An Exploratory Study of Sleep-Wake Disturbances in Advanced Lung Cancer Patients

by

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ABSTRACT

Sleep-wake disturbances are a common problem for people with cancer. Prior research of sleep-wake disturbances in cancer patients has focused predominantly on patients with early-stage disease. Consequently, little is known about sleep-wake disturbances in patients with advanced cancer. The significance of sleep-wake disturbances in advanced cancer patients and the factors associated with them is also not well understood. The purpose of this study was to identify the sleep-wake disturbances in individuals with advanced lung cancer and to explore the relationships amongst sleep, fatigue and quality of life in this population.

All patients with newly diagnosed advanced non-small cell lung cancer attending outpatient clinics at the Cape Breton Cancer Centre (01/06/2013 to 30/06/2014) were invited to participate in the study. Seventy-two patients agreed to participate. Data were collected during the pre-treatment period. Questionnaires were used to collect symptoms, sleep quality, fatigue and quality of life data. Demographic and clinical data including co-morbidities, stage of disease and use of medications were collected from patients' medical charts. Data were analyzed using SPSS-21. Descriptive statistics were computed to describe the characteristics of the study sample and the study variables. Bivariate correlations amongst all study variables were conducted using Spearman's rho correlation coefficient. Multiple regression analyses were performed to examine the associations between the predictor variables.

The conceptual framework that guided this study was the 'Borbely Two-Process Model of Sleep Regulation'. Borbely (1982) proposed two processes, a homeostatic process (Process S) and a circadian rhythm process (Process C) interact to regulate the timing and the duration of both sleep and wake states. A central hypothesis of this study was that Process S was influenced

by mediator factors (i.e. pain, dyspnea) and psychological factors (i.e. anxiety). It was proposed that Process C was affected by moderator factors such as age and sex. Medications were proposed to affect both Process C and Process S.

Findings showed that patients with advanced lung cancer experience very poor sleep quality and severe fatigue during the pre-treatment period. Difficulty initiating sleep, nocturnal sleep interruption, decreased sleep efficiency and daytime dysfunction were some of the experiences reported by patients. Difficulty starting and completing activities and requiring assistance with activities of daily living were reported because of severe fatigue. Poor sleep quality and severe fatigue predicted the quality of life of advanced lung cancer patients during the pre-treatment period.

The relationship between sleep quality, fatigue and quality of life in advanced lung cancer patients is complex. In the bivariate correlations conducted: pain, dyspnea, anxiety, tiredness, appetite and depression were significantly correlated with all three outcome variables but in the regression analysis, only drowsiness, dyspnea, and appetite predicted fatigue and only depression predicted quality of life. Lastly, the quality of life of participants was significantly associated with the severe fatigue and poor sleep quality reported. Poor sleep quality was the most significant predictor of quality of life.

Patients with advanced lung cancer should be screened for sleep disturbance and fatigue when initially diagnosed and those with scores of 3 out of 10 (with 0 being absent and 10 being severe) assessed using comprehensive, valid and reliable assessment tools. Both pharmacological and non-pharmacological evidence-based interventions should be considered to manage poor sleep quality and fatigue in these patients.

PREFACE

This thesis is the original work of Claudette Taylor. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, "An Exploratory Study of Sleep-Wake Disturbances in Advanced Lung Cancer Patients", No. 00034624, February 24, 2014. This thesis also references journal articles co-authored by Claudette Taylor. These journal articles were published when this research project was being conducted.

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CHAPTER 1

SLEEP-WAKE DISTURBANCE IN INDIVIDUALS WITH ADVANCED LUNG CANCER

Cancer is a major health problem in Canada. In 2011, the Canadian Cancer Society estimates 177, 800 Canadians will be diagnosed with cancer and 75, 000 Canadians will die from cancer. An estimated 43% of these new cases of cancer and 61% of cancer deaths will occur in individuals 70 years or older. Four types of cancer comprise over half of these new cases of cancer; in men (prostate, lung and colorectal) and in women (breast, lung and colorectal). To date, lung cancer is the leading cause of cancer death in Canadian men and women (Canadian Cancer Society, 2011).

In Nova Scotia, nearly 6,700 residents will experience a new cancer diagnosis in 2011. An estimated 2,650 people will also die of cancer this year. The incidence of cancer increases with age and in Nova Scotia, two-thirds of newly diagnosed cases of cancer occur in individuals 70 years or older (Canadian Cancer Society, 2011). Today, nearly 28,000 people in Nova Scotia are living with an invasive form of cancer. Prostate, lung and colorectal cancers are responsible for 59% of all cancers in Nova Scotian men. Breast, colorectal and lung cancers account for approximately 57% of all cancers in women, in Nova Scotia.

In Cape Breton, Nova Scotia, lung cancer rates are significantly higher, in both men and women, as compared to the rest of Nova Scotia (19% higher or 18 more cases per 100,000 men and 16% higher or 8 more cases per 100,000 women). There are several reasons which are responsible for the high rates of lung cancer in Cape Breton. First, Cape Breton is home to one of Canada's worst environmental disaster associated with known carcinogens–the tar ponds.

Second, for many years, most individuals were employed in steel producing and coal mining industries associated with exposure to carcinogens. Last, many individuals in this region of Canada continue to smoke (Cancer Care Nova Scotia, 2011).

Lung cancer is the leading cause of cancer death, in both men and women, in Cape Breton, as well as the rest of Nova Scotia. The five-year survival rates for Nova Scotians diagnosed with lung cancer are among the lowest in Canada. Both the age of the individual and the stage of the disease at presentation influence survival outcome of lung cancer patients (Cancer Care Nova Scotia, 2011; Canadian Cancer Society, 2011).

Lung Cancer

Lung Cancer is a malignant neoplasm in lung tissue. There are two main types of lung cancer, non-small cell lung cancer (NSCLC) and small-cell lung cancer. NSCLC is the most common form, comprising approximately 85% of all cases of lung cancer. The risk factors for NSCLC include cigarette smoking, air pollution and consistent exposure to lung carcinogens (Molina, Yang, Cassivi, Schild, & Adiel, 2008). NSCLC is further characterized as either *adenocarcinoma*, *squamous-cell carcinoma* or *large-cell carcinoma*. *Adenocarcinoma* typically presents in the lung periphery and may metastasize rapidly to the liver, adrenal glands, bones or brain. *Squamous-cell carcinoma* is usually found in the central part of the lung and typically grows relatively slowly doubling in size approximately every 88 days. The third type of NSCLC is *large-cell carcinoma* which is usually located in the lung periphery and grows at a rate comparable to squamous-cell cancers. Non-small cell lung cancer is staged from I (early) to IV (advanced), based on the extent of tumor involvement, presence or absence of lymph node involvement and presence or absence of distant metastasis (Cersosimo, 2002; Molina et al., 2008; Tod, Craven & Allmark, 2008; Yoder, 2006).

Small-cell lung carcinoma is the collection of neoplasms typically located in central regions of the lung. Small-cell lung cancer presents late and symptoms are generally present for a very short time, approximately 8-12 weeks. Small-cell carcinoma accounts for approximately 15 to 20% of all lung cancers and is predominantly found in patients with a significant smoking history. This type of lung cancer is staged as either limited or extensive disease. Patients with disease confined to one hemithorax are considered to have limited stage disease whereas those with disease involvement at any other location are considered to have extensive disease (Cersosimo, 2002; Cooper & Spiro, 2006; Molina et al., 2008; Tod, et al., 2008; Yoder, 2006).

Factors Affecting the Prognosis of Individuals with Lung Cancer

A cancer patient's prognosis may be influenced by multiple factors: age, gender, co-morbid conditions, socioeconomic factors, lifestyle factors, tumor-related factors (stage of disease, histological type) and system factors (availability of services). As with all cancers, early detection increases the likelihood that a curative treatment can be provided (Canadian Cancer Society, 2011). Unfortunately, most people with lung cancer are diagnosed late, when disease processes are advanced and are usually not curable (Cersosimo, 2002; Molina et al., 2008; Tod, et al., 2008). Due to the late presentation of this disease, the majority of patients diagnosed with lung cancer die within the year (Cersosimo2002; Montazeri, Milroy, Hole, McEwen, & Gillis, 2003; Pearman, 2008).

Symptoms Associated with Advanced Lung Cancer

Advanced lung cancer is associated with a wide range of distressing symptoms, many of which persist throughout the course of the disease and its treatment. The symptom burden of advanced lung cancer patients is particularly high as compared to other cancers (Fox & Lyon,

2006; Vena et al., 2006). This may be because of the simultaneous co-occurrence of multiple inter-related symptoms. Pain, breathlessness, fatigue, poor appetite, constipation, mood disturbance, functional decline and sleep-wake disturbance are especially common, occurring in some combination in almost all advanced lung cancer patients (Dodd, Miaskowski, & Paul, 2001; McMillan, Tofthagen & Morgan, 2008). Olson and colleagues have proposed that sleep-wake disturbance is a predictor of fatigue (2008). Management of the symptoms associated with lung cancer in a manner that also helps to promote the best possible quality of life is the primary focus of nursing care in individuals with advanced lung cancer.

My Personal Context

In the proposed study my central focus is on factors associated with sleep-wake disturbance and the relationship between sleep-wake disturbance and fatigue in individuals with advanced lung cancer. As a palliative care nurse I frequently encounter patients and their families living with advanced lung cancer. Multiple issues surround the care of these patients as they often suffer from numerous symptoms resulting from the disease itself, as well as from its treatment. Clinically it seems that sleep-wake disturbances increase as the number and severity of other symptoms increase.

Sleep-Wake Disturbance

Sleep-wake disturbance is a generic term used to describe a constellation of symptoms experienced as a result of an alteration in nighttime sleeping pattern and an associated impairment in daytime functioning (Delgado-Guay et al., 2011; Hearson & Sawatzy, 2008; Savard & Morin, 2001). Sleep-wake disturbances include difficulty initiating sleep, difficulty

maintaining sleep, early morning awakening and daytime sleepiness (Berger et al., 2009; Savard & Morin, 2001; Vena et al., 2006).

Sleep-wake disturbances are a common problem for people with cancer (Berger et al., 2005; Berger et al., 2009; Clark, Cunningham, McMillan, 2004; Vena, Parker, Cunningham, Clark & McMillan, 2004). Their prevalence increases in patients with advanced cancer (Mystakidou et al., 2009). It is now acknowledged at least one-fourth of cancer patients report some type of sleep-wake disturbance (Akechi, Okuyama & Akizuki, 2007).

The trajectories of sleep-wake disturbance vary. Some individuals report sleep-wake disturbance prior to their cancer diagnosis. For other individuals, sleep-wake disturbance seems to begin at the time of cancer diagnosis. Between 30% -50% of newly diagnosed cancer patients report sleep-wake disturbances (Savard & Morin, 2001; Chen, Yu & Yang, 2008).

Sleep-wake disturbances are influenced by the site of tumor and cancer treatment modalities. Decreased sleep efficiency, insomnia, nocturnal awakening, daytime sleepiness and daytime dysfunction have been reported by patients who have received chemotherapy, radiotherapy and hormonal therapy (Berger, Farr, Kuhn, Fischer, & Agrawal, 2007; Berger et al., 2009; Chen et al., 2008; Lee et al., 2003; Vena et al., 2006). Nocturnal sleep interruption and daytime sleepiness have been recognized as particularly problematic for patients being treated for lung cancer (Chen et al., 2008; Vena et al., 2006).

Unfortunately, sleep-wake disturbances are very difficult to measure as they are subjective in nature (Berger, Sankaranarayanan, & Watanabe-Galloway, 2007; Kvale & Shuster, 2006; Savard & Morin, 2001). This is particularly problematic because cancer patients consistently report that sleep-wake disturbances are one of the most distressing symptoms they

experience (Berger et al., 2007; Berger, 2009; Vena et al., 2006). In the proposed study I will measure sleep-wake disturbance using the Pittsburgh Sleep Quality Index (Buysse et al, 1989). This validated instrument, commonly used with cancer patients, provides a systematic approach to the collection of data about all major sleep-wake disturbances as well as information about the impact of these disturbances on daily life.

Problem Statement

Despite evidence documenting the high frequency and importance of sleep-wake disturbances, they have received very little attention from health care providers, researchers, and the oncology and palliative care community (Berger et al., 2009). Moreover, to date, the meaning of sleep-wake disturbances in advanced cancer patients and the factors associated with them is not well understood (Berger et al., 2009; Vena et al., 2006). Most of the research conducted on sleep-wake disturbances in cancer patients has focused on patients with early-stage disease. Consequently, there is little information about sleep-wake disturbances in patients with advanced cancer.

Purpose

The purpose of the study was to explore sleep-wake disturbances in individuals with advanced lung cancer and to identify factors associated with sleep-wake disturbance in this population.

Objectives

The objectives of this study are:

1. To identify the sleep disturbances reported by individuals with advanced lung cancer

2. To explore the relationships among sleep disturbance, fatigue, and quality of life.

Significance of the Study

This study will assist in understanding factors contributing to sleep-wake disturbances in individuals' with advanced lung cancer. An understanding of these factors could guide the development of interventions for managing sleep-wake disturbances in individuals with advanced lung cancer, thus assisting patients to live well as long as they possibly can. As the majority of patients with advanced lung cancer die of the disease within a year, optimal symptom management and quality of life are important health outcomes.

Research Questions

My research questions are:

1. What sleep disturbances are reported by individuals with advanced lung cancer during the pre-treatment period?

2. What factors influence the relationships among sleep, fatigue, and quality of life in individuals with advanced lung cancer during the pre-treatment period?

Definitions

Advanced Lung Cancer: In non-small cell lung cancer, advanced disease includes cases staged as IIIa, IIIb, and IV with or without nodal involvement. In small cell lung cancer, advanced disease includes cases staged as extensive.

Sleep-wake disturbance: An alteration in nighttime sleeping pattern with an associated impairment in daytime functioning (Berger et al., 2009; Savard & Morin, 2001; Vena et al., 2006).

Electroencephalography (EEG): A measure of electrical activity in the brain during sleep (Lee-Chiong, 2008).

Electromyography (EMG): An electrical measure of skeletal muscle activity during sleep (Lee-Chiong, 2008).

Electrooculography (EOG): An electrical measure of eye movements during sleep (Lee-Chiong, 2008).

Fatigue: A subjective multidimensional response to an illness which includes the physical, emotional, cognitive and behavioural perspectives of the individual, distinguished from the sense of 'tiredness' by its unrelenting, disruptive nature and its ability to foster hopelessness and despair (Olson, 2007).

Quality of Life: A multidimensional construct reflecting an individual's perception of physiological and psychological well-being, life satisfaction and social functioning (Fox & Lyon, 2006; Vena et al., 2006).

Organization of the Dissertation

This paper is organized into six chapters. In the first chapter I have provided some general background information relevant to the study of sleep-wake disturbance in individuals with advanced lung cancer. In Chapter 2, I discuss the literature relevant to my study in more detail. In Chapter 3, I outlined the methods I used to answer my research questions. In Chapter 4, I will present the results of the study. In Chapter 5, I will discuss my research findings in relation to the Two-Process Model of Sleep Regulation. Lastly, I outline the implication of my study for clinical practice, policy, education and research.

CHAPTER 2

REVIEW OF THE LITERATURE

In this chapter I begin with a discussion of sleep and its benefits. This will be followed by a discussion of the impact of sleep deprivation on the health of individuals. Next, I discuss sleep-wake disturbance in relation to cancer and the Two-Process Model of Sleep Regulation. Last, I identify gaps in knowledge related to sleep-wake disturbance in individuals with lung cancer and describe how I have oriented my study to begin addressing some of these gaps.

What is Sleep?

Sleep is a behavioral state of disengagement characterized by significantly reduced responsiveness, immobility and reversibility (Lee-Chiong, Jr, 2008; Roehers, 2001). Sleep is hypothesized as a "fundamental central nervous system phenomenon regulated by interactions between neurotransmitters, immunologically active peptides and hormones" (Dickstein & Moldofsky, 1999, p.220).

Normal Sleep Physiology

Sleep physiology is regulated by three intrinsic processes: sleep homeostasis, circadian rhythm and an ultradian process, the latter occurring within the sleep period and represented by alternating sleep states, non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep (Borbely & Achermann, 1999). Both the homeostatic process (Process S) and the circadian rhythm process (Process C) interact to regulate the timing and the duration of both sleep and wake states. The 'Borbely Two-Process Model of Sleep Regulation' provides a framework for understanding how this complex process takes place (Beersma & Gordijn, 2007; Borbely &

Acherman, 1999; Dijk & Schantz, 2005; Gapstur, Gross & Ness, 2009; Krueger et al., 1999; Taillard, Phillip, Coste, Sagaspe, & Bioulac, , 2003).

The two-process model of sleep regulation posits that the homeostatic component, Process S, acknowledges a 'need for sleep'. This need for sleep depends on prior patterns of wakefulness and sleep. This relationship is intuitive, that is, the longer an individual is awake, the greater the need for the individual to sleep (Gapstur et al., 2009; Taillard et al., 2003). Hence, Process S is the regulated variable in the model and is limited by two thresholds: sleep onset and sleep completion. In other words, when Process S reaches its lower limits during sleep, individuals wake up and when Process S reaches its upper limits individuals fall asleep (Beersma & Gordijn, 2007; Borbely & Acherman, 1999; Collop, Salas, Delayo & Gamaldo., 2008; Schwartz & Roth, 2008).

Process S alters sleep architecture primarily in relation to the intensity of Non-rapid eye movement (NREM) sleep, as shown by Electroencephalography (EEG) slow wave activity. In fact, slow wave activity is a key indicator of sleep homeostasis. For example, slow wave activity predominates in the initial part of sleep when process S is highest and progressively declines as Process S decreases. Moreover, the degree of slow wave activity is directly proportional to prior patterns of wakefulness (Beersma & Gorgijn, 2007; Borbely & Acherman, 1999; Borbely, 1998; Collop et al., 2008).

