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Continuous Positive Airway Pressure Use and Mild Obstructive Sleep Apnea Syndrome (OSAS)

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CONTINUOUS POSITIVE AIRWAY PRESSURE USE AND MILD OBSTRUCTIVE
SLEEP APNEA SYNDROME (OSAS)

by

Michelle L. Nelson

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ABSTRACT

CONTINUOUS POSITIVE AIRWAY PRESSURE USE AND MILD OBSTRUCTIVE
SLEEP APNEA SYNDROME (OSAS)

by

Michelle L. Nelson

The University of Wisconsin-Milwaukee, 2014
Under the Supervision of Jennifer Doering, PhD, RN

Obstructive sleep apnea syndrome (OSAS) is an increasingly recognized sleep disorder
that affects an estimated ten percent of middle-aged women and 25 percent of middle-
aged men. Continuous positive airway pressure (CPAP) is the standard treatment for
individuals with moderate to severe OSAS. However, it is estimated that 80 percent of
individuals with OSAS have a milder form of the disease. The use of CPAP therapy in
persons with mild OSAS has not been widely researched and whether CPAP is
efficacious in this population remains inconclusive. OSAS has both psychological and
physiological effects on people. Two common effects of CPAP use in persons with
moderate and severe OSAS are reduced excessive daytime sleepiness (EDS) and reduced
blood pressure. The purpose of this study was to examine the relationship of CPAP use to
the outcomes of EDS and blood pressure in persons with mild OSAS. CPAP use was
defined as using CPAP for more than 4 hours per night for more than 70 percent of nights
recorded by the CPAP machine.

The study design was a retrospective chart review of electronic medical records
(EMR) from a sleep medicine clinic in the southeastern United States. The sample
consisted of 60 participants with mild OSAS who were divided into two groups based
upon the amount of CPAP use recorded in the EMR (4 or more hours of nightly use 70%

of nights, $n = 45$ and less than 4 hours of nightly use 70% of nights, $n = 15$). Blood

pressure (systolic and diastolic) and daytime sleepiness (Epworth Sleepiness Scale) data

were collected on each participant before the initiation of CPAP therapy and at six weeks

follow up. Independent samples t-tests were conducted to examine the differences

between the groups from baseline to six-week follow-up on the outcome variables. No

statistical significance was found for daytime sleepiness (*t* [34] = .865, *p* = .393) or either

systolic (*t* [52] = .911, *p* = .367) or diastolic (*t* [52] = 1.002, *p* = .321) pressures.

Sleepiness scores in the group who used CPAP four or more hours a night 70% of nights

decreased 6.6 points from baseline to 6 weeks, and decreased 8.1 points in the group who

used CPAP less than 4 hours a night 70% of the nights. Both groups experienced

clinically significant decreases in daytime sleepiness from nearly excessive daytime

sleepiness (ESS score >10) before CPAP initiation to nearly no daytime sleepiness at six

weeks follow up. There were significant limitations in data collection around both the

EMR and the CPAP machine reporting that have implications for practice, research, and

policy. Recommendations include standardization of CPAP use reporting across machine

type, clearly defining the role of the nurse in the care of OSAS patients, and improving

quality around data entry in the EMR. These results support the continued need to

research the effectiveness of CPAP in persons with mild OSAS.

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CHAPTER ONE

STATEMENT OF THE PROBLEM

Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly recognized sleep disorder that is estimated to affect 10 percent of middle-aged women and 25 percent of middle-aged men (Yu & Berger, 2011). OSAS is characterized by repeated episodes of collapse or narrowing of the upper airway during sleep that result in fragmented sleep, blood oxygen desaturations, and sympathetic activation (Fletcher, 2000; Young, Peppard, & Gottlieb, 2002). Excessive daytime sleepiness (EDS) and hypertension are commonly associated with OSAS (Baguet, Barone-Rochette, & Pepin, 2009; Rosenberg & Doghramji, 2009).

EDS is the inability to stay alert and awake during the waking periods of the day, which often result in incidental lapses into sleep (Pagel, 2009). These periods may be accompanied by an uncomfortable feeling or struggle to stay awake when the sleep is inopportune. EDS also presents a safety concern when driving, operating machinery, and other similar activities. One of the leading causes of EDS is OSAS (Rosenberg & Doghramji, 2009).

OSAS is a progressive disease that has many cardiovascular effects with one primary effect being hypertension. The European and American recommendations on hypertension recognize OSAS as an accepted cause of hypertension (Baguet et al., 2009; Mansia et al., 2007). Recent studies suggest that even mild forms of the disease may be correlated with hypertension (Barnes et al., 2002; Jaimchariyatam, Rodriquez, & Budur, 2010). Hypertension can lead to damage to the structure and function of the eye (Wong &

Mitchell, 2007), stroke, cardiovascular disease (Woo et al., 2014), and kidney disease (Lim et al., 2012).

Diagnosis of OSAS

The number of persons identified with OSAS is expected to rise considerably in the coming years. This is due in part to heightened awareness and increased screening and diagnosis, which in turn, will lead to a rise in the actual number of patients diagnosed with OSAS (Holmdahl et al., 2009). The increase in the number of patients with OSAS will place a considerable demand on the health care system. The presence of OSAS is frequently initially recognized by the daytime experience (excessive daytime sleepiness) of the patient or the nighttime sleep disturbance experienced by the bed partner. Classic nighttime symptoms include nocturnal awakenings, gasping during the night, apneas witnessed by bed partner, and loud snoring (Wenner, Cheema, & Ayas, 2009).

Diagnosis of OSAS is based primarily on the number of apnea-hypopnea events per hour an individual has during sleep as measured objectively by an overnight sleep study. An apnea is defined as the cessation of airflow for a time of at least 10 seconds. A hypopnea exists when either there is a 30 percent decrease in airflow from baseline, for a minimum of 10 seconds duration, with at least 4 percent desaturation from baseline, or there is at least 50 percent decrease in airflow for a minimum of 10 seconds duration with at least a three percent desaturation or an arousal (American Academy of Sleep Medicine, 2007). Apneas and hypopneas are based on laboratory findings. The severity of the disease is determined by the apnea-hypopnea index (AHI) (i.e., the number of apneas plus hypopneas per hour of documented sleep). According to the American Academy of Sleep Medicine guidelines, OSAS can be diagnosed when the AHI is equal to or greater

than 15 or when the AHI is equal to or greater than 5 and accompanied by one or more of the typical associated symptoms of OSAS (witnessed apneas, regular snoring, excessive daytime sleepiness, restless sleep, fatigue or insomnia) (American Academy of Sleep Medicine, 2007). OSAS is further classified as mild, moderate, or severe. The severity of the disease is determined by the respiratory disturbance index (RDI). RDI is defined as the number of apneas, hypopneas, and respiratory effort related arousals (RERA) per hour of sleep. Mild OSAS is determined by a RDI of 5-14, moderate 15-30, and severe >30 (Epstein et al., 2009). Mild to moderate OSAS represents approximately 80 percent of the OSAS population (Young et al., 2008).

The most effective validated diagnostic tool for diagnosing OSAS is an overnight in-laboratory polysomnography (PSG) (Kushida et al., 2005). The PSG enables the practitioner to continuously monitor several physiologic variables including oxygen saturation, chest/abdominal movement, airflow, electroencephalography, and electromyography. The primary outcome measures examined from the PSG for a diagnosis of OSAS are: 1) AHI, 2) arousal index (a measure of sleep disruption per hour of sleep), and 3) various sleep scoring statistics describing overall sleep quality (e.g., sleep efficiency) (Ruehland et al., 2011). Many sleep laboratories also have an accompanying video and audio recording of the overnight session (Wenner et al., 2009).

Due to the resources required for PSG (personnel and laboratory availability), efforts have been made to develop and validate ambulatory devices that can be used to diagnose OSAS. In a population of patients where OSAS is likely (loud snoring, gasping during sleep, nocturnal awakenings, or witnessed apneas) an ambulatory study may provide sufficient evidence to initiate appropriate therapy (Mulgrew, Fox, Ayas, & Ryan,

2007). Ambulatory devices are capable of measuring many of the same physiologic variables as the overnight PSG. The primary difference is that ambulatory devices require fewer signals, which in turn allows them to be less expensive and more ambulatory (Domingo & Vigil, 2011). Ayas et al. (2003) found that the use of an overnight device worn on the wrist measuring physiologic markers of peripheral vasoconstriction and sympathetic activation in combination with oxygen desaturation index (number of ≥ 4 percent desaturations per hour) was a reasonably sensitive and specific means of diagnosing OSAS.

Treatment of OSAS

Individuals diagnosed with OSAS are often treated with continuous positive airway pressure (CPAP) devices. CPAP acts as a pneumatic splint to prevent airway collapse during sleep by providing continuous pressure to the airway. The result is an increase in the actual size of the airway during treatment, primarily in the lateral direction, as well as decreasing lateral pharyngeal wall thickness and reducing airway edema associated with chronic vibration (snoring) and airway occlusion (Yagi et al., 2009). CPAP therapy is not curative and could possibly be a lifelong treatment (Gami, Caples, & Somers, 2003; Schendel, Powell, & Jacobson, 2011). The guidelines for recommended CPAP use are 4 or more hours a night 70 percent of nights (Weaver & Grunstein, 2008).

The use of CPAP therapy for the treatment of patients with severe OSAS (apnea hypopnea index > 30) has been validated in the literature as being effective in reversing upper airway obstruction during sleep and also in reducing many of the troublesome consequences associated with this disorder, particularly, EDS (Antic et al., 2011;

Yaremchuk et al., 2011). However, the majority (80 percent) of individuals with OSAS has a milder form of the disease (apnea hypopnea index 5 - 30) (Young et al., 2005). CPAP therapy in persons with mild OSAS has not been widely used and previous research findings have been inconsistent in regards to the efficacy of CPAP in this population (Barnes et al., 2002; Engleman et al., 1997; Engleman et al., 1999; Marshall et al., 2005; Patel et al., 2003; Redline et al., 1998).

Purpose

EDS is the inevitable result of insufficient sleep. Individuals who experience EDS are at risk of falling asleep inadvertently and at times, inappropriately. They often require naps during the day, either planned or unplanned, and can remain asleep for a variable amount of time. The struggle to stay awake during inopportune times is overwhelming and the individual experiencing EDS may feel as if they are losing a fight to stay connected to the external world. During this struggle for wakefulness attention diminishes, learning decreases, and memory is altered (Vernet et al., 2011). EDS can be physiological (underlying medical condition) or psychological (disturbed sleep) (Pagel, 2009). The researcher for this study is concerned with EDS as a psychological aspect of OSAS. The amount of subjective daytime sleepiness a person reports is influenced by the number of respiratory events (AHI) that occur during sleep (Hayashida et al., 2007).

Hypertension is clearly demonstrated to be associated with OSAS (Baguet et al., 2009; Buchner et al., 2007; Jaimchariyatam et al., 2010; Mansia et al., 2007; Peppard et al., 2000). Effective treatment of OSAS with continuous positive airway pressure (CPAP) has been shown to dramatically and acutely decrease mean heart rate and decrease blood pressure throughout the day (Gapelyuk et al., 2011). The decrease in these two

physiological parameters suggests that cardiovascular consequences can be improved with adequate treatment of OSAS.

The progression of OSAS has been established in the literature (Berger, Berger, & Oksenberg, 2009; Fisher, Pillar, Malhorta, Peled, & Lavie, 2002; Pendlebury, Pepin, Veale, & Levy, 1997). Patients with untreated mild to moderate OSAS have been found to have an increase in AHI over time. More recently, Young et al. (2008) approximated the number of individuals with a mild to moderate form of OSAS to be 80 percent. Given the prevalence rates and the known progression of OSAS, it is imperative that additional studies involving patients with mild OSAS be conducted to assist in the establishment of guidelines for the treatment of OSAS in this population.

OSAS can lead to negative health outcomes at all levels of disease severity. The severity of OSAS depends on two separate parameters: AHI and level of EDS (Aurora et al., 2010). Being that OSAS is a progressive disease, diagnosis and treatment of OSAS in the mild form may prevent complications associated with EDS and hypertension by slowing or reversing the disease process. The purpose of this study was to examine the relationship of CPAP therapy on excessive daytime sleepiness and blood pressure in a population of patients with mild OSAS (AHI - 5-14).

Research Questions

To achieve the stated purpose, the research questions for this study were:

1.) How does continuous positive airway pressure use affect daytime sleepiness in persons with mild obstructive sleep apnea syndrome?

2.) How does continuous positive airway pressure use affect blood pressure in persons with mild obstructive sleep apnea syndrome?

Significance

      The initial nursing assessment is a critical first step to identifying individuals with OSAS. Advanced practice nurses (APNs) are primary providers in physicians' offices, clinics, as well as acute care and community-based settings. APNs have the opportunity to work with individuals with OSAS in the early stage of the disease process. These APNs are in a unique position to monitor patients, allowing opportunities for the detection of early signs and symptoms of OSAS, which may ultimately slow the progression of OSAS and its untoward effects. Routine nursing assessment in mild OSAS can identify risk factors associated with OSAS to include, but not limited to, metabolic syndrome, obesity, snoring, hypoxemia, apneic episodes, morning headaches, and hypertension. Risk identification and screening by APNs may enable patients to improve health outcomes over time through early diagnosis and ongoing monitoring and OSAS treatment.

      Healthcare providers specializing in sleep and sleep-related disorders have long been faced with the dilemma of when to treat OSAS. Historically, CPAP therapy has been reserved for patients with moderate to severe OSAS (AHI ≥ 15). However, recent studies demonstrate that even minor degrees of sleep disordered breathing can be associated with an increased risk of motor vehicle accidents (Komada et al., 2009), hypertension (Laaban et al., 2010), significant cognitive effects (Mathieu et al., 2008), decrease in quality of life (Zamarron, Garcia Paz, & Riveiro, 2008), and an increase in EDS (Bixler et al., 2005). This evidence suggests that patients with a milder form of OSAS can potentially benefit from treatment with CPAP; however studies are needed to

show direct and indirect improvements in outcomes to determine whether CPAP should be a standard of care in mild OSAS.

In addition to the aforementioned, mild OSAS patients treated with CPAP have the following potential benefits. First, research suggests that OSAS progresses over time. Therefore, a patient that presents initially with simple snoring could likely evolve over the course of time to a mild, moderate, or severe OSAS patient without early intervention (Berger et al.,2009). Secondly, when comparing CPAP to a placebo, even in the mildest forms of the disease, treatment effect is clinically significant (Jaimchariyatam et al., 2010). Thirdly, patients that present initially with mild OSAS have a high risk of developing hypertension due to the fact that even with low AHI levels cardiovascular risks can still exist (Takama & Kurabavashi, 2010). Lastly, excessive daytime sleepiness can be present in all forms of the disease. Patients that present with low AHI levels and report excessive daytime sleepiness have experienced significant relief of symptoms with adequate treatment (Barnes et al., 2002).

Treatment of patients with moderate to severe OSAS with CPAP therapy reverses upper airway obstruction while asleep as well as reducing many of the untoward side effects associated with OSAS such as excessive daytime sleepiness (Antic et al., 2011). The question of when to treat a patient with sleep apnea has long been debated and some research suggests that treating mild sleep apnea with CPAP is not warranted (Littner, 2007). However, many researchers do support the use of CPAP in this population (Brown, 2007; Jaimchariyatam et al., 2010; Levy, Pepin, & McNicholas, 2002; Takama & Kurabayashi, 2010). It should be noted that OSAS is only cured in specific patient cases with craniofacial or upper airway surgery or significant weight loss. Therefore,

CPAP, though not curative, is the initial and gold standard treatment for patients with severe OSAS (Gami et al., 2003).

Literature supporting the treatment of mild forms of OSAS is accumulating and clearly demonstrates that disease, even in this modest form, can lead to adverse symptoms and can be treated effectively. However, there remains a particular uncertainty regarding the effectiveness of CPAP therapy in mild cases of OSAS. Additional studies are needed to support the use of CPAP with this population providing supplemental evidence that increased adherence to CPAP in the mild OSAS population can lead to a decrease in EDS as well as a decrease in blood pressure. This study will help define the role of CPAP therapy and its effect on daytime sleepiness and blood pressure in this population.

Definitions

Sleep terminology is often used inconsistently across the sleep literature. For the purpose of this study the following definitions will be utilized.

Obstructive sleep apnea syndrome (OSAS) is characterized by a number of symptoms including snoring, interrupted sleep pattern, intermittent breathing cessations, morning headaches, concentration and memory difficulties, irritability, and excessive daytime sleepiness (EDS) (Partinen & Hublin, 2005; Young et al., 2002).

Excessive daytime sleepiness (EDS) refers to the tendency to fall asleep while involved in activities that are not stimulating, such as listening to a speaker or watching television (Rosenberg & Doghramji, 2009).

Apnea is defined as the cessation of airflow for a time of at least 10 seconds (American Academy of Sleep Medicine, 2007).

Hypopnea exists when either there is a 30% decrease in airflow from baseline, for a minimum of 10 seconds duration, with at least 4% desaturation from baseline, or there is at least 50% decrease in airflow for a minimum of 10 seconds duration with at least a 3% desaturation or an arousal (American Academy of Sleep Medicine, 2007).

Apnea – hypopnea index (AHI) is a summary measure of the number of obstructive apnea and hypopnea episodes per hour of sleep (Chervin, 2005).

Polysomnography (PSG) is an overnight sleep study that involves simultaneous recordings of several physiologic functions during the sleep period, including the electromyogram (EMG), the electroencephalogram (EEG), electrooculogram (EOG), oronasal airflow assessments, and oxyhemoglobin saturation (Punjabi, 2008).

Electromyogram (EMG) measures muscle tone and is helpful in distinguishing between REM sleep and NREM sleep. Electrodes are placed 2 cm below the inferior edge of the mandible and 2 cm to the right and left of the midline of the mandible (Vaughn & Giallanza, 2008).

Electroencephalogram (EEG) measures electrical activity of the brain and is essential for staging the sleep cycle. The electrodes are placed between four primary skull landmarks (nasion, inion, and both auditory canals (Vaughn & Giallanza, 2008).

Electrooculogram (EOG) measures eye movement during sleep for the purposes of sleep staging. Electrodes are placed just outside the outer canthus of each eye with the right outer canthus being 1 cm above the horizontal midline and the left being 1 cm below the horizontal midline (Vaughn & Giallanza, 2008).

Respiratory Disturbance Index (RDI) is defined as the average number of respiratory disturbances (obstructive apneas, respiratory hypopneas, and respiratory

event–related arousals [RERAs]) per hour (Amfilochiou, Papagrigorakis, Georgopoulos, & Liolios, 2009).

Respiratory Effort Related Arousal (RERA) may be estimated by flattening of the inspiratory airflow profile associated with an arousal, when airflow changes do not meet apnea or hypopnea criteria or by changes in the esophageal pressure recording (Amfilochiou, Papagrigorakis, Georgopoulos, & Liolios, 2009).

Continuous positive airway pressure (CPAP) is a device that generates positive pressure in the airway in order to prevent collapse of the upper airway (Yagi et al., 2009).

Adherence with CPAP usage is defined as 4 hours or greater of nightly use 70 percent of nights (Grunstein, 2005; Weaver & Grunstein, 2008).

Summary

OSAS is a progressive disease with many adverse health outcomes. The implementation of CPAP therapy to persons with mild OSAS may slow the progression of the disease and promote health outcomes. EDS and hypertension are commonly associated with OSAS and will be the focus of this study. The researcher of this study will investigate one outcome each from the psychological (EDS) and physiological (blood pressure) aspects of OSAS, which will be placed within a theoretical framework in chapter 2 in addition to a review and analysis of the literature. A literature review will be provided in chapter two to support this study and the methods used to obtain and analyze the data will be addressed in chapter three. The results of this study will be presented in chapter four with a discussion of the findings to follow in chapter five.

CHAPTER TWO

REVIEW OF LITERATURE

Obstructive sleep apnea syndrome (OSAS) is a progressive disease. Identifying and treating patients in the early stages of the disease can prevent numerous OSAS related health problems. The focus of this literature review is to provide an overview of the normal physiology of sleep and sleep regulation, discuss OSAS, and provide a review of CPAP as a treatment modality for OSAS.

Physiology of Normal Sleep and Sleep Regulation

A brief overview of the physiology of sleep is presented in order to lay the foundation of knowledge needed to establish the purpose for conducting the current study.

Stages of sleep. There are two types of sleep, non-rapid eye movement (NREM) and rapid eye movement (REM) (Hauw, Hausser-Hauw, Girolami, Hasboun, & Seilhean, 2011). The first type, NREM, is divided into four stages. The first stage of NREM sleep represents a small portion of sleep and occurs during the time the individual is falling asleep, approximately 5 percent of sleep occurs here. During this stage the individual is easily aroused and if arousal does occur it may feel as if he/she has been daydreaming and not actually sleeping. Stage 2 NREM involves about 50 percent of sleep time and is often referred to as the time when true sleep occurs. Stages 3 and 4 NREM sleeps are deep stages of sleep and constitute approximately 10-20 percent of sleep. It is during Stage 3 NREM that complete muscle relaxation occurs, which assists the body in restoration through energy conservation. Stage 4 NREM is considered to be the deepest

stage of sleep; it is difficult to arouse someone during this stage of sleep. Stages 3 and 4 usually occur within the first half of sleep time (Hauw et al., 2011).

The second type of sleep accounts for approximately 20-25 percent of sleep and is referred to as REM sleep. REM sleep alternates with NREM all through the sleep cycle. It most often begins within the first 90 minutes. It is during REM stage sleep that vivid full-color dreaming can occur. This stage is typified by the autonomic response of rapidly moving eyes, fluctuating heart and respiratory rates, and possibly an increase in blood pressure (Brown et al., 2012; Frey, 2001; Hauw et al., 2011).

Regulation of sleep. The two-process model is commonly used to explain the regulation of sleep through homeostatic and circadian drives. The two-process model postulates that a relationship between the homeostatic drive to sleep (Process S) and the circadian drive to sleep (Process C) interact to support the process of sleep (Rusterholz, Durr, & Achermann, 2010). Process C and Process S are independent processes; yet work synergistically to promote sleep and wakefulness. Process S is a homeostatic drive to sleep (influenced by an individual's history of sleep and waking), similar to a pressure system that builds during the waking hours of the day. Sleep pressure is released once a person falls asleep. Process C refers to the circadian rhythm.

