

Sleep Disturbance in Patients with Advanced Cancer

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### **Abstract**

As cancer detection and treatment improves, people with cancer diagnoses are living longer. Cancer as a chronic illness has led to new demands to manage the side effects of the disease. In cancer patients, one of the most common symptoms is sleep disturbance and fatigue. Sleep is critical for providing restorative, protective, and energy-conserving functions that are imperative for human life. The purpose of this study is to be able to describe sleep trajectories and symptom burden for hospitalized patients with advanced cancer over time. The Unpleasant Symptom Theory was used to explain how distressing symptoms, for example sleep disturbances, are a result of various factors. This study is a secondary analysis of a multi-site, prospective, observational study of palliative care consults in hospitalized patients with advanced cancer. Participants in this study included patients 18 years or older admitted to an acute care unit with advanced cancer that did not fit any of the exclusion criteria. The Condensed Memorial Symptom Assessment Scale (CMSAS) was used to assess sleep disturbances in study participants as well as co-occurring symptoms of pain, worry, nervousness, sadness, and lack of energy. We reviewed 12 adults that had complete data. Sleep disturbance was present in 90% of days measured and the patients endorsed an average of 5.5 concurrent symptoms when sleep disturbance was endorsed. Results from this study are consistent findings with others involving patients with cancer.

## **I. Statement of Problem**

### **Introduction**

On average, forty percent of Americans will at some point in their lifetime develop cancer, and nearly 600,000 American deaths will occur annual from this condition (May et al., 2016). As clinical care and research advances, cancer is being detected, diagnosed, and treated earlier. These improvements have led to more individuals surviving the initial period and to cancer being managed as a chronic, long-term illness (McCorkle et al., 2011). The disease itself as well as the forms of treatment cause a high symptom burden in patients, with sleep problems rated one of the most bothersome symptoms that cancer patients experience (Otte et al., 2015).

### **Background**

Sleep is critical for providing restorative, protective, and energy-conserving functions that are imperative for human life (Matthews et al., 2016). Lack of sleep, whether due to difficulty initiating sleep or problems maintaining sleep itself, interrupts normal functioning. Leaving these sleep problems uncontrolled can lead to a decrease in neurological abilities which in turn decreases one's quality of life (Coe, et al., 2018).

Chronic sleep loss is a serious health issue that affects millions of people (Basner, Dinges, Ma, Rao, 2015). Impacts on the brain from lack of sleep can be detrimental as it effects attention, memory, and learning. Patients experiencing poor sleep typically also face other burdensome symptoms. Feelings of pain, dyspnea, anxiety, and depression can further perpetuate sleep disturbance in already ill patients (Basara, Capezuti, Krieger, Woody, Zadeh, 2018).

Despite the importance of sleep, especially in ill patients, hospitals negatively impact sleep hygiene. Frequent periods of wakefulness by care providers, noise level, and light all add to sleep disruption in a hospital setting (Missildine, 2008).

Pain, fatigue, and sleep disturbance often exist as co-occurring symptoms and even more so in those with cancer (Coe, et al., 2018). These symptoms negatively affect quality of life and can furthermore negatively impact prognosis (Coe, et al., 2018).

Patients with advanced cancer may experience episodes of acute illness that require hospitalization. Hospitalized acutely ill patients, such as those with cancer, are at the highest risk for nonrestorative sleep leading to poor patient outcomes (Stewart & Arora, 2018). With rates of chronic cancer increasing, the need to care for the associated symptom burden, including sleep, is critical. Despite the acknowledgement that levels of sleep disturbance in advanced cancer patients is high, little advancements have been made to manage these issues (Coe, et al., 2018). More evidence is necessary to guide management of this disturbance.

### **Purpose of Study**

The purpose of this study is describe sleep problems and the co-occurring symptom burden for hospitalized patients with a diagnosis of cancer.