The circadian process, Process C, is a sinusoidal rhythm that occurs over a period of about 24 hours. Process C provides a wakefulness signal that progressively becomes stronger during the day and dissipates at night. This signal opposes the rising (during daytime) and dissipation (during nighttime) of sleep propensity - Process S. Process C, unlike process S, is not

affected by prior patterns of sleep and wakefulness and fluctuates during daytime and nighttime hours under the direction of a biological oscillator-the suprachiasmatic nucleus (Borbely & Acherman, 1999; Borbely, 1998; Dijk & Schantz, 2005; Kaplow, 2005; Schwartz & Roth, 2008; Taillard et al., 2003).

Most living organisms have developed an endogenous timing system that synchronizes cellular physiology and behavior along an approximate 24-hour time cycle. This timing system is known as the 'circadian' system, the word circadian derived from the Latin words *circa diem*- about a day (Levi & Schibler, 2007). The sleep-wake cycle is the most discernible of human circadian function. The light perceived by visual pathways and the secretion of melatonin, a hormone released by the pineal gland during darkness, regulates the timing of different body functions (Blask, 2009). Numerous physiological and behavioral processes display circadian rhythmcity and are associated with the sleep-wake cycle. For example, core body temperature is lower during nighttime hours while the secretion of melatonin is higher. The initial period of nocturnal sleep is characterized by elevated growth hormones and increased blood glucose concentrations (Dijk & Schantz, 2005; Fuller, Gooley & Saper, 2006; Levi, 2006). Toward the end of the sleep period, increased serum cortisol levels enhance glucose utilization (Laposky, Bass, Kohsaka & Turek, 2008).

Usually, salient features of the sleep-wake cycle of adults include an 8-hour sleep period and a 16-hour wake episode which generally recurs around the same time every day. In healthy adults, the sleep and wake states are highly consolidated. In ill individuals the sleep-wake cycle becomes increasingly fragmented (Dijk & Schantz, 2005; Mystakidou, Parpa & Tsilika., 2009).

Hormones that influence process C.

Melatonin. Melatonin, a hormone produced by the pineal gland, influences Process C. Melatonin production begins approximately 2 hours before an individual's usual bedtime and has been shown to correlates well with the onset of evening sleepiness (Berry, 2012). The amount of melatonin produced during the night appears to be greatest just prior to puberty with a steady decrease thereafter through middle and old age. The fact that melatonin is secreted primarily during nighttime hours and that sleep propensity increases during the night implies melatonin is involved in the physiological regulation of sleep. This hypothesis is also supported by the decrease in melatonin production during middle and old age and the accompanying age-related decline in sleep (Blask, 2009; Pandi-Perumal, Zisapel, Srinivasan & Cardinali, 2005).

Cortisol. Cortisol, a hormone produced by the adrenal glands, also appears to be associated with Process C. Cortisol production increases in the early morning, peaks at mid-morning and declines to its lowest point in the evening. Sleep is associated with a modest decline in cortisol secretions. A few hours prior to waking cortisol levels begin to rise. Awakening at the end of sleep is associated with a surge of cortisol secretion (Berry, 2012; Lee-Chiong, 2008).

Sleep architecture. The 'sleep period' is comprised of stages and cycles which collectively are known as sleep architecture. Stages of sleep are identified by defined parameters through the recording of brain activity (EEG), muscle activity (EMG) and eye-movements (EOG). Sleep is comprised of two distinct states: Non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. NREM sleep is characterized by three stages and with each

successive stage increasing sleep depth is achieved (Collop et al., 2008; Stanley, 2005; Roehrs, 2001; Lee-Chiong, 2008; Walker & Stickgold, 2004).

One sleep cycle is comprised of the three stages of NREM sleep plus a period of REM sleep (Lee-Chiong, 2008). In adults, each sleep cycle lasts approximately 90 to 120 minutes and is repeated 3-5 times per night. During the initial part of the night, NREM stage sleep predominates, whereas, REM sleep is more common during the latter part of sleep. The arousal threshold is lowest during NREM stage 1 sleep and highest during NREM stage 3 sleep (Stanley, 2005; Roehrs, 2001; Lee-Chiong, 2008; Walker & Stickgold, 2004).

At the onset of sleep, individuals enter NREM sleep. NREM Stage 1 is characterized by alpha and theta wave activity and is referred to as light or drowsy sleep. This stage is relatively short as it usually lasts only 5 to 10 minutes. During this stage parasympathetic activity is prominent as respirations become slower and regular, heart rate decreases, and eye movements are slow and rolling (Berry, 2012; Stanley, 2005; Roehrs, 2001; Walker & Stickhold, 2004).

Stage 2 is a deeper stage of sleep and is characterized by very little body movement, the relaxing of muscle tone, and the absence of eye movements. In this stage, EEG recordings depict theta wave activity, sleep spindles and K complexes (Berry, 2012; Dement, 2000; Stanley, 2005). Dement (2000) defines sleep spindles as "short burst of waves with a frequency two or three times that of the background theta waves" and K complexes as "large waves that usually seem to come out of nowhere and disappear (p.20). Approximately, 40 to 50% of an individual's sleep is spent in Stage 2 (Berry, 2012; Stanley, 2005).

Stage 3 is called deep sleep, and is characterized by delta sleep or slow-wave sleep. Stage 3 is dominated by delta wave activity. EEG recordings of stage 3 sleep depict the presence

of theta waves, sleep spindles and K complexes, although, they are now more difficult to observe. This is the deepest stage of sleep. People in stage 3 sleep are difficult to arouse and once awakened are dazed and confused (Berry, 2012; Stanley, 2005; Roehrs, 2001; Walker & Stickgold, 2004).

Stage 3 sleep is postulated to be the most restorative of all the sleep stages. This is because several physiological activities occur during this stage of sleep including: reduction in heart rate, blood pressure, sympathetic nervous system activity, decrease in brain glucose metabolism and an increase in vagal tone (Alvarez & Ayas, 2004; Walker, 2008). Additionally, during Stage 3 sleep the greatest amount of growth hormone is released and the stress hormone cortisol is inhibited (Van Cauter, Spiegel, Tasali & Leproult, 2008).

REM sleep is a state of high brain activity and is characterized by autonomic variability (increases in heart rate, respirations, blood pressure, cerebral blood flow and decreased temperature regulation), loss of muscle tone, dreaming and rapid eye movements. REM sleep is also known as paradoxical sleep because EEG recordings during this stage depict beta wave activity which usually is associated with wakefulness (Carskadon & Dement, 2000; Dement, 2000; Stanley, 2005).

Hirshkowitz (2004) & Stanley (2005) describe five generalizations about normal sleep architecture: Sleep onset occurs by the way of NREM sleep; NREM sleep and REM sleep states alternate approximately every 90 to 120 minutes; Stage 3 NREM (slow wave) sleep predominates in the first third of the night; REM sleep predominates in the last half of the night and 4 to 6 episodes of REM sleep occur each night and lengthen as the sleep period continues.

Benefits of Sleep

Although individuals spend a third of the day sleeping, the reasons why individuals sleep remains a topic surrounded by controversy. In fact, the "quest for a fundamental theory of sleep is considered one of the most important unsolved problems in science" (Savage & West, 2007, p.1460). Nevertheless, most authors acknowledge that sleep is essential for energy conservation, brain function, immune function, hormone production and metabolism (Collop et al., 2008; Roehers, 2001).

Continued development of the central nervous system. Numerous theoretical perspectives have been suggested as to the purpose of sleep. The first of these theories, a development theory, posits that the primary function of sleep, specifically REM sleep, is the continued development of the nervous system. The thesis of this theory is that REM sleep provides for the continued development of neural pathways. Accordingly, this is why infants, in their first few weeks of life, spend at least 80% of their sleep in REM sleep, more than three times the amount of adults. Moreover, this theory is further supported by the fact that across all species more time is spent in REM sleep, early in life, than at any other time in life (Roehers, 2001; Savage & West, 2007).

Memory. There is an increasing amount of evidence that supports a bidirectional and symbiotic relationship between sleep and memory. Two theories explain the role of sleep in memory consolidation. These are the dual process theory and the sequential hypothesis theory. According to the dual process theory, a single sleep stage (i.e. REM sleep) is responsible for declarative (knowing what) and procedural (motor skill) learning. The sequential hypothesis theory posits memories are consolidated through the ordered sequence of multiple sleep stages,

for example, non-REM sleep followed by REM sleep (Siengsukon & Boyd, 2009). To date, most of the studies investigating sleep and memory in humans have focused on declarative (knowing what) learning tasks (Walker & Stickgold, 2004). Yoo, Hu, Gujar, Jolesz & Walker (2007) also demonstrated that sufficient sleep prior to engaging in learning tasks is critical for next-day memory formation. In a study by Nishida & Walker (2007) daytime napping was also associated with an enhanced memory consolidation. Improved memory performance on paired word testing has also been associated with a good night's sleep (Gais & Born, 2004).

Learning. Individuals' ability to learn varies with the time of day. Learning is regulated by prior amounts of wakefulness, prior sleep history and circadian rhythmicity. The circadian timekeeping system interacts with homeostatic and circadian processes providing a pathway upon which learning occurs. Wright, Lowry & LeBourgeois (2012) describe a typical pattern of learning which occurs across a day of wakefulness. Specifically, high levels of cognitive ability are reached between 2 to 4 hours of wakefulness and are maintained across the remainder of the waking day, with the exception of a midday dip or afternoon slump. If wakefulness is extended beyond habitual bedtime, cognitive ability worsens and is impaired in the early morning hours.

Learning has also been shown to affect the structure of sleep. De Koninck, Lorrain, Christ, Proulx & Coulombe (1989), demonstrated through polysomnography that changes to sleep structure occur during learning. Specifically, language learning efficiency is positively correlated with increased REM sleep. It has also been suggested that sleep, after learning, allows for the plastic reorganization of memory within the brain which, in turn, facilitates memory recall the next day (Gais & Born, 2004).

Immune function. Adequate sleep is necessary for physical and mental health. It is acknowledged that sleep has a restorative function on immune processes (Irwin, 2002; Imeri & Opp, 2009). Increasingly, evidence also supports a bidirectional and symbiotic relationship between sleep and immune function. Cytokines, a diverse group of intercellular proteins, are the principal messengers of the immune system and are known to play an important role in the regulation of sleep (Motivala & Irwin, 2007; Kapsimalis, Richardson, Opp, & Kryger, 2005 ; Kapsimalis et al., 2008). Among cytokines, interleukin-1 (IL-1) and tumor necrosis factor (TNF) have been determined to be sleep-promoting substances (Krueger, Obal & Fang, 1999; Opp, 2005). According to Imeri & Opp (2009), IL-1 and TNF display circadian rhythmcity congruent with the sleep-wake cycle thus providing supporting evidence for the involvement of Il-1 and TNF in physiological sleep regulation.

Growth. It is acknowledged the growth hormone (GH) has a sleep-related secretory pattern as high levels of this hormone are found in deep slow wave sleep and in recovery sleep (Krueger et al., 1999; Berry, 2012). The amount of GH released is proportional to slow wave activity (Berry, 2012). Moreover, sleep-associated GH secretion is age and gender-dependent. In males, systemic levels of GH begin to decline when men reach their 30s and virtually disappear above the age of 50. These changes correlate with the decline of slow wave sleep seen in men as they get older. In females, a decrease in sleep-associated GH secretion occurs after menopause (Berry, 2012; Obal & Krueger, 2004).

Tissue repair. There is evidence suggesting that sleep is necessary for cell and tissue repair. Increased cell mitosis and increased protein synthesis have been observed during periods of NREM sleep (Obal & Krueger, 2004; Van Cauter et al., 2008). This is thought to occur because the anterior pituitary gland secretes growth hormones during NREM sleep. Growth

hormones enhance amino acid transport into cells and promote protein synthesis, which, in turn, stimulates the proliferation of granulation tissue in wounds thereby promoting wound healing (Krueger et al., 1999; Van Cauter et al., 2008).

Social and psychological functioning. In addition to physical functioning, sleep is essential for psychological and social functioning. Without sleep, individuals are irritable, anxious, stressed and frequently complain of being mentally exhausted. Sleep's effect on mood is related to brain activity. Dement (2000) states "the biochemistry of wakefulness and sleep is intimately tied in with the state of the emotional part of the brain" (p.110).

Consequences of Sleep Loss

Illness is frequently associated with sleep loss (Laposky et al., 2008; Matthews, 2011). One approach to understanding the functional significance of sleep is to consider the consequences of sleep loss. Numerous studies on animal models have evaluated the consequences of sleep deprivation. These studies have shown that sleep deprivation results in changes in: metabolism, (weight loss despite increased food intake and an increase in metabolic rate); neuron-endocrine abnormalities, (increase in plasma norepinephrine levels and decrease in plasma thyroxine levels); skin lesions; increased heart rate*;* decreased body temperature and with prolonged sleep deprivation, death (Carskadon, 2004; Knutson, Spiegel, Penev & Van Cauter, 2007; Laposky et al., 2008; Lee-Chiong, 2008).

It is well documented that sleep deprivation results in excessive daytime sleepiness, altered neuron-cognitive function; altered hormone production and altered immune function (Knutson et al., 2007; Spiegel, Leproult & Van Cauter, 1999). Short-term sleep deprivation in humans has been associated with adverse endocrine and cardiovascular effects (Troxel et al.,

2012). For example, the risk of a fatal heart attack increases by as much as 45% in individuals who regularly sleep only five hours per night (Imeri & Opp, 2009). Kato, Phillip, Sigurdsson, Krzysztof & Pesek , (2000) reported one night of total sleep deprivation in healthy adults' resulted in a significant increase in their systolic blood pressure readings. Spiegel et al. (1999) reported subjects, exposed to only 4 hours of sleep per night for six nights demonstrated impaired glucose tolerance, increased sympathetic nervous system activity, higher evening plasma cortisol levels and reduced leptin levels (an appetite-suppressing hormone). In a 'sleep debt study' of healthy adults subject to 4 hours of sleep per night, significant impaired glucose tolerance readings occurred during the sleep restriction period (Van Cauter et al., 2008). In another study, the authors found that C-reactive protein, a marker of systemic inflammation and a risk factor for cardiovascular disease, was elevated in healthy adults with sleep deprivation (Knutson et al., 2007).

Chronic sleep deprivation has been linked to the increased prevalence of obesity and diabetes in western countries populations. Studies in children have demonstrated shorter sleep duration is a risk factor for obesity (Liu, Zhang & Li, 2012). These studies found that children less than 10 years of age are at risk for being overweight or obese if they sleep less than 10 hours per night (Sekine et al., 2002; VonKries, Toschke, Wurmser, Sauerwald & Koletzko, , 2002). In a large cohort study of 5493 children, age 7 years, children who slept < 10.5 hours per night were more likely to be obese than those who slept >12 hours per night (Reilly, Armstrong & Dorosty, 2005).

Similar studies have been conducted in adults. A long-term (6 years) prospective study found that short-duration sleepers (defined as 5-6 hours) had a 27% increased risk for obesity as compared to individuals who, on average, sleep 7 to 8 hours (Chaput, Despres, Bouchard &

Tremblay, , 2008). Data extracted from the 'Nurses' Health Study' identified sleep duration of less than 5 and 6 hours in a 24-hour period was a risk factor for obesity (Patel, Malhotra, White, Gottlieb & Hu, 2006). Moreover, in a cross-sectional study of 983 people > 55 years of age, an association between short sleep duration and obesity was found, although age might have been a confounding variable given the changes that occur in older adults' sleep architecture (Van den Berg et al., 2008).

It is well acknowledged that sufficient amounts of nocturnal sleep are necessary for physical and psychosocial well-being (Durmer & Dinges, 2005; Lee, Cho, Miaskowski & Dodd, 2004; Vena et al., 2006). Poor sleep has been linked with increased levels of stress, irritability, anxiety, poor coping skills, impaired psychomotor skills, depression and mental fatigue. Depression, anxiety, poor symptom control and a decline in physical and cognitive functioning are more prevalent in cancer patients who report poor sleep quality (Mystakidou et al., 2009). Poor nocturnal sleep in patients with lung cancer has been associated with poorer perceived quality of life related to physical and mental health (Chen et al., 2008; Le Guen et al., 2007; Vena et al., 2006). Sleep deprivation is also associated with suicidal behaviors. Research on sleep deprivation and psychological well-being has found that sleep deprivation of one night results in impulsive behaviors (Kaplow, 2005; Mercadante, Girelli & Casuccio, 2004; Mystakidou et al., 2009).

The Two-Process Model of Sleep Regulation in Relation to Cancer

Gapstur et al., (2009) & Vena et al., (2004) used the Two-Process model as a framework for understanding how cancer, cancer treatment and related patient responses may affect sleep and wakefulness. In patients with advanced cancer, numerous factors may contribute to sleep-wake disturbance by altering the processes that regulate sleep. Factors that oppose or enhance

the homeostatic and circadian processes can affect the timing, duration and structure of sleep and wakefulness. These factors may be divided into the following categories: 1) demographic, 2) disease-related 3) psychological and 4) treatment factors.

Demographic factors.

Age-related sleep changes. Aging is accompanied by changes to both the endogenous and exogenous circadian control of sleep and wakefulness. A most significant endogenous change is a reduction in the amplitude of circadian sleep-wake rhythms resulting an increase daytime napping and nocturnal awakenings (Cajochen, Munch, Knoblauch, Blatter & Wirz-Justice, 2006). The circadian timing of sleep also changes, resulting in a 'phase advance' of temperature rhythms precipitating wakefulness towards the latter part of the sleep cycle in older individuals (Espiritu, 2008; Hood, Bruck & Kennedy, 2004; Phillips & Ancoli-Israel, 2001). Phase advancement may be related to several mechanisms including a weakening of the circadian pacemaker or entrainment mechanisms such as reduced morning light exposure or diminished retinal sensitivity to photic stimuli. Other endogenous changes include the weakening of homeostatic processes which results in difficulty in maintaining alertness during the day and increased daytime napping. (Ancoli-Israel, Poceta, Stepnowsky, Martin & Gehrman, 1997; Espiritu, 2008; Hood et al., 2004).