In the early morning hours the circadian rhythm encourages wakefulness, usually as a result of light (sunrise) which suppresses the release of melatonin. As the day becomes darker and melatonin levels increase so does the circadian drive to sleep. Process C and Process S collectively create a feeling of sleepiness at the end of each day (elevated sleep drive and elevated melatonin levels). Once sleep is initiated the drive to sleep (Process S) decreases. Process S will continue to decrease throughout the sleep

period until Process C initiates wakefulness starting Process S over again (Rusterholz et al., 2010).

The sleep – wake cycle is defined as a 24 hour period where approximately 16 hours are devoted to wakefulness and approximately 8 hours are devoted to sleep (Rosenberg & Doghramji, 2011). The term "circadian" refers to processes that occur in 24 hour period intervals. Circadian rhythms control many behaviors (e.g., sleep-wake, feeding), physiological functions (e.g., body temperature, blood pressure) and endocrine functions (corticosterone concentration) on a rhythmic 24 hour diurnal cycle (Kalsbeek et al., 2011). The circadian rhythms are influenced by an internal clock that is controlled by a pacemaker located in two clusters of nerve cells called the suprachiasmatic nuclei (SCN). The SCN is located in an area at the base of the brain called the anterior hypothalamus (Pail et al., 2011). This pacemaker is at the heart of the promotion of wakefulness during the day and sleep at night.

The natural inclination to sleep or sleep propensity function is comprised of three components that take place over a 24 hour period. Hilton (2002) identifies the three components as curves. These curves are used to describe sleep propensity function. The first curve takes place in the mid-afternoon. At this time, the body has an episode of high-sleep propensity and experiences sleepiness. The second curve, also known as the "forbidden zone", takes place in the early evening. At this time there is a low propensity for sleep and this period lasts approximately 2 to 3 hours. The third curve is the last curve and refers to the nocturnal sleep gate. This occurs late in the evening and during this time there is a steep rise in sleepiness (Hilton, 2002).

Light is the primary stimulus for coordinating the circadian system with the sleep-wake cycle (Schmidt, Chen, & Hattar, 2011). The cycle of light and dark intervals play the most important role in regulating the sleep – wake cycle and the circadian rhythm. Under normal light – dark conditions the human circadian system is synchronized with the geophysical day. The synchronous resetting of the circadian system is continuous, resetting every day. Even under circumstances when the cycle is delayed, or lengthened for example, by an hour, the delay remains at one hour due to the body's ability to reset itself day after day (Marhefka, 2011). As noted earlier, light is vital to the sleep – wake cycle. Limited or absent light adversely affects the sleep – wake cycle. This reduction in exposure can result from decreased sensitivity to light by the retina or to decreased exposure to light due to lifestyle.

Body temperature is a physiological circadian rhythm that is intricately related to the sleep process. Thermoregulation is the maintenance of a rather steady body temperature even under a variety of external conditions. About one to one and a half hours before falling sleep, the body starts to lose heat from its central core; this decrease in temperature brings on increased feelings of tiredness in normal healthy adults. These physiological changes happen well before going to bed and may occur without the person's awareness. The body achieves this temperature drop by shifting heat from the core of the body to the periphery of the body (Bach et al., 2011).

Sleep – related changes in body temperature and the effects of environmental temperature on sleep suggest that sleep regulation and body temperature are related. Evidence of this involves the preoptic area (POA) of the brain, specifically the medial preoptic area (mPOA), which participates in both the regulation of sleep and body

temperature (Kumar, 2004). The mPOA controls sleep and temperature through independent, but overlapping neuronal circuits (Kumar, 2004). The mPOA is located in a region of the hypothalamus between the anterior commissure and the optic chiasm. The anterior commissure is a round bundle of nerve fibers that crosses the midline of the brain near the anterior limit of the third ventricle. The optic chiasm is the part of the brain where the optic nerves partially cross, allowing for the parts of the right eye seeing things on the right side to be connected to the left side of the brain, and vice versa (Kidd, 2011).

Endocrine events, as previously mentioned, occur as a circadian rhythm. Melatonin, a small molecule produced in the pineal gland, is strongly linked to the sleep wake cycle. The pineal gland is considered part of the diencephalon, and sits near the base of the third ventricle, in approximately the anatomic center of the brain. Melatonin is synthesized from tryptophan, undergoes oxidation to serotonin, and is eventually converted to its active form (Paredes et al., 2009). Production and secretion of melatonin also follow a circadian pattern. As daylight approaches, light perceived by the retina is encoded and then sent to the pineal gland. Light serves to suppress the pineal activity, resulting in a decrease in melatonin levels, which remain low until secretion is once again stimulated by the onset of darkness (Borjigin, Zhang, & Calinescu, 2011). Melatonin levels closely correlate with sleep propensity. Melatonin secretion is at its highest level during high sleep propensity and is noticeably decreased during episodes of low sleep propensity.

Effects of disrupted sleep. The effect of sleep and sleeplessness-related problems has gained attention over the past several years. This may be in part due to the effect sleep has on the physiological function of the human brain (Couyoumdjian et al.,

2010). One particular area of the brain thought to be affected by sleep and sleeplessness is the prefrontal cortex (PFC). Ingvar (1979) studied PFC over 30 years ago and found that this area of the brain demonstrated a high metabolic rate even during periods of resting wakefulness. The frontal cortex is responsible for numerous thought processes including visual and auditory discrimination, task switching, semantics, and problem solving (Duncan & Owen, 2000) and is thought to receive much needed recovery during sleep (De Gennaro et al., 2007). Furthermore, Duncan and Owen (2000) assert that the PFC is the hardest working cortical area of the brain during wakefulness. Lim, Tan, Parimal, Dinges, and Chee (2010) conducted a study involving 23 participants comparing their ability to complete a selective attention task after a night of normal sleep and after a night of sleep deprivation (awake overnight). Each participant was asked to identify two different pictures by pressing a button when select images appeared. When this test was completed during the rested state (after a night of normal sleep) the participants accurately identified the pictures with high hit rates ($M = 91$, 11.0%). After sleep deprivation, a significant decline in hit rates was observed ($M = 4$, 4.6%). The authors concluded that sleep deprivation resulted in reduced visual selectivity.

Kim, Kim, Park, Choi, and Lee (2011) conducted a study involving 58 residents and interns and examined the effect disrupted sleep has on physical health, work performance, and cognition. The participants were divided into three groups: severe sleep deprived (S-SD, average less than 4 hours of sleep per night), mild-moderate sleep deprived (M-SD, 4-6 hours of sleep per night), and non-sleep deprived (Non-SD, more than 6 hours of sleep per night). The S-SD group had significantly higher Epworth Sleepiness Scale (ESS) scores than the M-SD and Non-SD groups ($p < 0.05$) as well as

higher levels of stress, more frequent attention deficit, and more difficulty learning ($p <$ 0.05). The primary physical health complaint was related to the specific work environment, such as standing or sitting all day. Participants reported sleep deprivation as having a negative impact on their social activities as well as experiencing difficulty in learning and concentration.

Behavioral challenges such as shift work also affect the sleep pattern and cause disrupted sleep. Shift work forces the person to be awake during the time when the circadian rhythm is promoting sleep, and likewise, attempting to sleep when the body is normally promoting wakefulness. This generally results in a reduction in the number of hours an individual is able to sleep during a 24 hour period. The misalignment in the sleep schedule can impair both sleep and waking alertness. The sleep loss that results from this disruption leads to an increase in the sleep drive during the hours in which work is required, thus resulting in impaired alertness (Kolla & Auger, 2011).

Jet lag is another example of a behavior influenced by the circadian rhythm. When individuals cross several time zones, there is a significant variation in sleep and wake times and the circadian system is altered. The result is a temporary misalignment in the new sleep/wake schedule that can lead to sleep disruption. The person attempts sleep during a time that wakefulness is being promoted and awakens when sleep is actively being promoted (Saksvik et al., 2011).

<center>**Obstructive Sleep Apnea Syndrome**</center>

Prevalence

Obstructive sleep apnea syndrome is characterized by repetitive episodes of complete or partial obstructions of the upper airway during sleep (Lurie, 2011).

Obstructive sleep apnea is a common sleep disorder in the United States. Data extracted from the Wisconsin Sleep Cohort found that state employees between ages 30 and 60 had a prevalence of 9 percent in women and 24 percent in men when OSA was defined by an AHI $\geq$ 5 events per hour during sleep. However, when OSA was more strictly defined as a syndrome (i.e., OSAS) which includes both AHI $\geq$ 5 and significant self-reported sleepiness, the prevalence was lower (women 2 percent, men 4 percent) (Young et al., 2008). Prevalence rates have been found to be similar to the Wisconsin Sleep Cohort prevalence in other diverse populations. Ip et al. (2004) conducted a community study involving middle aged Chinese women and found a prevalence rate of 2.1 percent. Udwadia, Doshi, Lonkar, and Singh (2004) found a 7.5 percent prevalence rate in middle aged Indian men. The authors of one study measuring the prevalence of OSAS in commercial drivers found that approximately 28 percent of commercial drivers in the United States suffered from at least a mild form of OSAS (AHI $\geq$ 5) (Pack, Dinges, & Maislin, 2002). Somers et al. (2008) suggest that as many as 85 percent of people with clinically significant OSAS are undiagnosed.

Despite the agreement between population-based studies, the true prevalence of OSAS is not easily estimated given the lack of clarity with cut-off measures distinguishing normal breathing during sleep from sleep disordered breathing (Kapur, 2010). The issue is primarily related to the definition of hypopnea. The American Academy of Sleep Medicine scoring manual provides two acceptable definitions for hypopnea: 1) $\geq$30 percent decline in nasal-pressure-transducer-signal (measurement of nasal airflow) excursions with a 4 percent desaturation from pre-event baseline, and 2) a $\geq$50 percent decline in nasal-pressure-transducer-signal excursions with a $\geq$3 percent

desaturation from baseline or arousal (Iber, Ancoli-Israel, Chesson, & Quan, 2007). A great deal of variance can occur with the use of different diagnostic criteria. For example, in the Sleep Heart Health Study the median AHI was almost 3–fold higher and the prevalence of moderate to severe OSAS was 2–fold higher when hypopneas with >3 percent desaturation or arousals were scored than when a >4 percent oxygen desaturation was required for hypopnea scoring (Redline et al., 2000).

The cut off for number of apneas / hypopneas per hour of sleep has traditionally been set at greater than or equal to 5 events per hour. However, not all evidence supports the use of this value. For example, in the Wisconsin Sleep Cohort (*n*= 709) the authors examined the association between sleep-disordered breathing and hypertension and found that participants with AHI values between 0.1 and 4.9 events per hour had 1.4 times the risk of developing hypertension when compared to participants with AHI of zero (Peppard et al., 2000). Additionally, researchers from the Sleep Heart Health Study examined the prevalence of sleepiness in the moderate to severe OSAS population and found that only 46 percent of the 6,440 participants with AHI > 15 (moderate to severe) reported excessive daytime sleepiness (Baldwin et al., 2010). The above results provide evidence that OSAS can lead to negative health outcomes at all levels of disease severity and that clinical significance can occur in any form of the disease based on individual susceptibility.

Pathophysiology of Obstructive Sleep Apnea Syndrome

The physiology of sleep is significantly impaired in the OSAS patient. In individuals without OSAS, wakefulness brings about an increase in cardiac vagal tone, resulting in an increase in the metabolic rate and an increase in the activity of the

sympathetic nervous system, resulting in micro-arousals (rapid changes in alertness) and an increase in blood pressure and heart rate. The opposite is true during times of normal sleep where there are decreases in cardiac vagal tone, metabolic rate, and sympathetic nervous system activity that all contribute to decreases in blood pressure and heart rate (Fava, Montagnana, Favaloro, Guidi, & Lippi, 2011).

Repeated bouts of wakefulness during sleep that are characteristic of OSAS patients are due to the repeated episodes of intermittent hypoxia and hypercapnia that occur in an attempt to surmount the pharyngeal obstacle. These episodes result in changes in pulmonary volume, intrathoracic pressure, and micro-arousals (Kario, 2009). After these hypoxia / hypercapnia events, OSAS patients demonstrate oscillations in hemodynamic parameters throughout the night. Heart rate, blood pressure, and cardiac output fluctuate constantly as a result of the repeated respiratory events and the rapid changes in alertness due to micro-arousals (Fava et al., 2011). Repeated arousals also result in less time spent in deep sleep (i.e., stages 3 and 4) among the OSAS population (Loureiro, Drummond, Winck, & Almeida, 2009; Sukegawa et al., 2009). Treatment of OSAS with CPAP has shown to decrease hypoxia - hypercapnia episodes (Garcia, Sharafkhaneh, Kirshkowitz, Elkhatib, & Sharafkhaneh, 2011; Lee & McNicholas, 2011), intrathoracic pressure (Kario, 2009) and micro-arousals (Sukegawa et al., 2009).

Factors Associated with Obstructive Sleep Apnea Syndrome

OSAS is a complex, multifactorial disease. Researchers have alluded to numerous associated factors. Epidemiological factors that are well documented to be associated with increased risk of developing OSAS are obesity, gender, and age. The following section will provide an overview of metabolic syndrome, obesity, craniofacial

morphology, gender, age, and race and the association each has with the pathogenesis of OSAS.

Metabolic Syndrome

The prevalence of metabolic syndrome is higher among OSAS patients. A diagnosis of metabolic syndrome is based on the occurrence of at least three out of five components of the syndrome. The components include elevated levels of plasma glucose (or previously diagnosed type 2 diabetes), elevated triglycerides, decreased HDL cholesterol, abdominal obesity (increased waist circumference), and increased arterial blood pressure (Kumor et al., 2013). Ambrosetti et al. (2006) examined 89 patients with OSAS and found metabolic syndrome in 53 percent of the cases. The link between OSAS and metabolic syndrome has been well established in the literature. Vgontzas, Bixler, and Chrousos (2005) reported that patients with OSAS had significantly higher fasting glucose and insulin levels compared to weight matched control subjects. Furthermore, Gruber, Horwood, Sithole, Ali, and Idris (2006) examined 38 subjects with OSAS and 41 controls and found that OSAS patients were nearly six times as likely to have metabolic syndrome as the control group.

It is plausible that metabolic syndrome and OSAS exert negative synergistic consequences on the cardiovascular system (Bonsignore & Zito, 2008; Levy et al., 2009). Su et al. (2013) reported that factors such as higher fasting blood glucose and body mass index (BMI) and lower high-density lipoprotein (HDL) cholesterol were more strongly associated with elevated cardiovascular disease than with OSAS. This finding suggests that metabolic parameters are important contributors to cardiovascular diseases and should be corrected in patients with OSAS. Sharma, Agrawal, and Damodaran (2011)

conducted a double-blind placebo-controlled trial in OSAS patients and found that blood pressure was lowered and metabolic abnormalities were partially reversed with three months of CPAP therapy.

There is increasing literature to support a causal relationship between OSAS and metabolic syndrome. The intermittent hypoxia that occurs with OSAS may induce or exacerbate metabolic syndrome. Additional clinical evidence is needed to identify direct and indirect associations between OSAS and metabolic syndrome, because such evidence could improve the understanding and management of both disorders (Zamarron, Cuadrado, & Alvarez-Sala, 2013).

Obesity

Researchers involved in the Sleep Heart Health Study assert that there is a relationship between rising BMI to increasing OSAS severity (Young, et al., 2002). The 2007-2008 prevalence of obesity among adult men was 32.2 percent and among adult women was 35.5 percent (Flegal, Carroll, Ogden, & Curtin, 2010). The term overweight refers to an individual who weighs more than a standard weight for height and age, whereas the term obesity is a much more complex term that refers to excessive body fat that places an individual at an increased risk for multiple health problems (Yu & Berger, 2011). Increased body weight above a standard level has been identified in epidemiologic studies from around the world as the strongest risk factor for OSAS (Punjabi, 2008). Obesity is defined as a body mass index (BMI, weight in kilograms divided by height in meters), of more than 27 kg/m^2 (Partinen & Hublin, 2005).

As noted previously in regard to metabolic syndrome, obesity also can be considered a consequence of OSAS. Anandam, Akinnusi, Kufel, Porhomayon, and El-

Solh (2011) reported a meta-analysis of nine articles that included data from patients experiencing both pre- and post- dietary weight loss PSG's where an AHI was obtained. The researchers found that the OSAS cure rate dropped from 61 percent at 3 months to less than 10 percent at one year. This was hypothesized to potentially be due to the challenge of maintaining large amounts of weight loss. Specifically, one of the studies reviewed by Anandam et al. was a study of 23 patients with various degrees of obesity (Pasquali et al., 1990). Only 30 percent of the participants were able to maintain a weight loss of greater than 10 percent after a two-year weight reduction program, and all AHI improvements were lost by the end of the study. Sampol et al. (1998) examined the efficacy of long term dietary weight loss and OSAS and found that after 5 years, 46 percent of those studied were not able to maintain a one half drop in BMI following dietary weight loss. Likewise, Greenburg, Lettieri, and Eliasson (2009) found that even when weight loss surgery resulted in dramatic weight loss, only 25 percent of patients achieved resolution of their OSAS. This suggests that weight loss is not curative in all cases of OSAS with significant weight loss. More importantly, the meta-analysis concludes that weight loss programs should not be considered curative of OSAS, but rather as an adjunct to other OSAS treatment. There are limited data available examining the effect of modest weight loss on OSAS, and additional studies are needed to examine the large number of patients who have residual OSAS following dietary weight loss.

Obesity affects breathing in several different ways, including alterations in the geometrical structure of the upper airway, increased collapsibility of the upper airway, or by exacerbating OSAS occurrences due to obesity related reductions in decreased residual capacity and increased whole – body oxygen demand (Yu & Berger, 2011).

Evidence does suggest, however, that weight loss can reduce the severity of OSAS and may be curative in isolated cases (Epstein et al., 2009; Fritscher, Mottin, Canani, & Chatkin, 2007). Researchers from the Wisconsin Sleep Cohort identified weight change as a significant determinant of disease progression or regression and evidence supports more severe OSAS in association with obesity in some adults. Participants with a 10 percent increase in weight demonstrated a 32 percent increase in AHI as well as a six fold risk of developing moderate to severe OSAS. Furthermore, participants with a decrease of 10 percent in weight demonstrated a decrease of 26 percent in AHI scores (Peppard et al., 2000). The association between body weight and OSAS has also been corroborated by the by researchers in the Cleveland Family Study, which confirmed that body weight, gender, and age (discussed below) were independent determinants in the incidence of OSAS (Tishler, Larkin, Schluchter, & Redline, 2003). A rigorous meta-analysis conducted by Anandam et al. (2011) found that weight loss is insufficient to eliminate OSAS and that the traditional approach of recommending weight loss as a first line of treatment is likely to be ineffective as well as very difficult to achieve due to hormonal disruption. Weight loss tends to normalize AHI rather than eliminate apneas in the majority of patients who are able to lose weight. In addition, the hormonal factors associated with OSAS can make it extremely difficult for people with OSAS to lose weight and maintain that loss if the OSAS is not treated with other interventions. The American Society of Sleep Medicine recommends CPAP as the first line of treatment for all cases of adult OSAS (Epstein et al., 2009).

Patients with a neck circumference greater than 40 cm tend to have a more collapsible airway during wakefulness (Tsai, Ho, Lee, & Tan, 2009). Inspiration and

airflow create negative pressure that can lead to airway collapse. The musculature surrounding the palate, pharynx, and tongue help to maintain airway patency and an increase in the load on the muscles can produce changes in the airway configuration and can alter the function of the airway. Fat deposits around the airway can potentially narrow the pharynx, changing the shape and mechanical properties, resulting in an increased risk for OSAS (Sutherland, Lee, & Cistulli, 2012). Hora et al. (2007) examined thirty-seven obese males with OSAS and fourteen obese control males and found that OSAS patients had statistically significant higher BMI, neck circumference, and waist circumference than the control group ($p < 0.05$). An additional study of 109 subjects (76 men, 33 women) was conducted and the authors revealed that BMI and neck circumference significantly increased the severity of OSAS in both men and women ($p < 0.001$, $p = 0.013$, respectively) (Tsai et al., 2009). Martinho et al. (2008) examined the head and neck measurements of 45 severely obese patients in order to determine if upper airway and facial skeleton was related to the severity of OSAS. A large neck circumference ($p = 0.02$), the presence of a voluminous lateral airway wall ($p = 0.04$), an anatomically posterior soft palate ($p = 0.03$), and a thick soft palate ($p = 0.04$) were all directly associated with the severity of OSAS. These data may mean that a thicker neck is a predictive factor for OSAS.

Consistent with the previous discussion about obesity and OSA, increased waist circumference is thought to play an integral role in sleep related disorders, specifically OSAS (Simpson et al., 2010). An increased waist circumference is defined by a measure of greater than 102 cm in men and 88 cm in women. The result of the additional weight combined with increased waist circumference is thought to displace the diaphragm,

leading to a decrease in tracheal traction on the upper airway, thereby resulting in an increased risk for upper airway collapse (Stadler, McEvoy, Bradley, Paul, & Catcheside, 2010). A study conducted by Angelico et al. (2010) of 281 subjects identified an independent association between OSAS severity and waist circumference ($t = 3.93$, $p = 0.000$). Any degree of excess body weight should be viewed as a potential risk factor or indicator of existing OSAS.

Craniofacial Morphology

While obesity is the primary risk factor for OSAS, craniofacial morphology is a major contributing factor. Several characteristics to be considered are skeletal morphology related to the hyoid and head position, mandible, maxilla, and cranial base. Soft tissue morphology of the upper airway is also considered a risk factor (Sutherland et al., 2011). The inferior displacement of the hyoid bone is thought to contribute to the pathogenesis of OSAS (Johal, Patel, & Battagel, 2007). Pressure exerted from excess pharyngeal tissues in the upper airway may contribute to a lower position of the hyoid bone in apneic patients due to the fact that when hyoid position between subjects (55 apneic and 55 non-apneic) was examined no difference was noted once tongue size was controlled (Chi, et al., 2011). Cephalometric studies (measurements of the head) indicated that OSAS patients have a smaller cranial base angle. Albajalan, Samsudin, and Hassan (2011) examined 25 OSAS patients and 25 non-OSAS patients and found that airway spaces were narrower (upper, middle, and lower), hyoid bone position was more posterior and inferior, and the angle of the cranial base was more acute in the OSAS group than the non-OSAS group suggesting a relationship between hyoid position and cranial base angle with the pathogenesis of OSAS.