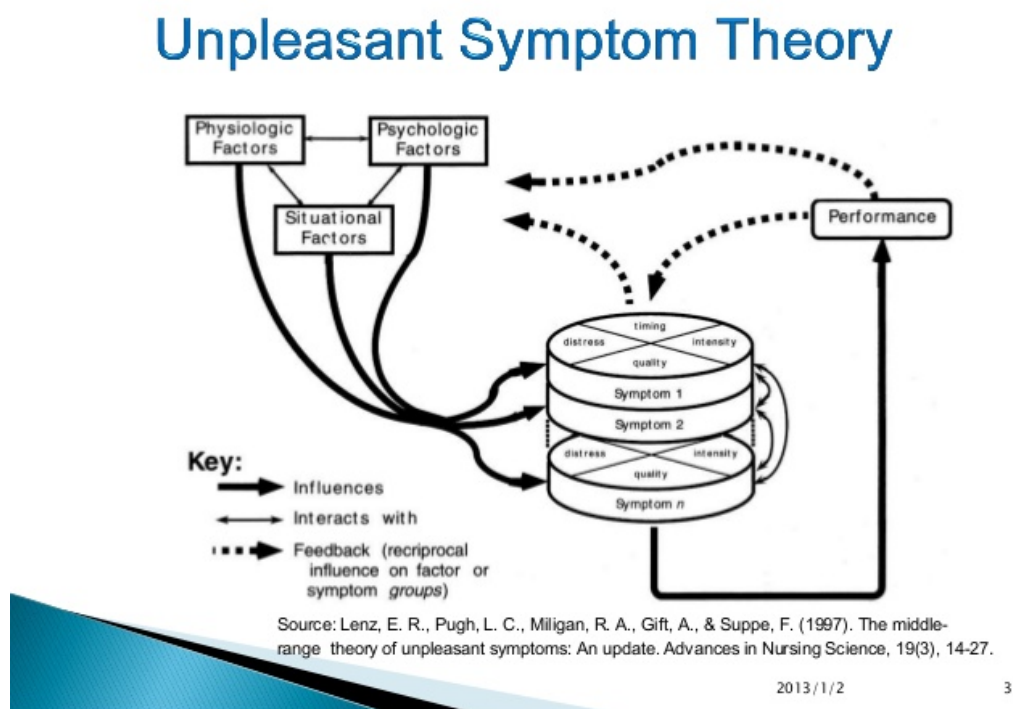
### **Significance of Study**

The increase in cancer survivorship has led to an increased need to care for the symptom burden that accompanies advanced cancer as it transitions from an acute to a chronic illness.

### **Theoretical Framework**

The Unpleasant Symptom Theory, demonstrated in Figure 1 below, was created by Elizabeth Lenz, a nurse researcher involved in clinical practice (Lenz, Pugh, Miligan, Gift, & Suppe, 1997). The theory is made up of three components including the symptoms experienced,

the factors influencing the symptoms, and what these factors and symptoms result in (Lopes-Junior, et al., 2015). The influencing elements include physiologic, psychological, and situational factors. The theory explains how distressing symptoms, for example sleep disturbances, are a result of various factors. The theory also demonstrates how co-occurring symptoms influence performance. The framework displays that in order to alleviate symptoms, interventions should also be aimed at the factors that alter them. This in turn results in better performance.



**Figure 1. Unpleasant Symptom Theory**

### Research Question

What is the rate of sleep disturbance and concurrent symptom burden in patients with cancer?

### Definition of Terms

*Advanced Cancer:* Diagnosis of cancer that is unlikely to be cured, the patient will have to live with as a chronic illness.

*Insomnia:* a report by an individual of difficulty sleeping.

*Sleep:* A time where eyes are closed, muscles are relaxed, allowing the mind and body to restore itself.

*Sleep Disruption:* Awakenings in the night.

*Sleep Latency:* When it takes a longer length of time to fall asleep.

*Symptom:* a feature, either physical or mental, that is apparent to the patient and a result of a disease.

## **II. Review of Literature**

### **Overview**

The purpose of this literature review was to investigate the association between sleep and cancer. Using the key words ‘cancer’, ‘oncology’, ‘sleep,’ ‘sleep disturbance,’ ‘sleep quality,’ with the following search engines: Google Scholar, PubMed, and CINHALL, the review of literature was conducted. Dates of articles were restricted to the past 10 years, 2008-2018, to keep the information gathered up to date. Overall, numerous studies have looked into the symptom burden of cancer patients and sleep disturbances were found amongst many of the participants in the articles examined.

