2021

Sleep-Related Problems, Sleep-Related Distress, and Sleep-Related Functional Status Among Adult Inpatients Receiving Palliative Care

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

by

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Richmond, Virginia
July 2021

Acknowledgments

I wish to thank the many advisors, colleagues, friends, and family that have supported me throughout my personal, professional, and academic journeys. You have helped me laugh, taught me about humanity, and given me solace when I needed it. Thank you for offering me kindness, wisdom, and enthusiasm which have made my life fascinating, enjoyable, and rich. My successes are also yours.

I would like to thank my previous advisor, Dr. Alison Montpetit, and previous committee chair, Dr. Beth Rodgers, for helping me build a strong foundation for success in my doctoral program.

I would like to thank my committee chair, Dr. Suzanne Ameringer; and committee members Dr. R.K. Elswick, Jr.; Dr. Shelly Orr; and Dr. Samuel Taylor, Jr. for helping me reach the finish line.

I would also like to thank Ms. Fonda Neal for helping me navigate the necessary steps to keep my doctoral program on track.

I sincerely appreciate the generosity of the VCU Health palliative care team for providing meaningful advice and assistance that enabled me to conduct my dissertation research so smoothly. I especially wish to thank Dr. Danielle Noreika, Mr. Barton Bobb, and Ms. Hope Coley of the palliative care team.

This dissertation was in part supported by Clinical and Translational Science Award No. UL1TR002649 from the National Center for Advancing Translational Sciences. Its contents are solely the responsibility of the author and do not necessarily represent official views of the National Center for Advancing Translational Sciences or the National Institutes of Health.

To those that participated in my study, thank you for your willingness to share personal aspects of your lives; it is my hope that your contributions will help those in the future better cope with severe illness.

Finally, to my husband, Mr. Eric Shoup, thank you for your love, and for your support of my dreams. May we enjoy a bountiful harvest.

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Abstract

SLEEP-RELATED PROBLEMS, SLEEP-RELATED DISTRESS, AND SLEEP-RELATED FUNCTIONAL STATUS AMONG ADULT INPATIENTS RECEIVING PALLIATIVE CARE

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Virginia Commonwealth University, 2021

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Palliative care patients may be at a higher risk for sleep-related problems and their negative effects compared to the general population, yet limited sleep research has been done with this population. The purpose of this dissertation was to determine prevalence rates for excessive sleepiness, insomnia, restless legs syndrome (RLS), and high risk for sleep apnea (HRSA); examine relationships between the aforementioned sleep-related problems, sleep-related distress (SD), and sleep-related functional status (SFS); and to determine which sleep-related problem measures along with age and gender predicted SD and SFS among a sample of adult palliative care inpatients. Secondary aims were to understand causes of SD and find out participant willingness to accept inconveniences/risks to alleviate SD. Participants (N = 38) were recruited from an urban, academic medical center in Virginia and asked to participate in an interview and complete sleep-related instruments. Measures included the STOP-Bang Questionnaire (STOP-Bang) for HRSA, Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), 2012 International Restless Legs Syndrome Study Group (IRLSSG) revised consensus diagnostic criteria, Sleep-Related Distress Thermometer (SDT), and Functional Outcomes of Sleep Questionnaire – 10 (FOSQ-10) for SFS. Prevalence rates were 62% for insomnia (ISI score > 7), 57% for HRSA (STOP-Bang score > 2), 41% for excessive sleepiness (ESS score > 10), and

14% for RLS (met all IRLSSG criteria). Significant relationships ($p < 0.05$) were found between insomnia and SD (Spearman's $\rho = 0.75$, $p < 0.0001$), and excessive sleepiness and SFS (Spearman's $\rho = -0.59$, $p = 0.0001$). Based on regression models, ISI score was found to be a predictor of SD ($F = 48.14$, $p < 0.0001$); and age, ISI score, and ESS score were found to be predictors of SFS ($F = 10.85$, $p < 0.0001$). The most frequently reported causes of SD were anxiety/distressing thoughts (32%) and pain/physical discomfort (19%). Most participants expressed willingness to accept minimal risk interventions (97%), prescription medication (68%) and positive airway pressure therapy (57%) to alleviate SD. In conclusion, sleep-related problems were found to be common among the study sample, frequent causes of SD included anxiety/distressing thoughts and pain/physical discomfort, and the majority of participants were willing to accept the inconvenience of standard treatment options to alleviate SD. While associations were found between variables, due to limitations of the study including small sample size and uncertainty of the reliability/validity of the measures used with this population, more research is needed to better understand these relationships. Future research is also needed to establish tolerability and efficacy of interventions for sleep-related problems among palliative care inpatients.

Sleep-Related Problems, Sleep-Related Distress, and Sleep-Related Functional Status Among Adult Inpatients Receiving Palliative Care

Chapter 1: Statement of the Problem, Purpose, and Philosophical Framework

Statement of the Problem

Sleep is a neurobehavioral phenomenon that takes up approximately one-third of a person's lifespan, with adults needing seven to eight hours of sleep nightly. Influenced by circadian, environmental, and societal factors, sleep involves entering an unresponsive but neurologically active state that serves to restore energy, maintain physiological homeostasis, strengthen host defenses, and consolidate knowledge (Buysse, 2014; Redeker & McEnany, 2011). Buysse (2014) describes good sleep health as a satisfying pattern of sleep and wakefulness that is associated with "appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours" (p. 12). With rising age, sleep patterns change slightly but sleep should continue to provide restorative benefits. Though older adults may have a greater health burden which can affect their sleep, the development of sleep-related problems is not considered an expected part of healthy aging (Vitiello, 2006).

The impacts of poor sleep are vast. Sleep deprivation induces excessive sleepiness which contributes to poor performance, daytime napping, reduced productivity, drowsy driving, and accidents (Redeker & McEnany, 2011). Daytime napping in turn can trigger insomnia. Biological consequences of sleep loss include elevated blood pressure, altered hormone production, increases in pain and hunger signals, lowered immune response to vaccinations, and increased inflammation (Besedovsky et al., 2019; Redeker & McEnany, 2011). Cognitive and psychological effects of poor sleep include lowered resilience to stress, negative mood, anxiety, reduced motivation, attention deficits, and challenges with comprehension. As a result of these

effects, social relationships can be impaired (Besedovsky et al., 2019; Redeker & McEnany, 2011).

Common sleep-related problems associated with poor sleep include excessive sleepiness, insomnia, sleep apnea and restless legs syndrome. Each can contribute to increased symptom burden, reduced functional status, and diminished quality of life (Redeker & McEnany, 2011). These sleep-related problems can also influence each other to raise the risk of other problems. For instance, sleep apnea and restless legs syndrome can both contribute to insomnia which then leads to sleep deprivation and excessive sleepiness. As described previously, sleep deprivation and excessive sleepiness have numerous potential negative outcomes. Additionally, sleep deprivation can cause or worsen the severity of restless legs syndrome (National Institute of Neurological Disorders and Stroke, 2017).

This dissertation focuses on the palliative care population which may be particularly prone to sleep-related problems. Palliative care is a form of healthcare which may be provided to any person at any age whenever it is needed. According to national clinical guidelines, palliative care should be considered for patients with serious acute or chronic, progressive, and/or life-threatening conditions that place a significant burden on the patient and are associated with poor quality of life (Dahlin, 2013). In the palliative care population, the frequent presence of factors such as advanced age, acute and chronic illnesses, weakness, dyspnea, anxiety, pain, stress, and certain medications (e.g., opioids, muscle relaxers, antiemetics, and hypnotics) may raise the risk for sleep-related problems (Mannarino et al., 2012; Redeker & McEnany, 2011).

The mission of palliative care is to manage distressing symptoms, promote comfort, and support patients to live to the fullest extent desired "with consideration of patient/family needs, preferences, values, beliefs, and culture" (Dahlin, 2013, p. 9). Palliative care providers strive to

alleviate distress and raise quality of life by “anticipating, preventing, and treating suffering” while addressing physical, intellectual, emotional, social, and spiritual needs. (US Department of Health and Human Services Centers for Medicare & Medicaid Services and the National Quality Forum, as cited in Dahlin, 2013, p. 9).

Palliative care is meant to be holistic for both patients and families. Major physical symptoms addressed in palliative care include “pain, shortness of breath, nausea, fatigue, anorexia, insomnia, restlessness, confusion, and constipation” (Dahlin, 2013, p. 20). Common emotional issues that need attention include fear, anxiety, sadness, distress, guilt, hopelessness, and loneliness (Limonero et al., 2018). Within the social domain, palliative care providers “[collaborate] with patients and families to identify, support, and capitalize on patient and family strengths” (Dahlin, 2013, p. 10). Palliative care incorporates elements related to resiliency, support networks, intimacy, and coping skills which may be thought of as part of the spiritual domain wherein spirituality refers to how people experience the world and the ways they find meaning and purpose in that world (Dahlin, 2013). Promoting good sleep quality is relevant to the provision of holistic care for palliative care patients due to the importance of sleep for health and well-being within each of the physical, emotional, social, and spiritual domains.

A central construct in palliative care is quality of life. It has been defined as “the overall state of well-being that individuals experience as assessed by subjective and objective measures of functioning, health, and satisfaction with the important dimensions of their lives” (Reimer & Flemons, 2003, p. 335). Health-related quality of life specifically deals with “physical function, social function, emotional or mental state, burden of symptoms, and sense of well-being” as affected by illness or injury and any corresponding treatment (Reimer & Flemons, 2003, p.336). Sleep is a critical aspect of quality of life (Lo & Lee, 2012; Marques et al., 2017; Zeitlhofer et

al., 2000), including health-related quality of life which may be of particular concern in palliative care.

Because disrupted sleep can heighten symptom burden and diminish functional capacity, it may prevent palliative care patients with sleep-related problems from achieving optimum health-related quality of life (Caresearch Palliative Care Knowledge Network, 2017; Hajjar, 2008; Loh et al., 2017). Sleep-related problems may reduce the ability of palliative care patients to engage in and sustain important or desired responsibilities, leading to hindered relationships, loss of professional and leisure occupations, financial instability, or other stressors (Dahlin, 2013; Reimer & Flemons, 2003). These outcomes can elevate distress and worsen overall quality of life. Family and friends who care about or depend upon a palliative care patient with sleep-related problems may also suffer as a result. For these reasons, detecting and managing sleep-related problems among palliative care patients is important.

The National Comprehensive Cancer Network (NCCN) recently developed enhanced assessment and intervention guidelines for sleep/wake disturbances in palliative care, adding recommendations to consider sleep apnea and restless legs syndrome as potential contributors to disturbed sleep (Dans & Kutner, 2018). The NCCN advises initially using the Epworth Sleepiness Scale (Johns, 1991) to evaluate for excessive sleepiness and taking a relevant history to determine what other sleep-related problems may be present. If sleep apnea is suspected, then a sleep study may be warranted. The updated guidelines newly incorporated positive airway pressure for sleep apnea and treatment of restless legs syndrome as interventions for palliative care patients (Dans & Kutner, 2018). With respect to insomnia, the guidelines continue to advise practitioners to address contributing factors such as pain, anxiety, mood problems, cognitive disturbances, and nausea; and support the use of cognitive behavioral therapy as well as sedating

medications such as lorazepam, zolpidem, quetiapine, trazodone, or mirtazapine for insomnia. The guidelines also continue to recommend trials of stimulant medications such as methylphenidate, dextroamphetamine, modafinil, or caffeine for excessive sleepiness (Dans & Kutner, 2018).

Despite the presence of these guidelines, comprehensive assessment for and appropriate management of sleep-related problems are not always done in palliative care (Yap, 2016), and the resulting negative impacts may go unaddressed. Several factors may influence this problem. Patients may underreport their experiences thinking that sleep-related problems are an expected part of illness that cannot be effectively helped (Hajjar, 2008). Consequently, sleep-related problems may first be recognized during an inpatient hospital stay when increased illness acuity exacerbates ongoing issues and hospital staff are able to make sleep-related observations (Auckley, 2018). Though sleep-related problems may be more evident in the hospital, their etiologies and urgencies may be obscured by other symptoms and concerns related to a palliative care patient's severe or life-threatening illness. A lack of awareness about sleep disorders among inpatient healthcare providers may also result in suboptimal management of palliative care patient sleep needs.

As an example of an issue that may apply to inpatient palliative care patients, the Joint Commission's Division of Healthcare Improvement has reported concerns regarding hospital practices related to sleep apnea. Specifically, they cite a "lack of training [among healthcare] professionals to screen for and recognize [sleep apnea,] failure to assess patients for [sleep apnea, and a] lack of guidelines for the care and treatment of [patients] at risk for [and those diagnosed with sleep apnea]" (Joint Commission, 2015, para. 6). Unfortunately, even if suspicion for a sleep-related problem like sleep apnea exists, there are multiple barriers to establishing a

diagnosis that might warrant symptomatic relief in the hospital. Inpatient sleep medicine consults are not always available. If a consult can be arranged, performing a diagnostic sleep study may not be feasible or tolerable. Studies are often invasive and disruptive to sleep. Supplemental oxygen used by some palliative care patients can conflict with portable sleep apnea testing equipment and it may not be feasible to accommodate a palliative care inpatient in a sleep lab if nursing support, lift equipment, or bed adjustability are lacking (Auckley, 2018).

Without the ability to fully identify and elucidate sleep-related problems such as sleep apnea or restless legs syndrome, palliative care providers may target resulting symptoms such as insomnia, dyspnea, or excessive sleepiness, rather than the underlying causative condition. This can lead to the utilization of interventions that may inadvertently worsen sleep-related problems and cause additional harm. Research with palliative care patients has demonstrated that treating insomnia with sedating medications can have limited long-term efficacy and contribute to cognitive impairment, sleep apnea, sleep walking, and excessive daytime sleepiness (Caresearch Palliative Care Knowledge Network, 2017; Zand, 2018b). In palliative care, dyspnea is sometimes managed with opioids to alleviate distress. This strategy can exacerbate confusion and trigger gasp-related arousals from sleep apnea which can then lead to panic and fearful avoidance of sleep (Bailey et al., 2010; Dahlin & Coyne, 2014). Using stimulants for excessive daytime sleepiness can cause or worsen anxiety, headaches, insomnia, appetite suppression and cardiovascular dysfunction without resolving the underlying sleep-related problem (Zand, 2018a). Additionally, caffeine can worsen restless legs syndrome (National Institute of Neurological Disorders and Stroke, 2017). As such, evidence-based means to correctly identify sleep-related problems and their appropriate treatments in palliative care patients should be utilized to alleviate symptoms and prevent additional discomfort.

Unfortunately, little sleep research has been done in palliative care, including validation studies of sleep-related instruments for use with palliative care patients (Caresearch Palliative Care Knowledge Network, 2017). Thus, knowledge of the nature, extent, and impact of sleep-related problems in this patient population is limited. Similarly, the risks, benefits, and acceptability of respective assessment and management options are not entirely known. This lack of research makes it difficult to develop evidence-based guidelines to mitigate suffering in the realm of sleep-related problems in palliative care.

Purpose

The purpose of this dissertation was to evaluate the frequency of sleep-related problems and their impact on distress and functional status among a sample of adult inpatients receiving palliative care, and to gain insight on participant willingness to accept risks or inconvenience for interventions that might alleviate sleep-related distress. Hospitalization is a time when palliative care needs may be high, risk of sleep-related problems may be elevated, and goals of care are being established. The hospital environment is an ideal setting for palliative care personnel to focus on intensive symptom monitoring and management. Understanding sleep-related problems among the inpatient palliative care population would allow for better recognition of patient needs and areas for enhanced staff competence. A pilot study was conducted to establish foundational knowledge, to elucidate feasibility and problems with studies of this nature, and to guide future research endeavors.

Specific Aims

The specific aims of the study are stated below.

1. To determine prevalence rates for four common sleep-related problems: excessive sleepiness, insomnia, restless legs syndrome, and high risk for sleep apnea.

2. To examine relationships between all measures for the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status.
3. To determine which of the sleep-related problem variables along with age and gender predict outcomes of sleep-related distress and sleep-related functional status.

Brief Description of Study

Data was collected by survey and a physical measurement of neck circumference from a sample of 38 adult inpatients receiving palliative care services. The sample was described with respect to participant demographics, contextual data, and sleep-related information including willingness to accept various risks or inconveniences to alleviate sleep-related distress. From the data, sample prevalence rates for excessive sleepiness, insomnia, high risk for sleep apnea, and restless legs syndrome were determined. Relationships between these sleep-related problems were examined to glean how one may affect another, and relationships between individual sleep-related problems and outcomes including sleep-related distress and sleep-related functional status were also examined. Pairwise associations between each of the following variables were determined: level of sleepiness, insomnia severity, sleep apnea risk score, restless legs syndrome status, sleep-related distress level and sleep-related functional status score. Two multiple regression models were constructed to look at how sleep-related problems, age, and gender might influence sleep-related distress and sleep-related functional status. For each of sleep-related distress level and sleep-related functional status score as dependent variables, a regression model was fit using level of sleepiness, insomnia severity, sleep apnea risk score, restless legs status, age, gender, and any interaction terms as independent predictors.

Critical Realism as a Philosophical Framework

The ideas of this dissertation are based on the assumptions of critical realism. Critical

realism began in the 1970's and grew from the work of philosophers including Archer, Bhaskar, Elder-Vass, Gorski, Lawson, Little, Porpora, Sayer, Steinmetz and Vandenberghe (Archer et al., 2016; Gorski, 2013). The philosophy draws from the work of Immanuel Kant's transcendental idealism (Bhaskar & Hartwig, 2010), wherein Kant believed that reality could not be known (only mentally conjured) and that human knowledge was based on socially shared judgements of empirical data (McCormick, n.d.). Critical realism shares the ideas that reality may not be known, and that knowledge is a human concoction based on research observations.

The primary tenets of critical realism include ontological realism, epistemic relativism, and judgmental rationality (Archer et al., 2016). It is assumed that there is a situational/contextual true reality, whether observable or not, and that representations of reality (i.e., knowledge) are constructed. All that can be known about reality is inference (Archer et al., 2016). As Archer et al. (2016) explain, "much of reality exists and operates independently of our awareness or knowledge of it" and it "may in fact resist articulation into theory, language, numbers, models, or empirical scrutiny" (Ontological Realism section). Judgmental rationality refers to the need to use critical reasoning to arrive at conclusions about the meaning of one's findings (Archer et al., 2016).

Critical realists recognize that reality may seem unpredictable from one circumstance to another, but this is assumed to be related to ontological stratification or underlying layers of truth/reality, in the form of interoperating mechanisms including physical, chemical, biological, psychological, historical, social, economic, and cultural processes (Archer et al., 2016; Bergin et al., 2008; Bhaskar & Hartwig, 2010). As such, observed events are not presumed to be directly linked to superficially apparent causes; rather, it is postulated that complex and often inconspicuous interactions lead to events (Bergin et al., 2008).

In critical realism, science and knowledge development are human activities that transform beliefs and improve understanding of reality, though one cannot necessarily decipher how well the resulting knowledge reflects true reality (Bhaskar & Hartwig, 2010). Bhaskar and Hartwig (2010) describe the steps of "scientific discovery" as "description of a non-random pattern in nature, …imagining a plausible model of a generative mechanism, …elimination of alternative accounts, [and] identification of the generative mechanism at work" (p. 70). Knowledge can be refined and improved over time through iteration (Archer et al., 2016; Bhaskar & Hartwig, 2010). Critique of current scientific practices and acceptance of emergent explanations that provide a better account of observations are features of critical realism.

Within the philosophical framework of critical realism, scientific knowledge is considered subject matter specific, and concepts/theories do not always transfer from one field to another (Bhaskar & Hartwig, 2010). A scientist's beliefs about what is or might be true influence the scientist's methodology for carrying out an investigation (Bhaskar & Hartwig, 2010). Methodological pluralism is embraced in critical realism (Archer et al., 2016) to gain better understanding of phenomena. Approaches may include mixed methods/triangulation utilizing statistical analyses, interviews, observation, case studies, purposive/theoretical sampling, constant comparative analysis, coding of qualitative data, thick description, thematic analysis, striving for data saturation, and reflexivity as part of ethnographic, phenomenological, or grounded theory-based studies (Archer et al., 2016; Bergin et al., 2008; D. Cohen & Crabtree, 2006; Speziale & Carpenter, 2007).