As individuals age, the quality of their sleep also deteriorates. Specifically, there is a gradual decline in sleep efficiency as older individuals spend more time in bed but less time sleeping. This is primarily the result of increased early-morning and nocturnal awakenings, some of which can be prolonged. Multiple awakenings are a common occurrence in this

population (Bloom et al., 2009; Collop et al., 2008; Espiritu, 2008; Feinsilver, 2003; Hirshkowitz, 2004; Stanley, 2005).

Aging is also accompanied by changes in sleep architecture. Sleep becomes more fragmented and there are fewer sleep cycles. The amount of time spent in stage 1 and 2 NREM sleep increases as a consequence of the reduced amount of time spent in slow-wave sleep. It is suggested that less time spent in slow-wave sleep is due to the weakening of the homeostatic process. The amount of time spent in REM sleep also declines and REM sleep occurs much earlier in the night's sleep of older individuals. (Bloom et al., 2009; Espiritu, 2008; Feinsilver, 2003; Hirshkowitz, 2004; Munch, Silva, Ronda, Czesler & Duffy,, 2010; Stanley, 2005).

Daytime functioning is a significant measure of sleep changes in older individuals. To date, the best validated measure of daytime functioning is the Multiple Sleep Latency Test (MSLT). This tool measures the propensity of a subject to fall asleep in a controlled setting. In several studies, sleep latency in older individuals, as measured by MSLT, was significantly reduced suggesting older individuals are more somnolent than the general population during daytime hours (Bloom et al., 2009; Feinsilver, 2003).

Although advancing age is responsible for changes in sleep architecture, there is also evidence that suggest co-morbidities, mental illness, pharmacological therapies, environmental, behavioral and psychosocial factors (retirement) contribute to sleep interruptions in older individuals (Ancoli-Israel et al., 1997;Bloom et al., 2009;Espiritu, 2008; Hood et al., 2004).

Overall, predictors of good sleep quality in older individuals include physical and psychosocial health, active participation and recurrent contact with exogenous *zeitgebers* (Espiritu, 2008). Zeitgebers are environmental cues that are capable of adjusting endogenous

circadian activity. Some examples of zeitgebers are physical activities, social interactions, meals and exposure to environmental light (Le-Chiong, 2008).

Sex. Although men have more objective changes in sleep architecture, women report poorer sleep quality (Arber, Bote & Meadows, 2009). Poorer sleep quality in women may be attributed to menopause and associated hormonal changes. Older women, in particular, are more likely to complain of insufficient or non-restorative sleep and daytime sleepiness. Older women also report their sleep is easily disrupted and a greater use of sedative-hypnotic agents. There appears to be an increase in NREM stage 1 sleep during perimenopause and post menopause. In addition to menopause, several factors related to sleep disturbance among older women have been identified in the literature. These include co-existing medical or psychiatric conditions, primary sleep disorders (i.e. obstructive sleep apnea, restless leg syndrome), stress, a decrease in daytime physical activity and caregiver responsibilities (Berry, 2012; Lee-Chiong, 2008; Phillips et al., 2008).

Disease-related factors. Sleep-wake disturbances in patients with cancer can be affected by: type and stage of cancer; other prevailing symptoms (pain, fatigue, nausea, depression, anxiety etc), and treatment-related effects (chemotherapy, radiotherapy, etc.) (Lee et al., 2003; 2004; Mystakidou, et al., 2009 ; Savard & Morin, 2001; Savard et al., 2009). Advanced lung cancer has been associated with a variety of symptoms attributed to the local and metastatic disease process and to the side effects of treatment (Temel, Pirl & Lynch, 2006).

Pain. The majority of patients with cancer experience pain in the course of their illness. In advanced cancer, pain is experienced by 60% to 80% of patients (Davidson, MacLean, Brundage & Schulze, 2002; Esper, 2010; Potter & Higginson, 2004). Lung cancer can cause

pain as a result of tumor burden and the extent of metastatic disease (Mystakidou et al., 2007; Potter & Higginson, 2004; Vena et al., 2006. Several authors have reported an association between pain and sleep-wake disturbance (Hearson & Sawatzky, 2008; Mystakidou et al., 2007; 2009). Moreover, the intensity of the cancer pain experience is inversely related with total sleep time; inadequate pain control is associated with sleep-wake disturbance in cancer patients (Davidson et al., 2002; Mercadante et al., 2004; Potter & Higginson, 2004).

Pain and sleep are often assumed to be reciprocally related, with pain adversely affecting sleep and poor sleep aggravating pain. Although intuitive, available evidence suggests this relationship may be more complex and further research is required (Esper, 2010). According to Tang, Goodchild, Sanborn, Howard & Salkovskis. (2012) the pain-sleep relationship may be mediated by factors not yet well understood. To date, animal and human studies suggest pain produces a persistent arousal state that interferes with sleep homeostatic processes (Lee-Chiong, 2008).

Fatigue. Fatigue is one of the most distressing symptoms experienced by patients with cancer. Fatigue is common symptom in cancer patients, affecting over 75% of patients with advanced cancer (Berger, 2009). Cancer-related fatigue has been defined as "a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (Berger, 2009, p.1). Moreover, fatigue has a negative impact on the performance status and quality of life of cancer patients (Berger, 2009).

The causes of fatigue in advanced cancer are multi-factorial. Several contributing factors have been suggested including pain, emotional distress, poor diet, sleep disturbances, cancer

treatment (i.e., anaemia), side effect of medications and co-morbidities (Berger, 2009; Minton, Strasser, Radbruch & Stone, 2012; Spichger et al., 2012). Previous research has identified possible associations between fatigue and a number of factors such as treatment, mood, pain and dyspnea in cancer patients. To date, the cause of fatigue and its relationship to sleep is not well understood in advanced cancer patients.

Dyspnea. The state of wakefulness and sleep are associated with distinctive patterns of breathing. When individuals are awake breathing is regulated by metabolic and behavioral mechanisms. During sleep breathing is controlled solely by metabolic processes and each stage of sleep is accompanied by varying clinical manifestations. NREM sleep is associated with a regular pattern of respirations, a decrease or no change in respiratory rate and diminished accessory muscle activity. Variable and irregular patterns of respirations and no accessory muscle activity occur during REM sleep. Both stages are characterized by higher arterial blood levels of carbon dioxide and lower arterial blood levels of oxygen (Berry, 2012; Lee-Chiong, 2008).

Dyspnea is defined as an uncomfortable subjective sensation of breathing and results from lower arterial blood levels of oxygen secondary to an airway obstruction, atelectasis, pleural effusion or other pathologies (Lee-Chiong, 2008). Dyspnea is common in advanced cancer, with reported incidence of up to 70%. Patients with advanced cancer often describe dyspnea as a feeling of breathlessness and suffocation. (Reddy, Parsons, Elsayem, Palmer & Bruera, 2009).

To date, we know that dyspnea interferes with sleep however the relationships among, dyspnea, sleep, and the respiratory patterns that normally occur during sleep are not well

understood. Aside from a physiological perspective, the relationships among dyspnea, sleep, and respiratory patters during sleep may be associated with and influenced by psychological factors such emotional distress and anxiety.

Altered hormone secretion. There is some evidence of altered cortisol production in some individuals with cancer. Normally, cortisol levels peak early in the morning and reach their lowest point at the end of the waking day. However, in women with metastatic breast cancer, cortisol levels reach their highest peak at the end of the day and are associated with nocturnal wake episodes (Palesh et al., 2008). Because the secretion of cortisol is associated with Process C, changes in the secretory pattern of this hormone may result in sleep-wake disturbance.

The risk of developing breast cancer is significantly higher in industrialized societies than in underdeveloped countries. Industrialized societies have increasingly become 24-hour a day societies and consequently individuals are being exposed to more artificial light during the night either at home or in the workplace. Exposure to artificial light at night is hypothesized to be a unique risk factor for breast cancer. This hypothesis is based on observations that light-at-night suppresses the nocturnal production of melatonin by the pineal gland which results in an increased production of estrogen and greater breast cancer risk (Blask, 2009). This postulate is further supported by data that suggest women who work at night have an increased risk of developing endometrial and colorectal cancer while men who are exposed to light at night have an increased risk of developing prostate cancer (Hansen, 2006; Kubo et al., 2006; Schernhammer, Kroenke, Laden & Hankinson, 2006).

Psychological. A cancer diagnosis is often accompanied by feelings of fear, stress, anxiety and depression. Anxiety and depression are the most common sources of psychological distress in cancer patients and are associated with changes to sleep architecture which may be caused by abnormalities in sleep homeostasis and circadian processes (Davidson et al., 2002; Hugel, Ellershaw, Cook, Skinner & Irvine, 2004; Vena et al., 2004; Zainal, Hui, Hang, Bustam, 2007). In particular, anxiety can interfere with the homeostatic processes by causing increased physiological arousal resulting in increased sleep latency, increased number of awakenings and decreased slow wave sleep (Thase, 2006; Vena et al., 2004). Mercadante et al., (2004) reports depression is a major cause of poor sleep in cancer patients and is associated with early morning awakening, non-restorative sleep, nightmares and difficulty resuming sleep. Numerous circadian disorders have also been reported in cases of major depression, including elevated nocturnal core body temperatures.

Socio-economic status and availability or lack of social support may also influence sleep disturbance. Koopman et al. (2002) studied sleep-wake disturbances in women with metastatic breast cancer patients in relation to depression and social support. These researchers found depressive symptoms and minimal social support were positively correlated with sleep-wake disturbances. Higher depression scores were associated with reduction in total sleep time, increased nocturnal awakenings, decreased sleep efficiency, problems initiating sleep and increased use of sleeping aids. Social support was identified as a fundamental coping resource, for example, spouse, child, siblings and close friends.

Treatment-related Factors.

Pharmacological agents. Many medications can alter the patterns of sleep and wakefulness (Berry, 2012; Lee-Chiong, 2008). Some agents can cause insomnia and excessive sleepiness while others may induce sleep disorders (i.e. restless leg syndrome) or exacerbate them (obstructive sleep apnea). Antidepressants interfere with sleep and cause daytime sleepiness. Others are sedating and improve sleep. Hypnotic agents, in general, are known to alter the perception of sleep and wakefulness, among other actions. Benzodiazepines reduce sleep latency but are potent suppressors of NREM sleep. REM sleep time is suppressed mildly. Newer non-benzodiazepines have very mild effects on REM sleep and tend not to alter slow wave sleep. Analgesic agents and narcotics have been associated with excessive sleepiness (Lee-Chiong, 2008).

Opioids are frequently prescribed for pain that accompanies advanced cancer. There are a few studies that report opioids, while sedating, actually interrupt sleep. This may occur because many opioids receptors are located in the same nuclei that are also involved in sleep regulation. To date, opioids are known to increase wakefulness, decrease total sleep time, sleep efficiency, slow-wave sleep and REM sleep (Dimsdale, Norman, DeJardin & Wallace, 2007; Wang & Teichtahl, 2007). If these effects are generalized to advanced cancer patients, the potential sleep disruption from opioids use may contribute to the fatigue that is frequently experienced by advanced cancer patients.

Corticosteroids are frequently used in the treatment of patients with advanced cancer. Although little is known about the mechanisms by which corticosteroids exert their therapeutic effects, a growing body of evidence supports their use in particular situations with this

population. For example, corticosteroids are effective as prophylaxis against chemotherapy-induced nausea and vomiting (CINV). Cisplatin is a type of chemotherapy commonly used to treat advanced NSLC. The risk of emesis associated with Cisplatin is greater than 90% (Grunberg, 2004). Corticosteroids, in particular, methyprednisolone and dexamethasone have proven to be effective against CINV in patients treated with Cisplatin. The most common side effect associated with the use of corticosteroids is insomnia most likely attributed to a weakening of the homeostatic process (Grunberg, 2004; Lee-Chiong, 2008).

Treatment modalities. Patients with cancer are subjected to multiple therapy modalities whose aim is either curative or control of disease and concurrent symptoms. These therapies include chemotherapy, radiotherapy, biotherapy and pharmacological agents. Sleep-wake disturbances have been associated with each of these therapies. Lee et al., (2003) reported changes in sleep pattern, in particular, increased nocturnal awakenings in fifty men undergoing nine weeks of radiation therapy. Palesh et al. (2007) also reported a high prevalence of insomnia in cancer patients undergoing chemotherapy. In a study by Savard et al. (2009), sleep disruption was reported by patients after the first cycle of chemotherapy, while repeated treatments were associated with progressively worse and of greater duration sleep-wake disturbances.

Nocturnal sleep interruption and daytime sleepiness have been reported by patients who have received chemotherapy, radiotherapy and hormonal therapy (Beck et al., 2009; Berger et al, 2005; Berger et al., 2009; Fortner, Stepanski, Wang, Kasprowicz & Durrence, 2002; Savard & Morin, 2001). Moreover, Savard et al. (2009) reported breast cancer patients reported progressively worse sleep-wake disturbances with repeated administrations of chemotherapy.

Sleep-Wake Disturbance in adults with cancer. Although the authors of studies about sleep-wake disturbance do not generally analyze their findings along the parameters outlined above, there is some evidence that may explain sleep-wake disturbance in adults with cancer. Sleep disturbances are more common in cancer patients than in the general population. As noted above, patients with cancer are at an increased risk for sleep-wake disturbances (Cheung, Le & Zimmermann, 2009; Le Guen et al., 2007; Vena et al., 2006). To date, several categories of pathophysiological sleep-wake disturbances have been identified in the cancer population (Ancoli-Israel, 2008; Berger, 2009; Davidson et al., 2002; Savard & Morin, 2001). These include: nocturnal awakening, daytime dysfunction, daytime napping, wake after sleep onset, alterations to sleep latency, and decreased sleep efficiency.

Sleep-wake disturbances are frequently reported by cancer patients. Upwards to 70% of cancer patients report some type of sleep-wake disturbance (Berger, 2005; Clark, Cunningham, McMillan, Vena & Parker, 2004; Vena et al., 2004). For example, nocturnal sleep interruption is reported by at least one-third of the cancer population (Clark et al., 2004; Davidson, et al., 2002; Fortner, et al., 2002). Daytime dysfunction and sleepiness is common and insomnia secondary to the cancer diagnosis is also reported by cancer patients (Ancoli-Israel, Moore & Jones, 2001; Davidson et al., 2002).

Sleep-wake disturbances are experienced by patients with many different cancers. Variable prevalence rates have been reported related to site-specific cancers. This variability is attributed to: the variety of approaches used to inquire about the nature of these disturbances; the subjective nature of this phenomenon and the diversity of cancer populations (Berger, 2009; Kvale & Shuster, 2006).

The characteristics of sleep-wake disturbances in patients with cancer are as heterogeneous as the underlying illness (Berger, 2009; Davidson, et al., 2002). In a study by Davidson et al. (2002) high rates of insomnia were reported by breast (37.8%) and lung cancer patients (36.8%). In the same study, lung cancer patients reported high rates of fatigue (56.1%), daytime sleepiness (56.1%) and 'sleeping more than usual' (34.2%). Being fatigued was also reported in other cancer types: breast (48%), GI (38.9%), GU (40%), GYN (46.1%) and Skin (31.7%). 'Sleeping more than usual' was also reported in other cancer types: breast (13.6%), GI (15.7%), GU (15.5%), GYN (20.0%) and Skin (18.7%).

It is important to remember, however, that sleep-wake disturbances may also occur prior to the diagnosis and treatment of cancer. Between 15 % -52% of patients report some type of sleep-wake disturbance prior to their diagnosis of cancer (Davidson et al., 2002; Ginsburg, Quirt, Ginsburg & MacKillop, 1995; Savard , Simard, Blanchet, Ivers & Morin, ., 2001). Others develop a sleep-wake disturbance following a cancer diagnosis. Several authors have found that between 30% -50% of newly diagnosed cancer patients report sleep-wake disturbances (Savard & Morin, 2001; Chen et al.,2008). In a study by Le Guen et al. (2007) 28% of recently diagnosed lung cancer patients reported daytime sleepiness. Fortner et al. (2002) studied breast cancer patients across their disease trajectory. Of the patients studied, 61% reported some type of sleep-wake disturbance.

Sleep-wake disturbances in advanced lung cancer. Sleep-wake disturbances are a common problem for lung cancer patients (Davidson et al., 2002; Le Guen et al., 2007; Vena et al., 2006; Wang, Chang & Lin, 2010). In particular, nocturnal sleep interruption and daytime sleepiness have been identified as being problematic for patients with lung cancer (Davidson et al., 2000. Laposky et al., 2008). . In a study by Degner & Sloan (1995), insomnia was a common

complaint of recently diagnosed lung cancer patients. In a comparative study of advanced lung cancer patients and healthy controls, lung cancer patients had significantly higher global sleep quality scores (poorer sleep) than the healthy control group (Vena et al., 2006). Furthermore, in a study by Silberfarb, Hauri, Oxman & Schnurr (1993), lung cancer patients were found to have longer sleep latencies, decreased sleep efficiency and increased sleep fragmentation as compared to non-cancer populations.

Chen et al (2008) compared the sleep of lung cancer patients receiving chemotherapy and those who were between cycles of chemotherapy. Sleep measures included sleep latency, duration of sleep, sleep efficiency, overall quality of sleep, daytime sleepiness, motivation in performance of tasks and use of hypnotic medications. For each measure, patients receiving chemotherapy reported poorer sleep, prolonged sleep latency, increased daytime sleepiness, decrease motivation and increase use of hypnotic medications.

A comparative study of the sleep of lung cancer and breast cancer patients with age and gender-matched healthy controls revealed lung cancer patients report poorer sleep quality compared to breast cancer patients and healthy control groups. Objective sleep measurements revealed increased sleep fragmentation in the lung cancer group compared to the other groups. Moreover, although lung cancer patients spent more time in bed, their sleep efficiency scores were the lowest of the three groups. Furthermore, in both cancer groups, the amount of time spent in deep sleep was considerably lower, 2% to 4%, compared to 15% to 20%, in healthy controls. This finding may be the reason why high levels of fatigue are reported by lung and breast cancer patients (Silberfarb et al., 1993; Stanley, 2005).