The skeletal morphology of the maxilla and mandible are also contributing factors to the pathogenesis of OSAS, specifically a short maxilla and a narrow maxillary arch (Schendel et al., 2011). Chi et al. (2011) found that when comparing apneic and non-apneic patients (25 apneic, 25 non-apneic), the male apneic patients presented with shorter mandibles. There was no significant difference in the female participants in this study. In addition to skeletal morphology, soft tissue morphology should also be considered as a contributing factor to the pathogenesis of OSAS. Johal et al. (2007) examined the skeletal and soft tissue anatomy of 99 OSAS patients and 99 non-OSAS patients. The researcher's results support the known existing evidence related to hyoid bone position and maxilla and mandibular size. The researchers also found that tongue size was increased ($p = 0.021$) as well as soft palate area, length, and thickness ($p = 0.001$) for those with OSAS.

Gender Differences in Obstructive Sleep Apnea Syndrome

For decades the male gender has demonstrated a higher prevalence for OSAS than the female gender (Block, 1979; Guilleminault, Van den, & Milter, 1978; Guilleminault, Quera-Salva, Partinen, & Jamieson, 1988). This is a direct result of the fact that all early studies of OSAS included men only. It was not until 1993 (Young et al., 1993) that females were included in a general population study of OSAS. Since this seminal study, gender differences in OSAS have been further refined. For example, men experience OSAS at two to three times the rate of women (Young et al., 1993), are diagnosed at a younger age (Young et al., 1997), and have a higher apnea-hypopnea index (AHI) than women (Shepertycky, Banno, & Kryger, 2005). Gender differences are in part, due to

differences in risk factors. The following section delineates the risk factors for both males and females.

There are several gender differences that suggest why men are more prone to obstructive sleep apnea than women. The male predisposition for OSAS has been attributed to sex differences in anatomical and functional properties of the upper airway, hormones, and respiratory control stability (Lin, Davidson, & Ancoli-Israel, 2008). Respiratory stability is determined by gas-exchange efficiency, circulatory delays to central and peripheral chemoreceptors, and chemo responsiveness (Wellman et al., 2003).

The "Great Leap Forward" hypothesis postulates that evolutionary changes in the upper respiratory tract predispose man to obstructive sleep apnea. The hypothesis suggests that the same anatomic features that support our ability to speak are the very same features that place our airway in jeopardy as we sleep and are more likely to occur in men than women (Davidson, 2003; Davidson, Sedgh, Tran, & Sepnowsky, 2005). The hypothesis asserts that the combination of laryngeal descent, shortening of the oral cavity and soft palate, and a tongue that resides partially in the pharynx can obstruct respiration during sleep (Davidson et al., 2005). Laryngeal descent elongates the oropharynx by reshaping the airway. Airway reshaping results in a slight separation of the epiglottis and the soft palate which in turn leads to the lengthening of the oropharynx. This elongation allows the tongue to collapse during sleep. While laryngeal descent does occur in both males and females during infancy it is the occurrence during puberty in males that predisposes men to OSAS (Lin et al., 2008).

Malhorta et al. (2002) found that when compared to women, men had a longer pharyngeal airway, an increased soft palate, and an increased pharyngeal volume. A

longer susceptible airway (hard palate to epiglottis) increases the propensity for airway collapse. During inspiration the extent of airway collapse is greater in men than women due to anatomic differences (Malhorta et al., 2002). Sawnani et al. (2010) supports the earlier study by Malhorta et al. (2002) asserting that the increased length of the oropharynx in the male airway is what leads to a greater risk of collapse during sleep (Sawnani et al., 2010).

The contribution of hormones to risk for OSAS is obscure due to the fact that the literature supports both elevated testosterone levels as well as decreased estrogen and progesterone levels (Behan & Wenninger, 2008; Lin et al., 2008; Myers & Meacham, 2003). Testosterone is thought to play a key role in the development of OSAS; however the mechanism of that relationship is unclear. The hypoxic ventilatory drive has been observed to increase with the administration of testosterone which may in turn contribute to OSAS (Myers & Meacham, 2003). This occurs in the following manner: ventilation is driven by increased carbon dioxide levels in the blood, testosterone is thought to lead to an increase in sensitivity to low oxygen levels; thus lowering carbon dioxide levels. Lowering carbon dioxide levels during sleep may possibly lead to periods of apnea (Hanafy, 2007).

Cistulli, Grunstein, and Sullivan (1994) found that testosterone leads to an increase in upper airway collapsibility as well as a possible link to a decrease in the dimensions of the upper airway. However, a more recent study conducted by Liu et al. (2003) did not support changes in the upper airway as specifically testosterone related. Liu et al. (2003) found that testosterone reduced total sleep time by approximately one hour, increased the duration of hypoxemia by approximately 5 minutes per night, and

disrupted breathing during sleep by approximately seven events per hour in healthy men over 60 years. Although the exact mechanism of testosterone and its interference with sleep is still disputed, the well-established male preponderance of sleep apnea does suggest that testosterone is somehow linked and therefore additional studies are needed to further evaluate the association between OSAS and testosterone levels.

Although many population studies support male predominance of OSAS, there is evidence that suggests women in the menopause transition have an increased risk of the disease (Anttalainen et al., 2006; Hachul et al., 2010; Kapsimalis & Kryger, 2009; Resta et al., 2003). Menopause lessens the excretion of estrogen and progesterone and is thought to contribute to the development of OSAS among women (Lin et al., 2008). Over 30 years ago evidence revealed that progesterone played a pivotal role in the mediation of respiratory stimulation, suggesting that progesterone was partially responsible for protecting females from OSAS and increasing the prevalence of OSAS among men (Skatrud, Dempsey, & Kaiser, 1978; Zwillich, Natalino, Sutton, & Weil, 1978).

The first robust data reported linking the menopause transition to OSAS was conducted by Young, Finn, Austin, and Peterson (2003) who examined 589 women to evaluate the effect menopause has on sleep disordered breathing (i.e. OSAS). Results revealed that postmenopausal women were 2.6 times more likely to have an AHI greater than 5 and 3.5 times more likely to have an AHI greater than 15 than their premenopausal counterparts. Hachul et al. (2010) examined a group of 931 women who sought treatment for a sleep complaint in an effort to study how the menstrual cycle affected sleep patterns. The researchers found that women taking hormonal contraceptives reported less snoring and had fewer arousals than women not taking hormonal contraceptives. In addition, the

researchers found that women taking hormone replacement therapy experienced less total awake time when compared to participants not taking hormone replacement therapy. Lastly, the researchers of this study suggest that menopausal women are more likely to demonstrate an apnea-hypopnea index greater than 5 events per hour. Interestingly, the researchers also found that women with a regular menstrual cycle reported less difficulty with sleep when compared to their irregular menstrual cycle counterparts. This finding supports a report of the data provided from the 2007 National Sleep Foundation annual Sleep in America Poll by Kapsimalis and Kryger (2009). This poll included 1,254 women in the United States who were polled by telephone and asked questions related to snoring, witnessed apneas, obesity, hypertension, and daytime sleepiness as well as questions related to general sleep habits, sleep problems, medical disorders, and menstrual cycle status. The report by Kapsimalis and Kryger (2009) concluded that women with regular menstrual cycles had a 16 percent risk for OSAS compared to 23 percent risk for women with irregular menstrual cycles.

Hachul et al. (2008) studied 33 postmenopausal women in an effort to examine the effects of estrogen and progesterone on sleep. Participants were randomly assigned to an estrogen or placebo group. After 12 weeks of receiving either the estrogen or placebo and while still taking the estrogen or placebo, all participants received progesterone for 12 weeks. The estrogen plus progesterone was more effective than the estrogen alone in decreasing several nighttime factors measured in the study such as, bruxism (11.1 percent vs. 0 percent), periodic limb movements (8.1 percent vs. 2.8 percent), and hot flashes (14.2 percent vs. 0 percent). The most significant finding the researchers of this study found for the present study is that once the progesterone therapy was added to the groups

both groups demonstrated a decrease in breathing irregularities and arousals from sleep, suggesting that progesterone has a protective effect against OSAS.

Age

Sleep – related difficulties become more common with advanced age (Berry & Foster, 2005; Malhorta et al., 2006; Punjabi, 2008). Although the underlying mechanisms are not quite clear it has been hypothesized that changes in pharyngeal collapsibility, ventilatory control stability, and possibly arousal responses are responsible for the increase of OSAS with age (Eikermann et al., 2007). The ventilatory control system is somewhat stable in the elderly, suggesting that ventilatory stability is not a probable cause of the increase in OSAS in this population (Wellman et al., 2007). However, pharyngeal collapsibility and arousal from sleep at the cessation of an apnea or a hypopnea do appear to play a role in the development of OSAS (Oliven, Aspandiarov, Gankin, Gaitini, & Tov, 2008; Thurnheer, Wraith, & Douglas, 2001). The increase in pharyngeal collapsibility has been attributed to an increase in airway length (women), an increase in the size of parapharyngeal fat pads, a decrease in the negative pressure reflex (reflex responsible for maintaining a patent upper airway), and an anatomical change in the bony shape of the pharynx (lower anteroposterior to lateral dimension ratio, indicating a more lateral skeleton and an increase in the length of the soft palate) (Malhorta et al., 2006).

Racial Differences in Sleep and Obstructive Sleep Apnea Syndrome

Several authors suggest that there may be important racial differences related to sleep disturbances (Fiorentino, Marler, Stepnowsky, Johnson, & Ancoli-Israel, 2006; Profant, Ancoli-Israel, & Dimsdale, 2002; Redline et al., 1998). African Americans spend

a smaller portion of time in deep sleep, or slow wave sleep, and spend more time in the light stages of sleep (stages 1 and 2) (Beatty et al., 2011; Hall et al., 2009; Mezick et al., 2008; Ruiter, DeCoster, Jacobs, & Lichstein, 2011). Redline et al. (1998) found that African Americans had a twofold higher risk for OSAS, a higher mean respiratory disturbance index, greater difficulty initiating sleep, reduced sleep satisfaction, and reported taking more naps than Caucasians. Tomfohr, Ancoli-Israel, Loredo, and Dimsdale (2011) conducted a study of 64 African Americans and 99 Caucasian Americans to investigate the differences in sleep architecture (i.e., sleep efficiency, total sleep time, sleep latency, time awake after sleep onset, time spent in various stages of sleep). The authors found that African Americans took longer to fall asleep, slept more in stage 2, and spent less time in slow wave deep sleep than did their Caucasian American counterparts.

Studies investigating racial differences in sleep apnea and OSAS are somewhat conflicting. Data involving African - Americans suggest that the prevalence of sleep apnea is equal to or higher than Caucasian counterparts and that sleep apnea may be more severe in this population (Durrence & Lichstein, 2006; Yaggi & Strohl, 2010). Ancoli-Israel et al. (1995) found that when compared to Caucasians (n=346), African Americans (n=54) had similar prevalence of OSAS (30 percent, 32 percent respectively) but a more severe form of the disease with 17 percent of the African Americans having an AHI greater than 30 compared to 8 percent of the Caucasians. Friedman et al. (2006) found that African Americans have a higher rate of daytime sleepiness and snoring when compared to Caucasian Americans. Ralls and Grigg-Damberger (2012) suggest that although there does seem to be a higher prevalence and severity in OSAS in African

Americans than Caucasian Americans, these differences may be due to environmental factors such as lower socioeconomic status and living in disadvantaged neighborhoods. Further research is needed to definitely determine the contribution of race to prevalence of sleep apnea and OSAS.

Complications Related to Obstructive Sleep Apnea Syndrome

The literature suggests that OSAS contributes to the evolution of health complications largely through excessive stimulation of the sympathetic nervous system (SNS). In medically uncompromised individuals, SNS activity (i.e., platelet aggregation, blood pressure, heart rate, metabolic rate) decreases during sleep. The opposite occurs with the OSAS patient due to recurrent respiratory events (apneas and hypopneas) and periods of alertness (micro-arousals) (Fava et al., 2011; Tazbirek, Slowinska, Kawalski, & Pierzchala, 2011). The result of the apneas and hypopneas is hypoxia (oxygen deficiency) and hypercapnia (increase in carbon dioxide), which in conjunction with the effects of excessive SNS activation, can lead to cardiovascular disease as well as EDS.

Cardiovascular Disease

It is unclear if OSAS is an independent risk factor for cardiovascular disease. There is, however, evidence of a well-established association with different types of cardiovascular disease including heart failure, hypertension, and stroke. Cigarette smoking is also an important factor to consider given the established relationship between cigarette smoking and cardiovascular disease (Lavie & Lavie, 2008).

Cigarette smoking. Cigarette smoking is linked to oxidative stress, and as a result is considered a risk factor for cardiovascular disease (Lavie & Lavie, 2008). A number of studies have identified an association between OSAS and underlying

predisposing factors to cardiovascular disease (Lavie, 2003; Lavie, Vishnevsky, & Lavie, 2004; Yamauchi et al., 2005). Lavie and Lavie (2008) compared 35 sleep apnea patients who smoke with 35 sleep apnea patients who do not smoke to investigate oxidative stress and inflammatory markers, important risk factors for cardiovascular disease. The authors found that OSAS patients who smoke 20 cigarettes or more a day for a period of 5 or more years have higher levels of oxidative stress and inflammatory markers and therefore, have a higher risk of cardiovascular disease than those who do not smoke.

Heart failure. Estimates are that 11 to 37 percent of patients with heart failure have moderate to severe OSAS (Wang et al., 2007). Obstructive respiratory events lead to significant temporary cardiovascular disturbances that may possibly lead to long-term cardiovascular remodeling. For example, the increase in negative intrathoracic pressure as a result of inspiratory efforts against an occluded airway increases venous return resulting in an enlarged right ventricle, which subsequently leads to slowed left ventricular filling and a decrease in stroke volume (Fava et al., 2011). It is also hypothesized that the intermittent hypoxia associated with OSAS may result in a disturbance between oxygen supply and demand, resulting in cardiac ischemia (Fava et al., 2011; Gami, Howard, Olson, & Somers, 2005; Schneider et al., 2000).

Kepez et al. (2011) conducted a study of 97 patients being evaluated for OSAS and found that as the severity of the OSAS disease progressed so did patient risk for coronary disease. The participants were grouped according to AHI scores (simple snoring, mild OSAS, moderate OSAS, severe OSAS) and coronary risk was assessed by tomographic calcium scoring (quantification of arterial calcification).The risk linearly increased from the simple snorers group to the severe OSAS group (Kepez et al., 2011).

Mechanical factors are considered in research examining the association between OSAS and cardiovascular risk. Left ventricular remodeling is thought to occur in OSAS patients as a result of oxidative stress as well as the effects of intrathoracic pressure (Kohler & Stradling, 2010; Singh, Patial, Vijayan, & Ravi, 2009). Kohler and Stradling (2010) assert that the increase in intrathoracic pressure results in an increase in the workload of the heart due to changes in venous return. Singh et al. (2009) sought to identify the effect of an anti-oxidant treatment to improve OSAS. Twenty male patients underwent PSG for diagnosis of OSAS and subsequently received two nights of CPAP therapy. Following the two nights of CPAP therapy the participants took an oral dose of the anti-oxidants vitamin C and vitamin E for 45 days. After 45 days of anti-oxidant treatment the participants underwent another PSG. The results revealed a decrease in the number of apneic events, more sleep time spent in stages 3 and 4, and a decrease in Epworth Sleepiness Scale scores.

Wang et al. (2007) found a relationship between untreated OSAS and mortality rates. The 164 heart failure patients who underwent PSG were grouped as follows: mild to no sleep apnea (n=113) (AHI $\leq$ 15 per hour of sleep), untreated OSAS (n=37) (AHI $\geq$ 15 per hour of sleep), and CPAP treated OSAS (n=14). Participants were followed up during a mean period of 2.9 and a maximum period of 7.3 years. Participants with untreated OSAS had a significantly higher rate of mortality than the participants with mild to no sleep apnea. The untreated OSAS group, 9 (24 percent) participants died. Five of the 9 were from sudden death, 1 from a myocardial infarction, and 3 from progressive heart failure. In the mild to no sleep apnea group, 14 (12 percent) participants died. Five died from sudden death, 3 from myocardial infarctions, and 6 from progressive heart

failure. There were no deaths in the treated OSAS group (Wang et al., 2007). The results from this study suggest that patients with heart failure and untreated OSAS have an increased risk of death regardless of the OSAS severity. It is important to note that it is possible that other factors, which could not be controlled for, might explain these differences.

Hypertension.

OSAS is an accepted cause of hypertension and is recognized as such by both European and American recommendations on hypertension (Baguet et al., 2009; Mansia et al., 2007). The primary mechanism behind the association between hypertension and OSAS is the increase in sympathetic activity during the apnea periods. Elevated sympathetic activity results in an increase in peripheral arterial resistance leading to an increase in diastolic pressure. Apneic patients develop cardiovascular sensitivity to the repetitive sympathetic stimulation and the blood pressure response to the CPAP depends on the severity of the OSAS, the more severe the disease the more effective the treatment (Baguet et al., 2009). The Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure (JNC7) classifies blood pressure as follows: optimal (normotensive) blood pressure is a systolic blood pressure less than 120 mmHg and a diastolic blood pressure less than 80 mmHg, prehypertension is a systolic blood pressure between 120 and 139 mmHg and diastolic blood pressure between 80 and 89 mmHg, a systolic blood pressure above 140 mmHg and / or a diastolic blood pressure over 90 is classified as hypertension. Hypertension is further divided into stage 1 (systolic between 140-159 mmHg), stage 2 (systolic between 160-179 mmHg, stage 3 (systolic

between 180-209 mmHg), and stage 4 (systolic greater than 210 mmHg) (Mancia et al., 2013; Miller & Jehn, 2004).

Peppard et al. (2000) conducted a prospective longitudinal evaluation to examine the association between objective measures of OSAS and hypertension (at least 140/90) or the use of antihypertensive medications over a decade ago. The study consisted of 709 participants that were evaluated at baseline and at a four year follow-up. Of the 709, 184 were followed for an additional four years, and reevaluated at 8 years. The researchers found that persons with few events of apnea or hypopnea (0.1 to 4.9 events per hour) at baseline were 42 percent more likely to have hypertension at follow-up than those with no events of apnea or hypopnea. Persons experiencing 5.0 to 14.9 events of apnea or hypopnea per hour were two times more likely to have hypertension at follow-up and those with apnea or hypopnea events of 15 or more an hour were three times more likely to have hypertension at follow-up. The authors of this early study suggest that OSAS in any form is a risk factor for hypertension.

Jaimchariyatam et al. (2010) conducted the first study comparing cardiovascular outcomes in the mild OSAS population. The study included 255 participants diagnosed with mild OSAS between 2004 and 2006. The participants were divided into two groups, CPAP ($n = 93$) and no CPAP ($n = 162$). At the end of the 2 year period the CPAP group had a 1.97 point reduction in mean blood pressure and the non CPAP group had a 9.61 point elevation in mean blood pressure. Ozeke et al. (2011) examined the influence of OSAS disease severity on nocturnal heart rate and hypertension. There were a total of 540 participants in the study by Ozeke et al. (2011), 166 mild OSAS patients (42 females, 124 males), 147 moderate OSAS patients (25 females, 122 males), and 227 severe OSAS

patients (25 females, 202 males). Group comparison regarding severity of OSAS and nocturnal mean HR was significant for both females and males ($p>0.001$), maximal heart rate ($p=0.004$ in females; $p=0.003$ in males), hypertension ($p=0.026$ in females; $p<0.001$ in males), as well as systolic ($p=0.004$ in females; $p<0.001$ in males) and diastolic ($p=NS$ in females; $p<0.001$ in males) blood pressure. Based on the evidence, hypertension should be explored in all apneic patients, regardless of disease severity.

Stroke. Recent data suggest that OSAS is associated with ischemic stroke (Somers et al., 2008). The physiological response to OSAS (i.e. blood pressure surges, increased sympathetic nervous system stimulation, hypoxia, and hypercapnia) is thought to increase stroke in OSAS patients. Redline et al. (2010) examined the prevalence of stroke among OSAS patients in a community based sample. A total of 5,422 participants were included in the study. The participants had no history of stroke and were identified as having OSAS (baseline PSG between 1995 and 1998) but were not being treated with pressure therapy. Participants were followed for 8.7 years, during which time a total of 193 strokes occurred (85 in men and 108 in women). Compared to men with low apnea hypopnea index scores, men with moderately severe OSAS had nearly a threefold increased risk of stroke. In the mild to moderate range (AHI - 5-25) the risk of stroke increased by 6 percent with each one unit increase in the AHI. There was no significant association between stroke and AHI in women.

The increased risk of stroke among patients with OSAS might be related to carotid artery thickness. Thirty men with severe OSAS (AHI >20) were included in a study conducted by Altin et al. (2005). All carotid arteries were found to be significantly thicker in participants with severe OSAS when compared to those with mild OSAS.

Severe OSAS participants also had more carotid plaque (thickening of at least 1.2 mm) than their mild OSAS counterparts, as well as more plague localizations. The relationship between plaque formation and OSAS is not fully understood. However, one author of a dated experimental study found a direct relationship between degenerative changes of the arterial walls and oxygen desaturations (Gainer, 1987).

Excessive Daytime Sleepiness

Excessive daytime sleepiness (EDS) affects an estimated 20 percent of adults in the United States and is the leading symptom reported by patients presenting to sleep clinics (Pagel, 2009). EDS refers to the tendency to fall asleep while involved in activities that are not stimulating, such as listening to a speaker or watching television. However, many individuals experiencing EDS are at risk for falling asleep at more inopportune times, such as while driving or working. Individuals experiencing EDS are at higher risk of motor vehicle accidents, work- related incidents, and overall poorer health than those individuals not experiencing EDS (Chen, Vorona, Chiu, & Ware, 2008; Drake et al., 2010; Gooneratne et al., 2003).