Assumptions

Below are assumptions for this dissertation, arising from a critical realist paradigm.

1. The inpatient palliative care experience is situationally/contextually based with multiple

factors affecting sleep.

2. Participants responded to questions honestly.
3. Full understanding of the phenomenon under investigation may not have been determined with this pilot study but the data provide useful information to guide future studies.

Conclusion

Good quality sleep is a vital requirement for health and well-being (Reimer & Flemons, 2003). When sleep is disturbed, people can experience negative impacts on their physical and cognitive performance, health outcomes, emotional states, and social lives. Palliative care patients deserve special attention to sleep-related issues because they are at high risk for sleep-related problems and associated negative sequelae. The central role of palliative care is to address multi-faceted aspects of the human experience in order to promote symptom relief, comfort, functional improvement, healthy relationships, and overall higher quality of life. Managing sleep-related problems is an important component of accomplishing these goals.

The delivery of palliative care during hospitalization occurs at an especially critical time when symptom management needs are high, sleep-related problems may be exacerbated, and goals of care are being established. While sleep issues are often addressed by inpatient palliative care providers as part of a comprehensive plan to alleviate distress and improve quality of life, some sleep-related problems may go unrecognized or be incompletely understood, and subsequent, well-intentioned interventions may inadvertently contribute to other problems. Sleep health in palliative care is under-researched and evidence is lacking for the best strategies to screen for and manage sleep-related problems in this population.

Conducting sleep research across the lifespan is a National Institutes of Health priority with respect to pathophysiology, mechanisms, risk factors, comorbidities, prevention, diagnosis,

treatment, healthcare improvement, and community awareness (National Institutes of Health, 2011). With this dissertation, the author strived to explore and better understand sleep-related problems, including their association with distress and functioning, and the inclination to accept risks or inconvenience for the alleviation of sleep-related distress among adult inpatients receiving palliative care. A pilot study was conducted wherein prevalence rates of common sleep-related problems were determined, and the relationships between those sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status were examined. Study procedures provided insight on the feasibility of the utilized methods with the selected population.

Critical realism provided a philosophical framework for the dissertation. Within this paradigm, it was recognized that study findings were influenced by the strategies used to obtain information and may only apply in the specific context of the phenomenon observed. Alternative circumstances and methods could reveal additional ways of understanding and interpreting the data as there may be multiple interacting layers of truth that are not obvious. The conclusions generated from this study will assist with iterative knowledge development and improved research methodology in the field of sleep health in palliative care.

Chapter 2: Relevant Concepts, Review of the Literature, and Conceptual Framework

The following chapter supports the development of a biobehavioral conceptual framework for studying sleep in palliative care. Biobehavioral aspects of sleep, common sleep-related problems, sleep-related distress, and sleep-related functional status are described. Updates on the field of palliative care and findings from palliative care research on associations between sleep-related problems and other health-related measures are then presented. This is followed by the introduction of a biobehavioral conceptual framework. Finally, implications of the preceding sections with respect to the proposed dissertation are discussed.

Biobehavioral Aspects of Sleep

Sleep is a neurobehaviorally regulated phenomenon involving temporary periods of unresponsiveness to the environment while the brain cycles through different stages of sleep as measured by an electroencephalogram (EEG). Sleep quality may be subjectively determined by a patient's perceived ability to obtain enough sleep of the appropriate depth at the needed time (Buysse et al., 1989). Good sleep has restorative and transformative properties that promote physiological and behavioral health (National Institute of Mental Health, 2012).

Underlying the neurological and behavioral aspects of sleep are numerous physiological processes. Emerging biomarkers in the field of sleep psychoneuroimmunology include the cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). Sleep deprivation raises IL-1, IL-6, and TNF levels (Irwin, 2015; Irwin et al., 2015; Krueger et al., 1995), thus enhancing their effects related to infectious and inflammatory processes which influence temperature regulation, appetite, and socialization (Besedovsky et al., 2019; Krueger et al., 1995). IL-1 and TNF are thought to act prominently in the brain as regulators of sleep by way of the endocrine and neurotransmitter systems and are associated with increased sleepiness

(Besedovsky et al., 2019; Krueger et al., 1995). Other research has shown that IL-6 and TNF have been found to be elevated in patients with sleep apnea as well as those with depression, suggesting one of many possible mechanisms between sleep-related problems and negative symptoms (Arnardottir et al., 2009; Kop et al., 2011; Prather et al., 2015; Weinberger et al., 2015; Zhou et al., 2010). As such, IL-1, IL-6, and TNF appear to work together, linking behavior with neurological and immunological function.

Common Sleep-Related Problems

The following sub-sections discuss four common sleep-related problems including excessive sleepiness, insomnia, restless legs syndrome, and sleep apnea. For each sub-section, first a definition is provided, then prevalence rates are presented. This is followed by a description of causes and treatments for each sleep-related problem.

Excessive Sleepiness

Excessive sleepiness is the propensity to fall asleep at inappropriate or undesired times. The prevalence of excessive sleepiness in the general population is 18% (Slater & Steier, 2012) but it has been found to be higher among palliative care populations. In a study of 60 participants diagnosed with advanced incurable cancer being cared for by a live-in non-professional caregiver, 26% were found to have excessive sleepiness (Gibbins et al., 2009). A study of 28 participants with advanced cancer receiving inpatient palliative care showed 36% had excessive sleepiness (Good et al., 2018).

Causes of excessive sleepiness may include insufficient sleep; neurological, psychological, cardiac, or pulmonary disorders; obesity; and sleep disorders such as sleep apnea. Excessive sleepiness has been linked to accidents, poor workplace performance, and reduced quality of life. Treatment consists of ensuring adequate rest, practicing good sleep hygiene,

managing any underlying disorder, and taking stimulant medications in refractory cases (Redeker & McEnany, 2011; Slater & Steier, 2012).

Insomnia

Insomnia is difficulty falling or staying asleep that leads to distress and/or daytime dysfunction. The prevalence of insomnia is estimated at 10-15% of the general population (Morin & Jarrin, 2013) however in patients with significant medical conditions such as heart disease, cancer, neurologic disease, and respiratory conditions prevalence rates are much higher ranging from 30 – 100% (Ancoli-Israel, 2015; Gibbins et al., 2009; Mercadante et al., 2017; Redeker & McEnany, 2011). This suggests that palliative care patients would be particularly susceptible to insomnia.

Life stressors, pain, depression, dyspnea, nocturia and other sleep disorders increase the risk for developing insomnia. Potential consequences of insomnia are decreased energy, difficulty concentrating, immune dysfunction, poor quality of life, increased healthcare costs, and injuries (Redeker & McEnany, 2011). Depression has a bidirectional relationship with insomnia, wherein each can contribute to the other (Redeker & McEnany, 2011). Treatments for insomnia include alleviation of underlying factors, taking hypnotic medications, receiving cognitive behavioral therapy, and practicing healthy sleep hygiene and relaxation exercises (Redeker & McEnany, 2011).

Restless Legs Syndrome

Restless legs syndrome (RLS) is a condition that causes nocturnal discomfort and an urge to move the limbs when motionless, thus making it difficult to initiate sleep. RLS has an estimated prevalence in the general population of 4 – 29% (Innes et al., 2011; Ohayon et al., 2012; Redeker & McEnany, 2011) but in a study of 76 palliative care clinic patients, the

prevalence was measured at 41% using a screening questionnaire (Walia et al., 2013). Contributing factors include iron-deficiency anemia, a ferritin level < 50, kidney disease, female sex, pregnancy, medications (e.g., antiemetics, antidepressants, antihistamines, and antipsychotics), caffeine, alcohol, nicotine, increased age, and a family history of RLS (Chokroverty, 2010; National Institute of Neurological Disorders and Stroke, 2017; Ohayon et al., 2012; Redeker & McEnany, 2011). RLS is associated with excessive sleepiness, poor daytime functioning, insomnia, depression, poor sleep quality, and lower quality of life (Broman et al., 2008; Molnar et al., 2007; Redeker & McEnany, 2011; Walia et al., 2013). Walia et al. (2013) specifically found that RLS is associated with reduced quality of life among palliative care patients. Treatments for RLS include iron supplementation, dopaminergic drugs, gabapentin, benzodiazepines, and addressing the underlying cause.

Sleep Apnea

Sleep apnea is a form of sleep-disordered breathing characterized by having five or more apneas and/or hypopneas per hour of sleep (American Psychiatric Association DSM-5 Task Force, 2013). Apneas are breathing pauses with complete (or nearly complete) cessation of airflow for at least ten seconds, whereas hypopneas are partial reductions in airflow for at least ten seconds with an associated oxygen desaturation of at least 3% (Collop et al., 2015; Mannarino et al., 2012; Ruehland et al., 2009). Apneas and hypopneas may be due to airway obstruction, or they may be neurologically/centrally mediated.

A small study of 28 adults with advanced cancer receiving palliative care found that 75% of participants had sleep apnea (Good et al., 2018). This compares to an estimated sleep apnea prevalence of 6 - 38% in the general population (Senaratna et al., 2017). Studies of other patient populations with characteristics commonly encountered in palliative care have also generally

shown elevated levels of sleep apnea. In studies of elderly patients, the prevalence of sleep apnea ranges from 20-60% (Netzer et al., 2016). Sleep apnea prevalence rates of 33-46% have been found among patients with heart failure (Arzt et al., 2016; Bradley & Floras, 2003) and greater than 50% among patients with severe COPD or COPD exacerbation (Shawon et al., 2017). Two studies of patients with head/neck cancer have reported sleep apnea prevalence rates of 12% (Nesse et al., 2006) and 76% (Payne et al., 2005). A study of patients with idiopathic interstitial lung disease found that 68% had sleep apnea (Mavroudi et al., 2018).

Risk factors for sleep apnea include advanced age, male sex or female postmenopausal status, obesity, reduced airway muscle tone, nasal congestion, enlarged tongue/uvula/tonsils, medication effects, neuromuscular disease, heart failure, alcohol consumption, smoking, and hypothyroidism (Mannarino et al., 2012; Senaratna et al., 2017). Symptoms and effects of sleep apnea may include snoring, nocturnal dyspnea/gasping, insomnia, excessive sleepiness, acid reflux, nocturia, nocturnal sweating, forgetfulness, decreased libido, reduced pain tolerance, dry mouth on awakening, morning headaches, depression, accidents, cerebral/cardiovascular disease, reduced functional status, and lower quality of life (American Psychiatric Association DSM-5 Task Force, 2013; Chokroverty, 2010; Onen et al., 2010; Redeker & McEnany, 2011).

Treatments for sleep apnea include treatment for any underlying contributing conditions, positive airway pressure (PAP), use of a mandibular advancement device (MAD), weight loss, positional management (e.g., avoiding supine sleep), and surgical interventions (Redeker & McEnany, 2011). After an extensive review of the literature, no studies were found examining sleep apnea treatment benefits with respect to quality of life elements among palliative care patients; however, research has shown improvements in pain tolerance, vitality, mental health, social functioning, marital satisfaction, sex life, and home management with sleep apnea

treatment in other populations (El-Sheikh et al., 2013; Onen et al., 2010; Reimer & Flemons, 2003; Troxel, 2010).

Sleep-Related Distress

The National Comprehensive Cancer Network (NCCN) has provided a definition of distress in cancer which may be applicable to the health situations experienced by palliative care patients: "Distress is a multifactorial unpleasant experience of a psychological (ie, cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with [illness], its physical symptoms, and its treatment" (Holland & Deshields, 2018, p. DIS-2). Studies have shown that more than one-third of palliative care patients experience significant distress (Gao et al., 2010; Thekkumpurath et al., 2009). Distress is linked to lower performance status (Jacobsen et al., 2005) and poor sleep (Fernandez-Mendoza et al., 2012). Sleep-related distress can be thought of as distress a person attributes to sleep-related problems.

Identifying specific causes of distress can be useful so that they can be addressed and the burden of the distress can be lessened. This is not always done in practice. Patients are often asked to rate the severity of their symptoms but not necessarily asked how much the symptoms are perceived to be bothersome. Research has shown that some symptoms rated as severe by a patient may not be as distressing as other symptoms that have been rated as less severe (Li et al., 2019). In studying 386 patients with advanced cancer, Li et al. (2019) found that while tiredness, sleep and appetite were often rated as the most severe issues, sleep and appetite were not as bothersome to patients as pain and tiredness which were considered the most bothersome symptoms. These results suggest that it is important to evaluate both the presence of sleep-related problems (i.e., excessive sleepiness, insomnia, high risk for sleep apnea, and restless legs

syndrome) as well as the perceived level of distress sleep issues generate. As such, a measure of sleep-related distress was sought in this dissertation research. Should certain sleep-related problems not contribute much to distress, then it may not be as necessary to address them as part of an overall strategy to promote quality of life in palliative care patients.

Sleep-Related Functional Status

Functional status refers to one's ability to meet basic needs and fulfill roles (Weaver et al., 1997) and is an important component to overall well-being and quality of life. Sleep-related functional status refers to one's ability to function as perceived to be impacted by sleep-related problems. Just as with sleep-related distress, it is relevant to measure sleep-related functional status alongside sleep-related problems. Should there be a strong relationship between sleep-related problems and sleep-related functional status, it would highlight an area worthy of greater research attention. It would be important to learn whether managing sleep-related problems would improve one's sleep-related functional status, and thereby increase quality of life.

Palliative Care

The World Health Organization (2019) provides an excellent definition and description of palliative care:

> Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. Palliative care:
>
> - provides relief from pain and other distressing symptoms;
> - affirms life and regards dying as a normal process;

- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patients [sic] illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
- will enhance quality of life, and may also positively influence the course of illness;
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications. (definition/description section)

This provides a solid framework for conceptualizing and understanding palliative care.

Palliative care is an evolving and expanding field. It is estimated that over 70% of hospitals have a palliative care program, with a 19% rise in the number of programs from 2008 to 2016 (Rogers & Heitner, 2018). According to recent survey results from the National Palliative Care Registry, over five percent of patients admitted to hospitals with palliative care programs receive palliative care services, with an average of three visits per patient from a member of the palliative care team. This rate of penetration is more than twice the rate observed in 2008 (Center to Advance Palliative Care & National Palliative Care Research Center, 2018a). Approximately 50% of hospitals surveyed utilized a palliative care interdisciplinary team (IDT) as required by the Joint Commission for advanced certification in palliative care. The Joint Commission defines a palliative care IDT as one that includes at least a physician, an advanced

practice or other registered nurse, a social worker, and a chaplain (Joint Commission on Accreditation of Healthcare Organizations, 2015; Rogers & Dumanovsky, 2017b).

Ninety percent of inpatient referrals for palliative care come from medical/surgical units (45%), intensive care units (24%), step-down units (13%), and oncology units (8%) with 53% of referrals being made by general hospitalists (Center to Advance Palliative Care & National Palliative Care Research Center, 2018a). While palliative care is often associated with cancer symptom management, only 26% of inpatients receiving palliative care have cancer as a primary diagnosis. Other primary diagnoses held by inpatient palliative care recipients include cardiac (15%), pulmonary (14%), neurological (9%), and infectious (7%) conditions (Center to Advance Palliative Care & National Palliative Care Research Center, 2018a). Palliative care patients have an average hospital length of stay of 10.4 days with 78% of patients being discharged from the hospital alive (Rogers & Dumanovsky, 2017a). Of those discharged alive, 26% go to a skilled nursing facility while 47% return to their homes. Roughly one-third of those that return home do so to receive home hospice care (Rogers & Dumanovsky, 2017b).

Adults make up the vast majority of palliative care patients, with only 0.2% of palliative care inpatients being under the age of 18 years. The elderly are the most likely to receive palliative care services however, adults between the age of 18 and 64 years make up 26.3% of the inpatient palliative care population (Center to Advance Palliative Care & National Palliative Care Research Center, 2018b). Females make up 51.5% of palliative care inpatients. Ethnic groups primarily receiving inpatient palliative care include white/Caucasian non-Hispanic (74.8%), black/African American non-Hispanic (13.4%), Hispanic/Latino (5.9%), and Asian non-Hispanic (2.6%) (Center to Advance Palliative Care & National Palliative Care Research Center, 2018b).

Inpatient palliative care has been shown to benefit patients by improving symptoms, quality of life, and satisfaction with care while reducing caregiver burden and family distress (Center for Advance Palliative Care & National Palliative Care Research Center, 2019; Smith et al., 2015). Palliative care is also associated with improved survival in some studies (Bakitas et al., 2015; Center for Advance Palliative Care & National Palliative Care Research Center, 2019; Temel et al., 2010). Despite this, palliative care has been shown to reduce healthcare costs and hospital length of stay without increasing mortality (Aslakson et al., 2014; Center for Advance Palliative Care & National Palliative Care Research Center, 2019; Fitzpatrick et al., 2018; May et al., 2018).

Spiritual care is a perceived area of weakness in palliative care (Center for Advance Palliative Care & National Palliative Care Research Center, 2019) and may be affected by sleep-related problems. Closely tied to quality of life, concepts related to spirituality include meaning, purpose, appreciation, healthy relationships, hope, self-acceptance, and peace (Chochinov & Cann, 2005; Edwards et al., 2010). Within relationships, patients want to feel loved while also providing support and care to others (Edwards et al., 2010). Many patients wish to maintain control over their lives and hope to accomplish important goals, such as financial and emotional preparation for the end of life (Edwards et al., 2010). To meet spiritual needs, patients often attempt to enjoy pleasurable activities with loved ones, including reviewing one's life or seeking out humor (Edwards et al., 2010). While receiving palliative care, there may be times of enhanced meaning and desire to make things special and memorable in positive and constructive ways. Loved ones may wish to bond by gathering for worship, watching a favorite movie together, or spending time romantically. In some cases, people have chosen to get married just prior to the expected death of oneself or one's partner. Lack of adequate spiritual well-being can

contribute to spiritual distress, anger, fear, depression, helplessness, despair, physical symptoms, and impaired quality of relationships (Chochinov & Cann, 2005; Edwards et al., 2010).

Meeting the spiritual needs of palliative care patients may be complicated by the ramifications of sleep-related problems. Excessive sleepiness, reduced functional status, and sleep-related distress may reduce capacity and motivation to achieve desired spiritual goals, thereby reducing hope, joy and spiritual fulfillment that had previously brought comfort (Chochinov & Cann, 2005; Edwards et al., 2010). As such, assessing for and promoting healthy sleep among palliative care patients is relevant to providing good spiritual care and enhancing quality of life.

Review of the Literature

Publications regarding sleep research with palliative care patients are limited. A search of PubMed, CINAHL Complete and Psychology and Behavioral Sciences Collection (PBSC) using EBSCOhost Research Databases was conducted using keywords and MeSH/subject headings related to palliative care, hospice, cancer and sleep to locate articles evaluating the presence of sleep-related problems and their association with other health-related measures of symptoms, distress, functional status and/or quality of life among those receiving palliative care and/or patients with advanced cancer. Additional relevant articles were found by reviewing reference lists of initial articles located and by reviewing various database suggestions for related articles. Advanced cancer patients were of interest because they are more likely to be receiving palliative care, either formally by a palliative care specialist or informally by an oncologist or other provider. Just as in palliative care, sleep research is limited among advanced cancer patients with many studies focusing on earlier stages of cancer (Akechi et al., 2007).

In all, twenty relevant articles written in English were located. Unfortunately, though the

term “advanced cancer” was frequently used by authors, it was typically not defined. One exception was a definition of advanced cancer offered by Delgado-Guay et al. (2011), “…cancer that is metastatic or recurrent” (p. 821). One article by Nishiura et al. (2014) involving inpatients with lung cancer did not specify whether patients were considered to have advanced cancer or were receiving palliative care, but it was reviewed because it was published in a palliative care journal and the patients were likely dealing with significant symptom management as part of the need for hospitalization.

