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Effects of Altitude on Sleep During Late Pregnancy

by

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DISSERTATION

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by

Gayle Kipnis
This dissertation is dedicated to Joyce Courtney Coleman for all of her support during my many years of nursing education and to Dr. Kathryn Lee, for her years of advising me during my doctoral studies at UCSF.
The majority of pregnancy sleep research has been conducted at sea level and relatively low elevations. Pregnancy at higher altitudes has distinctive physiologic attributes that affect perinatal outcomes and have been correlated with the duration and intensity of altitude. The effect of altitude on adult sleep has been studied at various elevations and has unique characteristics that may impact pregnant women. The effect of altitude on sleep during pregnancy is mostly unknown.

This dissertation research explored late pregnancy sleep quantity and quality characteristics at moderate altitude by comparing them to a similar sample at sea level, describing associations between moderate altitude sleep parameters and length of labor by self-report and medical records, and testing associations between sleep and pregnancy outcomes (length of labor and mode of delivery) at moderate altitude. Participants were nulliparous third trimester women (n=50) recruited in Flagstaff, Arizona (elevation 6910 feet [2106 meters]). A 3-day sleep diary and Pittsburgh Sleep Quality Index (PSQI) were completed between 35 gestational weeks and one week prior to delivery. Descriptive statistics, unpaired t-tests, Pearson product-moment correlation coefficients, ANCOVA, multiple regression, and logistic regression were utilized.

Results showed that after controlling for education, compared to nulliparous women at sea level, women at moderate altitude reported significantly higher sleep disturbance scores. After controlling for infant birth weight, length of labor was
associated with the PSQI self-report measure for sleep onset latency. Together, infant birth weight, maternal weight, age, income, and sleep onset latency, hours of sleep, sleep disturbance, and sleep quality accounted for 51.6% of the variance in length of labor.

Mode of delivery was also associated with sleep disturbance.
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Chapter 1

Effects of Altitude on Sleep in Late Pregnancy: An Introduction

Sleep disturbance is a common complaint during pregnancy even in women who have never had problems with their sleep in the past. According to the National Sleep Foundation’s 1998 Women and Sleep poll, 78% of women reported that their sleep during pregnancy was worse than at any other time in their lives (National Sleep Foundation, 2009). Effective assessment of the pregnant woman’s sleep history is often overlooked by health care providers as it is not viewed as a health priority.

Normal sleep for healthy adults consists of falling asleep within five to ten minutes of turning off the lights, sleeping seven to eight hours, and waking refreshed. Feeling ready to perform activities of daily living and remaining energetic through the day are indicators of a good night’s sleep (Lee, 2003). Sleep disturbance or insomnia can be categorized as either sleep deprivation resulting from an inadequate amount of sleep or sleep disruption that results from fragmented sleep during the night. Health related conditions often lead to sleep disruption whereas lifestyle or developmental issues lead to sleep deprivation. Getting additional sleep can often relieve the symptoms of sleep deprivation whereas sleep disruption can represent a pathological state.

What constitutes normal sleep during pregnancy has not been established. Although the first research on sleep during pregnancy was conducted in 1968, it has been over the past twenty years that the characteristics of sleep during pregnancy have been studied. Diminished sleep quality, greater fragmentation and a decreased duration of sleep during pregnancy are consistently observed. Pregnancy at altitude also has
distinctive physiologic attributes that affect perinatal outcomes and have been correlated with duration living at altitude as well as specific high altitudes compared to sea level. The effect of altitude on adult sleep has been studied at various altitudes and has unique characteristics that may impact pregnant women. The effect of altitude on sleep during pregnancy is mostly unknown.

The focus of this dissertation is to offer original research on pregnancy sleep at moderate altitude in order to describe characteristics of sleep during the third trimester and to explore associations with perinatal outcomes. This dissertation is being presented as three publishable papers. The second chapter is an extensive review of the literature on altitude, pregnancy and sleep with a focus on perinatal outcomes. The third chapter is a manuscript on the research comparing sleep characteristics of a sample of pregnant women living at moderate altitude with a sample living at sea level. The fourth chapter documents research on the association of sleep disturbance parameters with length of labor and mode of delivery. The fifth and final chapter is a synthesis of these research findings with implications for nursing practice and directions for future research.

**Altitude, Pregnancy & Sleep**

Altitude is defined as the vertical elevation of land above sea level. The specific elevations for low, moderate, and high altitudes vary throughout the literature (Hankins et al., 1996; Moore, 1987; Kametas, McAuliffe, Krampl, Chambers, & Nicolaides, 2004; Julian, Wilson, & Moore, 2009; Zamudio, 2007; Postigo et al., 2009). Altitude will be defined within this dissertation as: low (<4552 feet [ft] or 1387 m), moderate (4553 ft or 1388m) to 8858 ft (2700m) and high (> 8858 ft or 2700m).
Studies indicate that pregnancy at altitude can affect the mother and fetus on many physiologic levels. Maternal ventilatory adaptation at higher altitudes includes increases in functional residual, total lung, and forced vital capacities that increase oxygen transport to the uterus (Krampl, 2002). Elevated hemoglobin levels produce an arterial oxygen content that is higher at high altitude than at sea level (McAuliffe, Kametas, Krampl, Ernsting, & Nicolaides, 2001). Increased hemoglobin concentrations increase the oxygen transport capacity but also increase blood viscosity which combined have been shown to impair capillary tissue perfusion. Increased cardiac output and decreased blood viscosity are typical with pregnancy at sea level whereas high altitude is associated with lower cardiac output and increased viscosity (Kametas, Krampl, McAuliffe, Rampling, & Nicolaides, 2004).

Altitude has been shown to alter sleep in healthy adults by fragmenting sleep with brief arousals which are linked to periodic breathing. This form of breathing at altitude reflects stimulation of breathing by hypoxia (Weil, 2004). High altitude environments are characterized by low barometric pressure and lowered oxygen content. Multi-generational high altitude ancestry exerts a strong protective influence and adaptation to chronic hypoxia. Previous studies of pregnancy at higher elevations explored the role of chronic hypoxia, decreased blood flow, hyperviscosity, placental morphology, and genetics on incidence of adverse perinatal outcomes that included higher risk for pre-eclampsia (Moore, Hershey, Jahnigen, & Bowes, 1982), small for gestational age fetuses (Jensen & Moore, 1997) and fetal growth restriction (McCullough, Reeves, & Liljegren, 1977).
Altitude intensity and duration are factors to be considered when examining adverse perinatal outcomes at varying altitudes. Large epidemiologic studies at a variety of elevations in Colorado have shown that altitude has a direct independent effect on low birth weight resulting in a 102gm decrease for every 3300 ft elevation gain (1000m) that begins in the late second trimester (Jensen & Moore, 1997). There is population variation in the magnitude of the birth weight reduction at high altitude with those who have lived at high altitudes for 10,000 (Andeans) to 20,000 years (Tibetans) demonstrating one-third the reduction present in populations that had resided at high elevations for less than 500 years (Moore, 2001).

Studies of sleep disturbance during pregnancy at sea level and low altitudes have demonstrated changes in sleep patterns, more frequent awakenings, and lower quality and quantity of sleep. These changes are progressive reaching the most intense levels of sleep disturbance during the 28th to 40th gestational week, or last trimester of pregnancy. Reasons for pregnancy sleep disturbance include physiologic, psychological, and environmental origins. Physiologic reasons include general discomfort, fatigue, urinary frequency, restless leg syndrome (RLS), nausea, backaches, fetal movements, heartburn, and shortness of breath. Psychological reasons for sleep disturbance include anxiety, restlessness, dreams, and nightmares. Environmental reasons are often attributed to noise, co-sleeper disturbance, and child awakenings.

Sleep is measured at all elevations either objectively using polysomnography (PSG) or wrist actigraphy, or subjectively with sleep questionnaires and logs or diaries. PSG is considered the “gold” standard for estimating stages of sleep but requires an overnight stay in a sleep lab or clinic and may not be reflective of normal pregnancy
sleep. It is time-consuming, expensive, and labor intensive, producing enormous amounts of data that requires interpretation. Actigraphic data can be collected in the home for a naturalistic setting but equipment failure is common. When utilized alone, objective measures may not offer a comprehensive assessment due to aspects of sleep that cannot be quantified. There is a wide inter- and intra-individual variability that characterizes sleep and the perception of sleep. Subjective, self-report sleep measures report a history of sleep disturbance over time, are more sensitive to sleep behavior, and document the frequency and severity of sleep symptoms. Subjective sleep measures are less expensive but have a greater subject burden with participant compliance necessary for accurate data collection. Objective and subjective sleep measures are often combined within studies to gather an inclusive picture of sleep and to increase construct validity.

Sleep disturbance at lower elevations is most common during the third trimester of pregnancy (Baratte-Beebe & Lee, 1999; Beebe & Lee, 2007; Mindell & Jacobsen, 2000; Lee, Zaffe, and McEnany, 2000). Common sleep problems of this final trimester are waking to void, difficulty getting comfortable, heartburn, and restless sleep due to fetal movement (Pien & Schwab, 2004) and obstructive sleep apnea and sleep disordered breathing (Mindell & Jacobsen; Pien & Schwab). Baratte-Beebe and Lee examined midsleep awakenings in women prior to conception and during each trimester of pregnancy living at sea level in San Francisco. They documented a two-fold increase in the number of awakenings from pre-conception to the third trimester. Beebe and Lee also measured sleep in the last few days of pregnancy as women transitioned into labor at sea level and found that sleep quality deteriorated progressively over the last 5 days of pregnancy and was the lowest during the night before labor begins. Hall et al. (2009)
reported that 20.6% of their 650 subjects living at various elevations in British Columbia, Canada, reported sleeping less than 6 hours per night during their last trimester of pregnancy.

During the last decade, research has focused on sleep during pregnancy in association with pregnancy outcomes. Lee and Gay (2004) reported that women living at sea level in San Francisco who slept less than six hours at night during late pregnancy had longer labors and were 4.5 times more likely to have cesarean deliveries as compared to than those women who slept more than seven hours. Women with severely disrupted sleep had longer labors and were 5.2 times more likely to have cesarean deliveries. These findings were supported by two recent studies conducted in Tehran, Iran at an elevation of 3900 feet (1200m). Naghi et al., (Naghi, Keypour, Ahari, Tavalai, & Khak, 2011) reported that poor sleep quality during the last three weeks of pregnancy were associated with longer labors and a higher incidence of cesarean birth. Research by Zafarghandi and colleagues (Zafarghandi et al., 2011) revealed that women with a poorer quality and quantity of sleep had longer labors, a higher incidence of cesarean births and newborns with lower Apgar scores.

Third trimester pregnant women living in Providence, Rhode Island (elevation 6.6ft or 2m) who snored were found to have an 3.8 times greater likelihood of having an unplanned cesarean birth, 2.4 times greater likelihood of having gestational hypertension or pre-eclampsia, and a 2.1 times greater likelihood of having gestational diabetes (Bourjeily, Raker, Chalhoub, & Miller, 2010). Two recent studies in Chicago (587ft or180m) (Facco, Grobman, Kramer, Ho, & Zee, 2010a) and in Seattle, Washington (177ft or 54m) (Qiu, Enquobahrie, Frederick, Abetew, & Williams, 2010) supported these
findings by concluding that shorter self-reported sleep duration and frequent snoring were associated with development of gestational diabetes mellitus. Snoring is one of the categories of sleep-disordered breathing that is prevalent in pregnant women. Bachour and colleagues (Bachour, Teramo, Hiilesmaa, & Maasilta, 2008) found that pre-eclamptic women living in Helsinki, Finland (85ft or 26m) experienced more snoring and had higher levels of pro-inflammatory markers tumor necrosis factor alfa (TNF-α) and interleukin 6 (IL-6). The intermittent hypoxia of sleep disordered breathing plays a significant role in the cycle of systemic inflammation. Hypoxia leads to oxidative stress that can intensify inflammatory pathways. Hypoxia is known to intensify with elevation gain.

An extensive literature review revealed only two studies that have explored sleep disturbance during pregnancy at higher elevations. Both were of the same sample and conducted at moderate altitude in Denver, Colorado (5183ft or 1580m) by Okun and colleagues. They explored the association between sleep disturbance and inflammatory markers. Higher pro-inflammatory TNF-α was associated with increased subjective sleep complaints (Okun & Coussons-Read, 2007a) and sleep quality and continuity were correlated with late pregnancy levels of circulating and stimulated IL-6 (Okun, Hall & Cousson-Read 2007b).

Research shows that women in late pregnancy have increased inflammatory markers at low and moderate altitudes. Higher elevations are characterized by low barometric pressure and lowered oxygen content. Hypoxia leads to oxidative stress that can intensify inflammatory pathways. Pregnant women who live at higher elevations have the potential to be affected by the physiologic challenges of hypoxia combined with
increased inflammation which may lead to adverse pregnancy outcomes. To provide a foundation for meaningful research related to these findings, the Kipnis Conceptual Model of Pregnancy Sleep Disturbance at Altitude (Figure 1) was created from a synthesis of the Theory of Integral Nursing (Figure 2), the Theory of Symptom Management (Figure 3), and Lee’s Conceptual Model of Impaired Sleep (Figure 4).

**Synthesis of Theories & Conceptual Models**

Pregnancy should be viewed as a pathophysiologic state of holistic wellness. At the current time, pregnancy is viewed as a normal physiologic state that results in the birth of a newborn in the majority of cases. Sleep is also a normal physiologic state. With impaired sleep, the balance of body, mind, emotions, and spirit can begin to tip toward illness or suboptimal health.

The Theory of Integral Nursing (TIN) was developed by Barbara Dossey, PhD, in 2008. It is informed by integral theory, contains a philosophical foundation and applies a comprehensive integral process, dialogue, and worldview to expand nursing’s understanding of the complexity of human nature and healing. It is a grand theory that is complex but generalizable. The TIN encompasses both the art and the science of nursing (Dossey, 2009). It embraces and transcends holistic nursing and incorporates existing theoretical nursing work as well as concepts from various fields that include holism, multidimensionality, integral, chaos, complexity, and systems paradigms. The TIN combines the core concept of healing with the metaparadigm of nursing theory, patterns of knowing in nursing, the four quadrants (perspectives of reality) adapted from Wilber’s integral theory. The Kipnis Conceptual Model of Pregnancy Sleep Disturbance at Altitude integrates the overarching concept of holistic wellness and the nurse as a vital
component of the meta-paradigm of nursing from the TIN. Wellness is seen as the outer oval that surrounds the Kipnis model which symbolizes holistic wellness of body, mind, emotions, and spirit. The metaparadigm of nursing that includes the nurse as a vital component to wellness are seen as the four outer rectangles with interconnecting dotted lines.

The Theory of Symptom Management (TSM) was developed at the University of California, San Francisco in 1994 by the faculty in the symptom management group then revised in 2001 and again in 2008 (Humphreys et. al., 2008). It is a middle range theory that is highly generalizable with a focus directed towards clinical practice and research collaboration. Symptoms are described as subjective experiences that reflect changes in the biopsychosocial functioning, sensations, or cognition of an individual (Dodd et al., 2001). The theory of symptom management includes the three main concepts of symptom experience, symptom management strategies, and symptom status outcomes in the context of the dimensions of nursing science; person, environment, and health/illness. The Kipnis model integrates the concept of symptom experience and the dimension of nursing science which are seen as the symptom experience circle within the wellness oval and the dimensions of nursing science, which are similar to the TIN meta-paradigm of nursing.

The Lee Conceptual Model of Impaired Sleep (Lee, 2003) offers a detailed overview of sleep disturbance which adds an understanding of sleep disorders not addressed by the previous theories. It divides impaired sleep into sleep deprivation and sleep disruption that can both lead to physiologic, cognitive/behavioral, emotional, and social adverse health outcomes. It stimulates further understanding of the topic of sleep
disturbance and although it is not specific to pregnancy sleep disorders, it is very
generalizable. The concepts of sleep deprivation and sleep disruption are integrated into
the Kipnis model and are seen within the symptom experience circle.

The Kipnis Model of Pregnancy Sleep Disturbance at Altitude illustrates that
sleep disturbance during pregnancy at higher elevation is multidimensional and has a
broad scope. It illustrates that altitude can act independently and affect pregnancy
outcomes which has been validated through research of newborn birth weights being
lower at higher altitudes in Colorado. This model demonstrates that the intensity,
duration, and severity of symptoms create changes in pregnancy physiology at altitude
which has been well documented. Finally, the physiologic changes related to altitude are
depicted as leading to sleep deprivation or disruption which produces symptoms affecting
pregnancy outcomes. This will be explored through research presented within this
dissertation. Research on pregnancy, sleep, and altitude is in its infancy and this
conceptual model offers stimulus for questioning, study, and further exploration.

Conclusion

The systemic inflammation, periodic breathing, increased sleep fragmentation,
and chronic hypoxic that are common to increasing elevations may potentiate the usual
sleep deprivation and disruption seen at lower altitudes creating heightened sleep
disturbance for pregnant women at moderate altitude. The potential for an escalated
incidence of adverse perinatal outcomes is plausible. Conceptual organization is
accomplished through the Kipnis Model of Pregnancy Sleep Disturbance at Altitude.
The results of this dissertation research are presented in the following chapters.
Chapter 2

Sleep, Pregnancy, and Altitude: Implications for Adverse Perinatal Outcomes

Abstract

Objective: To synthesize the literature on pregnancy and sleep in relation to potential for adverse perinatal outcomes for women living at increased elevations.

Data Sources: PubMed, CINAHL, Web of Science, Cochrane, and Scopus databases

Study Selection: Studies published between 1995 and 2011 are included that examine perinatal outcomes related to sleep, altitude, or both sleep and altitude.

Results: Nineteen studies conducted on sleep during third trimester of pregnancy were evaluated based on altitude and perinatal outcomes. Physiologic hypoxia, as a function of intensity and duration of altitude, can fragment sleep during pregnancy by affecting breathing during sleep. Altitude can also have adverse effects on perinatal outcomes such as pre-eclampsia and intrauterine growth restriction.

Conclusions: There is a gap in knowledge related to how perinatal outcomes at higher elevations are affected by sleep disturbance during pregnancy. Research that addresses sleep disturbance at altitude and perinatal outcomes is warranted.

Keywords: sleep, pregnancy, altitude, sleep disturbance, perinatal outcomes
Introduction

It has been established that sleep disturbance is ubiquitous during pregnancy. Although the first research on sleep during pregnancy was conducted in 1968, it has been over the past twenty years that the objective and subjective characteristics of sleep during pregnancy have been studied and documented. Diminished sleep quality, greater fragmentation and decreased duration of sleep during pregnancy are consistently observed. Studies are now emerging that link sleep parameters during pregnancy with adverse perinatal outcomes. Maintaining a pregnancy at altitude has distinct physiological challenges that are associated with adverse perinatal outcomes. Studies that explore the characteristics of maternal sleep and adverse perinatal outcomes at elevations other than sea level are scarce. The purpose of this paper is to critique and synthesize the research evidence for adverse perinatal outcomes associated with sleep, pregnancy, and altitude.