A common problem encountered when a patient reports excessive sleepiness is distinguishing between sleepiness and fatigue. Sleepiness and fatigue are conceptually distinguishable but are continually confounded in research, research measurement instruments, health care settings, and in everyday spoken language. Sleepiness is generally described as a feeling associated with an overwhelming need to sleep and is associated with terms such as drowsy or somnolent. Fatigue, on the other hand, is related more to a feeling of the need to rest rather than sleep and descriptive terms such as

lethargy, listlessness, and exhaustion have been used to describe feelings of fatigue (Neu, Linkowski, & Bon, 2010).

EDS is prevalent among those with sleep disorders, particularly narcolepsy and OSAS. When addressing healthcare concerns related to sleep, the typical clinical interview involves the assessment of EDS, not fatigue. EDS can occur secondary to a number of things including side effects of medications, sleep deprivation, substance use, OSAS, circadian rhythm disorders, sleep – related movement disorders, psychiatric conditions (i.e., depression), and medical conditions (i.e., stroke, cancer, head trauma). EDS can also exist as a primary hypersomnia (i.e., idiopathic hypersomnia, narcolepsy). However, it should be noted that EDS of primary origin is far less common and a secondary origin should be considered initially (Pagel, 2009).

There are several assessment tools available to determine the severity of EDS. These include, but are not limited to, the Epworth Sleepiness Scale (ESS), the Stanford Sleepiness Scale (SSS), and the Multiple Sleep Latency Test (MSLT). The ESS and SSS both measure subjective daytime sleepiness while the MSLT measures objective daytime sleepiness. The ESS was used in this study and was developed in 1991 by Johns (Johns, 1991). The intent of the ESS is to differentiate alert individuals from those with excessive daytime sleepiness. The ESS presents eight various situations in which an individual self-scores (0-3) how likely they are to fall asleep in each situation, with a score of greater than ten suggesting significant daytime sleepiness (Johns, 1991).

Drake et al. (2010) conducted a study of 618 persons to determine the risk associated with sleepiness and motor vehicle accidents. The participants were divided into 3 groups based on sleepiness (excessively sleepy, $n = 69$; moderately sleepy, $n =$

204; alert, $n = 345$). Over a 10 year period the excessively sleepy group was found to be at a significant increase for motor vehicle accidents when compared to the moderately sleepy and alert groups. The positive linear relationship between the prevalence of motor vehicle crashes and physiological sleepiness was significant ($p < 0.05$) which supports EDS as a predictive factor in motor vehicle accidents. The relationship between commercial bus drivers and level of sleepiness has also been researched. Vennelle, Engleman, and Douglas (2010) examined 677 Epworth Sleepiness Scale (ESS) questionnaires completed by commercial bus drivers. Of the 677, 133 (20 percent) reported ESS scores > 10 (indicating excessive daytime sleepiness). Additional data obtained includes 8 percent reporting that they had fallen asleep at the wheel at least once, 7 percent reported having an accident due to sleepiness, and 18 percent reported a near miss accident as a result of sleepiness.

EDS has been associated with professional performance in physicians and judges. Chen et al. (2008) conducted a study of physicians and sleepiness. The study yielded 180 completed surveys. Of the 180, 41 had ESS scores of 11 or greater. The survey included numerous questions related to how sleepiness affected professional practice. When asked the following statement, "My work is unaffected by sleep loss and fatigue." Eighty-one percent disagreed or strongly disagreed. Additionally, 48 percent had worried about having a car accident on the way home post-call and 24 percent had made medical errors because of sleep loss and fatigue. Grunstein and Banerjee (2007) reviewed 15 judicial cases involving sleepiness and professional performance by judges. In 10 of the cases a retrial was ordered and in five of the cases there was either a dismissal of the case or retirement of the judge.

Sleep related problems are increasingly being recognized as a contributing factor to heightened pain perception, increased morbidity and mortality, as well as a decrease in overall quality of life (Taylor-Gjevre, Gjevre, Nair, Skomro, & Lim, 2011). A study conducted by Sforza, de Saint Hilaire, Pelissolo, Rochat, and Ibanez (2002) included 60 participants, 16 snorers and 44 with diagnosed OSAS. The purpose of the study was to evaluate the impact, if any, daytime sleepiness had on mood disorders. Anxiety was present in 16 percent of participants and depression was present in 7 percent of participants. The mean ESS score during the day was 10.9 with 29 participants having ESS greater than 11. Participants with a higher degree of subjective sleep propensity and daytime sleepiness were found to be at an increased risk for depression as evidenced by higher Hospital Anxiety (HAD-A) and Depression (HAD-D) Scale scores.

Continuous Positive Airway Pressure Treatment for Excessive Daytime Sleepiness

Continuous positive airway pressure (CPAP) is an effective method of treatment for individuals experiencing EDS. Avlonitou, Kapsimalis, Varouchakis, Vardavas, and Behrakis (2011) assessed the quality of life and symptoms in patients with OSAS after beginning CPAP therapy and adhering for 6 months to the regimen. A total of 50 patients (9 women, 41 men) underwent PSG, were diagnosed with OSAS, and prescribed CPAP therapy for treatment. Quality of life, as measured by the Sleep Apnea Quality of Life index (SAQLI), was significantly improved following 6 months adherence to CPAP therapy (total SAQLI scores -3.8 ± 0.9 before CPAP, 5.8 ± 0.8 after CPAP, $p < 0.01$). Other constructs of the SAQLI also demonstrated improvement; daily functioning (4.2 ± 1.4 before CPAP, 6.0 ± 0.9 after CPAP, $p < 0.01$), social interactions (4.8 ± 1.3 before CPAP, 6.3 ± 0.7, $p < 0.01$), emotional functioning (4.4 ± 1.4 before CPAP, 5.7 ± 1.0, p

<0.01) and symptoms (1.6 $\pm$ 0.8 before CPAP, 5.8 $\pm$ 1.2, $p < 0.01$). Overall ESS scores were decreased (13.7 $\pm$ 6.5 before CPAP, 3.9 $\pm$ 3.8 after CPAP, $p < 0.01$). The results of this study may provide evidence that adherence to CPAP therapy improves quality of life and decreases daytime sleepiness.

Excessive daytime sleepiness (EDS) is a primary symptom of, and a well-recognized consequence of OSAS (Rosenberg & Doghramji, 2009; Seneviratne & Puvanendran, 2004). While it is not unexpected for many people to fall asleep during boring situations it may be even more difficult for people with OSAS to remain awake even during times that demand sustained vigilance and concentration. EDS is exacerbated and more prominent in OSAS sufferers during times that would not normally evoke sleepiness in individuals without OSAS (Rosenberg & Doghramji, 2009). Patel et al. (2003) compiled the results of a meta-analysis regarding the effect of CPAP use on subjective and objective sleepiness. The most significant finding was that the more severe the OSAS, the more decrease in daytime sleepiness an individual experienced with CPAP.

Continuous Positive Airway Pressure. Continuous positive airway pressure (CPAP) is the primary treatment for OSAS. Nasal CPAP was first developed as a treatment for OSAS in 1981 (Sullivan, Berthon-Jones, Issa & Eves, 1981), but was not widely accepted until 1985 (Grunstein, 2005). The most significant effect of CPAP on the upper airway is that it acts as a pneumatic splint to prevent airway collapse during sleep by providing continuous pressure to the airway. The result is an increase in the actual size of the airway during treatment, primarily in the lateral direction, as well as decreasing lateral pharyngeal wall thickness and reducing airway edema associated with chronic

vibration (snoring) and airway occlusion (Yagi et al., 2009). CPAP therapy is not curative and should be expected as a lifetime treatment.

Currently there are three forms of positive airway pressure devices available: 1) continuous positive airway pressure (CPAP); 2) bilevel positive airway pressure (BiPAP); and 3) automatic self-adjusting positive airway pressure (APAP). CPAP uses a facial mask, or some other means of interface (such as intra-nasal tubes) with the upper airway, that is connected to an air pump that generates pressure in the airway while also allowing for the release of expired carbon dioxide. Therapeutic supplements can also be used with CPAP, such as oxygen for patients whose oxygen levels do not normalize and humidification to make use more comfortable by reducing the tendency of CPAP to cause nasal dryness (Chang, Cox, & Shaffer, 2011). The most common method of air pressure delivery is with a nasal mask, which is normally manufactured in standard sizes, however, some companies offer custom fitting for patients that present with unusual facial contours. Generally, the construction of the nasal masks consists of an outer shell of hard plastic with a soft inner seal constructed of rubber or rubber filled with silicone gel. One major variation of CPAP pressure delivery is nasal prongs, which enter the nostril and form a seal around the opening of the nostril (Haba-Rubio et al., 2011).

The first pressure generating devices for CPAP treatment were air compressors, which although effective, were considered by patients to be bulky and noisy. An advance in the CPAP delivery technology came with the replacement of air compressors with air blowers. Advantages of air blowers include smaller size, greatly reduced noise, and their ability to compensate for a loss of mask pressure due to an imperfect seal with the face (McNicholas, 2002). Due to the fact that inspiration and expiration are conducted through

the same nasal mask, it is necessary to provide a means for the removal of expired carbon dioxide. Common ways of dealing with this problem are to place a small hole in the mask or to attach a valve to the mask, which serves to remove expiratory flow from the system (Cistulli & Grunstein, 2005).

There are some variations in the pressure delivery of CPAP blower systems. Patients often find exhalation more difficult than inhalation on CPAP because they must exhale against the airflow. The first method of modified pressure delivery designed to address this problem was bi-level positive airway pressure (BiPAP). The BiPAP system allows for inspiratory and expiratory air pressure levels to be adjusted independently, and was designed to make the positive airway pressure more tolerable (Blau et al., 2011). This means of pressure delivery allows for a higher pressure level to be set for inspiration (inspiratory positive airway pressure), without equivalent high pressure for expiration (expiratory positive airway pressure) and the greater discomfort that this might cause.

The newest variation on pressure delivery is automatic CPAP (APAP), which delivers varying amounts of pressure throughout the night according to the amount required to eliminate snoring and sleep apnea. This system was developed in part due to issues surrounding the determination of what the ideal pressure for an individual would be throughout the entire night, in various sleeping positions and in various stages of sleep (McArdle et al., 2010). A specific range of CPAP pressures is set for the APAP device, with the lowest pressure being utilized at the beginning of any sleep period. The major theoretical advantage of APAP is increased patient comfort, because only the amount of pressure that is needed at any given point in the sleep period is delivered. APAP may be particularly useful in patients that are intolerant of higher pressures or in patients in

whom the ideal pressure is highly variable (McArdle et al., 2010). It is possible to also benefit economically with the APAP due to less technician time, the elimination of in-hospital polysomnography, and potentially reducing the number of clinic visits of patients with CPAP adherence issues (Grunstein, 2005; McArdle et al., 2010).

The use of CPAP therapy in patients with severe OSAS (apnea hypopnea index ≥30) has been studied for decades and has demonstrated reversal of upper airway obstruction during sleep as well as reducing the most notable consequence of OSAS, daytime sleepiness. The use of BiPAP and APAP is increasing. Marrone et al. (2011) found that when compared to CPAP, APAP was equally as effective at decreasing blood pressure during wakefulness and sleep. Reeves-Hoche et al. (1995) compared 36 CPAP patients and 26 BiPAP patients to determine if the use of BiPAP would result in an increase in the number of hours of use. The authors did not find a significant increase in the amount of time the device was used (80 percent CPAP; 82 percent BiPAP). Weber, Kellner, Burbach, Kirchheiner, and Ruhle (1995) studied the effect of CPAP and BiPAP on cardiac output and did not find a significant difference in hemodynamics between the two forms of positive pressure. Additional studies are needed to evaluate the effectiveness of APAP and BiPAP on hypertension and EDS.

The literature reviewed for this paper includes studies examining the use of CPAP. Two examples of early studies related to objective daytime sleepiness with moderate to severe OSAS were identified. Engleman, Martin, Deary, and Douglas (1994) examined 32 patients with OSAS and Engleman et al. (1999) examined 23 patients with OSAS. The researchers of each study found a decrease in objective daytime sleepiness with CPAP use. It should be noted that each study found improvement in daytime

sleepiness with less than ideal nightly use (3.4 hours per night, 3.2 hours per night). Two early studies examining subjective daytime sleepiness with moderate to severe OSAS were also reviewed. Hardinge, Pitson, and Stradling (1995) examined two groups, one (n = 50) at 2 months after the initiation of CPAP therapy and another (n = 25) at 1 year after initiation of CPAP therapy. Both groups demonstrated a decrease in ESS scores indicating a decrease in subjective daytime sleepiness. Ballester et al. (1999) conducted a study involving 105 participants in two groups, conservative treatment (n = 37) (complete enough hours of sleep each night, sleep on their side, lose weight by following a home diet prescribed by a dietician, and avoiding the use of sedatives and alcohol consumption) and CPAP group (n = 68) (CPAP therapy in addition to all criteria for conservative group). The authors found that the relief of sleepiness was greater in the group that used CPAP therapy in conjunction with conservative measures than in the conservative treatment group alone. Montserrat et al. (2001) conducted a study involving 48 patients comparing CPAP therapy to a placebo therapy (sham CPAP). The authors found that CPAP therapy was significantly more effective in reducing daytime sleepiness than the sham CPAP therapy. An earlier study conducted by Kingshott et al. (2000) examined 62 patients with moderate to severe OSAS and found a significant improvement in daytime function after 6 months of CPAP treatment. More recently Antic et al. (2011) examined 174 moderate to severe OSAS patients. The authors identified a greater achievement of overall daytime function with longer nightly CPAP use. A study by Machado et al. (2010) involving moderate to severe OSAS patients with coexisting chronic obstructive pulmonary disease (COPD) receiving long term oxygen therapy was reviewed. In this particular study 95 patients with moderate to severe OSAS and COPD were examined. Of

the 95, 61 were treated with CPAP therapy and 34 were not treated with CPAP therapy. The results of this study found 5 – year survival rate estimates of 71 and 26 percent, respectively. Therefore, based on these findings supporting the use of CPAP with moderate to severe OSAS, it can be concluded that CPAP is an effective choice of treatment with this population.

The effect of CPAP treatment in patients with mild OSAS severity has not been as well established as that of moderate to severe severity. Four studies were reviewed involving the use of CPAP with mild OSAS. Engleman et al. (1997) conducted a placebo controlled study involving 16 patients with mild OSAS. The participants received four weeks of placebo therapy and four weeks of CPAP therapy. Participants receiving CPAP therapy demonstrated an increase in cognitive performance and a decrease in psychological distress. However, it should be noted that Epworth Sleepiness Scale (ESS) scores for CPAP therapy did not reflect significant reduction in subjective daytime sleepiness when compared to the placebo therapy. The small sample size might explain the lack of statistical significance.

Engleman et al. (1999) conducted a second, larger study ($n = 34$) similar to the study previously discussed. Participants received CPAP therapy for four weeks and an oral placebo therapy for four weeks. CPAP therapy, when compared to placebo therapy, revealed a decrease in subjective daytime sleepiness as evidenced by a decrease in ESS scores. On the other hand, objective daytime sleepiness, as measured by the Maintenance Wakefulness Test, was not reduced. The researchers of this study support the use of CPAP therapy with mild OSAS but they also suggest that not all patients' sleepiness in this population will improve with CPAP therapy.

Monasterio et al. (2001) compared the effectiveness of CPAP therapy plus conservative therapy to conservative therapy alone in 125 mild OSAS patients (59 conservative therapy alone, 66 CPAP plus conservative therapy). Conservative therapy consisted of following a home diet plan for weight loss in individuals having a BMI greater than 27, avoidance of alcohol or sedative consumption, avoidance of the supine position for sleeping, and an acceptable number of hours of sleep per night. The authors did not find a significant benefit for CPAP therapy plus conservative therapy over conservative alone. ESS scores did improve slightly, but did not reach the level of significance. The authors did reveal an improvement in OSAS related symptoms (snoring, nocturia, concentration difficulties, breathing pauses, morning headache, morning drowsiness, and nonrestorative sleep), which suggests that CPAP therapy may have a role in the treatment of mild OSAS.

Barnes et al. (2002) studied 42 patients with mild to moderate OSAS over an 8 week trial period in which participants used CPAP for four weeks and took an oral placebo tablet for four weeks. Although self-reported symptoms of sleep quality were improved with CPAP, neither objective nor subjective symptoms showed improvement with CPAP over the oral placebo tablet. Based on the results of the above studies additional research is needed to validate the use of CPAP therapy in patients with mild OSAS.

Continuous positive airway pressure adherence. Despite the effectiveness of CPAP in the treatment of OSAS, treatment efficacy is limited by the lack of adherence to the prescribed therapy. Adherence is defined as 4 hours or greater of nightly use 70 percent of the nights (Grunstein, 2005; Weaver & Grunstein, 2008). The minimum

therapeutic usage of CPAP has been debated in the literature. Engleman et al. (1994) found a decrease in daytime sleepiness and improved cognitive function with as little as 3 hours of nightly use. Additional researchers have yielded results that suggest that a decrease in subjective sleepiness, objective sleepiness, memory, and daily functioning can be achieved at various levels of usage, ranging from 4 hours of nightly use to 7.5 hours of nightly use (Stradling & Davies, 2000; Weaver et al., 2007; Zimmerman, Arnedt, Stanchina, Millman, & Aloia, 2006). Despite the abundance of studies related to CPAP therapy use, the dose-response relationship between CPAP adherence and sleep apnea severity is not fully understood. Therefore, the minimum amount of nightly use has not been established (Stepnowsky & Dimsdale, 2002). Weaver et al. (2007) asserts that some individuals might have variation in the need for CPAP therapy. This suggests that individuals with shorter nightly use may be effectively treated with CPAP, particularly with respect to sleepiness. Furthermore, Weaver and Grunstein (2008) assert that the clinical evidence available, albeit variable, suggest that any use is better than no use. Despite the known variation related to dose-response, the arbitrary cut point of at least 4 hours per night 70 percent of the nights has become the standard usage to define adherence.

Estimates are that approximately 50 percent of patients prescribed CPAP therapy are nonadherent one year post prescription (Ballard, Gay, & Strollo, 2007) and that non-adherence rates are as high as 29 – 83 percent (Weaver & Grunstein, 2008). Several factors have been identified as possible causes of nonadherence including; 1) cost of CPAP therapy; 2) mask interface (discomfort); 3) nasal congestion; 4) difficulty adapting to the pressure; 5) social context (marital status and employment) (Beecroft, Zanon,

Lukie, & Hanly, 2003; Chasens, Pack, Maislin, Dinges, & Weaver, 2005; Gagnadoux et al., 2011); and 6) lack of personal involvement in care (Rodgers, 2014). These factors will be described further below.

CPAP therapy, when compared to the costs associated with untreated OSAS, is cost effective (Tzischinsky, Shahrabani, & Peled, 2011). Simon-Tuval et al. (2009) conducted a study involving 162 newly diagnosed OSAS patients that were prescribed CPAP therapy and found that only 40 percent of the patients purchased their CPAP machine. Of the 162 patients, 76 percent stated that the device was too expensive. Socioeconomic status plays a pivotal role in adherence to CPAP therapy. Insurance coverage related to CPAP treatment may vary considerably by insurance carrier, and studies demonstrate that non-adherence is higher in individuals with insufficient health coverage (Simon-Tuval et al., 2009; Tzischinsky et al., 2011).

Finding the most appropriate mask interface is a major challenge for many CPAP patients. There are a variety of interfaces available; nasal, oronasal (full face), and total face masks. Mask technology has improved greatly, and this is vital since mask discomfort remains a critical influence on adherence. An inappropriate mask fit can lead to air leaks, which appear to be the primary force behind mask discomfort. The air leaks can cause a drop in positive pressure, leading to sleep interruption as well as persistent OSAS. In addition, a poorly fitting mask can lead to facial bruising and possibly ulceration on the bridge of the nose (Grunstein, 2005). Despite the availability of various mask interfaces there remains a gap in the literature comparing the different mask types. However, it does appear that the newly developed mask interfaces are associated with fewer issues related to mask fit (Grunstein, 2005). For those patients who continue to

have mask-fit problems, despite the newly designed masks available, a change in mask interface may be necessary to improve fit and ultimately improve adherence. The nasal mask involves the use of nasal prongs and may be a solution for some patients. However, the use of nasal prongs does not come without problems as well and have been associated with nasal irritation and dryness of the mouth and throat (Ruhle & Nilius, 2008).

Nasal stuffiness is a commonly associated side effect of CPAP therapy (Weaver & Grunstein, 2008). Existing data available related to nasal congestion and CPAP therapy is somewhat limited in so far as it only addresses the fact that it occurs in this patient population. A few dated studies were identified and reviewed. Hayes, McGregor, Roberts, Schroter, and Pride (1995) found that mask mouth air leak was a factor in the nasal symptoms that many CPAP users experienced, however allergic conditions may also play a role. Data suggest that nearly all patients experience nasal stuffiness initially, and as many as 10 percent will continue to experience such symptoms after 6 months of treatment (Pepin et al., 1995). There are a number of potential reasons for the nasal stuffiness associated with CPAP therapy. It is possible that CPAP causes mucous production due to the pressure on the mucosal receptors, which may also lead to the reported side effect of significant nasal dryness (Grunstein, 2005). Another plausible explanation is that the CPAP treatment itself causes allergic reactions in some patients. Patients should also be screened for nasal polyps or a deviated septum, which could also contribute to the nasal symptoms (Grunstein, 2005). One of the primary treatments for the associated nasal stuffiness is heated humidification of the air within the device. The humidified air aids in the prevention of nasal dryness as well as nasal stuffiness. Koutsourelakis et al. (2011) conducted a study involving 25 patients receiving CPAP

treatment for OSAS and found that the relative humidity within the device was not significantly decreased when using heated humidification, even when a mouth leak occurred. Furthermore, it was discovered that when heated humidification was added to the face mask interface there was no decrease in the relative humidity at all, resulting in less nasal dryness and nasal congestion. Patients may also benefit from antihistamines or saline nasal sprays (Koutsourelakis et al., 2011).

Adapting to the pressure of the CPAP device can be challenging for some patients. However, there is little evidence that suggests that air pressure directly relates to low adherence rates (Grunstein, 2005). It has been reported that some patients will complain of too much pressure in the nose or difficulty resisting the pressure on exhalation. For this population of patients it is possible that a ramp feature might be helpful. A ramp feature is a delay timer that can be added to the CPAP system. The timer allows for the desired pressure to be reached gradually, thus reducing the resistance on exhalation. There is no evidence that use of the ramp feature actually increases adherence rates; however, most patients prefer using this feature to avoid the delivery of the therapeutic pressure all at once (McNicholas, 2002). An early study conducted by Pressman, Peterson, Meyer, Harkins, and Gurijala (1995) examined overuse of the ramp feature and found that "ramp abuse" can lead to under treatment of OSAS. It is therefore imperative that patients receive adequate education involving use of the ramp feature.