Sleep is critical. It provides for providing restorative, protective, and energy-conserving functions that are imperative for human life (Matthews et al., 2016). Disturbance in sleep can lead to disruption in behavioral processes as well as fatigue. Fatigue is a feeling of tiredness or weakness. This is a subjective feeling that, in the average healthy person, is caused by energy expenditure being greater than the amount of sleep that was had, often caused by poor sleep.

Poor sleep is determined by a number of present symptoms. Sleep disruptions throughout the night, sleep latency, an overall decreased number of hours of sleep, and the inability to function during the day without napping are all signs of dysfunctional sleep (Otte, et al., 2015). A sleep disorder affects nearly 70 million Americans suffer from (Stewart & Arora, 2018). Of those affected, a large majority of the sleep disturbance is caused by illness and hospitalization.

### **Sleep Disturbance in the Hospital Setting**

Being in a hospital environment often interferes with a proper sleep cycle. Between frequent visits from care providers, noise, and light disruptions, sleep barriers are common in this setting. These disturbances in the hospital that lead to acute sleep loss have been associated with overall poor patient outcomes and poor patient experience (Stewart & Arora, 2018).

Noise is one of the largest factors in sleep disturbance in a healthcare setting. In a publicly reported quality measure on noise, 42% of hospitalized patients considered their room to not be quiet overnight and ranked it as the worst of patient experience measures (Stewart & Arora, 2018). Much of the noise came from factors that were modifiable such as staff conversation (Stewart & Arora, 2018). Patients failing to receive quiet rooms often demonstrated clinical outcomes including, but not limited to, increased stress response and increased physiologic arousal adding to sleep disturbance (Stewart & Arora, 2018).

### **Sleep Disturbance in Cancer**

Due to underreporting, poor evaluation, and various types of sleep measures, both the severity and prevalence of sleep disturbance in patients with cancer is challenging to determine (Matthews et al., 2016). Despite the lack of complete data on sleep in cancer, the complaints of poor sleep are common in cancer patients. These complaints included difficulty falling asleep or staying asleep as well as frequent and prolonged awakenings overnight (Fiorentino & Ancoli-

Israel, 2007). The causes of these issues are multifactorial, resulting from various environmental factors, patient characteristics, and the disease, cancer, itself. Overall the rates of sleep disturbance in those with cancer are double that of the general population interfering with a patient's quality of life (Fiorentino & Ancoli-Israel, 2007).

Additionally, psychiatric issues have an effect on sleep. Problems such as anxiety and depression are often related to increased sleep disturbances in patients (Stewart & Arora, 2018). In an evaluation of fifty lung cancer patients, it was concluded that high levels of sleep dysfunction as well as other combined symptoms were present (Nishiura, Tamura, Nagai, Matsushima, 2015). The Athens Sleep Insomnia Scale (AIS) and Hospital Anxiety and Depression Scale (HADS) were used to assess the patients as well as asking about quality of life, pain, and overall fatigue. The results displayed that 56% of participants were facing sleep disturbance. The poor sleep correlated with high levels of anxiety and depression, higher pain levels, higher fatigue scores, and lower quality of life (Nishiura, Tamura, Nagai, Matsushima, 2015). The correlation between poor sleep and high levels of anxiety and depression could be due to the high levels of psychiatric symptoms leading to sleep disruption.

Pain is a major symptom associated with chronic illnesses. The frequently reported feeling of pain often experienced by cancer patients is a major cause of nighttime awakenings and overall poor sleep (Stewart & Arora, 2018). Pain is often treated with opioids. The use of opioids, although not well studied, has displayed a decrease in REM sleep causing a person who is using these medications to feel even less rested (Fiorentino, Ancoli-Israel, 2007). In a study of symptom burden done on adults receiving chemotherapy with advanced cancer, pain, sleep disturbance, and fatigue levels were high. This correlated with higher levels of stress and therefore higher levels of interference of daily life (Coe, et, al., 2018).



The disease of cancer itself has an effect on sleep. Both radiation and chemotherapy, treatments of cancer, have been known to create sleep issues as side effects from altered levels of inflammatory cytokines (Howell, et al., 2014). The distress associated with this chronic illness also effects the sleep-wake cycle. Maladaptive sleep behaviors then develop as a result of the long-term sleep disturbance which further perpetuates the issue (Fiorentino, Ancoli-Israel, 2007).