Though there were twenty articles, some involved secondary data analyses related to an earlier included publication. As such, 16 distinct sets of research participants were identified with research having been conducted in the following countries: the United States, Canada, Greece, Spain, Italy, the United Kingdom, Australia, and Japan. As a whole, the studies involved five groups of participants in the outpatient setting, seven in the inpatient setting, one in a hospice setting, and three in a mixed or unknown setting. Thirteen of the 16 groups were identified as palliative care or hospice patients. Eleven of 16 groups of participants focused specifically on cancer patients. Patients with cognitive impairment were excluded from nine of the 16 groups.

The largest study was by Mercadante et al. (2015) including 820 participants with advanced cancer across a variety of palliative care settings including oncology, home care, palliative care unit and hospice. This study found that 60.8% of patients experienced moderate to maximum levels of insomnia as defined by elevated scores on the Athens Insomnia Scale. They also found that low functional status based on Karnofsky Performance Status Scale scores, depression/anxiety based on the HADS, and certain medication use (opioids, corticosteroids, and hormone therapy) were associated with insomnia.

The next largest study involved 442 participants. Yennurajalingam et al. (2015) studied advanced cancer patients receiving outpatient palliative care, finding that 75% had sleep disturbance as defined by a score of three or greater on an Edmonton Symptom Assessment Scale (ESAS) sleep item score. Higher sleep disturbance intensity was associated with pain and fatigue based on other ESAS item scores.

Mercadante et al. (2017) studied 219 patients with advanced cancer admitted to a palliative care unit, finding that all patients met criteria for insomnia using the Athens Insomnia Scale with 84% experiencing severe levels of insomnia. Insomnia was positively associated with lower functional status, weakness, anorexia, drowsiness, depression, and anxiety based on Karnofsky Performance Status Scale, Edmonton Symptom Assessment System items, and Hospital Anxiety and Depression Scale scores.

Akechi et al. (2007) did a longitudinal study of 209 terminally ill cancer patients looking at prevalence of sleep disturbance upon registration with a palliative care unit and following up within a week of admission to the unit. Sleep disturbance was defined as "insomnia or hypersomnia nearly every day for at least 2 weeks" (p. 889) using the major depressive episode module of the Structured Clinical Interview for DSM-IIIR. At baseline 15.3% of patients experienced sleep disturbance which was significantly associated with younger age, distress, pain, diarrhea, being single and living alone. At follow up, 67% of patients had a change in sleep disturbance status with the overall prevalence of sleep disturbance increasing to 25.9%. It was determined that an increase in distress, based on the total score of the Japanese version of the Hospital Anxiety and Depression Scale (HADS), was a factor for the development of sleep disturbance from baseline to follow up.

Yennurajalingam et al. (2017) and Yennurajalingam et al. (2018) studied a group of 180

advanced cancer patients admitted to a cancer unit for at least 24 hours, looking at sleep apnea, restless legs syndrome and drowsiness. The data from these studies showed that 61% of participants were at high risk for sleep apnea based on a STOP-Bang Questionnaire score of three or more. Sleep apnea risk did not appear to be associated with sleep quality scores on the Pittsburgh Sleep Quality Index. The data also found an estimated prevalence of restless legs syndrome of 38% based on a single item question. Drowsiness based on the ESAS drowsiness item was associated with pain, fatigue, depression, anxiety, dyspnea, and anorexia according to these other ESAS item scores. Drowsiness as measured with the ESAS drowsiness item was associated with drowsiness as measured by the Epworth Sleepiness Scale. Their results are questionable though because researchers excluded patients with a score of zero on an "other" item of the ESAS which was designated as a sleep disturbance item.

Mercadante et al. (2004) studied 123 patients admitted to a pain relief and palliative care unit finding that a short total sleep time of less than 5 hours was associated with anxiety and nightmares, without being associated with functional status or depression. Functional status was measured with the Karnofsky Performance Status Scale while the other variables were measured using a custom questionnaire.

Mystakidou, Parpa, Tsilika, Galanos, et al., (2009); Mystakidou, Parpa, Tsilika, Pathiaki, Galanos, et al., (2007); Mystakidou, Parpa, Tsilika, Pathiaki, Gennatas, et al., (2007); and Mystakidou, Parpa, Tsilika, Pathiaki, Patiraki, et al., (2007) studied 102 advanced cancer patients with stage four cancer receiving palliative care. Seventy-four percent were found to have poor quality of sleep as defined by a score of greater than eight on the Greek version of the Pittsburgh Sleep Quality Index. Having worse quality sleep was associated with hopelessness, depression, worse quality of life, pain, worse functional status, and a desire for hastened death based on

results from the following respective instruments: Beck Hopelessness Scale, Greek Beck Depression Inventory, Medical Outcomes Study 12-item short form, Greek Brief Pain Inventory and a pain visual analogue scale, Eastern Cooperative Oncology Group performance status scoring, and Greek Schedule of Attitudes Toward Hastened Death.

Delgado-Guay et al. (2011) studied 101 advanced cancer patients receiving outpatient palliative care and found 85% had poor quality of sleep as defined by a score five or greater on the Pittsburgh Sleep Quality Index (PSQI). Those with poor quality of sleep were more likely to have worse depression and anxiety ESAS item scores compared to those with PSQI scores of less than five. Poorer quality of sleep was also associated with pain and dyspnea based on ESAS item scores.

Sela et al. (2005) studied 100 palliative oncology outpatients with incurable cancer. Participants were asked to rate various sleep-related concerns from zero to ten with five or greater representing evidence of a sleep disturbance. Sixty-three percent met sleep disturbance criteria related to difficulty staying asleep, 40% met sleep disturbance criteria related to difficulty falling asleep and 37% met sleep disturbance criteria related to early awakening. Each of these insomnia-related conditions was found to be associated with fatigue and pain according to fatigue and pain ESAS item scores. Interestingly, having a score of five or greater with respect to concern over one's sleep was associated with each of the three insomnia-related conditions but not with ESAS item scores for fatigue, pain, depression, or anxiety.

Mystakidou, Parpa, Tsilika, Gennatas, et al. (2009) studied a mixture of 82 inpatients and outpatients with advanced cancer receiving care at a palliative care center. Ninety-six percent were rated as having poor quality sleep according to a PSQI of five or greater. In this study, poor quality sleep was found to be associated with worse quality of life, depression, hopelessness, and

post-traumatic experience according to the following respective instruments: 12-item Short Form Health Survey, Greek Beck Depression Inventory, Beck Hopelessness Scale, and Impact of Event Scale - Revised.

Walia et al. (2013) studied 76 palliative care clinic patients, of which many were being seen for chronic pain rather than cancer. Based on a four-item questionnaire considering the essential diagnostic criteria of restless legs syndrome (without considering possible mimics of restless legs syndrome), 41% were considered to have restless legs syndrome. The researchers found that having restless legs syndrome was associated with a lower health-related quality of life based on the mental component score but not the physical component score of the 12-item Short Form Health Survey.

Hugel et al., (2004) studied 74 hospice patients finding that 70% complained of trouble sleeping based the answer to a single question and reported that 60% of participants experienced difficulty with sleep due to physical problems whereas 36% of participants struggled due to worry.

Renom-Guiteras et al. (2014) studied 61 patients admitted to a palliative care unit and found that 62% complained of insomnia, 74% complained of daytime sleepiness, 53% complained of non-restorative sleep, and 26% complained of nightmares based on the answer to a single question for each issue. Having insomnia was found to be associated with anxiety but not depression according to the HADS. Insomnia was also associated with a higher functional status as determined by the Karnofsky Performance Status Scale.

Gibbins et al. (2009) studied 60 patients with advanced incurable cancer. Poor sleep was assessed with a single question and found to be a problem among 47% of participants. Poor sleep was associated with pain according to the Short Form-36 and anxiety according to the HADS.

Nishiura et al. (2014) studied 50 inpatient lung cancer patients. They found that insomnia, measured by using the Athens Insomnia Scale, was associated with worse quality of life, pain, and fatigue according to European Organization of Research and Treatment Quality of Life Questionnaire – Cancer 30 scores. They also found that insomnia was associated with distress as measured by the HADS.

Good et al. (2018) studied 28 advanced cancer patients admitted to a palliative care service. Twenty-one participants were found have sleep apnea based on polysomnography, with ten meeting criteria for severe sleep apnea as categorized by an apnea-hypopnea index greater than 30. Only 12 of the 28 participants had been considered high risk for sleep apnea according to scoring on the Berlin Questionnaire. The researchers did not find significant associations between a diagnosis of sleep apnea by polysomnogram and excessive sleepiness by the Epworth Sleepiness Scale, fatigue by the Wu Index or anxiety/depression by the HADS.

Altogether, the cited research has shown that palliative care and advanced cancer patients have higher prevalence rates of common sleep-related problems compared to the general population with 38-41% found to have RLS (Walia et al., 2013; Yennurajalingam et al., 2017; Yennurajalingam et al., 2018), 26-36% found to have excessive sleepiness (Gibbins et al., 2009; Good et al., 2018), 37-100% found to have insomnia (Mercadante et al., 2015, 2017; Renom-Guiteras et al., 2014; Sela et al., 2005), and 43-75% found to have sleep apnea or high risk for it (Good et al., 2018; Yennurajalingam et al., 2017; Yennurajalingam et al., 2018). Some studies measured general sleep quality with the PSQI finding that 74-96% of participants had poor quality sleep based on PSQI score, and poor quality sleep was associated with hopelessness, depression, anxiety, post-traumatic experience, pain, dyspnea, worse quality of life, worse functional status, and a desire for hastened death (Delgado-Guay et al., 2011; Mystakidou, Parpa,

Tsilika, Galanos, et al., 2009; Mystakidou, Parpa, Tsilika, Gennatas, et al., 2009; Mystakidou, Parpa, Tsilika, Pathiaki, Galanos, et al., 2007; Mystakidou, Parpa, Tsilika, Pathiaki, Gennatas, et al., 2007; Mystakidou, Parpa, Tsilika, Pathiaki, Patiraki, et al., 2007). Insomnia was found to be associated with lower functional status, distress, worse quality of life, depression, anxiety, fatigue, pain, weakness, anorexia, and drowsiness (Mercadante et al., 2015, 2017; Nishiura et al., 2014; Sela et al., 2005). Excessive sleepiness was found to be associated with pain, fatigue, depression, anxiety, dyspnea, and anorexia (Yennurajalingam et al., 2017; Yennurajalingam et al., 2018). RLS was found to be associated with a lower health-related quality of life (Walia et al., 2013). No significant associations were found between sleep apnea and excessive sleepiness, fatigue, anxiety, or depression based on the study by Good et al. (2018).

Several limitations prevent generalizability of the results of these studies to the broad palliative care population. Some studies had small sample sizes and patient characteristics varied from study to study. Also, studies often measured sleep-related problems and other health-related outcomes with disparate instruments or non-standardized questions. Means for measurement were not always proven to be valid and reliable for the patient populations being studied. Studies often excluded patients with significant cognitive/psychiatric conditions and those deemed to be too ill to participate. Given the potential associations that sleep-related problems have with mental health conditions and physical illness, these exclusion criteria may have resulted in an underestimate of the true prevalence of sleep-related problems among palliative care and advanced cancer patients.

Biobehavioral Conceptual Framework for Sleep in Palliative Care

Sleep is a truly biobehavioral phenomenon involving strong links between neurology, immunology, and behavior. Palliative care patients carry a high risk for sleep-related problems

which may affect psychoneuroimmunologic pathways and a broad range of outcomes including symptoms, psychological factors, sleep quality, quality of life and functional status. Specifically, the research has shown that there are numerous links between various sleep-related problems and other distressing concerns among palliative care and advanced cancer patients including pain, anxiety, fatigue, diarrhea, weakness, drowsiness, post-traumatic experience, worse functional status, depression, reduced quality of life, anorexia, hopelessness, dyspnea, and desire for hastened death.

As a theoretical starting point and guide for determining methodology, this dissertation draws from two relevant models in the literature proposed by Redeker and Hedges (2002) and McCain et al. (2005). Redeker and Hedges (2002) present a model describing the environmental and situational influences on sleep during acute care recovery from coronary artery bypass surgery that might be applicable to palliative care patients. At the center of the model is the concept of sleep which is comprised of elements including quantity, continuity, diurnal timing, and depth. Surrounding the central concept of sleep are factors that influence sleep in the acute care recovery setting. The authors determined that some factors influence sleep without being affected themselves by the nature of sleep. These include age, gender, underlying health/illnesses, primary sleep disorders, the hospital environment, and treatments received. There are other factors which have a bidirectional relationship with sleep in that the nature of sleep experienced can influence change in those factors. The authors assert bidirectional interactions between sleep and the following factors: symptoms (e.g., pain, fatigue, dyspnea), emotional distress, functional status, quality of life and physiologic function.

The reported basis for the model by Redeker and Hedges (2002) is empirical data stemming from the literature as well as research conducted by the first author. According to

Redeker and Hedges (2002), studies have shown that the greater the number of factors disturbing sleep, the worse patients report their sleep being. Often in the acute care recovery stage after coronary artery bypass there is a high concentration of environmental noises (e.g., alarms, staff interactions) and healthcare interventions to manage post-operative issues. These have a strong influence on sleep. Some healthcare interventions may improve sleep by alleviating uncomfortable symptoms such as pain while others may disturb sleep such as vital sign monitoring and blood draws. Among palliative care patients, the balance between positive and negative influences on sleep may vary depending on the setting, the patient's physiologic/emotional status, and the goals of care.

The psychoneuroimmunology (PNI) model by McCain et al. (2005) provides an excellent guide to develop a conceptual framework for sleep and health-related phenomena in palliative care. The PNI model provides a holistic integration of factors affecting health dynamics including co-factors (e.g., age, gender, severity of illness, treatment adherence, treatment side effects), psychosocial moderators (e.g., affect, perceived stress, coping), biological mediators (e.g., immune, endocrine, and neurologic function), the lived experience (e.g., sociocultural and economic influences) and adaptational outcomes (e.g., psychosocial functioning, quality of life and physical health). The adaptational outcomes provide feedback to other aspects of the PNI model and may thereby influence treatment-related co-factors, psychosocial moderators, and biological mediators.

Tying in the reviewed findings from the palliative care literature, the Biobehavioral Conceptual Framework for Sleep in Palliative Care was constructed and is shown in Figure A1 (Appendix). The framework is informed by the PNI model of McCain et al. (2005) and incorporates aspects of the model of sleep during acute care recovery by Redeker and Hedges

(2002). This new framework represents the complex interactions between conceptual variables associated with sleep-related problems and other health-related outcomes among palliative care patients. Co-factors include age, gender, race, the state/severity of physical illness, palliative care interventions/effects, and sleep disorder risk factors. These have an impact on symptoms (sleep-related/other), psychosocial moderators (distress, affect, and coping) and biological mediators (sleep stages/fragmentation as reflected by encephalogram (EEG), sleep related biomarkers, and oxygen levels during sleep) which then affect adaptational outcomes (sleep quality, quality of life, and functional status). Symptoms and psychosocial moderators influence each other, while together interacting bidirectionally with biological mediators. Adaptational outcomes feed back into the intertwined system of symptoms, psychosocial moderators, and biological mediators. All variables/interactions occur within the context of socioeconomic and cultural factors.

Implications for the Dissertation

One might expect prevalence rates of sleep-related problems to be higher in the palliative care population than the general population, and the literature suggested this to be true for excessive sleepiness, insomnia, restless legs syndrome and sleep apnea. Due to the small amount of published data and limitations of the studies, current understanding of the nature of sleep-related problems and their true impact among palliative care patients is limited. As such, clinicians have difficult choices to make when selecting strategies to reduce suffering caused by sleep-related problems.

It is known that both obstructive sleep apnea and restless legs syndrome can both contribute to insomnia and excessive sleepiness (American Psychiatric Association DSM-5 Task Force, 2013; Broman et al., 2008; Chokroverty, 2010; Molnar et al., 2007; Onen et al., 2010; Redeker & McEnany, 2011). While these links have not been confirmed adequately with

palliative care patients, there is concern that certain treatments targeting insomnia (e.g., sedating medications) or excessive sleepiness (e.g., stimulants) may contribute to the worsening of sleep apnea or restless legs syndrome, respectively. Thus, in essence, some treatments could lead to a vicious cycle that deepens the negative impact of a sleep-related problem. It would be useful to know if symptoms of insomnia or excessive sleepiness might be associated with sleep apnea and/or restless legs syndrome among palliative care patients so that clinicians can consider this possibility when assessing for sleep-related problems. This would best allow clinicians to determine appropriate management strategies.

The Biobehavioral Conceptual Framework for Sleep in Palliative Care can assist investigators with the formulation of research questions and the identification of links between the proposed co-factors, symptoms, psychosocial moderators, biological mediators and adaptational outcomes of the framework. The specific elements of the overarching framework that were the foci of this dissertation are shown in Figure A2 (Appendix). A pilot study was conducted to examine the prevalence of and relationships between excessive sleepiness, insomnia, high risk for sleep apnea, and restless legs syndrome to increase our understanding of the relative importance of these sleep-related problems and their relationships with each other among adult inpatients receiving palliative care. The pilot study also examined relationships between the measured sleep-related problems, sleep-related distress, and sleep-related functional status.

Identifying causes of distress and functional impairment are important goals of palliative care so that contributing factors can be addressed, negative impacts can be ameliorated, and quality of life can be improved. Previous studies with palliative care patients have looked at associations between sleep-related problems and generalized measures of distress and functional

status, however, whether any identified associations reflect a true or direct relationship remains uncertain due to the numerous confounding factors present in the palliative care population. A patient's overall distress could easily be due physical pain or fear related to having a life-threatening illness. The pain or anxiety may prevent the patient from getting adequate sleep, and the patient may score high on an insomnia rating scale. This does not necessarily mean that insomnia is influencing distress. This dissertation will look at adult palliative care inpatients' perceptions of how sleep-related problems specifically factor into distress and functional status by using sleep-focused instruments including the Sleep-Related Distress Thermometer adapted from the National Comprehensive Cancer Network Distress Thermometer and the Functional Outcomes of Sleep Questionnaire – 10 (Chasens et al., 2009; National Comprehensive Cancer Network, 2018; Roth et al., 1998). Although sleep-related distress is depicted as a psychosocial moderator in the Biobehavioral Conceptual Framework for Sleep in Palliative Care, in this study it will be considered as an outcome. This will enhance awareness of the level of importance of sleep-related problems as influencers of distress and functional status.

Chapter 3: Methods

There is limited research on sleep-related problems, their causes, and their impact among palliative care patients. This study explored sleep-related problems in a sample of adults receiving palliative care in an inpatient setting. The aims were: 1) To determine prevalence rates for four common sleep-related problems: excessive sleepiness, insomnia, restless legs syndrome, and high risk for sleep apnea; 2) To examine relationships between all measures for the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status; and 3) To determine which of the sleep-related problem variables along with age and gender predict outcomes of sleep-related distress and sleep-related functional status.

Research Design

A descriptive, correlational, cross-sectional design was used to address the specific aims. A prospective study was necessary because of a lack of data previously collected relevant to the aims. A descriptive, as opposed to an interventional, study was warranted given the limited knowledge regarding the prevalence of the measured sleep-related problems and the lack of studies showing a connection between sleep-related problems and the outcomes of sleep-related distress and sleep-related functional status in the selected population. A cross-sectional design was selected in order to maximize the number of participants surveyed in a heterogeneous sample, which may allow for better likelihood of generalization of the findings among the adult inpatient palliative care population.

Setting

The study was conducted at the Virginia Commonwealth University Health System (VCUHS) hospitals in downtown Richmond, Virginia which is an 865-bed urban academic medical center and Level I trauma center (VCU Health, 2019) with an inpatient palliative care

unit and palliative care consultation service available to all other inpatients. This location has a large number of inpatient palliative care patients for potential recruitment, and inpatients reflect a wide diversity as the facility serves a large urban area surrounded by suburbs and sprawling rural areas.