Background and Significance of Sleep and Altitude

Sleep

It is estimated that 50 to 70 million Americans suffer from sleep disorders that interfere with their daily functioning and have adverse outcomes related to their health and longevity (Institute Of Medicine, 2006). Sleep can be defined as the periodic state of rest that is accompanied by periods of unconsciousness and relative inactivity. It is a normal biological function and imperative for the optimal functioning of the body and mind but exactly how it contributes to health and a feeling of wellbeing is not exactly understood. Normal sleep for healthy adults consists of falling asleep within five to ten minutes of turning out the light, sleeping seven to eight hours, and waking refreshed.
Feeling ready to perform activities of daily living and remaining energetic through the day are indicators of a good night’s sleep (Lee, 2003).

Sleep architecture refers to the basic organization of sleep with two basic states, rapid eye movement (REM) and non-REM sleep (NREM). NREM has four stages related to the continuum of the depth of sleep. These states alternate during the night with each cycle comprising approximately 90 to 120 minutes. NREM sleep composes approximately 75%-80% of the sleep cycle and REM sleep approximately 20%-25% with individual variations (Institute Of Medicine, 2006).

Sleep is measured either subjectively or objectively. Subjective sleep is measured with sleep questionnaires, sleep diaries, or sleep logs. Objective sleep is measured with polysomnography (PSG) or actigraphy. Different aspects of sleep that are commonly measured in sleep studies are: sleep onset latency (how long it takes to initially fall asleep), wake after sleep onset (total amount of time awaking during the night excluding latency and terminal wakefulness), number of awakenings (excluding the final awakening before the final arising), sleep quality (subjective), sleep efficiency (percent of time in bed spent asleep), time in bed (starting from the moment of intention to fall asleep, concluding with final arising), total sleep time (actual time slept) and terminal wakefulness (amount of awake time between the final awakening and arising).

Sleep Disturbance.

Sleep disturbance is defined in many ways throughout the literature but consists of either an inadequate amount of sleep, poor quality of sleep, or fragmented sleep. The Lee Conceptual Model of Impaired Sleep (Lee, 2003) points to potential adverse health outcomes but distinguishes sleep disruption from sleep deprivation. Sleep disruption is
the fragmented sleep due to pre-existing health problems, sleep disordered breathing, excessive leg movements, effects of caffeine or stimulants, anxiety, or other factors that disrupt sleep. Sleep deprivation is an inadequate amount of sleep due to such things as delayed bedtime, early wake time, or poor sleep hygiene. Orzel-Gryglewska (2009) defines sleep deprivation as either a shorter-than-optimal sleep time or a complete lack of sleep over a certain time period that leads to impaired perception, deterioration in wellbeing, difficulty concentrating, and slower reactions.

In the Lee Conceptual Model of Impaired Sleep, adverse health outcomes are physiological, cognitive/behavioral, emotional or social. Physiological outcomes include alterations in inflammatory processes and immune function as well as comorbidities such as hypertension. Cognitive/behavioral adverse outcomes include fatigue, increased risk for accidents, impaired short-term memory and coping whereas emotional outcomes include low motivation and altered mood. Adverse social outcomes can include impaired family interactions and increased health care utilization.

Outcomes of sleep disruption and sleep deprivation are dependent on individual awareness. The perception, evaluation, and response of sleep disorder symptoms by the person experiencing them vary greatly. If snoring with gasping, a significant symptom of sleep disordered breathing (SDB), is ignored and not reported to a healthcare provider or assessed, severe hypoxia results in adverse health outcomes.

**Sleep Disturbance during Pregnancy.**

Sleep disturbance has been documented through subjective self-report and objective polysomnographic and actigraphic studies to occur throughout all three trimesters of pregnancy (Lee, Zaffke, & McEnany, 2000; Schweiger, 1972). In the first
trimester, total sleep time and awakenings during the night have been observed to increase with a decrease in stage 3-4 non-REM sleep and sleep quality. In the second trimester sleep quality and total sleep time normalize but awakenings and stage 3-4 non-REM sleep increase with a decrease in REM sleep. In the third trimester, nocturnal awakenings increase, total sleep time decreases, and sleep quality is poor (Lee, et.al., 2000; Hertz et al., 1992; Santiago, Nolledo, Kinzler, & Santiago, 2001).

Initiation of sleep, referred to as sleep onset latency, is not usually a problem during pregnancy except for women with insomnia or sleep disorders, including the 23% who develop Restless Legs Syndrome (Lee, Zaffke, & Baratte-Beebe, 2001). In general, sleep fragmentation progressively increases throughout pregnancy and is estimated with number of awakenings or total minutes spent awake at night (Lee et al., 2000). The most common reasons for waking during the night (maintenance insomnia) during the third trimester are leg cramps (73%), need to urinate (47%), joint pain (23%), and interference by a bed partner (12%) (Lee & Caughey, 2006). Many symptoms of sleep disturbance are accepted as normal during pregnancy and are rarely discussed with their health care provider. Most physiological changes are routinely monitored in clinics or offices during prenatal visits, but it is not standard practice to assess sleep.

Sleep-disordered breathing (SDB), a form of sleep disruption, is defined as snoring, upper airway resistance syndrome, obstructive sleep apnea syndrome, or obesity hypoventilation syndrome. The prevalence of SDB during pregnancy is unknown but is associated with hypertension and chronic morbidity of cardiovascular disease, diabetes and obesity (Al Lawati, Patel ,&Ayas , 2009; Irwin et al., 2006).

Effects of Altitude
Altitude is defined as the vertical elevation of land above sea level. The specific elevations for low, moderate, and high altitudes vary throughout the literature (Hankins et al., 1996; Moore, 1987; Kametas, McAuliffe, Krampl, Chambers, & Nicolaides, 2004; Julian, Wilson, & Moore, 2009; Zamudio, 2007; Postigo et al., 2009). Altitude will be defined in this review as: low (< 4552 feet [ft.] or 1387 meters [m]), moderate (4553 ft. or 1388m)to 8858 ft. (2700m) and high (> 8858 ft. or 2700m). An estimated 140 million people world-wide are permanent residents at high altitude. In addition, it is thought that as many as 34 million people visit high altitude areas each year (Krampl, 2002; Kametas et al., 2004; Julian et al., 2009; Bobrowski, 2010). High altitude permanent residents are estimated to include 36% residing in Africa, 36% in Asia, 28% in South America and 1% in North America (Moore, 1987).

**Adult Sleep at Altitude.**

Studies of sleep architecture and characteristics in adults visiting at higher altitudes demonstrate similarities to sea level pregnancy sleep during the third trimester. At sea level, pregnancy sleep during the third trimester reveals an increase in the progressive nocturnal awakenings and Stage 1 NREM sleep with a decrease in total sleep time, sleep quality, stage 3-4NREM sleep and REM sleep (Lee, Zaffke, & McEnany, 2000; Hertz et al., 1992). Sleep fragmentation progressively increases through pregnancy (Lee et al., 2000). For adult, non-pregnant, sea-level residents that visit high altitude, sleep architecture shows an overall prevalence of lighter Stage 1 NREM, a lessening of deeper NREM Stages 3 & 4, REM sleep remaining the same or lessening, with fragmentation of sleep increasing with elevation gain. Periodic breathing increases with altitude gain, contributes to the arousals that constitute sleep fragmentation, and is most
prevalent during NREM sleep. There is a significant decrease in subjective sleep quality among sea-level residents when they ascend to higher altitudes and experience frequent awakenings and difficulty breathing (Szymcak et al., 2009). In multi-generational residents living at high altitude, fragmented sleep is 2-3 times greater than expected for age-matched males at sea level (Coote, Tsang, Baker, & Stone, 1993).

**Duration and Intensity of Altitude.**

Intensity and duration of altitude are significant factors to examine when looking at the effects of altitude on pregnancy and sleep. Ascending from sea level, the altitude at which arterial O\textsubscript{2} saturation falls below 90% is approximately 5800 ft. (1768 m) for visitors and 8400 ft. (2439m) for permanent residents (Moore, 1987). For visitors to high altitude, a time-dependent increase in ventilation occurs over 6 to 8 days, lowering oxygen saturation to below 90% (Moore, 1987). For long term residents at high altitude there is an adaptation to chronic hypoxia with multigenerational high-altitude ancestry exerting a strong, protective influence. Andeans and Tibetans who have adapted to high altitude for 10,000-50,000 years have a lower incidence of hypoxia-related intrauterine growth restriction (IUGR) than Europeans and other ethnic groups with ancestors living at high altitude less than 500 years (Bobrowski, 2010).

**Physiologic Changes in Adults at Altitude.**

Rapid responses to high altitude of approximately 10,000 ft. (3048m) are seen in the respiratory system of adults; slower responses occur in the nervous, muscular, and cardiovascular systems. Oxygen saturation in the first few days is lower during sleep possibly due to a decreased response to CO\textsubscript{2} that is common even at sea level. Digestion slows with reduced tone and mobility of the stomach due to hypoxia (Dill, 1968). Within
weeks, there is a decline in blood and plasma volume as well as an increase in pulmonary ventilation by sensitization to CO₂.

**Physiology of Sleep at Altitude.**

When adults first arrive at high altitude poor sleep quality is commonly experienced with reports of multiple awakenings (Weil, 2004). Sleep becomes more fragmented with frequent brief arousals linked to periodic breathing. Periodic breathing is the periodicity of hyperpnea ending in apnea similar to Cheyne-Stokes breathing observed in persons with congestive heart failure at sea level. This form of breathing at altitude reflects the stimulation of breathing by hypoxia, leading to hypocapnia which lessens the hypoxia, which during sleep can trigger apnea (Weil, 2004). Frequent brief arousals occur at apnea termination and at initiation of hyperpnea, but it is unclear whether arousals are triggered by apnea-induced asphyxia or by mechanics of abrupt resumption of breathing. At moderate altitude, periodic breathing decreases over successive nights as acclimatization progresses, but can persist at very high altitudes especially above 15,000ft. (Weil). Advantages to periodic breathing include energy conservation during apnea and enhanced alveolar ventilation during hyperpnea with its high tidal volumes. Sleep architecture shifts to lighter sleep stages with marked decreases in deep sleep (NREM stages 3 & 4) and REM sleep. During wakefulness, somnolence is experienced. Adults complain of shortened, restless sleep that is interrupted despite total sleep time being unaltered (Dill, 1968).

**Physiology of Pregnancy at Altitude.**

Altitude can affect the mother and fetus on many physiologic levels. High altitude environments have low barometric pressure and low oxygen content. At 14,108
ft. (4300m), the pressure is only 50% of that at sea level and creates a state of hypobaric hypoxia. Pregnant women at high altitude begin with 50% lower arterial pO2 and pCO2 values despite a higher tidal volume and minute ventilation. Maternal ventilatory adaptation at higher altitudes includes increasing functional residual, total lung, and forced vital capacities that increase oxygen transport to the uterus (Krampl, 2002). The elevated hemoglobin level seen at altitude increases oxygen transport capacity but also increases blood viscosity and can impair capillary tissue perfusion (Kametas, Krampl, McAuliffe, Rampling, & Nicolaides, 2004). It is unknown if cardiovascular changes during pregnancy at high altitude result in minimal myocardial strain due to an increase in oxygen content or whether sluggish placental circulation results from increased blood viscosity. Researchers are beginning to explore the role of chronic hypoxia, hyperviscosity, placental morphology, and genetics on perinatal outcomes at altitude that include pre-eclampsia, IUGR, and low birth weight.

Commercial aircraft are usually pressurized to 6000 to 8000 ft. above sea level, so flying results in a transient altitude exposure. Increased heart rate and blood pressure with symptoms of dyspnea and hyperventilation may occur. It is recommended that international air travel be restricted after 35 gestational weeks and domestic air travel be restricted after 36 gestational weeks (ACOG Committee on Obstetric Practice, 2001).

**Review Questions**

The two questions guiding this systematic review were: 1) Are there differences in perinatal outcomes at high altitude compared to sea level? and 2) Are there differences in sleep parameters during the third trimester for women who live at higher altitude compared to lower altitude?
**Review Method**

PubMed, CINAHL, Web of Science, Cochrane, and Scopus databases were searched for published research on pregnancy sleep disturbance at altitude with MESH terms *pregnancy, sleep* and *altitude*. Keywords also included *maternal or perinatal* combined with *altitude, high altitude, moderate altitude, elevation* and *sleep disorders, sleep disturbance, sleep disruption, sleep-disordered breathing, sleep quality, sleep quantity*, or *sleep deprivation*. The lack of literature from that process forced separate searches on pregnancy sleep, perinatal outcomes, and pregnancy at moderate and high altitude. A date limit of 1995-2011 was imposed. All studies were obtained from peer reviewed journals.

**Review Results**

**Question #1.** Are there differences in perinatal outcomes at high altitude compared to sea level? Keywords *pregnancy* and *altitude* revealed 575 publications. When the limits of English language, adult, female, and human were added, 141 articles were obtained. In order to compare and refine the search, MeSH terms *pregnancy* and *altitude* were used with the same limitations as above and narrowed to 111 publications. Keywords related to outcomes were added to *pregnancy* and *altitude* to expand the search and yielded 32 publications. The abstracts were examined and repeated authors searched resulting in 54 articles. Selection criteria were narrowed to identify research studies that targeted perinatal outcomes of pregnancy at altitude and sea level.

**Question #2.** Are there differences in sleep parameters during the third trimester for women who live at higher altitude compared to lower altitude? The search for pregnancy, sleep, and perinatal outcomes included the terms *pregnancy, perinatal,*
sleep, sleep disorders, sleep disturbance, sleep disruption, sleep deprivation, and outcomes and their variations as mentioned above. The limits of English language, adult, female, human, adolescent, and young adults were added. Utilizing MeSH terms produced 298 publications and key words for various perinatal outcomes were added resulting in 241 publications. Abstracts were reviewed for relevance to pregnancy sleep parameters during the third trimester and perinatal outcomes. Reference lists from the most focused articles were explored. Nineteen articles related to pregnancy and sleep, with adverse perinatal outcomes as a focus of study, are reviewed in this paper based on the altitude at which the study was conducted.

**Differences in Perinatal Outcomes between Low and High Elevations**

Studies in this section of the review indicate that higher altitude is associated with preterm labor, gestational diabetes, preterm birth, gestational hypertension, pre-eclampsia, intrauterine growth restriction (IUGR) and small-for-gestational age (SGA) infants, prolonged labor, and increased cesarean deliveries. To explore physiologic reasons for the adverse perinatal outcomes, Tissot van Patot et al. (2010) examined placental tissue at high altitude (10,171ft. or 3100m) and sea level and found that none of the placentas from high altitude showed metabolic markers of oxidative stress regardless of type of delivery. They concluded that the lack of oxidative stress in response to labor ischemia/hypoxia at high altitude suggests that adaptation to high altitude blunts the stress response of placental tissue and that hypoxic preconditioning may be occurring. Zamudio and colleagues (2010) compared maternal and fetal arterial and venous glucose concentrations at high altitude (11,811ft. or 3600m). Umbilical arterial and venous glucose concentrations were markedly lower than maternal levels indicating a lower
glucose delivery to the fetus. Fetal glucose consumption was decreased by 28% but strongly correlated with glucose delivery. They concluded that anaerobic consumption of glucose by the placenta spares oxygen for fetal use but limits glucose availability for fetal growth with a placenta-mediated decrease in glucose transport at high altitude.

Hypertensive disorders of pregnancy are more prevalent as altitude increases affecting as many as 12-28% of all pregnancies at 10,171ft. or 3100m (Moore, Hershey, Jahnigen, & Bowes, 1982; Palmer et al., 1999) as compared to 6-8% of all pregnancies at sea level. Pre-eclampsia occurs in 3-6% of all pregnancies and is a leading cause of fetal and maternal morbidity and mortality (Blackburn, 2007). High altitude was found to act independently of known risk factors with a 3.6 times greater risk for pre-eclampsia at 3100m than at 10m (Palmer et al., 1999). Yinon and colleagues (Yinon et al., 2006) found an association between pre-eclampsia and sleep disordered breathing with 71% of the neonates being small for gestational age (SGA) in Haifa, Israel (elevation 105ft. or 32m). Louis and colleagues (Louis, Auckley, Sokol, & Mercer, 2010) reported that pregnant women with obstructive sleep apnea residing in Cleveland, Ohio (elevation 653ft. or 199m) had a greater incidence of pre-eclampsia and preterm birth and were more likely to have primary cesarean deliveries for arrest of labor as well as higher rates of elective repeat cesarean births.

Snoring, a category of sleep disordered breathing and a risk factor for IUGR and pre-eclampsia, is common in pregnancy even in women without a history of snoring prior to pregnancy and has been reported to occur in 14% to 35% of pregnant women. Micheli and colleagues (Micheli et al., 2011) examined the association of sleep duration and snoring in late pregnancy with the risk of preterm birth and IUGR in Heraklion, Greece
Women with severe sleep disturbance (less than 5 hours) were at high risk for preterm births and women with severe snoring were at high risk for low birth weight and IUGR neonates. In Bursa, Turkey (elevation 476ft. or 150m) habitual snoring was found to be associated with the development of pre-eclampsia in 10.9% and gestational hypertension in 20% of 469 pregnant women as compared to 5.8% of non-snoring pregnant women (Ursavas, Karadag, Nalci, Ercan, & Gozu, 2008). In Umea, Sweden (elevation 89ft. or 27m), Franklin and colleagues (2000) studied 502 pregnant women and concluded that snoring is a sign of pre-eclampsia and a risk factor for IUGR. They reported that pre-eclampsia occurred in 10% of snorers (compared to 4% for non-snorers) and IUGR occurred in 7% of infants of snoring mothers (compared to 2.6% for the non-snoring mothers).

In Providence, Rhode Island (elevation 6.6ft. or 2m), third trimester pregnant women who snored were found to have an 3.8 times greater likelihood of having an unplanned cesarean birth, 2.4 times greater likelihood of having gestational hypertension or pre-eclampsia, and a 2.1 times greater likelihood of having gestational diabetes (Bourjeily, Raker, Chalhoub, & Miller, 2010). Two recent studies in Chicago (elevation 587ft. or 180m) (Facco, Grobman, Kramer, Ho, & Zee, 2010a; Facco, Kramer, Ho, Zee, & Grobman, 2010b) and in Seattle, Washington (elevation 177ft. or 54m) (Qiu, Enquobahrie, Frederick, Abetew, & Williams, 2010) also concluded that self-reported sleep duration and frequent snoring are associated with development of gestational diabetes mellitus.

Length of labor and type of delivery were associated with sleep during the last month of pregnancy in San Francisco at sea level (Lee & Gay, 2004) and in Tehran, Iran.
at 3900 ft. or 1200m (Zafarghandi et al., 2011; Naghi, Keypour, Ahari, Tavalai, & Khak, 2011). Results showed that sleep quality and quantity were significantly associated with type of delivery and with labor duration.