Cancer patients often experience insomnia, a subjective report of poor sleep. A study was done using a telephone help line to measure the prevalence of this disturbance using the Insomnia Severity Index. Out of the 500 patients surveyed, 59.4% reported some symptoms of insomnia with 27% of them stating that it was moderate to severe levels. This study concluded that these sleep disturbance issues are common and support is necessary for those affected (Morris et al., 2015). It was found that sleep pills did prove effective in inducing sleep in those facing disturbance, but they did not work well enough to improve overall sleep quality (Nishiura, Tamura, Nagai, Matsushima, 2015).

Similarly, a study done by Mercadante et al. (2015) found similar prevalence of sleep disturbances in patients with advanced cancer. Of the 820 patients surveyed, 60.8% of those that participated had consistent moderate-maximum sleep disturbance. These results were collected over a period of six months using the Athens Insomnia Scale and the Hospital Anxiety and Depression Scale (HADS). The use of the HADS displayed a positive correlation between sleep depression and anxiety and depression scores. The use of hormone therapy, opioids, and corticosteroids in patients also displayed higher disturbance in sleep. These results concluded that sleep issues are common in cancer patients and careful examinations should be done in order to treat the disturbances (Mercadante et al., 2015).

## Measuring Sleep

The Pittsburgh Sleep Quality Index (PSQI) is the most commonly used measurement tool for assessing sleep (Mollayeva et al., 2016). Searching for ‘Pittsburgh quality sleep index’ on PubMed resulted in 3,280 articles that used this tool. The PSQI was created in the 1980s to standardize the measure of sleep quality. It is aimed to provide both validity and reliability as well as help to discriminate “good” versus “poor sleepers. It was created in order to give patients something easy to complete that is also easy to interpret by researchers/clinicians (Mollayeva et al., 2016).

Actigraphy is another tool used for gauging sleep. It is a non-invasive and cost-effective monitor that tracks movement in order to analyze sleep-wake cycles (Roebuck et al., 2013). It can track movement 24 hours a day, and using the assumption that people move more while awake, it assesses sleep. Movement decreases with sleep and continues to decrease as people progress into the deepest stages of sleep (Massimiliano et al., 2015). Both the convenience and validity of actigraphy has led it to be the most accurate option to record sleep as an alternate to polysomnography (Van De Water et al., 2010).

Polysomnography (PSG) is considered the gold standard for sleep measurement. It is used widely to evaluate abnormal sleep to aid in diagnosing disorders through the measurement of brain waves, eye movement, muscle tension, respiration, heart rate, and leg movements (Fiorentino, & Ancoli-Israel, 2007). However, due to cost and user-related difficulties it is often impractical in a clinical environment which is why alternatives such as actigraphy and the PSQI exists (Van De Water et al., 2010).

Although all of these are examples of measuring sleep, each tool does so in a different way. The PSQI is a subjective self-report whereas actigraphy and polysomnography are

examples of objective and direct measuring. The PQSI is just one example collecting subjective sleep data as well as the Athens Sleep Insomnia Scale and the Condensed Form of the Memorial Symptom Assessment Scale.

### **Gaps in Literature**

In conducting the literature review, numerous areas of knowledge were lacking involving both sleep and cancer, and general sleep in the hospital setting. There is insufficient information regarding sleep loss in hospitalized patients. Often, studies focus only on measuring general symptoms of sleep. The underlying sleep disorders themselves are not always acknowledged. Underreporting and overall lack of assessment also leads to the gaps that exist in understanding and being able to better deal with sleep disruptions in patients.

### **Chapter Summary**

This review of literature was created to describe what current literature exists about sleep and cancer. It discusses the prevalence, causes, and perpetuating factors of the issue. It also identifies what gaps still exist in regard to underreporting and lack of assessment on sleep in cancer patients. With the number of people living with cancer as a chronic illness growing, treatment of symptom burden is becoming more prevalent and thus future studies are warranted in order to provide best evidenced-based care for patients.