Sample Population

The goal was to include a varied selection and sufficiently large sample of the adult inpatient palliative care population appropriate for the planned data analysis procedures. This would provide initial insights into what these patients may be experiencing with respect to sleep-related problems, sleep-related distress, and sleep-related functional status in conjunction with their current situation as recipients of palliative care services. This could provide guidance for future studies to focus on areas in need of attention to improve care for palliative care patients.

Study Eligibility

Inclusion criteria were: (a) inpatient status, (b) receiving direct or consultative services from a VCUHS palliative care provider while hospitalized, (c) age of at least 18 years, (d) able to communicate fluently in English, and (e) deemed to have independent decision-making capacity by the healthcare team. Inpatients receiving palliative care services were excluded from participation if they: (a) were known to be pregnant, (b) were prisoners, (c) had isolation precautions ordered, or (d) did not meet inclusion criteria.

Sample Size

To accomplish the aims of this study, proportions, two-tailed two-sample t-tests, correlational analyses, and multiple regression models were utilized (see Data Analysis Plan below). It is possible to calculate appropriate sample sizes that would increase the likelihood of identifying significant findings from the planned statistical tests if power, effect size, and

significance level are known (Abramowitz & Stegun, 1965; Chinese University of Hong Kong Centre for Clinical Research and Biostatistics, 2019; J. Cohen, 1988; J. Cohen et al., 2003; Kohn et al., 2019; Queensland Facility for Advanced Bioinformatics, 2019; Soper, 2019). Unfortunately, ideal effect sizes relating to group differences and variances for the population of interest are not known. For a larger study, robust sample sizes for estimating the prevalence of sleep-related problems would be 200-250, whereas 150-200 participants would be appropriate for the proposed multiple regression models (R.K. Elswick, personal communication, September 17, 2019). Because correlation tests and t-tests can be similarly powered using smaller sample sizes than multiple regression models, a sample size of at least 150 would also be adequate for the proposed correlation test and t-tests.

As this dissertation was a pilot study, a sample size of 40 was sought with an anticipated timeframe of up to three months for data collection, assuming recruitment of an average of three participants per week. Prior to the start of the study, a nurse practitioner on the VCUHS palliative care team had estimated that on a weekly basis approximately 10 inpatients receiving palliative care services at VCUHS would meet study inclusion criteria without meeting exclusion criteria. If 30% of those eligible for participation in the study agreed to participate, three months of data collection would yield a sample size of approximately 40. A sample size of 40 was thought to be enough to enable meaningful results while exploring feasibility of the study's components prior to conducting a larger study with a greater number of participants. As such, it would allow for the gathering of substantial data that could be used to initially estimate prevalence of sleep-related problems, assess relationship trends between sleep-related problem and outcome measures, and identify issues related to the research design.

Human Rights Protections

Virginia Commonwealth University (VCU) Institutional Review Board approval was obtained for all aspects of the study and all participant data were maintained confidentially. Age data was collected in years for those participants 18 – 89 years of age and recorded as 89 years old for anyone over 89 years old. This prevents the collection of identifiable private health information in order to protect participants. Consent forms were kept in a locked file drawer within the VCU School of Nursing. Paper study data was kept in a locked file drawer, separate from the locked drawer containing consent forms. Electronic data were stored securely within a password protected Research Electronic Data Capture (REDCap) (Harris, Taylor, Minor, et al., 2019; Harris, Taylor, Thielke, et al., 2009) account maintained by VCU. Study data was identifiable only by participant enrollment number (e.g., 101, 102, 103, etc.). Only the research team had access to the locked file drawers and REDCap account. Consent forms and study data will continue to be securely stored for the minimum time required by the VCU Data Retention Policy. After that time, the consent forms and study data will be destroyed.

Participant Recruitment

To identify potential participants, several days per week, information on adults receiving inpatient palliative care services was obtained by written or spoken communications from VCUHS palliative care team providers. Capacity for independent decision-making was verified with the person's healthcare team. The researcher introduced herself, including her role as a researcher and nursing Ph.D. student, to potential participants and explained that she was recruiting hospitalized adults for a study about sleep-related issues among inpatients receiving palliative care services. The researcher asked the person if he or she was interested in learning about participation in the study. If the person was interested, the researcher screened the patient to determine eligibility. If the patient was eligible to participate, the researcher verbally reviewed

the consent form. Those interested in participating were asked to sign the consent form after they had had a chance to review the entire form and have any questions answered. Upon signing the consent form, participants were given an enrollment number (e.g., 101, 102, 103, etc.) which were assigned sequentially and used to identify individual participant data.

Study Measures

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS), a reliable and valid instrument that is widely utilized and translated, was used to measure excessive sleepiness (Johns, 1991; Schotland, 2014). This instrument contains 8 items and allows participants to rate their chance of dozing from 0 ("would never dose") to 3 ("high chance of dozing") in the following situations: "sitting and reading," "watching TV," "sitting, inactive in a public place," "as a passenger in a car for an hour," "lying down to rest in the afternoon," "sitting and talking to someone," "sitting quietly after lunch without alcohol," and "in a car, while stopped for a few minutes in traffic." Possible scores range from 0 – 24 with higher scores indicating worse sleepiness and a score >10 indicating excessive sleepiness. The ESS has shown good test-retest reliability (r = 0.82) (Johns, 1992), internal consistency (Cronbach's alphas 0.73 - 0.88) (Johns, 1992; Kendzerska et al., 2014), and a single factor with factor analysis of item scores when tested in adults (Johns, 1992). A study with sleep clinic patients needing a multiple sleep latency test (MSLT) showed some correlation (rho = -0.37) between the MSLT and the ESS (Chervin et al., 1997). A study with older men found adequate internal consistency (Cronbach's alpha = 0.70) and construct validity when comparing the ESS with actigraphy and the Pittsburgh Sleep Quality Index (Spira et al., 2012).

Insomnia Severity Index

The Insomnia Severity Index (ISI) (Morin, 1993) was used to measure insomnia. It is a well-known, valid, and reliable instrument for assessing insomnia status in adults, and like the ESS, it has been translated for use in multiple languages (Bastien et al., 2001; Beckford, 2016). It is composed of seven items with rating scales ranging from 0 to 4, with different response options depending on the item. Items pertain to difficulty falling and staying asleep, waking up too early, satisfaction with sleep, sleep problem interference with functioning, impairment of quality of life, and distress. Total scores can range from 0 – 28 with higher scores indicating more problematic insomnia and a score >7 indicating presence of insomnia (Bastien et al., 2001). It has been shown to have internal consistency (Cronbach's alpha 0.75-0.92), convergent validity with the Pittsburgh Sleep Quality Index (PSQI) (r = 0.80), and criterion validity when compared to semi-structured interviews among adults (Albougami & Manzar, 2019; Gagnon et al., 2013; Morin et al., 2011). The ISI has also performed well with respect to internal consistency, temporal stability, sensitivity to change, and construct validity among a population of cancer patients (Savard et al., 2005).

International Restless Legs Syndrome Study Group (IRLSSG) Revised Consensus Diagnostic Criteria for Restless Legs Syndrome

The International Restless Legs Syndrome Study Group (IRLSSG) developed revised consensus diagnostic criteria for clinically significant restless legs syndrome (RLS) in 2012 and these were used to assess for the presence RLS in this study. According to the IRLSSG, clinically significant RLS involves having "an urge to move the legs usually but not always accompanied by, or felt to be caused by, uncomfortable and unpleasant sensations in the legs" (Allen et al., 2014, p. 861). Furthermore, the leg symptoms

- must “begin or worsen during periods of rest or inactivity such as lying down or sitting”;
- “are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues”, however “when symptoms are very severe, relief by activity may not be noticeable but must have been previously present”;
- “only occur or are worse in the evening or night”, however “when symptoms are very severe, the worsening in the evening or night may not be noticeable but must have been previously present”;
- are “not solely accounted for as symptoms primary to another medical or behavioral condition”; and
- “cause significant distress or impairment in social, occupational, educational or other important areas of functioning by the impact on sleep, energy/vitality, daily activities, behavior, cognition or mood.” (Allen et al., 2014, p. 861)

Participants were interviewed regarding the IRLSSG revised consensus diagnostic criteria above, and those affirming all items as having occurred within the past month were considered to have RLS.

Methods for identifying the presence of RLS vary greatly across studies (Innes et al., 2011; Ohayon et al., 2012) and often have significant challenges associated with their use in the palliative care population. This is due to the complex nature of RLS and its potential diagnostic mimics. Examples of RLS mimics include anxiety, neuropathic pain, myalgia, venous stasis, leg edema, arthritis, leg cramps, positional discomfort, and habitual foot tapping (Allen et al., 2014; Walters et al., 2014); and many of these conditions may be particularly relevant to palliative care patients. Given the lack of a standardized instrument to determine RLS status and no instrument

that has been validated for use with palliative care patients, careful consideration of the 2012 IRLSSG revised consensus diagnostic criteria for clinically significant RLS by a practitioner skilled at the diagnosis and management of RLS is appropriate for assessing the prevalence of RLS in this population. For those reasons, and because the student researcher had had multiple years of clinical experience as a sleep disorders nurse practitioner, the respective criteria were used to evaluate RLS status.

STOP-Bang Questionnaire

The STOP-Bang Questionnaire (STOP-Bang), a frequently used instrument that has been validated for use in multiple languages, was used to measure risk for sleep apnea (Chung et al., 2008; Sadeghniiat-Haghighi et al., 2015; Ursavaş et al., 2018). It is comprised of eight yes or no questions regarding sleep apnea risk factors related to snoring, tiredness, observed apneas during sleep, the presence of hypertension, body mass index, age, neck circumference, and sex. One point is given for each positive risk factor with total scores ranging from 0 – 8. Three or more yes responses suggest a high risk for sleep apnea. In a meta-analysis of 11 studies with 3175 sleep clinic patients with a sleep apnea prevalence of 85%, the STOP-Bang was found to have a pooled sensitivity of 90%, specificity of 49%, positive predictive value of 91% and negative predictive value of 46% (Nagappa et al., 2015). Nagappa et al. (2015) also determined from pooled data from two studies of 923 surgical patients with a sleep apnea prevalence of 68% that the STOP-Bang had a sensitivity of 84%, specificity of 43%, positive predictive value of 76% and negative predictive value of 55%. In a study of 123 asthma patients, with a 37% prevalence of moderate or severe sleep apnea (AHI >= 15), the STOP-Bang had a sensitivity of 84%, specificity of 80%, positive predictive value of 70%, and negative predictive value of 90% (Lu et al., 2017). A study of 100 male commercial drivers with a sleep apnea prevalence of 57% found

that the STOP-Bang had good test-retest reliability (Cohen's K = 0.89) (Popević et al., 2017). A validated Chinese version of the STOP-Bang has also shown good test-retest reliability (r = 0.85) (Hu et al., 2019). A validated Arabic version of the STOP-Bang has been shown to have internal consistency (Cronbach's alpha = 0.7) (BaHammam et al., 2015). The STOP-Bang has been shown to be more accurate a predictor of sleep apnea compared to alternative methods frequently used to screen for sleep apnea including the STOP Questionnaire, Berlin Questionnaire and Epworth Sleepiness Scale (Chiu et al., 2017; Luo et al., 2014).

Sleep-Related Distress Thermometer

The Distress Thermometer (DT), a commonly used instrument validated to measure distress in patients with cancer (Donovan et al., 2014; National Comprehensive Cancer Network, 2018; Roth et al., 1998; Snowden et al., 2011; Yeh et al., 2014), was adapted to a Sleep-Related Distress Thermometer (SDT) by asking research participants to consider distress attributed only to sleep-related difficulties within the past week. The SDT was used to measure sleep-related distress level as a continuous variable which was used for correlational analyses and for consideration as a dependent variable in a multiple regression model. In the same manner as the DT, the SDT has participants indicate their level of distress on a scale set within a thermometer image, with levels ranging from 0 (no distress) to 10 (extreme distress). While the SDT has not been previously validated, the traditional DT has been found to have criterion-related validity when compared to the Hospital Anxiety and Depression Scale (HADS), the General Health Questionnaire-12 (GHQ-12), and the Brief Symptom Inventory-18 (BSI-18), with scores changing together in the same direction over time (Gessler et al., 2008).

Functional Outcomes of Sleep Questionnaire – 10

The Functional Outcomes of Sleep Questionnaire – 10 (FOSQ-10) was used to measure sleep-related functional status (Chasens et al., 2009). The FOSQ-10 consists of ten items situated within the context of sleep impairment, representing five domains including activity levels, vigilance, intimacy, productivity, and social outcomes. Total scores range from 5 – 20 with higher scores corresponding to less functional difficulty. It was tested among patients with obstructive sleep apnea and found to have an internal consistency of $\alpha = 0.87$ and correlated well (> 0.90) with the original 30-item FOSQ (Chasens et al., 2009; Weaver et al., 1997). The FOSQ-10 has been validated for use in other languages and used with other populations including people with narcolepsy, pregnant women, family members of critically ill patients, and shift-workers (Rahavi-Ezabadi et al., 2016; Rey de Castro et al., 2018; Tsai et al., 2016; Weaver et al., 2018). Though it has not been used with palliative care patients, it served as a reasonable choice due to a lack of other succinct instruments available to measure sleep-related functional status.

Data Collection Procedures

Once a participant was enrolled, data collection began. The researcher, a nurse practitioner with expertise in the assessment and management of sleep disorders, first asked the participant his or her age. Age served as both a sample descriptor and as a necessary statistic for one of the eight items of the STOP-Bang Questionnaire (Chung et al., 2008) which was used to assess risk for sleep apnea.

After determining the participant's age, the researcher interviewed the participant utilizing the 2012 International Restless Legs Syndrome Study Group (IRLSSG) revised consensus diagnostic criteria (Allen et al., 2014) to establish the presence or absence of clinically significant restless legs syndrome. The presence of clinically significant restless legs syndrome was considered positive if the participant met all of the IRLSSG revised consensus diagnostic

criteria within the past month and the participant found the symptoms bothersome to the extent that the participant affirmed that the symptoms were contributing to "significant distress or impairment in social, occupational, educational or other important areas of functioning by the impact on sleep, energy/vitality, daily activities, behavior, cognition or mood" (Allen et al., 2014, p. 861).

Next, the researcher donned fresh gloves and used a new disposable paper tape measure to measure the participant's neck circumference around the laryngeal prominence (i.e., Adam's apple). Each tape measure was used only once with a single participant and then thrown away with the gloves in a biohazard bin at VCUHS. Neck circumference was needed for completion of a second item of the STOP-Bang Questionnaire and was documented on the investigator data collection form.

After the measurement of neck circumference, the participant was offered a writing implement if one was needed and a participant survey packet to fill out independently. As outlined in the consent form, an alternative option was for study personnel to provide assistance with completing the participant survey packet. The participant survey packet contained demographic and contextual items as well as instruments for measuring excessive sleepiness, insomnia, sleep-related distress, and sleep-related functional status. It also contained questions pertaining to six remaining items of the STOP-Bang Questionnaire, a question about what was thought to be causing sleep-related distress, and a question about what risks/inconveniences a participant would be willing to accept for an intervention to alleviate sleep-related distress.

Demographics and contextual data collected included who filled out the participant survey packet, race/ethnicity, sex, highest level of education, employment status, marital status, health insurance status, primary problems leading to hospitalization, the presence of

medical/psychiatric/sleep disorders, ongoing sleep disorder treatments, estimated total sleep time during a 24-hour period, and types/names of medications taken in the prior three days that might be expected to affect sleep-related symptoms (i.e., pain relievers, sedating medications, stimulating medications, anxiolytics, muscle relaxers, antidepressants, medications for restless legs, medications for weight loss, gabapentin, and supplemental oxygen). In order to assess whether participants may have received stimulating medication, they were asked if they had received a medication to help them stay awake or increase energy. To assess if a participant had received a sleep aid, they were asked if they had taken a medication to help them fall or stay asleep. The responses were used to describe the sample characteristics and to enhance understanding of study findings.

Having previously documented restless legs syndrome status and data (i.e., age and neck circumference) for two of eight items on the STOP-Bang Questionnaire to measure risk for sleep apnea on the investigator data collection form, the remaining information required to complete measurements for excessive sleepiness, insomnia and risk for sleep apnea was requested within the participant survey packet. For measurement of excessive sleepiness, participants completed the Epworth Sleepiness Scale (ESS) (Johns, 1991). For measurement of insomnia, participants completed the Insomnia Severity Index (ISI) (Morin, 1993). For measurement of risk for sleep apnea, items related to snoring, tiredness, apneas during sleep, hypertension, sex, and body mass index were included to allow for the calculation of a score using the STOP-Bang Questionnaire.

After the completion of items for calculating a STOP-Bang Questionnaire score, sleep-related distress and sleep-related functional status were assessed in the participant survey packet. Participants completed a modified version of the National Comprehensive Cancer Network Distress Thermometer (National Comprehensive Cancer Network, 2018; Roth et al., 1998) that

was adapted to measure sleep-related distress within the past week. Participants were then asked to identify what they thought might be causing sleep-related distress. Participants were also asked to indicate from a list of risks/inconveniences which ones they would be willing to accept for an intervention that would alleviate their sleep-related distress. For measurement of sleep-related functional status, participants completed the Functional Outcomes of Sleep Questionnaire – 10 (FOSQ-10) (Chasens et al., 2009).

Some participants were expected to require physical assistance completing the packet and the researcher provided this if necessary. Participants were asked to refrain from allowing someone other than the researcher or participant to fill out the participant survey packet. There was a question in the packet to identify which person(s) filled out the packet. It was anticipated that the total time to interview participants, measure neck circumference, and administer the participant survey packet would be less than 70 minutes. Writing implements were not shared between participants in order to avoid contamination or transmission of infectious processes. If a participant became tired or requested a break, he or she finished the participant survey packet within 24 hours and the participant survey packet was left with the participant to be completed and picked up at a later time. When this occurred, the participant was given a 9x12 envelope for securing the packet and the researcher established a time to return to retrieve it.

Upon collecting the participant survey packet, the researcher reviewed each page for completion. If any areas were missing data, the researcher followed up with the participant in person as soon as possible to go over those areas and ask if he or she would be willing to provide the requested information. If the participant was willing, the missing data were collected either by having the participant work independently or with researcher assistance as needed. Once data collection was completed for an enrolled participant, the participant's data were entered

manually into a password protected VCU REDCap account. REDCap data were later downloaded into an Excel software file (Microsoft Corporation, Richmond, WA) and then imported into JMP statistical software package (SAS, Cary, NC) for data analysis. Data plots were generated using Excel software and JMP software.

Data Analysis Plan

Descriptive Statistics

Sample characteristics with regards to demographics; contextual data; ESS scores, ISI scores, and STOP-Bang scores (corresponding to sleep-related problem severities); SDT scores (corresponding to sleep-related distress levels); and FOSQ-10 scores (corresponding to sleep-related functional status levels) were primarily described using measures of frequency and central tendency/variation. The distributions of relevant continuous variables were examined graphically using frequency histograms and normal quantile plots to evaluate evidence regarding normality. Means and standard deviations were reported for variables with symmetric distributions, while medians and ranges were reported for variables with skewed distributions.

Four open-ended questions were asked to obtain information about types/names of medications received, reasons for hospitalization, ongoing sleep disorder treatments, and causes of sleep-related distress. These data were categorized based on the type of question. With respect to medications, the proportion of participants specifying that they had taken a medication to help them fall or stay asleep was reported, as was the proportion of participants that reported taking any medication commonly known for sedating effects (e.g., sleep aids, opioids, benzodiazepines, mirtazapine, etc.). Responses regarding reasons for hospitalization, ongoing sleep disorder treatments, as well as caused of sleep-related distress were each categorized by themes and tallied.

Specific Aims

Analysis relevant to each specific aim will be discussed separately.

