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# Effect of Lung Cancer Treatment on Health-Related Quality of Life

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This is to certify that the doctoral dissertation by

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Abstract

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MSPH, Walden University, 2006

MBA, MA, Webster University, 2002

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Dissertation Submitted in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Philosophy
Public Health

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# Abstract

Advances in lung cancer treatment among older adults require a risk-benefit analysis for health professionals, patients, and family members to assess increased survival and health-related quality of life (HRQL). The purpose of this study was to assess the effect of lung cancer treatment with surgery or tumor ablation on HRQL domains. A lung cancer quality of life model guided the study. The research design was a quantitative ancillary study in which 70 participants were recruited from those who had already consented to undergo a randomized clinical trial of lung cancer treatment. Data consisted of repeated administrations (baseline, 1- and 3-months) of the lung cancer symptom scale. Participants indicated their physical function, symptomatic distress, and overall quality of life experience on an analogue response card. Although randomization in a clinical trial ensures equal groups at baseline, self-selection and loss to follow-up in this comparative survey led to significant differences between the 2 treatment groups in age ($p = .049$) and average symptomatic distress ($p = .007$). Statistical analyses were performed using generalized estimating equations assuming a negative binomial distribution. There were no significant effects from treatment with surgery or tumor ablation on HRQL (physical symptoms, symptomatic distress, and overall quality of life experience) at 1-month ($p = .7794$, $p = .6395$, $p = .9318$) and 3-months ($p = .2616$, $p = .1345$, $p = .5217$) based on Holm-Bonferroni correction ($p = .016$). The findings indicate that among older adults with lung cancer there is no advantage in selecting surgery or tumor ablation in terms of effect on HRQL. The study may contribute to positive social change by providing lung cancer treatment-specific risk-benefit information affecting patient HRQL, which may be useful to providers, patients, and family members.

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# Dedication

This dissertation is dedicated to my lovely wife, Agnes, and my children: Claramence, Raymond, Irene, and Rosemary for their support, and encouragement towards my schooling as well the entire Som and Dokyi families of Obosomase and Kukurantumi, Ghana, West Africa for making my education to this point a success.

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Table of Contents

# List of Tables

# List of Figures

# Chapter 1: Introduction to the Study

## Introduction

In this study, I examined issues surrounding the demographic imperative or the aging of the population and the corresponding pressure on the United States public health systems. These changes include rising life expectancy, aging of work force, ongoing migration, and increasing diversity (U.S. Census Bureau, 2015). An increase in life expectancy, however, is driving age-related lung cancer incidence. The implication is that older adults receiving cancer treatment face worsening health-related quality of life (HRQL; Damm, Roeske, and Jacob, 2013). I conceptualized this study based on the aging process, cancer incidence among older adults, variety of newer treatments amenable to improved survival, and assessment of HRQL physical functioning specifically on older adults with lung cancer. In particular, I assessed physical HRQL domain on older adult patients (65 years and older) newly diagnosed with lung cancer and undergoing one of two treatment modalities: surgery or tumor ablation.Throughout this chapter, I describe the background issues in detail, purpose, nature of study, theoretical framework, significance, definitions, assumptions, and limitations.

## Background of the Study

The leading cause of death in the United States was cardiovascular disease from 1950 to 2010 however, cancer is now by far the leading cause of cancer death among both men and women (American Cancer Society [ACS], 2017; National Cancer Institute [NCI], 2017). The incidence of most types of cancers is age-dependent and the number of older adults 65 years and above is projected to reach 88.5 million by the year 2050 (U.S. Census Bureau, 2010) due to better diagnostic technology, different treatment modalities, and disease prevention and control. The U.S. Census Bureau projects that 1 out of 8 Americans will reach the age of 65 by 2030 (U.S. Census Bureau, 2010; DHHS, 2010).

The ACS is the national organization that publishes estimates of all cancer statistics using projections from past years. The Centers for Disease Control and Prevention (CDC) reports actual data from cancer registries but the data are not for the most recent years. According to the ACS (2017), the lifetime probability or risk of developing lung cancer is 1 in 14 for men and 1 in 17 for women (SEER 2012-2014 statistics, Howlader et al., 2017). The ACS estimates that out of 234,030 patients newly diagnosed with lung cancer, 65.8% (154,050) will die in 2017, which is the highest number of deaths among all cancers (ACS, 2017). There are also gender differences in case-fatality; men are 2.3 times more likely die from lung cancer (78.8%) compared to women (33.6%) (ACS, 2017; CDC, 2016).

Lung cancer is predominantly a disease of older adults where incidence increases with age (NCI, 2017). Men at age 65 have a 50 times greater risk of developing lung cancer than men age 25 and three to four times greater risk than men age 45 to 64 (ACS, 2016). While two-thirds of people diagnosed with lung cancer are 65 years of age or older, less than two percent of all cases are among those younger than 45 (ACS, 2016). The latest age-adjusted cancer statistics are for years 2010-2014 based on the Surveillance, Epidemiology, and End Results (SEER) statistics (Howlader et al., 2017). During this period the median age at diagnosis of cancer of the lung and bronchus was 70 years of age (Howlader et al., 2017).

The incidence rates of lung and bronchus cancer between 2010 and 2014 were 55.8 cases per 100000 overall, and 65.7/100,000 among men, and 48.4/100000 among women (NCI, 2017). Mortality rates indicate that close to half of those diagnosed with lung and bronchus cancer (44.7/100,000) die, where men (55.9/100,000) are more likely to die than women (36.3/100,000).

Lung cancer is classified into four stages (Stages I, II, III, and IV) ranging from mild to severe. Only a small portion of cases are diagnosed early at stage I (13.4%) or II (2.8%), whereas most of the cases are either diagnosed at stage III (25.0%) or stage IV (37.3%) and on over a fifth (21.5%) of cases staging is unknown (Damm et al. 2013; Gloeckler, Ries & Eisner, n.d., NCI SEER Survival Monograph, p. 75). Stage IV lung cancer is an advanced form of the disease treated with chemotherapy or radiotherapy alone or in combination with another therapy. Therefore, due to the nature of the advanced stage of disease as well as the type of treatment involved, I limited this study to Stages I, II, and III, which were all treated by tumor ablation, or surgery.

The combination of lung cancer, other comorbidities among older adults (such as chronic obstructive pulmonary disease and emphysema), and treatment side effects often result in devastating physiological and psychological threats to an older adult patient (Wilders, 2006). Furthermore, older adult lung cancer patients usually present specific characteristics such as pain, weakness, shortness of breath, hemoptysis, and cough (Damm et al., 2013). These lung cancer-related characteristics make the choice of correct treatment more difficult because older patients are often undertreated and significantly underrepresented in cancer trials (Braun et al. 2011; Di Maio and Perrone, 2003; Pasetto et al. 2007). Treatment strategy for lung cancer is strongly dependent on the stage of the disease (Bircan et al. 2003).

Treatment therapies for lung cancer include surgery, chemotherapy, radiation therapy, embolization, drug therapy (Hoffman, Brintall, von Eye, & Jones et al. 2014), as well as minimally invasive therapy such as image-guided tumor ablation (cryoablation, radiofrequency ablation or microwave ablation). The treatment approach for lung cancer is more aggressive at certain stages of the disease; however, selection of a specific treatment is based on the stage of disease and patient's ability to tolerate aggressive interventions (Pasetto et al., 2007). Assessment of toxicity of lung cancer treatment and comorbidity has become a focal issue in cancer research because of concerns about the high number of older adults suffering from cancer in general (Pasetto et al. 2007). In addition to assessment of HRQL among older adults receiving treatment through clinical trials, the impact of comorbidity needs adequate exploration among older adults with lung cancer (Hoffman et al., 2014; Pasetto et al. 2007; Wao et al. 2013).

Despite advances in medical research technology and vast lung cancer clinical trials, there is little progress in survival from lung cancer among older adults during the last decade of their life (Howlader et al., 2017). For example, the overall 5-year relative survival for lung cancer patients between 2003 and 2009 was 16.6% (NCI, 2012) and increased slightly to 18.1% from 2007-2013 (Howlader et al., 2017). Based on the latest SEER data (2007-2014) women have the greatest gains (21.3%) in survival compared to men (15.2%).

Therefore, assessment of the effect of treatment on HRQL has become more relevant due to aging of the population living with lung cancer, and significant improvement in healthcare as well as medical technology (Bircan et al., 2003). This assertion stems from most literature, which emphasizes the importance and effectiveness of using HRQL in modern day oncology studies (Balduyck, Hendriks, Lauwers & Van Schill, 2007; Bircan et al., 2003; Hoffman et al., 2014; Lyons, Bennett, Nail, & Fromme et al., 2014). In the past, older adults over age 65 were considered too frail to undergo cancer treatment or the relative survival was inadequate benefit to outweigh the risk of treatment. This type of decision-making resulted in limited information on treatment effectiveness among those 65 and older (Hsu, Chen, Shih, Ho, Yang et al. 2012).

Several instruments to measure HRQL in lung cancer were developed for cancer clinical trials to assess survival (Anant et al., 2005; Moinpour et al. 2012; Moller and Sartipy, 2012; Montazeri et al., 1998). According to Balduyck et al. (2007), HRQL assessments obtained through self-administered questionnaires are gaining recognition in oncology research and becoming an important part of evaluation criteria in clinical decision-making. HRQL encompasses aspects of overall HRQL that affect health—either physical or mental (CDC, 2011). HRQL assessments are feasible, useful, and beneficial in cancer studies. These measures provide comprehensive assessment of the patient’s condition in terms of how the disease is affecting HRQL.

## Assessment of Health-Related Quality of Life Dimensions

HRQL instruments measure five basic human functioning domains: physical, social, and role functioning, mental health, and general health perceptions (Balduyck et al, 2007; Cella, et al., 1995; Wilson & Cleary, 1995). These areas of functioning include important symptoms such as physical domain (vitality or energy/fatigue, pain, shortness of breath, cough, hemoptysis, and lack of appetite, (Damm et al., 2013; Davis, 2012) and mental health (cognitive functioning) domain (Wilson & Cleary, 1995).

The importance of HRQL dimensions as the major physical symptoms associated with lung cancer treatment are recognized by several researchers (Anant et al., 2005; Balduyck et al, 2007; Cella, et al., 1995; Wilson & Cleary, 1995). These authors stated that while a patient may suffer distress initially during the duration of the lung cancer it may not impact his or her daily activities, but over an extended period, pain and other treatment-related stressors such as shortness of breath, poor appetite, and fatigue may dominate the patient's life and thereby cause significant impairment (Anant et al., 200; Balduyck et al, 2007; Cella, et al., 1995; Wilson & Cleary, 19955). Some common symptoms that influence a lung cancer patient's HRQL are anxiety, depression, pain, fatigue, dyspnea (shortness of breath), and cough (Salvo et al. 2009).

There are over 50 HRQL scaled instruments used in lung cancer clinical trials. The most widely used are the Functional Assessment of Cancer Therapy (FACT, L version), European Organization for Research and Treatment of Cancer (EORTC, both versions), and Lung Cancer Symptom Scale (LCSS) (Anant et al., 2005; Damm et al., 2013; Davis, 2012; Hoffmann et al., 2014; Lemonnier, Guillemin, Arveux, & Clement-Duchene et al., 2014; Wintner et al. 2013). The functional domain tested, and the abbreviation of the scale is shown in Table 1. The physical domain was assessed in the six scales used most often. The SF-36 scale was used to assess all five domains, including physical, social, role, mental health, general health, while the EORTC assessed all domains except mental health, and the FACT assessed all domains except role, and mental health (Anant et al., 2005; Moinpour et al. 2012; Moller and Sartipy, 2012; Montazeri et al., 1998; Hoffmann et al., 2014).

Table 1

*HRQL Functional Domains Tested by Scale*

| **Domain** | **LCSS** | **EORTC** | **FACT** | **SF 36** | **KPS** | **VAS** |
|---|---|---|---|---|---|---|
| Physical | X | X | X | X | X | X |
| Social |  | X | X | X |  |  |
| Role |  | X |  | X |  |  |
| Mental Health |  |  |  | X |  |  |
| General Health |  | X | X | X |  |  |

*Source*: Anant et al., 2005; Montazeri et al., 1998; Darke, Donaldson, Cespedes, Johnson et al., 2012; Hoffmann et al., 2014; Moinpour et al. 2012; Moller and Sartipy, 2012. LCSS—Lung Cancer Symptom Scale, FACT—Functional Assessment of Cancer Therapy, EORTC—European Organization for Research and Treatment of Cancer, SF—Short Form, KPS—Karnofsky Performance Scale, VAS—Visual Analog Scale.

## Health-Related Quality of Life by Lung Cancer Treatment Type

Although the impact of lung cancer treatment on HRQL was assessed through the use of different scales and functioning domains, such as physical, role, social, and emotional functioning, significant differences among the treatment modalities were not documented by researchers using the instruments (see Table 1). Claassens et al. (2011) conducted a literature review to determine which type of scales were used more often to measure HRQL. They reported that 57% of the authors used EORTC for chemotherapy, surgery, radiation therapy, and drug therapy while 13% used LCSS for drug therapy, surgery, and radiotherapy. Some studies used the FACT (Cella et al., 1994) while very few used the other scales under chemotherapy, drug therapy, surgery, and radiation therapy. My review of the studies using the scales in Table 1, indicated that tumor ablation has been understudied using scales except for one study that used the Karnofsky Performance Scale (KPS) to assess impact on HRQL from cryoablation treatment (Tse et al., 2005). Table 2 presents the frequency and type of HRQL scale used to assess lung cancer treatment. Although in Table 1 the evidence indicates that physical domain was assessed using all the scales, examination of the data by treatment modality reveals that assessment of tumor ablation on HRQL has received minimal attention. In this study, I sought to fill this gap by assessing physical functioning between tumor ablation and surgery.

Table 2

*Assessment of Lung Cancer Treatment by HRQL Scale*

| | LCSS | EORTC | FACT | SF36 | KPS | VAS |
|---|---|---|---|---|---|---|
| **Tumor Ablation** | | | | | | |
| Physical | | | | | + | |
| Cognitive | | | | | | |
| Mental | | | | | | |
| **Radiotherapy** | + | +++ | + | | + | |
| **Surgery** | | | | | | |
| Chemotherapy | + | +++ | + | + | | |
| Embolization | | ++ | ++ | + | | + |
| Drug Therapy | ++ | +++ | ++ | | | + |

+++: most clinical trials used the particular type of scale; ++: moderate use of the scale; +: few used the scale. LCSS—Lung Cancer Symptom Scale, FACT—Functional Assessment of Cancer Therapy, EORTC—European Organization for Research and Treatment of Cancer, SF—Short Form, KPS—Karnofsky Performance Scale, VAS—Visual Analog Scale.

## Problem Statement

Lung cancer is the cancer that results in the highest rate of death for both men and women, and lung cancer cases make up nearly a quarter of all cancer deaths in the United States (NCI, 2012). According to the ACS (2014), the lifetime probability or risk of developing lung and bronchus cancer in the United States (2007-2009 statistics) is 1 in 13 in men and 1 in 16 women. Men age 65 have a 50 times greater risk of developing lung cancer than men age 25 and three to four times greater risk than men age 45 to 64 (ACS, 2014). The U.S. Census Bureau estimates that by the year 2030, one out of eight Americans will reach age 65 (US Census Bureau, 2010; DHHS, 2010).

Lung cancer is age related and leads to higher mortality among older adults as compared to people younger than 65 years (ACS, 2014). Men currently age 70 are 38 times more likely to develop lung cancer in 2 decades compared to men age 30 and older women 25 times more likely than younger women are (SEER, 2014). Older adult lung cancer patients have complex medical histories as well as a myriad of comorbidities. Unique characteristics such as physiological changes in organ function and pharmacokinetics add to the risk compared to benefit assessment and are often untreated or not given the best treatment (Di Maio & Perrone, 2003). The combination of lung cancer comorbidity (such as chronic obstructive pulmonary disease and emphysema), and treatment side effects, often results in devastating physiological and psychological threats for older adults (Wilders, 2006). Some common symptoms that influence a lung cancer patient’s quality of life are anxiety, depression, pain, fatigue, dyspnea (shortness of breath), and cough (Salvo et al., 2009; Wintner et al., 2013). Anxiety and depression significantly correlate with impaired HRQL (Frick et al., 2007).

There is a paucity of literature in studies of HRQL among older adults diagnosed with cancer, especially lung cancer. The evidence on the ability of key instruments (EORTC, KPS, FACT, and LCSS) to predict the effect of treatment on HRQL among older adults with lung cancer is mostly conclusive. However, many researchers advocate for further studies as there is much to learn about HRQL’s role in cancer clinical trials, cancer research in general, utility in treatment planning, and appropriate therapeutic goals (Anant et al., 2005; Moinpour et al., 2012; Moller and Sartipy, 2012; Montazeri et al., 1998). Most of the HRQL literature on lung cancer physical domain is limited to scaled assessments on surgery treatment; however, assessment of HRQL on tumor ablation has received minimal attention. There are physiological and psychological problems in older adult lung cancer patients which could be assessed; however, I selected a conceptual model for this study that focuses on physical functioning, functioning well-being (assessment of well-being is well beyond the scope of this study), symptomatic distress, and overall quality of life for lung cancer experience. Therefore, I sought to fill the effect of tumor ablation and surgery treatment on HRQL gap by assessing physical functioning, symptomatic distress, and overall quality of life experience among older adults with lung cancer undergoing tumor ablation and surgery.

## Purpose of the Study

The purpose of this study was to assess the impact of two lung cancer treatment modalities on HRQL physical functioning, symptomatic distress among older adults, and the overall quality of life experience among older adults. Lung cancer treatment improves both survival and quality of life, yet treatment is underutilized among older adults. Insufficient evidence is available as to the extent that different treatments improve HRQL and survival. The reasons for underutilization include the unique alterations in physiology that place older adults at greater risk of toxicity, comorbid conditions which can further reduce tolerance, and underrepresentation of older adults in clinical trials (Anant et al., 2005; Balduyck et al, 2007; Di Maio & Perrone, 2003; Quoix, 2011). Although new lung cancer treatments are available, pessimism delays assessment of the effect of new treatment on older adults functioning and survival (Anant et al. 2005; Zimmermann et al. 2011). Both health care providers and patients need this information to use as evidence for decision-making regarding treatment and clinical trial participation.

Measurement of HRQL can be feasible, worthwhile, and beneficial in cancer studies of older adults. My study examined differences in HRQL among older adult lung cancer participants who underwent tumor ablation or surgery as part of their treatment and participation in a randomized clinical trial (Tse et al, 2005; Balduyck et al, 2007). Assessment of the effect of lung cancer treatment, such as surgery and tumor ablation, on HRQL yielded reliable information to some extent (Balduyck et al, 2007; Anant et al., 2005; Cella et al, 1995); however, lung cancer is not adequately assessed in terms of HRQL among older adults. Some researchers suggest the impact of HRQL domains on lung cancer treatment for the older adult and the need for additional studies and further evidence on the subject (Larsson, Ljung, and Johansson, 2012; Moller and Sartipy, 2012).

## Nature of the Study

I selected a quantitative comparative survey of HRQL on older adults newly diagnosed with lung cancer undergoing treatment with tumor ablation or surgery. The study approach involved an add-on ancillary study to an ongoing randomized clinical trial. I recruited participants from the cancer center of a hospital in the Northeastern part of the United States. I selected two lung cancer treatment modalities for this study which were surgery and an image-guided ablation (tumor ablation). I selected these two because surgery remains the most common treatment for lung cancer while tumor ablation is a new modality and literature on it is scanty (Anant et al., 2005; Balduyck et al, 2007; Cella et al, 1995; Osoba, 2011; Simon and Dupuy, 2005). Chemotherapy and radiotherapy, although major therapies used in lung cancer treatment were excluded in this study because they are usually used to treat more advanced lung cancer diagnoses such as stage IV. The inclusion criteria for the study included patients diagnosed with lung cancer stages I through III treated with surgery or tumor ablation; age 65 years and older; male or female; and able to speak, write or read English.

To test the effect of lung cancer treatment on physical pain HRQL domains, I proposed three research questions and three hypotheses. The dependent variables are the six major symptoms associated with lung malignancies, symptomatic distress, and overall quality of life for the lung cancer experience. Operational measures for these variables as well as detailed statistical plans are discussed in Chapter 3. Specific survey questions are listed in Appendices B & F.

## Research Questions and Hypotheses

Research Question 1: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 1$)*:* There are no significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a 1$): There are significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at1-month and at 3-months period.

Research Question 2: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 2$): There are no significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a 2$): There are significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Research Question 3: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 3$): There are no significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a 3$): There are significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

## Theoretical Base

The lung cancer quality of life model developed, by Hollen et al. (1995), titled "Quality of Life Dimensions for the Lung Cancer Experience" provided the foundation on HRQL (Haywood, Garratt, & Fitzpatrick, 2005; Hollen et al., 1995). The model represents the physical dimension as the basic factor that affects an individual’s functioning as well as overall perception of quality of life related to lung cancer (Hollen et al. 1995). According to Hollen et al (1995), the concepts of function and physical dimensions are different concepts; function is related to factors such as activities of daily living (walking, eating) and at the same time to activities related to cognitive and social functioning.

The focus of this study is on the physical domains since it is the primary way treatment affects older adults compared to young patients who are affected in terms of function (activities of daily living and social life), symptomatic distress of the patient as well as the overall quality of life experience (Damm et al. 2013; Davis, 2012; Hirsh, 2014). In addition, the other domains not measured in the study increase participants' burden, as they duplicate clinical notes that the cancer center already collects during regular doctor's visits (ADLs) and they are not available for research purposes. Overall quality of life experience is the outcome and represents the resulting effects of the disease on the physical and functional dimensions, and therefore is conceptualized separately. This theoretical model for quality of life may explain outcomes of subjective factors (pain, cough, fatigue, etc.) assessed in lung cancer therapies throughout the treatment (Hollen et al. 1995).

A set of related concepts and the linkages between them are described in the framework; the model is displayed in a diagram (Figure 1). This model allows visualization of a specific problem offering better understanding to the concepts and their interrelationships. This quality of life profile is based on the model developed for clinical and research use on the lung cancer population (Hollen et al. 1995). The model is consistent with World Health Organization’s (WHO’s) definition of health, which states health is “a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity” (Diwan and Moriaty, 1995 as cited in WHO

Constitution, 1946). These concepts and the associated diagram are described further in Chapter 2.

## Definitions of Terms

The following terms are defined for this study.

*Appetite:* a desire or relish for food (www.nlm.nih.gov).

*Cough:* Coughing is a reflex that keeps throat and airways clear or forces air from the lungs with short sharp noises often when sick. Although it can be annoying, coughing helps body heal or protect itself. Coughs can be either acute or chronic (US National Library of Medicine, 2014).

*Fatigue:* Fatigue can refer to a subjective symptom of malaise and aversion to activity or to objectively impaired performance. It has both physical and mental aspects. It can be used as a complaint of weariness from bodily or mental exertion, exhaustion, and/or toil (Sharpe, M. & Wilks, D., 2002).

*Health-related Quality of Life (HRQL)*: this construct encompasses those aspects of overall quality of life that can be clearly shown to affect health—either physical or mental (CDC, 2011). HRQL was measured in this study by a composite score on the Lung Cancer Symptom Scale (LCSS; Hollen et al. 1995).

*Hemoptysis:* may be defined as coughing up blood that has volume of about 100 mL in 24 h; causes abnormal gas exchange/airway obstruction; causes hemodynamic instability; expectoration of blood from some part of the respiratory tract (Ibrahim, W. H., 2008).