## **III. Methodology**

### **Research Design**

This study is a secondary analysis of an NIH-funded prospective trial of an intervention to improve communication between nurses and their critically ill patients. The focus for this study was in the number of concurrent symptoms with sleep disturbance present. A common

cancer symptom cluster is sleep disturbance, pain, fatigue, depression, and anxiety, so we selected the variables “pain”, “lack of energy”, “sadness”, “worried”, and “nervousness” from the Condensed Memorial Symptom Assessment Scale.

### **Population and Sample Design**

This study was conducted in 2 Intensive Care Units (ICUs) with 89 endotracheal intubated and mechanically ventilated, critically ill adults (Happ, et al., 2014; Tate, et al., 2013). Participants were over 21 years of age, able to understand English, were able to be aroused at baseline, and nonspeaking due to endotracheal intubation. Informed consent was obtained from participants or their legally authorized representative. We obtained approval from The Ohio State University Institutional review board (IRB) for a secondary analysis of a subset of this data that was specifically in participants with cancer. We selected a subset of patients that had a cancer diagnosis given our aim of describing sleep and concurrent symptoms in patients with cancer.

### **Data Collection Procedures**

Once informed consent was obtained, data collectors performed a baseline assessment of symptoms using the Condensed Form of the Memorial Symptoms Assessment Scale (CMSAS) (Chang, Hwang, Kasimis, & Thaler, 2004). Follow-up symptom assessment was conducted once per day for the following 2 days. Since participants were non-verbal, they pointed to responses on the CMSAS indicating the presence or absence of each symptom.

### **Data Collection Instrument**

We were particularly interested in sleep, so data was collected on sleep quality at baseline and during the next 2 days. These daily patient assessments were completed using the CMSAS. This is a 14-item scale, rated on a 5-point system. It measures the presence, frequency, and amount of distress associated with various symptoms including energy, appetite, pain, dry

mouth, weight loss, drowsiness, shortness of breath, constipation, difficulty sleeping, difficulty concentrating, nausea, worrying, feeling sad, and feeling nervous (Chang, Hwang, Kasimis, & Thaler, 2004). The Memorial Symptom Assessment Scale (MSAS) compared to other questionnaires is a valid and reliable instrument (Browall, Sarenmalm, Nasic, Wengström, & Gaston-Johansson, 2013). This was determined by a study of 206 participants with cancer who received the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC) (Montazeri, et al., 1999). And the MSAS (Chang, Hwang, Kasimis, & Thaler, 2004). Results concluded that the use of the Memorial Symptom Assessment Scale has both convergent validity and consistency (Browall, Sarenmalm, Nasic, Wengström, & Gaston-Johansson, 2013).

### **Data Analysis**

Descriptive statistics including percentages and means, were used to describe the presence of specific symptoms as well as the average symptom burden experienced.

## **IV. Results**

The first 30 patients were excluded from analysis due to a lack of sleep data leaving us with 12 patients that had complete data. We reviewed symptom data for these patients with a cancer diagnosis who were mechanically ventilated. The average age was 58 with a range of 36-80 years old. The majority of patients were female and white at 67% female and 92% white. All participants were on mechanical ventilation for an average of 33 days, with a minimum of 4 days and a maximum of 88 days. These patients were critically ill as indicated by the average APACHE III score of 48 with a minimum of 23 and a maximum of 70. See table 1.

The first 30 patients were excluded from the analysis due to a lack of sleep data leaving us with 12 patients that had complete data. We reviewed symptom data for these patients with a cancer diagnosis who were mechanically ventilated. The average age was 58 (sd = 13.2, range = 36-80 years old). The majority of patients were female (n = 8, 67% of study population) and white (n = 11, 92% of study population). All participants were on mechanical ventilation for an average of 33 days (sd = 28.3, range = 4-88 days). These patients were critically ill as indicated by the average APACHE III score of 48 (sd = 14.2, range = 23 – 70 Score; See Table 1).

Results display a high level of symptom burden. Patients endorsed difficulty sleeping on 90% of days measured. In addition to sleep, pain was present in 80% of the days measured, worrying in 88% of days, sadness in 100% of days, nervousness in 94% of days, and lack of energy in 80% of days measured. Interestingly, the results varied based on the order questions on the CMSAS were asked. Those that were asked early in the interview to rate such variables as “pain”, “difficulty sleeping”, and “lack of energy” have a greater percentage of responses than those who rated those items later (as participants became less responsive to questions; See Table 2). For those patients that endorsed difficulty sleeping, there was an average of 5.5 concurrent symptoms also endorsed (sd = 0.642, range = 5 – 7). This is consistent with other studies, displaying the severity of the patient’s symptom burden and disease (See Table 3).

