	.000	.000
DyspneaAnxiety	<---	Dyspnea	.113	.004	.897	.001	.005
DyspneaDiscomfort	<---	Dyspnea	.084	.003	.708	.001	.004
Insominfluence	<---	Insomnia	.000	.000	1.000	.000	.000
Insomserverity	<---	Insomnia	.209	.007	1.120	.024	.009
Anxietytotal	<---	Anxiety	.000	.000	1.000	.000	.000
TotalMET	<---	Physicalactivity	.000	.000	1.000	.000	.000
Serverity	<---	Severity	.000	.000	1.000	.000	.000
Nutritionscore	<---	Nutrition	.000	.000	1.000	.000	.000
Fatiguescore	<---	Fatigue	.000	.000	1.000	.000	.000
Coughtotal	<---	Cough	.000	.000	1.000	.000	.000

Standardized Regression Weights: (Group number 1 - Default model)

Parameter			SE	SE-SE	Mean	Bias	SE-Bias
Dyspnea	<---	Cough	.074	.002	.362	-.003	.003
Insomnia	<---	Cough	.077	.002	.169	-.006	.003
Insomnia	<---	Dyspnea	.082	.003	.316	-.001	.004
Anxiety	<---	Dyspnea	.080	.003	.266	-.003	.004
Physicalactivity	<---	Severity	.060	.002	-.169	.001	.003
Fatigue	<---	Physicalactivity	.052	.002	-.145	.002	.002
Fatigue	<---	Severity	.060	.002	.159	.005	.003
Fatigue	<---	Anxiety	.061	.002	.116	.001	.003
Fatigue	<---	Nutrition	.051	.002	-.156	.000	.002
Fatigue	<---	Cough	.070	.002	.143	.000	.003
Fatigue	<---	Dyspnea	.075	.002	.262	-.003	.003
Fatigue	<---	Insomnia	.069	.002	.317	-.001	.003
DyspneaEffort	<---	Dyspnea	.049	.002	.746	.003	.002

Parameter			SE	SE-SE	Mean	Bias	SE-Bias
DyspneaAnxiety	<---	Dyspnea	.049	.002	.801	.001	.002
DyspneaDiscomfort	<---	Dyspnea	.061	.002	.601	.002	.003
Insominfluence	<---	Insomnia	.073	.002	.824	.002	.003
Insomserverity	<---	Insomnia	.074	.002	.769	.007	.003
Anxietytotal	<---	Anxiety	.001	.000	.992	.000	.000
TotalMET	<---	Physicalactivity	.000	.000	1.000	.000	.000
Serverity	<---	Severity	.000	.000	1.000	.000	.000
Nutritionscore	<---	Nutrition	.000	.000	1.000	.000	.000
Fatiguescore	<---	Fatigue	.000	.000	1.000	.000	.000
Coughtotal	<---	Cough	.000	.000	.999	.000	.000

Variances: (Group number 1 - Default model)

Parameter	SE	SE-SE	Mean	Bias	SE-Bias
Severity	.067	.002	.880	.002	.003
Nutrition	6.825	.216	82.751	.068	.305
Cough	4.752	.150	62.798	.028	.213
r_dyspnea	.774	.024	4.672	.063	.035
r_insomnia	.928	.029	4.733	.010	.041
r_anxiety	1.083	.034	12.367	-.101	.048
r_physical_activity	137292.937	4341.584	1570010.364	-14314.612	6139.927
r_fatigue	7.686	.243	65.108	-2.194	.344
r_anxiety_score	.000	.000	.220	.000	.000
r_cough_score	.000	.000	.090	.000	.000
r_MET	.000	.000	.000	.000	.000
r_disease_severity	.000	.000	.000	.000	.000
r_nutrition_score	.000	.000	.000	.000	.000
r_fatigue_score	.000	.000	.070	.000	.000
r_dys_effort	.732	.023	4.255	-.062	.033
r_dys_anxiety	.540	.017	2.355	-.042	.024
r_dys_discomfort	.614	.019	4.693	-.054	.027

Parameter	SE	SE-SE	Mean	Bias	SE-Bias
r_insom_influence	1.018	.032	2.659	-.082	.046
r_insom_severity	1.268	.040	4.714	-.231	.057

Squared Multiple Correlations: (Group number 1 - Default model)