Strange and colleagues (Strange, Parker, Moore, Strickland, & Bliwise, 2009) did not find any difference in sleep quality and efficiency between preterm and full term birth groups in Atlanta, Georgia (elevation 1050ft. or 320m) but noted longer sleep onset latency in women who delivered preterm. Studies that document preterm labor and preterm birth at higher elevations are scarce. Gonzales, Steenlund, and Tapia (2009) conducted a multi-center analysis of 35,449 pregnancies at low altitude (492 ft. or 150m) and six other cities above 9843 ft. (3000m) in Peru. Proportions of stillbirths, preterm deliveries, and SGA were higher at high altitude than at low altitude.

Intensity and duration of altitude are factors to be considered when examining adverse perinatal outcomes at varying altitudes. Large epidemiologic studies in Colorado have shown that altitude has a direct independent effect on low birth weight through the effects of IUGR/SGA resulting in a 102 gram decrease for every 3300 ft. elevation gain (1000m) that begins in the late second trimester with gestational age decreased by 0.5 weeks (Jensen & Moore, 1997; Unger, Wiser, McCullough, Keefer, & Moore, 1988). Complications during pregnancy or labor and delivery occur more often at high altitude but low birth weight infants born above 9000ft. were more likely to survive (Unger et al., 1988). Long term pregnant residents with multigenerational exposure to high altitudes over 10,000 years, such as the Tibetans and Andeans, exhibit only one-third of the birth weight reduction than residents living at high altitude for fewer generations (less than 500 years) (Haas, 1981; Moore, 2001a). This was not found for high altitude residents in
Colorado living at higher elevations for less than 150 years (Moore, Young, McCullough, Droma, & Zamudio, 2001b).

**Differences in Sleep Parameters between Low and High Elevations**

Sleep characteristics during pregnancy at moderate to high elevations have only been described in two studies of third trimester women by Okun (Okun & Coussons-Read, 2007a; Okun, Hall, & Coussons-Read, 2007b) in Denver, Colorado (elevation 5183ft;1580m) and one study was a subset of the same sample. Adverse perinatal outcomes were not the main focus; however, sleep parameters were identified. Total sleep time ranged from 7.61 to 7.67 hours (refer to Table 1, Question 2). In other studies of healthy third trimester women at sea level, total sleep time ranged from 6.7 (Kennelly, Fallon, Farah, Stuart, & Turner, 2011) to 8.13 hours (Hedman, Pohjasvaara, Tolonen, Suhonen-Malm, & Myllyla, 2002).

Sleep onset latency, which is not a problem for pregnant women at sea level, seems to be more prevalent in adults at higher altitudes. Okun reported an average of 13.2 to 13.8 minutes in her sample at moderate altitude but the sample included multiparous women with children in the home that can impair many aspects of sleep. At sea level, sleep onset latency has been reported to range from an average 13.0 minutes (Lee, Zaffke, & McEnany, 2000) to 39.7 minutes (Mindell & Jacobson, 2000) in healthy third trimester women. Edwards and colleagues (2000) reported 50 minutes to fall asleep in hospitalized pre-eclamptic women taking clonidine which is known to suppress REM sleep but should not affect sleep onset latency.

Sleep quality as a sleep parameter was reported in the Okun studies with the Pittsburgh Sleep Quality Index (PSQI) where a score greater than 5 indicates severe sleep
disturbance. The sample at moderate altitude ranged from an average of 5.6 to 5.79. At sea level PSQI global scores range from an average of 5.26 (Okun, Schetter, & Glynn, 2011) to 6.06 (Tsai, Kuo, Yeur, & Lee, 2011). Okun and colleagues (2011) reported a PSQI global score mean of 7.79 for a subset of third trimester women that all delivered preterm at sea level.

Discussion

Although sleep parameters at sea level and moderate altitudes do not show major differences during the third trimester of pregnancy, there have been only two studies conducted at moderate altitude. The two studies included healthy third trimester women and sample sizes were small. From these studies, it is apparent that third trimester sea-level women with pre-eclampsia have the most prolonged sleep onset latency and women who delivered preterm had the highest PSQI global scores. No data were found in the published literature to compare sleep parameters and perinatal outcomes for women living at altitude with women at sea level.

The link between sleep and adverse perinatal outcomes at all elevations theoretically relates to similar inflammatory processes. The inflammatory pathway is stimulated during pregnancy (elevated CRP, IL-6, & IL-10), the birth process (elevated IL-1, IL-6 and IL-8), and with infections such as chorioamnionitis (TNF, IL-1, IL-6) (Arntzen, Kjollesdal, Halgunset, Vatten, & Austgulen, 1998). Elevated maternal inflammatory cytokines are also associated with sleep disturbance and adverse pregnancy outcomes. Increased TNF-α during the first trimester and decreased anti-inflammatory IL-4 was found in second trimester pregnant women with poorer subjective sleep quality in Denver, Colorado (elevation 5183 ft. or 1580m) (Okun & Coussons-Read, 2007a).
Sleep complaints in the third trimester, as reflected by higher PSQI scores, were associated with an increased circulating serum IL-6 concentration \((r=.56)\) at the same elevation (Okun et al., 2007b). Higher plasma levels of TNF-\(\alpha\) and IL-6 were found in women with pre-eclampsia who also developed snoring during pregnancy in Helsinki, Finland (elevation 85ft. or 26m). They also experienced significantly shorter gestation and lower birth weights than healthy pregnant controls (Bachour, Teramo, Hiilesmaa, & Maasilta, 2008). Snoring, a symptom of sleep disordered breathing, causes increased inflammation through the production of inflammatory cytokines and through hypoxia, which causes oxidative stress and an even greater inflammatory response (Jelic \& LeJemetel, 2008). The process of inflammation related to sleep, pregnancy, and altitude must be explored further to discover the association that may be leading to adverse perinatal outcomes.

**Implications for Practice and Research**

Researchers are beginning to explore sleep parameters during pregnancy that may influence perinatal outcomes. This review of the literature indicates a need for subjective and objective investigation of sleep at higher elevations related to perinatal morbidity with a focus on sleep disordered breathing and inflammatory markers. As research continues into how sleep is related to maternal and fetal outcomes at all altitudes, further knowledge will move us closer to interventions to improve birth outcomes for this very vulnerable population.

**Conclusion**

The studies reported in this review of the literature represent the current state of knowledge in regard to adverse perinatal outcomes associated with sleep at altitude.
Hypobaric hypoxia is inevitable with increasing altitude. Diminished sleep quality, greater fragmentation and decreased duration of sleep during pregnancy are consistently observed at sea level compared to non-pregnant controls. Pregnancy at sea level has distinct physiologic challenges that become even more critical to consider at increased elevation because of inflammatory cytokine processes, hypobaric hypoxia, and potential for growth restriction and low birth weight infants.

At higher elevations there is an increased prevalence of hypertensive disorders during pregnancy, which has been associated with sleep disordered breathing. Sleep disordered breathing has been associated with adverse perinatal outcomes. Elevated maternal inflammatory cytokines are also associated with sleep disturbance and adverse pregnancy outcomes. Periodic breathing and increased sleep fragmentation is common among healthy adults at higher altitudes. The potential combination of these factors for pregnant women living or visiting higher altitudes, especially in their third trimester, may further disturb maternal sleep parameters and lead to an increased risk for adverse perinatal outcomes.
Chapter 3
Pregnancy Sleep Disturbance Characteristics at Sea Level
and Moderate Altitude

Abstract

**Objective:** To compare subjective characteristics of sleep during late pregnancy at moderate altitude and sea level.

**Design:** Prospective descriptive comparison

**Setting:** The sea level group was located in the San Francisco Bay area and the moderate altitude group was in the Flagstaff, Arizona area (elevation 6910 feet or 2106 meters).

**Participants:** Nulliparous women during the last five weeks of pregnancy at sea level (n=126) and moderate altitude (n=50) were recruited through childbirth education classes, community clinics, physician offices and hospital prenatal pre-admission appointments.

**Methods:** Pittsburgh Sleep Quality Index (PSQI) and a 3-day sleep diary were utilized to gather data. Independent samples t-tests were used to compare the two altitude groups, and analysis of covariance (ANCOVA) were used to control for education in the analyses for sleep differences between groups.

**Results:** Compared to first-time pregnant women at sea level, women at altitude reported similar amounts of time in bed (9 hours) in the third trimester, a similar sleep onset latency (24 minutes), similar total sleep time (7.2 hours), and similar sleep quality. However, women living at altitude had significantly higher sleep disturbance scores on the PSQI (component 5) compared to their counterparts living at sea level.
Conclusion: Poor sleep quality and severe sleep disturbance was observed for women at both elevations. However, women in their third trimester living at moderate altitude perceived their sleep to be even more disturbed compared to women at sea level. Additional sleep studies need to be conducted at higher elevations to replicate and expand on these findings and assess sleep at altitude with objective measures for comparisons with women living at sea level and other altitudes.

Keywords: sleep, pregnancy, altitude, sleep disturbance
Introduction

Sleep disturbance is a common complaint during pregnancy even in women who have never had problems sleeping. According to the National Sleep Foundation’s 2007 *Women and Sleep* poll, 84% of pregnant women reported that they experience disturbed sleep at least a few days each week (National Sleep Foundation, 2012). What constitutes normal sleep during pregnancy is not known but sleep disturbance is most common during the third trimester of pregnancy. Diminished sleep quality, greater fragmentation and decreased duration of sleep during pregnancy at sea level are consistently observed (Baratte-Beebe & Lee, 1999; Beebe & Lee, 2007; Facco, Kramer, Ho, Zee, & Grobman, 2010a; Mindell & Jacobsen, 2000; Tsai, Kuo, Lai, and Lee, 2011). Pregnancy at altitude can affect perinatal outcomes and has been correlated with duration and intensity of altitude. Sleep during pregnancy while living at altitude has not been studied.

Pregnancy sleep disturbance at any elevation can include physiologic, psychological, and environmental origins. Physiologic reasons include general discomfort, fatigue, urinary frequency, leg cramps, nausea, backaches, fetal movements, heartburn, and shortness of breath. Psychological reasons for sleep disturbance include anxiety, restlessness, dreams, and nightmares. Environmental reasons are attributed to noise, co-sleeper disturbance, child awakenings, and altitude.

Altitude, as an environmental factor, has been shown to alter sleep in healthy non-pregnant adults at various levels of elevation. Even at moderate altitude that ranges from 4553 feet (1388m) to 8858 ft (2700m), hypobaric hypoxia places stress on physiologic parameters. The body adapts through functional and structural changes that
accommodate for the reduced oxygen in the air. As adaption to hypoxia occurs, there is polycythemia, a decline in blood and plasma volume, and an increase in pulmonary ventilation by sensitization to carbon dioxide. Acclimatization takes place in stages that occur over a period of days to months but can take up to a year or more with wide individual variation (Dill, 1968). Altitudes over 4500 meters (14,764 ft) have been shown to affect sleep quality in healthy adult male and female climbers (Szymczak et al., 2009). The studies of the effect of higher altitudes on pregnant women indicate an impact on perinatal outcomes that include preeclampsia, preterm birth, and impairment of fetal growth (Palmer et al., 1999; Julian, 2011). A study of Colorado pregnant women, living at elevations ranging from 3,000 to 11,000 feet, demonstrated that for every 3300 feet (1000m) elevation gain, birthweight declined an average of 102 grams, independent of all other factors (Jensen & Moore, 1997).

**Methods**

**Design and Sample**

Data were collected during prospective descriptive and observational studies that were approved by the University of California San Francisco Committee on Human Research. The moderate altitude study was also approved by the Northern Arizona Healthcare Institutional Review Board. Both were convenience samples of pregnant nulliparous women recruited through community clinics, childbirth education classes, physician offices and hospital prenatal pre-admission appointments. The participants at moderate altitude were recruited over a 6-month period between February and July 2011 in Flagstaff, Arizona and the sea level sample were a part of a larger randomized clinical trial recruited from 2004-2008 in the San Francisco Bay Area. For both samples,
inclusion criteria included age ≥ 18 years, healthy, singleton pregnancy, and able to read and write English. Exclusion criteria for both groups included working the night shift, planning a cesarean birth, having a diagnosed sleep disorder or a history of previous pregnancy loss. The altitude participants were also excluded if they had not lived at moderate altitude for at least 12 months with altitude determined by home zip code.

Informed consent was obtained for all participants in both groups. All study booklets were completed after the 35th gestational week and before the final week of pregnancy in both groups. Participants in both groups were contacted by phone between two to four weeks post-delivery to collect information about their birth experience and all participants from both cohorts were paid for their participation.

**Sleep-Related Measures**

Questionnaire booklets contained both the Pittsburgh Sleep Quality Index (PSQI) and a 3-day sleep diary. The sleep diary was used to collect data on subjective aspects of sleep over 72 hours and was completed at bedtime and morning for three consecutive days. It consisted of nine evening items and 16 morning items that asked about activity, diet, bed times, wake times, sleep latency, mid-sleep awakenings, and perception of sleep. The two diary variables included for this study were completed each morning and asked for estimated minutes to fall asleep and a rating of sleep quality on a scale of 1 (very poor quality of sleep) to 5 (very good sleep quality). The values for all three days were averaged for each participant and included in the analyses for group comparisons.

The Pittsburgh Sleep Quality Index (PSQI) was used to measure subjective dimensions of sleep quality over the previous month. It has 19 items with four additional open-ended questions regarding habitual bed time, wake time, sleep latency, and hours of
sleep. Within the 19-item tool, there are 9 questions about what specifically disturbs
sleep during the night, and the total score on this component can range from 0 to 27. As
part of computing the overall PSQI sleep quality score, there are seven component scores
obtained from recoded 0 to 3 scales, with zero signifying no sleep problem and 3
indicating a severe sleep problem within that component. The component scores are
added together to create a global score that ranges from 0 to 21. A PSQI global score
greater than 5 indicates a severe sleep disturbance (poor quality) in two or more
components or moderate sleep disturbance in three components yielding a diagnostic
sensitivity and specificity of 89.6% and 86.5% respectively, when compared with a
combination of clinical interviews and polysomnographic measures (Buysse, Reynolds,
Monk, Berman, & Kupfer, 1989). The Cronbach alpha coefficient for the 7-component
PSQI was .77 for the sample living at altitude and .70 for the sample living at sea level.

There were six variables from the PSQI used for analyses to compare the two
groups: 1) time in bed, computed in hours from self-reported bedtime and wake time; 2)
total hours of sleep; 3) minutes to fall asleep; 4) habitual sleep efficiency index
(calculated from the number of hours slept divided by the number of hours spent in bed
then multiplying the result by 100); 5) the total score from the 9-item sleep disturbance
subscale; 6) the global PSQI sleep quality index score that can range from 0 to 21, with
greater than 5 indicating severe sleep disturbance.

**Statistical Analyses**

All data were analyzed using SPSS for Windows (SPSS Inc., Chicago, Illinois)
version 18. Descriptive statistics and unpaired t-tests were used to compare the two
samples. Analysis of covariance (ANCOVA) was used to control for any altitude group
differences in potential demographic variables related to sleep. A two-tailed $p$ value of <.05 was considered statistically significant.

**Results**

For the sample at moderate altitude, 66 women were screened and 9 were ineligible due to reasons that included planning relocation to a lower altitude during pregnancy, twin gestation, not living at moderate altitude for at least 12 months, being less than 18 years old, diagnosed with insomnia and working the night shift. One mother enrolled in the study but did not complete her sleep booklet prior to a preterm delivery. Of the remaining 56 pregnant women, five had scheduled cesarean births and one did not complete her sleep booklet prior to labor. The final analyses were based on the results of 50 nulliparous women who had complete self-report data. The sea level sample screened 222 women and enrolled 152 women but 17 were excluded from analysis for insufficient data, four had scheduled cesarean births and delivered before onset of labor, and five did not fit the time frame for gestation greater than 35 weeks. The final analyses for the sea level sample included 126 nulliparous women.

As seen in Table 2, the mean age of the 50 participants at moderate altitude was $27 \pm 6.2$ years and the mean age for the 126 sea level participants was $26 \pm 6.6$ years. There were no significant differences between the two groups on age, body mass index, or gestation weeks when sleep data were collected (23-24 days prior to actual birth).

Ethnicity for the sample living at moderate altitude was 60% Caucasian and more varied at sea level (refer to Table 2). At moderate altitude 50% were college-educated and 80% were employed at the time of enrollment compared to 31% college-educated at sea level and 37% employed at the time of enrollment. Annual household income below
$36,000 was prevalent at sea level (86%) compared to 60% at moderate altitude. There was an expected difference in infant birth weight, with sea level infants weighing more at birth than infants at altitude (refer to Table 2). There was a significant difference in mean gestational weeks at time of delivery between sea level (40.1 ± 1.1) and moderate altitude (39.5 ± 1.1) ($t$ [174] = 3.55, $p < .001$) with a range for both groups of 37-42 gestational weeks. There were also significant differences between the two altitude groups for ethnicity/race, income, employment, and education. However, education was the only variable with trends in associations with the sleep outcome variables. The only significant association was between total sleep time reported for the women with a college degree (n = 63) having less sleep (6.9 ± 1.32 hours) compared to the sample with no college degree (n= 112) who averaged 7.4 ± 1.55 hours sleep ($t$=2.1, $p = .04$). Therefore, education (college/no college degree) was included as a covariate for sleep comparisons between altitude groups.

An independent sample t-test was conducted to compare all sleep variables between the groups at sea level and moderate altitude (refer to Table 3). While most sleep variables trended in the same direction for being worse for women at moderate altitude, the only variable that was significantly different between the two altitude groups was the PSQI sleep disturbance 0-27 scale that comprises Component 5 ($t$ [174] = -1.983, $p = .049$). The group at sea level averaged 12 ± 4.8 and the group at moderate altitude averaged 14 ± 3.7. The magnitude of the difference in the means (mean difference = -1.486, 95% CI: -2.966 to -.007) was small (partial eta-squared = .02). Despite reporting a slightly longer mean time in bed, the moderate altitude participants had a trend toward less total sleep time. This is reflected in the habitual sleep efficiency scores (HSE) which
were lower for moderate altitude (78%) than for sea level (82%). HSE is calculated by dividing the number of hours slept (TST) by the number of hours in bed (TIB). Less than 85% sleep efficiency is considered poor sleep, particularly in one’s own home environment without invasive monitoring protocols, and this was found at both elevations.

A one-way between-groups analysis of covariance (ANCOVA) was conducted to compare characteristics for the women in late pregnancy at sea level and moderate altitude. In these analyses, the dependent variables consisted of the sleep parameters and the independent variable was altitude. Although the two groups differed significantly on race/ethnicity, education, employment, and income, these variables were confounded with each other and only education itself was associated with the sleep outcomes variables. Therefore, education was then examined as a covariate using ANCOVA. Even after controlling for education, the PSQI sleep disturbance (component 5) score was the only sleep parameter that differed between sea level and altitude participants ($F[1,173] = 5.28, p = .023, \text{partial eta squared} = .030$). There were no group differences in self-report measures using either 3-day diary estimates of sleep onset latency or sleep quality, or using PSQI data for time in bed, total sleep time, sleep onset latency, or overall sleep quality. Habitual sleep efficiency (PSQI) trended in a similar direction, but did not reach statistical significance either before or after controlling for education.