Sleep-wake disturbances in advanced lung cancer in relation to the two-process model of sleep regulation

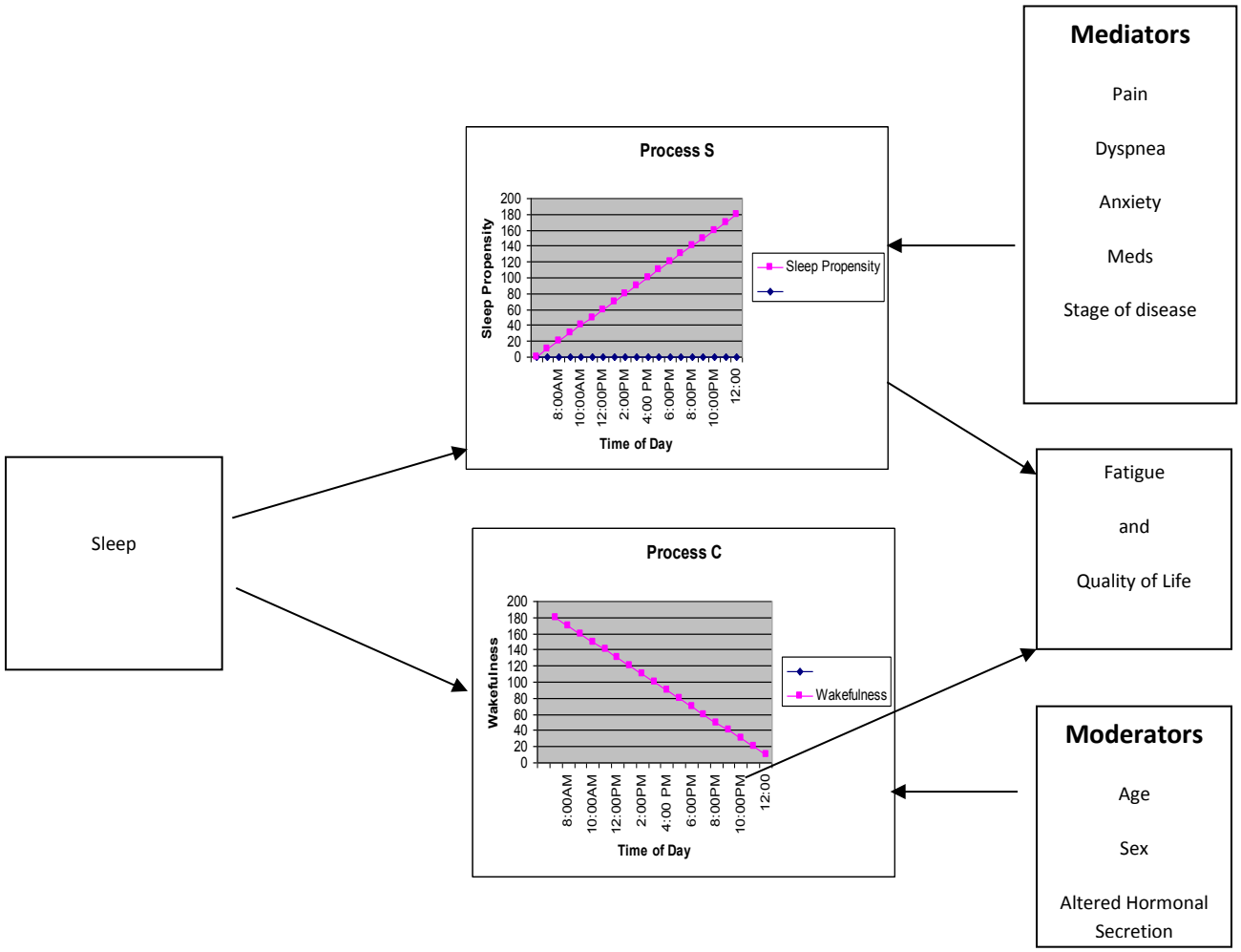
Although studies to date have not focused on the specific factors associated with sleep-wake disturbance in individuals with lung cancer, I have drawn some hypotheses from the perspective of the Two-Process Model of Sleep Regulation, about why this disturbance may exist (See Figure 1). I think the homeostatic process (Process S) is influenced by factors such as poor control of pain, anxiety, and dyspnea and lack of social support and this may have a significant impact on this process because these factors influence the two key thresholds in Process S–sleep onset and sleep completion. I think the circadian process (Process C), on the other hand, is likely to be more influenced by factors such as age, sex, altered hormonal secretion. Last, I think there is some evidence above to suggest that treatment modalities, and medications associated with symptom management could influence both the homeostatic and circadian processes.

Testing these hypotheses is complex because in addition to the influence of each factor within the two- stage model of sleep, one must also consider whether the factor is a mediator or a moderator of the proposed relationship. I understand moderating variables to be those that change the strength of the relationship between an independent and dependent variable and mediating variables to be those that explain why the causal relationship exists (Baron & Kenny, 1986). Based on this understanding I think that age and sex moderate the effect of sleep on fatigue and quality of life by acting on Process S, and that social support, symptoms and their related medications, and treatment modalities are mediators of the relationships among sleep, fatigue, and quality of life and act primarily on Process C. The design of my study was limited by the size of the population to which I have access and is intended as the first in a series of projects; remaining projects will be part of my research program following graduation. For this

reason, I limited my study variables to a subset of those listed above. The information obtained from this study will assist in developing interventions aimed at addressing sleep-wake disturbances in individuals with advanced lung cancer.

Conceptual Framework of Study

Figure 1



My conceptual framework is shown in Figure 1. In this study I examined relationships among some of the key variables in individuals diagnosed with advanced lung cancer who are

awaiting treatment. By choosing a homogeneous population, I was able to exert some control over effects associated with type of cancer and stage. Additional advantages were related to studying the pre-treatment time period. For example, I did not have to accommodate symptoms and other effects associated with treatment. Also, while the moderator variables are not modifiable, I hope my study will help to identify possible targets for interventions related to the proposed mediator variables that could eventually be implemented during the pre-treatment period, thus reducing sleep disturbance and increasing the ability of patients to adapt to the challenges associated with treatment.

CHAPTER 3

METHODS

The purpose of this study was two-fold: First, to identify the sleep disturbances reported by individuals with advanced lung cancer during the pre-treatment period. Secondly, to understand the relationship amongst sleep disturbances, fatigue and quality of life in advanced lung cancer patients during the pre-treatment period? In this chapter I will discuss the research questions for the study, study setting, design, study sample, data collection, instruments, data analysis procedures and ethical considerations.

Research Questions

1. What sleep disturbances were reported by individuals with advanced lung cancer during the pre-treatment period?
2. What factors influence the relationships among sleep, fatigue, and quality of life in individuals with advanced lung cancer during the pre-treatment period?

Study Design

A cohort study design was used in this study.

Setting

The setting for the study was the Cape Breton Cancer Centre, one of two cancer treatment centers in the province of Nova Scotia. The Cape Breton Cancer Centre offers a full range of services to patients living in Nova Scotia. This clinic treats a large population of oncology patients, including 100 individuals with lung cancer per year (Nova Scotia Cancer Care Registry, 2012).

Sample

Sample selection. Non-probability convenience sampling was used to recruit study participants. All individuals who attended a clinic for individuals with newly diagnosed lung cancer between 01/06/ 2013 to 30/06/2014 were invited to participate. Participants were recruited during regular appointments to the Cape Breton Cancer Centre. Based on information provided by the Nova Scotia Cancer Registry, we expected to recruit a cohort of approximately 75 individuals and roughly equal numbers of men and women. A sample of this size meets basic estimates as discussed by Cohen (1988) for multiple regression with six predictor variables.

Inclusion criteria. Adults, 18 years and above, of all ethnic backgrounds who met the following criteria were asked to participate in the study.

1. Primary diagnosis of Stage IIIA, IIIB or IV, non-small cell lung cancer.
2. Capable of reading and writing English as evidenced by the ability to read the consent form.
3. Planning to receive treatment through the Cape Breton Cancer Centre.

Exclusion criteria. Individuals with a diagnosed cognitive impairment that was documented in his or her medical record and that was sufficiently disabling that in the opinion of the attending physician would interfere with the ability of the person to complete the study questionnaires were excluded from the study.

Study Variables

A central aspect of this study was the operationalization of variables related to sleep-wake disturbances that could be incorporated into the Two-Process Model of sleep. The variables initially included in this study were based on existing research on sleep in cancer

patients. An increased number of variables would be required to fully test my model, but I have limited the number of variables due to the small population to which I had access. I selected fatigue, sleep-wake disturbance and quality of life as the predictor variables for the study. Proposed moderator variables were age and sex and proposed mediator variables included pain, dyspnea, anxiety, and medication. Table 1 shows the variables for the study and the source or instrument that I used to obtain the data. Following Table 1, I will provide psychometric information about the instruments I used in this study.

Table 1

Study variables

Suggested Variable	Description	Data Source/Instrument
Moderators	Age, gender	Demographic Sheet
Mediators	Pain, dyspnea, anxiety	Edmonton Symptom Assessment Scale (ESAS-r)
	Medication	Medical Chart
	Stage of Disease	
Outcome Variable	Sleep Quality	Pittsburgh Sleep Quality Index (PSQI)
Outcome Variable	Fatigue	Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-F)
Outcome Variable	Quality of Life	McGill Quality of Life Questionnaire (MQOL)

Data collection

Instruments including psychometric information and scoring. The instruments used in this study were the Edmonton Symptom Assessment System (ESAS-r), Pittsburgh Sleep Quality Index (PSQI), Functional Assessment in Chronic Illness Therapy Fatigue subscale (FACIT-F) and the McGill Quality of Life Questionnaire (MQOL). A description of each of these instruments follows and copies of these instruments are included in Appendix A.

The Edmonton Symptom Assessment System (ESAS-r)

The Edmonton Symptom Assessment System (ESAS) is a brief, practical clinical tool for self-reporting of symptom intensity at the time of completing the form. It includes nine common symptoms of advanced cancer (pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath). Each symptom is rated from 0 to 10 on a numerical scale, 0 meaning that the symptom is not present and 10 that it is of the worst possible severity (Nekolaichuk, Watanabe & Beaumont, & Mawani, 2009; Regional Palliative Care Program in Edmonton Alberta; Richardson & Jones, 2009).

The ESAS is a useful tool as it provides a clinical profile of symptom intensity of advanced cancer patients. The ESAS is easy to understand and patients can complete it in 5 minutes or less. Ideally, the ESAS should be completed by the patients themselves; however, if patients cannot independently do the ESAS, it can be completed with the assistance of a caregiver (family member or health professional) (Nekolaichuk et al., 2009; Regional Palliative Care Program in Edmonton Alberta).

The ESAS was first introduced in clinical practice in 1991 and has been adopted nationally and internationally for clinical, administrative and research purposes. Despite its overwhelming acceptance, concerns have been raised about its utility and feasibility in clinical practice. Specifically, a recent survey of palliative care nurses identified concerns about the potential for patients to misunderstand the tool when reporting symptom intensity (Nekolaichuk et al., 2009).

To date, two systematic reviews have been conducted on the reliability and validity of the ESAS. In the thirteen studies selected for an in-depth review by Nekolaichuk, et al. (2009), it

was noted numerous approaches were used to obtain reliability estimates and most of the reliability evidence focused on test-retest reliability measures. This led the authors to conclude the test-retest reliability estimates reported were neither accurate nor appropriate given the variable time period between assessments and the dynamic nature of the symptom experience of advanced cancer patients.

In terms of validity evidence, Nekolaichuk et al. (2009) reported most studies focused on gathering concurrent validity evidence. In some studies, the overall symptom distress score for the ESAS was used to compare with other global measures, for example, quality of life. In other studies, specific scales of the ESAS, for example, depression or anxiety, were compared with similar scales of another instrument. Moreover, there was very little evidence that addressed the format of the ESAS as evident by the following questions left unanswered: Do the nine scales of the ESAS function independently of one another; are patients' responses influenced by possible inter-scale relationships and to what extent does the total symptom distress score capture symptom burden?

Richardson & Jones (2009) reviewed thirty-nine studies published between 1991 and 2007, thirty-three of which were conducted predominantly in the context of cancer. Their review was itemized according to nine domains: population, characteristics, face and content validity, theoretical validity, scores distributions, reliability, structure, convergent and divergent validity, expected statistical associations and responsiveness. With respect to face and content validity, Richardson & Jones concluded too many versions of the ESAS were being used rendering comparative data across studies unreliable and invalid. In terms of reliability evidence, chronbach alpha scores ranged from 0.79 to 0.93. Furthermore, ESAS symptom scales correlated well with concurrent instruments, particularly for physical symptoms, but lower for

psychological symptoms. Specifically, moderate-to-good correlations for nausea (0.88), shortness of breath (0.84) and pain (0.80). Reliability by test-retest with the ESAS within one day is high, >.8. However, repeated measures of more than one day apart yield contradictory results thus suggesting lower reliability or a responsiveness to change.

The ESAS was recently revised to make it easier for patients to understand. All of the symptoms included in the ESAS are also included in the ESAS-r. This revised version, the ESAS-r was used in this study.

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index is a self-report questionnaire that requires participants to assess the quality of their sleep over the previous month. Nineteen questions evaluate sleep from the perspective of the following seven components: sleep quality; sleep latency; sleep duration; habitual sleep efficiency; sleep disturbances; use of sleeping medication and daytime dysfunction. Scores from each of these components, which can range from 0 to 3, are tallied to yield a global PSQI score. This global or total sleep score can range from 0 to 21 where higher scores signify poor sleep quality. A global sleep quality of 5 or more indicates moderate to severe sleep problems, in at least three sleep components or severe sleep problems in two components.

The PSQI was first implemented in clinical research in 1989 and since that time it has acquired widespread acceptance as a relevant, practical tool in measuring sleep quality in diverse populations (Buysse, 1989). The PSQI is easy to understand and can be completed in 5 to 10 minutes. It is self-administered and includes open-ended questions, semantic scales (paired words of opposite meanings) and questions which focus on event frequency. Sample questions

(Buysse, 1989) include "Over the past month, when have you usually gone to bed at night?", and "During the past month, how would you rate your sleep quality?"

This tool has demonstrated reliability and construct validity in studies of various populations. Carpenter & Andrykowski (1998) examined the psychometric properties of the PSQI in four populations: bone marrow transplant patients, renal transplant patients, women with breast cancer and women with benign health problems. To determine the reliability of the PSQI, Carpenter & Andrykowski (1998) calculated Cronbach α coefficients for the global PSQI score and for the sleep disturbance component score. Cronbach α score for the global PSQI score were consistent across all patient groups at 0.80 and for the sleep disturbance component score ranged from 0.70 to 0.78.

Pearson correlation coefficient scores were also calculated between PSQI and the seven component areas to determine convergent and discriminant validity, two aspects of construct validity. Carpenter & Andrykowski (1998) determined PSQI global scores correlated with single or multiple sleep component determinants of sleep quality or sleep disturbance (convergent validity) and poorly correlated with unrelated constructs (discriminant validity).

Beck, Schwartz, Towsley, Dudley & Barsevick (2004) evaluated the psychometric properties of the PSQI in a heterogeneous sample of cancer patients and determined was a reliable measurement as evident by a Cronbach α of 0.80. The findings from this study also supported the construct validity of the PSQI.

Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F)

The Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F) is a commonly used instrument that measures cancer-related fatigue over a seven day period. The

FACIT-F is a subscale of the Functional Assessment of Cancer Therapy Measurement System. It consists of 13 items each of which is measured by a five point rating scale (0= not at all to 4= very much). The FACIT-F scale evaluates fatigue as a multidimensional experience according to four domains: physical, family/social, emotional and functional well-being. The total score for the FACIT-F subscale can range from 0 to 52 with higher scores indicating less fatigue (Lai, Cella, Chang, Bode & Heinermann, 2003; Reddy, Bruera, Pace, Zhang & Reyes-Gibby, 2007).

In several studies, the FACIT-F scale has been validated as an appropriate measurement of symptom intensity of cancer patients. The FACIT-F scale has also demonstrated excellent internal consistency (Cronbach α =0.93) and test-retest reliability (r=0.90) over a time period of 3 to 7 days (Lai et al., 2003).

McGill Quality of Life Questionnaire (MQOL)

The McGill Quality of Life Questionnaire (MQOL) is a self-reporting questionnaire specifically developed to measure the quality of life of patients with a life-threatening illness. This tool measures quality of life with respect to four domains: physical well-being, psychological well-being, existential well-being and support. The MQOL consists of 16 items each assessed on a scale of 0 to 10 and global quality of life is measured on a single-item scale. In addition to the overall score for the questionnaire, each of the domains evaluated is given a score derived from its corresponding subscales (Cohen, Mount, Strobel, & Bui, 1995; Henry, Huang, Ferland, Mitchell & Cohen, 2008). The MQOL was first introduced into clinical practice in 1995. Since that time it has been widely adopted by the oncology and palliative care community. To date, an analysis of the psychometric properties of the questionnaire have determined the reliability (internal consistency) of the 16 item questionnaire and each of its

subscales is acceptable as demonstrated by calculated Cronbach $\alpha = 0.83$ for the questionnaire; $\alpha = 0.62$ for physical symptoms subscale; psychological symptoms subscale $\alpha = 0.81$; existential well-being $\alpha = 0.79$ and support $\alpha = 0.74$ (Cohen et al., 1997).

Bentur & Resnizky (2005) measured the reliability of the MQOL by calculating Cronbach α values for each of the sub-scores and reported an acceptable internal consistency with a Cronbach $\alpha > 0.65$, except for the physical domain which had a Cronbach $\alpha = 0.57$. Spearman correlation coefficient was also calculated to determine the degree to which a theoretical construct of the questionnaire (i.e. physical symptom subscale) was measured by the total quality of life score. All MQOL sub-scale scores were statistically significantly correlated with the overall quality of life score.

In addition, information was collected from participants' medical chart including demographics, medical history, social history, social support and any medications being taken at the time of the study that could alter sleep. To include this information in my analyses dichotomous variables were constructed for categorical variables.