Aim One. The first specific aim was to determine prevalence rates for four common sleep-related problems: excessive sleepiness, insomnia, restless legs syndrome, and high risk for sleep apnea. Using the relevant cutoff scores, the sample prevalence rates for excessive sleepiness (ESS score > 10), insomnia (ISI score > 7), high risk for sleep apnea (STOP-Bang score > 2), and restless legs syndrome (met all 2012 IRLSSG revised consensus diagnostic criteria for clinically significant RLS within the past month) were calculated.

Aim Two. The second specific aim was to examine relationships between all measures for the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status. To accomplish this, goals were to compare continuous variable means between groups for dichotomous variables, and perform correlation testing for pairs of continuous variables.

The only dichotomous variable was that of RLS status, while all other sleep-related problems and the outcome measures were continuous variables. A two-tailed two-sample Student's t-test, or an appropriate alternative test if assumptions of normality or equal variance were not met, was planned to determine if there was a significant difference between those with RLS and those without RLS for each of the continuous sleep-related problem measures and outcome measures. The distributions of each subsample (i.e., those with RLS and those without RLS) for each continuous variable were examined graphically using frequency histograms and normal quantile plots to evaluate evidence regarding normality. Variances were evaluated in two ways. If the linear fit lines of the normal quantile plots for the two subsamples appeared similar in slope and intercept, then equal variance between the subsamples was assumed. Another

method was to look at the *p*-value of the Brown-Forsythe test; if the *p*-value was > 0.05 then the variances were assumed to be equal. If both subsamples to be compared appeared to meet the assumption of normality, but did not have equal variances, then the Welch's t-test was planned to compare the subsample means. If one or both of the subsample distributions exhibited evidence of non-normality, then the non-parametric Mann-Whitney U test was to be used without regard for the equivalence status of the variances. For each test performed, a *p*-value of < 0.05 would be considered significant.

Correlations were estimated for all possible pairings among the continuous variables of sleep-related problem measures (ESS score, ISI score, and STOP-Bang score) and outcome measures (SDT score and FOSQ-10 score). Pearson's correlations were calculated unless one or both of the variables exhibited evidence of non-normality (e.g., an asymmetric or skewed distribution), in which case the Spearman's correlation was calculated.

Aim Three. The third specific aim was to determine which of the sleep-related problem variables along with age and gender predict outcomes of sleep-related distress and sleep-related functional status.

For each of the outcome measures of sleep-related distress and sleep-related functional status (i.e., SDT and FOSQ-10 scores), a regression model was fit considering the four sleep-related problem measures (ESS score, ISI score, STOP-Bang score, and restless legs status), age, and gender as potential predictors; and the outcome measure as the dependent variable. Hosmer and Lemeshow (2000) proposed an approach to building regression models in cases where the sample size may be considered small, and this method was used for building the models in a three stage process.

Stage One. For each outcome variable, bivariate models were fit with each potential

predictor variable. Potential predictor variables with a *p*-value of < 0.2 were considered to have some predictive ability and were candidates for Stage two.

Stage Two. An initial multivariable model was fit next using all potential predictor variables with $p < 0.2$ from Stage one. Using backward stepwise approach, potential predictors were removed one at a time from the model if their *p*-values were > 0.05 starting with the highest *p*-value.

Stage Three. For the predictor variables remaining after Stage two, all possible pairwise interaction terms were created and added to the model. Stepwise, backward elimination of interaction terms was then performed. With each step, the interaction term with the largest *p*-value was removed from the model until all remaining interaction terms had *p*-values < 0.05. The resulting model was considered the final prediction model.

All assumptions for multiple linear regression were checked for each final model. Assumptions checked included multicollinearity by checking variance inflation factors, influential data points, normality of the residuals, and homoscedasticity.

Due to the pilot nature of this study, no adjustments to alpha (e.g., Bonferroni adjustments) for multiple statistical tests were made. JMP software (SAS, Cary, NC) was used for all quantitative analyses. JMP software and Excel software (Microsoft Corporation, Richmond, WA) were utilized to produce data plots.

Chapter 4: Findings

Sample Characteristics

Recruitment for the study began in July 2020 and was completed in February 2021. As the study period progressed, the number of inpatients on contact precautions increased due to rises in the COVID-19 positivity rate within the hospital. This reduced recruitment opportunities due to the study's exclusion of persons on contact precautions. The palliative care team identified 146 patients deemed appropriate for study recruitment. Forty-seven patients were discharged prior to being screened for eligibility by the student researcher. Of the remaining 99 (68%) patients that were screened, 82 (83%) were initially found to be eligible for the study. Some of those found to be eligible requested extra time to think about participation, and of these, 14 (17%) were discharged prior to expressing a decision to the student researcher. Twenty-nine patients (35%) of those found eligible explicitly declined to participate, whereas 39 (48%) consented to enrollment in the study. Reasons for declining or delaying a decision to participate included fatigue, sleepiness, pain, shortness of breath, nausea/vomiting, urinary frequency, participation in another study, anticipating discharge or a procedure, unwillingness to sign a consent form, and not wanting to complete a survey. One of the 39 patients that consented to enrollment was later determined to be ineligible because he had not received palliative care services, and he was administratively withdrawn from the study. His data were excluded from all analysis procedures and results. The final study sample size was 38 participants. One of the 38 participants only completed a portion of the study due to fatigue; her data was included in analysis procedures and results when available.

See Table A1 (Appendix) for demographic and contextual data. The mean age was 57 (*SD* = 14) years. More than half (58%) were female. White participants made up the largest

racial/ethnic group at 66%, while black or African American participants made up the next largest group at 29%. Nearly one-third (32%) of participants' highest education level was a high school diploma, GED, or less. More than half of participants were not actively working, with retirees making up 39% of the sample and 37% of participants classifying their employment status as disabled. Half (50%) of participants were married or had a significant other. Most participants (92%) had health insurance.

Participants were asked to provide the primary reason for their current hospital stay, and whether they had certain medical or psychiatric conditions that may affect sleep. At the highest reported frequency, nearly one-quarter (24%) of participants reported pain as their primary reason for hospitalization, followed by the management of cancer (18%). Those in Table A1 characterized as having "other" primary reasons for hospitalization reported they had been admitted for bacteremia, neutropenia with fever, shortness of breath, weakness, or wound management. With respect to comorbid conditions that may affect sleep, the most frequently reported were cancer (78%), chronic pain (54%), and anxiety (46%).

Participants were asked whether they had insomnia, sleep apnea, restless legs syndrome, narcolepsy, rapid eye movement sleep behavior disorder, or any other sleep disorder; and whether they were receiving any treatments for a sleep disorder. Almost half of participants (47%) reported having at least one sleep disorder and insomnia (40%) was the most frequently reported. The "other" self-reported sleep disorder in Table A1 was frequent nocturia. The only sleep disorder treatments reported by participants were sleep aid medication (18%) and positive airway pressure therapy for sleep-related breathing disorders (8%).

Participants were also asked about their total sleep time in a 24-hour period and about medications they took in the past three days which might affect sleep. The median total sleep

time reported was 7.5 hours with a range of 3.5 – 20 hours. Thirty-seven percent of participants reported taking a sleep aid in the past three days. Including those participants taking a sleep aid, as much as 79% of the entire sample reported taking at least one medication commonly known to be sedating including opioids (63%), benzodiazepines (18%), and muscle relaxants (8%).

Participants can be further described by their mean and standard deviation or median and range (in the case of a skewed distribution) for ESS, ISI, STOP-Bang, SDT, and FOSQ-10 scores which are presented in Table A2 (Appendix). Scores ranged widely. The mean ESS score of 8.9 (*SD* = 5.4) is within the normal range for sleepiness with an ESS score above 10 indicating excessive sleepiness. The mean ISI score of 11.5 (*SD* = 7.9) and median STOP-Bang score of 3 are both elevated wherein an ISI score greater than seven suggests insomnia and a STOP-Bang score greater than two indicates a high risk for sleep apnea. Sleep-Related Distress Thermometer scores ranged from 0 to 10 (*Mdn* = 4). The median FOSQ-10 score was 18.5 with 20 being the highest possible score.

Findings for Specific Aims

Aim One

The first specific aim of the study was to determine the prevalence rates of four common sleep-related problems: excessive sleepiness, insomnia, restless legs syndrome, and high risk for sleep apnea. Prevalence was determined by using cutoff scores for the ESS (>10 indicates excessive sleepiness), ISI (>7 indicates insomnia), and STOP-Bang (>2 indicates high risk for sleep apnea) as well as utilizing the 2012 IRLSSG revised consensus diagnostic criteria for clinically significant RLS (meeting all criteria within the past month indicates the presence of RLS). Table A3 (Appendix) shows that insomnia was the most prevalent sleep-related problem affecting 62% of participants, followed by high risk for sleep apnea at 57%.

Aim Two

The second specific aim was to examine relationships between all measures for the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status.

Correlation testing only revealed significant relationships between insomnia and sleep-related distress (Spearman's $\rho = 0.75$, $p < 0.0001$), and excessive sleepiness and sleep-related functional status (Spearman's $\rho = -0.59$, $p = 0.0001$). For both correlations, the null hypothesis of no correlation was rejected, suggesting that higher levels of insomnia are associated with greater sleep-related distress, and that those with worse sleep-related functional status are more likely to be excessive sleepy. No causation between these variables can be assumed. All other correlation tests failed to reject the null hypothesis and therefore were unable to demonstrate significant relationships between variables. The results of all correlation tests can be found in Table A4 (Appendix).

Due to the low subsample size of only five participants with RLS, no testing was performed. Medians and ranges are reported in Table A5 (Appendix) for ESS, ISI, STOP-Bang, SDT, and FOSQ-10 scores by RLS status (absent versus present).

Aim Three

The third specific aim was to determine which of the sleep-related problem variables along with age and gender predict outcomes of sleep-related distress and sleep-related functional status. Using the method described by Hosmer and Lemeshow (2000), two multiple regression models were found for sleep-related distress (i.e., SDT score) and sleep-related functional status (i.e., FOSQ-10 score).

Stage One. With respect to sleep-related distress, it was determined that the tests with

gender ($p = 0.03$) and ISI score ($p < 0.0001$) had p-values < 0.2, permitting their entry as predictors into the initial model. Bivariate analysis with STOP-Bang score, ESS score, and age revealed p-values of 0.65, 0.31, and 0.39, respectively. Therefore, risk for sleep apnea, level of sleepiness, and age were eliminated as potential predictors in the model for sleep-related distress. The initial model for sleep-related distress therefore included only gender and ISI score as predictors.

For sleep-related functional status, it was determined that the tests with age ($p = 0.03$), ESS score ($p = 0.0006$), and ISI score ($p = 0.05$) had p-values < 0.2, permitting their entry as predictors into the initial model. Bivariate analysis with STOP-Bang score revealed a p-value of 0.91, so risk for sleep apnea was eliminated as a potential predictor in the model for sleep-related functional status. The test with gender also revealed a high p-value of 0.79. Therefore, gender was also eliminated as a potential predictor in the model for sleep-related functional status. Age, ESS score, and ISI score were the only remaining predictors in the initial model for sleep-related functional status.

Stage Two. Using backward elimination, gender was not significant in the model ($p > 0.05$) and, thus, it was removed from both multivariable models. No other predictors had a p-value > 0.05 in the initial model for sleep-related functional status from stage one.

Stage Three. There were no possible pairwise interaction terms to be added to the model for sleep-related distress in stage three. The final model for sleep-related distress ($F = 48.14$, $p < 0.0001$) is shown in Table A6 (Appendix). ISI score (β coefficient = 0.309, $p < 0.0001$) was the only independent variable. The variance inflation factor for ISI score was 1. Based on the adjusted R^2, the model shows that 57% of the variance in sleep-related distress is explained by insomnia severity with greater severity predicting higher levels of sleep-related distress. A

scatterplot of measured SDT scores against ISI scores and the predicted regression line for the model of sleep-related distress is shown in Figure A3 (Appendix). Those with an ISI score of zero are predicted to have no measurable sleep-related distress. The model predicts that for every 5 point increase in ISI score, the SDT score rises about 1.5 points. At the sample mean ISI score of 11.5, it is predicted that the SDT score will be 3.4. Those with the sample's highest measured ISI score of 25 are predicted to have a SDT score of 7.6.

With respect to the model for sleep-related functional status, all possible interaction terms were added for age, ESS score, and ISI score. After backward elimination, the only significant interaction term remaining was that for the ESS score by ISI score interaction. The final model for sleep-related functional status ($F = 10.85$, $p < 0.0001$) is shown in Table A7 (Appendix). Age (β coefficient = 0.040, $p = 0.0701$), ISI score (β coefficient = -0.108, $p = 0.0068$), ESS score (β coefficient = -0.251, $p = <0.0001$), and an interaction term for ESS score by ISI score (β coefficient = -0.021, $p = 0.0095$) were the remaining independent variables. Variance inflation factors for all independent variables were approximately 1. Based on the adjusted R^2, the model shows that 52% of the variance in sleep-related functional status is explained by age, insomnia, excessive sleepiness, and an interaction between insomnia and excessive sleepiness.

Generally, the final model for sleep-related functional status suggests that those with younger age, higher levels of sleepiness (i.e., higher ESS scores) or worse insomnia (i.e., higher ISI scores) are more likely to have poorer sleep-related functional status (i.e., lower FOSQ-10 scores). However, the interaction term suggests that when the level of sleepiness or insomnia is extremely low, sleep-related functional status will be high even if the level of the other is elevated. For example, when the ESS score is less than 3.8, FOSQ-10 scores range from approximately 17.5 to a maximum possible scale score of 20 across the sample age range,

regardless of ISI score. Additionally, when the ISI score is 0, FOSQ-10 scores remain high between approximately 17.5 and 19.5 across the sample age range, regardless of ESS score.

Figure A4 (Appendix) shows multiple interaction profiles (Profiles A – F) for the sleep-related functional status multiple regression model. It illustrates several examples of predicted FOSQ-10 scores across age, ESS score, and ISI score ranges while other variables are set to a sample mean, minimum or maximum. Profile A shows how the FOSQ-10 score changes with ESS score for the sample minimum age (red line) and sample maximum age (blue line) when ISI score is 11.5 (sample mean). Profile B shows how FOSQ-10 score changes with ISI score for the sample minimum and maximum ages when ESS score is set to the sample mean of 8.9. In Profiles A and B, as ESS score and ISI score increase by 4.0 and 9.3, respectively, FOSQ-10 scores decrease by 1. Profiles A and B also show that as age increases by 25.2 years, FOSQ-10 score increases by 1 across the sample ranges of ESS and ISI scores. Profiles C and E show similar data relationships as found in Profiles A and B, respectively, but instead graphically illustrate the FOSQ-10 score by age.

Profiles D and F illustrate the effects of the interaction term in the model for sleep-related functional status when ESS score and ISI score vary as age is held constant at the sample mean of 57 years. The red line in Profile D represents predicted FOSQ-10 scores when the ESS score is 0 (sample minimum), and shows that sleep-related functional status remains high with a FOSQ-10 score between 18.80 and the maximum possible scale score of 20 across the sample ISI score range of 0 – 25. In this case, the FOSQ-10 score rises by 1 point for every 12.6 point increase in the ISI score. The blue line in Profile D represents predicted FOSQ-10 scores when the ESS score is 19 (sample maximum), and shows that for every 3.1 point increase in the ISI score, FOSQ-10 scores drop by 1 point, reaching a low of 10.66 when the ISI score is 25 (sample

maximum). As such, the model predicts that those with both severe insomnia and severe excessive sleepiness are most likely to have the worst sleep-related functional status levels. In fact, the lowest possible FOSQ-10 score predicted by the model is 9.43 for someone who is 26 years old with an ESS score of 19 and an ISI score of 25.

The red line in Profile F represents predicted FOSQ-10 scores when the ISI score is 0 (sample minimum), and shows that sleep-related functional status remains high and relatively stable with a FOSQ-10 score between 18.63 – 18.80 across the sample ESS score range of 0 – 19. The blue line represents predicted FOSQ-10 scores when the ISI score is 25 (sample maximum), and shows that for every 1.9 point increase in the ESS score, FOSQ-10 scores drop steeply by 1, reaching a low of 10.66 when the ESS score is 19 (sample maximum).

All assumptions for multiple linear regression were met for both of the final constructed models.

Other Findings

After responding to the Sleep-Related Distress Thermometer (SDT), participants were asked to identify what they thought might be causing their sleep-related distress within the past week. Almost one-third of participants denied having sleep-related distress, and thus did not provide a response. Table A8 (Appendix) lists the frequencies of common concerns along with examples and quotes provided by participants. The two most common reported causes of sleep-related distress were anxiety or distressing thoughts (32%), and pain or physical discomfort (19%).

Participants were also asked to indicate from a list of risks/inconveniences which ones they would be willing to accept for an intervention that would alleviate sleep-related distress. These results are presented in Table A9 (Appendix). Nearly all participants (97%) were willing

to accept minimal risks from interventions such as relaxation or chamomile tea. While 68% of participants reported they were willing to take a prescription sleep aid or stimulant medication, percentages dropped to no more than 16% when asked about acceptance of various medication side effects such as leg discomfort, reduced appetite, headaches, or anxiety. Notably, one person was willing to risk a shortened lifespan from a medication if it would alleviate sleep-related distress; and no one was willing to experience confusion as a medication related side effect. More than half of participants (57%) were amenable to trying positive airway pressure (PAP) to relieve sleep-related distress, however, much fewer were willing if the PAP therapy was associated with commonly experienced side effects such as airway drying/irritation (19%), skin irritation (19%), or waking up from mask leak noise (19%).

Chapter 5: Discussion

The goals of this study were to investigate the prevalence of sleep-related problems among adult inpatients receiving palliative care, to examine relationships between the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status, to construct predictive multiple regression models for the two outcome measures, to determine causes of sleep-related distress, and to gauge willingness to accept various risks or inconveniences to alleviate sleep-related distress in this population. As a pilot study, a small sample of 38 adult inpatients receiving palliative care services at VCUHS in Richmond, Virginia was recruited to complete an interview, a neck measurement, and multiple sleep-related instruments. It was found that sleep-related problems were common among participants, with more than half of participants scoring positive for insomnia and for high risk for sleep apnea. Sleep-related distress was found to be significantly correlated with insomnia; and poor sleep-related functional status was found to be significantly correlated with excessive sleepiness. Anxiety or distressing thoughts were the most frequently cited causes of sleep-related distress. While more than half of participants were willing to take a prescription medication or use positive airway pressure (PAP) therapy to alleviate sleep-related distress, less than 20% would accept those interventions if they were accompanied by common side effects. This chapter further discusses these results, lessons learned, study limitations, and implications for future research and knowledge development regarding sleep-related problems, sleep-related distress, and sleep-related functional status in palliative care.

Sample Characteristics

Overall, the sample was partially representative of the larger inpatient palliative care population (PCP). The vast majority of palliative care inpatients are adults (99.8%) which were

the focus of this study. Sixty-three percent of study participants were under the age of 65 years compared to 26% of patients under 65 across the inpatient PCP (Center to Advance Palliative Care & National Palliative Care Research Center, 2018b).

Of 38 recruited participants, the sample had a higher proportion of females (58%) than males with slightly greater representation of females in this study than is found in the larger inpatient PCP (52%). The study sample was more racially diverse too, with a lower proportion of whites or Caucasians (66%) compared to the inpatient PCP (75%), and a higher proportion of blacks or African Americans (29% versus 13%) (Center to Advance Palliative Care & National Palliative Care Research Center, 2018b).

Cancer (78%) was very common among study particpants with 18% reporting cancer management as their primary reason for hospitalization. This compares to 26% of the overall population of palliative care inpatients having cancer as a primary diagnosis. The study sample had higher rates of heart disease (22%), lung disease (22%), and neurological disorders (19%) compared to the overall inpatient PCP (15%, 14%, and 9%, respectively) (Center to Advance Palliative Care & National Palliative Care Research Center, 2018a).