**Discussion**

At sea level, diminished sleep quality, greater sleep fragmentation and decreased duration of sleep during pregnancy are consistently reported. Fragmented sleep is a part of the PSQI sleep disturbance (Component 5) score obtained from nine questions related
to waking during the night, having to get up to urinate, and physiologic discomforts with a range of 0 (indicates not during the past month) to 3 (three or more times a week over the last month). Scores on the PSQI Component 5 differed by women’s level of education and even after controlling for education, there was a significant difference between the seal level participants and moderate altitude participants during their third trimester with higher scores indicating greater perception of sleep disturbance among the women at moderate altitude at a similar point during their pregnancy. After controlling for the effects of education, approximately 3% of the total variance in the PSQI sleep disturbance scores was explained by difference in altitude between the groups.

Poor sleep quality and greater sleep disturbance was common in both groups in this study as evidenced by the mean PSQI global score of 6.94 for sea level participants as compared to 7.64 for the moderate altitude cohort. A PSQI global score greater than 5 indicates poor sleep quality and was evident in 65% of the women at sea level and 64% at moderate altitude. The PSQI score reflects sleep quality over the previous month but as all participants completed their sleep questionnaires and diary after achieving their 35th gestational week of pregnancy and before the last week of pregnancy, these sleep quality findings are only generalizable to women in late pregnancy. The difference in sleep disturbance scores between the two altitude groups was an effect size of .33 standard deviation units, and this was statistically significant in our sample. Despite reporting a longer mean time in bed, the moderate altitude participants had a trend toward less total sleep time. This is reflected in the habitual sleep efficiency scores (HSE) which were lower for moderate altitude (78%) than for sea level (82%). HSE is calculated by dividing the number of hours slept (TST) by the number of hours in bed (TIB). Less than
85% sleep efficiency is considered poor sleep, particularly in one’s own home environment without invasive monitoring protocols, and this was found at both elevations. The difference in habitual sleep efficiency between the two altitude groups was an effect size of 0.29 standard deviation units, and did not reach statistical significance given our small sample size.

It would be important to replicate these findings in a larger sample, but it would also be important to consider using objective measures of sleep parameters in addition to self-report measures and to examine more closely the reasons for awakening and whether these reasons might differ by altitude.

**Implications for Practice**

Since poor quality sleep was evident at both sea level and moderate altitude during late pregnancy, obstetrical health care providers should advise women in late pregnancy to practice healthy sleep hygiene measures that include minimal stimulation prior to bedtime and making sleep a priority in her daily life in preparation for childbirth.

**Conclusion**

This is the first study that has explored late pregnancy sleep characteristics at moderate altitude. In this sample, PSQI sleep disturbance (Component 5) scores were significantly higher for women at moderate altitude compared to women at sea level. After controlling for the effects of education, approximately 3% of the total variance in the PSQI sleep disturbance scores was explained by the difference in elevation. PSQI global scores of greater than 5 were found at both elevations indicating poor sleep quality for all women in late pregnancy, regardless of altitude. Additional research needs to be
conducted at higher elevations to expand on these findings and include objective
measures of sleep onset latency and fragmented sleep during the night.
Chapter 4

Does Pregnancy Sleep Disturbance at Moderate Altitude Predict Length of Labor or Mode of Delivery?

Abstract

Objective: To test the hypothesis that self-reported sleep disturbance in late pregnancy is predictive of labor duration and mode of delivery at moderate altitude.

Design: Prospective, descriptive

Setting: Flagstaff, Arizona area at elevation 6910 feet (2106 meters).

Participants: Nulliparous women (n=50) at moderate altitude recruited through childbirth education classes, community clinics, physician offices and hospital prenatal pre-admission appointments.

Methods: Measures at 35-39 gestational weeks included demographic data, a 3-day sleep diary and Pittsburgh Sleep Quality Index (PSQI). Follow-up measures included self-report of labor, electronic medical record report of labor duration, and delivery experience.

Results: After controlling for infant birth weight (beta .315, R²= 8.0%, p<.05), length of labor was associated with the PSQI self-report measure for sleep onset latency (beta .593, R²= 21.7%, p<.001). Together, infant birth weight, maternal weight, age, income, and sleep onset latency, hours of sleep, and sleep quality accounted for 51.6% of the variance in length of labor. Mode of delivery was also associated with sleep disturbance.

Conclusion: For women living at moderate altitude, the aspect of sleep during late pregnancy that was most associated with length of labor was sleep onset latency.
Keywords: sleep, pregnancy, altitude, sleep disturbance, Pittsburgh Sleep Quality Index
Introduction

Sleep disturbance during late pregnancy is so commonly reported that it prompted the recognition of Pregnancy-Associated Sleep Disorder as a distinct entity in the revised International Classification of Sleep Disorders (American Academy of Sleep Medicine, 2001). Pregnancy sleep disturbance has been studied extensively both objectively and subjectively and diminished sleep quality, frequent mid-sleep awakenings, and decreased duration of sleep are consistently observed during the last trimester of pregnancy (Lee, Zaffke, & McEnany, 2000; Facco, Kramer, Ho, Zee, & Grobman, 2010a; Mindell & Jacobsen, 2000). Normal sleep for healthy adults consists of falling asleep (sleep onset latency) within five to ten minutes of turning out the light, sleeping seven to eight hours, and waking refreshed (Lee, 2003). Sleep onset latency has been significantly associated with diminished sleep quality and various parameters of sleep disturbance (Tsai, Kuo, Lai, & Lee, 2011). Sleep disturbance was associated with prolonged labor in women at sea level (Lee & Gay, 2004), however, length of labor was a self-report measure and no data on maternal weight was obtained in that study. Findings have been replicated in Tehran, Iran at 3900 feet elevation (Zafarghandi et al., 2011; Naghi, Keypour, Ahari, & Khak, 2011). These studies did not adequately control for mother’s weight or parity, or used data from medical records and sleep measures with questionable validity.

Sleep disturbance at higher altitudes has been studied however, pregnant women have been excluded from these studies. Pregnancy outcomes at extremely high altitudes in the Andes or Himalayan Mountains have been studied. Pregnant women at high altitude show negative perinatal outcomes related to the duration and intensity of the elevation (Gonzales, Steenlund, & Tapiz, 2009; Julian, Krampl, & Moore, 2009; Krampl,
The most common adverse perinatal outcomes include pre-eclampsia, intrauterine growth restriction, and lower birth weight related to chronic hypoxia, decreased blood flow, hyperviscosity, and altered placental morphology as part of adaptation to altitude (Kametas, Krampl, McAuliffe, Rampling, & Nicolaides, 2004a; Krampl et al., 2000; Moore, Young, McCullough, Droma, & Zamudio, 2001).

Adult sleep at higher elevations has been studied, mostly in men during treks to very high altitudes (Johnson, Edwards, Burgess, & Sullivan, 2010; Szymcak et al., 2009; Weil, 2004; Zielinski et al., 2000). Physiologic adaptation to altitude varies by duration and intensity and can take up to 12 months. Adults complain of restless interrupted sleep despite total sleep time being unaltered (Dill, 1968). After arriving at higher elevations, nightmares and multiple awakenings are common. Sleep becomes more fragmented due to periodic breathing at altitude (Salvaggio et al., 1998). The level at which arterial oxygenation saturation falls below 90% is approximately 5800 feet (1768 meters) for visitors or 8400 feet (2439 meters) for permanent residents (Moore, 1987; Weil, 2004).

An estimated 140 million people are permanent residents at higher elevations worldwide and as many as 34 million people visit high elevation destinations each year. Since air travel also exposes people to simulated moderate altitudes with airplane cabins pressurized to an altitude of 8202 feet or 2500 meters (Kametas, McAuliffe, Krampl, Chambers, & Nicolaides, 2004b), the American College of Obstetrics and Gynecology recommends restricted international air travel for pregnant women after 35 gestational weeks or domestic air travel after 36 gestational weeks (American College of Obstetrics & Gynecology, 2001).
This purpose of this study was to replicate findings previously reported a sea level and test the hypothesis that sleep at moderate altitude (6910 feet; 2106 meters) is predictive of labor duration and mode of delivery (cesarean or vaginal) after controlling for mother’s weight, income, age, and infant’s birth weight. Although specific definitions of altitude vary, moderate altitude is considered to be from 4553 feet (1388 meters) to 8858 feet (2700 meters)(Hankins et al., 1996; Moore, 1987; Zamudio, 2007).

**Materials and Methods**

**Design and Sample**

This prospective, descriptive study was approved by the University of California San Francisco Committee on Human Research and the Northern Arizona Healthcare Institutional Review Board. A convenience sample of pregnant nulliparous women were recruited through childbirth education classes, community clinics, physician offices and hospital prenatal pre-admission appointments over a 6-month period between February and July 2011 in Flagstaff, Arizona. Initial screening was conducted either in person or during a phone call with explanation of the study purpose and procedures. Inclusion criteria included age ≥ 18 years, healthy, able to read and write English, singleton pregnancy, planning to deliver in Flagstaff, Arizona and at least 32 gestational weeks at time of enrollment. Exclusion criteria included working the night shift, diagnosed sleep disorder, history of previous pregnancy loss, currently having labor contractions, planning a scheduled cesarean birth, or living at moderate altitude for less than 12 months. Altitude was determined by home zip code.

Once eligibility was established, an enrollment appointment was scheduled at about 35 gestational weeks. Table 4 depicts the demographic and clinical characteristics
of the sample. Height and pre-pregnancy weight were used to calculate body mass index (BMI). Informed consent, that included permission to access their medical record, was signed by participants at this appointment and a sleep booklet that contained a 3-day sleep diary and the PSQI was distributed. Instructions were given to start the 3-day sleep diary and complete the questionnaires after 35 gestational weeks with a reminder phone call offered. The sleep booklet was returned in a pre-addressed stamped envelope that was provided. All participants were contacted between two to four weeks post-delivery to collect information about their birth experience that included duration of labor, mode of delivery, maternal weight at delivery, and infant’s birthweight. Length of labor was defined as the time from onset of regular contractions that were painful until delivery. Electronic medical record length of labor was obtained through the hospital computer system. All women were paid for their participation. All eligibility screening, enrollment appointments, informed consent, and follow-up phone calls were conducted by the same researcher.

**Measures**

The 3-day sleep diary measured subjective aspects of sleep over 72 hours and was completed at each bedtime and each morning for three nights. It consisted of nine evening items and 16 morning items that described activity, diet, bed times, wake times, sleep latency, mid-sleep awakenings, and perception of sleep.

The Pittsburgh Sleep Quality Index (PSQI) was used to measure subjective dimensions of sleep over the previous month. It has 19 multiple-choice items with four additional open-ended questions regarding habitual bed time, wake time, sleep latency, and hours of sleep. Seven component scores were calculated into scales of 0-3 with zero
signifying no sleep disturbance and 3 indicating severe sleep disturbances. The component scores were added together to create a global score that ranged from 0-21. A PSQI global score of > 5 indicates a severe sleep disturbance in two or more component areas or moderate sleep disturbance in three areas yielding a diagnostic sensitivity and specificity of 89.6% and 86.5% respectively, when compared with a combination of clinical interviews and polysomnographic measures (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The Cronbach alpha coefficient for the current study sample was .77 for the 7-component PSQI global score.

All data were analyzed using SPSS software program version 18 for Windows (SPSS Inc., Chicago, Illinois). Pearson product-moment correlation coefficient, multiple regression and logistic regression were used for statistical analysis. A p value of < .05 was considered statistically significant.

Results

For this sample, 66 women were screened and 9 were ineligible due to reasons that included planning relocation to a lower altitude during pregnancy, twin gestation, not living at moderate altitude for at least 12 months, being less than 18 years old, to diagnosed with insomnia or working the night shift. One mother enrolled in the study but did not complete her sleep booklet prior to a preterm delivery. Of the remaining 56 pregnant women, six had cesarean births prior to labor or scheduled due to breech presentation, fetal distress, or maternal complications. The final analyses were based on the results of 50 women who had complete self-report data. Medical records data for length of labor was not available for four women; three had home deliveries and one had hospital data not retrievable.
The mean age of the 50 participants was 27.10 ± 6.2 years. The sample was 60% Caucasian, 50% percent college educated, 80% employed at the time of enrollment, and 60% had an annual household income of less than $36,000 (refer to Table 4). The majority of infants were born full term with delivery occurring at a mean of 39.5 ± 1.1 gestational weeks with a range of 37-42 gestational weeks. Self-reported length of labor ranged from 0 hours to 42 hours ($M = 12.9$, $SD ± 7.18$). Sleep onset latency from the item on the PSQI ranged from 5 minutes to 105 minutes ($M = 23.8$, $SD ± 21.57$) and PSQI sleep hours ranged from 2.5 hours to 10 hours ($M = 7.14$, $SD ± 1.55$). PSQI sleep quality (component #1) and sleep disturbance (component #5) were recoded from 0 (good sleep) to 3 (poor sleep) for the purpose of computing an overall PSQI 7-category sleep quality index score than can range from 0 to 21.

Length of labor did not significantly differ between self-report ($M = 13.3 ± 7.35$ hours) and medical record ($M = 11.7 ± 5.73$ hours), ($t [46] = 1.35$, $p = .183$) and values were significantly correlated ($r = .43$, $p = .003$). There was also no significant difference between sleep onset latency (SOL) for the diary mean of three nights ($M = 27.4 ± 26.12$ minutes) and PSQI minutes to fall asleep ($M = 23.8 ± 21.58$ minutes), ($t [50] = 1.72$, $p = .091$) and these values were significantly correlated ($r = .83$, $p < .001$).

The relationship between measurements of sleep disturbance and self-reported length of labor was investigated using Pearson product-moment correlation coefficient. Preliminary analyses were performed to ensure no violation of the assumptions of normality, linearity, and homoscedasticity. In this sample, there was a significant correlation between self-reported length of labor and the number of minutes to fall asleep
(r = .58, n = 50, p < .001). There was also a significant correlation between self-reported length of labor and infant birth weight (r = .33, n = 50, p < .01).

Hierarchical multiple regression was used to predict self-reported length of labor from the four sleep measures on the PSQI (sleep onset latency, hours of sleep, subjective sleep quality, and sleep disturbance) after controlling for infant birth weight, maternal income, age, BMI prior to pregnancy and BMI difference between pre-pregnancy and delivery. Maternal age, BMI prior to pregnancy, and income were entered in Step 1, explaining 12.7%, (F (3, 46) = 2.23, p = .098) of the variance in self-reported length of labor (refer to Table 2). After entering BMI difference and infant birth weight in Step 2, the total explained variance in self-reported length of labor was 26.2%, (F (5, 44) = 3.13, p < .017). In Step 3, the four sleep measures were entered and accounted for an additional 25.4% of the total explained variance in self-reported length of labor. After controlling for infant birth weight, maternal age, income, maternal BMI prior to pregnancy, and maternal BMI at delivery, the final model explained 51.6% (F (9, 40) = 4.74, p < .001) of the total variance in self-reported length of labor. Minutes to fall asleep (β = .593) and infant birth weight (β = .315) were statistically significant in the final model.

In this sample, for each one minute increase in sleep onset latency, the length of labor increased by .20 hours, holding the other eight variables constant. On average, for each additional minute it took to fall asleep, the length of labor increased by approximately 12 minutes for these pregnant women living at moderate altitude. For the women who reported falling asleep within 10 minutes, mean self-reported length of labor was 9 hours ± 4.4 hours. For the women who reported falling asleep in 10-20 minutes, length of labor was 13.4 ± 6.2 hours. Self-reported length of labor was 14.8 ± 4.8 hours
for women who reported falling asleep in 20-30 minutes. For the women who reported taking over 30 minutes to fall asleep, mean self-reported length of labor was 17.9 ± 10.3 hours.

For the women who reported getting less than 6 hours of sleep, the mean length of labor was 15.3 ± 13.1 hours. The mean length of labor was 14.7 ± 6.4 hours for the women who reported getting between 6 - 6.9 hours of sleep. For women in this sample who slept more than 7 hours, the mean length of labor was 12 ± 5.1 hours.

Logistic regression was utilized to predict mode of delivery from the same four sleep measures on the PSQI (sleep onset latency, hours of sleep, subjective sleep quality, and sleep disturbance) after controlling for infant birth weight, maternal income, age, BMI prior to pregnancy, and BMI difference between pre-pregnancy and delivery. The full model containing the predictors was not statistically significant, $X^2 (8, N = 50) = 4.161, \ p = .842$, indicating that self-reported sleep variables were not able to distinguish between women who had cesarean births from those who had a vaginal birth. The model as a whole explained between 13.8 and 21.9% of the variance in mode of delivery, and correctly classified 82% of cases. However, none of the independent sleep variables made a unique statistically significant contribution to the model after controlling for infant birth weight and maternal weight.

In this sample, of pregnant women living at altitude, nine women reported getting an average of less than 6 hours of sleep per night during their last month of pregnancy, and three had a cesarean birth (33.3%). There were five women who reported getting between 6 - 6.9 hours of sleep per night but none had cesarean births. Finally, of the 36
women who reported sleeping 7 hours or more per night, seven (19.4%) delivered by cesarean.

**Discussion**

In this study there was a correlation between self-reported length of labor and the PSQI global score \( r = .282, p < .05 \) as well as PSQI SOL \( r = .577, p < .001 \). An interesting finding is that 64% of this sample of pregnant women in late pregnancy had a PSQI global > 5. At lower altitudes, Facco et al.(2010a) reported that 53.5% of their sample of nulliparas (n= 189) located in Chicago (elevation 583 feet or 177 meters) had a PSQI > 5 in third trimester which became more common as pregnancy progressed compared to 39% at 6-20 gestational weeks. Lee and Gay (2004) had a PSQI global score of > 5 in 59.5% of their nulliparous sample from San Francisco (elevation 131 feet or 39 meters) and Tsai and colleagues (2011) reported that 50% of their sample of 30 nulliparas in Taipei, Taiwan (elevation 30 feet or 9.14 meters) had a PSQI > 5. At an elevation of 3900 feet (1200 meters) in Tehran, Iran, Naghi et al. (2011) reported 43.8% of primiparas and multiparas in their last trimester had a PSQI > 5.

The PSQI sleep onset latency was strongly predictive of length of labor even after controlling for known clinical characteristics such as maternal BMI and infant’s birth weight. Sleep onset latency is measured as the minutes it takes to fall asleep with greater than 30 minutes indicating insomnia. The PSQI mean sleep latency was 23.8 ± 21.58 minutes, the PSQI global score mean 7.6 ± 3.8, and PSQI habitual sleep efficiency was 78% ± 15.65%. Tsai and colleagues (2011) reported a PSQI sleep latency of 24 ± 22.0, PSQI global score mean of 6.06 ± 3.10, and PSQI habitual sleep efficiency of 86.6% ±
11.0% in their sample at sea level. This indicates that sleep efficiency was lower, and overall sleep quality, was worse in our sample at moderate altitude.