Data Collection Procedures

Patient recruitment. All patients with newly diagnosed advanced NSC lung cancer attending outpatient clinics for advanced lung cancer at the Cape Breton Cancer Centre were approached regarding participation in the study using a study recruitment form (Appendix B). This form was placed on the patients' chart and was given to them by the unit clerk when they reported for their appointment. Those interested in hearing more about the study were asked to sign the form and return it to the unit clerk. These forms were collected by the principal investigator who then contacted those interested in hearing more about the study, reviewed the

study information letter and consent (Appendix C) and obtained written consent from those who agree to take part.

Data Analysis

All data were analyzed using SPSS 21. Alpha was set at 0.05. Prior to any analyses, descriptive statistics (mean, median, standard deviation) on all variables were computed to describe the characteristics of the sample and the study variables. Graphs including histogram, scatter-plots and normal probability plots were constructed to explain the central tendencies of the data, variability of the variables and to observe for the presence of outliers and missing data. The level of measurement of the predictor variable, moderator, mediator and outcome variables influenced the analytic procedures I used. Correlations amongst all study variables were examined using Spearman's rho as the data for all variables were not normally distributed. Multiple regression analysis was used to examine the association between the predictor variables and the dependent variable. Study variables that were significantly correlated with the outcome variables were included in the regression equation.

Ethical Issues

Protection of human subjects. Prior to the initiation of data collection, approval for the study was obtained from the University of Alberta Institutional Review Board and the Research and Ethics Committee of the Cape Breton District Health Authority.

Informed consent was obtained prior to the enrollment of study participants. To ensure participation in the study was both informed and voluntary, the principal investigator (PI) thoroughly explained the purpose of the study, the data collection procedures, the time commitment required, risk and benefits, the reason why this study was being conducted and

potential information use that may be obtained from the study. Potential participants were informed they may withdraw from the study at any time and should they decide to do so the treatment of their cancer will not be compromised. Potential participants were also informed their cancer care will not be affected should they refuse to participate in the study.

Anonymity and confidentiality. To ensure the anonymity of study participants, each individual was assigned a unique code number. This unique code number appeared on all data collection forms (Appendix D) as no names appeared on these forms. A list of study participants together with their unique code number is kept in a locked drawer in the office of the principal investigator at Cape Breton University. All other data collection forms and consent forms are also contained in a separate locked drawer in the principal investigator's office.

Other considerations. Patients with advanced lung cancer are considered a vulnerable population. Flexibility and sensitivity to the issues confronting these patients was of paramount importance. The design and implementation of the study was sensitive to the burden of illness these patients. The time and place for data collection was discussed with each participant in an effort to minimize the effort required on their part for this study.

CHAPTER 4

RESULTS

In the following chapter, I will discuss the sleep-wake disturbances of NSC advanced lung cancer patients that I have identified in this study. Second, I will discuss the factors that influenced the relationship among sleep, fatigue and quality in life in individuals with NSC advanced lung cancer during the pre-treatment period. The research questions in this study were:

1. What sleep disturbances were reported by individuals with advanced lung cancer during the pre-treatment period?
2. What factors influence the relationships among sleep, fatigue, and quality of life in individuals with advanced lung cancer during the pre-treatment period?

Prior to answering these research questions, descriptive statistics including mean, median and standard deviations will be presented to characterize the study sample with respect to demographic, clinical, physical, psychosocial and quality of life variables.

Description of the Study Participants

Study invitations were extended to 97 individuals. Seventeen declined participation, two did not meet inclusion criteria, and six were deemed ineligible following recruitment, leaving 72 study participants. Data were collected prior to the start of treatment. In addition to data pertaining to the moderator variables (age, sex), mediator variables (pain, dyspnea, anxiety, medication, and stage of disease) and outcome variables (sleep quality, fatigue, and quality of life), history of co-morbidities was obtained to describe the sample.

The sample consisted of 40 males (55.6%) and 32 females (44.4%). Participants ranged in age from 52-90 years, with a mean age of 70.9 years. The majority of the sample was married (48.6%) and of the remaining, 9.7% were single, 13.9 % were divorced or separated and 27.8 %

were widowed. All participants had advanced non-small cell lung cancer, Stage IIIA, IIIB or IV. Approximately 50 participants (69.4%) had Stage IV lung cancer, 16 participants (22.2%) had Stage IIIB cancer and 6 participants (8.4%) had Stage IIIA cancer. At least 40% of participants reported an unintentional weight loss of at least 10% body weight in the six months prior to their diagnosis. A vast majority of study participants had co-existing co-morbidities including Chronic Obstructive Lung Disease (41.7%), Ischemic Heart Disease (15.3%), Diabetes (20.8%), Hypertension (55.6%) and Arthritis (16.7%). The mean number of co-morbid conditions per participants was 1.70 (SD= .429, median= 1.8 and range= 1). The demographic and clinical profile of the study participants are presented in Table 2.

Table 2

Demographic and Clinical Characteristics of Participants

Characteristics	N	%
Age (years)		
Mean = 70.9		
Median = 71.5		
SD = 8.57		
Range = 38		
Sex		
Male	40	55.6
Female	32	44.4
Marital Status		
Married	35	48.6
Single	7	9.7
Separated/Divorced	10	13.9
Widowed	20	27.8
Co-Morbid Conditions		
Chronic Obstructive Lung Disease	30	41.7
Diabetes	15	20.8
Arthritis	12	16.7
Ischemic Heart Disease	11	15.3
Hypertension	40	55.6
Median (per participant) = 1.7		

Descriptive statistics for proposed mediators

Pain, dyspnea and anxiety. The proposed symptom mediators were pain, dyspnea and anxiety. The ESAS-r is a validated assessment tool that includes these symptoms as well as tiredness, drowsiness, nausea, lack of appetite, depression, dyspnea (shortness of breath) and well-being. Participants were instructed to rate the severity of each symptom according to how he or she felt at the time of completing the form. An optional 'other symptom' could also be reported by participants.

The ESAS-r has a scoring range of 0 (absence of symptom) – 10 (worst possible severity). Each numerical scale was interpreted independently from each other. Previous studies have categorized the severity of ESAS scores as none (0), mild (1-3), moderate (4-6) and severe (7-10) and scores ≥ 4 as clinically significant (Dudgeon, 2009; Gill, Daines & Selby, 2010). In this study, shortness of breath, tiredness and anxiety were rated as the most severe symptom with median scores of 8.00, 8.00 and 7.00, respectively. This was followed by median values for appetite (5.00), pain (5.00), and depression (4.50). These results are presented in Table 3.

Table 3

The Edmonton Symptom Assessment System (revised)

ESAS-r	Mean	Median	SD
Pain	4.54	5.00	3.36
Tiredness	6.93	8.00	2.62
Nausea	.833	0.00	1.64
Depression	4.42	4.50	2.93
Anxiety	5.84	7.00	2.83
Shortness of Breath	7.04	8.00	2.93
Drowsiness	2.01	0.00	2.78
Appetite	5.13	5.00	3.04
Well-being	6.78	7.00	2.04

In their review of thirty-nine studies published between 1991 and 2007, Richard & Jones (2009) determined that the ESAS-r is a reliable measure of the symptom burden of patients with advanced cancer and has good internal consistency with Cronbach's alpha scores between 0.79 to 0.93. In this study, the overall Cronbach alpha was .784. This demonstrates the ESAS-r was a reliable measure of the symptom severity in study participants.

The median scores of the proposed mediators pain, dyspnea and anxiety were noted to be 5.0, 8.0 and 7.0 respectively. These findings indicate participants in this study were experiencing moderate to severe amounts of pain and anxiety and high levels of dyspnea. Participants also reported poor appetites, feeling depressed and feeling tired.

Medications. The majority of participants used medications on a regular basis. Medications were listed and categorized by class. Medications with sleep-altering properties were considered valid for review. Dichotomous variables for each category were constructed

and summary measures of frequency of use were calculated. Approximately 29.2 % of participants reported using benzodiazepines, 23.6%, anti-depressants and 23.6% beta-blockers. Hypnotics and both opioids and corticosteroids were used by 16.7% and 11.1% of participants, respectively. The median value of medications per participant was 1.7. This information is presented in Table 4.

Table 4

Medication Profile of Participants

Medications	N	% use
Benzodiazepines	21	29.2
Hypnotics	12	16.7
Anti-depressants	17	23.6
Beta-Blockers	17	23.6
Opioids	8	11.1
Corticosteroids	8	11.1

Stage of disease. All participants in this study had advanced non-small cell lung cancer, Stage IIIA, IIIB or IV. Approximately 50 participants (69.4%) had Stage IV lung cancer, 16 participants (22.2%) had Stage IIIB cancer and 6 participants (8.4%) had Stage IIIA cancer. This information is presented in Table 5.

Table 5

Stage of Disease of Participants

Stage of Disease	N	% by Stage
Stage IIIA	6	8.4
Stage IIIB	16	22.2
Stage IV	50	69.4

Descriptive statistics for outcome variables

The Pittsburgh sleep quality index (PSQI). Participants were asked to report their sleep habits for the majority of days and nights of the previous month. If applicable, a roommate or bed partner was asked to complete a section of the questionnaire. There were 19 individual questions on the PSQI. The scores from each of these questions were transformed into seven component scores, each ranging from 0 to 3, with higher scores indicative of poor sleep quality. The sum of these seven components yielded a Global Sleep Quality score with a possible range of 0 to 21. A PSQI global sleep quality score of 5 or higher indicates significance sleep disturbance.

Participants reported poor sleep quality as evident by a mean PSQI Global score of 13.4, which is greater than 5, the cutoff point associated with poor sleep quality. Aside from self-reported sleep quality, a median score of 2 (range 0-3) was obtained for all component scores. This implies that poor sleep quality is multi-factorial in origin. PSQI results revealed that 57 (79.2%) of participants reported sleep latency of 30 minutes or longer; sleep duration of less than 6 hours in 42 (58.4%) of participants and sleep efficiency of less than 85% in 62 (86.1%) of

participants. All participants had global PSQI scores greater than 5. Table 6 presents PSQI global sleep quality and component scores.

Research Question 1: What sleep disturbances were reported by individuals with advance lung cancer during the pre-treatment period?

Difficulty initiating sleep was reported by the majority (79.2%) of participants in this study. More time spent awake in bed than sleeping was also reported. A moderate degree of daytime dysfunction was experienced by participants (72%). Participants (51.4%) also reported trouble staying awake during the day. Participants reported their sleep at night was frequently interrupted. Nocturnal sleep interruption was related to difficulty breathing (80.6%), cough (83.3%), nocturia (97.2%), pain (75%), feeling too cold (18.1%), feeling too hot (27.8%), anxiety (51.3%) and depression (36.7%).

Table 6

The Pittsburgh Sleep Quality Index (PSQI)

PSQI	N	%
Sleep Latency > 30 minutes	57	79.2
Sleep Duration < 6 hours	42	58.4
Sleep Efficiency < 85%	62	86.1
Trouble staying awake during day	37	51.4
Sleep Disturbance	62	86.1
Daytime Dysfunction	54	72
Use of sleep medications	35	48.6

In other studies, the PSQI has proven reliability with Cronbach alpha of 0.80 (Carpenter & Andrykowski, 1999). In this study, the Cronbach alpha was .745 indicating the PSQI was a reliable measure of sleep quality.

Fatigue

The functional assessment of chronic illness therapy fatigue scale. (Facit-F). Prior to the analysis of the FACIT-F scores, each negatively-worded item response was recoded so that higher scores represented less fatigue and lower scores represented more fatigue. Scores range from 0-4 and the range of possible scores is 0-52. The total score was obtained by summing individual scores. A score of less than 30 indicated severe fatigue. The median value for the total FACIT-F score was 15 indicating participants were severely fatigued. In the study, 58 (80.6%) participants reported severe fatigue.

Participants reported difficulties initiating and finishing activities and indicated they required assistance with activities of daily living. Despite reports of severe fatigue and little energy, 29 (40.6%) participants reported they did not need to sleep during the day. Limiting social activities was also noted for the majority of participants given 77.8% of participants indicated the need to do so. This information is presented in Table 7.

Table 7

The Functional Assessment of Chronic Illness Therapy Fatigue Scale

FACIT-F	N	%
I feel fatigued	58	80.6
I feel weak all over	40	55.6
I feel listless (“washed out”)	51	70.8
I feel tired	52	86.1
I have trouble starting things because I am tired	59	81.9
I have trouble finishing things because I am tired	59	81.9
I have energy	6	8.4
I am able to do my usual activities	6	8.3
I need to sleep during the day	29	40.6
I am too tired to eat	29	40.3
I need help doing my usual activities	56	77.8
I am frustrated by being too tired to do the things I want to do	61	84.7
I have to limit my social activity because I am tired	62	86.1

According to Lai et al. (2003), the FACIT-F is a reliable measure of fatigue and has good internal consistency, with a Cronbach alpha of 0.93. In this study, the Cronbach alpha was .944. This demonstrates the FACIT-F scale was a reliable measure of fatigue.

Quality of Life

McGill quality of life questionnaire (MQOL). Participants were asked to rate their quality of life (QOL) for 'the past 2 days' with respect to five sub-scales of the MQOL: physical symptoms (items 1-3), physical well-being (item 4), psychological well-being (items 5-8), existential well-being (items 9-14) and perceived support (items 15-16). There is also a single-rating scale (SIS) to measure the overall QOL. All MQOL items sub-scale scores and total score had a possible range of 0 to 10. Prior to calculating MQOL scores for data analysis, scores were transposed for items 1, 2, 3, 5, 6, 7, and 8 so that 0 would indicate the worse score and 10, the best score. The single-rating (SIS) scale is not included in the total score and its raw scores are not transposed. In this study, participants, on average, reported a SIS score of 3.14. The MQOL total score is the mean of the five sub-scales scores. In this study, the mean value of the total MQOL was 6.03. This information is presented in Table 8.

Table 8

McGill Quality of Life (MQOL)

MQOL	Mean	Median	Standard Deviation
Physical Symptoms (Items 1-3)	5.48	5.3	2.02
Physical Well-Being (Item 4)	3.83	4.00	2.16
Psychological (Items 5-8)	5.08	4.5	2.46
Existential (Items 9-14)	6.52	6.3	1.58
Support (Items 15,16)	8.80	9.00	1.29
Quality of Life (SIS)	3.83	4.00	2.16
MQOL	6.03	5.93	1.31

According to Cohen et al. (1997), the MQOL is a reliable tool for assessing the quality of life of individuals with a terminal disease (Chronbach's alpha of 0.745 - 0.83). In this study the Chronbach's alpha computed was 0. 63, which is slightly lower than reported by Cohen, however, it is still acceptable by conventional standards.

Bivariate correlations among predictor variables (age, sex, pain, dyspnea, anxiety, medications, and stage of disease) and outcome variables (sleep quality, fatigue, and quality of life

In preparation for the regression equations needed to answer the second research question, I examined the correlations between each of the predictor variables with each of the outcome variables. The sample size for all correlations was 72 cases, unless otherwise stated. All correlations were conducted using Spearman's rho as the data were not normally distributed. The correlations among all predictors and outcome variables are presented in Table 9 and explained in the following paragraphs.

Table 9

Correlations between Moderators, Mediators, ESAS Subcales and Outcome Variables.

Age	Sex	Pain	Dyspnea	Anxiety	Medication	Stage of Disease	Tiredness	Drowsy	Nausea	Appetite
r= .246*	r=.164	r =.373**	r=.309**	r=.406**	Hypnotics r=.166 Antidepressants r=.101 Opioids r= .142 Benzodiazepine r= .096 Beta Blockers r=.-.018 Corticosteroids r= -.061	r=.126	r=.339**	r=.291*	r=.049	r= .345**
r=-.034	r=.124	r=.330**	r=-.484**	r=-.425*	Hypnotics r=-.064 Antidepressants r=-.048 Opioids r=.065 Benzodiazepine r=-.119 Beta Blocker r=-.169 Corticosteroid r=.034	r=.272*	r=-.718**	r=-.555**	r=-.213	r=-.620**
r=.431**	r=.091	r=-.294*	r= -.257*	r=.388**	Hypnotics r=-.043 Antidepressants r=-.208 Opioids r=-.165 Benzodiazepine r=.018 Beta Blocker r=.026 Corticosteroids r=.179	r=.288*	r=-.251*	r=-.136	r=.284*	r=-.257*

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

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

Correlations with sleep quality.

Age. Bivariate correlation analysis was performed to study the relationship between age and sleep quality. The results of this analysis revealed there was a significant, positive correlation between the two variables (r=.246, p=.037), with increasing age associated with poorer sleep quality.

Sex. The relationship between sex and sleep quality was also investigated. The correlation between the two variables was non-significant (r=.164, p=.169), indicating the sleep quality reported in this study was not significantly associated with the sex of study participants.

ESAS and Sleep Quality. Bivariate correlation analyses were conducted to study the relationship between each symptom of the ESAS and sleep quality. There were significant, positive correlations between the three proposed mediator variables (pain r=.373, p=.001; dyspnea r=.309, p=.008; anxiety r=.406, p >.001) and sleep quality.

The relationship between the remaining symptoms of the ESAS and sleep quality were also explored. Aside from the subscale 'nausea', there were strong positive correlations between each of the remaining symptoms of the ESAS and sleep quality. Specifically, tiredness (r=.339, p=.004), drowsiness (r=.291, p=.013), appetite (r=.345, p=.003) and depression (r=.282, p=.017).

Medications. The relationships between medications by class and sleep quality were also investigated. There was a non-significant relationship between each medication class (hypnotics r=.166, p=.163, antidepressants; r=.101, p=.400; opioids; r=.142, p=.233; benzodiazepines r=.096, p= .421; beta blockers r=-.018, p=.879; corticosteroids r= -.061, p=.611) and sleep quality. These results indicate that the poor sleep quality reported by participants was not significantly associated with the medications participants were taking.

Stage of disease. The relationships between stage of disease (Stage III A, III B and IV) and sleep quality were investigated. There was no relationship between stage of disease, (r= .126, p= .293) and sleep quality.

Correlations with Fatigue.