Some of the differences between the study sample and the inpatient palliative care population may be due to the location, type of facility, and procedures used for the study. A small sample size may be another reason for the differences. Epidemiological studies measuring population characteristics are often larger, include multiple sites, and don’t necessarily require alert or active participants. Data for age, gender, race, and diagnoses may be pulled from hospital system databases, without individual consent in some cases. The study sample was recruited at a large academic medical center located in a racially diverse urban area. Participants had to meet

specified inclusion criteria such as fluency in English and capacity for independent decision making.

Given the high level of specialty care available at the study facility, one might expect to see a more diverse range of diagnoses or a wider age range than is found among the general inpatient palliative care population. More aggressive or complex management options, such as experimental research protocols or highly specialized interventions, are often only available at a large academic medical center. The sample may have had more patients under the age of 65 (63%) compared to the inpatient palliative care population as a whole (26%) because of the availability of a palliative care consultation service available to assist with symptom management across all inpatient units. A consultation service may work with a more heterogeneous population of patients with varying goals of care. Active, life-prolonging treatments may be more likely on a consultation service whereas specialized palliative care on a designated palliative care unit may involve more elderly patients near the end of life receiving comfort and supportive care.

This study included patients with depression and mild cognitive impairment as long as they were deemed capable of independent decision making by the health care team. Therefore, the results from this study may be more reflective of the inpatient palliative care population than other studies of palliative care patients which often exclude patients with psychiatric illness or cognitive impairment. Given links between psychiatric conditions and sleep, such as the bidirectional relationship between depression and insomnia (Redeker & McEnany, 2011), other studies may underestimate sleep-related problems, sleep-related distress, or sleep-related functional status in the PCP.

Aim One

The first specific aim was to determine prevalence rates for four common sleep-related problems: excessive sleepiness, insomnia, restless legs syndrome, and high risk for sleep apnea. Insomnia (62%) was the most prevalent sleep-related problem in the study sample as determined from an ISI score > 7, though only 40% of participants self-reported having insomnia. The prevalence found in this study is similar to what others have found. Using the Athens Insomnia Scale, insomnia prevalence rates between 61 – 100% were found among a total of 1039 palliative care patients across mixed settings (Mercadante et al., 2015, 2017). Using a single item, 37-63% of 161 mixed setting palliative care patients were found to have insomnia (Renom-Guiteras et al., 2014; Sela et al., 2005). Potential contributors to insomnia in the study sample may have been anxiety, chronic pain, and depression which are known risk factors for insomnia (Redeker & McEnany, 2011) and were self-reported by 54%, 46%, and 35% of participants, respectively. More research is needed to establish whether these factors are significantly associated with insomnia among inpatient palliative care patients.

The Athens Insomnia Scale (AIS) (Soldatos et al., 2000) and the Insomnia Severity Index (ISI) are both extensively used for insomnia research and are both considered valid and reliable instruments (Lin et al., 2020). While Mercadante et al. (2017) and Mercadante et al. (2015) both used the AIS, the ISI was chosen for this study. This is because several items on the AIS may inappropriately inflate the score for insomnia severity among palliative care patients. For instance, palliative care patients may rate their sense of well-being and functioning as low, and their level of sleepiness as high (thereby raising their AIS score) due to illness-related factors rather than the impact of insomnia. The ISI, on the other hand, places all items in the context of sleep-related considerations such as satisfaction related to one's sleep pattern and the interference of one's sleep problem with functioning.

The use of cutoff scores for the ISI has been in question. While a score of 0 – 7 is labeled as "no clinically significant insomnia," scores of 8 – 14 are labeled "subthreshold insomnia," scores of 15 – 21 are labeled "clinical insomnia (moderate severity)" and scores of 22 – 28 are labeled "clinical insomnia (severe)" (Bastien et al., 2001, p. 299). In this context, scores of 8 – 14 were seen as reflecting mild insomnia. Bastien et al. (2001) suggest that scores > 10 may reflect a problem with or distress related to insomnia, and specifically state that more research is needed to determine an optimal cut off. Using alternative cut off scores, 51% of this study's participants had an ISI score > 10 and 38% of participants had an ISI score > 14. Using an ISI score > 7 to categorize the presence of insomnia, results aligned with the self-report of insomnia status 70% of the time, whereas using an ISI score > 10 aligned with the self-report 76% of the time and using an ISI score > 14 aligned with the self-report 73% of the time. All in all, the data suggests a large percentage of participants experience some level of insomnia, however there is a need for additional research on best ways for measuring insomnia in palliative care.

The sleep-related problem of excessive sleepiness also had a high prevalence rate (41%) as determined from an ESS score > 10. Using an ESS score > 10, Good et al. (2018) found that 36% of 28 palliative care inpatients were excessively sleepy, and Gibbins et al. (2009) found 26% of 60 outpatients with advanced incurable cancer to be excessively sleepy. One potential reason for a higher prevalence of excessive sleepiness found in this sample was that 79% of participants reported taking at least one medication commonly known to be sedating from sleep aids, opioids, benzodiazepines, muscle relaxants, and sedating antidepressants.

The optimum way to measure problematic sleepiness in palliative care remains uncertain. Additional research is needed to determine whether the ESS serves as a reliable and valid method for measuring excessive sleepiness in this population. Using a single question, Renom-

Guiteras et al. (2014) found that 74% of 61 palliative care inpatients complained of daytime sleepiness. In this study, 68% of participants gave a positive response to the first STOP-Bang item which contains a question about frequent tiredness, fatigue, or sleepiness, but only 46% of participants' responses aligned with their status as excessively sleepy or not according to their ESS score. How well these single items reflect a sleep-related problem is questionable.

Using a STOP-Bang score > 2, the sample prevalence of high risk for sleep apnea was 57%. Despite the high prevalence of high risk for sleep apnea, only 16% self-reported having a diagnosis of sleep apnea. Yennurajalingam et al. (2017) and Yennurajalingam et al. (2018) also used a STOP-Bang score > 2 as a measure of high risk for sleep apnea and found that 61% of 180 inpatients with advanced cancer met the criteria for high risk. Examining responses to individual items of the STOP-Bang, it is apparent that certain items may not adequately reflect sleep apnea risk in the palliative care population.

As previously mentioned, the first STOP-Bang item presents a question about frequent tiredness, fatigue, or sleepiness. While these concepts have overlapping features and the item may correlate well with the likelihood of having sleep apnea in the general population, it is not known if this item correlates well in the palliative care population. As multifactorial and disparate concepts, sleepiness and/or fatigue may represent separate phenomena related primarily to serious illness and not provide useful gauges for sleep apnea risk in palliative care patients. In that vein, the first STOP-Bang item could have contributed to an artificial inflation of the measured prevalence rate of high risk for sleep apnea in this study. If sleepiness, as measured by the ESS, were found to be a good predictor of sleep apnea in palliative care patients, a consideration could be to replace the first item of the STOP-Bang with an appropriate ESS cut off score to reflect a higher risk for sleep apnea.

Very few study participants had positive reponses to STOP-Bang items related to large neck circumference (19%), observed apneas (16%), and high BMI (i.e., BMI > 35) (8%) which are more commonly found among those with sleep apnea in the general population. Despite this, a high prevalence of sleep apnea confirmed by polysomnography might still be expected given the high prevalence of other sleep apnea risk factors found among the study participants. Besides the high positive response rate regarding sleepiness/fatigue (68%), more than half of study participants also had positive responses to STOP-Bang items related to advanced age (i.e., > 50 years) (68%) and snoring (59%).

In the palliative care population, the frequent use of sedating medications may also contribute to a high prevalence of sleep apnea. A study of 28 palliative care inpatients found that 75% had sleep apnea confirmed by polysomnography wherein 89% of participants were taking opioids (Good et al., 2018). Interestingly, in the study by Good et al. (2018), sleep apnea risk had only been considered high among 43% using the Berlin Questionnaire. As previously mentioned, 79% of this study's participants reported taking at least one sedating medication, with reported opioid use particularly high at 63%. The STOP-Bang does not include an item related to medication use and therefore it may underestimate risk for sleep apnea among palliative care patients in this respect. Adding an item related to medication use could be an adaptation to the instrument considered for future use with this population.

Overall, it is not yet feasible to associate STOP-Bang scores with sleep apnea prevalence in the palliative care population given the issues just discussed above. Specifically, reliability and validity of the STOP-Bang with palliative care patients is uncertain. More research is needed to optimize item contents and cut off scores that would accurately correlate with polysomnography, the gold standard for identifying the presence of sleep apnea.

Restless legs syndrome (14%) was the least prevalent sleep-related problem of the four measured in the study, and only 5% of study participants self-reported a diagnosis of RLS. Both of the participants that self-reported RLS were found to have RLS by the study measure. One common cause of RLS is iron-deficiency anemia with a ferritin level < 50 (Chokroverty, 2010; National Institute of Neurological Disorders and Stroke, 2017; Ohayon et al., 2012; Redeker & McEnany, 2011). Participant ferritin levels were not known but 27% self-reported having iron-deficiency anemia; and only one participant of five found to have RLS by the study measure also had iron-deficiency anemia.

It is difficult to compare prevalence rates for RLS from study to study. Two reviews of epidemiologic RLS studies with sample sizes of at least 300 participants found that methods for identifying the presence of RLS varied greatly across studies, as did estimated prevalence rates (Innes et al., 2011; Ohayon et al., 2012). Some studies incorporated only one or a few questions to elicit responses regarding RLS symptoms, while other studies asked questions formulated to determine if participants met some or all of the diagnostic criteria outlined by the IRLSSG.

The prevalence of RLS found in this study is much lower than that found by Walia et al. (2013) (41%) among 76 palliative care outpatients, and by Yennurajalingam et al. (2017) and Yennurajalingam et al. (2018) (38%) among 180 inpatients with advanced cancer. There may be several reasons for this discrepancy. The study by Walia et al. (2013) required 4 out of 4 positive responses to yes/no items related to the diagnostic criteria for RLS, and they did not attempt to exclude diagnostic RLS mimics. Yennurajalingam et al. (2017) and Yennurajalingam et al. (2018) assessed for the presence of RLS using a single item. The measure for RLS status used in this study was a non-structured interview conducted by an experienced sleep disorders nurse practitioner to determine if participants met all six of the 2012 IRLSSG revised consensus

diagnostic criteria for clinically significant RLS which account for diagnostic mimics. In that sense, the measured sample prevalence of RLS found in this study may more closely reflect the actual prevalence of active RLS in the inpatient palliative care population. Another reason for a lower prevalence rate of RLS may be due to the large portion of participants receiving opioids (63%) and benzodiazepines (18%), which can alleviate RLS symptoms.

Aim Two

The second specific aim was to examine relationships between all measures for the sleep-related problems and outcome measures of sleep-related distress and sleep-related functional status. Of the relationships examined, two were found to be significant. Insomnia severity was positively correlated with sleep-related distress levels (Spearman's $\rho = 0.75$, $p < 0.0001$), and level of excessive sleepiness was negatively correlated with sleep-related functional status level (Spearman's $\rho = -0.59$, $p = 0.0001$).

Other studies have looked at how sleep-related issues relate to global distress among palliative care patients, but there is a dearth of studies using a specific measure for sleep-related distress as was done in this study with the Sleep-Related Distress Thermometer (SDT). Operational measures of distress also vary from study to study. A frequently used measure of global distress with palliative care patients is the Distress Thermometer upon which the Sleep-Related Distress Thermometer was based. Nishiura et al. (2014) used the Hospital Anxiety and Depression Scale as a measure of distress with 50 inpatients with lung cancer and found that distress was associated with insomnia. This study's results using the SDT cannot be easily compared to studies using a measure of global distress.

A problem with using a global measure of distress is that palliative care patients are often dealing with a multitude of distressing issues (e.g., anxiety about one's illness, financial worries,

pain, dyspnea). Anxiety or physical discomfort may be highly distressing on their own and also make it difficult to sleep at night. However, the insomnia caused by worry or pain may not be distressing itself for some. Such patients would likely score high on a global distress scale and low on the Sleep-Related Distress Thermometer. Therefore, global distress is a confounding variable that makes it difficult to know whether altered sleep is contributing to distress or if other issues might be the primary cause of someone's distress. Even if sleep-related problems are somewhat distressing, other stressors may compound and raise global distress scores such that statistically significant associations with sleep-related problems are found that might not otherwise be there if only the portion of distress attributed to the sleep-related problems were considered.

Similar issues may arise with measures of global functional status. A frequently used measure for functional status in palliative care is the Karnofsky Performance Status Scale (KPS), though others are also used such as the European Organization of Research and Treatment Quality of Life Questionnaire–Cancer 30 (EORTC QLQ–C30). A number of palliative care studies have found a significant negative relationship between insomnia and global functional status. For instance, Mercadante et al. (2015) and Mercadante et al. (2017) found that low functional status based on KPS scores was associated with insomnia as measured with the Athens Insomnia Scale among their sample of 1039 palliative care patients across mixed settings. Nishiura et al. (2014) used the EORTC QLQ–C30 as a measure of functional status with their sample of 50 inpatients with lung cancer and also found that lower functional status was associated with insomnia based on AIS scores. Interestingly, the study by Renom-Guiteras et al. (2014) found that higher functional status based on KPS scores was associated with insomnia based on responses to a single question among their sample of 61 palliative care inpatients.

However, as with the use of a global measure for distress, global measures of functional status may not reflect functional alterations due to sleep-related problems. Palliative care patients often have many functional limitations due to the nature of their illnesses. The reasons for the functional limitations may not match the reasons for insomnia yet both high levels of insomnia and a high prevalence of poor functional status may coexist in the same sample. Because of the limitations of using a global measure of functional status, a sleep-related measure of functional status, the FOSQ-10, was used for this study. Due to the sleep focused nature of the FOSQ-10, it is difficult to compare the results from this study to studies that used a more global measure of functional status.

One might anticipate that insomnia and excessive sleepiness would each hamper sleep-related functional status. A significant association was found between excessive sleepiness and lower sleep-related functional status in this study, but insomnia was not found to be associated with sleep-related functional status. A likely reason for this is that all FOSQ-10 items involve questions about functional status in the context of sleepiness, such as "Do you have difficulty being as active as you want to be in the morning because you are sleepy or tired?" Insomnia can certainly worsen daytime sleepiness if one is unable to sleep adequately at night, so some questions may relate to insomnia in this way. However, adaptations to the FOSQ-10 that target insomnia as a potential contributor to functional alterations could better allow for the detection of significant relationships between insomnia and sleep-related functional status when present.

Though other studies with other populations have described relationships between sleep-related problems such as sleep apnea and RLS with excessive sleepiness and insomnia (American Psychiatric Association DSM-5 Task Force, 2013; Broman et al., 2008; Chokroverty, 2010; Molnar et al., 2007; Onen et al., 2010; Redeker & McEnany, 2011), this study did not

corroborate such findings. One reason is because the number of participants with RLS was too low to draw meaningful conclusions and so this measure was not considered for statistical testing. Additionally, this study did not include a measure for sleep apnea itself, but rather risk for sleep apnea (i.e., STOP-Bang score). With the limitations of the STOP-Bang discussed above, though a relationship between sleep apnea risk and excessive sleepiness or insomnia was not found in this study, it's possible that a relationship with sleep apnea itself exists.

Aim Three

The third specific aim was to determine which of the sleep-related problem variables along with age and gender predict outcomes of sleep-related distress and sleep-related functional status. To accomplish this task, regression models were constructed for sleep-related distress and sleep-related functional status as dependent variables using the approach for small sample sizes recommended by Hosmer and Lemeshow (2000).

Model for Sleep-Related Distress

In the model for sleep-related distress, only insomnia severity (ISI score) was found to be a significant predictor of sleep-related distress (SDT score). Considering that the standard deviation of the sample mean ISI score (mean = 11.5) was 7.9, the model predicts that within one standard deviation of the mean ISI score (i.e., ISI scores 3.6 – 19.4), SDT scores would range from 1.0 – 5.8. Without identifying a scale comparable to the SDT in the literature, it is difficult to determine how a SDT score within this range should be interpreted with respect to severity of sleep-related distress.

Researchers using the Distress Thermometer (DT), which is a global measure of distress, have suggested using various DT cut off scores to indicate significant distress. With respect to global distress, the DT has been found to have criterion-related validity using a cut-off score of 4

when compared to the Hospital Anxiety and Depression Scale (HADS), the General Health Questionnaire-12 (GHQ-12), and the Brief Symptom Inventory-18 (BSI-18) (Gessler et al., 2008). Cutillo et al. (2017) recommended a DT cut off score of 3 to detect significant distress based on research with a large, heterogeneous population of cancer patients across different time points of survival. Among palliative care patients, the DT has been shown to perform as well as longer screening methods (i.e., GHQ-12 and BSI-18) using a cut-off score of 5 wherein sensitivity was 0.77 and specificity was 0.59 (Thekkumpurath et al., 2009).

Adopting a SDT cut off score between 3 – 5 based on the cut off scores suggested by others for the global DT could be one option for interpreting SDT scores. In that case, the sleep-related distress model for this sample would predict high sleep-related distress among anyone with a score at or above an ISI score between 11 - 16, depending on the SDT cut off score selected from 3 – 5. Using a SDT score of 3 or greater to indicate high sleep-related distress, 51% of participants would be predicted to have high sleep-related distress based on their ISI score (i.e., 51% had ISI scores of 11 or greater). If a higher SDT score of 4 or greater (i.e., ISI score of 14 or greater) were used to indicate high sleep-related distress, the predicted prevalence would remain at 51%. If a SDT score of 5 or greater was used instead, the predicted percentage of those with high sleep related distress would drop to 32 (i.e., 32% had ISI scores of 16 or greater). For each of the three SDT cut off scores considered (i.e., 3, 4, and 5), the sleep-related distress model accurately predicts sleep-related distress status (i.e., high, or not high) 81%, 86%, and 81% of the time, respectively, based on measured participant ISI scores.

More research is needed to establish the best way to use an instrument like the SDT with palliative care inpatients. Some options for assessing the clinical significance of a SDT score could include adding facial expressions to the scale illustrative of distress level, or incorporating

descriptors. Examples of relevant descriptors might include “slight sleep-related distress” for a SDT score of 2, “moderate but tolerable sleep-related distress” for a SDT score of 4, “moderate sleep-related distress that is intolerable at times” for a SDT score of 6, and “severe sleep-related distress that is unacceptable” for a SDT score of 8.

Noting the lack of available instruments for specifically measuring sleep-related distress, Morrone et al. (2017) developed the Maugeri Sleep Quality and Distress Inventory (MaSQuDI-17) which they considered valid given its relationships with a variety of other measures including the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, the State-Trait Anxiety Inventory, and the Depression Questionnaire of the A-D Schedule. Item domains of the MaSQuDI-17 include daily routines, social factors, emotional/cognitive functioning, and somatic symptoms. It’s not clear whether this instrument would accurately measure the intended concept of sleep-related distress. While it may, it could be detecting the frequently observed associations between sleep-related phenomena and other mental or physical problems. Those associations, however, do not necessarily correspond to an inner sense of distress.

To know how distressing one’s sleep-related experiences are, one must ask the person directly how much they are affected or bothered by them. Culturally, genetically, and based on one’s health literacy, sleep-related distress levels may vary from person to person or change over time, despite similar circumstances (Jeon et al., 2021; Jones et al., 2019; Zhang et al., 2019). Ultimately, an ideal measure of sleep-related distress in palliative care would validly identify those suffering and in need of relief from distress caused by sleep-related issues, and reliably detect individual responses to interventions.

Model for Sleep-Related Functional Status

In the model for sleep-related functional status, age, insomnia severity (ISI score), level of sleepiness (ESS score), and an interaction term for ESS score by ISI score were found to be significant predictors of sleep-related functional status (FOSQ-10 score). It is interesting to note that while level of insomnia severity was not found to be significantly correlated with sleep-related functional status directly in Aim 2, it was when incorporated into the multiple regression model. This may have occurred in part because of the interaction between excessive sleepiness and insomnia which would not have been evident with the correlational analysis performed in Aim 2.