**Table 1. Demographics**

Variable	N (%)		
<b>Sex (female)</b>	8 (67)		
<b>Race (white)</b>	11 (92)		
	Mean (SD)	Minimum	Maximum
<b>Age</b>	58.08 (13.2)	36	80
<b>MV days</b>	33 (28.3)	4	88
<b>APACHE III (Knaus, et al., 1991)</b>	48 (14.2)	23	70

**Table 2. Symptoms**

Symptom	% (yes/n)
<b>Difficulty sleeping</b>	90 (17/19)
<b>Pain</b>	80 (16/20)
<b>Worrying</b>	88 (15/17)
<b>Sad</b>	100 (17/17)
<b>Nervous</b>	94 (16/17)
<b>Lack of Energy</b>	80 (16/20)

**Table 3. Mean number of concurrent symptoms when sleep disturbance present**

Minimum	Maximum	Mean	Standard Deviation
5	7	5.53	0.642

## V. Conclusions and Recommendations

### Summary of Findings

Results from this study displayed consistent findings with other studies involving patients with cancer. Hospitalized patients with cancer continue to have a high symptom burden especially when symptom disturbances are present. This study found sleep disturbance present in 90% of the days measured. Additionally, when sleep disturbance was endorsed, there was also an average of 5.5 concurrent additional symptoms being experienced. With the complex nature of concurrent symptoms, it is difficult to ascertain if their symptoms were cancer specific or due primarily to the hospitalization.

### Implications of Study

The results of this study are applicable to the clinical setting because data shows that there is a relationship between sleep disturbance and the presence of other unpleasant symptoms. Further exploration of management of sleep in the hospital setting is warranted to improve overall symptom management.

### Recommendations

Further studies with larger sample sizes that compare hospitalized patients without a diagnosis of cancer to hospitalized patients with a diagnosis of cancer are needed. This will help



to determine if it is the hospitalization that is related to the symptom burden or if it is the disease of cancer itself. Additionally, it would be helpful to identify if certain symptoms are treated, does it affect the entire symptom burden experience.

### VI. Appendix

**Condensed Memorial Symptom Assessment Scale (CMSAS)**

Patient Name: \_\_\_\_\_ Date: \_\_\_\_\_  
Last First MI

**Instructions:** Below is a list of symptoms. **Please circle either Y or N** to indicate whether or not you have experienced the symptom during the last week. **If YES**, please circle the number that best describes how much this symptom has bothered or distressed you in the past 7 days.

Symptom	Present		If the symptom is present, please indicate how much the symptom bothered you.				
			Not at all = 0	A little bit = 1	Somewhat = 2	Quite a bit = 3	Very much = 4
Lack of energy	Y	N	0	1	2	3	4
Lack of appetite	Y	N	0	1	2	3	4
Pain	Y	N	0	1	2	3	4
Dry Mouth	Y	N	0	1	2	3	4
Weight Loss	Y	N	0	1	2	3	4
Feeling Drowsy	Y	N	0	1	2	3	4
Shortness of Breath	Y	N	0	1	2	3	4
Constipation	Y	N	0	1	2	3	4
Difficulty Sleeping	Y	N	0	1	2	3	4
Difficulty Concentrating	Y	N	0	1	2	3	4
Nausea	Y	N	0	1	2	3	4

How frequently did the following symptoms occur?

Symptom	Present	Rarely = 1	Occasionally = 2	Frequently = 3	Almost Constantly = 4
Worrying	Y N	1	2	3	4
Feeling sad	Y N	1	2	3	4
Feeling nervous	Y N	1	2	3	4

Chang, V. T., Hwang, S. S., Kasimis, B., & Thaler, H. T. (2004). Shorter symptom assessment instruments: the condensed Memorial Symptom Assessment Scale (CMSAS). *Cancer investigation*, 22(4), 526-536.

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