Age. Bivariate correlation analysis was performed to explore the relationship the relationship between age and fatigue. There was a non-significant, negative correlation between the two variables (r=-.034, p=.779) indicating the severity of fatigue reported in this study was not associated with the age of participants.

Sex. Bivariate correlation analysis was performed to explore the relationship between sex and fatigue. The results of this analysis reveal a non-significant correlation between the two variables (r=. 124, p=.297). These results indicate the fatigue reported in this study was not related to the sex of study participants.

ESAS and fatigue. Bivariate correlation analysis was performed to also explore the relationships between the proposed mediator variables, pain, dyspnea, anxiety and fatigue. There was a significant, negative correlation between each of these variables (pain r=-.330, p=.005; dyspnea r=-.484, p <.001; anxiety r=-.425, p<.001 and fatigue. These results indicate that increasing severity of these symptoms was associated with increased fatigue.

Relationships between the remaining symptoms of the ESAS and fatigue were also explored. Aside from nausea, this analysis demonstrated there were significant, negative correlations between fatigue and tiredness (r=-.718), p< .001: appetite (r=-.620), p<.001; drowsiness (r= -.555), p<.001and depression (r=-.264, p=.025). These results indicate that increased severity of each of these symptoms was associated with increased fatigue.

Medications. Bivariate correlation analyses were conducted to study the relationships between medications by class and fatigue. There was a non-significant relationship between each medication class (hypnotics r=-.064, p=.595; antidepressants r=-.048, p=.689, opioids r=.065, p=.588; benzodiazepines r=-.119, p=.319; beta blockers r=-.169, p=.155, corticosteroids r=.034, p=.776) and fatigue. These results indicate fatigue severity was not related to the medications taken by participants.

Stage of disease. The relationships between stage of disease (Stage III A, III B and IV) and fatigue were investigated using Spearman's Rho coefficient. There was a significant relationship between the stage of disease (r= -.272, p value= .021) and fatigue.

Correlations with quality of life.

Age. To explore the relationship between age and quality of life, bivariate correlation analysis was performed. There was a significant, positive correlation between the age of study participants and the quality of life (r =.431, p<.001). The results of this analysis revealed the quality of life reported by participants was associated with the age of participants.

Sex. Bivariate correlation analysis was performed to explore the relationship between sex and quality of life. The results of this analysis reveal a non-significant correlation between the two variables (r=.091, p=.463). These results indicate the quality of life reported in this study was not related to the sex of study participants.

ESAS and quality of life. Bivariate correlation analysis was performed to also explore the relationships between the proposed mediator variables, pain, dyspnea, anxiety and quality of life. There were significant, negative correlations between pain (r=-.294, p =.015), dyspnea (r=-

.257, p=.034), anxiety (r=-.388, p= .001), and quality of life. These results indicate an increase in symptom severity was associated with a decline in quality of life.

The relationship between the remaining symptoms of the ESAS and quality of life was also explored. This analysis demonstrated there were significant, negative correlations between quality of life and tiredness (r=.251, p=.039), appetite (r=-.257, p=.035; nausea (r=-.284, p= 019) and depression (r=-.526, p<.000), indicating that an increase in the severity of these symptoms was also associated with a decline in quality of life.

Medications. Bivariate correlation analyses were conducted to study the relationships between medications by class and quality of life. There was a non-significant relationship between each medication class (hypnotics r=-.043, p=.726, antidepressants r=-.208, p= .089; opioids r=-.165, p=.178, benzodiazepines r=.018, p=.884, beta blockers r=.026, p=.836, corticosteroids r=.179, p=.144) and quality of life. These results indicate the quality of life reported by participants in this study was not related to the medications taken by participants.

Stage of disease. The relationships between stage of disease (Stage III A, III B and IV) and quality of life were investigated using Spearman's Rho coefficient. There was a significant relationship between stage of disease (r=-.288, p= .017) and quality of life.

Bivariate correlations among outcome variables

The correlations among the outcome variables are shown in Table 10.

Table 10

Bivariate Correlation of Outcome Variables

	Fatigue	Quality of Life
Sleep Quality	r= -.412**	r=-.388**
Fatigue		r=.330**

*Correlation is significant at the 0.05 level (two-tailed)
**Correlation is significant at the 0.01 level (two-tailed)

Sleep quality and fatigue. The relationship between the sleep quality and fatigue was explored. The results of this analysis revealed there was a significant, negative correlation between sleep quality and fatigue (r= -.412, p<.0001). This means that as sleep quality declined, (high score) fatigue became more severe (low score).

Sleep quality and quality of life. The relationship between sleep quality and quality of life was explored. There was a significant, negative correlation between these two variables (r= -.388), p=.001). This means that as sleep quality declined (high score) quality of life also declined (low score).

Fatigue and quality of life. A bivariate correlation analysis was performed to explore the relationship between fatigue and quality of life. There was a significant correlation between these two variables (r= .330, p=.006). This means that as fatigue increased (low score), quality of life declined (low score).

Predictors of Relationships among Sleep Quality, Fatigue, and Quality of Life

Based on the conceptual framework that guided this study, data were collected on moderator variables (age, sex), mediator variables (pain, dyspnea, anxiety), and outcome

variables including sleep quality, fatigue and quality of life. Based on the analysis above, however, additional predictors that were significantly correlated with a given outcome variable were added to the regression equation for that outcome variable.

Prior to running the regression I checked for multi-collinearity by performing collinearity diagnostics on these variables. Two values were examined, tolerance and Variance Inflation Factor (VIF). Tolerance values less than .10 and VIF values above 10 suggest multi-collinearity (Pallant, 2013). The variable 'tiredness' was removed from the regression equation for fatigue because of multi-collinearity.

Predictors of sleep quality. Mediator and moderator variables significantly correlated with sleep quality included: age (r=.246), pain (r=.373), dyspnea (r=.309), and anxiety (r=.406). Additional symptoms on the ESAS also significantly correlated with sleep quality included tiredness (r=.339), drowsiness (r=.291), appetite (r=.345) and depression (r=.282). These variables were entered into a standard multiple regression equation to determine their ability to predict sleep quality. These variables explained 30.3% of the variance in sleep quality ($F= 3.428$, $p < 0.001$). Drowsiness was the strongest independent predictor of sleep quality ($\beta=.205$, $p = .096$), followed by pain ($\beta=.139$, $p = .268$), appetite ($\beta=.135$, $p = .304$), depression ($\beta=.129$ $p = .373$), anxiety ($\beta.123$, $p =.417$), age ($\beta=-.115$, $p =. 386$), dyspnea ($\beta=.099$ $p = .444$) and tiredness ($\beta=.021$, $p= .890$), however, none of these variables made an independent statistically significant contribution to the variance of sleep quality. These results are presented in Table 11.

Table 11

Regression Analysis of Predictor Variables with Outcome Variable, Sleep Quality

	Age	Pain	Dyspnea	Anxiety	Tired	Drowsy	Appetite	Depression
B Coefficient	-.115	.139	.099	.123	.021	.205	.135	.129
p value	.386	.268	.444	.417	.890	.096	.304	.373
F (p value <0.001)	3.428							

Predictors of fatigue. Moderator and mediator variables significantly correlated with fatigue included: pain (r= -.330), anxiety (r=-.425), dyspnea (r=-.484) and stage of disease (r=-.272). Additional symptoms of the ESAS significantly correlated with fatigue included tiredness (r=-.718), drowsiness (r=-.555), appetite (r=-.620) and depression (r=-.264). Aside from tiredness, these variables were entered into a standard multiple regression equation to determine their ability to predict the variance in fatigue. These variables explained 59.1% of the variance in fatigue ($F=13.23$, $p<0.001$).

In this model, drowsiness was the strongest independent predictor of fatigue ($\beta= -.325$; p value of .000), followed by dyspnea s ($\beta=-.304$; p value of .000), appetite ($\beta=-.281$; p value of .004), depression ($\beta=-.126$; p value of .227), anxiety ($\beta=-.119$; p value of .295), pain ($\beta=-. 087$; p value of .351 and stage of disease ($\beta=-.017$, p value of .845. In this model, only dyspnea, drowsiness, and appetite were statistically significant independent predictors of the variance of fatigue.

Table 12

Regression Analysis of Predictor Variables with Fatigue

	Pain	Anxiety	Dyspnea	Stage of Disease	Drowsy	Appetite	Depression
B Coefficient	-.087	-.119	-.304	-.017	-.325	-.281	-.126
p value	.351	.295	.001	.845	.000	.004	.227
F (p< .001)	13.23						

Predictors of quality of life. Moderator and mediator variables significantly associated with quality of life included: age (r= .431), pain (r= -.294), dyspnea (r=-.257) anxiety (r= -.388) and stage of disease (r= -.288). Additional symptoms of the ESAS significantly correlated with quality of life included tiredness (r=-.257), nausea (r=-.284), appetite (r=-.257) and depression (r=-.526).

These variables were entered into a standard multiple regression equation to assess their ability to predict quality of life. These variables explained 43.3% of the variance in the quality of life (F=4.93, p<0.001). Depressive symptoms were determined to be strongest predictor of quality of life ((β=-. 403, p= .010), followed by age (β=-.242, p =.069,), appetite (β=-.216, p=.122), dyspnea (β=-. 196, p=.128), stage of disease (β=-.156, p =.153), tiredness (β=.090, p= .554), nausea(β=-.035, p= .780) , anxiety (β= .002, p= .988) and pain (β=.001, p=.991). In this model, depression was the only statistically significant independent predictor of quality of life. These results are presented in Table 13.

Table 13

Regression Analysis of Predictor Variables with Outcome Quality of Life

	Pain	Anxiety	Dyspnea	Stage of Disease	Tired	Appetite	Depressive Symptoms	Age	Nausea
B Coefficient	.001	.002	-.196	-.156	.090	.216	.403	.242	-.035
P value	.991	.988	.128	.153	.554	.122	.010	.069	.780
F (p <.000)	4.93								

Relationships among sleep quality, fatigue and quality of life. Given the significant correlations between sleep quality and fatigue, sleep quality and quality of life and fatigue and quality of life, I used standard multiple regression to assess the ability of fatigue and sleep quality to predict quality of life.

These variables were entered into a standard multiple regression equation to assess their ability to predict quality of life. These variables explained 16.9% of the variance in the dependent variable, quality of life. The unique contribution of each variable was also explored. Fatigue was entered first. In this model, fatigue (β=.224, p=.076) was not a significant predictor of quality of life. After the effects of fatigue were removed however, sleep quality (β=.263, sig=.038) significantly predicted the variance in quality of life.

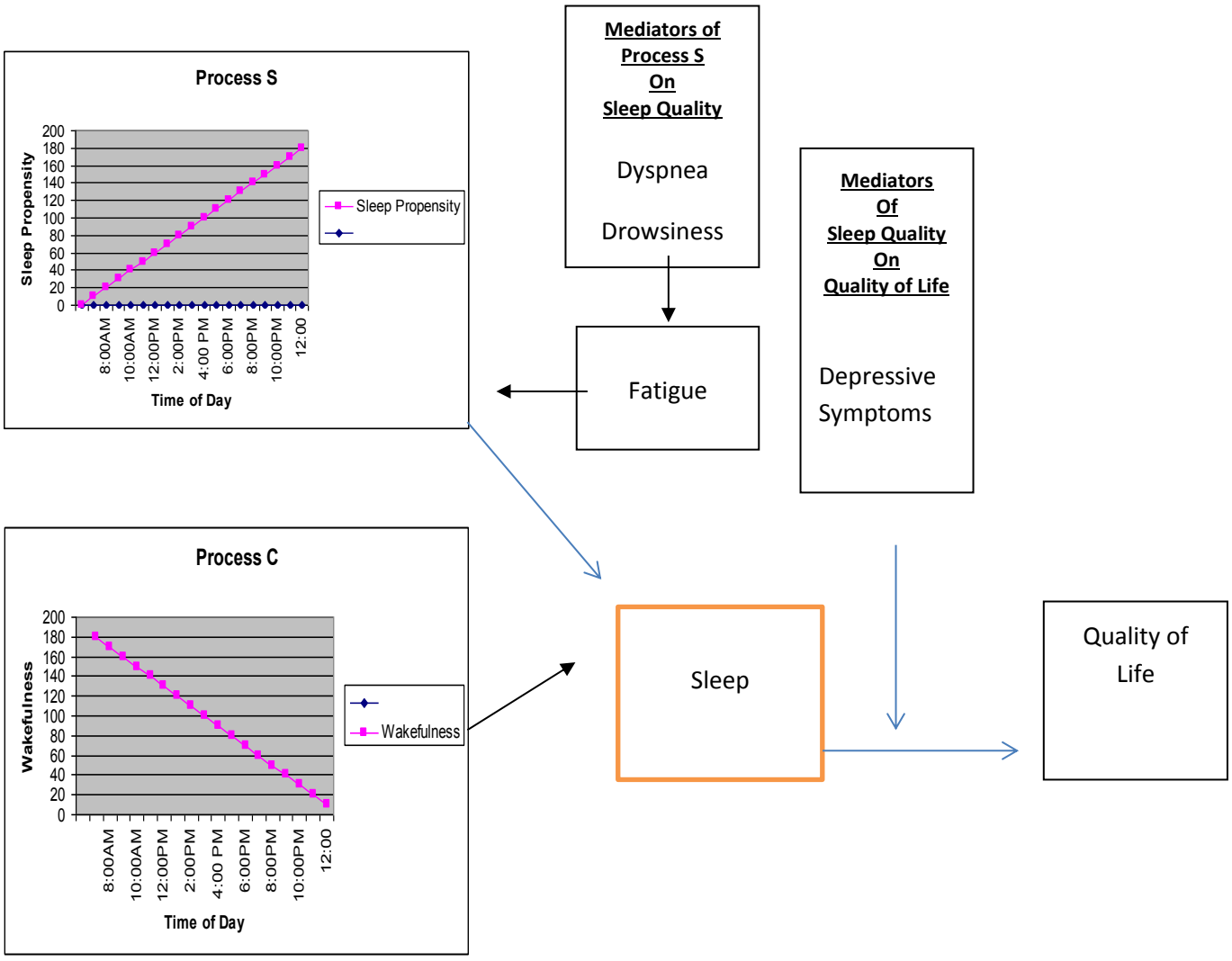
Research Question 2: What factors influence the relationships among sleep, fatigue and quality of life in individuals with advanced lung cancer during the pre-treatment period?

The relationship between sleep quality, fatigue and quality of life in individuals with advanced lung cancer is likely complex because each of these outcomes may be a consequence

of having cancer and may directly or indirectly influence the other outcome variables. Although sleep, fatigue and quality of life were significantly correlated, none of the proposed predictors of these outcomes were significant in the regression equations. Drowsiness, dyspnea and appetite were significant predictors of fatigue. In the regression equation for quality of life, depressive symptoms were the only significant predictor. Based on the Fatigue Adaptation Model (Olson et al., 2011), the ability of fatigue and sleep quality to predict the quality of life was tested. Fatigue severity was not a significant predictor, but after the effects of fatigue were removed, poor sleep quality was a significant predictor of quality of life. These relationships are depicted in Figure 2.

Revised Conceptual Framework

Figure 2



Chapter 5

DISCUSSION

The purpose of this study was to identify the sleep-wake disturbances of advanced lung cancer patients during the pre-treatment period and to understand what factors influenced the relationship amongst sleep, fatigue and quality of life in individuals with advanced lung cancer during this period. This study was conducted at the Cape Breton Cancer Centre, one of two regional cancer centres in Nova Scotia. A cohort study design was employed. Non-probability convenience sampling was used to recruit participants. Seventy-two individuals agreed to participate in this study. The sample consisted of 40 males and 32 females with advanced non-small cell lung cancer.

The conceptual framework that guided this study was the 'Borbely Two-Process Model of Sleep Regulation'. Borbely (1982) proposes two processes, a homeostatic process (Process S) and a circadian rhythm process (Process C) interact to regulate the timing and the duration of both sleep and wake states. Process S is a measure of sleep need and depends on prior patterns of sleep and wakefulness. Process C is not affected by prior patterns of sleep and wakefulness and fluctuates across the day and night influenced by the suprachiasmatic nucleus.

Although Process S and Process C are conceptually two separate processes, the interactions between the two determine the timing and duration of sleep and wake states. Therefore, factors that either enhance or oppose Process S or Process C may significantly affect sleep and wakefulness. As previously discussed, the initial central hypothesis of this study was that Process S was influenced by disease-related factors such as pain and dyspnea, and psychological factors such as anxiety and lack of social support. It was also proposed that

Process C was affected by physiological factors such as age, sex and altered hormone secretions. Moreover, medications prescribed for symptom management were proposed to affect both Process C and Process S. Based on the bivariate correlations and the multivariate analysis conducted in this study, I revised my conceptual framework to depict the significant relationships found in this study.

In the following chapter I will discuss the results of my study, their fit with my conceptual framework and current literature on this topic, and new findings not previously reported by others.

Research Question 1: What sleep disturbances were reported by individuals with advanced lung cancer during the pre-treatment period?

The PSQI was used to assess the sleep quality of participants because it provided a comprehensive assessment of their sleep patterns. The primary problems identified by participants were difficulty initiating sleep, waking after sleep onset, decreased sleep efficiency and a moderate degree of daytime dysfunction. Nocturnal sleep interruption was also frequently reported. The nature of the sleep disturbances reported in this study is consistent with previous studies of sleep disturbances in cancer patients (Ancoli-Israel, 2008; Berger, 2009; Clark et al., 2004; Davidson et al., 2002; Vena et al. 2004). These results suggest that patients with advanced lung cancer experience a disruption in sleep-wake regulation.