*Pain:* usually a localized physical suffering associated with bodily disorder, normally a disease or an injury; it also can be an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (International Association for the Study of Pain [IASP], 2012).

*Shortness of Breath:* a feeling of difficult or labored breathing that is out of proportion to the patient's level of physical activity. It is a symptom of a variety of different diseases or disorders and may be either acute or chronic (Frey, 2002).

*Symptomatic Distress:* a condition found to be associated with diagnoses in lung cancer (Hollen et al. 1995).

*Surgery*: an operative procedure for correction of deformities or a process that is used to treat lung cancer (ACS, 2015). Participants were placed into this option by physician referral.

*Tumor ablation*: a process whereby a needle applicator is placed into solid tumors using imaging guidance. This treatment option comprises of three major techniques (Simon and Dupuy, 2005). Applicators can deliver electric current (Radiofrequency ablation), electromagnetic energy (microwave ablation) or intense cold (cryoablation). All these ablative techniques destroy tumor in situ. Radiofrequency ablation uses an alternating electrical current operating in the frequency of radio waves (460-480 kHz) emitted from the tip of an electrode or needle placed directly into targeted tissues within the human body. The heat generated is used to destroy the tissues within the body. Microwave ablation is an electromagnetic method for inducing tumor destruction using devices with frequency of 900 MHz or greater. Cryoablation is a process whereby a local application of liquid nitrogen is used as an adjuvant to resection in treating tumors (Simon & Dupuy, 2005).

## Assumptions

There were three assumptions I made in developing this study. The first one is that the disease *sequelae* and treatment side effects of lung cancer are devastating and lasting longer than 3months. Second, that participants would answer the questionnaires openly and honestly because they were assured their responses would be kept confidential and anonymous. Third, that the selected instrument (LCSS) would accurately assess and differentiate HRQL measures since they were found to be valid and reliable tools and have been confirmed in international standards/studies (Hollen et al. 1995).

## Limitations

There were two limitations that I identified in this study, including generalizability and bias from refusal to participate, loss to follow-up, and mortality. The use of a small, sample from one hospital and geographic area may limit the generalizability of these findings. However, due to the lack of research on HRQL in the older adult participant, placing a higher burden on these participants was a concern, and additional studies can be designed later. The devastation of the diagnosis of lung cancer, the negative effects of the disease progression, and the treatment side effects may result in patients' reluctance to participate in the study and may cause sample bias and sample mortality. Participants will be encouraged but not coerced to participate in the study.

## Delimitations

There were two delimitations that I made in designing this study, including selecting only two lung cancer treatments to compare, and excluding combination therapies. This study is limited to examination of differences in older adults' HRQL from two treatment options (surgery and tumor ablation). The other treatment options such as chemotherapy and radiotherapy are used as advanced or stage IV therapies (Damm et al., 2013; Wao et al., 2013). The incidence of lung cancer is rare in young adults. The treatment modalities selected for this study are used to treat patients that can be followed-up regularly and who are expected to recover. There will be no studies of combination therapies. To avoid confounders, only stand-alone therapies were considered to capture changes in specific treatment. Because this study considered less advanced stages such as stages I, II, and III, combination therapies were not included as these are used with advanced staged IV lung cancer. The clinical design was not my decision but that of the core randomized clinical trial conducting the initial recruitment and enrollment of patients. However, a single treatment isolates the symptoms due to one treatment.

## Significance of the Study

The significance of this study stems from the fact that lung cancer ranks number one in incidence of cancer (Damm et al., 2013, SEER, 2014) among both males and females, young and old. There is also scarcity of research in lung cancer on older adults in terms of HRQL. Prior to this study, the effect of surgery and tumor ablation treatments on HRQL were not evaluated substantially. As reviewed in the literature, HRQL is the most important predictor of survival for older adult lung cancer patients (Cella et al., 1995; Damm et al., 2013; Davis, 2012; Hoffmann et al., 2014; Hollen et al., 1995; Wintner et al., 2013**).** The results of this study could be used to determine which cancer treatment option is more likely to be tolerated in older adults. Implications from the findings of this study may offer decision-making information suitable to older patients in clinical settings. This study may add to existing information on quality of life domains. Information on quality of life domains may offer patients the opportunity to identify the advantages and disadvantages of each treatment to HRQL. Furthermore, having knowledge of potential changes in HRQL over the course of treatment may add evidence-based information when selecting medical options. Medical practitioners, nurses, public health professionals, clinical social workers, chaplains and other professionals providing therapy and counseling to lung cancer patients can do a risk-benefit analysis in their decision-making. Evidence-based information may allow providers to understand the patients' perspective and their preferences in HRQL. Taking HRQL into consideration may help to provide humane treatment that will meet the potential needs of older adult lung cancer patients.

## Summary and Transition

Lung cancer incidence is higher in older adults compared to other age groups. Lung cancer is often not diagnosed until late in progress when case-fatality increases. Because of the aggressive process of late stage cancer, the frailty of older adults, and the significant impact on physiological and psychological effect that lung cancer treatment has on older adults, assessment of HRQL physical functioning, symptomatic distress, and lung cancer experience is of major importance. Although the need for humane, effective treatment exists, a review of the literature indicated there is a paucity of research on the impact various treatment options have on HRQL domains in older adults. The effectiveness of newer lung cancer treatment modalities on HRQL has not been thoroughly assessment. The purpose of this study was to compare three aspects of HRQL among older adult lung cancer patients undergoing treatment with surgery and tumor ablation. The physical domain includes individual pain, appetite, shortness of breath, fatigue, cough, and hemoptysis, as well as symptomatic distress, and overall quality of life experience. This chapter is followed by a review of the relevant body of literature on lung cancer treatment among older adults.

# Chapter 2: Literature Review

## Overview

The purpose of this study was to assess the effect of lung cancer treatment modality on HRQL among older adults. Lung cancer affects all age groups, but mainly diagnosed in older adults at a rate of two out of three individuals diagnosed at 65 years and older (ACS, 2013). Fewer than three percent of all lung cancers occur among those under the age of 45 years (ACS, 2013). The average age at diagnosis is approximately 70 years (ACS, 2013). Lung cancer consists of two types: small-cell lung cancer (SCLC) and non-small-cell (NSCLC). NSCLC constitutes about 80-85% of all lung cancers, while SCLC accounts for the remaining 15-20% (Gridelli, Langer, Maione, Rossi, & Schild, 2007). More than 50% of cases of advanced NSCLC were diagnosed among patients who were older than 65, and about 30-40% of incident cases were diagnosed among those older than 70 (SEER, 2016; Gridelli et al., 2005).

Although the older adult population makes up the fastest-growing segment in the United States (U.S. Census Bureau, 2012; 2014), older lung cancer patients are often excluded from participating in clinical trials (Gridelli et al., 2005; 2007). Older adult patients have traditionally been excluded based on age when enrolling in clinical trials involving lung cancer, especially stage III cancer (Gridelli et al., 2005; 2007). However, due to technological advances, standard treatment offered, and evidence from clinical trials, stage III older adult lung cancer patients are now enrolled without prejudice if they can tolerate the treatment offered and do not have significant limitations in functional ability (Schild et al., 2003; Wintner et al., 2013).

In this chapter, I describe the literature search strategy. I also describe the core issues related to the conceptualization of the study, such as the theoretical model, pathophysiology of lung cancer, relevant literature on HRQL, lung cancer, and the effects of changes in HRQL on lung cancer treatment.

## Literature Search Strategy

I used the following databases for my literature review: Ovid Online database (Health and Psychosocial Instruments), Lifespan Online library (Rhode Island and Miriam Hospitals), and Lifespan Library located on campus of a private hospital in Northeastern part of the United States. I also used the Walden University library, the United States Oncology Review, the Brown University library, and topic-related textbooks to search for the most relevant published articles related to this study. The search included articles published between 1992 and 2016. Literature published 5-10 years ago was included because the initial search for the proposal did not yield much literature passed 2005. Literature on quality of life for lung cancer patients resurfaced since 2014. Older published articles were included because they provided key relevant background information about the study topic. The following key words were used as the root of all inquiries: *health-related quality of life assessment*, *health-related quality of life assessment and lung cancer treatment*, *lung cancer and health-related quality of life measurements*, *lung cancer and the elderly*, and *lung cancer treatment modalities and the elderly*. With these terms, other search words were used to narrow the search: *health-related quality of life as related to tumor ablation and surgery*, *health-related quality of life and cancer in the elderly*, *health-related quality of life assessment in the elderly lung* *cancer patients*, and *different methods of cancer treatment*, were used to narrow the search.

In the remaining content of the literature review I highlighted seminal research capturing the effects of HRQL assessments on lung cancer treatment for older adults. The goal was to provide a better understanding of the physiological effects of quality of life domains among older adult lung cancer patients. The literature review is organized into six sections. The first section consists of the presentation of the conceptual model that I used to guide this study. The second section includes the pathophysiology of stages I, II, and, III lung cancer. The third section consists of a review of the two different therapies under consideration for this study. The fourth section consists of a review on aging process as it pertains to lung cancer in older adults. The fifth section consists of a review of the ethics of quality of life, while the sixth section includes a discussion of the quality of life tools used to guide this study as reviewed in the literature.

## Theoretical Model

The theoretical model I used to guide this study was the quality of life dimensions for the lung cancer experience developed by Hollen et al. (1995). The model is composed of three quality of life dimensions: a physical dimension, a functional dimension, and overall quality of life (Figure 1). The model conceptualizes a physical dimension as the basic dimension that influences functioning as well as overall experience of quality of life among those with lung cancer. The developers of the model conceptualized the dimension of function as distinct from the physical dimension where physical dimension is related to daily activities (walking, eating), and function reflects cognitive and social functioning. The functional dimension is separate from the physical dimension which is linked to activities such as walking, eating, resting, and is separate from those activities that reflect cognitive and social functioning. During the initial stages of lung cancer, it may not be evident that the disease is affecting cognitive and social functioning (Hollen et al., 1995). Overall quality of life represents a separate dimension and serves as the measure of the outcome variable or the effect of lung cancer on the physical and functional dimensions.

The study assessed physical dimensions, symptomatic distress, and overall quality of life for the lung cancer experience (Figure 1, pg. 28). The functional dimension, which measures functional activities such as walking, eating, resting or ADLs, is not captured in the cancer treatment experience until much longer than 3 months of progression and thus beyond the scope of this study (Lemonier et al, 2014). In addition, according to the principal investigator at the cancer center study site, this dimension is ascertained during the clinical process and is not available to link with research data. Attempts to collect this type of data represent an unnecessary participant burden, or duplicate clinical notes that the cancer center might have already collected during doctor's regular visits and these are not available for research purposes. However, symptomatic distress and overall quality of life experience among those with lung cancer was explored. There are preconditions, which may mediate experience with lung cancer and activity status (ADLs); however, these aspects are not as important in evaluating treatment interventions after initial diagnosis (Lima et al., 2011). Preexisting factors may have a direct negative effect on functional status and quality of life (Lima et al., 2011). According to Hoffman et al. (2014) preexisting factors such as unmanaged fatigue may become determining factors in evaluating treatment interventions of lung cancer.

The six major physical dimension symptoms (loss of appetite, cough, pain, shortness of breath, hemoptysis, and fatigue) of lung cancer are considered common and relevant symptoms of lung cancer by oncologists and lung cancer researchers (Damm et al., 2013; Davis, 2012; Hirsh, 2014). Alleviation of predominant physical manifestations of illness and other symptomatic distress and activity status may impact lung cancer treatment more than other dimensions, such as overall quality of life (Hollen et al., 1995; Hollen et al., 2006). To properly assess the subjective nature of psychological dimensions, the predominant six major symptoms should be assessed separately from other forms of symptomatic distress. However, in the conceptual model diagram (Figure 1) symptomatic distress falls under the physical dimension. Symptomatic distress refers to the way the individual perceives the severity of the symptom and occurs in conjunction with the major physical symptoms related to quality of life. Symptomatic distress was measured as one of the dependent variables. Activity status represents the functional dimension and includes social dimension to depict the association with the major physical symptoms. Global quality of life includes every dimension that was not detailed according to the model but could be linked to lung cancer (Figure 1; Hollen et al., 1995).

The diagram in Figure 1 was derived from the LCSS where I depict how the study was guided by this model. The figure highlights the two concepts (physical dimension and quality of life for those who experienced lung cancer) that are operationalized in this study to ascertain the HRQL following lung cancer treatment. HRQL physical domains which include shortness of breath, pain, fatigue, appetite, cough, hemoptysis, together with symptomatic distress (global symptomatic distress from lung cancer) make up the physical dimensions related to overall quality of life for the lung cancer experience. The overall quality of life for lung cancer experience captures global quality of life, which embodies other types of dimensions including cognitive, psychological, social, spiritual, and all others that might come into play in the patient's life.

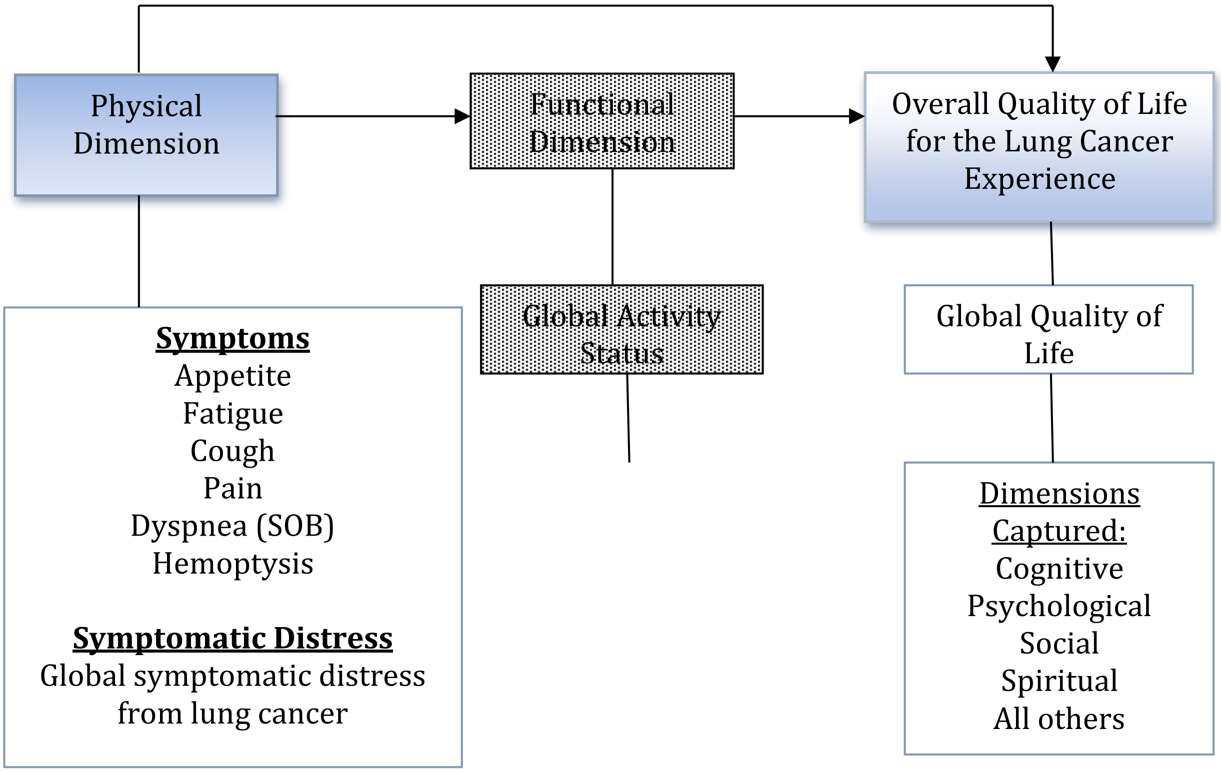

*Figure 1. Quality of Life Dimensions for the Lung Cancer Experience*

*Source:* Quality of Life during Clinical Trials: Conceptual Model for the Lung Cancer Symptom Scale. *Supportive Care Cancer*, 2, 213-222 (Hollen et al., 1995; Appendix D) *with permission*. The concepts highlighted indicate the constructs operationalized in the study.

The authors used the model as the basis for their study in measuring quality of life in patients with pleural mesothelioma to determine psychometric properties of the Lung Cancer Symptom Scale (LCSS)-mesothelioma—LCSS-meso (Hollen et al., 2006; Hollen et al., 2004). A modified version from the original LCSS 9-item patient reported scale and 6-item observer-reported scale of LCSS were used in two clinical trials. Improved scores were found in participants who scored better in terms of performance and had better symptom improvement among participants with tumor response (Hollen et al., 2006).

I presented discussion of literature on assessment of smoking and lung cancer quality of life due to the limited applied literature using the LCSS by Hollen et al. (1995, 2004, 2006). The literature on assessment of smoking and lung cancer quality of life adds supporting evidence of the model's ability to assess quality of life. Garces et al. (2004) used the LCSS based on the conceptual model by Hollen et al. (1995) to assess the relationship between quality of life and cigarette smoking after a diagnosis of lung cancer. The researchers recruited the sample between 1999 and 2002 and included 1028 respondents with lung cancer that were surveyed at the beginning and follow-up post-treatment for surgery, radiation, and chemotherapy. During diagnosis of lung cancer, there was a gradient of quality of life scores across smoking status where those who never smoked had the lowest scores (better quality of life), former scores had intermittent scores, and persistent smokers had higher LCSS scores (worse quality of life) (Garces et al., 2004; Sloan, Zhao, Novotny, Wampfler, Garces et al. 2012).

LCSS scores were contrasted with various groups of smokers using univariate independent group testing and multivariate linear models (Garces et al., 2004). The researchers of the study examined quality of life differences among groups of smokers, adjusting for gender, age, time of assessment, and stage at diagnosis (Garces et al., 2004). There was a clinically significant 10-point difference between groups as being clinically significant (Garces et al., 2004; Sloan et al. 2012). The adjusted average total LCSS scores for those who never smoked and persistent smokers were 17.6 and 28.7 (Garces et al., 2004). The authors found out of the seven individual LCSS quality of life components consisting of fatigue, appetite, shortness of breath, cough, lung cancer symptoms, illness affecting normal activities, and overall quality of life, were statistically different among those who never smoked compared to those who were persistent smokers (Garces et al., 2004). There were no clinically significant differences for pain or hemoptysis. In addition, former smokers had intermediate LCSS scores (Garces et al., 2004). The authors therefore concluded that the relationship between smoking status and quality of life were supported by their correlational study and that their findings suggested that continued cigarette smoking after diagnosis of lung cancer negatively impacted quality of life. There was a gradient of quality of life scores across smoking status where those who never smoked had the lowest scores (better quality of life), former scores had intermittent scores, and persistent smokers had higher LCSS scores (worse quality of life) (Garces et al., 2004; Sloan et al. 2012).

## Pathophysiology of Lung Cancer

Lung cancer forms in the lungs within the cells, which line the air passages (American Cancer Society [ACS], 2013). Lung cancer is a very aggressive disease and if not detected early enough can have a very poor outcome (ACS, 2013). According to the ACS recent estimates, in 2013 there were 228,190 new cases that included small cell and non-small cell lung cancer diagnoses in the United States and 159,480 deaths from lung cancer (ACS, 2013). Between both genders, lung cancer is the leading cause of cancer death (ACS, 2013). The American Cancer Society (2013) stated that lung cancer contributes to more deaths than a combination of colon, breast, and prostate cancer. Lung cancer tends to be less common in those under 45 years (Hsu et al., 2012). There are differences in gender where a man can develop lung cancer at a rate of 1 in 13, and women 1 in 16 (ACS, 2016).

There are four distinct stages of lung cancer that range from mild to the most severe form (ACS, 2013). Stage IV lung cancer is an advanced form of the disease treated with chemotherapy or radiotherapy alone or in combination with another therapy. Therefore, due to the nature of the advanced stage of disease and the type of treatment involved, this research study was limited to Stages I, II, and III that were treated by tumor ablation or surgery. Stage I lung cancer is the earliest stage of lung cancer diagnosis and the one where long-term survival is the best; stage II lung cancer is defined as *localized cancer* where a tumor is present in the lung and may have metastasized to local lymph nodes, but has not spread further (NCI, 2012); non-small cell lung cancer is diagnosed as Stage III when the tumor has protracted beyond the lung and into other structures in the mediastinum or chest wall, directly or through the lymph nodes.

### Stage I

Stage I lung cancer is the earliest stage of lung cancer diagnosis and the one where long-term survival is the best. About 30% of all lung cancer is at this stage or stage II (Henschke et al., 2006). Stage I lung cancer can present no symptoms; it can be detected when an individual at risk undergoes a computed tomography (CT) screening. Common symptoms may include persistent cough or recurrent episodes of pneumonia or bronchitis (NIH, 2010). Since the cancer does not spread easily, the major symptom associated with the disease is extreme fatigue, but weight loss or significant pain is usually absent (NCI, 2012). Surgery is usually considered the best treatment for stage I, but treatment also depends on where the tumor is located and the general health condition of the person. Three major types of surgery are performed, including video-assisted thoracoscopic surgery (VATS), stereotactic body radiotherapy (SBRT), and radiation therapy (ACS, 2014; NCI, 2012). VATS are minimally invasive and may be used for those who cannot tolerate the traditional surgery such as older adults. In addition to surgery, other options for treatment of stage I lung cancer include radiation therapy and SBRT (ACS, 2014; NCI, 2015). Radiation therapy can be an option for patients with inoperable tumors and has proven successful enough to result in a cure (ACS, 2013). The third type of treatment is a new technique, SBRT and tumor ablation, which appears to be quite promising for those who are unable to go through surgery for stage I lung cancer (Pennathur et al., 2009).

### Stage II

Stage II lung cancer is defined as localized cancer meaning that a tumor in the lung exists and has metastasized to local lymph nodes, but has not spread further (NCI, 2012). Stage II lung cancer is subdivided into stages IIA and IIB. The National Cancer Institute (NCI, 2012) defined stage IIA lung cancer as a tumor which is 3 centimeters or smaller and cancer has not spread to nearby lymph nodes at the same side of the chest containing the tumor, whereas in stage IIB, cancer has spread to nearby lymph nodes on the same side of the chest as the tumor. The most prevalent symptoms in stage II lung cancer include a persistent cough, hemoptysis, shortness of breath, and pain in the chest or back. Symptoms such as weight loss and fatigue are less commonly identified with this stage of lung cancer as they are found in more advanced forms of lung cancer (NCI, 2012). Once again, surgery is considered optimal for this stage of lung cancer. The three types of surgery for stage II lung cancer depend on the location of the tumor as well as general health concerns. Adjuvant chemotherapy or radiotherapy is recommended for those who are not able to undergo surgery for stage II lung cancer (Scott et al., 2007).

The recurrence rate for localized cancer is in the range of 20-50%, while the 5-year survival rate for stage II lung cancer is 40-50% (Kelsey, Clough, & Marks, 2006). This evidence indicates that lung cancer is highly recurrent and difficult to survive depending on the tumor and general health condition of the patient.

### Stage III

Non-small cell lung cancer (NSCLC) is diagnosed as Stage III when the tumor has protracted beyond the lung and into other structures in the mediastinum or chest wall, directly or through the lymph nodes (ACS, 2014; CDC, 2014). Cancer treatment becomes more difficult with increasing stage at diagnosis and greater severity (NCI, 2012). Compared to stages I and II, stage III lung cancer has a higher severity of disease and found near vital organs; thus, it is more difficult to treat with surgery (Lonardi et al. 2000). Although the recommendation for treating stage III lung cancer is a combination of radiation therapy and chemotherapy, individualized treatment depends on performance status, prior weight loss and overall health (Lonardi et al., 2000). Thus, stage III lung cancer tends to be more challenging to cure compared to stages I and II because the tumor may be problematic or impossible to remove by surgery because of the severity of disease and the location near vital organs (Lonardi et al., 2000).