Parameter	SE	SE-SE	Mean	Bias	SE-Bias
Dyspnea	.054	.002	.137	.004	.002
Physicalactivity	.021	.001	.032	.003	.001
Anxiety	.042	.001	.077	.005	.002
Insomnia	.064	.002	.178	.006	.003
Fatigue	.053	.002	.445	.016	.002
Fatiguescore	.000	.000	.999	.000	.000
Nutritionscore	.000	.000	1.000	.000	.000
Serverity	.000	.000	1.000	.000	.000
TotalMET	.000	.000	1.000	.000	.000
Coughtotal	.000	.000	.999	.000	.000
Anxietytotal	.001	.000	.984	.000	.000
Insomserverity	.113	.004	.597	.016	.005
Insominfluence	.121	.004	.684	.009	.005
DyspneaDiscomfort	.073	.002	.365	.006	.003
DyspneaAnxiety	.079	.002	.645	.005	.004
DyspneaEffort	.073	.002	.559	.007	.003

Matrices (Group number 1 - Default model)

Total Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.023	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	83.866	.000	.000	.000	.000
Anxiety	.017	.000	.000	.136	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insomnia	.026	.000	.000	.099	.000	.000	.000
Fatigue	.089	.059	.686	.351	.000	.181	.387
Fatiguescore	.089	.059	.686	.351	.000	.181	.387
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	83.866	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.017	.000	.000	.136	.000	.000	.000
Insomserverity	.027	.000	.000	.104	.000	.000	.209
Insominfluence	.026	.000	.000	.099	.000	.000	.000
DyspneaDiscomfort	.017	.000	.000	.084	.000	.000	.000
DyspneaAnxiety	.021	.000	.000	.113	.000	.000	.000
DyspneaEffort	.023	.000	.000	.000	.000	.000	.000

Standardized Total Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.074	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.060	.000	.000	.000	.000
Anxiety	.037	.000	.000	.080	.000	.000	.000
Insomnia	.077	.000	.000	.082	.000	.000	.000
Fatigue	.063	.051	.061	.066	.052	.061	.069
Fatiguescore	.063	.051	.061	.066	.052	.061	.069
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.060	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.037	.000	.000	.079	.000	.001	.000
Insomserverity	.059	.000	.000	.062	.000	.000	.074

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insominfluence	.069	.000	.000	.074	.000	.000	.073
DyspneaDiscomfort	.050	.000	.000	.061	.000	.000	.000
DyspneaAnxiety	.061	.000	.000	.049	.000	.000	.000
DyspneaEffort	.059	.000	.000	.049	.000	.000	.000

Direct Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.023	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	83.866	.000	.000	.000	.000
Anxiety	.000	.000	.000	.136	.000	.000	.000
Insomnia	.025	.000	.000	.099	.000	.000	.000
Fatigue	.095	.059	.685	.362	.000	.181	.387
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.209
Insominfluence	.000	.000	.000	.000	.000	.000	.000
DyspneaDiscomfort	.000	.000	.000	.084	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.113	.000	.000	.000
DyspneaEffort	.000	.000	.000	.000	.000	.000	.000

Standardized Direct Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.074	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.060	.000	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Anxiety	.000	.000	.000	.080	.000	.000	.000
Insomnia	.077	.000	.000	.082	.000	.000	.000
Fatigue	.070	.051	.060	.075	.052	.061	.069
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.001	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.074
Insominfluence	.000	.000	.000	.000	.000	.000	.073
DyspneaDiscomfort	.000	.000	.000	.061	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.049	.000	.000	.000
DyspneaEffort	.000	.000	.000	.049	.000	.000	.000

Indirect Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.017	.000	.000	.000	.000	.000	.000
Insomnia	.013	.000	.000	.000	.000	.000	.000
Fatigue	.068	.000	.145	.201	.000	.000	.000
Fatiguescore	.089	.059	.686	.351	.000	.181	.387
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	83.866	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.017	.000	.000	.136	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insomserverity	.027	.000	.000	.104	.000	.000	.000
Insominfluence	.026	.000	.000	.099	.000	.000	.000
DyspneaDiscomfort	.017	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.021	.000	.000	.000	.000	.000	.000
DyspneaEffort	.023	.000	.000	.000	.000	.000	.000

Standardized Indirect Effects - Standard Errors (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.037	.000	.000	.000	.000	.000	.000
Insomnia	.039	.000	.000	.000	.000	.000	.000
Fatigue	.049	.000	.013	.038	.000	.000	.000
Fatiguescore	.063	.051	.061	.066	.052	.061	.069
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	.060	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.037	.000	.000	.079	.000	.000	.000
Insomserverity	.059	.000	.000	.062	.000	.000	.000
Insominfluence	.069	.000	.000	.074	.000	.000	.000
DyspneaDiscomfort	.050	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.061	.000	.000	.000	.000	.000	.000
DyspneaEffort	.059	.000	.000	.000	.000	.000	.000