In general, participants reported poor sleep quality, a finding consistent with previous studies involving individuals with cancer (Humpel & Iverson, 2009; Nishiura, Tamura, Nagai &Matsushima, 2014; Phillips, Jim, Donovan, Pinder-Schenck & Jacobsen, 2012) and with previous studies of sleep quality of advanced lung cancer patients (Dean et al., 2013; Lin, Chen,

Yang, Zhou, 2013; Wang et al., 2010). To date, however, little is known about the sleep quality of advanced lung cancer patients during the pre-treatment period. In this study, the global sleep quality score on the PSQI for all participants was greater than 5, which is the cut-off point associated with poor sleep quality. This was an unexpected finding as the participants were newly diagnosed advanced lung cancer patients who had not yet begun treatment for their cancer. In my future studies, I plan to explore this issue more fully using a mixed methods approach that would include interview data and a measure of social support. Social support was part of my initial conceptual framework but was not included in this study because of the small sample.

Research Question 2: What factors influence the relationships among sleep, fatigue and quality of life in individuals with advanced lung cancer during the pre-treatment period?

Although all initial variables of interest were individually correlated with each outcome variable, only a few significant predictors were identified when the regression equations were evaluated. In this study, there were no significant independent predictors of sleep quality,, but the amount of variance explained by the model was significant. The significant independent predictors of fatigue identified were dyspnea, drowsiness and appetite and depressive symptoms and the model as the amount of variance of fatigue explained by the model was significant. Seep were significant predictors of quality of life. These findings are reflected in my revised conceptual framework. Because fatigue was entered first in the regression equation exploring fatigue and sleep quality as predictors of quality of life, I have shown fatigue as a predictor of sleep. For this reason, one may view dyspnea, drowsiness, and appetite as indirect predictors of

sleep quality, via fatigue. This hypothesis could be tested in future studies using structural equation modeling (Field, 2013).

The etiology of fatigue in cancer patients is complex and not completely understood. Previous studies have reported possible causes including physiological factors (anemia, pain, and sleep disturbances), psychological factors (anxiety, stress and depression), side effect of medications, co-morbidities and chronobiological factors (altered circadian rhythm activity) (Berger, 2009; Olson, 2007; Payne, 2011; Spichger et al., 2012) but none of these findings were supported by the results of my study. Because all data were self-report, it was difficult to sort out the relative contribution of these factors, cancer itself, and various co-morbidities to the fatigue reported in this study.

In the multivariate analyses, significant predictors of fatigue included dyspnea, drowsiness and appetite. In a study by Minton et al., (2012) dyspnea and appetite were also found to be significant predictors of fatigue (Minton et al., 2012). Dyspnea was a common symptom reported in this study. This was an expected finding as dyspnea is common in advanced cancer, with reported incidence of up to 70% (Reddy et al., 2009). Dyspnea was also one of the most distressing symptoms reported by my study participants. Previous studies have reported that high levels of symptom distress appear to be associated with high levels of cancer-related fatigue (Parsall et al., 2011; Reddy et al., 2009). To date, the exact relationship of dyspnea to fatigue has not been fully explained. I think that in advanced cancer the work of breathing likely takes an inordinate amount of energy, and thus patients report fatigue. This could be because even before treatment begins, patients are beginning to experience loss of muscle function, which could include the smooth muscles associated with respiration.

Dyspnea was often accompanied by the presence of cough in this study. Many participants reported difficulty in both initiating and maintaining sleep because of these two symptoms. The cause of dyspnea in advanced lung cancer may result from many factors including pleural effusion, lymphadenopathy and bronchial obstruction from the disease process and co-existing co-morbidities such as chronic obstructive pulmonary disease (Dean et al., 2013; Nations & Nathan, 2009; Reddy et al., 2009; Thomas, Bausewein, Higginson & Booth, 2011). In this study approximately 41.7% of participants reported having chronic obstructive pulmonary disease (COPD). This co-morbid condition has been linked to poor sleep quality because of the physiological changes that accompany this disease. In particular, COPD is frequently associated with lung hyperinflation which over time weakens respiratory muscles and results in a sensation of 'air hunger' and 'breathlessness', symptoms that can interfere with sleep maintenance and initiation (Lee-Chiong,Jr., 2008; Nations & Nathan, 2009; Thomas et al., , 2011).

Loss of appetite was a problem for some of participants in this study. Loss of appetite commonly occurs in cancer patients (Minton et al., 2012; Spichger et al., 2012). The significant relationship found between loss of appetite and fatigue in this study was an important finding. Loss of appetite may have resulted in reduced dietary intake and this may have contributed to fatigue. There is very little research on the relationships between poor dietary intake and fatigue

This loss of appetite resulted in major weight loss for some participants, even before treatment started. At least 40% of participants reported an unintentional weight loss of at least 10% body weight in the six months prior to their diagnosis. A weight loss of $\geq$ 10% of body weight in six months is defined as cachexia (Minton et al., 2012; Stewart, Skipworth & Fearon, 2006). Cachexia is considered a contributing factor to cancer-related fatigue (Minton et al., 2012; Roberts, Frye, Ahn, Ferriera & Judge, , 2013). Cachexia is a complex metabolic syndrome

commonly associated with advanced lung cancer, characterized by progressive weight loss and skeletal muscle wasting (Roberts et al., 2013). I did not include measurements of malnutrition or cachexia in this study, but in my future research I will add a measure of dietary intake, such as a 3 day diet record, and a measure of lean muscle mass, so that the possible role of nutritional status and cachexia in relation to fatigue can be assessed.

Drowsiness was found to be the most significant predictor of fatigue even though the ESAS score for drowsiness was low. Surprisingly, participants did not rate drowsiness as one of their most distressing symptoms nor did they feel the need to sleep during the day as measured by the FACIT-F scale. This finding may speak to a lack of understanding about the relative importance of sleep and suggests sleep may not have been a priority for participants. The latter assumption was also a theme that emerged out of a recent qualitative study of patients with advanced lung cancer (Dickerson et al., 2012).

A significant predictor of quality of life in this study was depressive symptoms. I anticipated this finding because the mean score of the psychological domain of the MQOL was one the lowest scores reported. Depressive symptoms are one of the most common sources of psychological distress in individuals with cancer (Davidson et al., 2002; Hugel et al., 2004; Vena et al., 2004). In this study, approximately 23.6% of participants reported regular use of anti-depressants. Previous studies have shown depressive symptoms adversely affects quality of life (Brown, Brodsky & Cataldo, 2012; Hutter et al., 2012; Mystakidou et al., 2009). In future studies, I will consider using instruments that are diagnostic for depression to further examine this relationship.

In this study, I found fatigue and sleep to be significant predictors of quality of life. This finding has also been identified by others (Chen et al., 2008; Le Guen et al., 2007; Vena et al., 2006). I anticipated this finding as previous research studies have shown a significant association between fatigue and sleep variables and quality of life (Berger, 2009; Chen et al., 2008; Le Guen et al., 2007; Vena et al., 2006).

I had proposed that pain and anxiety would have an effect on all of my outcome variables. In this study, participants reported a moderate degree of pain, a finding consistent with other studies involving advanced cancer patients (Knudsen et al., 2012; Laird et al., 2011; Lin et al., 2013; Mystakidou et al., 2007).

Although the bivariate correlation between pain and sleep quality was significant, pain was not a significant predictor of sleep quality in this study. This is in contrast to the work of other who reported that poor sleep quality lowered pain threshold and that increased pain was associated with poor sleep quality (Finan, Goodin & Smith, 2013; Lautenbacher, Kundermann & Krieg, 2006; Ma, Chang & Lin, 2013; Onen, Onen, Coupron et Dubray, 2005). In order to explore this issue more fully, I plan to interview participants in the next phase of my research about their perceptions regarding pain and sleep quality. One possibility is that pain may interfere with some aspects of sleep quality, such as the initiation of maintenance of sleep, but not have an overall effect on sleep quality.

A moderate relationship between pain and fatigue was also found in this study, but once again, pain was not a significant predictor of fatigue. I think the severe fatigue experienced by participants in this study may be a maladaptive response to pain (Olson, 2007; Olson et al., 2011), as undertreated pain stimulates a stress response resulting in the activation of

physiological mechanisms (i.e., increased heart rate and increased blood pressure), which if sustained over a period of time, could result in fatigue.

The bivariate correlation between pain and quality of life was significant but once again, pain was not a significant predictor of quality of life. I anticipated this finding because the mean score for the physical symptom domain of the MQOL was one of the lowest reported. Previous studies have also demonstrated an association between pain and quality of life in advanced cancer patients (Larson & Johansson, 2012; Mystakidou et al., 2009). In future studies I plan to explore the relationship between pain and each of the subscales of the MQOL, using a qualitative approach, in order to understand more about the relationship between pain and quality of life.

One of the most distressing symptoms reported in this study was anxiety. In this study, anxiety was a significant correlate of sleep quality, fatigue and quality of life. These findings have also been found in previous studies of patients with advanced cancer (Du-Quiton et al., 2010; Mystakidou et al., 2007; Mystakidou et al., 2009). Although this study did not objectively measure sleep architecture, there is evidence from previous studies which suggests that anxiety may cause abnormalities in sleep homeostasis and circadian processes (Davidson et al.,2002; Hugel et al., 2004; Vena et al., 2004; Zainal et al., 2007). Thus I was surprised to find that anxiety was not a significant predictor of sleep quality. In future studies, I will consider using instruments that are diagnostic for anxiety to further study this relationship.

In this study, a moderate relationship between anxiety and fatigue was found. Few studies have explored the relationship between anxiety and cancer-related fatigue (Brown & Kroenke, 2009). To date, most of the research on psychological correlates of cancer-related fatigue has focused on depression. Although anxiety was not a significant predictor of fatigue I

plan to continue including it in my studies in order to understand the relationship between anxiety and fatigue more clearly.

A moderate relationship between anxiety and quality of life was also found in this study. I anticipated this finding because the mean score of the psychological domain of the MQOL was one the lowest scores reported. Aside from depressive symptoms, anxiety is one of the most common sources of psychological distress in individuals with cancer (Davidson et al., 2002; Hugel et al., 2004; Vena et al., 2004). In this study approximately 29.2% of participants reported regular use of benzodiazepines, pharmacological agents frequently prescribed for anxiety. Previous studies have shown that anxiety adversely affects quality of life (Arrieta et al., 2013; Mystakidou et al., 2009), and yet anxiety was not a significant predictor of quality of life. In future studies, I will consider using instruments that are diagnostic for anxiety. Moreover, I will use an alternative quality of life measure as the MQOL cronbach's alpha was low in this study.

Limitations

The study enrolled a convenience sample of advanced lung cancer patients from the Cape Breton Cancer Centre in Nova Scotia. To control for variability in the study sample, eligibility criterion was limited to cancer stage and timing of data collection. The data obtained from this study was based on self-reports of sleep disturbance, fatigue and quality of life, therefore, this data does not reflect physiologic measures. The study design was not longitudinal; consequently, the data obtained from this study does not provide information about sleep disturbance, fatigue and quality of life of advanced lung cancer patients over time or in relation to treatment or disease progression. Finally, the Cronbach's alpha for the MQoL was lower than

reported by others, suggesting that it was not a particularly good for measuring quality of life in this population. In my future studies, I plan to use a disease-specific quality of life measure.

Summary

In this chapter, I have discussed my findings in relation to advanced lung cancer patients' reports of sleep quality, fatigue and quality of life during the pre-treatment period. I was surprised to find that none of the symptoms I initially proposed were significant predictors of sleep quality, but found that dyspnea, drowsiness, and appetite appeared to have an indirect effect on sleep quality via fatigue.

In this study, I found that depressive symptoms, fatigue and sleep quality all were significant predictors of quality of life. This finding is in keeping with the work of others who have studied advanced cancer populations.

Chapter 6

CONCLUSION

In this chapter, I will discuss the implication of my study findings for clinical practice, policy, education and research.

Clinical Practice

Sleep Quality

Patients with advanced lung cancer appear to be particularly susceptible to poor sleep quality prior to treatment (Dean et al., 2015). Therefore, all patients with advanced lung cancer should be screened for sleep disturbance when initially diagnosed using an instrument such as the ESAS-r. Those with scores of 3/10 or more may benefit from a full sleep assessment. This assessment should identify the type and severity of sleep problems, symptoms (e.g. pain, dyspnea) associated with the sleep problems, risk behaviors, factors that seem to provoke it or make it better, and the meaning of the sleep disturbance to the patient (Howell et al.,2013). This assessment should be conducted using a validated sleep instruments used in cancer populations, such as the Pittsburgh Sleep Quality Index, and should be included in assessments conducted throughout the treatment trajectory so that the effectiveness of any interventions can be monitored and adjusted as needed.

The results of this assessment should be person-centered, and interventions should be based on existing evidence for managing sleep disturbances (Howell et al., 2013). These may include the use of both pharmacological and non-pharmacological interventions. Non-pharmacological interventions including providing resources on self-management strategies and

sleep hygiene education should also be provided (Dickerson, Connors, Fayad & Dean, 2014; Howell et al., 2013). This information is presented in Table 14.

Table 14

Sleep Hygiene Strategies

Establish regular activity-rest behaviours

1) Wake up and go to bed at the same time every day
2) Avoid napping during the day
3) If required, limit daytime naps to brief naps (1 hour or less)
4) Exercise regularly, particularly in the afternoon. Avoid exercise within 2 hours of bedtime

Engage in dietary practices that promote sleep

1) Avoid caffeine, alcohol, and nicotine products 4-6 hours before bedtime
2) Avoid eating a heavy meal 4-6 hours before bedtime
3) A light snack before beds is appropriate. Warm milk and foods high in the amino acid tryptophan may encourage sleep

The Sleep Environment

1) Minimize noise/disruption
2) If noise is a problem, use ear plugs
3) Keep room dark. Avoid exposure to bright light.
4) Keep room well ventilated and room temperature at a comfortable level
5) Use comfortable bedding
6) Associate your bed with sleep

Establish a relaxing bedtime routine

1) Listen to relaxing music
2) Practice relaxation exercises such as yoga or deep breathing
3) Assume your favorite sleep position
4) Designate a "clear- your- head time

Cognitive Behavioural Therapy has been a particularly useful approach to the management of sleep disturbances (Dickerson et al., 2014; Howell et al., 2013). Cognitive

behavioral therapy should be person-centered and patients should be provided with several strategies including guided imagery, relaxation and distraction etc. to determine which strategy is most effective for their particular sleep disturbance (Kwekkeboom, Abbot-Anderson, & Wanta, 2010; Howell et al., 2013).

Fatigue

Based on the findings of this study, patients with advanced lung cancer appear to be particularly susceptible to severe fatigue. Therefore, the initial pre-treatment symptom screen for all patients with advanced lung cancer should include fatigue, using a validated instrument such as the ESAS-r. Those with scores greater than 3/10 warrant further assessment including the identification of factors that provoke fatigue or make it better, the nature of the fatigue, the regions of the body effected, an assessment of whether the fatigue is worse at any particular time of day, and the meaning of the fatigue. Again, these assessments should be conducted using validated fatigue instruments used in cancer populations. Given the severity of fatigue pre-treatment, it should be monitored throughout the treatment trajectory in order to assess the effectiveness of any interventions.

Depending on the cause of fatigue, both evidence-based pharmacological and non-pharmacological interventions can be implemented (Howell et. al., 2011; Koornstra. Peters, Donofrio, Van den Borne & DeJong., 2014). Potential pharmacological interventions should target symptoms associated with fatigue. Based on the results of this study, dyspnea, drowsiness, and appetite warrant close attention. A low dose of an opioid such as morphine may alter perceptions of dyspnea (ref), and maxeran 10 mg orally 30 minutes before meals and at bedtime may promote gastric motility, and thus improve appetite (LeGrand, Khawan, Walsh & Rivera,

2003; Lorenz et al., 2008). Recent studies show that other medications such as modafinil are not effective (Spathis et al., 2009; Spathis et al., 2014). The relief of dyspnea and an improvement in appetite may reduce fatigue and improve sleep quality. Given the significance of appetite as an independent predictor of fatigue, nurses should refer those who report poor appetite to a dietician prior to treatment.

Non-pharmacological approaches have proven to be effective for managing the severe fatigue reported in this study. A self-paced exercise program of light intensity has been determined to be a safe and effective intervention for fatigue in lung cancer patients (Hoffman et al., 2013). Conserving energy is another practical and useful approach for managing fatigue in this population. Daily self-monitoring and identification of triggers of fatigue may assist patients to establish rest-activity behaviors conducive to minimizing fatigue. Complimentary therapies including listening to relaxing music, massage therapy, yoga and acupuncture may also provide relief from severe fatigue (Finnegan-John, Molassiotis, Richardson & Ream, 2014). Consultation with other healthcare professionals including dietitians, physiotherapists, psychologists and counselors may provide patients with strategies to minimize their fatigue experience. Moreover, providing patients with other resources including home care services and volunteer organizations may also be beneficial.

Quality of Life

Based on this study's findings, health care providers should screen all individuals with advanced lung cancer quality of life when they are initially diagnosed. Those with scores greater than 3/10 should be further assessed. This assessment should include the identification of symptoms, as symptoms are known to be associated with poor quality of life. In this study,

depressive symptoms were a significant predictor of quality of life. This assessment should also include the use of validated quality of life instruments used in advanced cancer populations. Advanced lung cancer has a poor prognosis, and thus quality of life is the focus of care in this population. For this reason, ongoing assessment of the quality of life should occur and regular intervals both during and after any planned treatment in order to monitor the benefits of interventions.

Cognitive-reframing interventions may increase the hope of individuals with advanced cancer and have a positive impact on their quality of life (Herth, 2000). These interventions consist of a series of cognitive exercises designed to assist individuals in maintaining or enhancing their situational hope. Previous studies have demonstrated the efficacy of hope-focused intervention in enhancing the quality of life of individuals with advanced cancer (Duggleby et al., 2007).

Policy

The findings of this study have implications for policy related to increasing public awareness about the significance of sleep. The lack of distress regarding poor sleep quality suggests that the participants in this study may not have been knowledgeable about the importance of sleep. One approach may be to include messages about sleep hygiene and the importance of sleep in health promotion initiatives.

Education

My study findings have implications for nursing education in relation to the curriculum of baccalaureate nursing educations programs. I think that information on sleep, fatigue and quality of life, should be horizontally threaded through the curriculum of oncology, palliative

care and nursing courses, particularly those that focus on older adults. This same content should be included in educational program in all health disciplines.