## Surgery and Tumor Ablation Treatments for Lung Cancer

Many therapies such as surgery, embolization, drug therapy, chemotherapy, radiotherapy, and tumor ablation are conventional lung cancer treatments. Although these therapies have advantages and drawbacks in lung cancer treatment, surgery and tumor ablation were selected as the primary focus of the study. Surgery and tumor ablation are the two treatments selected for this study. Definitions of these lung cancer therapies or treatments have been discussed in Chapter 1.

Surgery refers to an operative procedure for correction of deformities or a process that is used to treat lung cancer (ACS, 2015), and radiotherapy were documented in the literature to yield effective results (Chen & Johnston, 2002; Kelsey et al., 2006; Salati, Brunelli, Xiume, Refai & Sabbatini, 2009). Tumor ablation is a process whereby a needle applicator is placed into solid tumors using imaging guidance. This treatment option comprises of three major techniques (Simon and Dupuy, 2005). Applicators can deliver electric current (Radiofrequency ablation), electromagnetic energy (microwave ablation) or intense cold (cryoablation); although a relatively new modality, has achieved laudable results in the treatment of nonsurgical lung cancer patients by improving quality of life, survival, and overall prognosis (Dupuy et al., 2006; Jian, Dupuy, Cardarelli, Zheng, & DiPetrillo, 2003). Tumor ablation also reduces morbidity and mortality compared to surgery at a lower cost as well (Jian et al. 2003). Jian et al. described three older adult lung cancer patients who underwent radiofrequency ablation successfully; Belfiore et al. (2004) reported 35 successful radiofrequency ablation treatments that were performed with very encouraging results; and Tse et al. (2005) conducted a study in which transvenous catheter cryoablation was done successfully on atrial fibrillation (AF) patients. The study was conducted to determine the effects and the improvement of quality of life of the AF patients. Patients who had AF had significantly lower quality of life scores (Tse et al., 2005). However, patients who underwent successful cryoablation showed significant improvement overall and in five out of eight SF-36 quality of life subscale scores compared with baseline (Tse et al., 2005).

Surgery and tumor ablation play a role in the treatment of lung cancer as indicated in the literature. Evidence indicated that the two lung cancer therapies proposed in this study were recognized for their effectiveness and the associated promising results (Balducci, 2003; Bircan et al., 2003; Dupuy et al., 2006). Owonikoko et al. (2007) conducted an analysis of lung cancer in older adults to determine differences in survival based on treatment modality. The distribution of cancer stage was not significantly different across age groups (less than 70, 70-79, and 80 and older), but the pattern of improved overall prognosis was observed across all stages. Between 1988-1997 and 1998-2003 use of surgery increased while use of radiation decreased. Owonikoko et al.'s findings indicated that the respective therapies yielded good survival benefits. Of the 316,682 patients eligible, 14% were 80 years or older, 33% were 70-79 years, and 53% below 70 years. Patients who were 80 or older were less likely to avoid surgery or radiation than those who were younger (47% compared to 28% and 19% for age subgroups greater or equal to 80 years, 70-79 years, and < 70 years, respectively). In general, prognosis for patients who had surgical therapy or radiation was similar among the three age groups (Owonikoko et al., 2007). In addition, there is an evidence of significant improvement in outcome for all groups with any treatment (Owonikoko et al., 2007). However, evidence of disease progression was found in neither participant who received either therapy, surgery, nor radiation during the period 1998-2003 (Owonikoko, et al., 2007).

Salati et al (2009) conducted a study of 279 patients who went through major lung resection where 98% of the patients survived the surgery. In this study, quality of life assessment was done using the SF-36 before the operation and at 3 months after the surgery measuring eight health concepts (bodily pains, physical functioning, vitality, physical role limitation, general health perception, social functioning and emotional role limitation, and mental health). The authors observed and reported that older adult lung cancer participants experienced a level of postoperative individual physical, emotional, and social well-being comparable to the mean of a general population of older adults (Salati et al., 2009).

A study by Win et al. (2005) assessed 150 patients for consideration of lung cancer treatment using surgery. Twenty-one percent of patients were excluded for several reasons; not fit for surgery, refusal to go through surgery (12), or had more advanced disease at the final pathologic review (20). In addition, tumors found in eight were unresectable at the time of the surgery (open and closed thoracotomy), making it impossible to be studied further (Win et al., 2005). The study sample consisted of the remaining 110 patients (30% had borderline lung function). Evaluation using the EORTC QLQ-C30 included measuring emotional, social and cognitive functioning as well as physical role. The instrument also includes three symptom scales, one that measures pain, fatigue, nausea, and vomiting, a quality of life scale, as well as single items that assess additional symptoms (Win et al., 2005). The supplementary lung module LC 13 was also used to measure lung cancer associated symptoms that included hemoptysis, cough, shortness of breath, chest or body pain, and chemotherapy or radiotherapy side effects that may include peripheral neuropathy, sore mouth, dysphagia, and hair loss (Win et al., 2005). Before the 110 patients underwent surgery, both instruments were administered and at 1, 3 and 6 months postoperatively (Win et al., 2005). The authors reported that those identified as operable lung cancer patients had a reasonable quality of life compared with a general lung cancer population (Win et al., 2005). Furthermore, the short-term surgery for lung cancer had a short lived negative effect on quality of life that dissipated at 6 months post-surgery. Unfavorable HRQL scores did not predict poor surgical outcome, defined as death or major complication, although poor surgical outcome was correlated with a worse postoperative quality of life at 6 months (Win et al., 2005).

Radiofrequency ablation reduces morbidity and mortality as compared to surgery and together with its lower cost makes it suitable for older adult lung cancer patients to be able to opt for such therapy (Dupuy et al., 2006; Jain et al., 2003). In addition, palliative care symptoms associated with quality of life such as cough, hemoptysis, shortness of breath, and pain were reduced with radiofrequency ablation (Jain et al., 2003). To determine the importance of tumor ablation as an upcoming viable lung cancer treatment therapy, Jain et al. (2003) described how three patients (ages 78, 61, and 65 years old) were treated with combined radiofrequency ablation and brachytherapy guided by computer tomography. The authors stated that the three patients tolerated the combination therapy well (Jain et al., 2003). The authors determined that percutaneous radiofrequency ablation in conjunction with brachytherapy is feasible and suggested that a minimally invasive combination modality can be used to eradicate local tumors (Jain et al., 2003). In addition, radiofrequency ablation, a new therapy used to remove lung tumors, could provide significant advantages to nonsurgical candidates who undergo lung cancer therapies (Jain et al., 2003). Jain et al. (p. 712) therefore reported that “percutaneous image-guided tumor ablation with radiofrequency is an expanding minimally invasive modality for the local treatment of solid malignancies”.

In a study conducted by Belfiore et al. (2004), 35 successful radiofrequency ablation treatments were performed where the objective was to investigate the safety, effectiveness, technical feasibility/possibility, and possible complications of palliative CT-guided radiofrequency ablation of unresectable primary pulmonary malignancies. Complications included were three cases of minor pneumothorax, five cases of sputum cruentum, and three asymptomatic pleural effusions in the periprocedural period (Belfiore et al., 2004). The authors suggested that radiofrequency ablation could be successful for unresectable lung cancer in addition to radio- or chemotherapy (Belfiore et al., 2004).

Clinical and treatment-related data regarding 129 consecutive percutaneous radiofrequency ablation treatment sessions for 100 patients with inoperable lung tumors were analyzed for risk factors following procedures that included pleuritic chest pain, overall morbidity, pleural effusions, hemoptysis, pneumothorax, and chest drain requirement (Zhu, Yan, Glenn, & Morris, 2009). Researchers found that for lung tumors radiofrequency ablation was considered as a safe procedure with low incidence of complications and that better understanding of any risk factors because of adverse events could help in preventing and recognizing any potential complications (Zhu et al., 2005).

Tse et al. (2005) conducted a study in which transvenous catheter cryoablation was done on atrial fibrillation patients. This study was conducted to determine the effects and the improvement of quality of life of the atrial fibrillation patients. Quality of life was assessed using Medical Outcomes Study Short Form 36 and Symptom Checklist at baseline and 3-months post treatment. Participants were compared with sex-age matched normal controls. The authors reported that at baseline, patients with atrial fibrillation had lower quality of life scores overall and five out of eight subscales of SF-36 compared to the sex-age matched control group ($p < 0.05$). On the other hand, patients who had successful cryoablation showed significant improvement in overall and in five out of eight subscales of SF-36. Quality of life scores have significantly increased as compared with the baseline ($p < 0.05$; Tse et al., 2005). However, at the 3-month follow-up, there was a significant reduction in both symptom frequency and symptom severity scores as compared with the baseline scores ($p < 0.05$; (Tse et al., 2005).

The benefit of selecting which treatment modality yields positive outcomes for both the patient and the clinician had been elaborated in the literature. Several authors suggest that positive outcomes will better assess the prevailing symptoms suffered by the patient as well as the relative importance given by both the patient and the provider (Balduyck et al., 2007; Cella et al., 1995; Montazeri et al., 2003; Pasetto et al., 2007; Sloan et al. 2012). This will help in formulating better plan for best treatment strategy.

## The Aging Process and Lung Cancer among Older Adults

According to the 2014 U.S. Census, the population of older adults grew at a faster rate than the younger population indicating that the older adult population is one of the fastest-growing populations in the United States (U.S. Census Bureau, 2014). The 65 and over population was 43.1 million persons (13.7% of the general population) and the population aged 65 and over grew at a faster rate of 15.1% than the population under age 45 (Howden & Meyer, 2011; Ortman, Velkoff, & Hogan, 2014; U.S. Census Bureau, 2014). Furthermore, the older adult population in the U.S. is estimated to double from 35 million to 72 million by the year 2030 and to 83.7 million by 2050 (Ortman et al., 2014; Owonikoko et al., 2007; U.S. Census Bureau, 2012). Research has also shown that more than half of all non-small cell lung cancer patients are older than 65 years of age, whereas about one-third are older than 70 years old (Owonikoko et al., 2007). Lung cancer continues to be a global problem and affects both young and old, but the incidence of the disease has decreased for individuals aged 50 and younger while it has increased among 70 years old and above (Gridelli et al., 2005). Age is known to be associated with increased risk for surgical and radiation complications, but surgery and radiation therapy are beneficial to older adult lung cancer patients (Balducci, 2003).

The selection of optimal treatment for older adult lung cancer patients face medical challenges such as chronic obstructive pulmonary disease and emphysema, and treatment side effects as well as physiologic challenges (Frick et al., 2007; Wilders, 2006). Anxiety and depression in functional status as well as challenges in lean body mass and marrow reserve or drug clearance were cited as examples (Gridelli et al., 2007). Older adult patients may be denied potentially beneficial treatment and participation in clinical trials solely because of old age and because medical professionals have the perception that those older adults are too frail to withstand any type of lung cancer treatment (Owonikoko et al., 2007). However, the process of aging is multidimensional, and assessment needs to be comprehensive of function, comorbidity, and personal and social resources (Balducci, 2003). Owonikoko et al. (2007) stated that age alone might not be a significant prognostic factor in lung cancer treatment. His argument stemmed from the fact that the European Organization for Research and Treatment Center (EORTC) reported that increase in age is a good prognostic factor for response to some lung cancer therapies such as radiotherapy or chemotherapy (Balducci, 2003).

Advances in medical science and technology have resulted in enabling more people to survive into old age, nevertheless, with longer life spans there has been an increased incidence of acquiring pathologies in cancer (Gridelli et al., 2007). Hence, the frequency with which older adults develop carcinogenic pathologies in the lung is a prevalent and societal burden (Gridelli et al., 2007). The above result as an opinion confirmed that older adult lung cancer patients have the potential to survive if they adhere to a standard course of daily activities such as exercise, eating healthy, and following the ADLs in addition to responding to their medical appointments.

## Health-Related Quality of Life in Lung Cancer Patients

Quality of life studies can be feasible, useful, and beneficial in cancer studies. Previous quality of life studies indicated comprehensive assessment and self-report methodology from the responders because they allowed the patients to answer questions and discussed issues that related to their condition and well-being (Di Maio & Perrone, 2003). The answers obtained help medical providers have greater understanding in evaluating the patients' problems to offer better plan for treatment (Di Maio & Perrone, 2003).

Some clinical trials were conducted to show how useful HRQL is in treating NSCLC (Hirsh, 2013; Lemonnier et al., 2014; Wintner et al., 2013). A clinical trial comparing NSCLC and HRQL was conducted by Lemonier and colleagues to show the predictive role of HRQL on NSCLC after initial treatments on survival (Lemonnier et al., 2014). This study was done to determine whether there is correlation between perceived health in HRQL and initial treatment for NSCLC patients. Researchers found that there was a persistent relationship between better perceived health in HRQL after initial treatment of NSCLC and better survival prognosis (Lemonnier et al., 2014). The study emphasized the importance the researcher of the present study seeks to address, whereby HRQL assessment done on lung cancer patients at initial treatment would benefit older adult lung cancer patients.

According to Balduyck et al. (2007) self-administered quality of life questionnaires in oncological research are becoming an important part of evaluation criterion for clinical decision-making, thereby stressing the importance of its future use. An important aspect of HRQL instrument's validity is responsiveness to change over time as well as performance status rating, which is commonly used as an indicator for participant functional status in a clinical trial (Cella et al., 1993). The evaluation of HRQL has become important in lung cancer patients because of high-symptom burden and severe morbidity (Anant et al., 2005). HRQL measures also help providers and patients to compare different treatment modalities in lung cancer, thus allowing for selection of the appropriate modality (Anant et al., 2005).

Researchers recognized that quality of life needs is a key goal when considering treatment options of older patients with lung cancer (Cella et al., 1995; Hollen et al., 1995). However, apart from Cella et al., Balduyck et al. (2007), Hollen et al. (1995), and Pasetto et al. (2007), who have done a few studies in this area, a limited number of studies have specifically focused on the topic (Braun et al., 2011; Damm et al., 2013; DiMaio & Perrone, 2003). Reiterating the importance of quality of life DiMaio and Perrone (2003) and Braun et al. (2011) reported that the assessment of HRQL in older adult patients with lung cancer was areas of contention in research especially the measurement and assessment of outcomes**.** The efficacy of lung cancer treatment among older adult patients later was determined to depend on the sound judgment bordering the effects of both quantity and quality of life (Braun et al., 2011). Damm et al., reported on the satisfactory quality of life in lung cancer, stated that as the number of treatment alternatives increases, the need for comparable assessments of HRQL parameters grows as well. The area has not been fully studied and therefore the authors postulate more assessment in the field. This is one of the reasons for designing the present study. There is also a gap in this field of research; hence, there is a need for assessment of HRQL in lung cancer of older adults.

The role of HRQL assessment in lung cancer research is promising, but many methodological problems such as the reliability of the survey responses received from older adults need to be resolved to allow the best use of potential utility of instruments (Hirsh, 2013; 2014; Lima et al. 2011). In addition, HRQL assessment in clinical practice may be beneficial to older adult patients and could provide good rapport or better communication between the patient and clinician, hence, the need for more application of properly selected instruments (Lemonnier et al., 2013). The emphasis of clinical trials specifically dedicated to older adult participants needs to be stressed, because systematic HRQL assessment in clinical practice using self-reported questionnaires have proven feasible and useful (Di Maio & Perrone, 2003; Hirsh, 2013; Lemonnier, 2013). This has given prognostic power for survival of patients by allowing for the discussion between the clinician and the lung cancer patient about the answers given on the questionnaires (Di Maio & Perrone, 2003).

To support the importance of HRQL assessment, the following studies are discussed. A prospective study by Balduyck et al. (2007) was conducted to examine the quality of life evolution after lung cancer surgery in 100 patients using the instruments EORTC QLQ-C30 and EORTC QLQ-LC13. Reliability and validity of these two instruments was previously confirmed in international studies (Balduyck et al., 2007). The study focused on role functioning, emotional functioning, physical functioning, cognitive functioning, social functioning, and global quality of life, and was a first step in evaluating intermediate to long-term quality of life evolution in participants undergoing pulmonary surgery (Balduyck et al., 2007). Questionnaires were given to participants to complete 1 day before surgery and at 1, 3, 6, and 12 months after surgery. Thirteen women and 87 men were selected to participate in the study. At baseline, questionnaire response rate was 100%, while at 1, 3, 6, and 12-month response rates dropped to 71%, 77%, 83% and 76%, respectively (Balduyck et al., 2007). Comparison of quality of life and shortness of breath (dyspnea), coughing, general pain, thoracic pain, and shoulder dysfunction were obtained using EORTC QLQ-C30 (Balduyck et al., 2007). The authors found that quality of life in lung cancer patients who underwent surgery tended to diminish significantly as the disease progressed. This was mostly associated with cancer symptoms like fatigue, chronic pain, and weakness. They also postulated that those symptoms were linked to recurrent disease, which was a determinant of post-operative quality of life (Balduyck et al., 2007).

Montazeri et al. (2004) also conducted a prospective population-based study in Glasgow, Scotland on quality of life in lung cancer participants to determine whether the knowledge about lung cancer diagnosis could affect quality of life. In this study, 129 lung cancer participants were interviewed to determine their knowledge of the disease at baseline assessment. Thirty (23%) participants were aware of their lung cancer diagnosis and 99 (77%) participants did not know about their diagnosis. Montazeri et al. (2004) found that knowledge of diagnosis of lung cancer did not affect participants’ responses to the quality of life questionnaire. According to the authors, their assertion is because regardless of awareness of lung cancer diagnosis, participants responded in a comparable manner on most measures or domains studied, typically the psychosocial domains (Montazeri et al., 2004). This assumption was assessed before, during, and after the research. Montarezi's study showed that if participants know about their disease (lung cancer), they will be more proactive to look at quality of life dimensions. Participants who were more proactive in their quest for information on quality of life dimensions may relate to the present study in a way that they will have knowledge about which therapy to opt for as well as the benefits of healthcare cost associated with their disease as stated in the change of social impact. This research may also help reduce health costs that may be incurred by patients by engaging in and adhering to HRQL activities.

Socioeconomic status plays a key role in an individual’s behavioral life. As a result, Montazeri et al. (2003) prospectively studied the association between quality of life and socioeconomic status of lung cancer participants. Out of 129 participants, 82 participants completed both baseline and follow-up measures, including physical mobility, energy, role functioning, physical functioning, and breathlessness (Montazeri et al., 2003). Fifty-seven percent of participants came from low socioeconomic status, had more health problems, were less functioning, and had more symptoms as compared to affluent participants (Montazeri et al., 2003). The authors found that patients with lower socioeconomic status had more health problems, less functioning and global quality of life as well as more symptoms at baseline assessment (Cassedy et al., 2013; Montazeri et al., 2003; Ma & McGhee, 2013; Mielck, Vogelmann, & Leidi, 2014). Ma and McGhee stated that economic hardship and HRQL are strongly related, in that more attention should be placed on subjective SES indicators when dealing with HRQL. Similarly, other authors such as Cassedy et al. and Mielck et al. reported that having a clear idea of relationship between SES and HRQL will help researchers make unbiased assessments of results obtained from studies, which could help develop more effective interventions to improve HRQL. This could show that socioeconomic status may play key role in HRQL assessment. It might also test the confounding that people with low socioeconomic status might have problems accessing good and quality medical care.

Salati et al. (2008; 2009) assessed HRQL in older adult patients after major surgical resection for lung cancer. The purpose was to determine the difference observed in younger patients to provide additional information that could help to clarify the role of surgery in high-risk group older adult lung cancer patients. Salati and colleagues (2008) observed that few lung cancer studies have focused on participants reported outcomes such as quality of life, thus limiting the capability of surgeons to exhaustively counsel patients about their perioperative risk and residual function (Salati et al. 2008; 2009). Resuming an acceptable daily lifestyle is a crucial factor that may critically influence the decision to undergo lung resection (Salati et al., 2008; 2009).

Quality of life was measured using the administration of Short Form-36 Health Survey (Salati et al., 2008; 2009). The survey was used to assess physical role limitation, physical functioning, physical pain, health perception, social functioning, vitality, emotional role limitations, and mental health (Salati et al., 2008; 2009). In the study, Salati et al. (2008) reported that older adult patients older than 70 years of age (85 patients, mean age = 75 years) had worse exercise performance on the stair climbing test ($p < 0.0001$) as compared to younger patients (133 patients, mean age = 59.4 years). It appears that although the patients were conscious of their poorer physical conditions, they were also more prepared to be sick and to face the challenge of cancer and the treatment associated with it. The authors reiterated the importance of providing reliable information on older adult lung cancer patients' psychological and physical function. The patients with a limited cardiorespiratory function remained in the balance between oncological radicality and the prospect of an inadequate quality of life, which may have ethically influenced the decision to proceed to surgery (Salati et al., 2008). This means that although older adult lung cancer patients were fearful about their diagnosis, they were also conscious about the fact that something had to be done about the disease to increase their health performance status. Finally, the authors noted that measures of quality of life reflected patients' perspectives and these measures could be affected by other factors associated with emotion such as social support, the radicalness of the procedure, and satisfaction with care. Therefore, there is the need for further studies to account for social support and degree of satisfaction factors on postoperative residual quality of life. Patients after the postoperative procedure were to make sure that there were family members to take care of them, help them go through their medical appointments, and can do their ADLs or house chores.

Pain is a subjective factor and its measurement depends on the individual. In terms of lung cancer treatment, pain is more likely to be associated with surgery as compared to tumor ablation; hence, pain could be measured as part of the quality of life assessment (Salati et al., 2008; 2009). The authors observed that further studies are needed to confirm their results in a larger population and to identify strong predictors of residual quality of life that may further assists surgeons and/or medical practitioners in counseling their patients as well as planning perioperative physical and psychological supportive programs which will help improve lung cancer patients' health perception (Salati et al., 2008; 2009).

A randomized trial was done by the Elderly Lung Cancer Vinorelbine Italian Study Group (ELVIS) to determine the effects of vinorelbine—a semisynthetic vinca alkaloid on quality of life and older patient survival who had advanced non-small cell lung cancer (ELVIS, 1999; Winton et al., 2005). This study reinforces the importance of the role quality of life plays in the survival of older adult patients with non-small cell lung cancer, even though chemotherapy was not particularly studied. The study included patients 70 years of age and older, stage IV or IIIB NSCLC, who were ineligible for radiotherapy (ELVIS, 1999); patients 65 years and older with completely resected T2N0, T1N1, T2N1 NSCLC (Winton et al., 2005). EORTC questionnaires (QLQ-C30 and QLQ-LC13) and the Cox regression model, stratified according to nodal status (Winton et al., 2005) was used to analyze the results by fitting a linear mixed model for each quality of life scale. Data from 161 and 482 (including 242 patients and 240 observation) patients were analyzed respectively. The investigators found out that patients who were treated with vinorelbine scored better than control patients on quality of life functioning scales and reported fewer lung cancer-related symptoms. However, they found that these patients reported worse toxicity-related symptoms, such as constipation, nausea, vomiting, hair loss, and peripheral neuropathy (ELVIS, 1999). Cognitive function was statistically significant but borderline significant for global health status (ELVIS, 1999).