Bootstrap Confidence (Group number 1 - Default model)

Bias-corrected percentile method (Group number 1 - Default model)

95% confidence intervals (bias-corrected percentile method)

Scalar Estimates (Group number 1 - Default model)

Regression Weights: (Group number 1 - Default model)

Parameter			Estimate	Lower	Upper	P
Dyspnea	<---	Cough	.106	.060	.152	.004
Insomnia	<---	Cough	.053	.005	.104	.021
Insomnia	<---	Dyspnea	.328	.149	.525	.004
Anxiety	<---	Dyspnea	.427	.153	.678	.004
Physicalactivity	<---	Severity	-231.347	-408.833	-62.778	.004
Fatigue	<---	Physicalactivity	-.001	-.002	.000	.006
Fatigue	<---	Severity	1.780	.125	2.958	.037
Fatigue	<---	Anxiety	.339	-.007	.722	.052
Fatigue	<---	Nutrition	-.186	-.316	-.076	.003
Fatigue	<---	Cough	.196	.000	.380	.046
Fatigue	<---	Dyspnea	1.250	.579	1.991	.003
Fatigue	<---	Insomnia	1.447	.638	2.267	.005
DyspneaEffort	<---	Dyspnea	1.000	1.000	1.000	...
DyspneaAnxiety	<---	Dyspnea	.895	.716	1.160	.003
DyspneaDiscomfort	<---	Dyspnea	.707	.554	.879	.004
Insominfluence	<---	Insomnia	1.000	1.000	1.000	...
Insomserverity	<---	Insomnia	1.096	.715	1.540	.006
Anxietytotal	<---	Anxiety	1.000	1.000	1.000	...
TotalMET	<---	Physicalactivity	1.000	1.000	1.000	...
Serverity	<---	Severity	1.000	1.000	1.000	...
Nutritionscore	<---	Nutrition	1.000	1.000	1.000	...
Fatiguescore	<---	Fatigue	1.000	1.000	1.000	...
Coughtotal	<---	Cough	1.000	1.000	1.000	...

Standardized Regression Weights: (Group number 1 - Default model)

Parameter			Estimate	Lower	Upper	P
Dyspnea	<---	Cough	.365	.227	.515	.002

Parameter			Estimate	Lower	Upper	P
Insomnia	<---	Cough	.175	.021	.330	.018
Insomnia	<---	Dyspnea	.317	.159	.468	.004
Anxiety	<---	Dyspnea	.269	.086	.409	.007
Physicalactivity	<---	Severity	-.170	-.293	-.046	.004
Fatigue	<---	Physicalactivity	-.148	-.238	-.039	.007
Fatigue	<---	Severity	.154	.008	.259	.041
Fatigue	<---	Anxiety	.115	-.005	.244	.056
Fatigue	<---	Nutrition	-.156	-.264	-.061	.003
Fatigue	<---	Cough	.143	.000	.275	.047
Fatigue	<---	Dyspnea	.266	.100	.401	.005
Fatigue	<---	Insomnia	.318	.168	.443	.004
DyspneaEffort	<---	Dyspnea	.743	.638	.832	.006
DyspneaAnxiety	<---	Dyspnea	.800	.694	.892	.006
DyspneaDiscomfort	<---	Dyspnea	.599	.483	.721	.004
Insominfluence	<---	Insomnia	.822	.685	.971	.004
Insomserverity	<---	Insomnia	.762	.596	.889	.008
Anxietytotal	<---	Anxiety	.992	.990	.993	.004
TotalMET	<---	Physicalactivity	1.000	1.000	1.000	...
Serverity	<---	Severity	1.000	1.000	1.000	...
Nutritionscore	<---	Nutrition	1.000	1.000	1.000	...
Fatiguescore	<---	Fatigue	1.000	1.000	1.000	.003
Coughtotal	<---	Cough	.999	.999	.999	.004

Variances: (Group number 1 - Default model)

Parameter	Estimate	Lower	Upper	P
Severity	.878	.735	1.009	.006
Nutrition	82.683	69.385	95.423	.004

Parameter	Estimate	Lower	Upper	P
Cough	62.770	53.743	72.015	.004
r_dyspnea	4.609	3.163	6.050	.008
r_insomnia	4.724	3.204	7.194	.002
r_anxiety	12.468	10.077	14.608	.003
r_physical_activity	1584324.976	1326272.909	1878083.975	.002
r_fatigue	67.301	54.875	86.886	.000
r_anxiety_score	.220	.220	.220	...
r_cough_score	.090	.090	.090	...
r_MET	.000	.000	.000	...
r_disease_severity	.000	.000	.000	...
r_nutrition_score	.000	.000	.000	...
r_fatigue_score	.070	.070	.070	...
r_dys_effort	4.317	2.973	5.983	.002
r_dys_anxiety	2.397	1.301	3.440	.003
r_dys_discomfort	4.747	3.461	5.926	.003
r_insom_influence	2.742	.657	4.617	.027
r_insom_severity	4.945	2.679	7.652	.004