My study findings have implications for healthcare providers currently employed in oncology and palliative care centres. I think the findings of this study speak to the need for professional development opportunities focused on screening, assessment, and interventions for sleep disturbances and fatigue in advanced lung cancer patients and as well as to the importance of understanding the factors that impact the quality of life of these patients.

Research

The findings of this study also have implications for research. I have ethical clearance to continue following my study participants through any treatments and into the post-treatment period. The availability of longitudinal data will make it possible to ascertain ways in which sleep quality changes over time, and the factors that influence sleep quality at each of these time points. The longitudinal data will also make it possible to explore relationships between fatigue, sleep quality and quality of life over time.

As noted in Chapter 5, I plan to add close monitoring of dietary intake to my future studies so that I can appraise the relationship between dietary intake and appetite, and also assess the benefits of interventions intended to improve appetite. Based on the results of this study, I am particularly interested in developing nurse-led interventions that will improve the quality of life of this population.

Sub-group analyses, for example, comparing the level of social support and its relationship to sleep quality, fatigue and quality of life is another area of potential research. The

relationship between co-morbidities and sleep quality, fatigue, and quality of life in this population should also be further studied.

Summary

Currently, advanced lung cancer patients in the setting where I collected data are not routinely screened for sleep disturbance, fatigue or quality of life at initial diagnosis. The results of this study suggest that pre-treatment screening, assessment, and treatment of sleep disturbance and fatigue, is very important as they are significant predictors of quality of life. I am very interested to see whether these relationships remain significant as the participants move through the illness trajectory.

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APPENDIX A: INSTRUMENTS

Edmonton Symptom Assessment System:
(revised version) (ESAS-R)

Please circle the number that best describes how you feel NOW:

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Drowsiness
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Nausea
No Lack of Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Lack of Appetite
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Wellbeing
No _____ Other Problem *(for example constipation)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible _____

Patient's Name _____

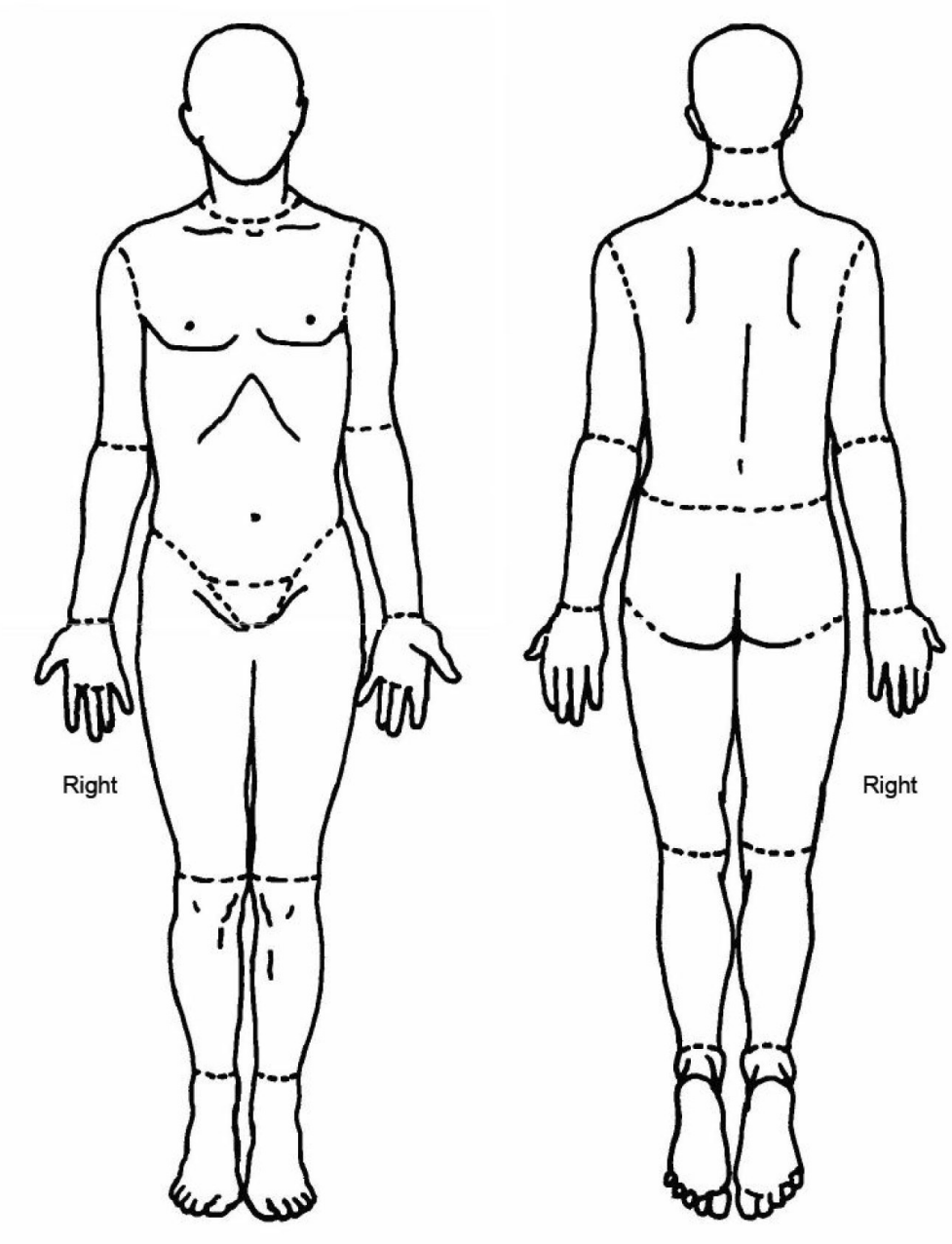
Date _____ Time _____

Completed by (check one):
- ☐ Patient
- ☐ Family caregiver
- ☐ Health care professional caregiver
- ☐ Caregiver-assisted

BODY DIAGRAM ON REVERSE SIDE

ESAS-r
Revised: November 2010

Please mark on these pictures where it is that you hurt:



Subject's Initials_____ID#_____Date_____Time_____AM PM

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?

   BED TIME _____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

   NUMBER OF MINUTES _____

3. During the past month, what time have you usually gotten up in the morning?

   GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

   HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

f) Feel too cold

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

g) Feel too hot

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

h) Had bad dreams

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

i) Have pain

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

j) Other reason(s), please describe_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good _____

Fairly good _____

Fairly bad _____

Very bad _____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____

_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: Psychiatry Research, 28:193-213, 1989.

FACIT Fatigue Scale (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

		Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

McGILL QUALITY OF LIFE QUESTIONNAIRE

STUDY IDENTIFICATION #:_____ DATE: _____

Instructions

The questions in this questionnaire begin with a statement followed by two opposite answers. Numbers extend from one extreme answer to its opposite.
Please circle the number between 0 and 10 which is most true for you.
There are no right or wrong answers.
Completely honest answers will be most helpful.

EXAMPLE:

I am hungry:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

- If you are not even a little bit hungry, you would circle 0.
- If you are a little hungry (you just finished a meal but still have room for dessert), you might circle a 1, 2, or 3.
- If you are feeling moderately hungry (because mealtime is approaching), you might circle a 4, 5, or 6.
- If you are very hungry (because you haven't eaten all day), you might circle a 7, 8, or 9.
- If you are extremely hungry, you would circle 10.

BEGIN HERE:

IT IS VERY IMPORTANT THAT YOU ANSWER ALL QUESTIONS FOR HOW YOU HAVE BEEN FEELING *JUST IN THE PAST TWO (2) DAYS*.

PART A

Considering all parts of my life - physical, emotional, social, spiritual, and financial - *over the past two (2) days* the quality of my life has been:

very bad 0 1 2 3 4 5 6 7 8 9 10 **excellent**

Please continue on the next page...

PART B: Physical Symptoms or Physical Problems

(1) *For the questions in Part "B", please list the* **PHYSICAL SYMPTOMS OR PROBLEMS** *which have been the biggest problem for you over the past* **two (2)** *days. (Some examples are: pain, tiredness, weakness, nausea, vomiting, constipation, diarrhea, trouble sleeping, shortness of breath, lack of appetite, sweating, immobility. Feel free to refer to others if necessary).*

(2) *Circle the number which best shows how big a problem each one has been for you* ***OVER THE PAST TWO (2) DAYS.***

(3) *If, over the past two (2) days, you had* **NO** *physical symptoms or problems, or only one or two, answer for each of the ones you have had and write "none" for the extra questions in Part B, then continue with Part C.*

1. Over the past two (2) days,
one troublesome symptom has been:_____.
(write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

2. Over the past two (2) days,
another troublesome symptom has been:_____.
(write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

3. Over the past two (2) days,
a third troublesome symptom has been:_____.
(write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

Please continue on the next page...

4. Over the past two (2) days I have felt:

physically terrible	0	1	2	3	4	5	6	7	8	9	10	**physically well**

PART C *Please choose the number which best describes your feelings and thoughts* ***OVER THE PAST TWO (2) DAYS.***

5. Over the past two (2) days, I have been depressed:

not at all	0	1	2	3	4	5	6	7	8	9	10	**extremely**

6. Over the past two (2) days, I have been nervous or worried:

not at all	0	1	2	3	4	5	6	7	8	9	10	**extremely**

7. Over the past two (2) days, how much of the time did you feel sad?

never	0	1	2	3	4	5	6	7	8	9	10	**always**

8. Over the past two (2) days, when I thought of the future, I was:

not afraid	0	1	2	3	4	5	6	7	8	9	10	**terrified**

9. Over the past two (2) days, my life has been:

utterly meaningless and without purpose	0	1	2	3	4	5	6	7	8	9	10	**very purposeful and meaningful**

10. Over the past two (2) days, when I thought about my whole life, I felt that in achieving life goals I have:

made no progress whatsoever	0	1	2	3	4	5	6	7	8	9	10	**progressed to complete fulfillment**

Please continue on the next page...

11. Over the past two (2) days, when I thought about my life, I felt that my life to this point has been:

completely worthless	0	1	2	3	4	5	6	7	8	9	10	**very worthwhile**

12. Over the past two (2) days, I have felt that I have:

no control over my life	0	1	2	3	4	5	6	7	8	9	10	**complete control over my life**

13. Over the past two (2) days, I felt good about myself as a person.

completely disagree	0	1	2	3	4	5	6	7	8	9	10	**completely agree**

14. To me, the past two (2) days were:

a burden	0	1	2	3	4	5	6	7	8	9	10	**a gift**

15. Over the past two (2) days, the world has been:

an impersonal unfeeling place	0	1	2	3	4	5	6	7	8	9	10	**caring and responsive to my needs**

16. Over the past two (2) days, I have felt supported:

not at all	0	1	2	3	4	5	6	7	8	9	10	**completely**

Please continue on the next page...

PART D

Please list or describe the things which had the greatest effect on your quality of life in the past two (2) days. Please tell us whether each thing you list made your quality of life better or worse during this time. If you need more space, please continue on the back of this page.

Thank you very much for your help.

APPENDIX B: RECRUITMENT LETTER

U of A Letterhead/Cape Breton Cancer Centre Letterhead

An Exploratory Study of Sleep-Wake Disturbances in Advanced Lung Cancer Patients

RECRUITMENT INVITATION

Dear Sir/Madam,

I am conducting a study here at the Cape Breton Cancer Centre about the sleep problems frequently experienced by individuals with lung cancer. My focus is on things that may contribute to sleep problems. I would like to meet with you to tell you more about my study and to see whether you would be interested in participation. If this would be okay with you please print your name below, and provide your phone number. Thank you for considering this request.

Sincerely,

Claudette Taylor

NAME

PHONE NUMBER

OKAY to leave a message? _____ Yes _____No

If you have any questions about the research now or later, please contact the researcher at (902) 563-1961 or Dr. Karin Olson, her supervisor, at (780) 935-1186. Collect calls will be accepted.

Recruitment Form, Version 1, August 2012

APPENDIX C: STUDY INFORMATION LETTER AND CONSENT FORM

U of A Letterhead/Cape Breton Cancer Centre Letterhead

An Exploratory Study of Sleep-Wake Disturbances in Advanced Lung Cancer Patients

Research Investigator:	**Supervisor:**
Claudette Taylor	Dr. Karin Olson
PhD Nursing Student, University of Alberta	Professor, Nursing Faculty
623 Lisa Drive	4-359 Edmonton Clinic Health Academy
Albert Bridge, Nova Scotia, B1K 3V2	University of Alberta, Edmonton, AB,
EMAIL: claudett@ualberta.ca	EMAIL: Karin.Olson@ualberta.ca
Phone: (902) 563-1961	Phone:(780) 492-6403 or (780) 935-1186

Why am I being asked to take part in this study?

You are being asked to take part in a research study because you have recently been diagnosed with lung cancer. . The goal of this study to learn more about the sleeping problems experienced by people with advanced lung cancer. In the long term, the results of this study will be used to find ways to help people with advanced lung cancer sleep better. Before you make a decision about whether to participate, the researcher will go over this form with you. You are encouraged to ask questions if you feel anything needs to be made clearer. You will be given a copy of this form for your records.

What is the reason for doing this study?

A growing number of researchers have reported on the links between good sleep and health and quality of life. Clinicians have reported that people with lung cancer have trouble sleeping. Only a few studies of sleep problems among people with lung cancer have also been conducted. In order to solve this problem, we need to know more about factors that may be contributing to the sleep problems experienced by people with lung cancer. This study has been designed to help address this gap in our understanding. It is being conducted as part of the researcher's PhD studies in the Faculty of Nursing at the University of Alberta.

What will I be asked to do?

You will be asked to complete four questionnaires prior to the start of your treatments. These questionnaires will include the Pittsburgh Sleep Quality Index, the McGill Quality of Life Questionnaire, the Edmonton Symptom Assessment Scale and the Functional Assessment of Chronic Illness Therapy Fatigue Subscale. It will take about 30 minutes to complete these questionnaires. You can either complete the forms at the Cape Breton Cancer Centre or in the convenience of your home. If you complete the forms at home, you will be provided with self-addressed stamped envelope so that you can mail them back.

What are the risks and discomforts?

There are no known risks associated with this study. If some of the questions on the questionnaires are distressing to you, please leave them blank. If you require some support in dealing with this distress, the researcher will speak to the clinic nurse at the Cape Breton Cancer Centre for you.

What are the benefits?

You may not get any benefit from being in this research study, but the study may help other people with lung cancer in the future."

Do I have to take part?

Being in this study is your choice. If you decide to be in the study, you can change your mind and stop being in the study at any time, and it will in no way affect the care or treatment that you are entitled to.

What will it cost me to participate?

There are no costs for participating in this study.

Will my information be kept private?

During the study we will be collecting some information about your health. Specifically, we will be collecting information about your past health, current medications and social support. . We will do everything we can to make sure that this data is kept private. No data relating to this study that includes your name will be released by the researcher or published by the researcher.

As part of this study the researcher will look at your personal health records held at the Cape Breton Cancer Centre. These records contain information about your past health, current medications and information related to your cancer. Any personal health information that we get from these records will be only what is needed for the study.

All study participants will be assigned a study number. All information collected for this study will be labeled with this number, rather than your name or health care number. A document linking the names of study participants and their study number will be stored in a locked drawer in the office of the researcher, separate from all other study information.

.

By signing this consent form you are saying it is okay for the researcher to collect and use information about you from your personal health records as described above.

After the study is over, we will keep your health data that was collected as part of the study for 5 years. This information will be kept in a locked drawer at the Cape Breton Cancer Centre. All electronic information related to this study will be on a computer that is password-protected.

The information collected for this study will only be available to the researcher and her supervisors in the Faculty of Nursing at the University of Alberta and will only be used for the research outlined above. It is possible the information obtained from this study may be used in future research, but this would first be approved by a Research Ethics Board.

What if I have questions?

If you have any questions about the research now or later, please contact the Claudette Taylor, the researcher, at (902) 563-1961 or Dr. Karin Olson, her supervisor, at (780) 935-1186.

If you have any questions regarding your rights as a research participant, you may contact the Health Research Ethics Board at 780-492-2615. This office has no affiliation with the study investigators.

This research has also been reviewed and approved by the Cape Breton District Health Authority Research Ethics Board. If you have any questions or concerns about the study, you may contact the Chair, District Research Ethics Board @ 902-563-1833.

U of A Letterhead/Cape Breton Cancer Centre Letterhead

CONSENT

Title of Study: An Exploratory Study of Sleep-Wake Disturbances in Advanced Lung Cancer Patients

Principal Investigator(s): Claudette Taylor **Phone Number(s): 902)-563-1961**

PhD Supervisor: Karin Olson **Phone Number(s): (780)492-6403**
(780) 935-1186

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	☐	☐
Has the issue of confidentiality been explained to you?	☐	☐
Do you understand who will have access to your records, including personally identifiable health information?	☐	☐
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, give his/her name _____	☐	☐

Who explained this study to you? _____

I agree to take part in this study:

Signature of Research Participant _____

(Printed Name) _____

Date:_____

Signature of Investigator or Designee _____ Date _____

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH PARTICIPAN

APPENDIX D: DATA COLLECTION FORM

Data Collection Form

Demographic:

Age: _____ Sex: _____

Menopausal Status: Post-Menopausal _____

Social History:

Marital Status: Married _____ Single _____Separated _____ Divorced _____

Widowed _____ Common Law _____

Number of Children _____ Close _____ Elsewhere _____

Lives alone _____ With Family _____ In Nursing Home _____

Support Systems: _____

Chart Review:

History of Present Illness:

Diagnosis: _____ Stage: _____

Date of Diagnosis: _____

Diagnosis known by: Family _____ Patient _____

Medical History:

_____

_____

_____

_____

History of Sleep Disorders:

_____

_____

_____

_____

Questions to Assess Decision-Making Capacity

Understanding

Can you tell me in your own words what is the purpose of this study?

_____

_____

_____

Appreciation

Whether or not you enroll in this study, what do you see as the risks?

_____

_____

_____

Reasoning

How is enrolling in this study better than not enrolling in it?

_____

_____

_____

What are some ways that enrolling in the study might affect your life?

_____

_____

_____