Birth weight was also found to be predictive of self-reported length of labor in this study. For every SD unit increase in infant birth weight (SD= 444 gms), self-reported length of labor (SD= 7.35 hours) increased by .315 SD units. In this sample, each additional pound of infant birth weight increased labor by 2.32 hours. Although birth weight has long been known to effect labor and delivery it has special significance at altitude. Jenson & Moore (1997) conducted a retrospective cohort study of an altitude-stratified random sample of 3836 Colorado birth certificates from 1989-1991 to examine whether the decline in birth weight with increasing altitude was due to an independent effect of altitude or an exacerbation of other risk factors that included gestational age, maternal weight gain, parity, smoking, number of prenatal visits, and hypertension. None of the characteristics related to birth weight interacted with the effect of altitude and birth weight declined 102 grams for every 3300 feet (1000 meters) in elevation gain. The mean weight of the newborns in this study at 6910 feet elevation was 3231 ± 444 grams. Naghi reported the mean newborn birth weight of their 488 participants at 3900 feet to be 3284 ± 439 grams. Lee and Gay (2004) reported a mean birth weight of 3543 ± 513 grams at sea level, which also correlated with length of labor (r = .32, p< .01).

With no significant difference between self-reported length of labor and electronic medical record length of labor, this sample of pregnant women at moderate altitude demonstrated an accurate recall of labor length that correlated with the medical record. All study participants were advised to specifically define the beginning of labor as the onset of regular contractions that were painful. This eliminated potential outliers due to
contractions that did not produce cervical dilation. There was also a high correlation between sleep onset latency (SOL) in the diary over three nights and the PSQI minutes to fall asleep considering the past month.

As self-reported total sleep time increased, there were fewer cesarean births but it was not statistically significant in this small sample. This finding replicates the results reported by Lee & Gay (2004) in their study of sleep predicting length of labor and type of delivery in their sample of 131 nulliparous women living at sea level. They reported cesarean rates of 36.8%, 34.2%, and 10.8% for participants who had less than 6, 6-6.9 and ≥ 7 hours of sleep per night, respectively. This sample living at altitude had cesarean rates of 33.3%, 0%, and 19.4%, respectively.

In the logistic regression for mode of delivery, maternal BMI prior to delivery \( (p = .144) \), PSQI sleep quality \( (p = .149) \), and maternal age \( (p = .133) \) approached statistical significance. Maternal BMI prior to delivery was higher for mothers who had cesarean births \( (M = 27.3, N = 10) \) than for mothers who had vaginal deliveries \( (M = 24.9, N = 40) \). A power analysis revealed that to achieve 80% power, with a .05 two-sided significance level, 155 participants would have been required to show statistical significance. Within this sample, there was a non-significant trend for an increase in cesarean births with an increase in maternal BMI prior to delivery and maternal age, and with a decrease in PSQI sleep quality.

**Limitations**

This study has some limitations to consider. The sample size was small with 50 participants and most of the data were based on subjective reports. Although three participants in this study reported 0-3 hours of labor, their electronic medical records
showed between 4 to 19 hours of labor. Participants were instructed to consider labor to start when the contractions were regular and painful but the experience of pain during labor is very individual. Sleep diaries were completed each evening and morning but the PSQI was a retrospective recall over the last month. The use of self-report data to study sleep during pregnancy are common and the various tools have been shown to be valid and reliable. Reporting errors that may occur during completion of these types of questionnaires are likely to be the same across study participants. The sample size was small and was not randomly selected but data were collected prior to onset of labor. Conducting a study in late pregnancy can be complicated by health issues that develop during the 40 weeks of gestation. Unlike other studies that explored the relationship between sleep and labor in which all participants in late pregnancy were healthy (Lee & Gay, 2004), this study had four participants with pregnancy complications of hypertension or gestational diabetes that developed after enrolling in the study.

**Conclusion**

This is the first study that has explored pregnancy sleep at moderate altitude which has unique influences on prenatal sleep. In this sample, sleep latency and infant birth weight were predictors of self-reported length of labor at moderate altitude. As research develops into how sleep is related to maternal and fetal outcomes at all altitudes, new discoveries will move us closer to interventions and treatment for this very vulnerable population.
Chapter 5: Synthesis and Conclusions

The effects of altitude on sleep during late pregnancy have been mostly unknown. The focus of this dissertation is to offer original research on pregnancy sleep at moderate altitude and to utilize the data to describe characteristics of sleep during late pregnancy through comparison to a similar sample at sea level, and to explore associations between late pregnancy sleep at moderate altitude with perinatal outcomes. Prior to preparing the dissertation proposal and conducting research, a review of the literature was completed.

Review of the Literature

An extensive literature search was conducted on the topics of pregnancy sleep related to perinatal outcomes, pregnancy at altitude and sleep at altitude. Literature confirms that the progressive severe sleep disruption and fragmentation during pregnancy combined with a progressive decrease in the quality and quantity of sleep may tip the balance and create harm to both mother and fetus. Research has shown that sleep disturbance during pregnancy is associated with pre-eclampsia, intrauterine growth restriction (IUGR), small for gestational age newborns (SGA), preterm labor, preterm birth, length of labor, and mode of delivery. The physiologic plausibility for the association between sleep disturbance and adverse perinatal outcomes points to changes in hormones, metabolic processes and insulin resistance but more specifically to the association between sleep duration and sleep disordered breathing with inflammatory cytokines and oxidative stress markers. The only two publications that were found that studied late pregnancy sleep at moderate altitude examined sleep disruption and disturbance in late pregnancy in relation to inflammatory pathways and pregnancy complications (Okun & Coussons-Read, 2007a; Okun, Hall, & Coussons-Read, 2007b).
The relationship with altitude was not the focus of the research but it did occur in Denver, Colorado (elevation 5183 feet [ft.] or 1580 meters [m]). Circulating cytokines and systemic inflammation were associated with altered sleep during pregnancy but it is unclear whether their presence alters sleep or they are produced by the altered sleep. The intermittent hypoxia of sleep disordered breathing, which is progressive in pregnancy, also plays a significant role in the cycle of systemic inflammation. Hypoxia leads to oxidative stress that can intensify inflammatory pathways. Hypoxia is accentuated with increasing altitude.

The literature search on pregnancy and altitude revealed that the chronic hypoxia of high altitude plays a significant role in perinatal outcomes including IUGR, SGA, low birthweight, preeclampsia, preterm delivery, and stillbirths. High altitude also creates adaptive responses over generations in long term residents of extremely high altitudes (Bobrowski, 2010). Birthweight has been shown to progressively fall with increasing altitudes at a rate of 102 grams per 1000 meters in elevation gain but without an increase in neonatal and infant morbidity (Jensen & Moore, 1997). Additional studies suggest that the oxidative stress noted in placentas of women who have undergone labor at sea level is not seen at high altitude but that under conditions of chronic hypoxia, placental-mediated reduction in glucose transport is the etiology for reduced fetal growth at altitude (Zamudio et al., 2010). The publishable paper in Chapter 3 also indicates that infant birth weight is significantly lower at moderate altitude compared to a similar sample at sea level.

Literature reviewed on sleep disturbance and higher altitudes stress that the underlying physiological change of high altitude is hypobaric hypoxia due to the decrease
in partial pressure of oxygen with the increasing altitude. People become more hypoxic and hypocapnic with increasing altitude (Weil, 2004). The studies reviewed were divided between sea-level residents visiting higher altitudes and multi-generational residents of very high altitude. Very few sleep studies at higher altitudes included women and no studies that included only women were found. For sea-level residents a common theme emerged from the literature: sleep fragmentation increases progressively with elevation gain (Johnson, Edwards, Burgess, & Sullivan, 2010; Salvaggio et al., 1998; Zielinski et al., 2000). The associated arousals are produced by various sources that include periodic breathing which increases with altitude gain and is most prevalent during non-rapid eye movement sleep (NREM) (Salvaggio et al., 1998; Zielinski et al., 2000).

These findings are in alignment with the Kipnis Conceptual Model of Pregnancy Sleep Disturbance at Altitude presented in Chapter 1. According to this model, altitude can act independently to influence pregnancy outcomes or can create physiologic changes that relate to the symptom experience and impact pregnancy outcomes. Literature indicates that research on adverse perinatal outcomes might best be conducted at altitude, as altitude provides a natural experiment for testing maternal, fetal, and placental responses to chronic hypoxia.

**Dissertation Research**

Research for this dissertation was conducted in the moderate altitude of Flagstaff, Arizona (elevation 6910 ft. [2106m) and data were collected from February through October 2011.

**Sleep Characteristics**
Sleep characteristics that were measured were derived from the Pittsburgh Sleep Quality Index (PSQI) and a 3-day sleep diary. The specific characteristics were PSQI mean sleep onset latency (SOL) as minutes to fall asleep, mean sleep quantity as reported by mean total sleep time (TST) and mean time in bed (TIB), global PSQI score as a measurement of mean sleep quality, and habitual sleep efficiency (HSE). Components 1 and 5 of the PSQI were utilized to measure subjective sleep quality and sleep disturbances respectively. The sleep diary measured mean 3-night sleep quality and mean SOL as minutes to fall asleep.

**Sleep Characteristics at Moderate Altitude Compared to Sea Level**

A one-way between-groups analysis of covariance (ANCOVA) was conducted to compare sleep characteristics for the women in late pregnancy at sea level and moderate altitude. A significant difference between the two elevations was found with a greater sleep disturbance for the sample living at moderate altitude (13.78) than for women living at sea level (12.29). Research has shown that in the general population, progressive elevation gain increases sleep fragmentation and when combined with the physiologic changes in late pregnancy that also increase fragmentation, greater sleep disturbance at moderate altitude seems likely. This aspect of sleep disturbance was measured with PSQI component 5, which is comprised of nine questions that relate to fragmentation; waking during the night, having to get up to urinate, and physiologic discomforts.

Despite reporting a longer mean time in bed, the moderate altitude participants had a trend toward less total sleep time. This is reflected in the habitual sleep efficiency scores (HSE) which were lower for moderate altitude (78%) than for sea level (82%). HSE is calculated by dividing the number of hours slept (TST) by the number of hours in
bed (TIB). Less than 85% sleep efficiency is considered poor sleep, particularly in one’s own home environment without invasive monitoring protocols, and this was found at both elevations.

Poor sleep quality was also found in both groups in this study as evidenced by the mean PSQI global score of 6.94 for sea level participants as compared to 7.64 for the moderate altitude cohort. PSQI global scores greater than 5 indicate severe sleep disturbance and this was observed in 65% of the women at sea level and 64% at moderate altitude. Sleep quality has been reported to be lower for all women during late pregnancy. At lower altitudes, Facco et al. (2010a) reported that 53.5% of their sample of nulliparas (n= 189) located in Chicago (elevation 583 feet) had a PSQI > 5 in third trimester compared to 39% at 6-20 gestational weeks. Lee and Gay (2004) had a PSQI global score of > 5 in 59.5% of a nulliparous sample from San Francisco (elevation 131 feet) and Tsai and colleagues (2011) reported that 50% of their sample of 30 nulliparas in Taipei, Taiwan (elevation 30 feet) had a PSQI > 5. At an elevation of 3900 feet (1200 meters) in Tehran, Iran, Naghi et al. (2011) reported 43.8% of primiparas and multiparas in their last trimester had a PSQI > 5. When compared to all of these studies of pregnant women in their third trimester, the highest incidence of poor sleep (PSQI > 5) is reported within this study of women in Flagstaff.

Newborn birth weights for the two elevations were significantly different by 175 grams (gm.) which is close to the 204 gm. predicted for the elevation of 6910 ft. (102 gm. decrease for every 3300 ft.) reported in the literature (Jensen & Moore, 1997).

Adverse Perinatal Outcomes at Moderate Altitude
Length of labor and mode of delivery were chosen as the perinatal outcomes to assess as perinatal outcomes with the sample at moderate altitude. Hierarchical multiple regression was used to predict self-reported length of labor from the four sleep measures on the PSQI (SOL, TST, subjective sleep quality component #1, and sleep disturbance component #5). Together, infant birth weight, maternal weight, age, income, SOL, TST, sleep disturbance, and sleep quality accounted for 51.6% of the variance in length of labor. SOL uniquely accounted for 21.7% of the variance in length of labor.

Length of labor was significantly associated with SOL. On average, for each additional minute it took to fall asleep, the length of labor increased by approximately 12 minutes for pregnant women living at moderate altitude in this sample. Although the mean length of labor was 12.9 hours, the women who reported taking over 30 minutes to fall asleep had a mean self-reported length of labor of almost 17.9 hours. PSQI SOL was 23.8 minutes for this cohort, and other studies have reported a mean range at sea level from 13 to 39.7 minutes (Lee, Zaffke & McEnany, 2000; Greenwood & Hazendonk, 2004; Mindell & Jacobson, 2000). However, the Mindell and Greenwood studies each reported that only 86% of their samples were without medical/obstetrical problems whereas Lee and colleagues reported healthy women in their sample. Edwards et al. (2000) reported a SOL for preeclamptic women at 50 minutes in Sydney, Australia (121 feet). At moderate altitude, Okun reported that it took participants in Denver (elevation 5180 feet) a mean of 13.8 minutes to fall asleep (2007a) and in the subset from the previous study 13.2 minutes (2007b). Strange and colleagues (2009) studied the sleep disturbance of second trimester women in Atlanta (elevation 1050 feet) and reported that
mean PSQI SOL was significantly longer in the women who eventually delivered preterm (26 minutes) than in those who delivered at term (18.5 minutes).

Length of labor did not significantly differ between self-report and medical record and values were significantly correlated. There was also no significant difference between sleep onset latency (SOL) for the 3-day diary means and PSQI minutes to fall asleep, and these values were significantly correlated. When conducting studies with subjective measures that require self-reported data, it is reinforcing to have results that affirm their use. The PSQI takes 5-10 minutes to complete, is retrospective over the previous month, and proved to be as accurate as the prospective diary that required six entries in a 72-hour period.

Pregnancy is a time of joy, yet it can be a time of increased sleep disturbance and prolonged latency to sleep onset for women living at moderate altitude. Researchers need to develop and test interventions to improve sleep onset latency and minimize this type of insomnia, particularly at higher altitudes where length of labors may be negatively influenced by ability to fall asleep.

**Implications for Nursing Practice & Future Research**

Education is the key to bringing light to the need for women to allow themselves the time to sleep, especially during pregnancy at higher altitudes. Educating health care providers and nurses about the importance of assessing for sleep disturbance during pregnancy is vital to the well-being of all mothers-to-be and their newborns. Nurses have the most access to pregnant women that come for care to clinics and in the hospital setting. A nurse-led educational campaign could provide information to the general public on the need for good sleep hygiene and to schedule sleep as we would an
appointment to ensure optimal health during pregnancy. Preventing longer labors and pregnancy complications could be strong motivating factors for optimizing time available for sleep.

As this is the first research that has been dedicated to exploring pregnancy sleep characteristics at moderate altitude, additional studies are needed to describe the sleep characteristics that are innate at moderate altitude. Associations between late pregnancy sleep at moderate altitude with perinatal outcomes needs to be explored. Continuity within the research community to assure that studies report data similarly would make sharing information more cohesive. An example is that the PSQI item for SOL was reported as minutes, while others report percentage of individual nights or percentage of nights per week, making comparisons between studies impossible.

Although the PSQI was not initially designed for use with pregnant women, the use of the Component #5 score for sleep disturbance focused on the fragmented sleep that is inherent in late pregnancy as well as the physiologic discomforts. It can be used as a continuous variable (0-27) by not recoding it into the 0 to 3 final component score. Significant findings were made more accessible by using the component scores and not just the global score.
References


Table 1. Literature Review of Third Trimester Sleep Parameters & Implications for Adverse Perinatal Outcomes
19 Publications: 1995-2011

<table>
<thead>
<tr>
<th>Author, Year, Location &amp; Elevation</th>
<th>Design &amp; Parity</th>
<th>Sample Size, Age/weight &amp; Weeks Gestation (Wk/G)</th>
<th>Sleep Measures</th>
<th>Sleep Onset Latency</th>
<th>Sleep Disruption: WASO or # Arousals</th>
<th>Sleep Quantity: Total Sleep Time (TST) or Time in Bed (TIB)</th>
<th>Sleep Quality (mean)</th>
<th>Perinatal Outcomes/Sleep Efficiency/Sleep Architecture</th>
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</thead>
<tbody>
<tr>
<td>Bachour et al. (2008) Helsinki, Finland 85ft. (58m)</td>
<td>Observational cohort M &amp; D</td>
<td>Pre-eclamptic (PE) n=15, Age=33.7± 6.9 yrs Control n=14 Age = 31.7±5.7 All WkG=11</td>
<td>Nordic Sleep Questionnaire, serum for inflammatory markers &amp; medical records</td>
<td>Difficulty falling asleep PE.1±1±1.6 n Control 0±1±1.1 nights/wk</td>
<td>PE 2.7±1.1; Control 2.3±1±0.9 episodes/night</td>
<td>Poor Sleep 3rd &amp; worse than weak prior: PE= 27%,67% Control=14%,36%</td>
<td>Gestational duration shorter &amp; birth weight lower in PE than Control. PE had higher TGF-α plasma levels than Control</td>
<td></td>
</tr>
<tr>
<td>Edwards et al. (2009) Sydney, Australia 121ft. (37m)</td>
<td>Observational cohort M &amp; P</td>
<td>Pre-eclamptic (PE) n=2; Age=32±1 WKG=33±1 Controls n=17 Age=30±3.5yr WKG=31±4.1</td>
<td>Portable PSG</td>
<td>PE 5±1min Healthy controls: 4±1min</td>
<td></td>
<td></td>
<td></td>
<td>Sleep efficiency: PE = 72±2% Controls=74±2% PE: ↑SW5, ↑Latency to REM, ↓ L, RRE than Controls. Possible mechanism: ↑SW5 due to circulating cytokines</td>
</tr>
<tr>
<td>Facco et al. (2010) Chicago, IL 587ft. (180m)</td>
<td>Prospective cohort O</td>
<td>n=189 Age=29.7±5.5 WKG=30±2.2</td>
<td>PSQI, Berlin SD8, ESS, NIH RLS, VHI R5</td>
<td>PSQI: 7±1±1±3 hrs 40% sleep &lt;7 hr/night</td>
<td>PSQI: 6±3±5±2</td>
<td></td>
<td></td>
<td>Short sleep duration &amp; SDB implicates inflammation as a key factor in PTSD &amp; PE</td>
</tr>
<tr>
<td>Facco et al. (2000) Chicago, IL 587ft. (180m)</td>
<td>Prospective cohort subset of above study: O</td>
<td>n=189 Age=29.7±5.5 WKG=28±4±9 wks</td>
<td>PSQI, Berlin SD8, ESS, NIH RLS, VHI R5</td>
<td></td>
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<td></td>
<td>Short sleep duration (&lt;7hr/night) &amp; frequent snoring associated with higher GDM</td>
</tr>
<tr>
<td>Kennedy et al. (2016) Dublin, Ireland;43 F (13m)</td>
<td>Retrospective descriptive M=55.5% O=44.5%</td>
<td>n=200 Age=31±5±5.6 WKG=3±2±2±3 trimester</td>
<td>SOLL: 6±2%</td>
<td></td>
<td></td>
<td></td>
<td>Mode of delivery related to TST: &gt;6 hrs/night significantly associated with vaginal delivery</td>
<td></td>
</tr>
<tr>
<td>Lee &amp; Gay (2004) San Francisco, CA 52ft. (35m)</td>
<td>Prospective, observational O</td>
<td>n=131 Age=32±2±4yr WKG=36</td>
<td>PSQI, Actigraphy</td>
<td>Actigraphy WASO=13±0±1±7.4%</td>
<td></td>
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<td>Poor sleep quality: ↑T/↓S</td>
</tr>
<tr>
<td>Michieli et al. (2011) Heraklion, Crete, Greece;108ft (35m)</td>
<td>Prospective, cohort O (58%) O=42%</td>
<td>n=109±1 Age=36±16 yrs WKG=28±3±2 wks</td>
<td>ESS &amp; unnamed sleep questionnaire (retrospective)</td>
<td>≤3 hrs/night=6±7% 6-7 hrs/night=28% 8hrs/night=65%</td>
<td></td>
<td></td>
<td></td>
<td>Poor quality sleep: ↑RRI</td>
</tr>
<tr>
<td>Naghi et al. (2011) Tehran, Iran 3900ft. (1200)</td>
<td>Prospective, descriptive M &amp; P (Not reported)</td>
<td>n=488 Age=25.2±8±5 yrs</td>
<td>PSQI global score = 5±6±1±8±6±1 systolic ≥3±6</td>
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<td></td>
<td></td>
<td></td>
<td>Poor quality sleep: ↑RRI</td>
</tr>
<tr>
<td>Okun &amp; Coussens-Read (2007) Denver, CO 5183± (1550m)</td>
<td>Longitudinal cohort M=42.3% O=57.1%</td>
<td>n=45 Age=31±8±3.7 WKG ≥ 36</td>
<td>PSQI, Daily sleep Diary, ASPQ &amp; ESS serum cytokines</td>
<td>PSQI: 13±8±1±7±1min PSQI-TST (hrs): 7±6±1±3±9 min; TIB =5±5±4±1±6 min</td>
<td></td>
<td></td>
<td></td>
<td>Poor quality sleep: ↑10% more likely to have C/S &amp; longer labors than good quality sleepers</td>
</tr>
<tr>
<td>Okun &amp; Coussens-Read (2007) Denver, CO 5183± (1550m)</td>
<td>Longitudinal cohort M=42.3% O=57.1%</td>
<td>n=45 Age=31±8±3.7 WKG ≥ 36</td>
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<td>PSQI: 13±8±1±7±1min PSQI-TST (hrs): 7±6±1±3±9 min; TIB =5±5±4±1±6 min</td>
<td></td>
<td></td>
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<td>Poor quality sleep: ↑10% more likely to have C/S &amp; longer labors than good quality sleepers</td>
</tr>
</tbody>
</table>