Due to the number of independent variables and an interaction term, the model is complex. Figure A4 illustrates how the FOSQ-10 score changes with various relationships between age, ISI score, and ESS score. One major finding was that the model suggests younger palliative care inpatients are more likely to have worse sleep-related functional status than older palliative care inpatients. The model also suggests that palliative care inpatients with a very low ESS score or a very low ISI score are more likely to have normal or high sleep-related functional status. Another important trend suggested by the model was that palliative care inpatients with both severe insomnia and severe excessive sleepiness are likely to have the worst sleep-related functional status. The FOSQ-10 has been found to have a mean of 17.81 with a standard deviation of 3.10 among normal controls (Chasens et al., 2009). In this sample, only 19% of participants had a FOSQ-10 score more than one standard deviation below the mean for normal controls found by Chasens et al. (2009), suggesting that poor sleep-related functional status is not a problem for the majority of palliative care inpatients. The lowest possible FOSQ-10 score predicted by the model is 9.43 for someone 26 years old with an ESS score of 19 and an ISI score of 25. This compares to the lowest measured FOSQ-10 score in the sample of 11.33 for

someone between 40 – 50 years old with mild excessive sleepiness and moderately severe insomnia.

The model's prediction that sleep-related functional status is most negatively impacted by the presence of severe insomnia and severe excessive sleepiness together coincides with aspects of other studies of functional status. It has been found that comorbidity, having two or more conditions, diminishes global functional status more than having a single condition alone (Mozes et al., 1999; VanderZee et al., 1996; Wensing et al., 2001). A study using the full length 30-item FOSQ found that older adults with daytime sleepiness and three or more medical conditions had worse sleep-related functional status (Gooneratne et al., 2003). Furthermore, severe conditions with higher symptom burden have been shown to reduce global functional status significantly more than disease states that are less noticeable or bothersome (McHorney et al., 1993; Mozes et al., 1999). If low sleep-related functional status were truly indicative of a greater degree of sleep-related difficulties, then measuring sleep-related functional status along with sleep-related distress could be an effective way to differentiate which palliative care inpatients may benefit from a more thorough assessment of their sleep and intervention to improve outcomes.

Typically, one would expect functional status to decline with advanced age due to normal biological changes associated with aging, and research has shown this to be the case (Wensing et al., 2001). However, the model for sleep-related functional status predicts an opposite relationship; as age increases, sleep-related functional status improves. There may be several reasons for this among palliative care inpatients. For one, extreme biological compromise is common for all palliative care inpatients, regardless of age. Next, the FOSQ-10 is a purely subjective measure whereas other measures of functional status may incorporate objective findings (e.g., parameters of physical strength, recent fall history) that often yield lower

functional status scores as age increases. Wensing et al. (2001) asserts that in the face of deteriorating health, psychological adaptation can occur with aging to temper the experience of functional losses, resulting in the revision of subjective ideals of good functional status. Younger palliative care inpatients may be less flexible in this regard.

Sprangers and Schwartz (1999) developed a theoretical model of factors that may influence perceived functional status which included age, expectations, coping, social comparison, and conceptualization among others. Younger inpatients receiving palliative care may self-report worse sleep-related functional status based on social comparisons with others their age that are actively working and functioning without the limitations of a severe and/or life-threatening illness. Of those under age 65 years in the study sample, 25% were still employed while 54% considered themselves disabled. Of elderly participants 65 years of age or older, 85% reported having retired. With retirement and older age, palliative care inpatients may not expect or regard with as much importance to be as active or healthy as they once were, thereby influencing their responses to self-reported measures of sleep-related functional status. Further research is needed to elucidate the relationship between age and sleep-related functional status found with this sample.

Other Findings

Causes of Sleep-Related Distress

In Table A8, it is evident that a large portion of the sample reported anxiety and distressing thoughts (32%) as causes of sleep-related distress. Many of the descriptions of thoughts that participants gave suggested that the thoughts triggered insomnia. This is similar to a study with 74 hospice patients that found that 36% of participants had trouble sleeping due to worry (Hugel et al., 2004). Pain/physical discomfort (19%) and hospital noises/disruptions (11%)

were other reported causes of sleep-related distress in this sample. Among those domains, most of the descriptive examples again suggested that the causes of sleep-related distress (e.g., pain, noise) were triggers of insomnia. A positive relationship between these specific causes of sleep-related distress and insomnia may explain the association found between insomnia and sleep-related distress with this sample.

Limited productivity or activity (11%) was another domain reported to cause sleep-related distress but within this domain, participant descriptions seemed to be more closely tied to problems with excessive sleepiness than insomnia. Given that relatively few participants reported this domain as a cause of sleep-related distress, there is less support for an association between excessive sleepiness and sleep-related distress; and no such relationship was found with this sample. That said, level of sleepiness and sleep-related functional status were found to be negatively correlated in this study, which may align with the way some participants explained their struggles to function as being due to low energy or somnolence.

Willingness to Accept Inconveniences or Risks to Alleviate Sleep-Related Distress

Table A9 relates to what participants are willing to accept for an intervention that can help to alleviate sleep-related distress. Virtually all participants were open to options with minimal risks (97%) and, at first, a majority was open to the inconvenience of taking a prescription medication (68%) or wearing a positive airway pressure mask (57%). However, once participants were asked about their willingness to accept common risks and side effects, less than a fifth of participants gave positive responses for any one item. The least acceptable were headaches (8%), difficulty falling or staying asleep (5%), anxiety (5%), reduced ability to interact with others (3%), abdominal discomfort (3%), less time to live (3%), and confusion (0%). It would seem that avoiding additional pain, emotional distress, insomnia, social

disruption, or loss of meaning may be areas of importance to palliative care inpatients that few would want to sacrifice for less sleep-related distress.

PAP therapy for sleep apnea is often thought of as cumbersome and undesirable for palliative care patients due to a perception that it would add to a patient's distress level. However, this study found that 57% of participants would be interested in trying PAP therapy. Not everyone experiences side effects, and some find the benefit of PAP therapy so great that they accept problems like minor skin irritation or airway drying. Additionally, there are often ways to reduce side effects such as adjusting air humidity or changing the mask style. If someone decides they do not want to use PAP therapy, there are other treatment options available, such as mandibular advancement or upper airway stimulation devices to improve airway patency. Research trials would be useful to establish the actual tolerability of sleep apnea treatments with palliative care inpatients, however, the lack of such studies should not be a barrier to offering palliative care patients standard interventions known to be effective and beneficial for other populations.

Study Strengths and Limitations

This study was intended as a pilot to gather preliminary data and assess feasibility of methods. As a descriptive and cross-sectional study, procedures were not designed to examine longitudinal aspects of sleep-related issues in palliative care; nor were they meant to establish evidence of instrument reliability/validity or efficacy of any particular intervention. The participants in this study constituted a small convenience sample limited to one health care setting and the results may not be applicable to other inpatient palliative care settings.

While the sample size was small with 38 total participants and 37 that completed all study measures, the size was reasonable to accomplish most study goals. The measured

prevalence of RLS was too low to obtain meaningful statistical results related RLS status; and in this case, a larger sample size of approximately 120 may have yielded enough participants with RLS to perform the planned analyses.

The array of demographic and contextual data collected in conjunction with the study measures provided useful insights related to study findings and procedures, as discussed earlier in Chapter 5. Each of the measures used in this study had advantages and disadvantages as discussed earlier in Chapter 5, and various potential modifications were proposed there. Using the multiple regression modeling procedure recommended by Hosmer and Lemeshow (2000) for small sample sizes, the likelihood of a type II error was reduced by lowering the chance that predictors able to explain part of the variance in the dependent variable would be eliminated. Due to the pilot nature of this study, the same level of significance was used for all statistical tests without correcting for multiple tests. However, the results provide trends which may suggest areas for future research.

Those receiving treatment for sleep disorders were not excluded from the study. For this reason, the measures of sleep-related problems could have underestimated prevalence rates if participants were already receiving treatment. Treatments also could have influenced the outcome measures of sleep-related distress and sleep-related functional status such that the negative effects of sleep-related problems were less appreciable with respect to these outcomes.

With respect to data collection, it was evident early on that most participants were unable to complete survey forms independently without great difficulty due to severe physical problems such as weakness, fatigue, motor incoordination, and visual problems. All participants were offered the opportunity to fill out forms on their own, however, all preferred to have the researcher provide assistance by reading questions aloud and writing in their responses. Future

study designs should account for the likelihood of physical limitations within this population and consider ways to reduce data collection burden for participants. Planning for the researcher to perform all physical data collection would promote standardization of this procedure with all study participants.

While assisting with the completion of study forms, it became evident that participants often struggled to mentally process components of the study. Many times, instructions, items, or response choices had to be repeated by the researcher; yet very few participants expressed difficulty hearing the researcher. To maintain overall integrity of participant responses, the researcher provided clarification as needed when participants found instructions or terminology confusing. There is a possibility that this biased study results, however, this type of interaction is similar to everyday clinical scenarios where it is necessary to have back and forth dialogue to ensure that both parties understand one another. This is especially important when there are cognitive limitations due to illness or when health literacy is low.

The amount of time it took to complete study procedures after consent had been obtained ranged from about 15 minutes to 1 hour. Occasionally, the researcher had to return the next day to complete study procedures due to patient fatigue. A benefit of having the researcher maintain and complete all forms directly with participants was that study procedures could be streamlined. The researcher was more able to recognize and intervene when a participant misunderstood an item or was unable to concentrate on study tasks. There was less chance for participants to miss items or for study documents to become lost. Additionally, by having the researcher alleviate participants of the work of steadily holding a document, reading numerous pages with small print, and maintaining control of a writing implement; study procedures could be completed more quickly with less possibility of participants becoming overly fatigued or frustrated. This

likely improved the legibility and accuracy of responses and facilitated the high survey completion rate, with only one participant failing to complete the survey due to fatigue.

Despite missing approximately one-third of patients identified by the palliative care team for potential recruitment due to the rapid discharge of many patients, the participation rate of those found eligible was high at 48%. Physical symptoms (e.g., fatigue/sleepiness, pain, and nausea/vomiting) were common reasons given for declining, though some patients requested that the researcher return later because they wished to participate once they felt better. There were many patients who could not be approached due to clear incapacitation related to severe cognitive impairments, delirium, or reduced consciousness. They may have initially been recommended by the palliative care team for recruitment but deteriorated prior to being approached by the researcher. In this sense, the very nature of being a palliative care patient made it difficult to participate in the study. As such, those unable to participate due to the severity of their illness were likely underrepresented in the sample.

Unfortunately, many studies with palliative care patients exclude those with cognitive impairment or psychiatric illness, however this study did not, and this is a strength of the study. Cognitive impairment and mental health concerns may be primary conditions or they may arise as a result of severe illness or sleep-related problems. It is important to include these patients when feasible so that they're experiences are represented in the data and their struggles are not overlooked.

It is not known how many palliative care patients were not considered for this study, as the palliative care team was not asked to provide this information. However, it was notable during recruitment that the palliative care team deemed the majority of their patients to be inappropriate for the study. Given a lack of representation for so many palliative care patients,

it's difficult to know how well the results of this study reflect the inpatient palliative care population as a whole. Potential ways to include patients with limited capacity in future studies could be to obtain consent from legally authorized representatives (e.g., responsible family members), to use images in conjunction with words for assessments (e.g., a facial expressions pain rating scale), and to seek input from a patient's bedside nurse or family members. Understanding the sleep-related experiences and needs of the sickest patients is certainly a relevant component of the philosophy of palliative care and this is an area that deserves more attention.

Conclusion

For each person, the need for regular, high quality sleep never abates; and sleep health is one area that is universal to all palliative care patients. Preventing the negative consequences of poor sleep aligns with the goals of palliative care which aims to alleviate distress, promote comfort, and improve quality of life across physical, intellectual, emotional, social, and spiritual realms. Sleep touches all of these realms, and there is a need for ongoing sleep research and provider education in palliative care.

In this pilot study of palliative care inpatients, preliminary data was obtained to investigate sleep-related problem prevalence rates and relationships between sleep-related problems, sleep-related distress, and sleep-related functional status. Among a convenience sample of 38 palliative care inpatients recruited from an urban, academic medical center, there was a high prevalence of insomnia (62%), high risk for sleep apnea (57%), and excessive sleepiness (41%). Significant positive correlations were found between insomnia severity level and sleep-related distress, and between excessive sleepiness and poor sleep-related functional status. Linear regression models suggested that of multiple variables considered, level of

insomnia severity was a significant predictor of sleep-related distress; and age, level of insomnia severity and level of sleepiness were significant predictors of sleep-related functional status. Participants were asked to share their reasons for sleep-related distress and willingness to accept various inconveniences and risks to alleviate sleep-related distress. The most common reasons given for sleep-related distress involved difficulty sleeping due to anxiety or distressing thoughts. Most participants reported they would be willing to take prescription medication or utilize a positive airway pressure device if they would alleviate their sleep-related distress, however much fewer maintained their willingness if the intervention caused noticeable side effects.

The results of this study provide foundational information regarding sleep-related issues and methodological considerations with palliative care inpatients upon which future studies can build. Future efforts should focus on the development of valid and reliable instruments to measure sleep-related phenomenon with this population. Subsequently, these instruments can be used to screen individual palliative care patients and more accurately identify the prevalence of sleep-related problems and their associations with other aspects of well-being. Over time, risk factors for sleep-related problems in palliative care can be better recognized, new interventions can be trialed, and clinical guidelines can be updated to reflect the evidence and improve outcomes.

Appendix

Tables and Figures

Table A1

*Sample Descriptive Statistics (*N = *38)*

Variable	***M***	***SD***
Age (years; range 26 - 78)	57	14
	n	**%**
Sex		
Female	22	58
Male	16	42
Race / Ethnicity		
White	25	66
Black or African American	11	29
Asian	1	3
Hispanic or Latino	1	3
Highest educational level		
High school diploma, GED or less	12	32
Trade / technical / vocational training	4	11
Some college or university education	6	16
Bachelor's degree	8	21
Graduate degree	6	16
Post-graduate education	2	5
Employment status		
Retired	15	39
Disabled	14	37
Employed	7	18
Homemaker	2	5
Marital status		
Married / partnered	19	50
Divorced / separated	10	26
Single, never married	6	16
Widowed	3	8
Health insurance status		
Insured	35	92
Not insured	3	8
Self-reported reason for hospitalization [a]		
Pain	9	24
Cancer management	7	18
Heart disease	6	16
Gastrointestinal / hepatic condition	5	13
Dehydration	2	5
Intravenous medication administration	2	5

Surgical complication management	2	5
Other	5	13
Self-reported presence of a sleep disorder		
No	20	53
Yes	18	47
Self-reported sleep disorders [b]		
Insomnia	15	40
Sleep apnea	6	16
Restless legs syndrome	2	5
Narcolepsy	0	0
REM sleep behavior disorder	0	0
Other	1	3
Self-reported sleep disorder treatments [a]		
Sleep aid medication	7	18
PAP therapy	3	8
Self-reported total sleep time in 24 hr [c] (*Mdn* = 7.5, range: 3.5 – 20)	37	97
Other self-reported medical / psychiatric conditions [b]		
Cancer	29	78
Chronic pain	20	54
Anxiety	17	46
Depression	13	35
Iron deficiency anemia	10	27
Heart failure	8	22
Lung disease	8	22
Stroke or traumatic brain injury	6	16
Thyroid disease	6	16
Kidney disease	5	14
Autoimmune disorder	4	11
Neuromuscular disease	1	3
Dementia	0	0
Self-reported medication use in last 3 days [b]		
Sedating medications	30	79
Opioids	24	63
Antidepressants	16	42
Sleep aids	14	37
Supplemental oxygen	12	32
Benzodiazepines	7	18
Gabapentin	3	8
Muscle relaxants	3	8
Stimulants	0	0

Note. *M* = mean; *SD* = standard deviation; REM = rapid eye movement; PAP = positive airway pressure; *Mdn* = median. Means and standard deviations are reported for continuous variables

with symmetric distributions, while medians and ranges are reported for continuous variables with skewed distributions.

[a] Participants were asked an open-ended question and responses were sorted into relevant categories. [b] Participants could check all that apply. [c] One participant did not provide a numerical response, stating she was “uncertain” how many hours she slept in a 24 hr period.

Table A2

*Sleep-Related Problem, Sleep-Related Distress and Sleep-Related Functional Status Severities (*N = *37)* [a]

Variable	***M***	***SD***
Excessive sleepiness		
ESS score	8.9	5.4
Insomnia		
ISI score	11.5	7.9
	Mdn	**Range**
Sleep apnea risk		
STOP-Bang score [b]	3	0 – 8
Sleep-related distress		
SDT score	4	0 – 10
Sleep-related functional status		
FOSQ-10 score	18.5	11.3 - 20

Note. *M* = mean; *SD* = standard deviation; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; STOP-Bang = STOP-Bang Questionnaire; *Mdn* = median; SDT = Sleep-Related Distress Thermometer; FOSQ-10 = Functional Outcomes of Sleep Questionnaire - 10. Means and standard deviations are reported for continuous variables with symmetric distributions, while medians and ranges are reported for continuous variables with skewed distributions.

[a] One of the 38 study participants did not complete the ESS, ISI, STOP-Bang, SDT, and FOSQ-10. [b] The STOP-Bang score for one participant was calculated based on an assumption that neck circumference was < 41 cm, given a very slender appearing neck on visual inspection; the participant refused measurement due to the presence of a cervical central line.

Table A3

Prevalence of Sleep-Related Problems

Sleep-Related Problem	*n*	%
Insomnia [a]		
ISI score > 7	23	62
High risk for sleep apnea [a]		
STOP-Bang score > 2 [b]	21	57
Excessive sleepiness [a]		
ESS score > 10	15	41
Restless legs syndrome [c]		
Met all 2012 IRLSSG revised consensus diagnostic criteria for clinically significant RLS within the past month	5	14

Note. ISI = Insomnia Severity Index; STOP-Bang = STOP-Bang Questionnaire; ESS = Epworth Sleepiness Scale; IRLSSG = International Restless Legs Syndrome Study Group; RLS = restless legs syndrome.

[a] $N = 37$ because one of the 38 study participants did not complete the ISI, STOP-Bang, and ESS.

[b] The STOP-Bang score for one participant was calculated based on an assumption that neck circumference was < 41 cm, given a very slender appearing neck on visual inspection; the participant refused measurement due to the presence of a cervical central line. [c] $N = 38$.

Table A4

*Correlations for Measures of Sleep-Related Problems, Sleep-Related Distress, and Sleep-Related Functional Status (*N = *37)* [a]

Variable	1	2	3	4	5
1. Excessive sleepiness (ESS score)	—				
2. Insomnia (ISI score)	-.03 [b]	—			
3. Risk for sleep apnea (STOP-Bang score) [c]	-.02 [b]	.18 [b]	—		
4. Sleep-related distress (SDT score)	.19	.75*	.09	—	
5. Sleep-related functional status (FOSQ-10 score)	-.59*	-.22	-.07	-.19	—

Note. ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; STOP-Bang = STOP-Bang Questionnaire; SDT = Sleep-Related Distress Thermometer; FOSQ-10 = Functional Outcomes of Sleep Questionnaire - 10.

[a] One of the 38 participants did not complete the ESS, ISI, STOP-Bang, SDT, and FOSQ-10. [b] Pearson's correlation coefficient; all others are Spearman's correlation coefficients due to evidence of non-normal distribution of at least one of the variables tested. [c] The STOP-Bang score for one participant was calculated based on an assumption that neck circumference was < 41 cm, given a very slender appearing neck on visual inspection; the participant refused measurement due to the presence of a cervical central line.

*$p \leq .001$.