Bi-level pressure is another feature that can assist with the difficulty experienced by some patients during exhalation. As mentioned previously, BiPAP allows for the inspiratory and expiratory pressures to be set independently. The underlying principle is that the expiratory pressure setting can be lowered, thus reducing the difficulty with

expiration. Early studies indicate however, that BiPAP may be less effective in maintaining the upper airway patency than CPAP (Gugger & Vock, 1992; Sanders & Kern, 1990). The authors of these early studies suggest that BiPAP should not be a first line therapy, and should be considered only for those patients that have extreme difficulty adjusting to standard CPAP.

The social context of daily life should be taken into account when screening patients for CPAP adherence. Gagnadoux et al. (2011) conducted a study involving 1,141 patients prescribed CPAP for nightly use for at least 90 days. The researchers sought to examine the impact of socioeconomic factors, as well as patients and disease characteristics prior to the initiation of CPAP therapy, on long term adherence. The researchers found that marital status and employment status are associated with CPAP adherence. Patients living alone and / or working are at a greater risk for non-adherence than their married and retired counterparts. Relationship quality is also a factor to be considered when exploring non-adherence. Baron, Smith, Czajkowski, Gunn, and Jones (2009) examined relationship quality and CPAP adherence in 42 married males. They found that patients with higher levels of relationship conflict were less likely to adhere to CPAP therapy and averaged lower nightly adherence rates over the first 3 months of treatment than those with lower levels of relationship conflict.

Lewis, Seale, Bartle, Watkins, and Ebden (2004) sought to identify factors associated with non-adherence prior to the initiation of CPAP therapy in a group 80 patients. The authors found that patients living alone used CPAP an average of 3.2 hours a night during the first week of treatment, whereas patients living with a partner averaged 4.5 hours a night. Cartwright (2008) examined the sleep of 10 married couples to

determine how CPAP adherence was affected by sleeping with a partner. This author asserted that adherence is strongly related to the bed partner's sensitivity to arousal related to the CPAP apparatus and that assessing and addressing the partner's response to the treatment may improve treatment adherence. Marital status is related to higher levels of CPAP adherence and should be considered when evaluating patients for adherence.

Lack of personal involvement in the management of OSAS potentially reduces adherence to CPAP therapy. Rodgers (2014) conducted a grounded theory study involving 82 adults who were at various stages in the process of being diagnosed and living with OSAS. The researcher sought to examine the experiences of adults who live with the condition. Rodgers found that participants expressed a desire to be more involved in the management of their care, particularly at the onset of disease management with positive airway pressure machine selection and delivery interface. Participants also reported the desire to be able to monitor their own therapy. Based on the findings, Rodgers suggests that CPAP adherence rates may be increased by involving the patients in their care and placing an emphasis on self-management.

Adherence monitoring. Early efforts at objective monitoring of adherence with CPAP were built-in timers that actually provided information related to when the machine was switched on. This time was referred to as "machine-on" time (Collard et al., 1997). However, there was no way to determine whether the mask was being worn during the time that the machine was on. The ability to differentiate between "machine-on" time and the amount of time the mask was actually worn, referred to as "mask-on face" time, was achieved with the advent of the new CPAP machines. This is accomplished with built-in pressure transducers that are able to detect variations in pressure; therefore a

significant drop in pressure indicates that the mask is not being worn. In addition, CPAP machines are equipped with an electronic memory card that records the aforementioned information. Patients are instructed to bring the memory card with them to either the physician's office or the medical supply company. If the information is supplied to the medical supply company it will be forwarded to the physician prior to the patient's follow up visit. This information allows the clinician to assess both how many hours the machine was functioning as well as how many hours the mask was worn (Cistulli & Grunstein, 2005).

Theoretical Framework

The researcher of this study is concerned with the effect CPAP use has on daytime sleepiness and blood pressure in persons with mild OSAS. Daytime sleepiness and elevated blood pressure can have both psychological and physiological antecedents and sequela and can interact with one another. In order to adequately support the psychological component of daytime sleepiness and the physiological component of blood pressure a synthesized model approach was taken. Daytime sleepiness is routinely assessed in the clinical setting as a subjective complaint. Bebee and Gozal's prefrontal cortex model of the effects of OSAS (Figure 1) was modified for the current study. The modified theoretical model presented in figure 2 illustrates both physiological and psychological changes that occur as a result of OSAS and the impact CPAP use has on each. CPAP use will be divided into two categories, use four or more hours nightly 70 percent of the nights and use less than four hours nightly 70 percent of the nights. The cut point of at least four hours of nightly use 70 percent of nights has been used in numerous research studies (Aloia, Arnedt, Stepnowsky, Hecht, & Borrelli, 2005; Bachour &

Maasilta, 2004; Chasens et al., 2005; Lindberg, Berne, Elmasry, Hedner, & Janson, 2006).

There is a preponderance of evidence indicating that untreated OSAS leads to physiological changes in the cardiovascular system that can result in hypertension (Buchner et al., 2007; Jaimchariyatam et al., 2010; Laaban et al., 2010; Peppard et al., 2000). The primary mechanism behind the association between hypertension and OSAS is the increase in sympathetic activity during the periods of apnea. Elevated sympathetic activity results in an increase in peripheral arterial resistance leading to an increase in diastolic pressure. CPAP use decreases sympathetic activity resulting in a decrease in blood pressure (Penzel et al., 2012). As indicated in figure 2, when CPAP is used four or more hours a night 70 percent of the nights, there is a reduction in sympathetic activity resulting in a decrease in blood pressure (Weaver & Grunstein, 2008). When CPAP is used less than four hours a night 70 percent of the nights the clinical benefits are not as great. Loube et al. (1999) and Arias at al. (2008) found significant reductions in systolic and diastolic blood pressure ($p = 0.001$ and $p = 0.006$, respectively) when patients used the CPAP device for greater than four hours a night. Dorkova, Petrasova, Molcanyiova, Popovnakova, and Tkacova (2008) and Jelic et al. (2008) found that patients who used the CPAP device less than four hours a night did not experience reductions in systolic or diastolic blood pressure. Faccenda, Mackay, Boon, and Douglas (2001) also found a greater reduction in blood pressure with greater CPAP use.

EDS is a common finding in persons with OSAS (Tomfohr et al., 2011). The literature suggests that CPAP use can reduce associated daytime symptoms (Avlonitou et al., 2011). Figure 2 illustrates how mild OSAS leads to sleep disruption that then leads to

adverse daytime effects such as excessive daytime sleepiness. Avlonitou et al. (2011) conducted a study involving 50 OSAS patients in all degrees of disease severity (mild *n* = 8, moderate *n* = 8, and severe *n* = 34) and found a significant decrease ($p = 0.001$) in excessive daytime sleepiness where CPAP use was defined as at least four hours of nightly use 70 percent of the nights per week. Weaver et al. (2007) found that four hours of nightly use improved daytime sleepiness as measured by the Epworth Sleepiness Scale and increased the likelihood that normal levels of sleepiness could be achieved. Donadio et al. (2007) examined 10 newly diagnosed OSAS patients with EDS and found a consistent decrease in daytime sleepiness with CPAP use of six hours ($\pm$ 3) per night. It can be concluded from the previous literature that CPAP use of four or more hours nightly for 70 percent of the nights leads to a decrease in daytime sleepiness. As the feedback loop illustrates for both physiological and psychological components, less than four hours of CPAP use can lead to progression of the disease which in turn can lead to an increase in blood pressure and an increase in daytime sleepiness.

Beebe and Gozal Theoretical Model

Beebe and Gozal theorized that the disruption in sleep within the context of OSAS prevents restorative sleep from occurring. This is in part due to the intermittent hypoxemia and hypercarbia that occur as a result of OSAS. They further assert that in addition to the blood gas abnormalities and sleep disruption that occurs a chemical and structural central nervous system cellular injury takes place as well, leading to a dysfunction of the prefrontal regions of the brain cortex (PFC). The dysfunction in the PFC is manifested behaviorally in what has been termed by neuropsychologists as executive dysfunction. Executive dysfunction is theorized to significantly affect the

functional application of cognitive abilities which in turn leads to adverse daytime effects (Beebe & Gozal, 2002; Jackson, Howard, & Barnes, 2011).

Beebe and Gozal's theoretical model bridges the gap between the physiological and psychological aspects of OSAS by depicting the effect the intermittent hypoxia and hypercarbia have on daytime function (Figure 1). The authors propose a relationship between limited tissue oxygen delivery (hypoxia), decreases in intra – and extra – cellular pH (hypoxia and hypercarbia), and sleep restoration. Beebe and Gozal further assert that blood gas abnormalities and sleep disruption can lead to changes within the central nervous system (CNS) that can in turn affect executive dysfunction (Beebe & Gozal, 2002). The prefrontal model proposed by Beebe and Gozal is not the first model to depict an association between the prefrontal cortex and disordered sleep (Harrison & Horne, 2000). However, no previous studies were identified using the prefrontal model proposed by Beebe and Gozal (2002) within the context of OSAS.

Figure 1 – Beebe and Gozal's Prefrontal Model depicting effects of OSAS.
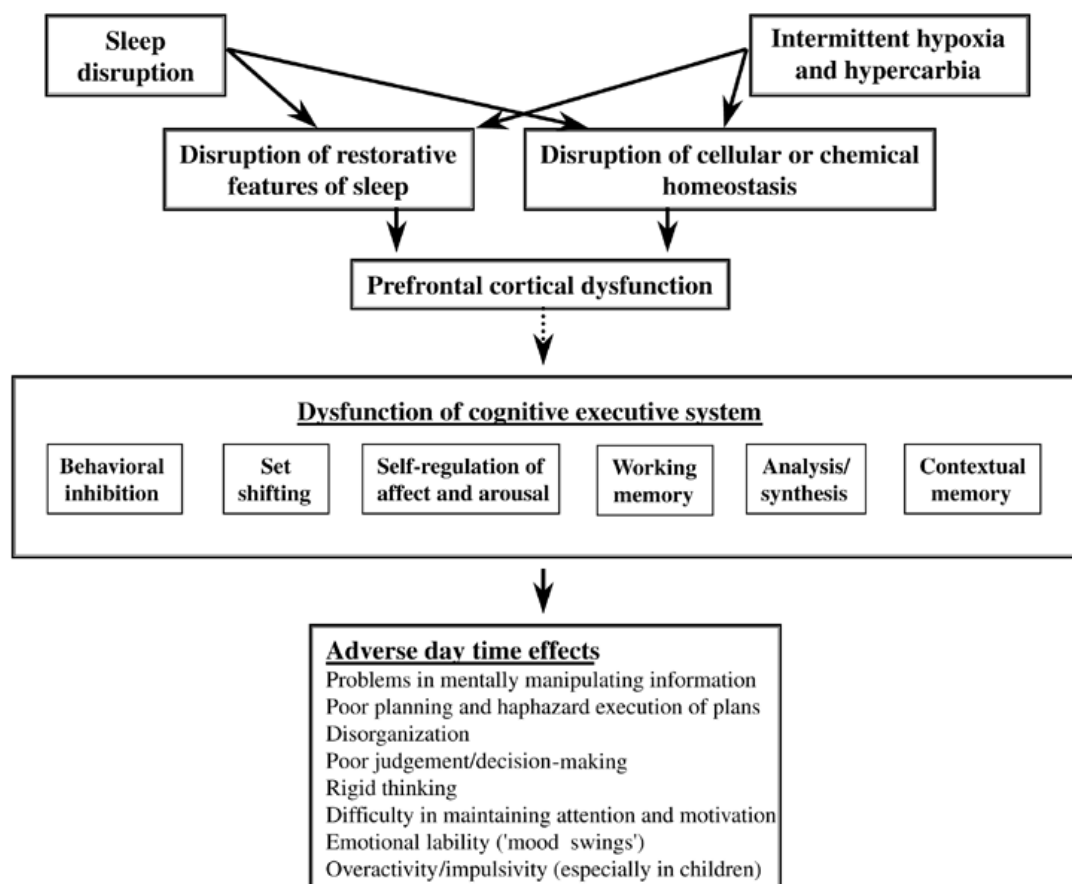
Modified Theoretical Model

A synthesized theoretical model will serve as the underpinning for the proposed study. The model used for this study was modified from Beebe and Gozal's (2002) prefrontal model of OSAS related sleep disruption to further enhance the applicability of the model. As Figure 2 illustrates the modified model is divided into psychological and physiological components. The left side of the model illustrates the psychological effect of mild OSAS on daytime function. OSAS leads to arousals during sleep that in turn result in sleep disruption.

Sleep disruption leads to adverse daytime effects such as EDS. This study proposed that CPAP use will decrease the associated EDS by minimizing sleep disruption from occurring. The recommended amount of nightly CPAP use is defined as machine placement of four or more hours a night 70 percent of the nights (Weaver & Grunstein, 2008), and although widely accepted in clinical practice, this definition is not based upon evidence of physiological of psychological response to a particular dose of CPAP. The recursive arrows included in the model delineate CPAP use of four or more hours 70 percent of the nights from CPAP use of less than four hours a night 70 percent of the nights. As the arrows infer when CPAP is used four or more hours a night a decrease in daytime sleepiness will occur. The feedback loop indicates that when CPAP is used less than four hours a night there is minimal improvement in the mild OSAS with possible disease progression.

The current study modified Beebe and Gozal's model to replace the blood gas abnormality hypercarbia with increased sympathetic activity, increased oxidative stress, and intermittent hypoxemia. It is clearly demonstrated in the literature that untreated OSAS leads to physiological changes in the cardiovascular system that can result in hypertension (Buchner et al., 2007; Jaimchariyatam et al., 2010; Laaban et al., 2010; Peppard et al., 2000). The primary mechanism behind the association between hypertension and OSAS is the increase in sympathetic activity during the periods of apnea. Elevated sympathetic activity results in an increase in peripheral arterial resistance leading to an increase in diastolic pressure. CPAP use decreases sympathetic activity resulting in a decrease in blood pressure. As the arrows suggest in figure 2 when CPAP is used four or more hours a night 70 percent of the nights, there is a reduction in

sympathetic activity resulting in a decrease in blood pressure. When CPAP is used less than four hours a night 70 percent of the nights there is minimal reduction in sympathetic activity.

The number of hours of CPAP use per night to achieve clinical benefits has been the focus of several studies. The evidence suggests that better clinical outcomes will be achieved with greater use (Engleman et al., 1999; Faccenda at al., 2001; Stradling & Davies, 2000; Zimmerman et al., 2006). It should be noted that clinical benefits have been observed with less use than the present CPAP guidelines suggest (Barnes et al., 2004; Weaver et al., 2007). Campos – Rodriquez et al. (2005) found that CPAP use of one hour per night lowered five year mortality rates when compared to no CPAP use. The cut point of at least four hours of nightly use 70 percent of nights (although arbitrarily assigned) has been used in numerous research studies and will serve as the guidelines for recommended use for this study (Aloia et al., 2005; Bachour & Maasilta, 2004; Chasens et al., 2005; Lindberg et al., 2006).

Figure 2 – Theoretical model of Mild Obstructive Sleep Apnea and Continuous Positive Airway Pressure use
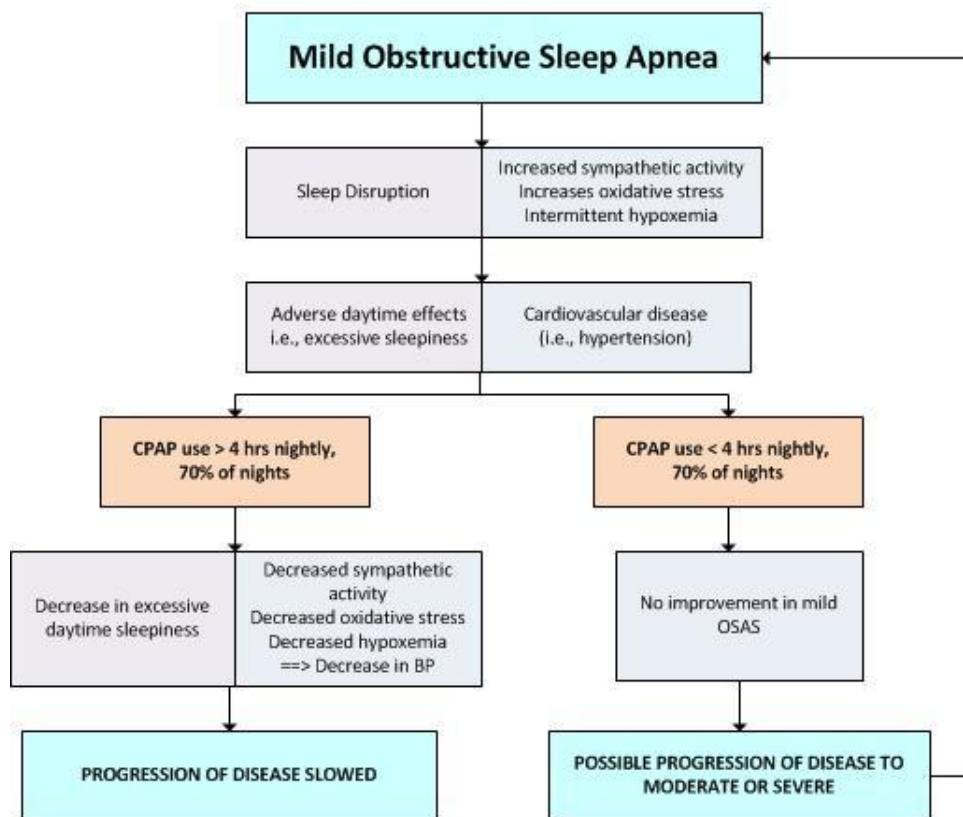
Summary

The literature was reviewed and gaps were identified. Clinical research has focused much of its attention on moderate to severe forms of OSAS. Several studies were identified examining the effectiveness of CPAP in persons with mild OSAS and the impact it has on excessive daytime sleepiness and hypertension, although, additional studies are needed. OSAS is a progressive disease and early intervention is imperative. OSAS can lead to negative health outcomes at all levels of disease severity.

CHAPTER THREE

METHODS

Introduction

The previous chapter's literature review examined the concepts of sleep, sleep apnea, CPAP therapy, and adherence to CPAP therapy. Many studies have been conducted examining the relationship between adherence to CPAP therapy and moderate to severe sleep apnea. This study addressed the gap that exists in the literature related to the effects of CPAP therapy use in mild OSAS. The following chapter describes this study's design and methods.

Research Design

In order to establish additional evidence of the relationship between CPAP use and the outcomes of EDS and blood pressure, a retrospective chart review was conducted. A retrospective chart review enabled the researcher to use existing data to examine past events and factors to answer the research questions. The following hypotheses were addressed:

H1: Individuals who use continuous positive airway pressure four or more hours a night for at least 70 percent of nights recorded will report less daytime sleepiness than those who use continuous positive airway pressure less than four hours a night at least 70 percent of nights.

H2: Individuals who use continuous positive airway pressure four or more hours a night for at least 70 percent of nights recorded will demonstrate a greater decrease in systolic and diastolic blood pressure from baseline than those who use

continuous positive airway pressure less than four hours a night at least 70 percent of nights.

Sample Selection and Setting

The sample for this study was taken from a physician's office in a southern state. This multi-disciplinary medical clinic specializes in pulmonary diseases and sleep disorders with approximately 400 patients seen annually with a diagnosis of obstructive sleep apnea. The office manager estimated that of these 400, approximately 120 had a diagnosis of mild obstructive sleep apnea. The goal of this study was to examine the relationship of CPAP use on daytime sleepiness and blood pressure. In order to test whether CPAP use results in decreases in daytime sleepiness and in systolic and diastolic blood pressure from the baseline measure in individuals with mild obstructive sleep apnea a priori power analysis was necessary. Conducting a priori power analysis reduces the risk that a type II error (accepting a false null hypothesis) will occur (Heavey, 2011). The criterion for significance, alpha, was set at 0.05. Alpha is often referred to as a type I error. Alpha is the probability that the data analysis will reveal an effect of CPAP use on daytime sleepiness and blood pressure that does not actually exist. Power, the probability that CPAP use will result in a statistically significant decrease in daytime sleepiness and a decrease in systolic and diastolic blood pressure from baseline, was set at 80 percent. According to Polit and Beck (2004) 0.8 or 80 percent is the conventional standard for power. Using the power program G*Power 3.1.9.2 for the t test family, difference between two independent means (two groups) with alpha set at 0.05 and power set at 0.80 the estimated target sample size was 176, or 88 subjects per group.

The sleep clinic office converted to an electronic medical record (EMR) charting system in 2010. Only data within the electronic medical records were collected. Patient records were selected for review based on the inclusion criterion: a diagnosis of mild obstructive sleep apnea as evidenced by an AHI score between 5 and 14 (i.e., the clinical equivalent of mild OSAS), as determined during a full, supervised, standard polysomnographic study. Patients were excluded for several reasons including: 1) no documented blood pressure or ESS prior to CPAP therapy initiation, 2) no documented six week follow up blood pressure or ESS data, 3) no documented data related to CPAP use; or 4) diagnosis of cognitive impairment of any type, restless legs syndrome, or narcolepsy documented in the EMR. Clinic protocol for patient follow up visits is six weeks and annually thereafter.

Clinic process for reporting CPAP use. After diagnosis of OSAS with overnight PSG, the patient is advised to visit the medical supply company of his or her choice to obtain the CPAP machine. At that time, the patient is provided with information related to proper use of the machine by the medical supply company worker. Each patient is also educated regarding how to meet the requirement for a download of CPAP use data. According to the sleep clinic office manager where data were collected, patients can either, 1) link electronically to the medical supply company and have CPAP use automatically downloaded, or 2) visit the medical supply company in person prior to their sleep clinic follow up visit and have the data extracted from the machine memory card. Regardless of the method of CPAP use data extraction, the medical supply company is responsible for sending the CPAP use reports to the sleep clinic office wherein the data

are automatically populated into the electronic medical record. The clinic physician then has the ability to refer to CPAP machine use at follow-up visits with patients.