**Note:** WASO = Wake After Sleep Onset, TIB = Total In Bed, TST = Total Sleep Time, C/S = Cesarean Section.
<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>n</th>
<th>Age/Outcome Measures</th>
<th>PSQI: 13±2±6 min</th>
<th>PSQI: 3±1±1.4</th>
<th>PSQI: 7.61 hs ± 0.35</th>
<th>PSQI: global score: 5.6 ± 2.3</th>
<th>Sleep quality &amp; continuity correlated with circulating and stimulated IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okun et al. (2007)</td>
<td>Longitudinal cohort</td>
<td>n=19</td>
<td>Age: 30±4 yrs; WkG≥36</td>
<td>PSS, STAI, &amp; CES</td>
<td></td>
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<tr>
<td>Denver, CO</td>
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<tr>
<td>513±6 (180±50)</td>
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<tr>
<td>Okun et al. (2011)</td>
<td>Observational cohort</td>
<td>n=166</td>
<td>Age: 28±5.5; WkG≥30±12</td>
<td>PSS, STAI, &amp; CES</td>
<td></td>
<td></td>
<td>PSQI: Preterm delivery: 7.79±4.13; Term delivery: 5.2±2.73</td>
<td>Poor sleep quality predictor of PTB</td>
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<td>Irvine, CA</td>
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<td>50±17 (44±4)</td>
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<tr>
<td>Zafarghandi et al. (2011)</td>
<td>Cross-sectional</td>
<td>n=457</td>
<td>Age: 27.4±5.6; WkG≥31</td>
<td>Unnamed sleep questionnaire</td>
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<td>Tehran, Iran</td>
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<td>390±6, (120±5)</td>
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<td>Question 2: Sleep Parameters (15)</td>
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<tr>
<td>Beebe &amp; Lee (2007)</td>
<td>Descriptive, longitudinal, correlational</td>
<td>n=35</td>
<td>Age: 21±5 yrs; WkG≥38</td>
<td>Actigraphy</td>
<td></td>
<td></td>
<td>WASO 5th night prior delivery 12±4% 7.8% Night prior to delivery 32±6±7.2%</td>
<td>Sleep duration &amp; length of labor, mode of delivery and neonate Apgar score</td>
</tr>
<tr>
<td>San Francisco, CA</td>
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<td>52±15 (15±5)</td>
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<tr>
<td>Edwards et al. (2000)</td>
<td>See above</td>
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<tr>
<td>Facco et al. (2010)</td>
<td>See Above</td>
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<tr>
<td>Greenwood &amp; Hazendonk (2004)</td>
<td>Prospective &amp; retrospective cohort</td>
<td>n=209</td>
<td>Age: 29±3.8; WkG≥32±2.6</td>
<td>Sleep diary-prospective (Pro) &amp; questionnaire-retrospective (Reto)</td>
<td>Retro: 19.6±17.20 min</td>
<td>Retro: 21.10±15.97 min</td>
<td>TST: Retto: 7.79±1.45 Pro: 36.98±25.72 min</td>
<td>Sleep efficiency: Retro: 89.6±7.6% Reto: 88.5±5.7%</td>
</tr>
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<td>Melbourne, Australia;</td>
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<td>115±8 (35±9)</td>
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<td>Ballarat, Victoria, Australia</td>
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<td>1480±450 (45±50)</td>
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<td>Hedman et al. (2002)</td>
<td>Longitudinal cohort</td>
<td>n=325</td>
<td>Age: 21±5.2; WkG≥31±5.2</td>
<td>Basic Nordic Sleep Questionnaire</td>
<td>No: 1.5%</td>
<td>no: 8.3±1.2 hrs</td>
<td>Restless sleep: 30.3%</td>
<td>Sleep efficiency: 89.6±7.6%</td>
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<tr>
<td>Helsinki, Finland</td>
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<td>85±16 (36±5)</td>
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<tr>
<td>Kennedy et al. (2011)</td>
<td>See above</td>
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<tr>
<td>Lee &amp; Gay (2004)</td>
<td>See Above</td>
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<tr>
<td>Lee, Ziffka &amp; McEnany (2000)</td>
<td>Longitudinal cohort</td>
<td>n=33</td>
<td>Age: 31±6; WkG≥35±36</td>
<td>Home PSG on 2 consecutive nights &amp; 7-day sleep diary</td>
<td>13±11.1 min</td>
<td>45±24.1 min</td>
<td>6.92±6.45 min</td>
<td>NREM: Stage 1: 4±5±1.2%; Stage 2: 56±5% ±7.3%; Stage 3±4: 8±4±3.8; Sleep efficiency: 89.0±8±5.8%</td>
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<tr>
<td>San Francisco, CA</td>
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<td>52±15 (15±5)</td>
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<td>Minneci &amp; Jacobson (2000)</td>
<td>Cross-sectional cohort</td>
<td>n=38</td>
<td>Age: 29±5.1; WkG≥35±38</td>
<td>Retrospective questionnaire created &amp; ESS</td>
<td>39.72±50 min Fasting asleep</td>
<td>NWAS: 3.1; 97.3% wake during noc</td>
<td>7.77 hours</td>
<td>Sleep efficiency: 88.6%</td>
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<td>Philadelphia, PA</td>
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<td>39±12 (12±3)</td>
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<tr>
<td>Naghi et al. (2011)</td>
<td>See Above</td>
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<tr>
<td>Okun &amp; Cousens-Read (2007)</td>
<td>See Above</td>
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<tr>
<td>Okun et al. (2011)</td>
<td>See Above</td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>Method</td>
<td>n</td>
<td>Age (Mean ± SD)</td>
<td>Weight (Mean ± SD)</td>
<td>ACT (Mean ± SD)</td>
<td>TST (Mean ± SD)</td>
<td>TIB (Mean ± SD)</td>
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</tr>
<tr>
<td>Signa et al. (2007)</td>
<td>Wellington, New Zealand</td>
<td>Longitudinal M (58%) &amp; O (42%)</td>
<td>19</td>
<td>34 ± 16.54</td>
<td>39 ± 9.17</td>
<td>21.46 ± 3.69</td>
<td>7.14 ± 0.25</td>
<td>7.54 ± 0.15</td>
</tr>
<tr>
<td>Tsai et al. (2011)</td>
<td>Taipei, Taiwan</td>
<td>Prospective Observational O</td>
<td>30</td>
<td>30.80 ± 4.75</td>
<td>32.87 ± 2.68</td>
<td>54.96 ± 11.20</td>
<td>6.55 ± 0.30</td>
<td>6.71 ± 0.15</td>
</tr>
<tr>
<td>Zafarghandi (2011)</td>
<td>See Above</td>
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<td></td>
<td>21.20 ± 2.60</td>
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</table>
Table 2. Chapter 2: Demographics and Birth Characteristics of Sleep Study Women by Altitude

<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>Sea Level (n=126)</th>
<th>Altitude (n=50)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean ± SD)</td>
<td>26.3 ± 6.6</td>
<td>27.1 ± 6.2</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index (mean ± SD)</td>
<td>24.3 ± 5.1</td>
<td>25.4 ± 4.3</td>
<td>NS</td>
</tr>
<tr>
<td>Days prior to delivery (mean ± SD)</td>
<td>23.0 ± 9.3</td>
<td>24.2 ± 8.9</td>
<td>NS</td>
</tr>
<tr>
<td>Length of labor (hrs) (mean ± SD)</td>
<td>17.3 ± 10.8</td>
<td>12.9 ± 8.9</td>
<td>(t = 2.63, p = .009)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Asian</td>
<td>30% (n=38)</td>
<td>0% (n=0)</td>
<td>(X^2(5) = 61.7, p &lt; .001)</td>
</tr>
<tr>
<td>Native American</td>
<td>0% (n=0)</td>
<td>20% (n=10)</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>13% (n=16)</td>
<td>4% (n=2)</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latina</td>
<td>24% (n=30)</td>
<td>10% (n=5)</td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>23% (n=29)</td>
<td>60% (n=30)</td>
<td></td>
</tr>
<tr>
<td>Mixed/Other</td>
<td>10% (n=13)</td>
<td>6% (n=3)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>College degree</td>
<td>31% (n=39)</td>
<td>50% (n=25)</td>
<td>(X^2(1) = 5.6, p = .015)</td>
</tr>
<tr>
<td>No college degree</td>
<td>69% (n=87)</td>
<td>50% (n=25)</td>
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<tr>
<td>Employment</td>
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<tr>
<td>Employed at enrollment</td>
<td>37% (n=47)</td>
<td>80% (n=40)</td>
<td>(X^2(1) = 26.1, p &lt; .001)</td>
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<tr>
<td>Not employed at enrollment</td>
<td>63% (n=79)</td>
<td>20% (n=10)</td>
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<tr>
<td>Annual household income</td>
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<tr>
<td>&lt;$36,000/year</td>
<td>86% (n=100)</td>
<td>60% (n=30)</td>
<td>(X^2(1) = 13.2, p &lt; .001)</td>
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<tr>
<td>≥$36,000/year</td>
<td>15% (n=17)</td>
<td>40% (n=20)</td>
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<tr>
<td>Mode of Delivery</td>
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<tr>
<td>Cesarean Birth</td>
<td>30% (n=38)</td>
<td>20% (n=10)</td>
<td>NS</td>
</tr>
<tr>
<td>Vaginal Birth</td>
<td>70% (n=88)</td>
<td>80% (n=40)</td>
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<tr>
<td>Birth Characteristics</td>
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<tr>
<td>Infant birthweight (gm) (mean±SD)</td>
<td>3406 ± 492</td>
<td>3231 ± 444</td>
<td>(t = 2.19, p = .030)</td>
</tr>
<tr>
<td>Gestational age at birth (weeks)</td>
<td>40.1 ± 1.1</td>
<td>39.5 ± 1.1</td>
<td>(t = 3.55, p &lt; .001)</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>54% (n=68)</td>
<td>46% (n=23)</td>
<td>NS</td>
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Table 3. Sleep Parameters of Sleep Study Women by Altitude (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Sea Level (n=126)</th>
<th>Altitude (n=50)</th>
<th>Statistics</th>
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<tbody>
<tr>
<td><strong>Pittsburgh Sleep Quality Index (PSQI)</strong></td>
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<tr>
<td>Time in bed (hrs)</td>
<td>8.9 ±2.23</td>
<td>9.2 ± 1.20</td>
<td>NS</td>
</tr>
<tr>
<td>Total sleep time (hrs)</td>
<td>7.26 ± 1.46</td>
<td>7.15 ± 1.55</td>
<td>NS</td>
</tr>
<tr>
<td>Time to fall asleep (minutes)</td>
<td>25.4 ± 21.5</td>
<td>23.8 ± 21.6</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 30 minutes</td>
<td>22% (n=28)</td>
<td>20% (n=10)</td>
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<tr>
<td>Habitual sleep efficiency (%)</td>
<td>82.2 ± 13.5</td>
<td>78.1 ± 15.7</td>
<td>t= 1.72, p=.088</td>
</tr>
<tr>
<td>&gt; 5 (poor sleep)</td>
<td>6.94 ± 3.04</td>
<td>7.64 ± 3.83</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep global quality index (0-21)</td>
<td>65% (n=82)</td>
<td>64% (n=32)</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep disturbance (comp5) (0-27)</td>
<td>12.29 ± 4.8</td>
<td>13.78 ± 3.7</td>
<td>t= -1.98, p = .049</td>
</tr>
<tr>
<td><strong>3-Night Sleep Diary</strong></td>
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<tr>
<td>Time to fall asleep (minutes)</td>
<td>38.3± 59.9</td>
<td>27.4 ± 26.1</td>
<td>t= 1.68, p=.094</td>
</tr>
<tr>
<td>Sleep quality (1 – 5)</td>
<td>3.3 ± 0.72</td>
<td>3.1 ± 0.65</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table 4. Demographics & Labor Characteristics of Sleep Study Women at Moderate Altitude (n=50)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>(M ± SD or %)</th>
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<tbody>
<tr>
<td>Maternal Characteristics</td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>27.10 ± 6.2</td>
</tr>
<tr>
<td>BMI prior to pregnancy</td>
<td>25.35 ± 4.3</td>
</tr>
<tr>
<td>BMI at delivery</td>
<td>30.94 ± 4.6</td>
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<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Native American</td>
<td>20% (10)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>4% (2)</td>
</tr>
<tr>
<td>Hispanic/Latina</td>
<td>10% (5)</td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>60% (30)</td>
</tr>
<tr>
<td>Mixed/Other</td>
<td>6% (3)</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
</tr>
<tr>
<td>Employed at enrollment</td>
<td>80% (40)</td>
</tr>
<tr>
<td>Not employed at enrollment</td>
<td>20% (10)</td>
</tr>
<tr>
<td>Annual household income</td>
<td></td>
</tr>
<tr>
<td>&lt;$36,000/year</td>
<td>60% (30)</td>
</tr>
<tr>
<td>≥$36,000/year</td>
<td>40% (20)</td>
</tr>
</tbody>
</table>

| Labor Characteristics | | |
| Length of Labor (hrs) | | |
| Self-reported | 13.13 ± 7.35 |
| Electronic medical record | 11.71 ± 5.73 |
| Birth Characteristics | | |
| Infant birthweight (gm) | 3230.5 ± 444 |
| Gestational age at birth (wks) | 39.5 ± 1.1 |
| Cesarean Births | 20% |
Table 5. Multiple Regression Model Accounting for the Variance in Self-Reported Length of Labor (n = 50)

<table>
<thead>
<tr>
<th>Scale</th>
<th>Variables</th>
<th>Beta</th>
<th>Unique R²</th>
<th>p value</th>
<th>F</th>
<th>R Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSQI</td>
<td>Minutes to fall asleep</td>
<td>.593</td>
<td>.217</td>
<td>.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hours of sleep</td>
<td>.078</td>
<td>.032</td>
<td>.604</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subjective sleep quality</td>
<td>-.029</td>
<td>.0004</td>
<td>.846</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sleep disturbance</td>
<td>-.09</td>
<td>.006</td>
<td>.490</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Covariates</td>
<td>Birth weight (gms)</td>
<td>.315</td>
<td>.081</td>
<td>.014</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI prior to pregnancy</td>
<td>-.188</td>
<td>.031</td>
<td>.118</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Income</td>
<td>-.231</td>
<td>.026</td>
<td>.148</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maternal age</td>
<td>.193</td>
<td>.017</td>
<td>.245</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI difference</td>
<td>.115</td>
<td>.012</td>
<td>.331</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Model</td>
<td></td>
<td></td>
<td>≤ .001</td>
<td>4.743</td>
<td>.516</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1: Kipnis Conceptual Model of Pregnancy Sleep Disturbance at Altitude
Figure 2: Theory of Integral Nursing

Theory of Integral Nursing
Barbara Dossey, PhD, RN, AHN-BC, FAAN © 2007

Figure 1.1a. Healing

Figure 1.1b. Healing and Meta-Paradigms of Nursing
(Nurse, Person, Health, Environment)

Figure 1.1c. Healing and Patterns of Knowing in Nursing
(Personal, Aesthetic, Ethic, Not Knowing, Socio-Political)
Adapted from A. Casap (1979)

Figure 1.1d. Healing and Four Quadrants
Adapted from K. Wilber (2000)

Figure 1.1e. Healing and AQAL (All Quadrants, All Levels)
Adapted from K. Wilber (2000)

Integral and Holistic Nursing: Local to Global.
In B. M. Dossey & L. Kegode,
Holistic Nursing: A Handbook for Practice (5th ed.)
Sudbury, MA: Jones & Bartlett.
Figure 3: Theory of Symptom Management
Figure 4: Lee’s Conceptual Model of Impaired Sleep

**Lee’s Conceptual Model of Impaired Sleep**

**SLEEP DEPRIVATION**

Inadequate amount of sleep due to:
- Delayed bedtime
- Early wake time
- Poor sleep hygiene
- Multiple roles/responsibilities: caregiving
- Circadian phase desynchronosis:
  - Jet lag
  - Shiftwork
  - Seasonal light/dark exposure
- Developmental adaptations during:
  - Infancy/childhood
  - Adolescence/puberty
  - Pregnancy/postpartum
  - Aging

**SLEEP DISRUPTION**

Fragmented sleep due to:
- Disordered breathing
- Leg movement
- Esophageal reflux
- Parasomnias
- Environmental noxious stimuli
- Caffeine/stimulants
- Iatrogenic med/surgtx effects
- Substance abuse/withdrawal
- Violence/PTSD
- Hyperarousal/stress/anxiety

**ADVERSE HEALTH OUTCOMES**

Physiological-
- Altered immune function
- Altered metabolic/endocrine function
  - (ie., stress response, metabolic syndrome, dyslipidemia, insulin resistance)
  - Comorbidities (ie., HTN, depression, impaired wound healing)

Cognitive/Behavioral- Impaired daytime functioning
- Fatigue
- Increased risk for accidents/errors
- Excessive daytime sleepiness
- Impaired short-term memory
- Impaired problem solving/coping

Emotional-
- Altered Mood
- Low motivation

Social-
- Impaired social interactions
- Impaired family interactions
- Impaired work performance/productivity
- Increased health care utilization
Human Research Protection Program
Committee on Human Research

Notification of Expedited Review Approval

Principal Investigator: Kathryn A Lee
Co-Principal Investigator: Gayle J Kipnis

Type of Submission: Initial Review Submission Packet
Study Title: Late Pregnancy Sleep and Birth Outcomes at Moderate Altitude
IRB #: 10-04562
Reference #: 013182
Committee of Record: Laurel Heights Panel
Study Risk Assignment: Minimal
Approval Date: 12/22/2010 Expiration Date: 12/21/2011

Regulatory Determinations Pertaining to this Approval:
The research meets all of the conditions of 45 CFR 46.204 for the involvement of pregnant women or fetuses.
Individual HIPAA authorization is required.