In terms of symptom scales and items, results obtained from the participants treated with vinorelbine were more encouraging than from the control patients for pain and shortness of breath (dyspnea) (ELVIS, 1999). The investigators concluded that vinorelbine may have improved survival of older adult patients with lung cancer and had a low enough level of toxicity. Patients remained free of disease that had completely resected early-stage NSCLC, and vinorelbine may have improved overall quality of life (ELVIS, 1999; Winton et al., 2005).

LCSS is another HRQL tool which is responsive to changes in performance status signifying the different scores for individuals with different states of disease. In a study conducted using LCSS with 207 NSCLC patients and 21 observers, Hollen et al. (1995) reported a comparison with the Karnofsky scale indicating that results from the study supported the premise that the primary factors assessed by LCSS (physical and functional domains) were predictors of quality of life for those with lung cancer who used some sort of therapy. The authors reported the Cronbach’s alpha coefficients were 0.82 for the participant scale, 0.71 for the average symptom burden subscale, and 0.75 for the observer scale (Hollen et al., 1995). The authors concluded that measurement of less relevant factors may be assessed in less depth through summation items and that the explained variance of quality of life (about half) by the LCSS is reasonable for evaluation of new therapies such as tumor ablation (Hollen et al., 1995).

Generally, the above studies have shown how HRQL in lung cancer could be important for older adults such that the possibility to resume an acceptable daily lifestyle becomes a crucial factor and may critically influence the decision of the elders undergoing a therapy. They also show how HRQL may help provide reliable information on older adult lung cancer patients' physical well-being and functioning well being as well as patients who have limited cardiorespiratory performance. Therefore, care must be taken when considering the lung cancer therapy. Although the conceptual model of quality of life used as the guide for this study includes both a physical and functional dimension, the LCSS instrument only measures physical well-being, symptom distress and global quality of life, but not the functional dimension. The functional dimension is measured by assessing activities of daily living. It was mentioned previously that these are beyond the scope of this study.

## Health-Related Quality of Life Tools

There are several tools described in the literature to measure quality of life and HRQL and to some degree these may be interchangeable. The instruments described below are tools that have been used in HRQL assessment. They have been tested and found to be valid and reliable as well as conforming to international standards. These tools were already described briefly in Chapter 1 by domain tested (Table 1) and type of treatment (Table 2). The researcher of the present study aims to fill the research gap in assessing HRQL in physical function among older adults being treated with either surgery or tumor ablation using the LCSS questionnaire. The LCSS tool is short and not time consuming. It offers the participants relatively shorter time to complete the survey as compared to the other tools. Participants generally will use about 8 minutes to complete the survey while EORTC and FACT-L use about 11-15 minutes to complete. The review presented in the next sections encompasses a broader assessment than physical function and has a focus on the psychometric properties of the Functional Assessment (FACT-Lung), European scales (EORTC-QLC-30 and EORTC-LC-13), and the LCSS.

## Functional Assessment of Cancer Therapy—Lung

The Functional Assessment of Cancer Therapy-Lung (FACT-L) scale is a 44-item instrument, which measures multidimensional quality of life. It can be used in clinical trials. It is a tool that was developed in 1987 by David F. Cella and colleagues and has been used since then as a testing and comprehensive measurement system for HRQL for lung cancer patients. It measures social and emotional well-being, physical, and functional status of the patient (Cella et al., 1995; Browning, Ferketich, Otterson, Reynolds, & Wewers, 2009; Busarik et al., 2013). The reliability and validity (multiple studies had been conducted to obtain same or almost same results) had been published using international standards (Cella et al., 1995; Browning et al., 2009; Busarik et al., 2013). The construct validity and reliability of FACT-L to measure quality of life has been done over a period since 1987 by Cella and colleagues using factor analysis (Tulsky et al., 1993). This has confirmed hypothesized multidimensional structure of the instrument and patterns of correlation coefficients. Correlations had been predicted between FACT-L and other instruments such as FACT-General (FACT-G), Functional Living Index-Cancer (FLIC), and Lung Cancer Subscale (LCS). The correlation between FACT-G and FLIC is 0.58; between the FACT-L and FLIC is 0.60; and among FACT-G, FACT-L, and LCS is 0.66 (Table 3).

Table 3

*Reliability and Validity Coefficients among Lung Cancer Quality of Life Measures*

| **Instrument** | **FACT-G** | **FACT-L** | **EORTC-QLC-30** | **EORTC-LC-13** |
|---|---|---|---|---|
| FLIC | 0.58 | 0.68 | - | - |
| LCS | 0.66 | 0.66 | - | - |
| α coefficient | - | - | > or = 0.70 | > or = 0.70 |

Source: Cella et al. (1995). Reliability and validity of the functional assessment of cancer therapy—lung (FACT-L) quality of life instrument. *Lung Cancer,* 12, 199-220; Balduyck, et al. (2007) Quality of Life evolution after lung cancer surgery: a prospective study in 100 patients. *Lung Cancer*; *56,* 423-431.
FLIC--Functional Living Index-Cancer
LCS--Lung Cancer Subscale

## EORTC QLC-30 and LC-13

In 1986, an organization called European Organization for Research and Treatment of Cancer started a research program to "develop an integrated, modular approach for evaluating the quality of life of patients participating in international clinical trials" (Aaronson et al., 1993, p. 365). This group conducted two international field studies to evaluate how practical, reliable, and valid the core questionnaire (EORTC QLQ-C30) and a supplemental 13-item lung cancer-specific module, the EORTC QLQ-LC13 (Balduyck et al., 2007; Damm et al., 2013). The organization reported the reliability and validity of their results by using 30 core questions, which came to be known as EORTC QLQ-C30 (Aaronson et al. 1993). The EORTC QLQ-C30 is a self-rating questionnaire that consists of 30 questions and uses nine multi-item scales. It includes 5 functional scales (physical, role, cognitive, emotional, and social), 3 symptom scales (fatigue, pain, nausea/vomiting), a global health or quality of life scale, and items that assess additional symptoms such as constipation, dyspnea, sleep difficulties, and diarrhea (Aaronson et al., 1993, p. 366; Wintner et al., 2013). The purpose of this instrument is to determine self-reported methodology from patients. Its reliability and validity have been confirmed in international studies (Balduyck et al., 2007; Damm et al., 2013).

To determine the reliability and validity, the questionnaire was administered to 305 patients from 13 countries, who had nonresectable lung cancer. Variables included weight loss, disease stage, performance status, and treatment toxicity (Aaronson et al., 1993). On the average, the minimum time required to complete the questionnaires where no assistance was needed by most patients was 11 minutes (Aaronson et al., 1993). Data supported the hypothesized scale structure of the questionnaire except for role functioning, such as work and household activities which did not meet the minimal standards for reliability (Cronbach’s ά ≥ 0.70) (Aaronson et al., 1993). Validity was based on moderate interscale correlations, components of quality of life constructs including the functional and symptom measures, weight loss, as well as treatment toxicity (Aaronson et al., 1993). In addition, performance status, physical, and role functioning, global quality of life, fatigue, nausea, and vomiting results provided statistically significant changes for lung cancer patients (Aaronson et al., 1993).

According to Aaronson et al. (1993), reliability and validity of the questionnaire were highly consistent among the three groups of individuals from Northern Europe, English-speaking countries, and Southern Europe. In addition, it was shown that the results supported the EORTC QLQ-C30 as a reliable and valid measure of quality of life in cancer patients from many distinct cultural clinical settings (Aaronson et al., 1993; Balduyck et al., 2007; Damm et al., 2013).

### EORTC Quality of Life Questionnaire-Lung Cancer

The lung cancer specific module LC13 (EORTC QLQ-LC13) is a supplementary questionnaire to the EORTC QLQ–C30 module designed for use among patients receiving treatment in lung cancer (Balduyck et al., 2007). The module was comprised of multi-item and single-item measures of lung cancer-associated symptoms (Balduyck et al., 2007; Damm et al., 2013). The module was administered to lung cancer patients with nonresectable tumors. The purpose was to determine self-reported questionnaires from participants who have been diagnosed with lung cancer (Balduyck et al., 2007; Damm et al., 2013). The module contained 13 questions that assessed lung cancer as well as related symptoms like side effects of chemotherapy or radiotherapy, cough, dyspnea, hemoptysis, site-specific pain, peripheral neuropathy, dysphagia, and alopecia (Balduyck et al., 2007). Its reliability and validity have also been confirmed in international standards (Balduyck et al., 2007). It is scored in the same manner as EORTC QLQ-C30 described above.

Participants were gathered from 17 countries and submitted the questionnaire once while undergoing treatment. From these participants 883 completed the questionnaire before treatment and 735 completed it once during treatment (Bergman et al., 1994). Cronbach’s alpha coefficient greater or equal to 0.70 was reported to emphasize that the study supported the scale structure (Bergman et al., 1994). However, items that pertained to pain did not form a scale that was reliable for group comparisons (Bergman et al. 1994). Nevertheless, the findings partially supported the minimal standards for reliability of the 23 multi-item dyspnea scales (Bergman et al., 1994). Results from international field testing supported the EORTC QLQ-LC13 as a valid instrument that is useful for measuring disease- and treatment-specific symptoms among patients with lung cancer who participate in clinical research in combination with the EORTC core QL questionnaire (Bergman et al., 1994). The patterns of these correlations to substantiate the validity and reliability of the tool are seen in Table 1.

### Lung Cancer Symptom Scale

The Lung Cancer Symptom Scale (LCSS) is a quality of life instrument used to evaluate physical and functional domains of individuals diagnosed with lung cancer at a specific site, but devoid of treatment toxicity (Hollen et al., 2005). LCSS is a HRQL tool that is responsive to changes in performance status signifying the different scores for individuals with different states of disease (Hollen et al., 2005; Hollen et al., 2012; Iyer, Taylor-Stokes, & Roughley, 2013). The advantage of the LCSS instrument is its simplicity (Earle, 2004). This scale consists of two symptoms scales administered to patients and health professionals completing a form as observers. The patient scale consists of nine items. Six of these items measure symptoms for lung cancer that include fatigue, appetite loss, dyspnea, cough, hemoptysis, and pain. Three summary items that measure total symptom distress include normal activity status and overall quality of life (Hollen et al., 2005; Iyer et al., 2013). The primary developers of the LCSS were Patricia Hollen, Richard J. Gralla, and Mark G. Kris (1995). In developing this scale, the purpose was to develop a tool for measuring quality of life to ease patient and staff in serial measurement of quality of life during a clinical trial. The scale captured in detail the dimensions most likely to be influenced by therapeutic interventions and evaluates other dimensions globally (Iyer et al., 2013).

The LCSS focuses on physical and functional aspects of the participants (Iyer et al., 2013), which is what I sought to assess in the present study. The LCSS measures physical functioning through six symptoms of lung cancer that include fatigue, dyspnea, appetite loss, cough, hemoptysis, and pain. Three summary items measure total symptom distress, normal activity status, and overall quality of life experience (Hollen et al., 2005; Hollen et al., 2012; Iyer et al., 2013). This study assesses eight of the nine physical quality of life dimensions of the LCSS. However, the normal activity status component is not measured in this study because it requires measurement beyond the 3-month period.

The scoring system of the LCSS is measured as scores of equal lengths of line marked by patient and an average of the aggregate score of all nine items is used for a total score" (Hollen et al., 1995, p. 6; Appendix F). In addition, a subscoring system is used to determine the mean of all 6 major symptoms that make up the average symptom burden index. Specific areas of change can be represented by a quality of life aggregate of several items or individual items. The LCSS was tested in over 1000 patients with lung cancer in about six different published studies (Browning et al., 2009; Gralla et al., 2009; Hollen et al., 2005; Hollen et al., 2012; Iyer et al., 2013). In a study with 207 NSCLC patients and 21 observers, Hollen and colleagues reported that the Cronbach's alpha coefficients were 0.82 for the patient scale, 0.71 for the average symptom burden subscale, and 0.75 for the observer scale (Hollen et al. 1995).

Comparison of the LCSS with the Karnofsky scale indicated that the LCSS is sensitive to changes in functioning status as demonstrated by disease stage-specific differences in scores (Hollen et al. 1995). The results from that study supported the premise that the primary factors assessed by LCSS, the physical and functional domains, are important predictors of quality of life for individuals with lung cancer undergoing some sort of therapy (Hollen et al., 1995). Therefore, the authors concluded that measurement of less relevant factors may be assessed in less depth through summation items and that the explained variance of quality of life (about half) by the LCSS is reasonable for evaluation of new therapies (Hollen et al., 1995). The concept of minimally important difference (MID) for HRQL instruments is equated with half of the variance explained in a review of 38 studies (Norman, Sloan & Wyrwich, 2003). The threshold of discrimination for changes in HRQL for chronic disease appears to be about half of the standard deviation (Norman, Sloan & Wyrwich, 2003).

The LCSS was also validated with patients diagnosed with mesothelioma (Hollen et al., 2004). To test the conceptual model of the instrument, LCSS-meso, 495 patients undergoing chemotherapy with unresectable malignant pleural mesothelioma were randomized to undergo two clinical trials with pemetrexed (Hollen et al., 2004). Poisson regression was used for predictive value of physical symptoms, symptomatic distress, activity level, and global quality of life at baseline, 40 days, and 82 days post-treatment (Hollen et al., 2004). More than 85% of the patients reported pain, dyspnea, fatigue, and appetite loss (Hollen et al., 2004). The researchers concluded that for both mesothelioma and lung cancer, most of the symptoms within the LCSS model supported the use of LCSS as a "sensitive instrument for serial measurement during clinical trials involving patients with lung malignancies" (Hollen et al., 2004).

Browning et al. (2009) examined both the FACT-L and LCSS as instruments to assess quality of life in recently diagnosed lung cancer patients and found both were psychometrically valid instruments and widely used in literature. However, I found the LCSS was better suited for the present study because it measures physical and functional domains of quality of life, while the FACT-L includes social and emotional domains as well. Browning et al. reported on the internal consistency and validity of both instruments from data collected from a larger study examining smoking behavior in newly diagnosed patients. Descriptive statistics were calculated for internal consistency on the FACT-L and LCSS by estimating Cronbach's alpha coefficients and Pearson correlation coefficients between the two scales. Browning et al. found that internal consistency coefficients demonstrated good reliability for both scales and both instruments demonstrated a strong correlation, suggesting good convergence validity.

Gralla et al. (2009) also used the LCSS to assess the impact of neoadjuvant therapy on quality of life and noted that the LCSS was a validated instrument designed for clinical trials and patient management. Symptoms in this study were measured on a 100-mm visual analogue scale (VAS) and scores ranged from 0 to 100 (0 meaning no impairment, 100 most impairment). Gralla et al. noted that this scale has been shown to have good psychometric properties and used the patient-based LCSS, which included three symptoms from a thoracic subset (i.e., cough, dyspnea, and hemoptysis), three from a general subset (anorexia, fatigue, and pain), and three summary items (symptom distress, interference with daily activities, and global quality of life).

Nowak et al. (2004) reporting from a study conducted by Vogelzang et al. stated that LCSS results from their study gave evidence that dyspnea and pain scales showed improvements with pemetrexed and cisplatin as compared with cisplatin alone. Similarly, in a systematic literature review looking at HRQL instruments, Damm et al. (2013) reported the need for LCSS as one of the tools for measuring HRQL in lung cancer, even though it has been used in a few studies as compared to EORTC LC 13.

LCSS has been used in other studies after its development by Hollen et al. as well. For example, Garces et al. (2004) conducted a study using the tool to find relationship between cigarette smoking and quality of life after lung cancer diagnosis. The instrument was mailed to 1,506 patients between the years 1999 and 2002, where LCSS scores were compared among diverse groups of cigarette smokers through univariate independent group testing and multivariate linear models (Garces et al., 2004). The results from the study showed that seven of the individual LCSS quality of life components (i.e., appetite, fatigue, cough, shortness of breath, lung cancer symptoms, illness affecting normal activities such as walking, and overall quality of life) were statistically and clinically significant ($p < 0.001$) and were different between nonsmokers and persistent smokers. Researchers also found no significant differences in pain or hemoptysis (Garces et al., 2004). The authors concluded that the relationship between smoking status and quality of life was supported by the correlational study, and that persistent cigarette smoking status and quality of life after a lung cancer diagnosis impacted quality of life scores negatively (Garces et al., 2004).

The LCSS was used in another therapy involving quality of life and non-small cell lung cancer where pemetrex maintenance was conducted on patients (Belani et al., 2012). Researchers found that through LCSS the therapy significantly improved overall survival and progression-free survival with patients diagnosed with non-small cell lung cancer as compared to placebo (Belani et al., 2012). Four cycles of platinum-based induction therapy were given to 663 patients with stage IIIB or stage IV NSCLC between March 2005 and July 2007. Patients completed the LCSS from baseline, after each cycle, and at post-discontinuation (Belani et al., 2012). The authors reported that baseline characteristics to include LCSS score were well balanced between groups, which were low, thereby, indicating low symptom burden for patients without disease progression after completion of first-line treatment (Belani et al., 2012). According to the authors, the results proved that with pemetrexed maintenance therapy there was amelioration in overall and progression-free survival and treatment of this type can be helpful for patients with advanced NSCLC (Belani et al., 2012)

LCSS is the preferred choice of tool for the present study because of its high acceptance rate by patients and professionals, the rapid completion time, ease of use, and strong psychometric properties it possesses (Hollen et al., 2012). In addition, the LCSS is a simplified version among the discussed instruments and the tool is more user-friendly and beneficial to the older participants than the other two instruments FACT-L and EORTC QLQ 30 and LC-13, which consist of many questions and take longer time (11-15 minutes) to answer. The ease with which the participants might find the tool together with shorter time to answer the questionnaires emphasize the importance of the choice of LCSS as the appropriate tool for this study in the HRQL assessment of lung cancer.

There are equally other studies such as EORTC studies and LCSS whose validity and reliability have been confirmed and conformed to international standards. These studies have become useful in quality of life studies and are specific for lung cancer. The EORTC QLQ-C30 and QLQ-LC 13 look at physical, role, cognitive, emotional, social, and symptoms scales (Balduyck et al., 2007), while the LCSS looks at six measuring major symptoms for lung cancer (appetite loss, fatigue, cough, dyspnea, hemoptysis, and pain) and three summary items related to total symptom distress, normal activity status, and overall quality of life (Hollen et al., 2005). The EORTC and LCSS instruments have reported extensively on quality of life studies and other researchers have used these tools in their studies to find the viability and the usefulness of them in quality of life studies. For example, Nowak et al. (2004) used EORTC in their studies to find the feasibility and the validity of results in quality of life studies in chemotherapy for pleural mesothelioma.

Salvo et al. (2009) examined different tools used to assess either quality of life or palliation of lung cancer-related symptoms by conducting a literature review of quality of life measurement in cancer patients receiving palliative radiotherapy for symptomatic lung cancer. The most common tool used was EORTC QLQ-C30. Fourteen of 43 studies (32%) identified out of which eight used EORTC QLQ-C13—a supplemental version of a lung cancer-specific questionnaire. The questionnaire consisted of items concerning lung cancer symptoms and the side effects of conventional treatments used for lung cancer (Salvo et al., 2009). Some of the quality of life domains considered was dyspnea, diarrhea, and loss of appetite, among others (Salvo et al., 2009). FACT-L, which is analogous to EORTC QLQ-LC13 and includes additional questions that relate specifically to quality of life in patients with lung cancer, was used in two studies. Spitzer quality of life index, a third validated quality of life tool and covers 5 dimensions of quality of life was used. The 5 dimensions covered were activity, daily living, and health, support of family and friends, and outlook (Salvo et al., 2009). A study-specific method to determine quality of life was used in three trials, and nineteen trials attempted to evaluate symptom palliation using a study-designed questionnaire.

The authors found out that in a total of twenty identified trials that were considered for palliative radiotherapy for lung cancer and evaluation of quality of life, 11 used a tool that was specific to patients with lung cancer, while the remaining nine used overall quality of life questionnaires for cancer patients or a study-designed questionnaire (Salvo et al., 2009). Also, in 31 identified studies, the level of symptom palliation, one aspect that contributes to a quality of life measure was assessed, where the authors concluded that more trials should use a validated lung-specific tool to allow for comparisons between trials which will in turn increase the internal validity of individual studies (Salvo et al., 2009). The authors therefore, recommended that lung-specific validated tools that would be beneficial for the measurement of quality of life in trials evaluating palliative thoracic radiotherapy should be FACT-L and the EORTC QLQ-LC13 (Salvo et al., 2009). Nevertheless, FACT-L was not chosen for the proposed study because it goes well beyond the scope as it is some broader instrument measuring social and emotional domains.

Another study involving HRQL assessment in lung cancer was conducted using lung cancer tools EORTC QLQ-C-30 version 3.0 and C-13 at baseline and at day 1 of 2, 4, and 6, and after 6, and 8 weekly thereafter until disease progression (Nowak et al., 2004). In the same way, Earle (2004), studied and compared five quality of life instruments (FACT-G, FACT-L, EORTC QLQ-C30, EORTC QLQ-LC 13, and LCSS) noting merits and demerits and concluded that the use of these instrument in measuring quality of life is decreasing, but suggested that their use should be encouraged. As this study assesses HRQL in lung cancer treatment, it was imperative that it followed the timeline documented in literature. For example, a study involving HRQL assessment in lung cancer was conducted using lung cancer tools EORTC QLQ-C-30 version 3.0 and C-13 at baseline and at day 1 of 2, 4, and 6, and after 6, and 8 weekly thereafter until disease progression (Nowak et al., 2004). Similarly, Balduyck et al. (2007) in their study on quality of life evolution after lung cancer surgery predicted “changes in 1, 3, 6, and 12 months after the surgery” (p. 429). Other studies have been done using these same instruments and span over a period of 1-4 months (Lemonnier et al., 2014; Nowak et al., 2004; Tse et al., 2005).

## Literature on Research Design and Conceptual Framework

This section reviewed studies that used analysis derived from comparative design and the conceptual model. Holland et al. (2009) listed different interventions that have been used to help older adult patients with lung cancer. The older lung cancer patients exhibited cognitive coping skills by showing improvement in processing difficult events. Interventions that focused on anxiety reduction (including loss of appetite) were provided as helpful tools to assist processing of painful past and present events. These interventions were effective. The article reported, in two studies, a psychoeducational intervention delivered via a telephone showed efficacy of interpersonal psychoeducational intervention in reducing distress in older women with breast and lung cancer (Holland et al., 2009). Similarly, several psychoeducational techniques were tested in samples of cancer patients with older adult patients (Holland et al., 2009). In addition, Holland et al. (2009) reported that after reviewing men who are 65 years old with cancer found that a group-based cognitive behavioral stress management intervention improved quality of life and helped patients find benefits from their cancer experience. The preceding evidence from research helped to buttress the fact that psychoeducational intervention aids older adult cancer patients improve disease regimen if they are engaged in quality of life activities. The authors therefore concluded that a review of literature supports that psychoeducational interventions assisted in improving quality of life in older adult lung cancer patients (Holland et al., 2009). Additionally, the authors stated one cannot manipulate treatment or therapy of lung cancer patients, and therefore, postulated that an observational study is best rather than an experimental study in which the criterion is used to manipulate the independent variable (Holland et al., 2009).

A review of randomized controlled trial data showed that early palliative care improved survival, quality of life, and depressive symptoms in those with NSCLC compared to standard care (Davis, 2012). However, symptom burden of lung cancer was great and at least 80% of the patients experienced fatigue, 65% suffered loss of appetite, 77% exhibited cough, 73% exhibited dyspnea (from both local symptoms and weight loss), 57% had chest pain, and 17% had hemoptysis (Davis, 2012). In addition, symptom frequency and severity could be worse in individuals who survived 3 months or less (Davis, 2012). Therefore, early palliative care improves quality of life and decision-making in patients with advanced lung cancer and may improve survival (Davis, 2012).