Institutional Review Board (IRB) approval was obtained for this retrospective chart review through the University of Wisconsin-Milwaukee (UWM) #13.204 (see IRB letter in Appendix A). A letter of support from the clinic physician is located in Appendix B.

A total of 139 EMR's were reviewed for this study. Initial review revealed that 79 participants had incomplete data; meaning one or more of the exclusion criteria were met such as no CPAP use documented, incomplete or missing data related to ESS scores or blood pressure, or a diagnosis of narcolepsy or restless legs syndrome. The final sample size reviewed for this study was 60. Table 1 provides additional data for the excluded participants.

Table 1

Demographics for Excluded Participants

	Mean, standard deviation or percent of sample *N = 79*		
	Incomplete data *N = 13*	*No CPAP use reported* *N = 60*	*Excluding chronic medical condition* *N = 6*
Age	51.8 (*SD* 13.60)	59.7(*SD* 12.51)	55.0 (*SD* 13.93)
Gender			
Male	9 (69.2)	34 (56.7)	2 (33.3)
Female	4 (30.8)	26 (43.3)	4 (66.7)
Race			
Caucasian	12 (92.3)	57 (95)	6 (100)
African American	1 (7.7)	3 (5)	
Marital status			
Married	12 (92.3)	50 (83.3)	3 (50)
Divorced		8 (13.3)	2 (33.3)
Single/never married	1 (7.7)	2 (3.3)	
Widowed			1 (16.7)

Measures

Age, race, gender, and marital status provided information for describing the demographics of the sample. Age was determined from the date of birth. Age is a significant variable due to the existing research that suggests that sleep related difficulties increase with increased age (Malhorta et al., 2006). Race was recorded as Caucasian, African American, or other, since no other races or ethnicities were represented within this patient population. A study conducted by Means, Ulmer, and Edinger (2010) found that African Americans used their CPAP therapy one less night per week and one less hour per night than their Caucasian American counterparts. Gender was recorded as male or female. The male predisposition for OSAS has been attributed to sex differences in anatomical and functional properties of the upper airway, hormones, and respiratory control stability (Lin et al., 2008). Marital status was recorded as married, divorced, single / never married, widowed, or separated. Marital status data were collected in the sleep clinic office as a single question, "marital status." This collection method may have led to heteronormative data. Gagnadox et al. (2011) conducted a large clinical study involving patient's prescribed CPAP therapy and found marital status to be an independent factor of CPAP adherence.

AHI scores were recorded for each participant from the polysomnogram prior to CPAP therapy initiation. The sleep clinic office uses both AHI and RDI scores to diagnose mild OSAS. AHI and RDI values were reportedly used by this sleep medicine practice to categorize OSAS as mild, moderate, or severe (mild OSAS AHI – 5-14, moderate OSAS AHI – 15-30, severe OSAS AHI - >30,) (Berry et al., 2012). However, for this study, OSAS was categorized by AHI value only, since this is standard practice in

OSAS research (Jainchariyatam et al., 2010; Takama & Kurabayashi, 2010). Additional information was gathered related to smoking and positive airway pressure use. Current smoking status was recorded as "yes" or "no". Positive airway pressure was recorded as continuous positive airway pressure, automatic positive airway pressure, or bilevel positive airway pressure. Machine manufacturer, machine pressure setting, and the use of supplemental oxygen with the positive airway pressure were also recorded. Machine manufacturer responses were RESMED, Respironics, Sandman, Fisher and Paykel, Cascade, and other. Machine pressure setting was measured in centimeters of water pressure and supplemental oxygen use was recorded as "yes" or "no". CPAP use was documented as the number of days included in the most recent report available to the sleep clinic office and the percent of days during the report when CPAP was used greater than or equal to four hours a night and the percent of days when CPAP was used less than four hours a night.

Information related to current medications was gathered from the EMR. Of specific interest to this study were antihypertensive medications. Antihypertensive medication classifications included angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, beta blockers, diuretics, and calcium channel blockers. A wide range of other medications was gathered from the EMR that were not thought to affect blood pressure or daytime sleepiness. These included, but were not limited to, medications used to treat diabetes, gastrointestinal disorders, hyperlipidemia, and vitamins.

Diagnoses related to chronic medical conditions were recorded as follows; hypertension, restless legs syndrome, narcolepsy, diabetes mellitus, depression,

cardiovascular disease, obstructive sleep apnea syndrome, and other. Data were collected on chronic medical conditions for descriptive purposes as well as participant exclusion (i.e., narcolepsy, restless legs syndrome).

Epworth Sleepiness Scale (ESS) scores, blood pressure, oxygen saturation, neck circumference, and weight information were collected from the EMR from the initial visit (prior to CPAP therapy), and at follow up visits that occurred at or around six weeks, one year, two years, and 3 years.

Daytime sleepiness was measured by the patient's ESS scores, which was completed at each patient visit. Blood pressure measurements were also recorded at each patient visit. The amount of CPAP use for each patient was made available to the sleep clinic via fax from the medical supply company that supports the particular sleep apnea machine used by the patient as previously described. Some patients had the option to have their CPAP use automatically downloaded and sent to the medical supply company without having to physically go to the medical supply company. The EMR did not record whether patients physically delivered their memory storage device to the company or used the automatic download option. CPAP use was summarized in each EMR and included the number of days included in the report (which varied depending on the last time the report was downloaded from the CPAP machine) and the percent of days that the patient used the device for 4 or more hours a night.

Epworth Sleepiness Scale. The following evidence demonstrates that the Epworth Sleepiness Scale (ESS) is a widely used questionnaire designed to measure subjective sleepiness (Johns, 1991). The ESS questionnaire consists of eight items that address typical day- to- day situations and is intended to differentiate individuals with

excessive daytime sleepiness from alert individuals (see Appendix C). Each item is scored from 0 to 3 points (0 = would never doze, 3 = high chance of dozing). Responses to individual questions are summed for a possible range of 0 to 24. A score of 10 or greater is indicative of excessive daytime sleepiness (Gander et al., 2005).

Evidence for the validity of the ESS was reported by Johns (1991) who conducted a study of 180 adults, including 150 patients with a range of known sleep disorders and 30 normal women and men as controls. This study was conducted to assist in determining whether the ESS was a valid tool for assessing daytime sleepiness. Lower ESS scores were reported for controls than for OSAS, narcolepsy, and idiopathic hypersomnia ($p < 0.001$). In addition, concurrent validity of the ESS was established in this study. ESS scores were significantly correlated to sleep latency (the amount of time it takes an individual to fall asleep after the lights are turned off) as measured by overnight polysomnography ($p < 0.001$). Furthermore, in subjects with OSAS, ESS scores were significantly correlated with the apnea - hypopnea index ($p < 0.001$) (Johns, 1991).

The reliability of the ESS was investigated in a second study conducted by Johns (1992). Eighty-seven healthy subjects were asked to complete the ESS at baseline and again 5 months later. Test – retest reliability was demonstrated by a high correlation ($r = 0.82$) between the paired tests. Item analysis of two different groups of subjects (healthy subjects and individuals with a variety of sleep disorders) demonstrated a reliability of $\alpha = 0.88$ and 0.73, respectively. Factor analysis of the items on the ESS demonstrated that the questionnaire measures only one factor (Johns, 1992).

Spira et al. (2012) conducted a study to examine the reliability and validity of the ESS. In the study involving 3,059 men the ESS demonstrated moderately adequate

internal consistency as measured by Cronbach's alpha of $\alpha = .70$ and an item-total correlations range from .30 to .51. Beaudreau et al. (2012) also examined the validity of the ESS in a study involving 2,968 women. The ESS demonstrated adequate reliability in the total sample ($\alpha = .76$). Correlations between the ESS and theoretically relevant measures were weak but were statistically significant (daytime inactivity, $p = <0.001$, $r = 0.15$; total sleep time, $p = <0.001$, $r = -0.19$; wake after sleep onset, $p = 0.01$, $r = 0.05$).

Blood pressure. The standard of practice at the sleep clinic is to assess blood pressure at each visit using a manual sphygmomanometer. Both systolic and diastolic pressures readings were extracted from the electronic medical record.

Procedure for Data Collection

IRB approval was obtained and the PI met with and trained the office manager on the use of the data collection tool (Appendix D). The office manager worked on her own time to collect the data and was compensated. Data were collected on mild OSAS patients from electronic medical records (EMR) only. After the data collector collected data from 25 EMR's the PI reviewed the data that had been collected for quality control purposes. The data collector coded the data collection sheets prior to PI review to ensure anonymity. Blood pressure and ESS scores were extracted from the EMR for each participant prior to the initiation of CPAP therapy and at six weeks follow up, 1 year follow up, 2 year follow up, and 3 year follow up. The time period for the follow up visits is based on clinic protocol. The 3 year follow up is the last visit for data collection due to the length of time the clinic has been using the EMR system.

Independent variable

The independent variables for this study were the two groups of CPAP use; those who used CPAP four or more hours a night and those who used CPAP less than four hours a night. CPAP use is defined by the number of hours a person uses the device during a 24 hour period. The recommended amount of use is four or more hours of nightly use 70 percent of the nights (Weaver & Grunstein, 2008). Data were recorded in the EMR as the percent of days with CPAP use of four or more hours and the percent of days with CPAP use less than four hours as reported by the manufacturer of each CPAP machine and entered into the EMR.

Dependent Variables

The dependent variables in this study were daytime sleepiness and blood pressure. Daytime sleepiness was measured using the ESS. Blood pressure and ESS scores were documented in the EMR at each clinic visit. Blood pressure was represented by two values, diastolic and systolic. This study examined both values separately to determine if one or both values were affected by CPAP use. The standard of practice at the clinic is that after a diagnosis has been made of OSAS the patient will follow up at six weeks, and then annually thereafter. The time periods for data collection for this study were baseline (prior to CPAP therapy initiation), 6 weeks, 1 year, 2 years, and 3 years. The collection time points are based on clinic protocol.

Human Subjects Protection Procedures

Data were extracted from the EMR by the data collector. At the time of data extraction each data collection sheet was assigned a study identification number. The data collector will keep a list that links the study identification number with the medical

record in her office for a period of two years after the study at which point the list will be

shredded. After IRB approval was obtained the PI received de-identified data. The PI

made no attempt to identify study participants. All information obtained for this study is

stored on a secure, password protected computer.

Data Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS)

Version 21.0. Descriptive statistics were used to analyze the demographic data obtained.

Frequencies were computed for age, race, gender, and marital status. Descriptive

statistics provided a description of the research participants.

The aim of this study was to examine the effect CPAP use had on daytime

sleepiness and blood pressure. The final sample was divided into two groups, those who

used CPAP four hours or more a night for 70 percent of nights (Group A) and those who

used less than this amount (Group B). Both research questions were answered by

comparing group means using independent *t*-tests. A *t*-test at baseline demonstrated no

differences between the groups. As a result, the difference in scores between baseline and

follow-up were calculated for each study variable (ESS scores, systolic blood pressure,

diastolic blood pressure) and three independent t-tests were run (see Table 8).

Summary

This retrospective chart review provided quantitative data to address the research

questions "How does continuous positive airway pressure affect daytime sleepiness?" and

"How does continuous positive airway pressure therapy affect blood pressure?" This

methodology section provided the following information: a description of the research

design, sample selection and setting, instrumentation, procedure for data collection, a

description of the independent and dependent variables, as well as the statistical

procedures that were utilized.

CHAPTER FOUR

RESULTS

This chapter presents study analysis results. First there will be discussion of the study participants' sample size and demographics. Then the final data analysis will be presented.

Demographics

The final sample included only participants who had documented CPAP use ($n = 60$). These participants were further divided into two groups:

- Group A: Those with documented use of CPAP four or more hours a night 70% of the recorded nights ($n = 45$), and
- Group B: Those with documented use of CPAP for less than four hours a night 70 percent of the recorded nights ($n = 15$).

Each of the 60 participants had pre-CPAP and six week follow up visits for ESS scores, blood pressure, or both (see Table 2). This study experienced significant loss of participants due to lack of complete EMR data (see Figure 3). The data available at the one, two, and three year follow ups were limited and therefore were not included in the final analysis.

Table 2

Patients with Documented Blood Pressure, ESS, or Both

Variable	Pre CPAP and 6 week follow up		Pre CPAP, 6 week, and 1 year follow ups		Pre CPAP, 6 week, 1 and 2 year follow ups		Pre CPAP, 6 week, 1, 2 and 3 year follow ups
	N	%	*n*	%	*n*	%	*n*
Blood pressure only	54	90	26	43	8	15	0
ESS score only	36	60	10	17	1	2	0
Blood pressure and ESS score	30	50	6	10	1	2	0

Figure 3

Number of Participants with Documented Blood Pressure, ESS Scores, or Both
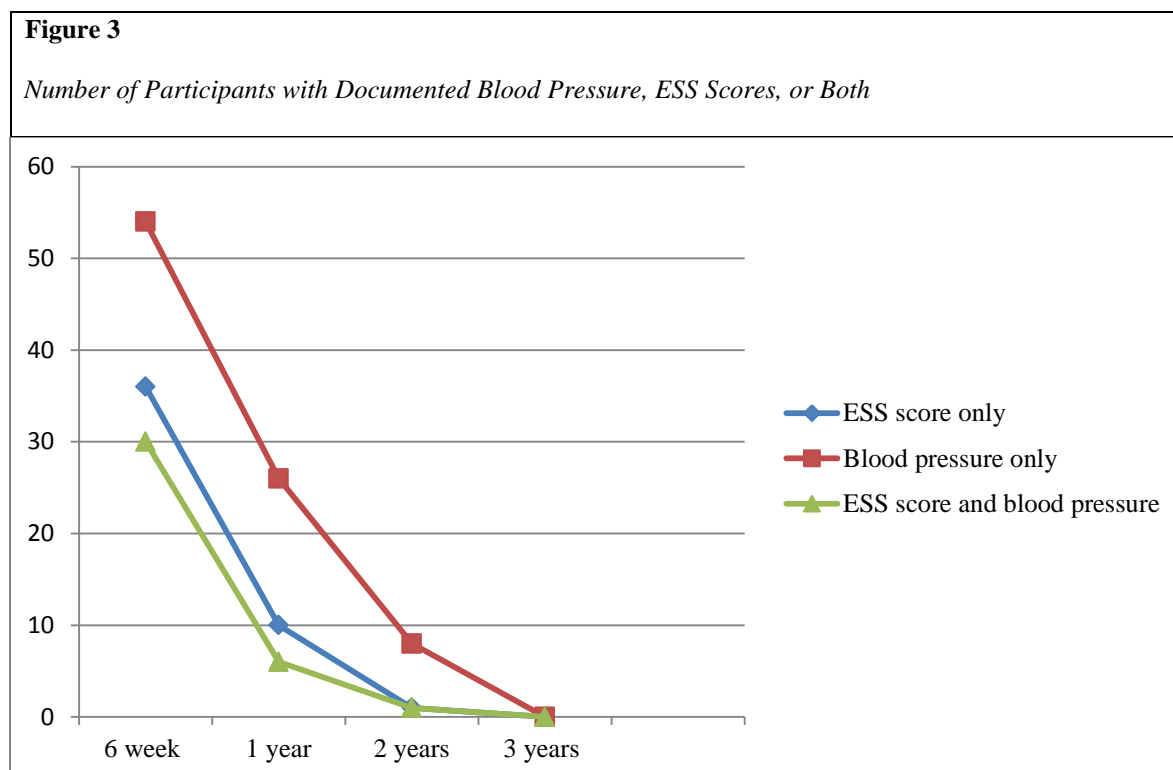
The final sample (*n* = 60) was 56.7 percent male, 43.3 percent female, and 98.3 percent Caucasian (see Table 3). Forty four participants (73%) were currently taking a medication(s) that could be used to treat hypertension and 96.7 percent had at least one chronic medical condition other than OSAS. The three most frequent conditions reported were obesity (55%), hypertension (58.3%), and diabetes mellitus (15%). The mean AHI

score was 9.7(2.89) and RDI was 10.0(3.12). CPAP was the only type of positive airway pressure reported as being used and 95 percent reported not using supplemental oxygen with the CPAP. Clinic protocol for OSAS treatment is six week follow up followed by annual follow up visits. It is not uncommon for a patient to seek medical treatment for OSAS complications outside of the clinic protocol. For the sample above, 9 (15%) sought treatment outside of the clinic protocol once and 2 (3.3%) sought treatment outside of the clinic protocol twice. No further exploration of frequency of follow up visits outside of clinic protocol was conducted due to limited data.

The demographic characteristics of Groups A and B were similar (see Table 3). The mean ages of participants in Group A was 62 and Group B was 59. Both groups were approximately one half male, predominately Caucasian, married, and non-smokers. A t-test was conducted to compare age between the groups and found no statistical difference t (58) = .770, p = .445 between Group A (μ = 62, SD 11.82) and Group B (μ = 59.1, SD = 14.40). There were 2 (4.4 percent) in Group A and 1 (6.7 percent) in Group B who used supplemental oxygen with their CPAP. The mean age for the two in Group A who received supplemental oxygen with their CPAP was 64 (9.90); they were white, non-smokers, one widowed female and one married male. The one participant in Group B receiving supplemental oxygen was a 62 year old white, non-smoking, married female.

	Group A	Group B
	n= 45	*n* = 15
Age	62 (11.82)	59.1 (14.40)
Gender		
Male	27 (60)	7 (46.7)
Female	18 (40)	8 (53.3)
Race		
Caucasian American	45 (100)	14 (93.3)
African American		1 (6.7)
Marital Status		
Married	36 (80)	12 (80)
Divorced	2 (4.4)	3 (20)
Single/never married	2 (4.4)	
Widowed	3 (6.7)	
Separated	1 (2.2)	
Smoker		
No	39 (86.7)	14 (93.3)
Yes	6 (13.3)	1 (6.7)
Supplemental oxygen therapy with CPAP		
No	43 (95.6)	14 (93.3)
Yes	2 (4.4)	1 (6.7)

Table 3

Demographics, Supplemental Oxygen Use, and CPAP use for Both Groups

CPAP Use

The number of days included in the CPAP use report is highly variable with a range of 354 days for those who used CPAP four or more hours a night and a range of 104 days for those who used CPAP less than four hours a night (see Table 4). Data collected related to CPAP use included the number of days in the most recent report submitted to the sleep clinic, percent of days with usage of four or more hours a night, and percent of days with usage of less than four hours a night. The average number of days included in the CPAP use report for Group A was 69.4 (66.90) days and the average number of days included for Group B was 53 (34.74). The median for number of days included in the CPAP report was 37 (Group A) and 42 (Group B).

Table 4	
Days of CPAP Use Reported	
	μ, SD, M
Group A, *n*= 45	69.4 (66.90), 37
Group B, *n* = 15	53 (34.74), 42
Note. Range of days included in CPAP use report for Group A was 11-365. Range of days included in CPAP use report for Group B was 13-117.	

Findings for Analysis

Table 5 illustrates the mean changes in ESS scores for the two groups. The ESS score range for Group A was 0-20 and the range for Group B was 0-16. The mean ESS score prior to starting CPAP (i.e., baseline) did not vary significantly between Group A (10.2) and Group B (10.0); however both groups met the criteria for having clinically significant levels of daytime sleepiness. Prior to being prescribed CPAP therapy, 55 percent (*n* = 15) of Group A reported ESS scores greater than or equal to 10, while 63 percent (*n* = 5) of Group B reported ESS scores greater than or equal to 10. At the six week follow-up, both groups reported a dramatic decrease in sleepiness to clinically insignificant levels (see Table 5) with 11 percent (*n* = 3) of Group A reporting ESS scores greater than or equal to 10 (clinically excessive daytime sleepiness) and none of those in Group B reporting ESS scores greater than or equal to 10.

| Table 5		
ESS Scores at Six Week Follow Up, n = 36		
	Group A, *n*=28 μ (SD)	Group B, *n* = 8 μ (SD)
preCPAP	10.2 (4.58)	10.0 (4.63)
6 week follow up	3.6 (4.17)	1.9 (1.73)
Note: ESS reference norms – 0-9 = average amount of daytime sleepiness, 10 or > = excessive daytime sleepiness. Maximum possible score is 24 (Johns, 1991).		

Table 6 illustrates the effects on blood pressure based on the American Heart Association (AHA) guidelines on hypertension in blood pressure from baseline to six

week follow up. In order to examine the groups more closely for blood pressure changes, baseline and six week follow up blood pressure readings were reviewed based on the AHA hypertension guidelines. There were a total of 54 participants who had blood pressure data available at baseline and the six week follow up visit. Of the 54, eight were normotensive at baseline, four demonstrated no change in blood pressure at six week follow up (Group A, $n = 3$; Group B, $n = 1$) and four demonstrated an increase in blood pressure (prehypertension, stage 1, or stage 2 hypertension) (Group A, $n = 4$). There were 24 participants who were prehypertensive at baseline. Of the 24 with prehypertension, 13 demonstrated no change in blood pressure at the six week follow up (Group A, $n = 11$; Group B, $n = 2$), three demonstrated a decrease (normotensive) (all Group A), and eight demonstrated an increase (stage 1 hypertension) (Group A, $n = 5$, Group B, $n = 3$). Of the 54 participants with blood pressure data at the six week follow up, 16 had stage 1 hypertension (Group A, $n = 13$, Group B, $n = 3$) and six had stage 2 hypertension (Group A, $n = 2$, Group B, $n = 4$) at baseline. A total of five with stage 1 hypertension demonstrated no change (Group A, n = 4, Group B, n = 1) and 11 demonstrated a decrease (Group A, $n = 9$, Group B, $n = 2$). Of those with stage 2 hypertension, one demonstrated no change (Group B) and five demonstrated a decrease (Group A, $n = 1$, Group B, $n = 4$). Eighty five percent of those who had blood pressure data at baseline and six week follow up were either prehypertensive (44 percent) or hypertensive (41 percent) (stage 1 – 11 percent, stage 2 - 30 percent).

Table 6		
Effects on Blood Pressure, n = 54		
	Group A, *n* = 41	Group B, *n* =13
No change	*n* = 18 (44)	*n* = 5 (38.5)
Decrease	n = 14 (34)	*n* = 5 (38.5)
Increase	*n* = 9 (22)	*n* = 3 (23)

Table 7 and Figure 4 illustrate the mean decrease in blood pressure for both

groups. There was a decrease in systolic blood pressure of 1.1 mmHg for Group A

compared to a decrease of 5.8 mmHg for Group B. Decreases in diastolic blood pressure

were similar; Group A demonstrated a decrease of 0.4 mmHg while Group B

demonstrated a decrease of 4 mmHg. A greater decrease in mean systolic and diastolic

blood pressures was noted for Group B than for Group A.