IRB Comments:
The iMedRIS system will generate an email notification eight weeks prior to the expiration of this project’s approval. However, it is your responsibility to ensure that an application for continuing review approval has been submitted by the required time. In addition, you are required to submit a study closeout report at the completion of the project.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to CHR approval. The CHR website has more information.
Human Research Protection Program
Committee on Human Research

Notification of Expedited Review Approval

Principal Investigator: Kathryn A Lee
Co-Principal Investigator: Gayle J Kipnis

Type of Submission: Continuing Review Submission Form
Study Title: Late Pregnancy Sleep and Birth Outcomes at Moderate Altitude

IRB #: 10-04562
Reference #: 035579

Committee of Record: Laurel Heights Panel

Study Risk Assignment: Minimal

Approval Date: 12/08/2011 Expiration Date: 12/21/2012

Regulatory Determinations Pertaining to this Approval: This study is in data analysis and involves no greater than minimal risk for the population being studied.

All changes to a study must receive CHR approval before they are implemented. Follow the modification request instructions. The only exception to the requirement for prior CHR review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103.b.4, 21 CFR 56.108.a). In such cases, report the actions taken by following these instructions.

Expiration Notice: The iMedRIS system will generate an email notification eight weeks prior to the expiration of this study’s approval. However, it is your responsibility to ensure that an application for continuing review approval has been submitted by the required time. In addition, you are required to submit a study closeout report at the completion of the project.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to CHR approval and follow all applicable VA and other federal requirements. The CHR website has more information.
Dear Dr. Lee and Ms. Kipnis:

Thank you for submitting your study/activity proposal to the Northern Arizona Healthcare Institutional Review Board (NAH IRB). I, along with a fellow IRB committee member, have reviewed your proposal and noted the following:

This is a prospective study to describe the characteristics of sleep quality and quantity as self-reported by pregnant women during late pregnancy and describe associations between moderate altitude and birth outcomes that include length of labor and mode of birth. The study will specifically examine sleep in late pregnancy (35-38 gestational weeks) at moderate altitudes (4500-8858 ft. elevation). Sleep disturbances at lower altitudes have been associated with increased incidence of preeclampsia and adverse birth outcomes such as longer labors and increased cesarean birth rates. You plan to recruit 125 nulliparous women over the age of eighteen (18) for this study. You will recruit patients from physicians’ offices, childbirth education classes, Flagstaff Medical Center, and/or community prenatal clinics. It is your intention to publish the results of this study, and to submit this dissertation to obtain your PhD at University of California San Francisco (UCSF). IRB approval from the Human Research Protection Program Committee on Human Research at the University of California San Francisco has been received. The influence on altitude on pregnancy sleep has not been studied. You are hoping that important knowledge gained through the study will assist health care providers to understand and anticipate patients’ needs who give birth at moderate altitudes.

Also, please be advised of the following stipulations of continuing approval for all NAH IRB studies/activities, as applicable (please contact the IRB Administrator to request the appropriate IRB submission form):

- Review/Continuation of Study/Activity: Must be submitted to the IRB three (3) weeks prior to the study/activity review date and you will receive a reminder notice in advance of the deadline for submission (Next Review Date is noted above, if applicable). Note that late submissions may result in studies/activities being temporarily suspended and/or closed to accrual of new subjects, or permanent closure;
Amendments or Changes (Protocol or Consent Form): Unless done to eliminate immediate hazard to the subject/patient, any and all changes in the study/activity must be promptly submitted to the IRB and approved by the IRB prior to their implementation (i.e., Protocol revisions, Investigator/Treating Physician changes, consent form revisions, etc.);

Risks and Information: Unanticipated risks and new relevant information that may impact the risk/benefit ratio of the test article for the subject must be submitted to the IRB within five (5) working days;

Adverse Events: Prompt reporting is required for events that are (a) unanticipated (i.e., not identified as reasonably foreseeable in the protocol and/or consent form and (b) of sufficient seriousness to affect the relative risks and benefits of participating in the study/activity as contemplated by the approved protocol and/or consent form). "Prompt" is defined to mean as soon as the seriousness of the issue reasonably demands. Serious adverse events should be reported to the IRB within one (1) week of Investigator/Treating Physician becoming aware of the event; any other unanticipated problem should be reported to the IRB within two (2) weeks;

Life threatening/Death Events: Any life-threatening event or study-related death must be submitted to the IRB within twenty-four (24) hours;

Emergency Use: Emergency use of an Investigational Drug in a life-threatening situation, which must be documented and certified by an uninvolved Hospital physician, i.e., that the emergency existed which required use of the investigational article, must be submitted to the IRB within five (5) working days; and

All forms approved by the IRB, such as the informed consent document (noted below if enclosed), must be presented to all study subjects/patients.

This study represents no more than minimal risk to subjects; therefore, it does qualify for expedited approval under the Expedited Review/Approval Guidelines of the Northern Arizona Healthcare IRB and based on my review of the following materials; NAH IRB Initial Protocol Form w/ attachments; Informed Consent; Curriculum Vitas (Lee, Kipnis); UCSF Permission to Use Personal Health Information for Research form; Dear Expectant Mom letter; Advertisement flyer; Birth Information Form; Eligibility Screening Form; Pregnancy Sleep Study log; Study Sign-up Form and Research Curriculum Completion Report, Notification of Expedited Review Approval (UCSF), approval to commence your study is herewith granted effective this date, subject to review in one (1) year.

The IRB maintains the authority to terminate or suspend approval of research that is not being conducted in accordance with stated IRB requirements or that has been associated with unexpected serious harm to subjects. The IRB operates in compliance with 21 Code of Federal Regulations ("CFR") Part 56 and 45 CFR Part 46.

Should you have any questions, please feel free to contact me directly or contact Gretchen McMasters in NAH IRB Administration at 928.773.2346 or via email at gm18754@nahealth.com.

Sincerely,

Samuel Butman, MD
Chair, NAH Institutional Review Board

Enclosure: NAH IRB Approved Consent Form (approved 1/24/11)
November 16, 2011

Kathryn A. Lee, RN, PhD, FAAN, CBSM
Gayle J. Kipnis PhD(c), RNC-OB, AHN-BC
University of California (UCSF) School of Nursing
Department of Family Health Care Nursing
2 Koret Way, Room #N-411Y
UCSF Box 0606
San Francisco, CA 94143-0606

Re: EXPEDITED PERIODIC REVIEW APPROVAL
NEXTREVIEW: 11/16/2012
Study/Activity Title: Late Pregnancy Sleep and Birth Outcomes at Moderate Altitude.
FWA# 00009566

Dear Dr. Lee and Ms. Kipnis:

Thank you for submitting your study/activity proposal to the Northern Arizona Healthcare Institutional Review Board (NAH IRB). I, along with a fellow IRB committee member, have reviewed your proposal and noted the following:

Enrollment to date
Nationally: 56        This Hospital: 56

Enrollment since last review
Nationally: 56        This Hospital: 56

Amendments None: Study is closed to accrual.

Withdrawals/Reasons None

Unanticipated or Unexpected AEs None

P.I.’s Synopsis The data collection phase of this study completed in late October 2011 and data analysis is just beginning. This is an observational study and not interventional research; effectiveness is not calculated. There are no preliminary results or changes made in scientific knowledge at this time. There are no other centers conducting this study.

Consent Form No consent submitted: Study is closed to accrual

This submission qualifies for expedited approval/acceptance; therefore, approval/acceptance is herewith granted, effective this date, per the Expedited Review/Approval Guidelines of the NAH IRB.

Full committee review will be provided at the next scheduled meeting.

Also, please be advised of the following stipulations of continuing approval for all NAH IRB studies/activities, as applicable (please contact the IRB Administrator to request the appropriate IRB submission form):

- Review/Continuation of Study/Activity: Must be submitted to the IRB three (3) weeks prior to the study/activity review date and you will receive a reminder notice in advance of the
deadline for submission (Next Review Date is noted above, if applicable). **Note that late submissions may result in studies/activities being temporarily suspended and/or closed to accrual of new subjects, or permanent closure:**

- **Amendments or Changes (Protocol or Consent Form):** Unless done to eliminate immediate hazard to the subject/patient, any and all changes in the study/activity must be promptly submitted to the IRB and approved by the IRB prior to their implementation (i.e., Protocol revisions, Investigator/Treating Physician changes, consent form revisions, etc.);
- **Risks and Information:** Unanticipated risks and new relevant information that may impact the risk/benefit ratio of the test article for the subject must be submitted to the IRB within five (5) working days;
- **Adverse Events:** Prompt reporting is required for events that are (a) unanticipated (i.e., not identified as reasonably foreseeable in the protocol and/or consent form and (b) of sufficient seriousness to affect the relative risks and benefits of participating in the study/activity as contemplated by the approved protocol and/or consent form). "Prompt" is defined to mean as soon as the seriousness of the issue reasonably demands. Serious adverse events should be reported to the IRB within one (1) week of Investigator/Treating Physician becoming aware of the event; any other unanticipated problem should be reported to the IRB within two (2) weeks;
- **Life threatening/Death Events:** Any life-threatening event or study-related death must be submitted to the IRB within twenty-four (24) hours;
- **Emergency Use:** Emergency use of an Investigational Drug in a life-threatening situation, which must be documented and certified by an uninvolved Hospital physician, i.e., that the emergency existed which required use of the investigational article, must be submitted to the IRB within five (5) working days; and
- **All forms** approved by the IRB, such as the informed consent document (noted below if enclosed), must be presented to all study subjects/patients.

The IRB maintains the authority to terminate or suspend approval of research that is not being conducted in accordance with stated IRB requirements or that has been associated with unexpected serious harm to subjects.


Should you have any questions, please feel free to contact me directly or contact Gretchen McMasters in NAH IRB Administration at 928.773.2346 or via email at gm18754@nahealth.com.

Sincerely,

Samuel Butman, MD
Chair, NAH Institutional Review Board
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Protocol IND or IDE #: N/A
Phase of Study: N/A
Principal Investigator: Kathryn Lee, RN, PhD, FAAN
University of California (UCSF) School of Nursing
Department of Family Health Care Nursing
2 Koret Way, Room #N-411Y
UCSF Box 0906
San Francisco, CA 94143-0606
(415) 476-4442

Co-Principal Investigator: Gayle Kipnis PhD(c), MSN, AHN-BC
University of California (UCSF) School of Nursing
Department of Family Health Care Nursing
2 Koret Way, Room #N-411Y
UCSF Box 0906
San Francisco, CA 94143-0606
(928) 642-2173

Sponsor: None

Research Participant’s Name:

This Consent Form may contain words that you do not know. You should ask the study investigators to explain any words or information that is not clear.

BACKGROUND
You are being invited to participate in this research study because you are pregnant with your first baby and living at moderate altitude. If you choose to participate, your participation will last for approximately four (4) months. This study is being conducted at one (1) hospital in Northern Arizona at Flagstaff Medical Center and approximately 125 research participants will be enrolled. The individuals chiefly responsible for this study are Gayle Kipnis, a PhD student in the UCSF School of Nursing, who can be reached at (928) 642-2173 and Kathryn Lee, a professor in the UCSF School of Nursing, who can be reached at (415) 476-4442.

PURPOSE OF THE STUDY AND WHAT IS EXPERIMENTAL
The purpose of this study is to find out if pregnancy sleep at moderate altitude is different from sleep at lower altitudes and whether it is associated with birth outcomes. The primary objectives are to describe the characteristics of sleep quality and quantity as self-reported by pregnant women during late pregnancy and describe associations between moderate altitude and birth outcomes that include length of labor and mode of birth.

Study Title: Late Pregnancy Sleep and Birth Outcomes

Consent Version Date: [date]

Approved by the NH IND [date]
Approved by the UCSF CIBR [date]

(patient’s initials)
PROCEDURES
If you decide to take part in this study, this study will involve the following procedures:
1. We will provide you with a booklet to complete when you are between 35 and 38 weeks pregnant. This includes two (2) questionnaires that you will need to fill out once which will take approximately 15 minutes and a sleep log to be filled out each morning and evening for three days. In the sleep diary, you will keep track of the time you go to bed, the time you wake up, where you sleep, if you take any naps, and your daily routine. The sleep diary takes less than five (5) minutes to fill out each time, for a total of 30 minutes, over the three days. You will receive a phone call as a reminder to complete these. You will return the completed booklet in a pre-addressed stamped envelope that will be provided to you.
2. Two (2) to four (4) weeks after your baby is born, we will call you and ask you some questions about your pregnancy, labor and delivery. This will take approximately 15 minutes.
3. We will ask you for your written permission to access your medical record. The information that we will collect from your medical record will include your prenatal visits and details about your labor and delivery.

This study will last for approximately four (4) months. Data will be collected from your sleep booklet after you return it to us and from your answers to the telephone questions two (2) to four (4) weeks after you deliver. If you decide to participate in this study, you will be asked to sign this consent form.

RISKS AND DISCOMFORTS ASSOCIATED WITH THIS STUDY
There is no risk of injury for you or your baby from participating in this study. It may be inconvenient for you to answer questions about your sleep and how you are feeling. You may feel uncomfortable or become upset answering the questions. You are free to skip any question.

BENEFITS ASSOCIATED WITH THIS STUDY
There is no direct benefit to you or your baby from participating in this study. However, we hope that the study will help us learn more about sleep during pregnancy at higher elevations and how it may be associated with birth outcomes.

COSTS AND COMPENSATION ASSOCIATED WITH THIS STUDY
There are no costs to you for this research study. You have not been promised a cure. If you finish all parts of the study, you will receive a total of $25.00. This cash payment will be mailed to you after you return the study questionnaire and complete the postpartum phone call. This payment will cover your time, effort, and inconvenience.

PRIVACY & CONFIDENTIALITY
Participation in research may involve some loss of privacy. However, we will make every attempt to minimize that loss. Your identity and the identity of your baby will be kept confidential. We will use a number, not your name, to identify your data. We will keep your data in a locked file. Only the research team will be allowed to see your data and access your medical records. We will not use any names in reports or publications resulting from this study. If you tell us that you plan to hurt yourself or someone else, we will need to notify the appropriate authorities.
If you participate in this study, it will involve the use and disclosure of your information, including your name, address, phone number, zip code, age, weight, gender, ethnic origin, current and previous health status, and other similar data.
resulting from research-related activities. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

The following persons and classes of persons are authorized to use and/or disclose your information: The study investigators identified elsewhere in this consent form as being responsible for this research. Your information may be disclosed to the following persons or classes of persons (recipients):

- The Food and Drug Administration (FDA)
- The Northern Arizona Healthcare Institutional Review Board (IRB)
- The University of California San Francisco Committee on Human Research (CHR)

It is possible that information which is disclosed to one or more of the above recipients will be re-disclosed and will no longer be protected by the terms of use and disclosure described in this consent form.

The purposes for which you would be authorizing the use and disclosure of your information, as a participant in this research project would be to promote the objectives of this research project as described elsewhere in this consent form, and to facilitate related monitoring, regulatory oversight, and quality assurance activities.

There is no expiration date to your authorization for the use of disclosure of your information as described above. However, you may revoke your authorization at any time, and the revocation will be effective upon receipt. Please note that if you revoke your authorization, information that has already been obtained will continue to be used and disclosed as described above. Your revocation must be made in writing and addressed to the person noted below:

Principal Investigators names: Gayle Kipnis & Kathryn Lee

Principal Investigators address:
University of California (UCSF) School of Nursing
Department of Family Health Care Nursing
2 Koret Way, Room #N-411Y
UCSF Box 0606
San Francisco, CA 94143-0606

By signing this consent form, you are authorizing the above uses and disclosures of your information as described above. If you do not sign this consent form, including this authorization, you will not be eligible to participate in this research project.

ALTERNATIVES
There are no alternatives to participating in this research study.

CONTACT PERSONS
Gayle Kipnis or Kathryn Lee have discussed this research study with you and you have been given the opportunity to ask questions which have been answered to your satisfaction. If you have any further questions regarding this treatment, you should call Gayle Kipnis at (928) 642-2173 or Kathryn Lee at (415) 476-4442.

An Institutional Review Board has been established at NORTHERN ARIZONA HEALTHCARE, composed of physicians, community representatives and members of the Hospital Administration. The purpose of this Board is to protect the interests of human research participants participating in research. The Board is an impartial third party not directly involved with the research. The Board invites any comments, questions or complaints which you may have

Study Title: Late Pregnancy Sleep and Birth Outcomes

(please fill in each time Consent is revised)
Approved by the NAH IRB (to be filled in by IRB Coordinator)
Approved by the UCSF CHR (to be filled in by IRB Coordinator)
Regarding: 1) this research study, and, 2) patient's rights as investigational research participants. Comments may be addressed to:

Chair, Institutional Review Board – NORTHERN ARIZONA HEALTHCARE
c/o IRB Manager, c/o NAH IRB Office
1200 N. Beaver St, Flagstaff, AZ 86001
Telephone: (928) 773-2346 - 8:00 AM to 5:00 PM Monday through Friday.

In addition, you may contact the University of California San Francisco Committee on Human Research, which is concerned with protection of volunteers in research projects. You may reach the Committee office by calling: (415) 476-1814 from 8:00 a.m. to 5:00 p.m., Monday through Friday, or by writing to the Committee on Human Research, Box 0962, University of California San Francisco, San Francisco, CA 94143.

VOLUNTARY PARTICIPATION
Participation in this study is voluntary. You understand that you are free to withdraw your consent to participate in this research study at any time without prejudice to your subsequent care. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.

You are free to seek care from your health care provider at any time. If you do not take part in or withdraw from the study, you will continue to receive care as usual.

Your study investigator(s) may withdraw you from the study at any time she feels it is in your best interest.

SIGNATURES

Research Participant Signature  Date

By signing above, you acknowledge that you have read this Consent Form, you have been given the opportunity to ask questions and you understand what participation in this study will involve. You freely consent to participate, with the understanding that you may withdraw your consent at any time without penalty or loss of benefits to which you are otherwise entitled. You also acknowledge that you have received an appropriately executed copy of this informed consent and the Medical Research Subject Bill of Rights.