The ability to evaluate and apply evidence-based guidelines into daily practice has become an important aspect of medical care. Integrating evidence-based guidelines in lung cancer treatment involves the development of theory and a method of action from a systematic review of current evidence (Pearson, Field, & Jordan, 2007). Given the ability to incorporate assessment of HRQL dimensions in lung cancer treatment, the findings from this study will be used to complement the existing evidence on treatment effectiveness.

## Summary and Transition

Treatment of older adult lung cancer patients is historically understudied. Because most lung cancer clinical trials are linked to younger patients, older adult lung cancer patients have been under-represented and, as such, treatment recommendations based on extant data are inadequate in routine clinical practice with older adults. However, to thoroughly characterize the scope of the under-representation that older adult lung cancer patients face and to obtain data regarding outcomes, it should be a consensus approach. A quality of life assessment may be very helpful and useful for older adult lung cancer patients by improving rapport or better communication between the patient and the provider. This relationship could improve recommendations for a wider application of properly selected treatments.

The two previous chapters detailed the increased incidence in lung cancer among older adults. While modern medicine and technology has increased the number of treatment options, there is a paucity of research related to the impact these options have on HRQL in older adults with lung cancer. Patients undergoing any treatment need to understand the impact it will have on their quality of life. Ethically, in making their decision, it is the patients’ right to be informed of all sequelae of any treatment or no treatment. Chapter 3 will provide the description of the study design, participant' procedures, and data collection, as well as data analysis, and protection of human research participants.

# Chapter 3: Research Method

## Introduction

The purpose of this study was to assess the effect of lung cancer treatment modality on HRQL among older adults. I carried out an ancillary comparative survey to determine whether there were differences in physical functioning, symptom burden, and overall quality of life experience between surgery and tumor ablation lung cancer treatment modalities. This chapter begins with an overview of the study research design and the rationale for why this research design and approach were selected. The rest of the chapter includes discussion of the setting where the study took place, participant recruitment, sample characteristics and sample size, and materials and instrumentation. The logistics entailed in obtaining and scoring data for the comparative survey of HRQL is described in the data collection process. I describe the operational measures of the independent and dependent variables in the statistical analysis section as well as statistical tests performed for hypothesis-testing, followed by ethical considerations.

## Research Design and Approach

The research design of this study was a quantitative, comparative survey based on treatment modality and assessment with repeated measures. In a comparative study, the critical issue is to determine whether the participating groups differ with regards to the dependent variable (HRQL dimensions) without manipulating the independent variable (treatment). This rationale forms the basis of the research design of the study.

My approach was to carry out an ancillary study to an existing randomized clinical trial of lung cancer in older adults. The participants were assigned to one of the two cancer treatment groups prior to the proposed ancillary research, and as such, their randomization to either group does not present additional ethical concerns within the scope of this research. The ancillary component to the clinical trial consisted of a comparative survey research design. According to Mills, van de Bunt, and de Bruijn (2006), the comparative nature of a study constrains the researcher to observe the effects of the independent variable (treatment) on a dependent variable (outcome), without direct intervention or manipulation of the former.

I considered other methods of quantitative inquiry but determined that they would less effective in providing the insight relative to a randomized clinical trial with comparative survey follow-up. I also considered a multiple case study; however, this design is not as powerful as the comparative survey. One of the advantages of the randomized clinical trial design is the ability to control for immutable characteristics (e.g. age, ethnicity, or place of birth) which are unlikely to have a direct effect on the outcome when participants are grouped at random (Stevens, 2009). The quantitative approach is the preferred design for a comparative study with repeated-measures because the interval and ratio scales are conducive to parametric statistics.

The nature of the HRQL scale I selected is continuous and this level of measurement is frequently used because they are numerical and are often used in quantitative studies. The quantitative method is more useful in testing effects than the qualitative method. The quantitative method maximizes similarities and differences on the information gathered (Creswell, 2003). The goal of a quantitative study is to determine, with a degree of statistical certainty, whether an effect is likely to exist (Tabachnick & Fidell, 2012). Therefore, I selected the quantitative method in place of the qualitative

I used generalized estimating equations (GEE) to model self-reported quality of life measures over time between ablation and surgery conditions (Hanley et al., 2003). GEE provides a semiparametric approach to longitudinal analysis of categorical response and can also be used with continuous measurements. Instead of attempting to model the within-subject covariance structure, the GEE procedure treats the covariance structure as a nuisance and simply models the mean response. Count data rarely fit the restrictive assumptions of the Poisson distribution and violation of these assumptions frequently result in overdispersion (Hammami, Garcia & Nuel, 2013); data that are overdispersed have a variance that is larger than the mean. Therefore, to account for the overdispersion, I assumed a negative binomial distribution because patient scores were nested within patients. When the data have a heterogeneous compound symmetry covariance structure, the sandwich estimator is used to correct for model misspecification (Guillaume, Hua, Thompson, Waldorp & Nichols, 2014). For example, in my study the sandwich estimator accounts for the repeated measures correlation from baseline to 1-month and 3-month follow-up.

Changes in quality of life dimensions were compared between treatment modalities' negative binomial distribution with one three-level within-subjects factor (i.e., time: baseline, 1 month, and 3 month), and one two-level between-subjects factor (i.e., modality: surgery versus tumor ablation). The within-subject’s changes from baseline were compared between each pair of modalities at each follow-up time using six orthogonal contrasts. The comparison of the repeated measures was between baseline and 1-month, baseline and 3-months and between baseline and 3-months since the emphasis was on changes between the various time points. There were no appreciable changes between 1-month and 3-months, thus analysis was made between those two times. All statistical analyses and modeling were conducted using SAS$^{©}$ Software 9.4 with PROC GLIMMIX procedure.

I planned repeated measures of HRQL and these introduced an effect of repeated testing upon statistical analyses. To correct for the effect of repeated testing, orthogonal contrasts are computed within and between conditions using the *Holm-Bonferroni* correction. Orthogonal contrasts for analysis of variance are independent linear comparisons between the groups of a factor with at least three fixed levels, such as the three-time periods and two treatment groups in my study.

The *Holm-Bonferroni* correction represents an adjustment made to *p*-values when several repetitive statistical tests are performed simultaneously on a single data set (Stevens, 2009). The *Holm-Bonferroni* correction is based on the idea that if an experimenter is testing *n* dependent or independent hypotheses on a set of data, the probability of type I error is offset by testing each hypothesis at a statistical significance level 1/*n* times what it would be if only one hypothesis were tested (Napierala, 2012). As suggested by Napierala (2012), to perform a Holm-Bonferroni correction, the critical *p* value (α) is divided by the number of comparisons being made. For example, if 10 hypotheses are tested, the new critical *p*-value would be α/10. The statistical outcomes of the study are then determined based on this modified *p*-value (Napierala, 2012). The *p*-value used in this study was .05 and the number of hypotheses tested on the data set was three, hence, the chance of obtaining a false-positive result was 15% percent. The *Bonferroni correction* required an adjustment to the *p*-value from .05 to .016 to neutralize the inflated risk of Type I error. In this study, statistical significance was established *a* *priori* at the .05 level and all interval estimates were calculated for 95% confidence. Thus, the effect assessed in each hypothesis tested was considered significant only if the *p*-value was below .016.

Nowak et al. (2004) and Win et al. (2005) suggested follow-up for 3-months after treatment to provide adequate time to compare differences from baseline and 1-month and 3-months. In addition, Hollen et al., (1999) suggested that the most important response and toxicity assessment is reached within 90 days (p. 141). Balduyck et al. (2007) and Cella et al. (1995) concurred that observations for studies of this nature have a duration between baseline and 1, 2, 3, 6-12 months. Balduyck et al. (2007) used a comparative design for their study on quality of life evolution after lung cancer surgery and predicted changes at 1, 3, 6, and 12 months after the surgery. Similarly, Cella et al. (1995) reported a 2-month follow-up time for their study on reliability and validity test using FACT-L (p. 205). Other studies I reviewed spanned over a period of 1 to 4 months (Nowark et al. 2004; Tse et al. 2005). Considering the average timeframe, I chose a data collection period of baseline, 1-, and 3-months.

## Setting and Sample

The setting of the study was a private hospital with a National Cancer Institute-designated cancer center in the Northeast part of the country. Participants were volunteers who underwent stand-alone tumor ablation, or stand-alone surgery procedures for small-cell lung cancer. Inclusion criteria were 65 years and older, previously randomized to undergo surgery or tumor ablation as the treatment modality, diagnosed with lung cancer stages I, II, and III, and agreement to participate in the 3-month HRQL survey. Participants who had received combined therapies were excluded. Based on the procedures and policies of the hospital, participants meeting the inclusion criteria described above were selected from diagnosed lung cancer patients who visit the cancer center and had been randomized to a treatment group. These patients were referred to participate in the ancillary survey research study by oncologist, diagnostic imaging researcher/principal investigator, and a thoracic surgeon at the cancer center.

The oncologists arranged for the patients to be contacted ahead of time using the established hospital's IRB rules and regulations affecting research (Appendix A). At the doctor's visit, I was present to discuss the study with the participants (as discussed it with the oncologist beforehand) and if they had agreed, I contacted them using the preferred method of contact, which they had selected either by phone or mail. Although the participants were referred to me by the principal investigator and the oncologist, it was their choice to provide their contact information during the first meeting to me.

Written information introducing the study and an informed consent form were disseminated via individual patients' chosen mailing addresses. The informed consent form included brief background information on the study, the procedures for participation, a discussion of confidentiality, the voluntary nature of the study, and other ethical concerns. The participants were asked to arrive 30 minutes early for their oncology appointments or be available 30 minutes after their appointment, depending upon which was more convenient for them. The extra time allowed for the visit gave them an opportunity to ask questions on the informed consent and complete the LCSS and demographic surveys.

The cancer center examines between 100 and 120 adult cancer patients per day or about 500-600 per week, Monday through Friday. Estimates on patient census were provided by tally from an oncologist of the cancer center (A. Birnbaum, personal communication, March 10, 2015). About 250-300 (50%) of these patients are 65 years and older, of which 75-105 (30%-35%) have non-small cell lung cancer. Out of a maximum number of 105 older adult lung cancer patients who are seen at the oncology clinic on a weekly basis, it was assumed that about 94 participants could be approached for the study each week. Allowing a refusal rate for the randomized study to be about 10% (RIH Cancer Center), 80 patients were recruited for the ancillary survey.

Effect size was based on the means and standard deviations from previously published literature, where the assumption was that with a “within-subjects” correlation of 0.5, power would exceed 80% to detect a difference of 0.7 standard deviations between groups. I used one between-subjects factor with two levels (i.e., treatment) and one within-subjects factor with three levels (i.e., time point) to determine the differences between the group means, after *Holm-Bonferroni* adjustment (Cleophas et al., 2009; Gravetter & Wallnau, 2004).

Based on previous studies with medium effect sizes (Damm et al. 2013; Davis, 2012; Hoffmann et al. 2014; Kasymjanova, Grossman, Tran, Jagoe, Cohen, Pepe et al. 2013), I expected to find a medium effect size as well. To determine the sample size, I calculated the power analysis for ANOVA designs as discussed in Cohen (1988) and Stevens (2009). Using the medium effect size of 0.40 (f squared), significance level ($a$) of 0.05, and power of 0.80 yielded population size of 66 ($N = 66$) for the two therapies (Stevens, 2009). To confirm the results, the University of Colorado, Colorado Springs sample size and effect size calculators were used. Becker (2014), based his calculations on the interpretation of Cohen's *d* (medium effect size of 0.40, power of 0.80, and significance level of 0.05) and calculated a sample size of 66. Using another medium effect size of 0.30 but same power and significance level produced a sample size of 62 (Becker, 2014). Based on the above calculated results, I estimated for my study a sample size a total of about 60-70 participants for both modalities, with a minimum of 30 participants per modality. However, the sample recruited my study with complete administration of all three forms was 70 participants for the two therapies (35 participants for each modality).

## Instrumentation and Materials

Two instruments were used to collect data for this study: a brief demographic survey and the LCSS analogue scale. Both instruments were administered to older adult lung cancer patients who volunteered to participate in the study and met the inclusion criteria prior to beginning one of the two selected treatment options. The survey administration prior to treatment represented the baseline measurement. At 1, and 3-month interval post-treatment had commenced, the two instruments were administered again. Each of the instruments is described below.

***Demographic Survey***. I obtained basic information regarding the type of treatment selected, age, gender, education, race/ethnicity, marital status, and income above or below $75,000. This demographic data collection tool is found in Appendix B. Demographic data collected was used to determine the demographic composition of the sample, which was matched to data at the baseline, 1-month and 3-month follow-up responses. Participants were not required to provide demographic information at either of the two follow up assessments. Using the data that participants consented to provide on their demographic sheet bypassed the need to access to hospital data, which required extensive permission to access. These data were used as controls prior to analysis. In doing so, I compared the two groups based on their demographic features to determine how comparable they are.

***Lung Cancer Symptom Scale***. The Lung Cancer Symptom Scale (LCSS) was first developed in 1995; the primary developers were Patricia Hollen, Richard J. Gralla, and Mark G. Kris (Hollen et al. 1995). LCSS is a “quality of life instrument used to evaluate physical and functional domains of individuals diagnosed with lung cancer at a specific site devoid of toxicity of treatment" (Hollen et al. 2005; Earle, 2004). The patient scale used originally consisted of nine items: six measuring major symptoms for lung cancer— “appetite loss, fatigue, cough, dyspnea, hemotypsis, pain, and three summation items related to total symptomatic distress, activity status and overall quality of life” (Hollen et al., 2005; Hollen et al. 1995, p. 57). The idea behind the development of the scale was to provide a practical quality of life measure that will reduce patient and staff burden in serial measurement of quality of life during a clinical trial (Hollen et al. 1995). The scale captures the dimensions most likely to be influenced by therapeutic interventions and evaluates other dimensions globally (Hollen et al. 1995).

The participant assigns an individual score on each item on the scale by placing a line across an analogue 100mm line that ranges from zero (better status) to 100 (worst status) (Appendix D) (Hollen et al. 1995). The LCSS has been tested in over 1000 patients with lung cancer in many international studies (Browning et al. 2009; Hollen et al. 1993; 1995). The LCSS has undergone comprehensive testing for psychometric properties of feasibility, reliability (coefficient alpha for internal consistency, test-retest for stability, and inter- and intra-rater agreement), and validity (contrasted groups approach, relationship testing, multitrait-multimethod approach, and criterion-related validity) (Hollen et al., 2005). Good sensitivity to all levels of the Karnofsky scale is reported as part of the construct validity of the LCSS (Hollen et al., 1995). Scoring is done by measuring equal lengths of line marked on analogue cards and an aggregate score of all nine items is used for the total score (Hollen et al., 1995).

The LCSS scoring is computed by adding the scores from 0-100 from the responses received from the participants of all eight patient items to determine the total score and then the average (mean). The single quality of life is evaluated based on responses to item nine (item eight is not evaluated), then the average symptom burden index is obtained based on a mean of items one through six (Hollen et al., 1995). This scoring procedure results in one continuous quality of life score, a continuous average symptom burden index, and a total score, resulting in a total of three scores (Hollen et al., 2005). A scoring guide for the LCSS can be found in Appendix E.

Table 4

*Description of Demographic and HRQL Operational Measures*

| **Variable** | **Brief Description** | **Response Categories** | **Variable Type** |
|---|---|---|---|
| Physical Functioning | | | |
| Shortness of Breath | Amount of SOB | 0-100mm | Continuous |
| Appetite | How good is appetite | 0-100mm | Continuous |
| Cough | Cough frequency | 0-100mm | Continuous |
| Fatigue | Amount of fatigue | 0-100mm | Continuous |
| Hemoptysis | Amount of blood in cough | 0-100mm | Continuous |
| Pain | Amount of pain | 0-100mm | Continuous |
| Overall Quality of Life Experience | Overall quality of life experience rating | 1=Mild<br>2=Moderate<br>3=Strenuous | Ordinal |
| Average Symptom Burden Index | Mean of 6 Domain items | 0—600 ÷ 6 | Continuous |
| Demographic Factors | | | |
| Race/Ethnicity | Participant self-identified race/ethnicity | 1=White<br>2=Black/African American<br>3=Asian<br>4=AI/AN<br>5=Native Hawaiian/PI<br>6=Hispanic or Latino<br>7=Preferred not to answer | Nominal |
| Income | Total income in past year | 0=≤$75, 000<br>1=>$75, 000 | Ordinal |
| Education | Level of education | 1=Not a High School graduate or equivalent<br>2=High School graduate or equivalent<br>3=Some college<br>4=College graduate<br>5=Post-graduate or professional school | Ordinal |

## Data Collection

The data collection followed a sequence of steps to recruit, inform participants, and collect data. The IRB approval was received from both the private hospital and Walden University to conduct the study (Appendix A). The principal investigator of the lung cancer clinical trial at the private hospital served as the onsite principal investigator of the ancillary protocol on HRQL that used to collect data for this dissertation study. At the private hospital, I served as co-investigator of the ancillary study. The hospital IRB had the primary responsibility for overseeing the data collection of the comparative survey. Walden had secondary responsibility as the institution supervising student research, by coming into agreement with the hospital to protect the data rights to carry out this dissertation study. The dissertation proposal was submitted to Walden University IRB as an ancillary study added onto an existing randomized clinical trial. The ancillary component consisted of a comparative survey research design intended to assess additional symptomatic changes not examined in the existing randomized clinical trial.

***Baseline Survey***. I met with the research oncologists at the cancer center of the hospital to explain the study, reviewed necessary documents, as well as to elicit support for referral of patients who met the inclusion criteria. During the initial meeting, participants who agreed to volunteer in the study were asked to provide contact information using their preferred method, either by phone or mailing address. This contact information was only used to send information regarding the study and to arrange a time during their hospital visit to complete the demographic and LCSS forms. I spent some time in the waiting room to find out the process of how the participants would be cycled through their appointment as well as being processed for initial treatment. During this time, I obtained the consent from the participant/patient in the presence of the doctor.

I then contacted the patients referred by using their preferred mailing method explaining the nature of the study and providing a contact telephone number. In the letter, I asked the referred patients to contact me through a phone call or e-mail to arrange for them to arrive at least a half hour early to their next oncology visit or half an hour after their doctor's visit, whichever one was convenient for them. I explained and discussed the ancillary study survey and the separate consent form to them. Each participant was asked if they were willing to participate. All participants who consented were contacted promptly to ensure speedy screening. All these instructions were explained at the initial meeting before participation starts. Once they agreed to participate in the study and select a convenient timeframe, they were asked to sign a consent form and complete the survey. The discussion took place in a private consultation room in the cancer center.

After diagnosis, the patient is contacted by the cancer center for follow up computed tomography (CT) scan of the chest. At the consultation, the patient and the doctor discussed the different treatment modalities available to include the advantages and disadvantages associated with each treatment. The consultation takes place to enable the patient to decide which modality he/she would opt for. After this consultation, the patient was scheduled for the procedure depending on availability of the hospital's schedule which normally takes anywhere from three weeks to two months. Patients went through the necessary preparation for the chosen modality to include mental preparation, availability, and procedures. On the day of the procedure, the patients arrive about 1-2 hours early, consult with a physician assistant, who works with the oncologist, and makes sure that the patient followed the rudiments of the procedure. The patient awaits in a recovery room to talk to the oncologist to get signatures, consent forms, or anesthesia. After the consultation with the physician assistant, the patient is admitted to the procedure room and waits anywhere from 1-3 hours. During this 1 to 3-hour period, the patient's heart rate, and blood pressure, are monitored and "time out" (procedures are conducted. Time out refers to all personnel involved in the procedure consulting each other to make sure all paperwork and other pertinent information about the patient are concluded. During the 1 to 2- hour time out period, I met with the patient to go through the baseline survey (this had been communicated to the patient during the earlier doctor's visit).

***Follow-up Surveys***. Participants were scheduled to complete the 1-month and 3-months follow-up surveys at the same time when they had appointments for follow-up of their cancer treatment. In case follow-up surveys were not completed at the 1- or 3-month timeframe, the lung cancer symptom scale questionnaire was mailed to the participants' home asking them to complete and mail back to the cancer center using enclosed self-addressed stamped envelopes. The 1- and 3-month periods are a standard follow-up time at the hospital after surgery and ablation (personal communication with D. Dupuy, tumor ablation doctor, researcher, and principal investigator; T Ng, researcher and thoracic surgeon as well as A. Birnbaum, oncologist, April 15, 2015).

In addition to prior communication, there was discussion with the above-named physicians to confer the participants' follow-up schedules (with permission from the participants) to contact them for the follow-up survey. The surveys were administered prior to the medical appointment. A unique study identification number for the comparative survey was used to link all completed surveys and clinical data on the participants (clinical trial participant and treatment modality). The ancillary study data were not made available to anyone outside the ancillary study team. I input the data into a computer. Hard copy questionnaires were kept in a locked file in the investigator’s office and electronic data files password protected. The hard copy questionnaires will be destroyed after five years.

A follow-up phone call was used to gather information from participants that were hospitalized; participants that were too ill or did not wish to respond were excluded from the survey and another participant was recruited. Early evaluation helped to alleviate or minimize any refusals to participate in the next phase of the study. This also helped me to ascertain if the participants were continuing with original treatment, had adopted combination treatment or any other treatment option, and to assess their quality of life changes as enumerated in the questionnaires. Participants who adopted any combination of therapy were excluded from the study and new participants were sought via the research oncologist.

***Administration of Survey***. Data were collected through two sets of survey questions at baseline, including both the LCSS and a brief demographic questionnaire. Following this baseline survey, participants were not required to provide demographic information at follow-ups. The demographic information was used to describe baseline treatment group differences.

The LCSS tool is meant to elucidate participant physical and functional well-being while undergoing lung cancer treatment. The literature suggests that the majority of older adult lung cancer patients who undergoes surgery or tumor ablation may experience a change in at least one of the HRQL domains under consideration as described in chapter 2. The LCSS instrument was selected because the symptoms included are parallel to the symptoms experienced by patients during lung cancer treatment. These symptoms are the participants' pain, shortness of breath, appetite, cough, hemoptysis, and fatigue as well as symptomatic distress and overall quality of life for the lung cancer experience. The LCSS tool helped evaluate the participants' experience across the quality of life dimensions after going through the procedures during the two treatment modalities. Permission was granted to use the LCSS scale by the authors (see Appendices D and E). In addition, IRB procedures from the hospital were obtained to conduct ancillary study and permission to do this study under a qualified principal investigator (see Appendix A).

The LCSS instrument uses a scale consisting of continuous numbers ranging from 0-100, with zero corresponding to the lowest rating—best status and 100 representing the highest rating—worst status (Hollen et al., 1995 p. 3; Appendix F). This scoring system was used to score the three dimensions (Appendix E). As per the original methodology, participants were asked to indicate their rating of symptoms on a set of cards provided. They were asked to mark a small line to indicate the severity of each symptom, as well as the overall quality of life. Each item was scored to the length of the line marked by the participant equivalent from 0 to 100 on the line in millimeters. A marked ruler was used to measure the exact value indicated as the measure for the variable (Appendix F). To create aggregate scores for a total score, average symptom burden index, and quality of life measure, means were calculated using the following procedures: A mean of all eight items was calculated for the total score, a mean of items one through six was calculated for the average symptom burden index, and raw score was examined for overall quality of life for the lung experience (see Appendix E).