Squared Multiple Correlations: (Group number 1 - Default model)

Parameter	Estimate	Lower	Upper	P
Dyspnea	.133	.052	.265	.002
Physicalactivity	.029	.002	.086	.004
Anxiety	.072	.007	.167	.007
Insomnia	.172	.055	.298	.007
Fatigue	.429	.307	.518	.027
Fatiguescore	.999	.999	.999	.003
Nutritionscore	1.000	1.000	1.000	...

Parameter	Estimate	Lower	Upper	P
Serverity	1.000	1.000	1.000	...
TotalMET	1.000	1.000	1.000	...
Coughtotal	.999	.998	.999	.004
Anxietytotal	.984	.981	.986	.004
Insomserverity	.581	.355	.790	.008
Insominfluence	.675	.469	.943	.004
DyspneaDiscomfort	.359	.234	.520	.004
DyspneaAnxiety	.640	.481	.795	.006
DyspneaEffort	.552	.407	.692	.006

Matrices (Group number 1 - Default model)

Total Effects (Group number 1 - Default model)

Total Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.060	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-408.833	.000	.000	.000	.000
Anxiety	.015	.000	.000	.153	.000	.000	.000
Insomnia	.040	.000	.000	.149	.000	.000	.000
Fatigue	.295	-.316	.448	1.255	-.002	-.007	.638
Fatiguescore	.295	-.316	.448	1.255	-.002	-.007	.638
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-408.833	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.015	.000	.000	.153	.000	1.000	.000
Insomserverity	.048	.000	.000	.181	.000	.000	.715

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insominfluence	.040	.000	.000	.149	.000	.000	1.000
DyspneaDiscomfort	.044	.000	.000	.554	.000	.000	.000
DyspneaAnxiety	.057	.000	.000	.716	.000	.000	.000
DyspneaEffort	.060	.000	.000	1.000	.000	.000	.000

Total Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.152	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-62.778	.000	.000	.000	.000
Anxiety	.086	.000	.000	.678	.000	.000	.000
Insomnia	.147	.000	.000	.525	.000	.000	.000
Fatigue	.651	-.076	3.256	2.741	.000	.722	2.267
Fatiguescore	.651	-.076	3.256	2.741	.000	.722	2.267
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-62.778	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.086	.000	.000	.678	.000	1.000	.000
Insomserverity	.153	.000	.000	.592	.000	.000	1.540
Insominfluence	.147	.000	.000	.525	.000	.000	1.000
DyspneaDiscomfort	.115	.000	.000	.879	.000	.000	.000
DyspneaAnxiety	.141	.000	.000	1.160	.000	.000	.000
DyspneaEffort	.152	.000	.000	1.000	.000	.000	.000

Total Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.004	...	...	...	...	...	...

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Physicalactivity	...	...	.004	...	...	...	...
Anxiety	.002	...	...	.004	...	...	...
Insomnia	.002	...	...	.004	...	...	...
Fatigue	.003	.003	.024	.002	.006	.052	.005
Fatiguescore	.003	.003	.024	.002	.006	.052	.005
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	.004	...	...	...	...
Coughtotal	...	...	...	...	...	...	...
Anxietytotal	.002	...	...	.004	...	...	...
Insomserverity	.002	...	...	.003	...	...	.006
Insominfluence	.002	...	...	.004	...	...	...
DyspneaDiscomfort	.003	...	...	.004	...	...	...
DyspneaAnxiety	.004	...	...	.003	...	...	...
DyspneaEffort	.004	...	...	...	...	...	...