Witness Signature  Date

Investigator Signature  Date

The above-signed study investigator hereby certifies that she has discussed the research project with the participant and has explained all of the information contained in the Consent Form to the participant, including any adverse reactions that may reasonably be expected to occur. The above-signed study investigator further certifies that the participant was encouraged to ask questions and that all questions were answered.

Study Title: Late Pregnancy Sepsis and Birth Outcomes

Consent Version Date: 12/29/2011 (must be filled in each time consent is revised)
Approved by the NAH IRB: [ ]
Approved by the UCSF CHE: [ ] (to be filled in by IRB Coordinator)
MEDICAL RESEARCH SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to participate in medical research.

As a research subject (participant), you have the following rights:

1. To be told the nature and purpose of the research.

2. To be told what will happen and whether any of the procedures, drugs or devices are different from what would be used in standard practice.

3. To be told about any significant risks, side effects or discomforts that can be reasonably expected from the research.

4. To be told of any expected benefits from participating in the research.

5. To be told the other available treatments that could be chosen instead, and how they may be better or worse than participating in the research.

6. To be allowed to ask any questions concerning the research both before agreeing to be involved and during the course of the study.

7. To be told what sort of medical treatment is available if any complications arise.

8. To refuse to participate at all or to withdraw consent to participate at any time, without jeopardizing the right to receive present or future care.

9. To receive a copy of the signed and dated consent form.

10. To be free of pressure when considering whether to agree to participate in the research.

Date: 

Time:

Signature: _______________________________ (patient)

Witness: ________________________________

Study Title: Late Pregnancy Sleep and Birth Outcomes

Consent Version Date: 1 [to be filled in by patient] (to be filled in by IRB Coordinator)

Approved by the NAc IRB [ ]

Approved by the UCSF IRB [ ]

Page 5 of 5
Pregnancy Sleep Study

ELIGIBILITY SCREENING FORM

TO SEE IF YOU CAN BE IN THE STUDY, I HAVE A FEW QUESTIONS ABOUT YOUR HEALTH HISTORY AND LIVING SITUATION. YOU CAN STOP ME AT ANY TIME AND YOU CAN SKIP ANY QUESTION YOU DON’T WANT TO ANSWER. OK?

1. So how is your pregnancy going? BOY GIRL DK

(Do you know if you’re having a boy or girl? Have you had any contractions yet?)

2. Have you been having any problems/complications with this pregnancy?
   NO YES
   [If YES, explain]: ________________________________
   ________________________________

3. When are you due? _____/_____/______ Current gestational weeks_______

4. Are you having one baby? More than one?
   =1 – continue with #5
   >1 – INELIGIBLE, skip to Not Eligible section, p.3

5. How many times have you been pregnant before? _______ times
   = 0 – skip to #7
   > 0 – continue with #6

6. How many times have you given birth (> 20 gestational weeks)?
   _____ times
7. What is your current age? ________ years
   ≥ 18  – continue with #8
   < 18  – INELIGIBLE, skip to Not Eligible section, p.3

8. Do you work nights? [at least 4 hrs between 12am-6am]
   NO  – continue with #9
   YES  – INELIGIBLE, skip to Not Eligible section, p.3

9. Did your pregnancy begin in Flagstaff or above 4500 feet elevation?
   NO  – continue with #10
   YES  – continue with #10

10. How long have you lived above 4553 feet elevation? (circle one)
    <12 months – INELIGIBLE, skip to Not Eligible section, p.3
    ≥12 months - continue with #11

11. Do you plan on delivering your baby in Flagstaff?
    NO – INELIGIBLE, skip to Not Eligible section, p.3
    YES – continue with #12

12. Are you able to read and write English?
    NO – INELIGIBLE, skip to Not Eligible section, p.3
    YES – continue with #13

NOW I’M GOING TO ASK YOU SOME QUESTIONS ABOUT YOUR HEALTH HISTORY:

13. Have you ever been diagnosed with a sleep disorder, such as insomnia or apnea?
    [If YES]  Describe: ________________________________
14. Do you have a history of previous pregnancy loss?
   
   [If YES] Describe: ________________________________
   
   NO – continue with #15
   
   YES – INELIGIBLE, skip to Not Eligible section, p.3

15. Are you planning to have a cesarean birth?
   
   NO – continue with #16
   
   YES – INELIGIBLE, skip to Not Eligible section, p.3

16. Are you taking any meds for sleeping problems?
   
   NO – ELIGIBLE, continue with #17
   
   YES – INELIGIBLE, skip to NOT ELIGIBLE below

17. Are you currently having labor contractions?
   
   NO – ELIGIBLE, continue with #18
   
   YES – INELIGIBLE, skip to NOT ELIGIBLE below

18. What was your weight prior to pregnancy? ______________lbs.

19. How tall are you? _____feet _____inches

---

**ELIGIBLE:** Based on your answers, it seems that you CAN be in our study. Before I tell you more about the study, is it OK if I ask a few more questions about your background?

**NOT ELIGIBLE:** It turns out that you can’t be in our study because ______. Even though you won’t be able to participate in our study, is it OK if I asked you just a few more questions about your background?

---

**DEMOGRAPHICS**
THESE QUESTIONS WILL HELP US COMPARE THOSE WHO CAN BE IN THE STUDY WITH THOSE WHO CAN’T. OK?

20. Are you currently in a relationship with someone that you consider your partner and that you sleep with?

NO       YES

[If YES:]
How long have you been with him/her? _______ mos / yrs

21. Are you single or married? Which category best describes your marital status?

Single or Unmarried..........1
Married .........................2
Separated.......................3
Divorced .......................4
Widowed.......................5

22. Do you consider yourself Hispanic or Latino?   NO   YES

23. Which of the following categories best describes your race?

American Indian or Alaska Native .........................1
What is your tribe?
  Navajo.................................................8
  Hopi.....................................................9
Asian .......................................................2
Native Hawaiian or Other Pacific Islander ...............3
Black or African-American .................................4
White or Caucasian ......................................5
More than one race ........................................6
Other, describe: ____________________________________7

24. What language do you feel most comfortable speaking?

English ......................................................1
Spanish ......................................................2
Other: ____________________ ............................3

25. What is the highest level of school you completed?

Grade school or less .........................................1
Some high school ..........................................2
High school diploma/equivalent ............................3
Vocational or trade school ................................4
Some college ..............................................5
College diploma ............................................6
26. Are you currently working?

- Employed full-time for wage or salary ...................... 1
- Employed part-time for wage or salary ...................... 2
- Self-employed business ....................................... 3
- On Maternity Leave and returning ............................ 4
- On Maternity Leave and not returning ....................... 5
- Homemaker/Work without pay in a family .................. 6
- Unemployed, looking for work .................................. 7
- Unemployed, not looking for work .............................. 8
- Student .................................................................. 9
- Unable to work because: _____________________________ 10
- Other (please specify): ________________________________ 11

27. How many people live in your household (including yourself)? ______

28. What was your household income from all sources, after taxes last month? ______

[if she'd prefer to choose from a category:]

- Less than $1,000 ........... 1
- $1,000 to $1,999 ............. 2
- $2,000 to $2,999 ............. 3
- $3,000 or more.............. 4

---

**NOT ELIGIBLE**

Thank you for answering our questions and for your interest in our study.

Refer when appropriate:  
www.sleepfoundation.org  
Sleep Disorders Center of Flagstaff  
(928) 214-7400

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**ELIGIBLE**

That was my last question. Now let me tell you a little more about the study. We are studying late pregnancy sleep in women that live at moderate altitude. We will make an appointment for you to come in and sign an informed consent form to be in the study when you are in your last two months of pregnancy. We will give you a study booklet to complete. The booklet consists of two self-report sleep questionnaires and a sleep diary. These are to be completed after you are 35 weeks...
pregnant but prior to delivery. You will receive a reminder phone call from us to do this. After completion, you will return the booklet in the self-addressed stamped envelope. Two to four weeks after you deliver, we will contact you by phone to ask you questions about your pregnancy, labor, and delivery outcomes. You will receive $25 for your participation.

Do you have any questions? Do you want to participate in this study? If you are unsure, would you like to talk with your partner and I can call you back?

[Did she agree to participate?] NO UNSURE YES → [assign Study ID on p1]

Let’s schedule a date & time for you to come in and sign informed consent

Agreed upon private location at the hospital

Date & time [at least 32 weeks gestation]
PREGNANCY SLEEP STUDY

University of California San Francisco
School of Nursing
Department of Family Health Care Nursing

UCSF Pregnancy Sleep Study
2700 S. Woodlands Village Blvd.
Suite 300-455
Flagstaff, Arizona 86001
(928) 642-2173
FIRST, SECOND & THIRD EVENINGS
(Complete this section before going to sleep)

1. Today's date: ___________   Time : ___________ AM / PM

2. Did you take any naps today?   _____ Yes   _____ No

If yes, what times and where did you nap (in bed, on sofa, in chair, in car, etc)

Nap #1: from _______ to _______; location: ___________________
Nap #2: from _______ to _______; location: ___________________
Nap #3: from _______ to _______; location: ___________________

3. Today I did:       _____ no activity
                     _____ basic activity (light housekeeping, running errands, etc.)
                     _____ mild exercise (walking, isometrics, etc.)
                     _____ moderate exercise (heavy housework, gardening, etc.)
                     what time(s)?: ___________ AM/PM
                     _____ strenuous exercise (jogging, swimming, etc.)
                     what time(s)?: ___________ AM/PM

4. Today I ate:       _____ my usual diet
                     _____ an unusual diet, describe: ___________________

5. Today I ate:       _____ my typical amount
                     _____ less than usual
                     _____ more than usual

                     Dinner: ___________ Snacks: ___________

7. What alcohol or caffeine beverages did you consume today?
Examples: Type of beverage Approximate time Amount (cups)

<table>
<thead>
<tr>
<th>Coffee</th>
<th>Coke/Pepsi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decaf coffee</td>
<td>Mountain Dew</td>
</tr>
<tr>
<td>Tea</td>
<td>Jolt</td>
</tr>
<tr>
<td>Herbal tea</td>
<td>Beer</td>
</tr>
<tr>
<td>Decaf tea</td>
<td>Wine</td>
</tr>
<tr>
<td>Cocoa</td>
<td>Liquor</td>
</tr>
</tbody>
</table>

8. Did you encounter any particular stress today?   _____ Yes   _____ No

describe: _____________________________________________________

9. What, if any, problems did you experience today?

describe: _____________________________________________________
FIRST, SECOND & THIRD MORNINGS
(Complete this section before going to sleep)

1. Today's date: _______________ Time: ___________ AM / PM

2. What time did you go to bed last night? ___________ AM / PM

3. Where did you sleep last night? ______ in your bed
   (check all that apply) ______ somewhere else: ____________

4. Falling asleep took ______ minutes, which was:
   ______ less than usual ______ longer than usual
   ______ the usual amount of time ______ way too long

5. Did you do/take something to help you fall asleep last night? ___ Yes ___ No
   If yes, describe: ______________________________________________________

6. How many times did you awaken during the night? _______ times
   If 1 or more, what awakened you? ______________________________________

7. Were any awakenings longer than 5 minutes? _____ Yes _____ No
   If yes, describe: ______________________________________

8. The number of awakenings was: _____ fewer than usual _____ way too many
   _____ typical for me _____ don’t remember _____ more than usual

9. The time I spent awake was: ______ no time at all ______ longer than usual
   ______ less than usual ______ way too long ______ about the usual

10. Did you snack during the night? ______ Yes, please describe: ____________
     ____________________________  ______ No

11. I awoke this morning at _______ AM and got up at _______ AM.

12. I awoke:
   ______ much too early ______ later than usual
   ______ earlier than usual ______ way too late
   ______ the usual time

- go on to next page –
13. I feel
   ______ very alert ______ somewhat drowsy
   ______ alert ______ very drowsy

14. I feel:
   ______ very rested ______ somewhat rested
   ______ rested ______ not at all rested

15. My sleep was:
   ______ very poor ______ good
   ______ poor ______ very good
   ______ fair

16. I dreamt:
   ______ not at all ______ more than usual
   ______ very little ______ don’t remember
   ______ a normal amount
QUESTIONNAIRES

(This section can be completed any time during the 3-day measurement period)
The following questions relate to your usual sleep habits during the PAST MONTH ONLY. Your answers should indicate the most accurate reply for the majority of days and nights in the PAST MONTH. Please check one box for each item.

<table>
<thead>
<tr>
<th>How often have you had trouble sleeping because you:</th>
<th>Not during the past month</th>
<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cannot get to sleep within 30 minutes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Wake up in the middle of the night or early morning</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Have to get up to use the bathroom</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Cannot breathe comfortably</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Cough or snore loudly</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feel too cold</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feel too hot</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Had bad dreams</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Have pains</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>10. Other reason(s) you had trouble sleeping.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Please describe:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. How often have you taken medicine (prescribed or “over the counter”) to help you sleep?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>12. How often have you had trouble staying awake while driving, eating meals or engaging in social activity?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>13. During the past month, how would you rate your sleep quality overall?</td>
<td>Very good………………1</td>
<td>Fairly good……………2</td>
<td>Fairly bad……………3</td>
<td>Very bad……………4</td>
</tr>
</tbody>
</table>
14. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?
   No problem at all…………1
   Only a very slight problem……….2
   Somewhat of a problem…………..3
   A very big problem……………...4

15. During the past month:
   a. When have you usually gone to bed at night?  Usual bed time: ________
   b. How long has it usually taken you to fall asleep each night?
      Number of minutes: ____________
   c. When have you usually gotten up in the morning?
      Usual getting up time: ____________
   d. How many hours of actual sleep did you get at night?
      (This may be different than the number of hours you spent in bed).
      Hours of sleep per night: __________

16. Do you have a bed partner or roommate?
   No bed partner or roommate ..............................1 ➔ [skip to next page]
   Partner/roommate in other room ..............................2 ➔ [skip to next page]
   Partner in same room, but not same bed ....................3
   Partner in same bed .............................................4

   Ask your partner how often in the past month you have had...

<table>
<thead>
<tr>
<th></th>
<th>Not during the past month</th>
<th>Less than once a week</th>
<th>Once or twice a week</th>
<th>Three or more times a week</th>
</tr>
</thead>
</table>
   17. Loud snoring     | 0                         | 1                     | 2                    | 3                         |
   18. Long pauses between breaths while asleep | 0                     | 1                     | 2                    | 3                         |
   19. Legs twitching or jerking while you sleep | 0                     | 1                     | 2                    | 3                         |
   20. Episodes of disorientation or confusion during sleep | 0                     | 1                     | 2                    | 3                         |
   21. Other restlessness while you sleep; please describe: | 0                     | 1                     | 2                    | 3                         |
The next questions ask about your sleep during the **PAST WEEK**. Circle one number for each item.

<table>
<thead>
<tr>
<th>How many days in the <strong>PAST WEEK</strong> did you:</th>
<th>NO DAYS</th>
<th>EVERY DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. have difficulty getting to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>2. wake up during your sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>3. wake up too early at the end of a sleep period</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>4. feel rested upon awakening at the end of a sleep period</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>5. sleep poorly</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>6. feel sleepy during the day</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>7. struggle to stay awake during the day</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>8. feel irritable during the day</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>9. feel tired or fatigued during the day</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>10. feel satisfied with the quality of your sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>11. feel alert and energetic during the day</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>12. get too much sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>13. get too little sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>14. take a nap at a scheduled time</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>15. fall asleep at an unscheduled time</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>16. drink an alcoholic beverage to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>17. use tobacco to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>18. use marijuana to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>19. use an over-the-counter sleeping pill to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>20. use a prescription sleeping pill to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>21. use aspirin or other analgesic to help you get to sleep</td>
<td>0 1 2 3 4 5 6 7</td>
<td></td>
</tr>
</tbody>
</table>

K. Lee, c1992
Pregnancy Sleep Study

BIRTH INFORMATION FORM

Study ID: ___ ___ ___ Date: ____/_____/_____

1. Did you have a boy or a girl? □ Boy □ Girl

2. What did you name him/her? ______________________________________

3. What day was he/she born? _____/_____/_____. Time of birth: ____ am/pm

4. Where did you deliver? ____________________________________________

5. How much did he/she weigh? _____ lbs _____ ozs or _____ kg

6. What was his/her length? _____ inches / cm

7. Did you have a vaginal birth or a c-section?
   □ Vaginal → Did they need to use…[circle]: forceps? vacuum?
   □ C-section → Was it…[circle one]: scheduled? emergency?
   reason: _______________________________________________________

8. Did you have any problems/complications during your pregnancy?
   □ No □ Yes describe:
   ________________________________________________________________

9. Did you have any hypertensive disorders of pregnancy?
   Preeclampsia
   □ No □ Yes describe:
   ____________________________
   Gestational hypertension
   □ No □ Yes describe:
   ____________________________
   Chronic hypertension
   □ No □ Yes describe:
   ____________________________
Preeclampsia superimposed onto chronic hypertension

☐ 0 No  ☑ 1 Yes describe:

Eclampsia

☐ 0 No  ☑ 1 Yes describe:

10. On a scale of 0-5 (0=none to 5=extreme), how much did you snore prior to pregnancy? (circle one)

0 1 2 3 4 5

11. On a scale of 0-5 (0=none to 5=extreme), how much did you snore during your last month of pregnancy? (circle one)

0 1 2 3 4 5

12. On a scale of 0-5 (0=none to 5=extreme), how much did your legs jump during your last month of pregnancy? (circle one)

0 1 2 3 4 5

13. Did you have diabetes prior to your pregnancy?

☐ 0 No  ☑ 1 Yes

14. Did you develop diabetes during your pregnancy?

☐ 0 No  ☑ 1 Yes

15. Did you have any complications during labor or delivery?

☐ 0 No  ☑ 1 Yes describe:

16. Did your baby have any complications?

☐ 0 No  ☑ 1 Yes describe:
17. Was your baby smaller than expected?

☐ No  ☐ Yes  describe:
_________________________________________________________
_________________________________________________________

18. Was your baby larger than expected?

☐ No  ☐ Yes  describe:
_________________________________________________________
_________________________________________________________

19. How long did your labor last? ______ hrs  (labor = regular painful contractions)

20. Was your labor induced?  ☐ No  ☐ Yes  →  How?

_________________________________________________________
_________________________________________________________

21. Did you get an epidural?  ☐ No  ☐ Yes

How many centimeters was your cervix dilated when the epidural was administered?

_______________ cms.

22. Did you get any other medications during labor?

☐ No  ☐ Yes  describe:
_________________________________________________________

23. What was your last weight prior to delivery? _____________ lbs.

24. How many prenatal appointments did you have during your pregnancy?

___________

25. How many weeks pregnant were you when you stopped working outside of your home?

_____________ wks.
26. Did you travel below 4500 feet during the last month of your pregnancy?

☐ No  ☐ Yes  

describe:

________________________________________________________________________

________________________________________________________________________

If yes, How long did you stay?

________________________________________________________________________
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Author Signature

[Date]
5/27/12