## Statistical Analysis

The characteristics of the participants included bivariate analysis to compare demographic differences among the two treatment groups on age, gender, ethnicity, marital status, and income. Demographics and clinical characteristics were compared between two treatment groups involving quality of life dimensions using descriptive statistics such as means, medians, percentages and *p-values.*

Means from all eight items were computed to develop a single total score. Average symptom burden index of the six major lung cancer symptoms was obtained as the average of items one through six. An overall quality of life score was obtained. This allowed me to compare the means responding to the various treatments and corresponding quality of life domains (Rudestam and Newton, 2001).

The study sought to answer three research questions with three hypotheses based on comparisons of the effect of treatment on quality of life measures. Self-reported quality of life measures was modeled over time between ablation and surgery conditions using generalized estimating equations (GEE) (Hanley et al., 2003). A negative binomial distribution was assumed (for overdispersion), where patient scores were nested within patients, assuming a heterogeneous compound symmetry covariance structure with sandwich estimator to correct for model misspecification. Planned comparisons (Orthogonal contrasts) within and between conditions were examined using *Holm-Bonferroni* corrections. Statistical significance was established *a priori* at the .05 level and all interval estimates were calculated for 95% confidence. All statistical analyses and modeling were conducted using SAS Software 9.4 with PROC GLIMMIX.

Research Question 1: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 1$)*:* There are no significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a 1$): There are significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at1-month and at 3-months period.

*Statistical Plan 1:* Independent variables: Treatment modalities and time periods; dependent variable: Physical functioning (LCSS total score); statistical test: Generalized Estimating Equation; criteria to reject Null: $p < .016$.

Research Question 2: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 2$): There are no significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a2$): There are significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

*Statistical Plan 2:* Independent variables: Treatment modalities and time periods; dependent variable: Average symptom burden index score; statistical test: Generalized Estimating Equation; criteria to reject Null: $p < .016$.

Research Question 3: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_03$): There are no significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a3$): There are significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

*Statistical Plan 3:* Independent variables: Treatment modalities and time periods; dependent variable: Overall quality of life for the lung cancer experience score; statistical test: Generalized Estimating Equation; criteria to reject Null: $p < .016$.

## Protection of Human Participants

The participants in this study were patients who are 65 years and older who underwent surgery and tumor ablation for lung cancer as part of their enrollment in a randomized clinical trial, and who spoke English language. Informed consent for this ancillary comparative survey study on HRQL was obtained from each subject prior to commencement of the cancer treatment. Each participant was informed that participation is separate from enrollment in the clinical trial and was entirely voluntary and regardless of their participation, it would not impact their treatment at the private hospital's oncology department, that there were minimal risks associated with the study, and that there was no compensation for their participation.

The Hospital where the clinical trial took place oversaw the data collection of the ancillary study and served as the primary supervising institution. I served as the Co-investigator of record and its IRB approved the collection of data for the study. I collected the ancillary study data as part of my role at the hospital. Therefore, Walden and the Hospital had a data use agreement to make sure that the data were clearly mine to analyze as part of this dissertation study.

The participants were informed that they could decline to be part of the study at any time or refuse to answer any questions without penalty to treatment. Patients were informed that the sole benefits of the study will be to help health care professionals provide better care to future patients' treatment for lung cancer. Any information they provide would be strictly confidential and all documents pertaining to this study would be assigned subject numbers to be able to match the records of the same patient. No names or any other form of identification would be permitted on any data or document received.

I was the only person who had access to the information or the documents. All information was reported in aggregate and no individual responses were shared. Precautions were taken to ensure the validity and reliability of the findings of the study. If participants needed any assistance to cope with the findings, they would be informed of resources for follow-up support.

## Summary and Transition

The approach to the study was a quantitative comparative survey, carried out as an ancillary study to an ongoing randomized clinical trial of non-small cell lung cancer. Newly diagnosed older adults who underwent surgery or tumor ablation treatment modalities for their lung cancer and who had already consented to participate in the clinical trial were asked to volunteer in the ancillary study. Participants were asked to complete a survey including demographic information and an 8-item symptom scale. Baseline data were collected in person by the researcher and follow-up at 1- month and 3-months post treatment. Surveys were completed during appointments for follow-up of their cancer treatment or by mailing the lung cancer symptom scale questionnaire to the participants' home. The next chapter, Chapter 4, will discuss the results following implementation of data collection.

# Chapter 4: Results

## Introduction

The purpose of this study is to assess the effect of two lung cancer treatment modalities on HRQL physical functioning, symptomatic distress and overall quality of life experience among older adults. I used a quantitative, ancillary study approach that consisted of a comparative survey based on treatment modality and examined baseline and two follow-up time points. A comparative study helps to find already-existing groups categorized by an independent variable (treatment) that differ in dependent variables (HRQL dimensions). The data collection spanned over 5 months. The results of Chapter 4 are divided into four sections, including: (a) sample characteristics, (b) research question and hypotheses testing (c) statistical analysis, and (d) summary and transition.

## Participant Recruitment and Attrition

The study participants were patients enrolled in a randomized clinical trial for the treatment of non-small-cell lung cancer using either tumor ablation or surgery. The patients were treated at a cancer center in a hospital in the Northeastern part of the United States. The inclusion criteria for the comparative survey was that they be 65 years and older and spoke English. Eighty (*n* = 80) participants signed the consent form to take part in the comparative survey. Out of the 80 patients who volunteered for the ancillary study, 42 were randomized in the clinical trial to the tumor ablation group and 38 to the surgery group. Two tumor ablation patients and one surgery patient (out of the 80 who consented) changed their minds and withdrew before providing baseline information. Out of the 38 surgery patients, one withdrew, and another died before completing the baseline survey, and a third did not complete the follow-up surveys. The final sample for the surgery group with complete data was 35 (*n* = 35). The tumor ablation group was reduced from 42 to 35 because two patients withdrew and two died before baseline, and three did not meet the study inclusion criteria (two patients had stage IV lung cancer and one had ablation of the esophagus not lung). While the two treatment groups in the ancillary study ended up with equal numbers, the initial participation and loss to follow up had different pathways.

## Characteristics of Sample

Newly diagnosed patients enrolled in a randomized clinical trial of lung cancer were recruited to participate in the comparative survey to test the effect of two treatments on repeated measures of HRQL. The ancillary study sample consisted of 70 volunteers (35 in each treatment) that met the inclusion criteria and completed the three surveys. Although randomization in a clinical trial ensures equal groups at baseline, the 70 participants for the comparative survey were self-selected and not randomized. At baseline there were significant differences between the two treatment groups in average symptomatic distress ($p$ = .0070) but not physical functioning ($p$ = .0240; *Bonferroni* adjusted $p < .016$), and overall quality of life experience scores ($p$ = .1893).

The demographic characteristics of the baseline participants by treatment modality are shown in Table 5. The two groups were only statistically significant in age ($p$ = .0049) with mean age 65 years for surgery patients and 66 for tumor ablation. Two-thirds (65.8%) of surgery patients were female, over half (55.3%) were married, and over two-thirds (68.4%) earned less than $75,000 annually. Two-thirds (65.4%) of tumor ablation patients had high school or less education, one-third (34.6%) were widowed and over a fourth (27.3%) refused to provide their income.

Table 5

*Distribution of Demographic Characteristics by Treatment Domain*

| Demographic Domains | Surgery (%) N = 35 | Tumor Ablation (%) N = 35 | *p-value* |
|---|---|---|---|
| Age | | | .0049 |
| Mean | 65 | 66 | |
| Age Range | 65-87 | 65-90 | |
| Gender | | | .2065 |
| Male | 34.2 | 50 | |
| Female | 65.8 | 50 | |
| Education | | | .1574 |
| Not a High School graduate | 23.7 | 26.9 | |
| High School Graduate/GED | 18.4 | 38.5 | |
| Some College | 23.7 | 7.7 | |
| College Graduate | 18.4 | 23.1 | |
| Post Graduate/Professional | 15.8 | 3.8 | |
| Race/Ethnicity | | | .9999 |
| White | 94.7 | 100 | |
| Black | 5.3 | 0 | |
| Preferred not Answer/other | - | - | |
| Marital Status | | | .6832 |
| Single | 3.9 | 3.9 | |
| Married | 55.3 | 46.2 | |
| Divorced | 15.8 | 15.4 | |
| Widowed | 21.1 | 34.6 | |
| Income | | | .6173 |
| <$75,000 | 68.4 | 81.8 | |
| >$75,000 | 13.2 | 9.1 | |
| Refused to Answer | 18.4 | 27.3 | |

## Statistical Analysis

Three research questions and three hypotheses were tested using generalized estimating equations (GEE; Hanley et al., 2003). GEE is a multilevel regression technique that adjusts standard errors to account for correlated data, such as the correlation of repeated measurements in a longitudinal study (Huh, Flaherty, and Simoni, 2012). Huh et al. first described the GEE statistical test along with its assumptions and steps taken to test these assumptions. In the GEE statistical analysis to test hypotheses, I present each research question and hypothesis with associated findings in sequential order. In addition, least mean squares estimates were computed and graphed for baseline, 1-month, and 3-months for the LCSS total scores of the HRQL physical functioning symptoms, average symptom burden index scores as well as overall quality of life experience. The least mean squares estimates were elucidated to show the mean, the minimum and maximum means, the *t*-values and the adjusted *p-values* for the dependent variables listed and at the different time points.

Self-reported health-related quality of life was measured sequentially to determine the effect of time between tumor ablation and surgery treatment. The quality of life dependent variables has data that are right skewed and where the variance is much greater than the mean; these distributions lead to overdispersion and violate the assumption that the mean and variance are the same (Byers, Allore, Gill & Peduzzi, 2003). GEE analyses assume a negative binomial distribution for overdispersion, where patient scores are nested within patients. To correct for model misspecification, a heterogeneous compound symmetry (all response variables have the same variance) covariance structure with sandwich estimation was assumed (Gurka, Edwards & Muller, 2012).

Regression parameters in GEE are first estimated through a generalized linear regression that initially ignores whether the data are longitudinal (Huh et al., 2012). A correlation structure is specified *a priori* and defines the hypothesized relationship between repeated observations on a subject (Huh et al., 2012). GEE approach is an extension of generalized linear models. GEE provides a semiparametric approach to longitudinal analysis of categorical responses; it can also be used for continuous measurements (Byers, Allore, Gill, & Peduzzi, 2003; Odueyungbo, Browne, Akhtar-Danesh, & Thabane, 2008; Zhu & Lakkis, 2013). Instead of attempting to model the within-subject covariance structure, the core of GEE is designed to treat the covariance structure as a nuisance and simply model the mean response (Byers et al., 2003; Odueyungbo et al., 2008; Zhu et al., 2013). GEE involves specifying a model relating covariates to outcomes and a plausible correlation structure between responses at different time periods (Byers et al., 2003; Odueyungbo et al., 2008; Zhu et al., 2013).

The key assumptions to do a GEE analysis include: (a) The responses: $Y_1$, $Y_2$, ..., $Y_n$ should be correlated or clustered, i.e., cases are NOT independent; (b) covariates can be the power terms or some other nonlinear transformations of the original independent variables, which can have interaction terms; (c) the homogeneity of variance does not need to be satisfied; (d) errors are correlated; (e) covariance specification are typically four or more correlation structures that are assumed *a priori;* and (f) it uses quasi-likelihood estimation rather than maximum likelihood estimation (MLE) or ordinary least squares (OLS) to estimate the parameters, but at times these will coincide (Byers et al., 2003, pg. 560; Odueyungbo et al., 2008, pg. 30).

To visualize the differences or changes in the types of variation I assumed that the raw scores received from the participants would be different in wide margins and that there would be no overlap between the two treatment modalities in terms of the outcome measure. The assumptions were tested using *t*-test, which is a test of two population means using statistical examination; a *t*-test is a test with two samples commonly used with small sample sizes, testing the difference between the samples when the variances of two normal distributions are not known (Trochim, 2006). To test the differences or changes in the types of variation in the variables, orthogonal contrasts were used. Within and between conditions where two treatment therapies were compared across three different time points were examined using *Holm-Bonferroni* corrections. Statistical significance was established *a priori* at the $p < .05$ level and all interval estimates were calculated for 95% confidence. All statistical analyses and modeling were conducted using SAS Software 9.4 with PROC GLIMMIX.

The *p*-value was set at 0.05 and the number of hypotheses tested was three, hence, the chance of obtaining a false-positive result would be 25%, and the Holm-Bonferroni correction to adjust the *p* value for each hypothesis was .016 to neutralize the risk. The change in treatment differences over time were compared using results from baseline; between baseline and 1-month, and baseline and 3-months since there were no significant changes between 1-month and 3-months. The results were used to test whether the between-group variation exceeded the within-group variation.

Research Question 1: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 1$)*:* There are no significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a 1$): There are significant differences in LCSS total scores between the two lung cancer therapies (surgery or tumor ablation) measured at1-month and at 3-months period.

No significant differences in physical functioning were observed between surgery and tumor ablation patients at 1-month follow up (*p* =.7794) or at 3-month follow up (*p* =.2616). Thus, the null hypothesis is supported. The least mean squares estimate for baseline, 1-month, and 3-months for the LCSS total scores of the HRQL symptoms is presented in Table 6. Data include the mean, the minimum and maximum means, the *t*-values and the adjusted *p-values* for the total scores of symptoms listed and at different time points. Following this table, the least squares means across the three-time periods were graphed in Figure 2. The means indicate that physical functioning was higher for tumor ablation compared to surgery at baseline, 1- and 3-months, while surgery was almost equal to tumor ablation only at 1-month post-treatment but lower than the mean of tumor ablation at baseline and 3-months. The scores of symptoms in the table above (Table 4) can range into the hundreds, yet the means are around 4 or 5. The scores are absolute values. The means were computed for statistical analysis using SAS. To obtain absolute values for the means, exponent of the mean needs to be calculated. For example, to calculate the absolute value of the mean of surgery at 1 month (4.6695), it was $e^{(4.6695)}$

= 106.64 and that of tumor ablation (4.7205) is $e^{(4.7205)}$ = 112.22. Similar calculations were done at 3-months, where the mean values for surgery (4.4508) was $e^{(4.4508)}$ = 85.70 and that of tumor ablation (4.4508) is $e^{(4.8367)}$ = 126.05.

Table 6

*Least Means Squares Estimates for Physical Functioning (LCSS Total Symptom Scores): Baseline, 1-Month, and 3-Months*

| **Interval** | **Treatment** | **Mean** | **Lower Mean** | **Upper Mean** | ***t*- value** | **Adjusted *p*** |
|---|---|---|---|---|---|---|
| Baseline | Tumor Ablation | 4.5920 | 4.3471 | 4.8369 | 37.12 | - |
| Baseline | Surgery | 3.9072 | 3.5325 | 4.2819 | 20.64 | - |
| 1-Month | Tumor Ablation | 4.7205 | 4.4629 | 4.9782 | 36.27 | - |
| 1-Month | Surgery | 4.6695 | 4.4180 | 4.9210 | 36.75 | - |
| 3-Months | Tumor Ablation | 4.8367 | 4.6539 | 5.0195 | 52.37 | - |
| 3-Months | Surgery | 4.4508 | 4.0847 | 4.8169 | 24.06 | - |
|  | Tumor Ablation at baseline | 0.6848 | 0.2372 | 1.1324 | 3.03 | 0.0240 |
|  | Tumor Ablation at 1-month | 0.0511 | -0.3090 | 0.4111 | 0.28 | 0.7794 |
|  | Tumor Ablation at 3-months | 0.3859 | -0.0234 | 0.7951 | 1.87 | 0.2616 |
|  | Tumor Ablation 1-month-baseline | 0.1285 | -0.1503 | 0.4073 | 0.91 | 0.7268 |
|  | Surgery 1-month-baseline | 0.7623 | 0.4269 | 1.0976 | 4.50 | 0.0001 |
|  | Delta Delta 1-month baseline | -0.6338 | -1.0699 | -0.1976 | -2.88 | 0.0332 |
|  | Ablation 3-months-baseline | 0.2447 | -0.0025 | 0.4919 | 1.96 | 0.2616 |
|  | Surgery 3-months-baseline | 0.5436 | 0.1130 | 0.9743 | 2.50 | 0.0827 |
|  | Delta Delta 3-months-baseline | -0.2989 | -0.7955 | 0.1976 | -1.19 | 0.7071 |

Alpha= 0.05; Delta-Delta 1-baseline=change/difference in 1-month and baseline; Delta-Delta 3-month-baseline=change/difference in 3-months-baseline.

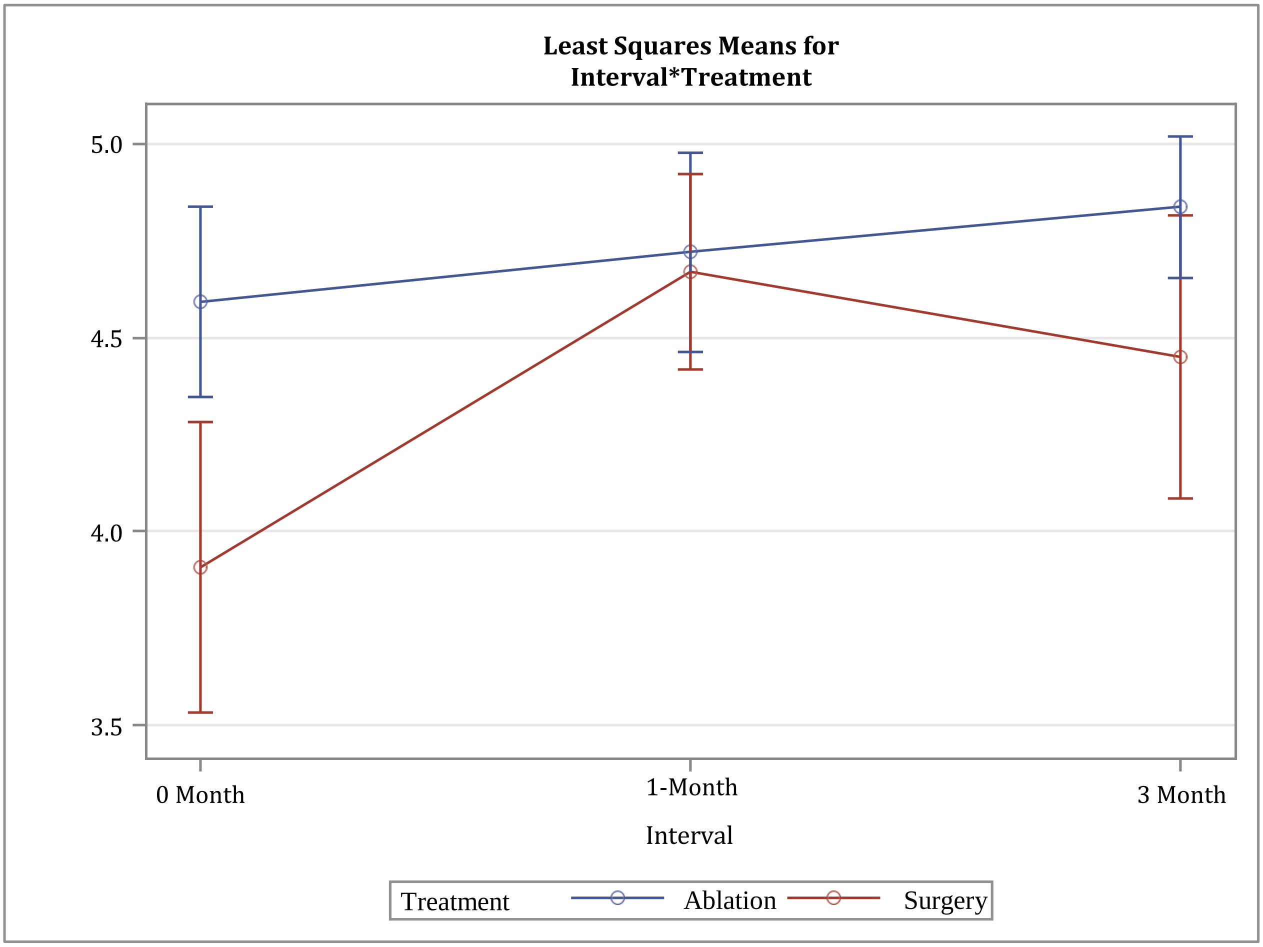

*Figure 2*. Quality of life changes in physical functioning between the two treatments for LCSS total scores

Research Question 2: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0 2$): There are no significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a2$): There are significant differences in average symptom burden index scores between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

There were no significant differences between surgery and tumor ablation patients at 1-month follow up ($p$ =.6395) or at 3-month follow up ($p$ =.1345). Thus, the null hypothesis is supported. The least mean squares estimate for baseline, 1-month, and 3-months for the average symptom burden index score of the HRQL symptoms is presented in Table 7. Data include the mean, the minimum and maximum means, the t-values and the adjusted *p-values* for the total scores of symptoms listed and at different time points. Following this table, the least squares means across the three-time periods were graphed in Figure 3. The means indicate that symptom burden was higher for tumor ablation compared to surgery at baseline, and 3-months, while the mean symptom burden for surgery was slightly higher than the mean of tumor ablation only at 1-month.

Table 7

*Least Means Squares Estimates for Average Symptom Burden Index Scores: Baseline, 1-Month, and 3-Months*

| **Interval** | **Treatment** | **Mean** | **Lower Mean** | **Upper Mean** | ***t*- value** | **Adjusted *p*** |
|---|---|---|---|---|---|---|
| Baseline | Tumor Ablation | 2.7060 | 2.4370 | 2.9750 | 19.91 | - |
| Baseline | Surgery | 1.8821 | 1.4801 | 2.2841 | 9.27 | - |
| 1-Month | Tumor Ablation | 2.8764 | 2.5884 | 3.1643 | 19.77 | - |
| 1-Month | Surgery | 2.9652 | 2.7254 | 3.2051 | 24.47 | - |
| 3-Months | Tumor Ablation | 3.0458 | 2.8594 | 3.2323 | 32.33 | - |
| 3-Months | Surgery | 2.5703 | 2.1738 | 2.9668 | 12.83 | - |
| | Tumor Ablation at Baseline | 0.8239 | 0.1341 | 1.5137 | 3.37 | 0.0070 |
| | Tumor Ablation at1-month | -0.0889 | -0.6233 | 0.4455 | -0.47 | 0.6395 |
| | Tumor Ablation at 3-months | 0.4756 | -0.1492 | 1.1004 | 2.15 | 0.1345 |
| | Tumor Ablation at 1-month-baseline | 0.1703 | -0.2068 | 0.5475 | 1.27 | 0.5501 |
| | Surgery at 1-month-baseline | 1.0831 | 0.6154 | 1.5509 | 6.54 | <.0001 |
| | Delta Delta 1-month-baseline | -0.9128 | -1.5137 | -0.3119 | -4.29 | 0.0003 |
| | Tumor Ablation at 3-months-baseline | 0.3398 | -0.0056 | 0.6852 | 2.78 | 0.0317 |
| | Surgery at 3-months-baseline | 0.6882 | 0.0395 | 1.3369 | 2.99 | 0.0199 |
| | Delta Delta 3-months-baseline | -0.3484 | -1.0833 | 1.3369 | -1.34 | 0.5501 |

Alpha= 0.05; Delta-Delta 1-baseline=change/difference between 1-month and baseline; Delta-Delta 3-months-baseline=change/difference between 3-months-baseline.