Standardized Total Effects (Group number 1 - Default model)

Standardized Total Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.227	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.293	.000	.000	.000	.000
Anxiety	.035	.000	.000	.086	.000	.000	.000
Insomnia	.120	.000	.000	.159	.000	.000	.000
Fatigue	.207	-.264	.039	.276	-.238	-.005	.168
Fatiguescore	.207	-.264	.039	.276	-.238	-.005	.168
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-.293	.000	1.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.035	.000	.000	.086	.000	.990	.000
Insomserverity	.111	.000	.000	.126	.000	.000	.596
Insominfluence	.109	.000	.000	.124	.000	.000	.685
DyspneaDiscomfort	.129	.000	.000	.483	.000	.000	.000
DyspneaAnxiety	.185	.000	.000	.694	.000	.000	.000
DyspneaEffort	.154	.000	.000	.638	.000	.000	.000

Standardized Total Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.515	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.046	.000	.000	.000	.000
Anxiety	.187	.000	.000	.409	.000	.000	.000
Insomnia	.437	.000	.000	.468	.000	.000	.000
Fatigue	.456	-.061	.283	.532	-.039	.244	.443
Fatiguescore	.456	-.061	.283	.531	-.039	.244	.443
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	-.046	.000	1.000	.000	.000
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.185	.000	.000	.406	.000	.993	.000
Insomserverity	.335	.000	.000	.359	.000	.000	.889
Insominfluence	.385	.000	.000	.411	.000	.000	.971
DyspneaDiscomfort	.337	.000	.000	.721	.000	.000	.000
DyspneaAnxiety	.423	.000	.000	.892	.000	.000	.000
DyspneaEffort	.384	.000	.000	.832	.000	.000	.000

Standardized Total Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.002	...	...	...	...	...	...
Physicalactivity	...	...	.004	...	...	...	...
Anxiety	.002	...	...	.007	...	...	...
Insomnia	.004	...	...	.004	...	...	...
Fatigue	.004	.003	.024	.002	.007	.056	.004
Fatiguescore	.004	.003	.024	.002	.007	.056	.004
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	.004	...	...	...	...
Coughtotal	.004	...	...	...	...	...	...
Anxietytotal	.002	...	...	.007	...	.004	...
Insomserverity	.003	...	...	.004	...	...	.008
Insominfluence	.002	...	...	.003	...	...	.004
DyspneaDiscomfort	.003	...	...	.004	...	...	...
DyspneaAnxiety	.003	...	...	.006	...	...	...
DyspneaEffort	.004	...	...	.006	...	...	...

Direct Effects (Group number 1 - Default model)

Direct Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.060	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-408.833	.000	.000	.000	.000
Anxiety	.000	.000	.000	.153	.000	.000	.000
Insomnia	.005	.000	.000	.149	.000	.000	.000
Fatigue	.000	-.316	.125	.579	-.002	-.007	.638
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	1.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.715
Insominfluence	.000	.000	.000	.000	.000	.000	1.000
DyspneaDiscomfort	.000	.000	.000	.554	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.716	.000	.000	.000
DyspneaEffort	.000	.000	.000	1.000	.000	.000	.000

Direct Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.152	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-62.778	.000	.000	.000	.000
Anxiety	.000	.000	.000	.678	.000	.000	.000
Insomnia	.104	.000	.000	.525	.000	.000	.000
Fatigue	.380	-.076	2.958	1.991	.000	.722	2.267
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	1.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	1.000	.000
Insomserverity	.000	.000	.000	.000	.000	.000	1.540
Insominfluence	.000	.000	.000	.000	.000	.000	1.000
DyspneaDiscomfort	.000	.000	.000	.879	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	1.160	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
DyspneaEffort	.000	.000	.000	1.000	.000	.000	.000

Direct Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.004	...	...	...	...	...	...
Physicalactivity	...	...	.004	...	...	...	...
Anxiety	...	...	...	.004	...	...	...
Insomnia	.021	...	...	.004	...	...	...
Fatigue	.046	.003	.037	.003	.006	.052	.005
Fatiguescore	...	...	...	...	...	...	...
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	...	...	...	...	...
Coughtotal	...	...	...	...	...	...	...
Anxietytotal	...	...	...	...	...	...	...
Insomserverity	...	...	...	...	...	...	.006
Insominfluence	...	...	...	...	...	...	...
DyspneaDiscomfort	...	...	...	.004	...	...	...
DyspneaAnxiety	...	...	...	.003	...	...	...
DyspneaEffort	...	...	...	...	...	...	...

Standardized Direct Effects (Group number 1 - Default model)

Standardized Direct Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.227	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.293	.000	.000	.000	.000
Anxiety	.000	.000	.000	.086	.000	.000	.000
Insomnia	.021	.000	.000	.159	.000	.000	.000
Fatigue	.000	-.264	.008	.100	-.238	-.005	.168

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.990	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.596
Insominfluence	.000	.000	.000	.000	.000	.000	.685
DyspneaDiscomfort	.000	.000	.000	.483	.000	.000	.000
DyspneaAnxiety	.000	.000	.000	.694	.000	.000	.000
DyspneaEffort	.000	.000	.000	.638	.000	.000	.000