Table A5

*Measures of Sleep-Related Problems, Sleep-Related Distress, and Sleep-Related Functional Status by Restless Legs Syndrome Status (*N = *37)* [a]

Variable	RLS Absent (*n* = 32)		RLS Present (*n* = 5)	
	Mdn	Range	*Mdn*	Range
Excessive sleepiness				
ESS score	8.5	0 – 19	15	4 – 18
Insomnia				
ISI score	11	0 – 25	12	0 – 25
Sleep apnea risk				
STOP-Bang score [b]	3	0 - 8	4	2 – 6
Sleep-related distress				
SDT score	4	0 – 9	0	0 – 10
Sleep-related functional status				
FOSQ-10 score	18.415	11.33 – 20	18.5	16.17 – 19.33

Note. There were *n* = 32 (86%) participants without RLS and *n* = 5 (14%) participants with RLS. RLS = restless legs syndrome; *Mdn* = median; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; STOP-Bang = STOP-Bang Questionnaire; SDT = Sleep-Related Distress Thermometer; FOSQ-10 = Functional Outcomes of Sleep Questionnaire - 10. For purposes of comparison between groups, only medians and ranges are reported, without regard for normality of distributions, due to a very small subsample size of participants with RLS.

[a] One of the 38 study participants did not complete the ESS, ISI, STOP-Bang, SDT, and FOSQ-10. [b] The STOP-Bang score for one participant without RLS was calculated based on an assumption that neck circumference was < 41 cm, given a very slender appearing neck on visual inspection; the participant refused measurement due to the presence of a cervical central line.

Table A6

*Multiple Regression Model for Sleep-Related Distress (*N = *37*) [a]

Variable	Estimate	*SE*	*p*	Adjusted R^2
Sleep-Related Distress Model				.567
Intercept	-.159	.619	.799	
Insomnia (ISI score)	.309	.045	<.0001	

Note. ISI = Insomnia Severity Index.

[a] One of the 38 participants did not complete the ISI and sleep-related distress measure.

Table A7

*Multiple Regression Model for Sleep-Related Functional Status (*N = *37*) [a]

Variable	Estimate	*SE*	*p*	Adjusted R^2
Sleep-Related Functional Status Model				.523
Intercept	18.703	1.483	<.0001	
Age	.040	.021	.0701	
Insomnia (ISI score)	-.108	.037	.0068	
Excessive sleepiness (ESS score)	-.251	.053	<.0001	
Interaction term (ESS score – 8.946)*(ISI score – 11.541)	-.021	.008	.0095	

Note. ISI = Insomnia Severity Index; ESS = Epworth Sleepiness Scale.

[a] One of the 38 participants did not complete the ISI, ESS, and sleep-related functional status measure.

Table A8

*Self-reported Causes of Sleep-Related Distress in the Past Week (*N = *37)* [a]

Cause [b]	*n*	%	Example Description / Quote
Not applicable [c]	12	32	Denies sleep-related distress
Anxiety / Distressing thoughts	12	32	Shortness of breath causing anxiety and participant feeling worried he will stop breathing during sleep
			"My brain doesn't quiet down"
			"My mind running"
			Racing thoughts possibly due to the “psychological effect of receiving chemotherapy”
			Sitting around thinking “this might be my last summer”
			Feelings of aggravation
			Worries about work/future make it hard to shut off brain
			Thinking about things she can't do anymore
			Mind on thoughts that make it hard to sleep
			Anxiety causing insomnia
			Can't sleep due to stressful thoughts about cancer/family and can't turn thoughts off
Pain / physical discomfort	7	19	Waking up choking and gagging
			Waking up in pain
			Shortness of breath
			Due to pain participant has to sleep with head of bed partially elevated and cannot sleep in comfortable positions on side/stomach
Limited productivity or activity	4	11	Not being able to work at a job due to excessive sleepiness
			Not having energy to do things she wants to do and is capable of doing
			Unable to be up and walking due to daytime drowsiness
			Distressed that he can't be more productive during the day due to poor sleep

Cause [b]	*n*	%	Example Description / Quote
Hospital noises / disruptions	4	11	Interruptions by staff
			Hospital noises waking participant up
			Not being able to fall back to sleep if woken up by something
Other	5	14	"I'm not sure but probably my cancer"
			Dreams
			Waking up at 3:00 a.m. to use the bathroom
			Trouble falling and staying asleep
			Waking up a lot at night

[a] One of the 38 study participants did not complete the Sleep-Related Distress Thermometer nor answer the question regarding causes of sleep-related distress. [b] Participants were asked an open-ended question regarding the cause of their sleep-related distress and were permitted to provide multiple responses. [c] One participant scored 0 on the Sleep-Related Distress Thermometer but gave pain as a cause of sleep-related distress.

Table A9

*Risks and Inconveniences Participants Would Be Willing to Accept for Interventions That Alleviate Sleep-Related Distress (*N = *37)* [a]

Condition	*n* [b]	%
Intervention with minimal risk (e.g., relaxation, chamomile tea)	36	97
Taking a prescription medication (e.g., sleep aid, stimulant)	25	68
Medication risks / side effects		
Uncomfortable feelings / urge to move legs	6	16
Breathing pauses during sleep	5	14
Reduced appetite	5	14
Less daytime alertness	4	11
Headaches	3	8
Difficulty falling or staying asleep	2	5
Heightened anxiety	2	5
Reduced ability to interact with others	1	3
Shortened lifespan	1	3
Confusion	0	0
Wearing a breathing mask (e.g., PAP therapy)	21	57
PAP therapy risks / side effects		
Airway drying / irritation	7	19
Skin irritation from mask	7	19
Waking from occasional mask leak noise	7	19
Stomach discomfort from aerophagia	1	3

Note. PAP = positive airway pressure.

[a] One of the 38 study participants did not provide responses regarding risks and inconveniences she would be willing to accept. [b] Participants could check all that apply.

Figure A1

Biobehavioral Conceptual Framework for Sleep in Palliative Care

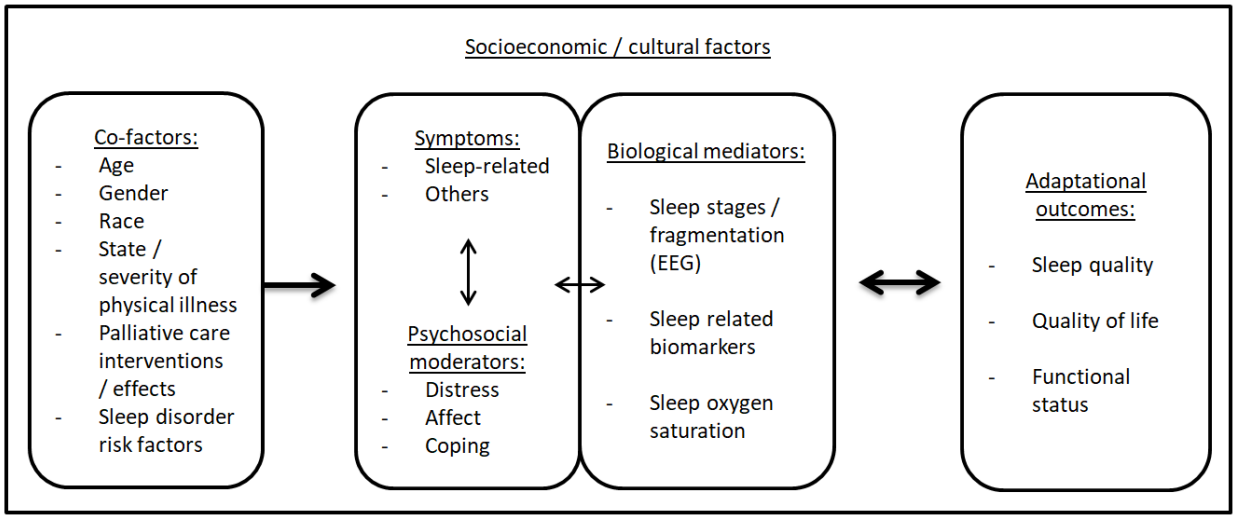


Figure A2

Dissertation Foci

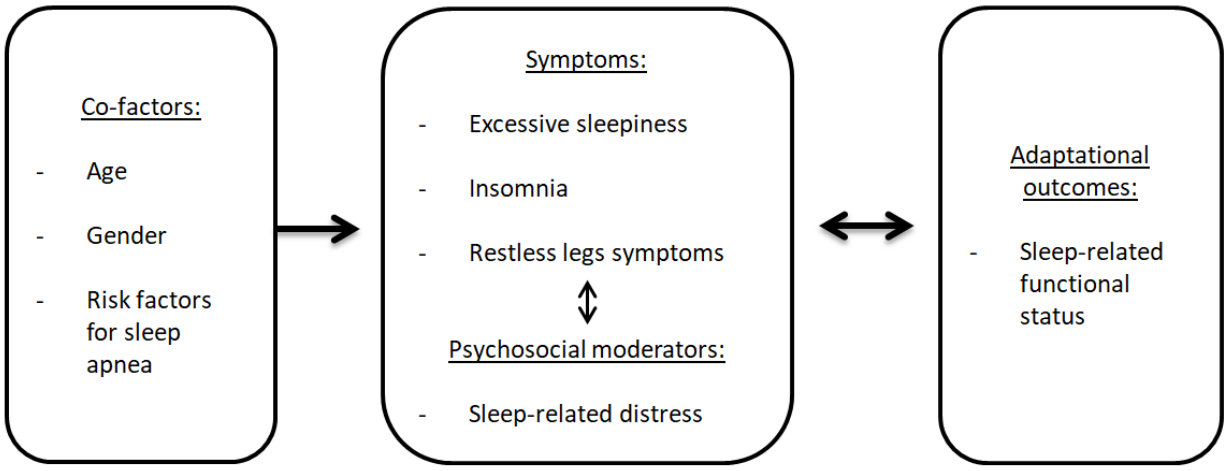
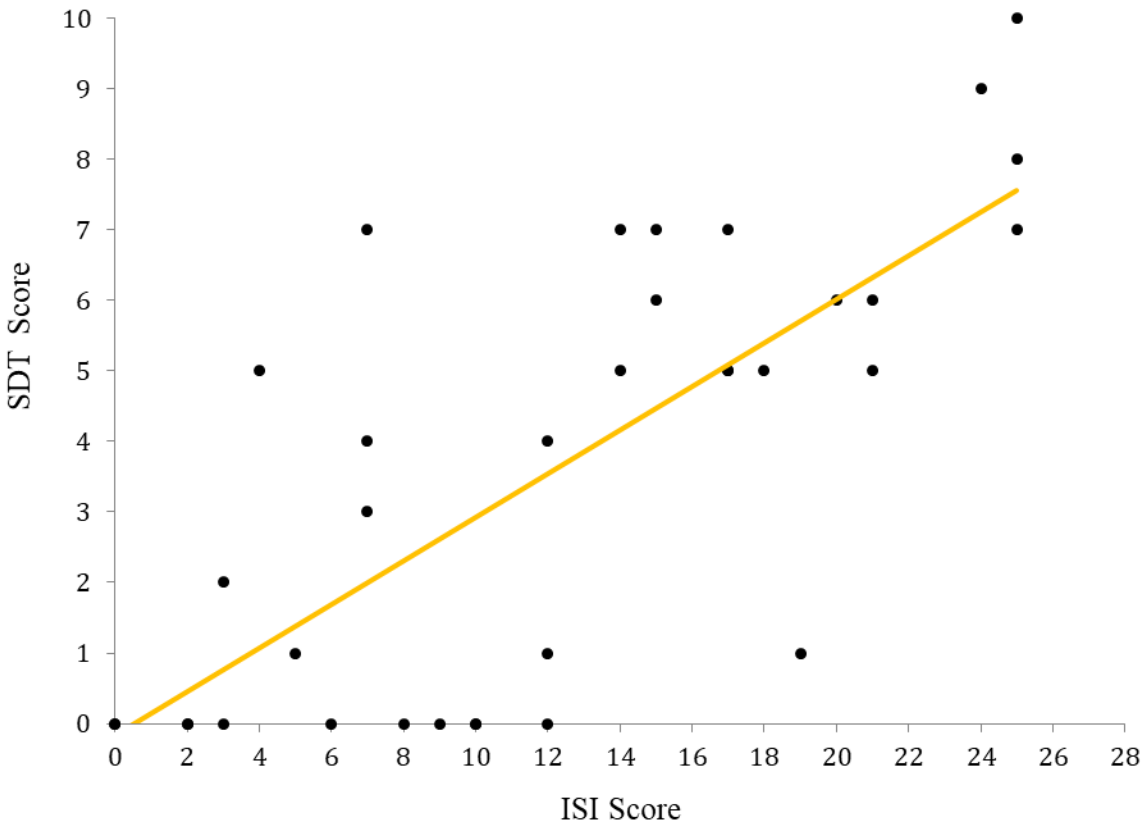


Figure A3

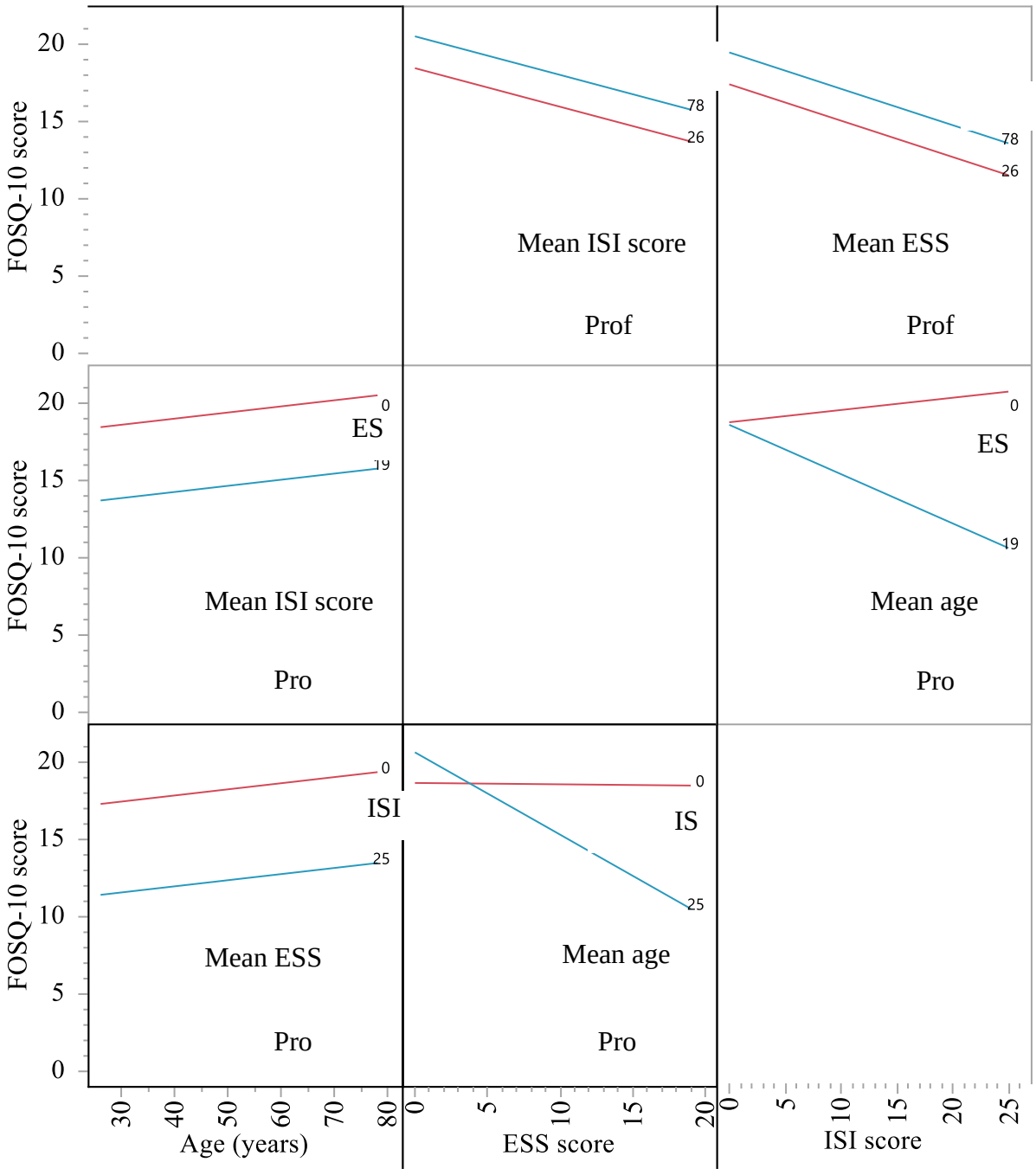
Scatterplot of Sleep-Related Distress Level (SDT Score) Against Insomnia Severity (ISI Score) and Predicted Regression Line for Model of Sleep-Related Distress



Note. SDT = Sleep-Related Distress Thermometer and ISI = Insomnia Severity Index.

Figure A4

Interaction Profiles for Sleep-Related Functional Status (FOSQ-10 Score) Regression Model



Note. FOSQ-10 = Functional Outcomes of Sleep Questionnaire - 10, ISI = Insomnia Severity Scale, and ESS = Epworth Sleepiness Scale.

Vita

Lisa C. Sievers attended Smith College in Northampton, Massachusetts and graduated with a Bachelor of Arts degree in Physics in 2000. During Summer 1999 she participated in the Research Experiences for Undergraduates program, supported by the National Science Foundation, as a medical physics research assistant at the University of New Mexico in Albuquerque, New Mexico. She accepted a graduate fellowship at the University of Rochester in Rochester, New York where she obtained a Master of Science degree in Biomedical Engineering in 2002. While in Rochester she volunteered as a responder with the Rochester Police Department to support neighborhoods affected by homicide, an inpatient mental health assistant at the Rochester Psychiatric Center, and a basic emergency medical technician at Honeoye Falls – Mendon Volunteer Ambulance. In 2006, she took a position as a patent examiner at the United States Patent and Trademark Office in Alexandria, Virginia where she reviewed patent applications for measuring and testing devices until 2008. She enrolled in an accelerated nursing program at Virginia Commonwealth University (VCU) in Richmond, Virginia in 2008 and earned a Bachelor of Science degree in Nursing, cum laude with a GPA of 4.0/4.0 in 2009, and a Master of Science degree in Nursing with a GPA of 4.0/4.0 in 2011. In support of her bachelor's and master's nursing education, she received a Theresa Thomas Scholarship, a Virginia League of Nursing Scholarship, a VCU Phi Kappa Phi Honor Society Graduate Scholarship, and a MCV Hospital Auxiliary Scholarship. While in the accelerated nursing program, she was inducted into several honor societies including Sigma Theta Tau International Honor Society of Nursing, Golden Key International Honour Society, and Honor Society of Phi Kappa Phi. She also worked as a care partner in the VCU Health System Emergency Department, a graduate resident director for VCU Residential Life & Housing, and a graduate research assistant at the VCU School of Nursing. During her research assistantship, she provided support for a National Institutes of Health-funded study on the effect of backrest elevation on skin integrity in the critically ill, under principal investigator Dr. Mary Jo Grap. Related to this research, she won the Best Poster Presentation Award at the VCU Graduate Student Association Research Symposium & Exhibit in 2010. She also received the VCU Emerging Leader Award in 2009, the VCU Residential Life & Housing Outstanding Community Developer Award in 2009, and the Virginia Council of Nurse Practitioners Richmond Region Outstanding Nurse Practitioner Student Award in 2011. She obtained board certifications as an acute care nurse practitioner in 2011, a family nurse practitioner in 2013, and a psychiatric mental health nurse practitioner in 2016. She has held nurse practitioner positions with the Medical Critical Care Service at Inova Fairfax Hospital in Falls Church, VA; and at VCU Health System in the Cardiothoracic Surgery step-down unit, the Center for Sleep Medicine, and the Adult Inpatient Psychiatry unit. While at the VCU Center for Sleep Medicine, she supervised medical students as a clinical instructor appointed by the VCU School of Medicine. In 2013, with support from the Jessie Ball du Pont Foundation, she participated in an advanced practice palliative care externship at the VCU Massey Cancer Center and this experience inspired her dissertation topic on sleep in palliative care. She completed the requirements for the Doctor of Philosophy degree in Nursing at VCU in 2021.

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