Table 7		
Blood Pressure Measurements (mmHg) at Six Week Follow Up		
	Group A, *n* = 41 μ (SD)	Group B, *n* = 13 μ (SD)
Pre CPAP systolic	130.6 (15.02)	139.5 (15.71)
6 week systolic	129.5 (13.42)	133.7 912.02)
Pre CPAP diastolic	79.3 (9.26)	84.8 (13.03)
6 week diastolic	78.9 (8.91)	80.8 (9.00)

Figure 4

Blood Pressure Measurements (mmHg) at Six Weeks Follow Up
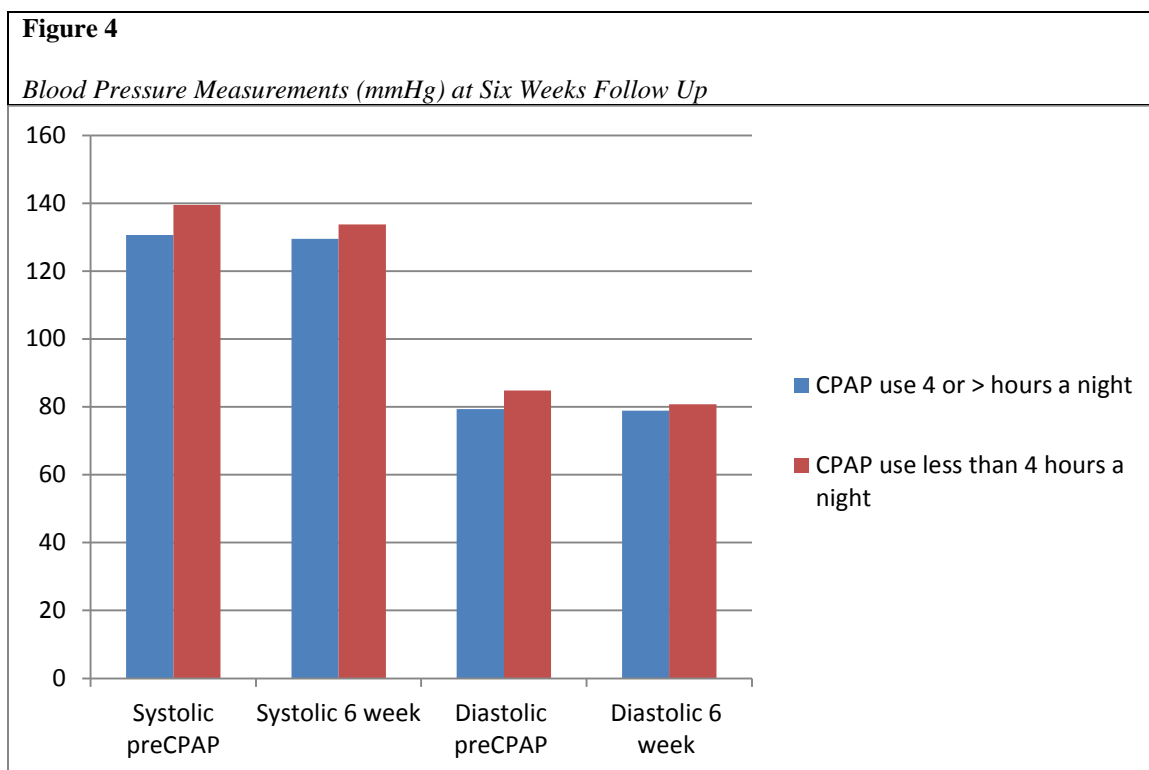
T – tests were run at baseline for daytime sleepiness (t [43] = .411, p = .683),

systolic blood pressure (t [57] = 1.200, p = .235), and diastolic blood pressure (t [53] =

1.133, p = .176) to determine if significant differences existed between the groups at

baseline. It was determined that there were no differences between Groups A and B at

baseline. Therefore, difference scores were calculated on each variable for each group

from baseline to 6 weeks follow up. Three independent samples t – tests were conducted

on the difference scores to examine the effect CPAP use had on daytime sleepiness,

systolic blood pressure, and diastolic blood pressure (Table 8).

Table 8

Independent Samples t Test Results on Difference Scores for Daytime Sleepiness, Systolic Blood Pressure, and Diastolic Blood Pressure

	M	t (df)	p	CI (95%)
ESS	1.5	.865 (34)	.393	-2.049 – 5.084
Systolic blood pressure	4.7	.911 (52)	.367	-5.653 – 15.053
Diastolic blood pressure	3.6	1.00 (52)	.321	-3.617 – 10.837
Note. Mean reported is the mean difference score for each variable.				

Summary

Overall, the findings did not reveal significant differences between those who used CPAP four or more hours a night 70 percent of reported nights (Group A) and those who used CPAP less than four hours a night 70 percent of reported nights (Group B) from baseline to six-weeks follow-up. However, both groups demonstrated clear reductions in daytime sleepiness from baseline to six week follow-up. Paradoxically, Group B demonstrated greater decreases at the 6 week follow-up on all three variables than Group A. These findings will be placed in the context of the literature in chapter five.

CHAPTER FIVE

DISCUSSION

The purpose of this study was to examine the relationship of CPAP use to the outcomes of daytime sleepiness and blood pressure in persons with mild obstructive sleep apnea. Although this study found no significant differences between CPAP use and daytime sleepiness or blood pressure, these results can still inform future directions for research, policy, and practice. This chapter will address findings and limitations of this retrospective chart review on daytime sleepiness, blood pressure and blood pressure medication use, and CPAP use reporting within the context of the existing literature. As a reminder, obstructive sleep apnea is categorized as mild (AHI 5-14), moderate (AHI 15-30), or severe (AHI >30).

Continuous Positive Airway Pressure (CPAP) Use and Daytime Sleepiness

In this retrospective chart review, the data available at the one, two, and three year follow up were so limited that this time point was not included in the final data analysis. Hypothesis 1: *Individuals who use continuous positive airway pressure four or more hours a night will report less daytime sleepiness than those who use continuous positive airway pressure less than four hours a night.* Although daytime sleepiness scores decreased substantially for both groups, the reduction did not reach the level of statistical significance when the groups were compared. The decrease was, however, clinically significant for both groups. Noting that an ESS score ≥ 10 is considered clinically significant sleepiness, the percent of participants in each group with clinically significant sleepiness dropped dramatically from baseline to six weeks (Group A dropped from 55% to 11%; Group B dropped from 63% to 0%). That both groups changed from having

clinically significant sleepiness before CPAP initiation to having nearly no daytime

sleepiness is a clinically significant finding. Paradoxically, those in Group B reported a

greater decrease in daytime sleepiness than those in Group A. Due to the small sample

size, the findings may be indicative of random variability, especially given the lack of

statistical significance between the groups.

Marshall et al. (2006) found ESS scores to be significantly reduced (1.2 points)

with the use of CPAP in the mild to moderate OSAS population. However, ESS scores

were not significantly decreased in the mild OSAS population in several other studies

previously reviewed (Barnes et al., 2002; Engleman et al., 1997; Monasterio et al., 2001).

A large amount of the current literature related to treatment of mild OSAS involves the

use of oral appliances (Doff et al., 2013; Leite et al., 2013) and surgical treatment with

uvulopalatoplasty (Balsevicius, Uloza, Vaitkus, Sakalauskas, & Miliauskas, 2013). CPAP

use is currently optionally indicated for the treatment of patients with mild OSAS.

Kushida et al. (2006) recommends that additional research is needed to validate its use in

this population, and the findings from the current study also support this

recommendation.

Continuous Positive Airway Pressure (CPAP) Use and Blood Pressure

Similar to daytime sleepiness scores, data collected at the one, two, and three year

follow up visits were so limited that they were not included in the final data analysis. H2:

Individuals who use continuous positive airway pressure four or more hours a night will

demonstrate a greater decrease in systolic and diastolic blood pressure from baseline

than those who use continuous positive airway pressure less than four hours a night. The

results of this study did not find statistically significant differences in blood pressure

between the groups for either systolic or diastolic blood pressure at six weeks. There was a mean decrease in systolic blood pressure of 1.1 mmHg for Group A and a mean decrease of 5.8 mmHg for Group B. Results were similar for diastolic pressure where Group A decreased on average 0.4 mmHg and Group B decreased 4 mmHg. Similar to sleepiness scores, Group B demonstrated greater decreases in both systolic and diastolic pressure at six week follow up than Group A, which was an unexpected finding.

Based on the AHA hypertension guideline definitions of hypertension, 44 percent of Group A demonstrated no change in blood pressure, 34 percent demonstrated a decrease in blood pressure, and 22 percent demonstrated an increase in blood pressure. In Group B, 38 percent demonstrated no change in blood pressure, 38 percent demonstrated a decrease in blood pressure, and 23 percent demonstrated an increase in blood pressure. Although not statistically significant, perhaps due to the small sample, overall those in Group B demonstrated greater reductions in both systolic and diastolic blood pressure than those in Group A.

It is noteworthy to mention that 83 percent of those with either prehypertension or hypertension at baseline demonstrated no change or a decrease in blood pressure, and 17 percent demonstrated an increase in blood pressure at the six week follow up. This finding suggests that CPAP use, at varying doses, may effectively reduce or prevent further progression of hypertension in some OSAS patients, but further investigation of this relationship is necessary.

Changes in blood pressure (systolic and diastolic) have been observed in as little as one month in a population with an AHI of 10 or greater (Pepperell et al., 2002), two months with an AHI of 10 or greater (Logan et al., 2003), and three months in a

population with a mean AHI of 30 or greater (Hui et al., 2006). Pepperell et al. (2002) found significant decreases ($p = 0.0013$) in mean arterial blood pressure with therapeutic CPAP use at one month. Based on the above studies, the current study should have revealed a decrease, or at the minimum, a trend toward lower blood pressure. It should be noted that Pepperell et al. (2002) found a greater benefit for those taking blood pressure medications than for those not taking blood medications. The current study was unable to control for blood pressure medications due to insufficient data available in the EMR (i.e., medication name, dose, frequency) to accurately control the variable. Furthermore, it was not known if the prescribed medication was primarily being used to treat hypertension or another medical condition.

Pepperell et al. (2002) found a greater decrease with those who had a more severe form of the disease. Jaimchariyatam et al. (2010) conducted a retrospective study of mild OSAS subjects comparing those who used CPAP ($n = 93$) to those who did not use CPAP ($n = 162$) over a two year period. Those who used CPAP experienced a 1.97 point decrease in mean blood pressure compared to a 9.61 point increase in those who did not use CPAP. Based on the results of Jaimchariyatam et al. (2010) it is plausible that persons with mild OSAS could experience a decrease in blood pressure with long term use. Additional studies are needed to confirm this supposition. The small sample size for the current study may explain the lack of statistical significance. Complexities in defining groups by the definition of four or more hours per night for 70 percent of recorded nights may also have washed out an existing effect, which will be further discussed later.

Several studies have shown that CPAP use can reduce the blood pressure of OSAS patients (Akashiba et al., 1999; Faccenda et al., 2001; Pepperell et al., 2002).

However, these studies included primarily patients with moderate to severe OSAS. The study with the largest patient population was conducted by Borgel et al. (2004) on 196 moderate to severe OSAS patients. The authors found a statistically significant decrease in diastolic blood pressure among those participants using CPAP for six months ($p = .001$). Borgel et al. (2004) also found independent relationships between the severity of the OSAS and diastolic blood pressure ($p = .003$) and systolic blood pressure ($p = .014$). The relationship between disease severity and CPAP use contributes to the ambivalence related to treating persons with mild OSAS with CPAP therapy. Baguet et al. (2009) assert that CPAP is more effective on blood pressure if the OSAS is severe.

Results from another study conducted with persons with mild OSAS are conflicting. Barnes et al. (2002) conducted a study involving 28 patients with mild OSAS where mild OSAS was defined as an AHI of 5 - 30. The participants had 24 hour blood pressure measurements obtained at baseline, after eight weeks of CPAP treatment, and after eight weeks of treatment with an oral placebo tablet. CPAP use did not result in statistically significant findings related to 24 hour blood pressure readings. The authors did not postulate as to why the CPAP users did not have a decrease in blood pressure. The results of the Barnes et al. (2002) study are similar to those found in the current study. Given the progressive nature of OSAS, additional studies examining the effectiveness of treating the disease during the early stages are warranted. The results of this study were based on intermittent clinic-acquired readings. A better measurement plan for understanding the effects of CPAP use on psychological and physiological outcomes would involve more frequent readings.

Findings Summary

The purpose of this study was to examine the relationship of CPAP use on the outcomes of daytime sleepiness and blood pressure in persons with mild OSAS, however no statistically significant differences were noted at the six week follow up for daytime sleepiness or blood pressure. The small sample size might explain the lack of significance. Another possible explanation for lack of significance in blood pressure was not controlling for blood pressure medications.

A common clinical dilemma in the literature appears to be at what level of disease severity a person with OSAS should be treated with CPAP (Barnes et al., 2002; Engleman et al., 1997; Marshall et al., 2005). The literature examining the use of CPAP in persons with mild OSAS continues to evolve. Although the use of CPAP in the sample for this study did not result in statistically significant findings in regards to daytime sleepiness or blood pressure, clinical significance could be considered in regards to daytime sleepiness. The mean reduction in ESS scores for participants in this study was 6.6 points for those who used CPAP four or more hours a night 70 percent of nights, compared to a mean reduction of 8.1 points for those who used CPAP less than this amount. Considering that an ESS score of 10 or greater is indicative of excessive daytime sleepiness this reduction, which was seen in both groups, may be clinically significant even though the level of statistical significance was not reached between groups. The mean reduction in blood pressure for those participants who used CPAP four or more hours a night 70 percent of nights was 1.1 mmHg decrease in systolic and a 0.4 mmHg decrease in diastolic, compared to a mean reduction of 5.8 mmHg decrease in systolic and a 4 mmHg decrease in diastolic for those who used CPAP less than four hours a night

70 percent of nights. Neither group had a decrease in blood pressure (systolic or diastolic) that reached the level of significance. A decrease of 5.8 mmHg systolic and 4 mmHg diastolic for those who used less than four hours a night 70 percent of nights may be clinically significant, however, this finding is limited by the small ($n = 13$) sample size.

Limitations

Limitations to this study involved data collection, CPAP usage reporting, CPAP use definition, and generalizability of the results. The retrospective chart review conducted for this study presents several limitations, including but not limited to incomplete or missing data within the medical record, difficulty verifying documented information, and variability in the quality of documentation by health care personnel. Data available in the patient medical record are primarily collected for the purpose of providing clinical care and are often not comprehensive.

The sleep clinic office where data were collected converted to an EMR system approximately three years before these data were collected. All patients seen in the sleep clinic office in the last three years were included in the study. However, it became apparent that some of the participants had data from earlier than three years and had begun CPAP therapy prior to the initiation of the EMR system. Therefore, original data had to be manually transferred from the paper record to the EMR. The process of manual entry may have resulted in data being missed, skipped, or incorrectly entered. Several variables collected for this study are subject to change over time (marital status, chronic medical conditions, and current medications) and it is plausible that these changes were not reflected in the EMR. A total of 73 participants were excluded from this study due to incomplete or missing data (13 incomplete data, 60 missing CPAP use data). The author

does not presume those with incomplete or missing data to be any different from those who had complete data documented. Review of the data collection sheets led the author to reach the conclusion that the incomplete and missing data is either the result of the data entry process during the transition from paper to electronic records or lack of documentation.

For healthcare researchers, there are obstacles to digitalization of medical records. The data collected for the EMR are not done so for research purposes, therefore lack of standardization related to medical conditions, laboratory tests, disease staging, etc., can hinder the data collection phase of the research process. Additionally, inconsistent data entry across sites also presents challenges for health care researchers (Dean et al., 2009). Overall, current methods of utilizing EMR systems are not sufficient. The quality of care provided, as well as the utilization of data for research, may be compromised due to incomplete or missing data.

One of the aims of this study was to examine the effect of CPAP use on blood pressure. Due to insufficient data related to medication use it was not possible to control for blood pressure medication use in this study. Data were gathered regarding medication use specific to those medications that could be used to treat hypertension. However, medications used to treat hypertension can also be used to treat various other medical conditions (i.e., congestive heart failure, vascular headaches, and cardiac dysrhythmias). It was unknown from the data collected whether the participant was taking a specific blood pressure medication to treat hypertension or for another health condition. Identifying those who take multiple medications for the treatment of hypertension would have provided data related to individuals with resistant hypertension (requiring at least

three antihypertensive medications). It is estimated that greater than 70 percent of individuals with resistant hypertension also have a diagnosis of OSAS (Logan et al., 2001). Those data could have provided additional information regarding the resistant hypertension population. It was also unknown how each participant took their blood pressure medication (e.g., dosage, frequency). It is also plausible that changes in medication use could have occurred and not been documented in the EMR.

The sleep clinic procedure for documenting CPAP use was also a limitation of this study. The actual number of hours a patient used CPAP was not available. The data available in the EMR was the number of days included in the report and the percent of the days when the CPAP was used four or more hours a night and the percent of the days when the CPAP was used less than four hours night. In light of the findings of this study, and given a possible dose-response relationship between CPAP use (Stepnowsky & Dimsdale, 2002; Weaver et al., 2007) and possible health benefits, more specific data related to the number of hours a patient used the CPAP would have been beneficial to this study.

The reporting method by manufacturer for CPAP use was another limitation of this study. CPAP machine type varied among participants. There were a total of five different machines identified as used by participants in this study. There were three participants who used a machine other than the five listed on the data collection tool. While all machines used in this study have the capability of providing a summary report of usage, there is some degree of variability in how the reports are compiled. Compliance summaries are provided by request from either patient or physician for whatever time period desired. Therefore, reports frequently vary in the number of days summarized.

CPAP use reports are generated by the medical supply company that supports the particular CPAP machine used by the patient. The patient is responsible for taking the data storage device from their machine to the medical supply company prior to the visit so the report can be generated and faxed to the sleep clinic. Patients are also able to perform automatic downloads from the machine. It was not known from the EMR how the patient provided data on CPAP use to the sleep clinic. The method in which the data is provided should not have any impact on the results of this study, but the lack of control in this variable is a data collection limitation.

A major point of concern for this study was the lack of data available in the EMR related to CPAP use. It may be presumed that those who use the CPAP machine likely follow up with their sleep medicine provider and that those who do not use the CPAP machine are less likely to follow up with their sleep medicine provider. With that presumption, it is plausible that those without CPAP uses documented are in fact using their CPAP machine, but do not have evidence to support the use in the EMR. This lack of evidence could be due to the patient or the medical supply company failing to make the CPAP use data available or it could be that data were lost or not properly entered into the EMR during the transition from paper records. Direct data collection from participants in future studies would help to minimize these limitations.

This study provides evidence to support the need for development of a standard reporting procedure for companies that manufacture CPAP machines. Requiring machine manufacturers to report usage following the same format could result in more accurate tracking of patient use. Positive airway pressure machine manufacturers could also be required to link CPAP use data to EMR's providing automatic population of data to entry

fields needed for health care providers to adequately evaluate CPAP use. Patients are treated at the sleep clinic office with or without a CPAP usage report. If a usage report is not available, the physician gathers the patient's subjective report of use and bases treatment on that report.

Generalizability of this study's findings is limited due to a lack of power resulting from the small sample size. The initial data collection included 139 participants. A number of participants were excluded from this study ($n = 79$) for lack of data availability. The lack of data available in the EMR for data collection likely impacts generalizability.

Theory Implications

The Beebe and Gozal Prefrontal Model (Figure 1) was modified (Figure 2) and served as the theoretical underpinning for this study. When re-visiting the theoretical model in light of these findings it seemed that although not statistically significant, the initiation of CPAP brought about more changes to daytime sleepiness in persons with mild OSAS than changes in blood pressure. Those who used CPAP and those who did not use CPAP decreased from clinically excessive daytime sleepiness (ESS >10) to virtually no daytime sleepiness at the six week follow up.

In light of these findings, the model was revised (Figure 5). The revised model removes the specified number of hours per night of CPAP use. The revision will allow for future studies to explore the dose-response relationship between CPAP use and positive health outcomes.

Figure 5 – (Revised) Theoretical model of Mild Obstructive Sleep Apnea and Continuous Positive Airway Pressure use
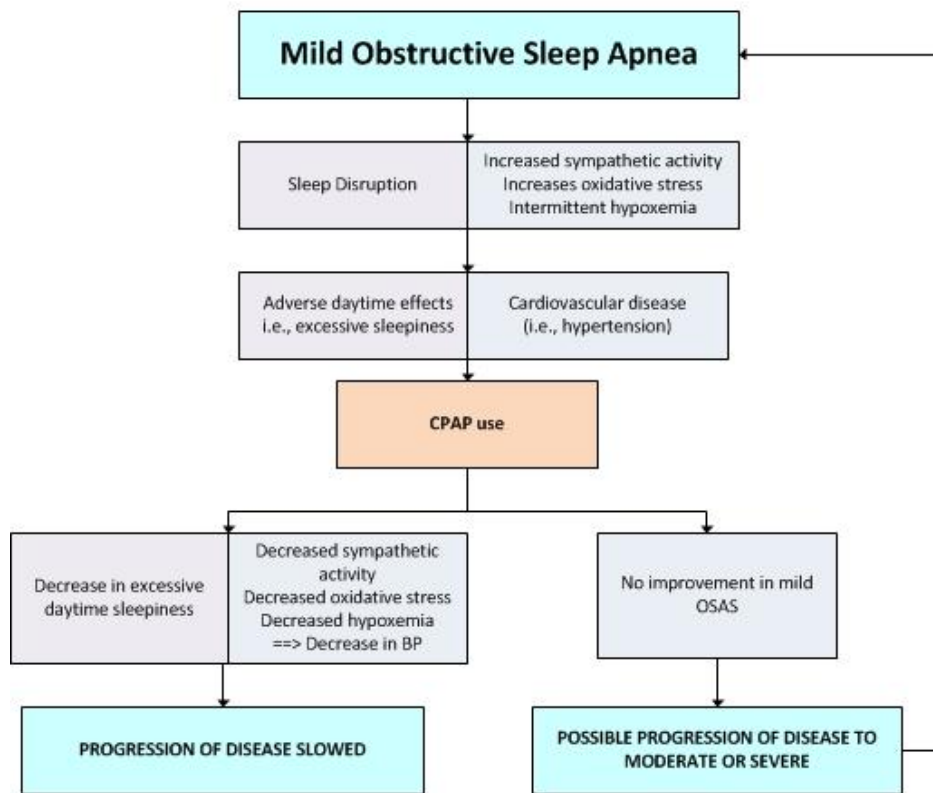
According to Beebe and Gozal (2002) many health care providers may be inclined to dismiss the psychological effects of OSAS due to a lack of understanding related to the link between the two. These findings will hopefully increase awareness related to the link between OSAS and daytime psychological consequences, especially daytime sleepiness. It is estimated that approximately 80 percent of persons with OSAS have a milder form of the disease (Young et al., 2008). Healthcare providers should routinely assess OSAS patients for daytime sleepiness.