Standardized Direct Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.515	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	-.046	.000	.000	.000	.000
Anxiety	.000	.000	.000	.409	.000	.000	.000
Insomnia	.330	.000	.000	.468	.000	.000	.000
Fatigue	.275	-.061	.259	.401	-.039	.244	.443
Fatiguescore	.000	.000	.000	.000	.000	.000	.000
Nutritionscore	.000	1.000	.000	.000	.000	.000	.000
Serverity	.000	.000	1.000	.000	.000	.000	.000
TotalMET	.000	.000	.000	.000	1.000	.000	.000
Coughtotal	.999	.000	.000	.000	.000	.000	.000
Anxietytotal	.000	.000	.000	.000	.000	.993	.000
Insomserverity	.000	.000	.000	.000	.000	.000	.889
Insominfluence	.000	.000	.000	.000	.000	.000	.971
DyspneaDiscomfort	.000	.000	.000	.721	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
DyspneaAnxiety	.000	.000	.000	.892	.000	.000	.000
DyspneaEffort	.000	.000	.000	.832	.000	.000	.000

Standardized Direct Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.002	...	...	...	...	...	...
Physicalactivity	...	...	.004	...	...	...	...
Anxiety	...	...	...	.007	...	...	...
Insomnia	.018	...	...	.004	...	...	...
Fatigue	.047	.003	.041	.005	.007	.056	.004
Fatiguescore	...	...	...	...	...	...	...
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	...	...	...	...	...
Coughtotal	.004	...	...	...	...	...	...
Anxietytotal	...	...	...	...	...	.004	...
Insomserverity	...	...	...	...	...	...	.008
Insominfluence	...	...	...	...	...	...	.004
DyspneaDiscomfort	...	...	...	.004	...	...	...
DyspneaAnxiety	...	...	...	.006	...	...	...
DyspneaEffort	...	...	...	.006	...	...	...

Indirect Effects (Group number 1 - Default model)

Indirect Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.015	.000	.000	.000	.000	.000	.000
Insomnia	.016	.000	.000	.000	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Fatigue	.146	.000	.080	.347	.000	.000	.000
Fatiguescore	.295	-.316	.448	1.255	-.002	-.007	.638
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-408.833	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.015	.000	.000	.153	.000	.000	.000
Insomserverity	.048	.000	.000	.181	.000	.000	.000
Insominfluence	.040	.000	.000	.149	.000	.000	.000
DyspneaDiscomfort	.044	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.057	.000	.000	.000	.000	.000	.000
DyspneaEffort	.060	.000	.000	.000	.000	.000	.000

Indirect Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.086	.000	.000	.000	.000	.000	.000
Insomnia	.070	.000	.000	.000	.000	.000	.000
Fatigue	.420	.000	.687	1.251	.000	.000	.000
Fatiguescore	.651	-.076	3.256	2.741	.000	.722	2.267
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-62.778	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.086	.000	.000	.678	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Insomserverity	.153	.000	.000	.592	.000	.000	.000
Insominfluence	.147	.000	.000	.525	.000	.000	.000
DyspneaDiscomfort	.115	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.141	.000	.000	.000	.000	.000	.000
DyspneaEffort	.152	.000	.000	.000	.000	.000	.000

Indirect Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	...	...	...	...	...	...	...
Physicalactivity	...	...	...	...	...	...	...
Anxiety	.002	...	...	...	...	...	...
Insomnia	.002	...	...	...	...	...	...
Fatigue	.002	...	.003	.002	...	...	...
Fatiguescore	.003	.003	.024	.002	.006	.052	.005
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	.004	...	...	...	...
Coughtotal	...	...	...	...	...	...	...
Anxietytotal	.002	...	...	.004	...	...	...
Insomserverity	.002	...	...	.003	...	...	...
Insominfluence	.002	...	...	.004	...	...	...
DyspneaDiscomfort	.003	...	...	...	...	...	...
DyspneaAnxiety	.004	...	...	...	...	...	...
DyspneaEffort	.004	...	...	...	...	...	...