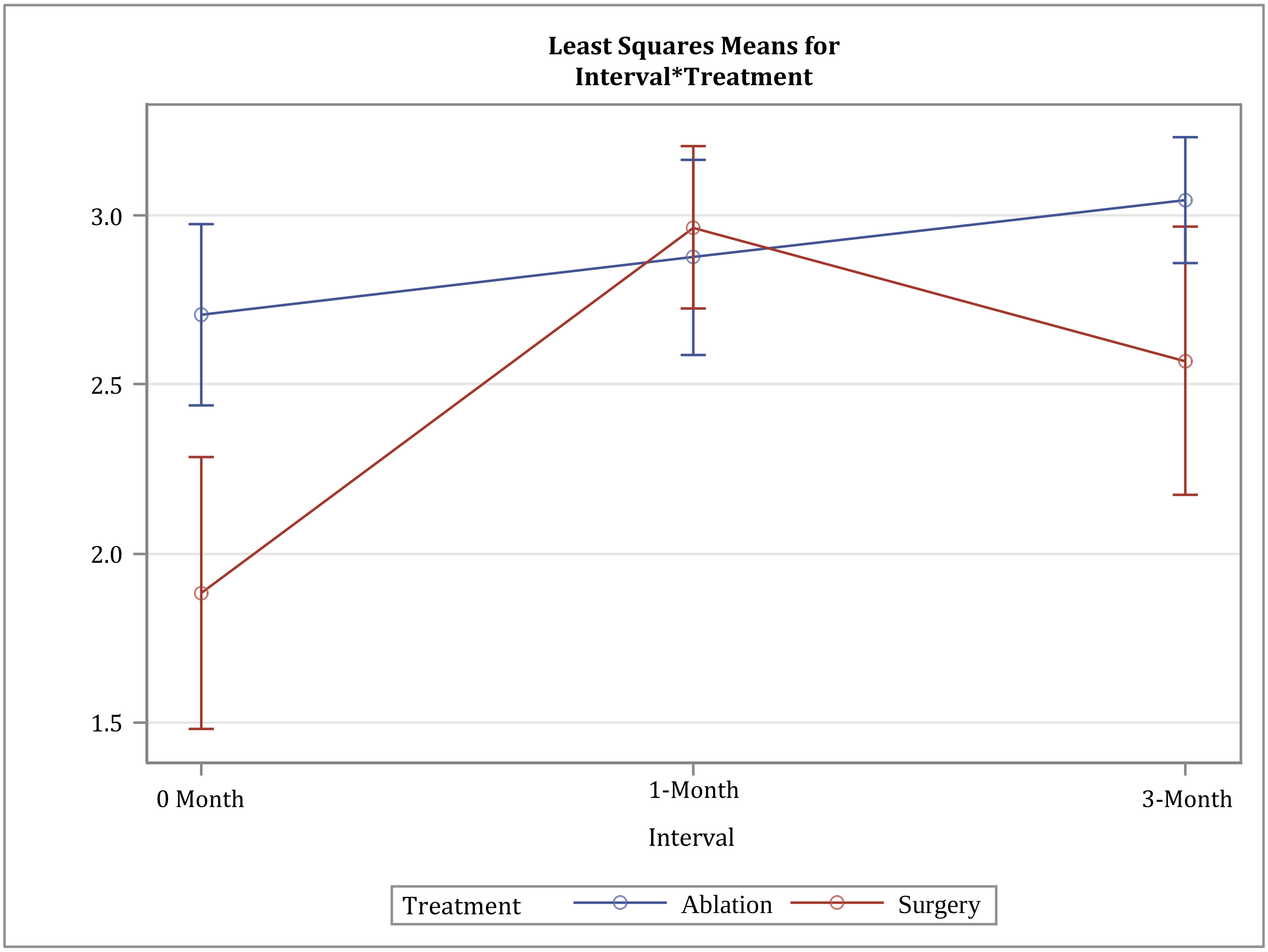

*Figure 3*. Quality of life changes in symptom burden between the two treatments

Research Question 3: Are there differences in health-related quality of life physical functioning, symptomatic distress, and overall quality of life experience among older adult lung cancer participants undergoing two-treatment modalities--surgery and tumor ablation--for small-cell lung cancer at 1-month and 3-months period?

Null Hypothesis ($H_0$3): There are no significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Alternative Hypothesis ($H_a3$): There are significant differences in quality of life between the two lung cancer therapies (surgery or tumor ablation) measured at 1-month and at 3-months period.

Interaction effect refers to the relationship among three or more variables, and describes a situation in which the simultaneous influence of two variables on a third is not additive (Aguinis, Gottfredson and Culpepper, 2013)

No significant differences were observed between surgery and tumor ablation patients at 1-month follow up ($p$ =.9318) or at 3-month follow up ($p$ =.5217). Thus, the null hypothesis is supported. Both ablation and surgery patients did not report significant changes after treatment at 1 month, (interaction effect, $p$=.1893) [Figure 4].

The least mean squares estimate for baseline, 1-month, and 3-months for the overall quality of life experience of the HRQL symptoms is presented in Table 8. Data include the mean, the minimum and maximum means, the t-values and the adjusted *p-values* for the total scores of symptoms listed and at different time points. Following this table, the least squares means across the three-time periods were graphed in Figure 4. The means indicate that overall quality of life experience was higher for tumor ablation compared to surgery at baseline, and 3-months, and the means were about the same for surgery and tumor ablation only at 1-month.

Table 8

*Least Means Squares Estimates for Overall Quality of Life Experience at 1-Month, and 3-Months*

| **Interval** | **Treatment** | **Mean** | **Lower Mean** | **Upper Mean** | ***t*- value** | **Adjusted *p*** |
|---|---|---|---|---|---|---|
| Baseline | Tumor Ablation | 2.9669 | 2.5562 | 3.3776 | 14.37 | - |
| Baseline | Surgery | 2.2418 | 1.7496 | 2.7340 | 9.06 | - |
| 1-Month | Tumor Ablation | 3.2161 | 2.8869 | 3.5453 | 19.43 | - |
| 1-Month | Surgery | 3.2367 | 2.8900 | 3.5834 | 18.57 | - |
| 3-Months | Tumor Ablation | 3.2830 | 3.0152 | 3.5508 | 24.38 | - |
| 3-Months | Surgery | 2.9096 | 2.5039 | 3.3153 | 14.26 | - |
|  | Tumor Ablation at baseline | 0.7251 | 0.08406 | 1.3662 | 2.25 | 0.1893 |
|  | Tumor Ablation at 1-month | -0.02062 | -0.4987 | 0.4575 | -0.09 | 0.9318 |
|  | Tumor Ablation at 3-months | 0.3734 | -0.1128 | 0.8595 | 1.53 | 0.5217 |
|  | Tumor Ablation at 1-month-baseline | 0.2492 | -0.1252 | 0.6236 | 1.32 | 0.5676 |
|  | Surgery at 1-month-baseline | 0.9949 | 0.4526 | 1.5373 | 3.65 | 0.0041 |
|  | Delta Delta 1-baseline | -0.7457 | -1.4047 | -0.08674 | -2.25 | 0.1893 |
|  | Tumor Ablation at 3-months-baseline | 0.3161 | -0.04731 | 0.6794 | 1.73 | 0.4367 |
|  | Surgery at 3-months-baseline | 0.6678 | 0.1520 | 1.1837 | 2.57 | 0.0944 |
|  | Delta Delta 3-months-baseline | -0.3517 | -0.9827 | 0.2792 | -1.11 | 0.5676 |

Alpha = 0.05; Delta-Delta 1-baseline=change/difference in 1-month and baseline; Delta-Delta 3-month-baseline=change/difference in 3-months-baseline.

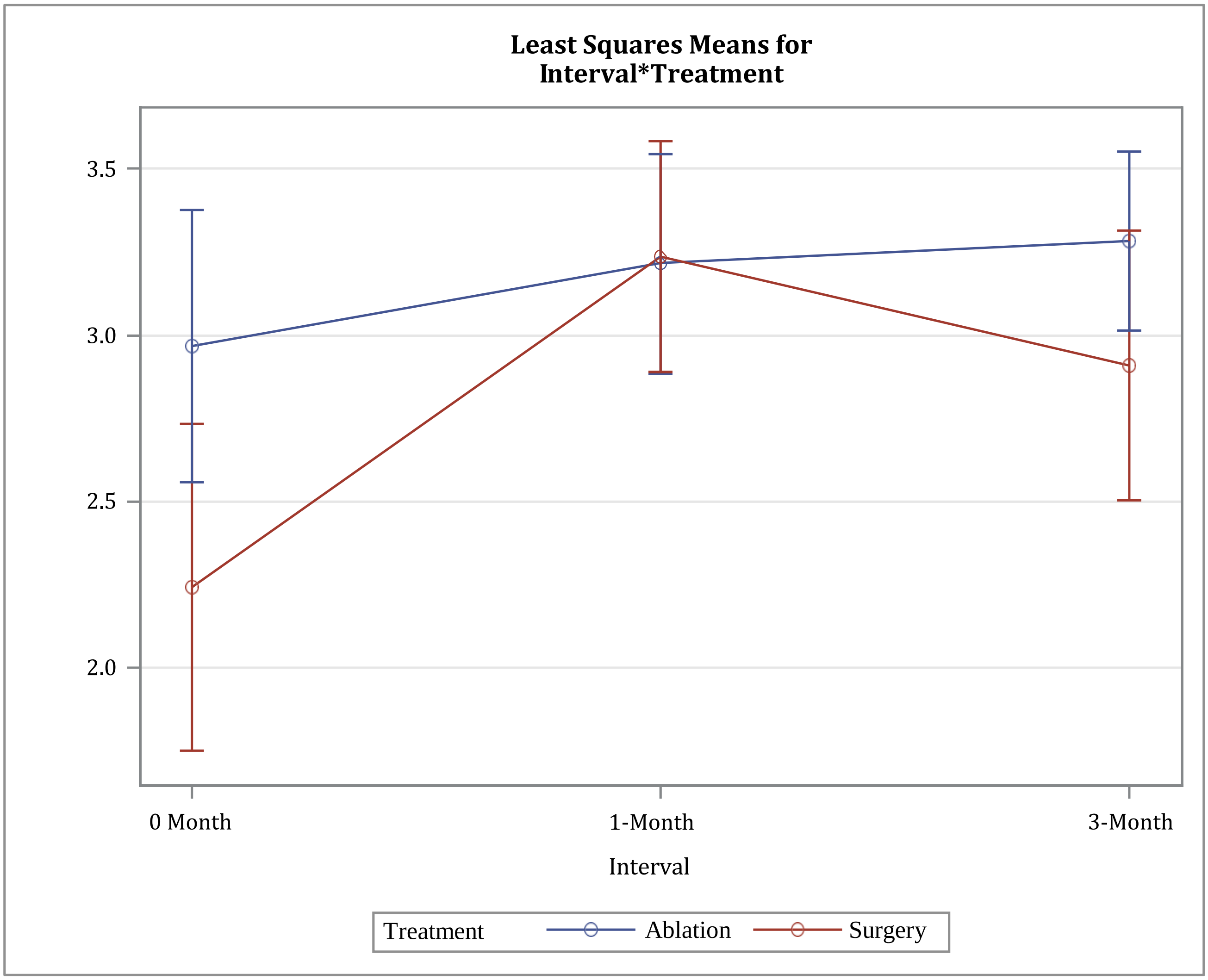

*Figure 4* Overall Quality of Life Experience between the two treatments.

## Summary and Transition

This chapter presented characteristics of the study population and hypotheses-testing results using GEE. Patients enrolled in a randomized clinical trial for lung cancer were asked to volunteer in this comparative survey to test the effect of two treatments on HRQL at 1- and 3-months. Seventy volunteers (35 in each treatment) met the inclusion criteria and completed the surveys at the three points in time. Although randomization ensures equal groups at baseline, the 70 participants were self-selected and not randomized. There were significant differences between the two treatment groups in physical symptoms and average symptomatic distress but not overall quality of life experience.

Testing of the GEE assumptions indicated that the assumptions were met. The research questions investigated the association for physical functioning, symptomatic distress, symptom burden, and overall quality of life experience of HRQL dimensions between two treatments and at three different time points. The null hypothesis was not rejected for physical functioning, symptomatic distress, and overall quality of life experience; there were no significant differences in the effect of surgery and tumor ablation treatment on all three HRQL domains at 1-month and at 3-months.

In this chapter, I presented findings for the research questions and hypotheses, characteristics of sample, and statistical analysis. Chapter 5 includes the interpretation of findings, limitations of the study, recommendations for future research, practice, implications for social change, and a conclusion.

# Chapter 5: Discussion, Conclusions, and Recommendations

## Introduction

The purpose of this study was to assess the effect of lung cancer treatment on HRQL domains. I assessed the impact of surgery or tumor ablation treatment on HRQL physical functioning, symptomatic distress, and the overall quality of life experience among older adults. In this chapter I present a summary of key findings and interpretation of findings, along with study limitations, recommendations for future studies, and implications for practice and social change.

The incidence of most types of cancers is age-dependent and the number of older adults 65 years and above is expected to reach 88.5 million by 2050 (U.S. Census Bureau, 2010). Both life expectancy and lung cancer survival are expected to increase due to better diagnostic technology, different treatment modalities, and disease prevention and control. I designed my study with three research questions to assess the effect of treatment modality on HRQL among older adults with small-cell lung cancer. The design of the study was an ancillary comparative survey among older adults undergoing treatment with either surgery or tumor ablation as part of a randomized clinical trial of lung cancer. Seventy patients completed an HRQL analog assessment with repeated measures of physical functioning, symptomatic distress, and overall quality of life experience.

## Summary of Findings

Patients who were newly diagnosed and already enrolled in a randomized clinical trial of lung cancer treatment were recruited to participate in a comparative survey ancillary study to test the effect of two treatments on repeated measures of HRQL. Three

HRQL domains, physical functioning, symptomatic distress, and overall quality of life for the lung experience were assessed using analog scales to measure the effect of the treatment on HRQL. Seventy volunteers (35 in each treatment) met the inclusion criteria and completed all the surveys. Although randomization ensures equal groups at baseline, the 70 participants for the comparative survey were self-selected and not randomized. At baseline there were significant differences between the two treatment groups in average symptomatic distress ($p = .0070$) but not physical functioning ($p = .0240$; Bonferroni adjusted $p < .016$), or overall quality of life experience scores ($p = .1893$).

The demographic characteristics by treatment modality at baseline were only significantly different in age ($p = .0049$) with mean age 66 for tumor ablation and 65 years for surgery patients. Two-thirds (65.8%) of surgery patients were female, over half (55.3%) were married, and over two-thirds (68.4%) earned less than $75,000 annually. Two-thirds (65.4%) of tumor ablation patients had high school or less education, one-third (34.6%) were widowed and over a fourth (27.3%) refused to provide their income.

The three research questions I proposed were analyzed using GEE to test whether there were differences in the effect of two treatment modalities and repeated measures on HRQL among older adult lung cancer patients already participating in a randomized clinical trial. Each research question focused on a different HRQL domain, including self-reported horizontal visual analog measures of physical functioning, symptomatic distress, and overall quality of life for the lung cancer experience. Since repeated measures introduce an inflated risk of Type I error, a Bonferroni correction to adjust the $p$-value was required. The calculated criteria to reject the null thus was $p < .016$ instead of $p < .05$. In addition to result tables displaying the GEE results, the means for each treatment domain were graphed for visual comparison between the two treatments over time.

The first research question examined the effect of surgery and tumor ablation treatments on physical functioning during the first three months after treatment. GEE analysis indicated that there were no significant differences in treatment effect on physical functioning between patients treated with surgery and tumor ablation at both follow-up times. However, the graph of computed means indicated that physical functioning was higher for tumor ablation compared to surgery at 3-months after treatment, while surgery was almost the same as the mean of tumor ablation at 1-month post-treatment. The null hypothesis was not rejected.

The second research question examined the effect of surgery and tumor ablation treatment on symptomatic distress during the first three months after treatment. GEE analysis indicated that there were no significant differences in treatment effect on symptomatic distress between patients treated with surgery and tumor ablation at both follow-up times. However, the graph of computed means indicated that symptomatic distress was higher for tumor ablation compared to surgery at 3-months after treatment, while the mean symptom burden for surgery was slightly higher than the mean of tumor ablation at 1-month. The null hypothesis was not rejected.

The third research question examined the effect of surgery and tumor ablation treatment on overall quality of life lung experience during the first 3 months after treatment. GEE analysis indicated that there were no significant differences in treatment effect on overall quality of life experience between patients treated with surgery and tumor ablation at both follow-up times. However, the graph of computed means indicated that overall quality of life experience was higher for tumor ablation compared to surgery at 3-months, while surgery was almost the same as the mean of tumor ablation only at 1-month. The null hypothesis was not rejected.

## Interpretation of Findings

The findings from the present study are consistent with prior literature in that none of the studies whether using EORTC, FACT-L, or LCSS document significant differences among the treatment modalities. A comparison of studies that examined physical and quality of life domains using all the scales developed to date were presented in Chapter 1 (Tables 1 and 2). A synthesis of the quality of life domains by treatment modality revealed that assessment of tumor ablation on HRQL has received minimal attention. In this study, I sought to fill this gap by assessing the effect of treatment with tumor ablation and surgery on HRQL domains of physical functioning, symptomatic distress, burden index, as well as overall quality of life of the lung cancer experience. Although no further interpretation can be made on the hypotheses-testing findings, the independent prognostic value of HRQL domains on survival merits interpretation and discussion (Yun et al., 2016).

***Physical functioning***. Physical functioning consists of six symptoms: pain, dyspnea, appetite, fatigue, cough, and hemoptysis. Findings from the comparative survey indicated that some symptoms developed or increased with time progression (1-month through 3-months after treatment). The four most prevalent symptoms were pain, appetite, fatigue, and dyspnea. The development of these four symptoms implies that older lung cancer patients who go through surgery or tumor ablation may develop all or some of the above symptoms during their treatment, causing disease deterioration. The four most prevalent symptoms in this study drove the physical functioning and lung cancer experience.

According to Yun et al. (2016) scores for poor indicators of survival after surgical treatment suggest that physical functioning (dyspnea, anorexia, diarrhea, cough, personal strength, anxiety, and depression) were associated with poor survival. The adjusted Cox proportional hazard ratio, for example, for overall physical functioning was 2.39 while for dyspnea was 1.56; the authors concluded that these predictor symptoms retained their independent prognostic power of survival. Family members, spouses, and care givers need to be educated about the possible development of these major lung cancer symptoms that affect physical functioning in order to prepare and educate patients when the need arises.

However, Poghosyan, Sheldon, Leveille and Cooley (2013) found that a different set of symptoms drive the physical functioning and lung cancer experience. At 1 month after surgery, the most prevalent symptoms were pain, fatigue, dyspnea, and coughing (Poghosyana et al. 2013). Pain and dyspnea scores remained significantly worse compared to baseline when measured 3-4 months after surgery in five of the eight studies reviewed by Poghosyana et al. However, the significance of these symptoms varied by the type of surgery and patient's age. Yang et al. (2012) also reported that almost all symptom scales indicated a 10% or greater reduction and clinically important decline including pain, fatigue, cough, dyspnea, and appetite. Wildstein, Faustini, Henschke, and Ostroff (2011) found that dyspnea and distressed mood were associated HRQL impairments. Since a majority of those who develop lung cancer are smokers or exposed to second-hand smoke, new interventions that focus on smoking cessation, improving symptom control, and physical function, are needed to enhance HRQL after lung cancer treatment.

***Symptomatic Distress.*** Hollen et al. (1999) and Yang et al. (2012) reported lack of differences in symptomatic distress across repeated measures using the LCSS. However, Yang et al. (2012) reported that among patients whose quality of life declined, significantly worsened symptoms were fatigue, pain, dyspnea, and appetite. Symptom burden did not lessen among participants who reported improvement, suggesting survivors might have adapted to their physical condition (Yang et al., 2012). The study by Hollen et al. (1999) measured symptomatic distress on patients treated with chemotherapy. The results indicated that fatigue, appetite, dyspnea, and pain contributed the greatest variance toward symptomatic distress. Other studies reported similar outcomes where all the same four predictors contributed the greatest variance toward symptomatic distress (Hollen et al., 1999; 2004; Wildstein, et al., 2011; Yang et al., 2012).

***Overall Quality of Life Experience for Lung Cancer.*** Findings from the present study found no significant differences in overall quality of life for patients who had surgery or tumor ablation. Because HRQL outcomes research in lung cancer focuses mainly on short-term survival and quality of life, findings are not conclusive and require longer periods of observation (Yang et al., 2012). Some studies report overall quality of life for the lung cancer experience significantly lower at repeated measures but a clinically important decline and improvement in overall quality of life. Yang et al. (2012) found a clinically important decline and improvement in overall quality of life, where the overall quality of life experience score was high (80) within 3 years of diagnosis and decreased to 75 at 4 years. A score of 80 is equivalent to healthy populations. Lower quality of life warrants a design that provides frequent quality of life assessment throughout a clinical trial and use of instruments that focus on the primary issues of concern (Hollen et al., 1999; 2004; Wildstein, et al., 2011; Yang et al., 2012). The findings from this study suggest that the use of HRQL questionnaires during the first three months after surgery and tumor ablation may provide prognostic information but further studies are needed to evaluate the potential clinical value of these instruments. Recommendations include a demand for targeted interventions to improved HRQL.

## Theoretical Application

The framework that guided this study was the lung cancer quality of life model. I used only three of the model's quality of life dimensions to conceptualize my study: the physical, functional, and overall quality of life dimension (Figure 1). The physical dimension is the basic dimension that influences functioning as well as overall experience of quality of life among those with lung cancer. The developer of this model conceptualized the dimension of function as distinct from the physical dimension, where physical dimension is related to activities of daily living (walking, eating, bathing), and function reflects cognitive and social functioning. During the initial stages of lung cancer, the level of function may not be evident, and that the disease is affecting cognitive and social functioning (Hollen et al., 1995). HRQL represents a separate dimension and serves as the measure of the outcome or the effect of lung cancer on the physical and functional dimensions.

The findings from this comparative survey study confirm the application of the lung cancer quality of life model. Although there were no significant differences in the three domains studied, the mean HRQL scores were higher for tumor ablation compared to surgery at 3 months across the three domains, and about the same for physical functioning and overall quality of life for the lung cancer experience at 1-month follow-up. However, the mean HRQL for symptomatic distress at 1 month was higher for surgery compared to tumor ablation. This reversal favoring the less invasive treatment suggests that symptomatic distress is associated with severity of treatment, which in the case of surgery makes sense. In the case of lung cancer treatment burden symptoms parallel disease symptoms. HRQL is a multidimensional concept that interprets a patient's health status because proliferation of disease-related symptoms and treatment-induced toxicity are inversely related to HRQL (Bottomley et al., 2003; Echteld et al., 2007; Pallis et al., 2010).

## Strengths and Limitations of the Study

The findings of this study have significance for several reasons. First, the analysis supports current practice patterns where there is no reported effect of treatments on HRQL physical functioning, symptomatic distress, and overall quality of life for the lung cancer experience. Second, although the sample size was 35 for each treatment and considered a small sample, it had at least 80% power to detect differences. Another strength of the study was the fact that to be eligible for the randomized clinical trial, participants in the comparative survey underwent pathological staging which is more objective than clinician-base and allows precise exclusion of stage IV lung cancer patients. Most studies rely on clinically staged lung cancer.

There were limitations to the generalizability, validity, and reliability, either imposed by me or challenging to control. The discussion includes ways in which the study was designed to minimize, or actions taken during the study. The use of a small sample from one hospital and geographic area may limit the generalizability of the findings. Most studies in cancer treatment and HRQL are either underpowered or fail to report any power calculations (Echteld et al., 2007; Melin-Johansson et al., 2010). Sample size calculations for the present study indicated that 30 patients in each treatment group would yield an 80% power to detect differences at the $p < .05$ significance level.