Severity of OSAS is based on the number of apnea – hypopnea episodes per hour of documented sleep (American Academy of Sleep Medicine, 2007). The apnea – hypopnea episodes result in oxygen desaturations and an increase in sympathetic activity (Kario, 2009). The desaturations and increased sympathetic activity result in increased

arterial pressure (Nieto et al., 2000; Peppard et al., 2000). The Wisconsin Sleep Cohort Study found a dose response relationship between the number of apnea hypopnea episodes and the development of hypertension at four year follow up (Peppard et al., 2000). Haentjens et al. (2007) found a greater reduction in blood pressure with CPAP use among patients with a more severe form of the disease. The progressive nature of OSAS requires that health care providers examine the effectiveness of treating the disease during the early stage to prevent untoward effects associated with the disease.

Practice Implications

The implementation of EMR's in primary care settings hold great potential for improving quality of care. However, the process requires effective communication and planning between EMR creators, physicians, nurses, and clinic / hospital assistive personnel (Crosson, Stroebel, Scott, Stello, & Crabtree, 2005). Primary care settings present issues specific to the practice, such as treatment protocols for specific disease conditions. Effective implementation will require high levels of collaboration within the practice. Nursing is in a unique position to facilitate the adoption of EMR systems in this setting by working with other practice leaders to address specific implementation issues as they arise.

The transition from paper records to electronic records requires meticulous attention to data entry accuracy. Nursing can lead efforts with clerical staff and other allied health team members to clarify health related terminology questions that could potentially affect the quality of documentation within the medical record. Nursing is also in a position to lead efforts to evaluate the quality of the EMR system adopted. It is imperative that the EMR contain features that specifically address quality measures such

as blood pressure checks, smoking cessation counseling, and controlled blood pressure for hypertensive patients (Hsiao, Marstellar, & Simon, 2014). Hsiao et al. (2014) assert that EMRs that are not fully functional (i.e., measuring appropriate quality of care) are associated with lower odds of blood pressure checks, inappropriate urinalysis, and inappropriate prescribing of antibiotics for urinary related infections when compared to no EMR use. Nurses employed outside of inpatient facilities (e.g., schools, university health centers, primary care offices, health departments, employee health clinics, and occupational health clinics) can provide important insight in the EMR selection process to ensure quality data is collected. The results of this retrospective chart review confirm the importance of collecting quality data, because several aspects of the study design and analysis needed to be re-configured due to inadequacies of the EMR chart availability and documentation quality. Clinical decisions in research and practice in the treatment of OSAS are based on data collected. Incomplete or missing data can skew research findings and practice decision and delay advancements in areas of science that depend on chart reviews for uncovering those advances.

When data are collected and entered correctly the EMR system can provide a rich source of clinical information, not only for point-of-care clinical practice, but also for research and quality performance evaluation (Tu et al. 2014). However, incomplete or missing data can lead to patient safety concerns as well as problems with data collection for research and quality evaluation. One solution to the safety concerns associated with lack of or incomplete data may be to implement a follow-up and feedback system such as the one proposed by Gandhi and colleagues to address the reporting of errors (Gandhi, Graydon-Baker, Huber, Whittemore, and Gustafson, 2005). Follow-up involves assigning

responsibility and accountability for the plan of action set forth to address specific safety issues. Feedback refers to following up with those who report the safety issues and communicating the issue and plan of action to the broader staff and clinicians participating in patient care. Nurses specializing in informatics should be included in the action plan and should be consulted when evaluating the best approach for dissemination of feedback to the broader audience of health care professionals. The use of a complete and current EMR system in sleep clinics could potentially alert health care providers in this area to changes in patient conditions that could be impacted by OSAS (hypertension, daytime sleepiness) as well as provide current data related to CPAP use.

Policy Implications

The American Recovery and Reinvestment Act (ARRA) of 2009 stimulated the adoption of health information technology (HIT). The law provides an unprecedented $19 billion to promote the adoption and use of HIT. The President of the United States vowed to provide every American with the benefit of an electronic health record by 2014 (Blumenthal, 2009). Physicians who adopt EMR's in their practice are rewarded with financial incentives, while those who do not adopt EMR's in their practice by 2015 will lose a percentage of Medicare fees. This loss will continue to increase until 2017 (Blumenthal, 2009). The transition to EMR's is critical to the nursing profession. Physicians who lose funding will likely cut back in other areas of their practice (e.g., staffing, salaries) which will have a direct impact on nursing. Nurses play a pivotal role in supporting legislation aimed at increasing the adoption rate of EMR systems. Nursing research is one area that stands to be enhanced from legislation promoting HIT. One provision of the Patient Protection and Affordable Care Act specifically addresses the

need for clinical registries and networks where health information data can be shared among health care providers (Buntin et al., 2010). This type of registry and networking would facilitate nursing research that mines EMRs for linking care to quality, safety, and health outcomes.

Recommendations

Several recommendations that are supported by the challenges experienced in this study are put forward. The first recommendation relates to collecting data on persons diagnosed with mild OSAS. Currently, data may not be consistently collected on patients at all levels of disease severity. OSAS is a progressive disease and aggressive early treatment can deter negative health outcomes associated with the disease. Increasing awareness among health care practitioners, particularly nurses, could lead to more complete and accurate documentation in persons with mild OSAS.

Next, it is recommended that this study be replicated using wider sampling by including additional sleep clinic offices. This would allow for a larger and more diverse sample size and could lead to more generalizability of findings. Decreases were identified in daytime sleepiness and blood pressure for those who used CPAP four or more hours a night and for those who used CPAP less than four hours a night in this study but did not reach the level of significance. The small sample size likely contributed to low power to detect significant differences between the groups. In addition, future studies of this type should control for blood pressure medication use. Data should be obtained specific to whether a medication was taken for hypertension or another disease that could also be treated with blood pressure medications (i.e., vascular headaches). Data related to sleep hygiene, work / shift schedules, lifestyle, and alcohol use could

potentially offer additional valuable information related to excessive daytime sleepiness and hypertension in this population (National Sleep Foundation, 2013). Conducting a study examining a time point beyond the six week follow up may also offer plausible explanations related to CPAP use. Participants who used CPAP less than 4 hours night may have experienced more difficulty adjusting to the CPAP machine than participants who used greater than 4 hours a night. It is possible that study participants who used CPAP less than 4 hours a night may increase use over time with CPAP machine adjustment. A future study may also employ the use of a more rigorous measure of sleep quality, such as the Pittsburgh Sleep Quality Index (Sitasuwan, Bussaratid, Ruttanaumpawan, & Chotinaiwattarakul, 2014) or the Functional Outcomes of Sleep Questionnaire (Korpe, Lundgren, & Dahlstrom, 2013) and also extend follow-up data collection to points beyond only 6 weeks after CPAP initiation to account for the time needed to adapt to the machine and any machine adjustments. Findings from this study also recommend that future studies seeking to improve upon the study design to establish causal relationships between CPAP use and outcomes should also utilize random assignment of participants.

Another recommendation is related to CPAP use reporting. Future studies should consider using CPAP data collected at a specific time point (i.e., 30 days). It is assumed from this study that all machines report the same type of data, varying primarily in how the usage data is presented (graph, table, etc.). The results of this study do not suggest that one machine is better than another at providing essential data needed related to usage, only that data collection time points were widely variable. Standardization of CPAP machine use reporting in future studies would also strengthen the study. Future

studies may also be strengthened by obtaining CPAP summaries directly from the medical supply company rather than the sleep clinic office, since the sleep office may choose not to enter all variables from the CPAP summaries needed for research studies into the EMR. This method of CPAP use data collection may potentially provide additional information related to the dose –response relationship between CPAP use and possible health benefits.

Finally, this study recommends that nurses partner with other healthcare professionals in sleep medicine to define nursing's contribution to early detection and treatment of OSAS. Nurses should be more integrally involved with sleep centers in ways that could benefit patient outcomes. The role of the nurse in identification of those with or at risk for developing OSAS warrants expansion. This expansion could be enhanced through educational opportunities aimed toward increasing awareness among nurses related to identifying the signs and symptoms of OSAS (i.e., snoring, morning headaches, and excessive daytime sleepiness) across all patient populations and across the lifespan. Nurses also have the capacity to be ideal providers to teach patients how to both use CPAP machines, but perhaps more importantly, integrate CPAP use into their lives, troubleshoot problems and challenges, and promote follow-up and coordination of care between sleep medicine specialists and other health care team members (Rodgers, 2014). Furthermore, nurses may also play a pivotal role in educating patients regarding sleep hygiene (practices associated with sleep) and modifications to the sleep environment (www.nationalsleepfoundation.org). Patient education regarding sleep practices that potentially interfere with sleep such as ingesting stimulants prior to bedtime (alcohol, caffeine, nicotine), staying in the bed too long or not long enough, food intake and

exercise regimen close to bedtime, and not creating a relaxing environment prior to bedtime could potentially result in higher quality sleep and potentially lead to enhanced outcomes of CPAP therapy. Aggressive, early identification and treatment of OSAS is crucial to slowing the progression of the disease and promoting the health of persons experiencing this disease.

Conclusion

Knowledge regarding the effectiveness of CPAP use in persons with mild OSAS and daytime sleepiness and blood pressure is critical to the treatment of this population. This evidence is needed to demonstrate the need to intervene and treat early in the disease process. The results of this study do not support the use of CPAP therapy in persons with mild OSAS; however, this finding should be interpreted cautiously given the results were limited by several methodological issues. The question of when to implement CPAP as treatment for a person with OSAS has long been debated (Barnes et al., 2002). Although the results of this study did not reach the level of statistical significance, it should be noted that a reduction in daytime sleepiness and blood pressure was identified in both groups, irrespective of amount of CPAP use.

A retrospective chart review was used for this study employing an analysis of patient electronic medical records from a local sleep clinic in the southern United States. The challenges encountered in the collection of the patient data had a major impact on the outcome of this study. Sample size was severely limited as a result of incomplete or missing data. These issues suggest that greater attention be given to securing adequate collecting and input of data into EMR in persons with mild OSAS.

This study found no evidence to support the use of CPAP in persons with mild OSAS. The reductions noted in daytime sleepiness and blood pressure did not reach the level of statistical significance. The results from other studies examining the effect of CPAP use on blood pressure and daytime sleepiness in the mild OSAS population are conflicting. The results of this study and the findings of other studies (contradictory, little effect, no effect) support the need to question when to implement CPAP as treatment for OSAS.

It is crucial for the nursing profession to continue to conduct methodically sound research examining the effect CPAP use has on patients with mild OSAS. Nursing needs to be concerned with evolving existing research in the area of OSAS and expanding the knowledge base related to treating persons with mild OSAS. This is a responsibility the nursing profession should embrace, since nurses both care for patients with OSAS and may be best positioned to understand how to promote the self-management of OSAS and CPAP to optimize health outcomes.

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Appendix A.

UNIVERSITY of WISCONSIN

UWMILWAUKEE

Department of University Safety & Assurances

Melissa Spadanuda
IRB Manager
Institutional Review Board
Engelmann 270
P. O. Box 413
Milwaukee, WI 53201-0413
(414) 229-3173 *phone*
(414) 229-6729 *fax*

http://www.irb.uwm.edu
spadanud@uwm.edu

New Study - Notice of IRB Expedited Approval

Date: December 10, 2012

To: Jennifer Doering, PhD
Dept: College of Nursing

Cc: Michelle Nelson

IRB#: 13.204
Title: Positive airway pressure use and mild obstructive sleep apnea syndrome (OSAS)

After review of your research protocol by the University of Wisconsin – Milwaukee Institutional Review Board, your protocol has been approved as minimal risk Expedited under Category 5 as governed by 45 CFR 46.110. In addition, your protocol has been granted approval to waive informed consent as governed by 45 CFR 46.116 (d).

The Institutional Review Board has also approved a waiver of authorization to access protected health information for the purpose of this study which includes the following data:

- Date of birth, Smoker / Non-smoker, Weight, Gender, Blood pressure, Chronic medical conditions, Ethnicity, Neck circumference, Current medications, Marital Status, Oxygen saturation, Type of CPAP device used

This protocol has been approved on December 10, 2012 for one year. IRB approval will expire on December 9, 2013. If you plan to continue any research related activities (e.g., enrollment of subjects, study interventions, data analysis, etc.) past the date of IRB expiration, a continuation for IRB approval must be filed by the submission deadline. If the study is closed or completed before the IRB expiration date, please notify the IRB by completing and submitting the Continuing Review form found on the IRB website.

Unless specifically where the change is necessary to eliminate apparent immediate hazards to the subjects, any proposed changes to the protocol must be reviewed by the IRB before implementation. It is the principal investigator's responsibility to adhere to the policies and guidelines set forth by the UWM IRB and maintain proper documentation of its records and promptly report to the IRB any adverse events which require reporting.

It is the principal investigator's responsibility to adhere to UWM and UW System Policies, and any applicable state and federal laws governing activities the principal investigator may seek to employ (e.g., FERPA, Radiation Safety, UWM Data Security, UW System policy on Prizes, Awards and Gifts, state gambling laws, etc.) which are independent of IRB review/approval.

Contact the IRB office if you have any further questions. Thank you for your cooperation and best wishes for a successful project

Respectfully,

Melissa C Spadanuda

Melissa C. Spadanuda
IRB Manager

Appendix B.

FELIX MORRIS, M.D., LLC

Pulmonary Diseases, Critical Care and Sleep Disorders
416 North Seminary Street
Suite 2500
Florence AL 35630

256-764-7710   Fax 256-765-3888

November 29, 2012

Institutional Review Board
University of Wisconsin – Milwaukee

Dear Institutional Review Board members:

I give Michelle Nelson permission to conduct her study at my practice. I have a multi-discipline clinic in Florence, Alabama which specializes in Pulmonary Diseases and Sleep Disorders with approximately fifty percent of the practice dealing with Sleep Medicine. Patients with obstructive sleep apnea are a primary type of patient I see and treat. I am interested in Ms. Nelson's study and believe is has potential to contribute to a better understanding of how to best treat patients with mild obstructive sleep apnea.

This study will involve data extraction from medical charts of patients who receive care at my clinic. My permission does not include direct access to the charts. No identifiable data will leave the clinic. My office administrator, Dana Mullen, will extract the data from the charts and keep a list linking the study ID with the medical record number in her office for a period of two years after the study at which point the list will be shredded.

Sincerely,

Felix Morris, MD

fam/dam

Appendix C.

Epworth Sleepiness Scale

Situation	Chance of Dozing 0 = would never dose, 1= slight chance of dozing, 2= moderate chance of dozing, 3= high chance of dozing
Sitting and reading	
Watching TV	
Sitting, inactive, in a public place	
As a passenger in a car for an hour	
Lying down in the afternoon	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in traffic	
Total	

Appendix D.

Michelle Nelson, RN, MSN
University of Wisconsin – Milwaukee

Study ID # : _____

Date of birth: _____

Gender: ☐ Male ☐ Female

Ethnicity: _____

Marital status : _____

Smoker: ☐ Yes ☐ No
If yes, how many packs per day? _____
How many years? _____

Apnea hypopnea index AHI (Respiratory disturbance index RDI) - _____

Number of OSA associated visits outside of the clinic protocol (initial, 6 weeks, 1 year, annually):
☐ Once ☐ Twice
☐ Three times
☐ Four or more times

ESS score:
prior to CPAP _____
At or around: _____
6 week follow-up _____
1 year follow-up _____
2 year follow-up _____
3 year follow-up _____
If greater than 3 years, how many years? _____

Blood pressure:
Prior to CPAP _____
At or around : _____
6 week follow-up _____
1 year follow-up _____
2 year follow-up _____
3 year follow-up _____
If greater than 3 years, how many years? _____

Oxygen Saturation:
Prior to CPAP _____
At or around: _____
6 week follow-up _____
1 year follow-up _____
2 year follow-up _____
3 year follow-up _____
If greater than 3 years, how many years? _____

Neck circumference :
Prior to CPAP _____
At or around: _____
6 week follow-up _____
1 year follow-up _____
2 year follow-up _____
3 year follow-up _____
If greater than 3 years, how many years? _____

Weight:
Prior to CPAP _____
At or around: _____
6 week follow-up _____
1 year follow-up _____
2 year follow-up _____
3 year follow-up _____
If greater than 3 years, how many years? _____

Positive Airway Pressure:
☐ Continuous positive airway pressure
☐ Automatic positive airway pressure
☐ Bilevel positive airway pressure

Machine type (manufacturer): _____

Pressure setting: _____

Supplemental oxygen with positive airway pressure: ☐ Yes ☐ No
If yes, how many liters? _____

CPAP use:
Number of days included in report _____
Percent of days with usage >= 4 hours _____ %
Percent of days with usage < 4 hours _____ %

Chronic medical conditions:
☐ Hypertension
☐ Restless leg syndrome
☐ Narcolepsy
☐ Diabetes Mellitus
☐ Depression
☐ Cardiovascular disease
☐ Obstructive sleep apnea
☐ Obesity
☐ Other
_____
_____
_____

Current medications:
☐ Lotensin / benazepril
☐ Capoten / captopril
☐ Vasotec / enalapril
☐ Prinivil, Zestril / lisinopril
☐ Avapro / irbesartan
☐ Cozaar / losartan
☐ Diovan / valsartan
☐ Inderal / propranolol
☐ Lopressor, Toprol XL / metaprolol
☐ Normodyne / labetalol
☐ Coreg / carvedilol
☐ Lasix / Furosemide
☐ Hydrochlorothiazide / HCTZ
☐ Aldactone / spironolactone
☐ Zaroxolyn / metolazone

Current medications cont:
☐ Verapamil / Isoptin, Calan, Covera, Verelan
☐ Diltiazem / Cardizem
☐ Amlodipine / Norvasc
_____
_____
_____

Other:
_____
_____
_____

Michelle Nelson

EDUCATION

University of Wisconsin-Milwaukee, Milwaukee, Wisconsin
PhD, Nursing, May, 2014
Dissertation: Continuous Positive Airway Pressure Use and Mild Obstructive Sleep
Apnea Syndrome (OSAS)
Advisor: Dr. Jennifer Doering

University of Alabama, Tuscaloosa, Alabama
Master of Science, Nursing, July, 2001
Nursing Case Management

University of North Alabama, Florence, Alabama
Baccalaureate of Science, Nursing, December 1997
Cum laude

Northwest Shoals Community College, Muscle Shoals, Alabama
Associate in Applied Science, Nursing, May, 1995

WORK EXPERIENCE

Assistant Professor   **August 2002 - present**
University of North Alabama, College of Nursing
Florence, Alabama
Currently teach the Fundamentals of Nursing – two sections of lecture, one clinical
rotation.
- Course coordinator – responsible for all student clinical rotation assignments.
- Collaborate with local health care facilities for student placement.
- Supervise clinical adjunct faculty.
- Maintain two on - campus lab facilities.
- Coordinate all classroom activities (i.e., lectures, exams)

Staff nurse   **1995 – 2002**

HealthSouth Florence Surgery Center
Florence, Alabama
Duties included:
- Pre-operative patient interviews
- Preparing patients for surgery
- Circulating nurse
- Specialty charge nurse, ENT

- Specialty charge nurse, Orthopedic
- Post anesthesia care unit (PACU)

Assessment Nurse   **2000-2001**

Tim Melson, M.D.
Clinical drug trial
Muscle Shoals, Alabama
Duties included:
- Collaborating with physician on patient assessments during clinical drug trial
- Physical assessments
- Phlebotomy and specimen handling
  ### HONORS / PROFESSORSHIPS

  - Julie Haddons Matthews Professorship – 2012-2013
  - Jessie Barnes Edwards Professorship – 2013-2014
  - Nominated - Eleanor Gaunder Teaching Excellence Award, Phi Kappa Phi - 2008
  - Academic scholarship – University of Alabama, 2001
  - Cum Laude – University of North Alabama, 1997

Professional Organizations

Sigma Theta Tau International Nursing Honor Society – 1/2008 - present
Upsilon Omicron Chapter (served as Vice President – 2008-2011)

American Nurses Association - 2003 -2012

University of North Alabama – 8/2002 – 1/2008
Nursing Honor Society

Committee Membership at University of North Alabama (2007-present)
College of Nursing, Level I, secretary – 2011-present
Traditional Student Guidelines and Resources Committee – 2014-present
Faculty Advisor, Student Nurses Association, 3/2003 – present
Academic Affairs Service Award Selection Committee – 2014
SOAR Summer Session Advising – 2002 – present
Undergraduate Readmissions Committee – 2013-present
Traditional Faculty Development Student Scholarship Committee - 2012-2013
Shared Governance, Human Subjects Protection Committee – 2007-2008

Community Service (2009-present)
Volunteer – MUNCH 2013
Volunteer – Hospice of North Alabama Adopt a Stocking - 2013
Volunteer – Hospice of North Alabama Adopt a Stocking – 2012
Volunteer – Hospice of North Alabama Adopt a Stocking – 2011
Volunteer – Supply Collection Alabama Tornado Relief - 2012

Volunteer – University of North Alabama Bone Marrow Screening – 2011
Volunteer – Salvation Army Angel Tree Collection – 2011
Volunteer – Student Nurses Association Blue Jeans for Haiti – 2009
Volunteer – Toys for Tots – 2009
Volunteer – Girl Scout Health Presentation - 2009