Standardized Indirect Effects (Group number 1 - Default model)

Standardized Indirect Effects - Lower Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.035	.000	.000	.000	.000	.000	.000
Insomnia	.056	.000	.000	.000	.000	.000	.000
Fatigue	.116	.000	.006	.076	.000	.000	.000
Fatiguescore	.207	-.264	.039	.276	-.238	-.005	.168
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-.293	.000	.000	.000	.000
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.035	.000	.000	.086	.000	.000	.000
Insomserverity	.111	.000	.000	.126	.000	.000	.000
Insominfluence	.109	.000	.000	.124	.000	.000	.000
DyspneaDiscomfort	.129	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.185	.000	.000	.000	.000	.000	.000
DyspneaEffort	.154	.000	.000	.000	.000	.000	.000

Standardized Indirect Effects - Upper Bounds (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	.000	.000	.000	.000	.000	.000	.000
Physicalactivity	.000	.000	.000	.000	.000	.000	.000
Anxiety	.187	.000	.000	.000	.000	.000	.000
Insomnia	.225	.000	.000	.000	.000	.000	.000
Fatigue	.303	.000	.061	.232	.000	.000	.000
Fatiguescore	.456	-.061	.283	.531	-.039	.244	.443
Nutritionscore	.000	.000	.000	.000	.000	.000	.000
Serverity	.000	.000	.000	.000	.000	.000	.000
TotalMET	.000	.000	-.046	.000	.000	.000	.000

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Coughtotal	.000	.000	.000	.000	.000	.000	.000
Anxietytotal	.185	.000	.000	.406	.000	.000	.000
Insomserverity	.335	.000	.000	.359	.000	.000	.000
Insominfluence	.385	.000	.000	.411	.000	.000	.000
DyspneaDiscomfort	.337	.000	.000	.000	.000	.000	.000
DyspneaAnxiety	.423	.000	.000	.000	.000	.000	.000
DyspneaEffort	.384	.000	.000	.000	.000	.000	.000

Standardized Indirect Effects - Two Tailed Significance (BC) (Group number 1 - Default model)

	Cough	Nutrition	Severity	Dyspnea	Physicalactivity	Anxiety	Insomnia
Dyspnea	...	...	...	...	...	...	...
Physicalactivity	...	...	...	...	...	...	...
Anxiety	.002	...	...	...	...	...	...
Insomnia	.002	...	...	...	...	...	...
Fatigue	.002	...	.003	.002	...	...	...
Fatiguescore	.004	.003	.024	.002	.007	.056	.004
Nutritionscore	...	...	...	...	...	...	...
Serverity	...	...	...	...	...	...	...
TotalMET	...	...	.004	...	...	...	...
Coughtotal	...	...	...	...	...	...	...
Anxietytotal	.002	...	...	.007	...	...	...
Insomserverity	.003	...	...	.004	...	...	...
Insominfluence	.002	...	...	.003	...	...	...
DyspneaDiscomfort	.003	...	...	...	...	...	...
DyspneaAnxiety	.003	...	...	...	...	...	...
DyspneaEffort	.004	...	...	...	...	...	...

Minimization History (Default model)

Iteration		Negative eigenvalues	Condition #	Smallest eigenvalue	Diameter	F	NTries	Ratio
0	e	4		-.238	9999.000	582.848	0	9999.000
1	e	1		-.037	1.756	162.537	20	.611
2	e	1		-.014	.630	70.253	4	.771
3	e	0	26.491		.431	54.290	6	.774
4	e	0	21.701		.180	51.592	1	1.019
5	e	0	21.970		.026	51.556	1	1.015
6	e	0	21.949		.001	51.556	1	1.001

Bootstrap (Default model)

Summary of Bootstrap Iterations (Default model)

(Default model)

Iterations	Method 0	Method 1	Method 2
1	0	0	0
2	0	0	0
3	0	0	1
4	0	0	29
5	0	0	48
6	0	0	14
7	0	0	6
8	0	0	0
9	0	0	1
10	0	5	0
11	0	18	0
12	0	65	0
13	0	88	0
14	0	90	0
15	0	66	0
16	0	35	0

Iterations	Method 0	Method 1	Method 2
17	0	17	0
18	0	9	0
19	0	8	0
Total	0	401	99

0 bootstrap samples were unused because of a singular covariance matrix.

0 bootstrap samples were unused because a solution was not found.

500 usable bootstrap samples were obtained.

Bootstrap Distributions (Default model)

ML discrepancy (implied vs sample) (Default model)

```
                          |--------------------
                 53.145   |*
                 60.648   |******
                 68.151   |*********
                 75.654   |**********
                 83.157   |******************
                 90.661   |**********************
                 98.164   |**********
N = 500          105.667  |**********
Mean = 89.718    113.170  |******
S. e. = .772     120.673  |*****
                 128.176  |***
                 135.680  |*
                 143.183  |
                 150.686  |*
                 158.189  |*
                          |--------------------
```

ML discrepancy (implied vs pop) (Default model)

```
                        |------------------
                64.845  |*
                71.500  |**
                78.156  |*******
                84.811  |*****************
                91.466  |******************
                98.122  |**************
                104.777 |*************
N = 500         111.432 |*********
Mean = 96.404   118.088 |****
S. e. = .564    124.743 |**
                131.399 |*
                138.054 |*
                144.709 |
                151.365 |
                158.020 |*
                        |------------------
```