Despite a 12.5% (10/80) attrition rate after consenting to participate in the ancillary study, the resulting sample with complete baseline and follow-up data was above the calculated sample size ($n$=35 for each group). Movsas et al. (2016) conducted a secondary analysis of pooled data from 185 institutions in the U.S. and Canada enrolling patients with lung cancer stage III in randomized clinical trials. Movsas et al. (2016) wanted to test the effect of high-dose radiation compared to standard dose on HRQL. All the sites were part of the Radiation Therapy Oncology Group which uses the FACT-Lung Cancer Subscale to measure HRQL. Movsas et al. (2016) reported a 30% attrition rate from baseline to 3-months. The attrition rate of the present study (12.5%) was much lower than published studies (Movsas et al., 2016) and especially stage IV lung cancer (average attrition rates 29.1 and 46.6%) where palliative care is the intervention (Kassianos, Loannou, Koutsantoni & Charalambous, 2018).

## Recommendations for Research

The recommendations for further research are grounded in the strengths and limitations of the current study, as well as the literature reviewed in chapter 2. Comparing the effectiveness of tumor ablation and surgery is difficult. Randomized trials either have failed to accrue an adequate number of participants or are many years from completion.

One suggestion is the need to determine whether the LCSS instrument would work for all age groups who may be diagnosed with lung cancer. Another school of thought is that this study may help health care providers, public health professionals, oncologists and other professionals in the field of cancer research to make informed decisions on lung cancer for older adults.

While different instruments have been used to examine HRQL to guide physicians and health care providers in their decision-making to select a cancer treatment, such instruments have measured a range of conditions, but the LCSS in this study was developed specifically to measure the effect of treatment for lung cancer. The ease with which participants find the LCSS survey analogue questions and the short time span to answer the questions could make the LCSS the instrument of choice for HRQL studies. There are numerous studies assessing the effect of chemotherapy on lung cancer HRQL as chemotherapy is the treatment of choice for early stage lung cancer as well as nonresectable cancers for which surgery is not an option (Kassianos et al. 2018).

The data gathered from this study using 70 older adult lung cancer patients can be used to extrapolate for interpretation of scores of the LCSS in larger populations. The results and findings from this study might also be interesting to use to bridge the gap in the literature especially in the field of tumor ablation where quality of life is not adequately investigated. Physicians face barriers to make consistent decisions during treatment, such as cost control, professional judgment, as well as demands to include patients in decision-making (Parker, Ritchie, Kirchner, & Owen, 2009, p. 972-973).

There should be a study using this instrument as a pretest and posttest after an educational conference about lung cancer treatment therapies for older adults. In addition, existing educational treatment and management guidelines could be of help to oncologists, and healthcare providers to gain more insight into management and treatment of lung cancer especially in the older adult. Finally, for researchers looking to design studies with endpoints of mortality and morbidity, the findings from this study suggest stratifications of patients by life expectancy and examination of complications and mortality for at least 2 years after treatment.

## Recommendations for Practice

HRQL research is an important aspect of cancer clinical trials and a major concern for cancer patients and their families. Findings from HRQL research are key to the provision of evidence that addresses how much additional time a patient can gain with a particular treatment and how valuable that time can be made. Thus, HRQL impacts both future research and treatment decisions for clinicians (Bottomley et al., 2003; Yun et al., 2016). HRQL is a multidimensional concept that interprets a patient's health status because increases in disease-related symptoms and treatment-induced toxicity are inversely related to HRQL (Bottomley et al., 2003; Echteld et al., 2007; Pallis et al., 2010; Yun et al., 2016).

Evidence-based clinical recommendations are difficult to reach because evidence on adults 65 years of age and older is dismal. Despite the high incidence of lung cancer in older adults, they are underrepresented in clinical trials (Sacher, Le, Leighl, & Coate, 2013). Providers and patients lack certainty as to the optimal treatment for lung cancer. Recommendations for practice include increasing knowledge and awareness of the importance of educating high-risk individuals about lung cancer. The results of this study may lead to more information on lung cancer HRQL treatment especially in surgery and more importantly tumor ablation where there is scant amount of knowledge in the field. For the clinician counseling patients, this study provides further incentive for frank discussion and individualized decision-making, considering a patient's life expectancy, desire for a long-term cure, and appetite for treatment-related complications

## Implications for Social Change

The study may influence positive social change by providing information that may improve both survival and HRQL of older lung cancer patients, reducing self-care, healthcare cost, and complement existing information available to patients, family, and providers. Most older lung cancer patients have complex medical histories as well as a myriad of comorbidities. Older lung cancer patients present unique characteristics such as physiological changes in organ function and pharmacokinetics, that make the choice of the best treatment more difficult and therefore are often undertreated (Di Maio & Perrone, 2003).

Lung cancer is often not diagnosed until late in progress when disease-mortality is increased. Because of the aggressive process of late stage cancer, the frailty of older adults, and the impact on physiological and psychological effect that lung cancer treatment has on older adult assessment of physical functioning, symptomatic distress and lung cancer experience as HRQL is of major importance. Lung cancer treatment improves both survival and quality of life, yet treatment is underutilized among older adults.

Hence, the results of this study may help healthcare providers and older lung cancer patients to decide the mode of lung cancer treatment to adopt based on symptoms. The information in this study may help researchers and public health officials provide educational programs related to the diagnosis and treatment of lung cancer or any other type of cancer to the older adult community. Findings from this study may also provide evidence-based guidelines on lung cancer to the lung cancer patients.

Effective educational programs and guidelines may influence how oncologists and other healthcare providers, manage and perceive lung cancer. The potential impact for positive social change may be positioned at the provider, organizational, and policy levels. The results of this study may help providers, research and cancer centers to tap into the information which might aid their current treatment and standard of care to include evidence based medical practices.

## Conclusion

The purpose of this study was to assess the effect of lung cancer treatment on HRQL domains. The study assessed the impact of surgery and tumor ablation treatment on HRQL physical functioning, symptomatic distress, and the overall quality of life for the lung cancer experience among older adults. The research design and approach of the study was an ancillary comparative survey among older adults undergoing treatment with either surgery or tumor ablation as part of a randomized clinical trial of lung cancer. Seventy patients completed an HRQL analog assessment with repeated measures of physical functioning, symptomatic distress, and overall quality of life experience.

This ancillary comparative survey study examined three dimensions of HRQL among older adult lung cancer participants undergoing treatment with surgery and tumor ablation. The physical domain included individual pain, appetite, shortness of breath, fatigue, cough, and hemoptysis. In addition, the domains of symptomatic distress and overall quality of life of the lung cancer experience were included. Repeated measures of

HRQL at 1-month and 3-months did not indicate significant differences in the effect from treatment with surgery and tumor ablation on physical functioning symptoms, symptomatic distress, average symptom burden index, and overall quality of life experience. The lack of significant differences in HRQL domains between the two treatments implies that either treatment is adequate for older adults with non-small cell lung cancer. Because participant attrition biases the findings towards the “healthy-effect” with participants with better well-being, more studies are needed to improve treatment decisions for more frail lung cancer patients and those with higher co-morbidity.

Lung cancer incidence is increasing with the increasing aging of the U.S. population. In addition, the number of women with lung cancer has increased dramatically in the last decades and represent almost half of patients with lung cancer (Howlader et al., 2017). Lung cancer is the leading cause of death among all cancers. Despite a high incidence and median age of 70 years, uncertainty about the optimal treatment remains due to the systematic under-representations of older adults in clinical trials, and evidence exists that elderly patients are specifically excluded in the trial designs (Howlader et al., 2017; Pallis, et al., 2010); Sacher, Le, Leighl, & Coate, 2013).

Both life expectancy and lung cancer survival are expected to increase due to better diagnostic technology, different treatment modalities, and disease prevention and control. Although the prognosis of lung cancer is poor, the quality of life is at least as important as the quantity of remaining life. HRQL is a useful concept which might be considered intangible to define; however, there are several important contributing factors. Culture, religion, prior experience, and the individual’s point of view may contribute to their preferences. As a result, quality of life assessment may only generalize to a defined community. The measurement of quality of life in cancer clinical trials should concentrate on a few important categories such as physical symptoms, psychosocial factors, and should be simple rather than comprehensive.

The representation of age and gender in the present study contributes to the literature in increasing evidence to better define the effect of treatment on HRQL and reduce uncertainty for selection of optimal treatment for older adults. The review by Sacher et al. (2013) of the 100 most cited trials of NSCLC, revealed that 33% of elderly were excluded and the average patient median age was 60.9 years. The mean age of the comparative survey sample was 66 and 65 for the two treatment groups, and two-thirds were women. However, according to the EORTC Elderly Task Force, Lung Cancer Group (Pallis, et al., 2014), treatment decisions should not be based just on chronological age but on functional age (Pallis, et al., 2010; Pallis, et al., 2014). Functional age includes evaluation of health, functional status, nutrition, cognition, and the psychosocial and economic context (Pallis, et al., 2010). The EORTC also recommends inclusion of patient's life expectancy, preferences, functional age, comorbidities, and estimated benefits and risks in treatment decisions.

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# Appendix A: Demographic and Health Data

**Participant** #_____

Interviewer_____

**Protocol**: Surgery: [___] Tumor Ablation: [___]

Your answers will help to facilitate a health-related quality of life study on surgery and tumor ablation. All of the information you give me will be strictly confidential, and when I report my results I will do it by groups and not by individuals. Do you have any questions before we start?

1. What is your date of birth? _______________

2. What is your gender? (Check one) M [__] F [__]

3. What is the highest grade you completed in school?
   a. Not a High School graduate or equivalent [ ]
   b. High School graduate or equivalent [ ]
   c. Some college [ ]
   d. College graduate [ ]
   e. Post-graduate or professional school [ ]

4. What race do you consider yourself?
   a. White [ ]
   b. African-American or Black [ ]
   c. Asian [ ]
   d. American Indian or Alaskan Native [ ]
   f. Native Hawaiian or other Pacific Islander [ ]
   g. Hispanic or Latino [ ]
   h. Prefer not to answer [ ]

5. What is your marital status?
   a. Single [ ]
   b. Significant Other [ ]
   c. Married [ ]
   d. Separated [ ]
   e. Divorced [ ]
   f. Widowed [ ]

**Participant**#[___] [___] [___]

Interviewer: [___] [___][___]

Now I would like to ask you some questions about your health. I am interested in knowing if you have gone through any of the following two treatment options or any other lung cancer therapy not mentioned below.

6. Has your lung cancer been treated with any other therapy other than surgery, or tumor ablation?

[ ] No
[ ] Yes→ If yes, what type of therapy did you receive?
a. ____________________________
b. ____________________________
c. ____________________________
d. ____________________________

7. What was your household income for the [ENTER LAST CALENDARYEAR]?

[ ] $75, 000 and over or
[ ] Less than $75,000

# Appendix B: Questionnaire Permission Letter

You have our permission to use the data

kind regard,
brambalduyck

[redacted]

---

> From: fesdok@juno.com
> Date: Mon, 29 Sep 2008 16:27:27 +0000
> [redacted]
> Subject: Re: Standard Deviations

Sir,

Thank you very much for the response. I am looking forward for it. Sir, one more thing. Do I have your permission to use your data as stated in my first e-mail? I really appreciate your help.

\>
\> Festus
\>

# Appendix C: Lung Cancer Symptom Scale (LCSS)

Fee Waiver Agreement Form

The **Lung Cancer Symptom Scale (LCSS),** a site-specific quality of life instrument, provides a practical measure for the lung cancer population. The scale developers, ***Quality of Life Research Associates, LLC***, having a business address at 3445 Seminole Trail, Suite 214, Charlottesville, VA, 22911, and the ***other entity)*** [see below] agree to the following conditions:

User's Name (*Typed*): FESTUS F. DOKYI

Organization: WALDEN UNIVERSITY

Address: [redacted]

Telephone #: [redacted]

Fax #: [redacted]

E-mail: FESDOK@JUNO.COM

Name of Study (*Typed*): QUALITY OF LIFE ASSESSMENT OF LUNG CANCER TREATMENT IN THE ELDERLY

Sponsor: NONE
(*If none, so state*)

Special Circumstances (e.g., Student Status, Non-Sponsored Study): STUDENT STATUS

**Terms of Agreement:**

1. User sends an <u>abstract</u> of the proposed study at the time of sending the agreement form.

2. User agrees to use the *LCSS* for her/his own work, <u>without distribution</u> to other colleagues other than those involved in the trial, unless written approval is obtained from the scale developers.

3. User agrees to use the *LCSS* for <u>one trial only</u> (as specified above). For additional trials, new agreements will be needed.

4. User agrees to cite <u>all</u> primary references for this measure by the *LCSS* developers.

5. User agrees to send a copy of the <u>final published report</u> of the study for the *LCSS* bibliography.

______Festus F. Dokyi________________________6/8/10________________

Signature of Applicant Date

____________________________________________________

Signature of Developer Date

# Appendix D: Scoring The LCSS

## Scoring Instructions Located at LCSS Website

The LCSS is designed as a site-specific measure of quality of life (QL), particularly for use in clinical trials. It evaluates six major symptoms associated with lung malignancies and their effect on overall symptomatic distress, functional activities, and global QL. The philosophy behind the development of the LCSS is to provide a practical QL measure that reduces patient and staff burden in serial measurement of QL during the course of the trial. It captures in detail those dimensions most likely to be influenced by therapeutic interventions and evaluates other dimensions globally. It consists of two scales: one completed by the patient and an optional one for health care professionals ("counterpart observer") to provide context.

**Number of QL Dimensions/Domains:**

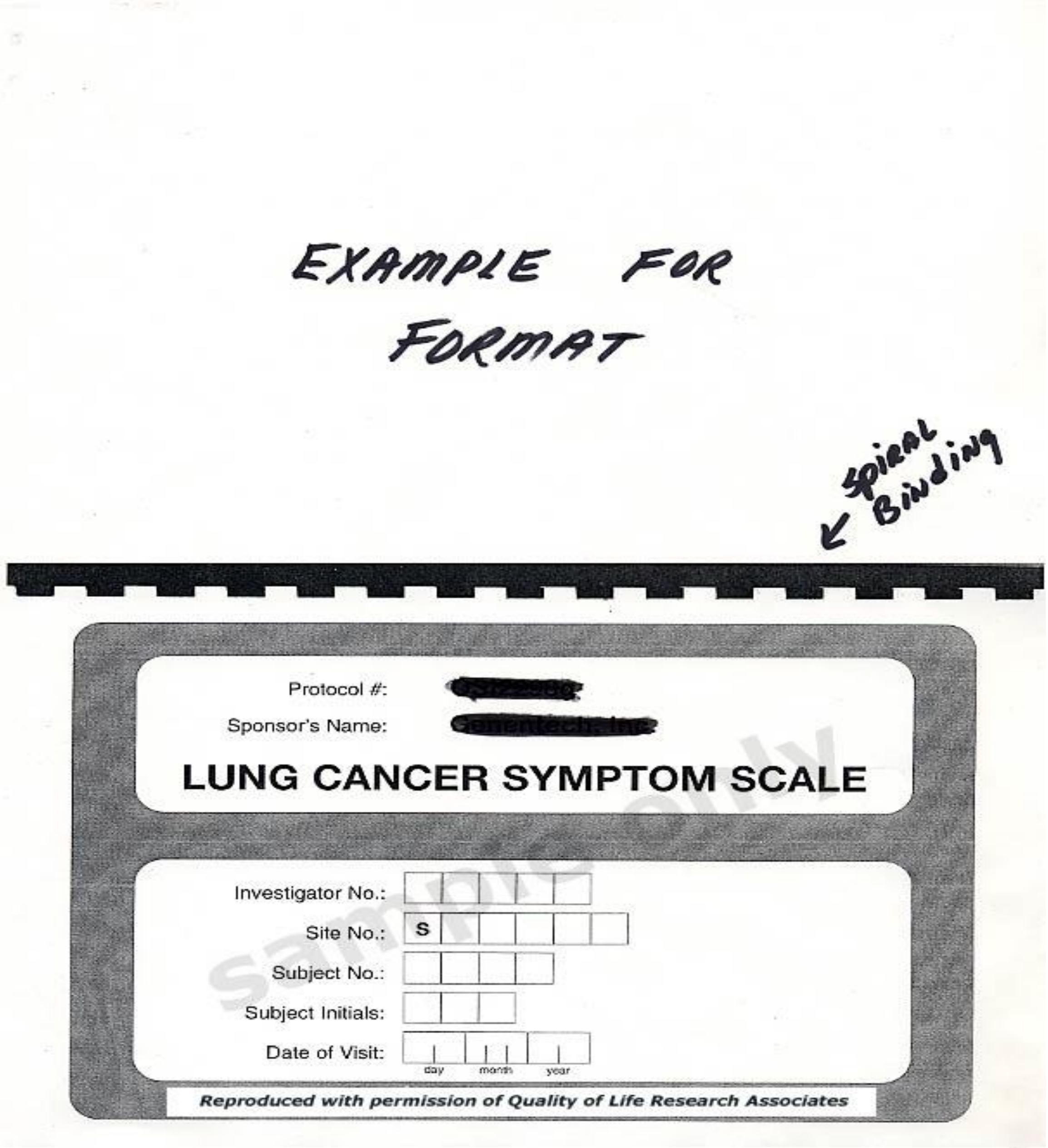
Five, with physical and functional in detail, and others captured globally.

**Scaling of items:**

***Patient scale:*** 9 visual analogue scales (100 mm horizontal line). Patient puts a mark on line to indicate intensity of response to the items in question (0 = lowest rating; 100 = highest rating). ***Observer scale:*** 5-point categorical scale (100 = none; 75 = mild; 50 = moderate; 25 = marked; 0 = severe).

**Scoring:**
***Patient scale:*** Scores equal length of line marked by patient. An average of the aggregate score of all 9 items is used for a total score. In addition, a subscore using the mean of all 6 major symptoms ("average symptom burden index"), the single QL item, and/or individual items to report specific areas of change can be used. ***Observer scale:*** Score equals point value chosen by observer for each item. Aggregate score is used as well as average symptom burden index and/or individual items for specific areas of change.

# Appendix E: Example LCSS Patient Form



EXAMPLE FOR
FORMAT

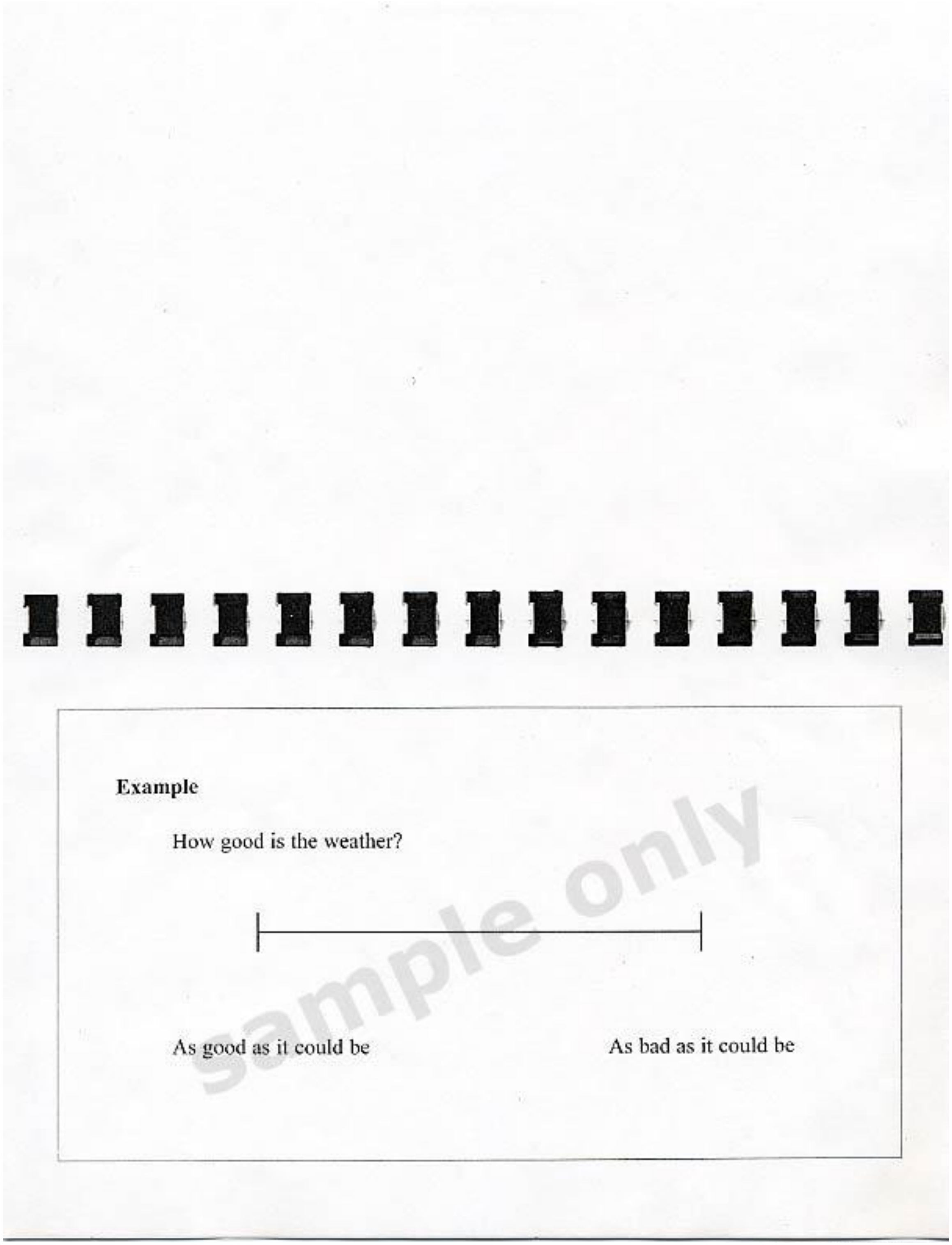
↙ Spiral
Binding

Protocol #: [redacted]
Sponsor's Name: [redacted]

**LUNG CANCER SYMPTOM SCALE**

Investigator No.: ☐☐☐☐☐
Site No.: S☐☐☐☐☐
Subject No.: ☐☐☐☐
Subject Initials: ☐☐☐
Date of Visit: ☐☐ day ☐☐☐ month ☐☐ year

*Reproduced with permission of Quality of Life Research Associates*



**Example**

How good is the weather?

As good as it could be

As bad as it could be

Actual example will include a mark across one end of the range and this will be explained to patients face-to-face until they are able to express their symptom severity on the cards.

## Lung Cancer Symptom Scale Symptoms and Patient Scoring Ranges

**Directions:**
Please place a mark along the line where it would best describe the symptoms of your lung cancer DURING THE PAST DAY (within the last 24 hours)—The questions here represent the actual Cards on Spiral Binding shown on prior page.

| Q# | Question assessing severity of symptoms | Lower Range<br>0 | Upper Range<br>100 |
|---|---|---|---|
| 1. | How good is your appetite? | As good as it could be | As bad as it could be |
| 2. | How much fatigue do you have? | None | As much as it could be |
| 3. | How much coughing do you have? | None | As much as it could be |
| 4. | How much shortness of breath do you have? | None | As much as it could be |
| 5. | How much blood do you see in your sputum? | None | As much as it could be |
| 6. | How much pain do you have? | None | As much as it could be |
| 7. | How bad are your symptoms? | I have none | As bad as they could be |
| 8. | How much has your illness affected your ability to carry on normal activities? | Not at all | So much that I can do nothing for myself? |
| 9. | How would you rate the quality of your life today? | Very high | Very low |