K-L overoptimism (unstabilized) (Default model)

```
                        |------------------
                -164.160|*
                -125.989|*
                -87.818 |****
                -49.647 |******
                -11.477 |************
                26.694  |***************
                64.865  |*****************
N = 500         103.036 |******************
```

Mean = 80.967	141.206	|**********
S. e. = 3.894	179.377	|**********
	217.548	|******
	255.719	|**
	293.890	|*
	332.060	|
	370.231	|*
		|----------

K-L overoptimism (stabilized) (Default model)

		|----------
	22.875	|*
	32.884	|*
	42.893	|****
	52.903	|******
	62.912	|**********
	72.921	|**********
	82.930	|**********
N = 500	92.939	|**********
Mean = 86.938	102.949	|**********
S. e. = 1.068	112.958	|**********
	122.967	|*****
	132.976	|**
	142.985	|**
	152.995	|*
	163.004	|*
		|----------

ML discrepancy (implied vs pop) (Default model)

```
                    |-------------------
          64.845    |*
          71.500    |**
          78.156    |*******
          84.811    |*****************
          91.466    |*******************
          98.122    |**************
          104.777   |*************
N = 500   111.432   |*********
Mean = 96.404 118.088 |****
S. e. = .564 124.743 |**
          131.399   |*
          138.054   |*
          144.709   |
          151.365   |
          158.020   |*
                    |-------------------
```


Model Fit Summary

CMIN

Model	NPAR	CMIN	DF	P	CMIN/DF
Default model	28	51.556	38	.070	1.357
Saturated model	66	.000	0		
Independence model	11	567.465	55	.000	10.318

RMR, GFI

Model	RMR	GFI	AGFI	PGFI
Default model	131.863	.963	.937	.555
Saturated model	.000	1.000		

Model	RMR	GFI	AGFI	PGFI
Independence model	298.896	.638	.566	.532

Baseline Comparisons

Model	NFI Delta1	RFI rho1	IFI Delta2	TLI rho2	CFI
Default model	.909	.869	.974	.962	.974
Saturated model	1.000		1.000		1.000
Independence model	.000	.000	.000	.000	.000

Parsimony-Adjusted Measures

Model	PRATIO	PNFI	PCFI
Default model	.691	.628	.673
Saturated model	.000	.000	.000
Independence model	1.000	.000	.000

NCP

Model	NCP	LO 90	HI 90
Default model	13.556	.000	36.450
Saturated model	.000	.000	.000
Independence model	512.465	439.709	592.676

FMIN

Model	FMIN	F0	LO 90	HI 90
Default model	.210	.055	.000	.149
Saturated model	.000	.000	.000	.000
Independence model	2.316	2.092	1.795	2.419

RMSEA

Model	RMSEA	LO 90	HI 90	PCLOSE
Default model	.038	.000	.063	.764
Independence model	.195	.181	.210	.000

AIC

Model	AIC	BCC	BIC	CAIC
Default model	107.556	110.440	205.705	233.705
Saturated model	132.000	138.798	363.352	429.352
Independence model	589.465	590.598	628.024	639.024

ECVI

Model	ECVI	LO 90	HI 90	MECVI
Default model	.439	.384	.532	.451
Saturated model	.539	.539	.539	.567
Independence model	2.406	2.109	2.733	2.411

HOELTER

Model	HOELTER .05	HOELTER .01
Default model	254	291
Independence model	32	36

Execution time summary

Minimization:	.000
Miscellaneous:	.343
Bootstrap:	.530
Total:	.873

VITA

Mr. Nguyen Hoang Long was born in Bac Ninh province, Vietnam on 5th January, 1984. He completed his Bachelor program in Nursing Science at Ha Noi Medical University, Ha Noi, Vietnam in 2006. After graduation, he became an instructor at Faculty of Nursing, Thang Long University, Ha Noi, Vietnam. He also worked as a clinical nurse in Viet Duc Hospital, Ha Noi, Vietnam.

In 2008, Vietnam Government granted him scholarship to study his master course in Adult nursing at Burapha University, Chonburi, Thailand. After finished the program in 2010, he served as acting head of Nursing Division, Faculty of Health Science, Thang Long University, Ha Noi, Vietnam.

In 2012, he enrolled to the Doctor of Philosophy in Nursing program at Chulalongkorn University under the full financial support of this university. He finished the program in 2015 and came back to his position in Thang Long University, Vietnam.