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Depressive Symptoms, Sleep Disturbance and Chronic Illness in
Diverse Midlife Women: A Longitudinal Study

by

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DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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Acknowledgements and Dedication

I acknowledge and give heartfelt thanks to the following:

The village of many who helped me in large and small ways along this journey that cannot be accomplished alone,

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UCSF School of Nursing faculty--inspiring from the start and into the future,

Abstract

Depressive symptoms, sleep disturbance and chronic illness are seldom studied together. Depression is higher in women and insomnia is a common sleep problem for women. Both are nurse-managed symptoms. This dissertation first proposes a theoretical nursing perspective of insomnia guided by four theoretical perspectives. The concepts from these perspectives were incorporated into a proposed model focused on mechanisms of insomnia and insomnia symptom experience.

The research involved a community-based sample of 347 healthy, ethnically diverse, premenopausal women between 40-50 years of age. The purpose was to describe patterns of depressive symptoms across time as a function of fixed demographic factors and time-varying biological and social factors, and describe the relationship between depressive symptoms and physical illness. The women with hypertension provided a group with a chronic physical illness.

Longitudinal data included the Center for Epidemiologic Studies – Depression (CES-D) scale, investigator-designed questionnaires about sociodemographics, medical history, and health problems, Pittsburgh Sleep Quality Index, social support subscale of the Interpersonal Relationships Inventory, and the health perception item from the Medical Outcomes Study Short Form. Biometric measures included: follicle stimulating hormone assays, blood pressure, and height and weight for calculating body mass index (BMI). Group comparisons used t-tests, ANOVA, chi square, and Mann-Whitney U.

Negative binomial regression was used for analysis of CES-D due to its skewed distribution in this sample. A significant model of predictors of CES-D scores was identified. Prevalence of depressive symptoms was 30% at study initiation and 26% at 30

months. Predictors of high CES-D scores were poor sleep quality, presence of chronic illness at 30 months, high BMI, and the interaction of time and poor sleep quality. Time, having a partner, positive social support and the interaction of time with low BMI predicted low CES-D scores.

A higher proportion of African American women scored $\geq$ 16 on the CES-D. Number of health conditions, presence of chronic illness, and hypertension were significantly higher for women scoring $\geq$16 on CES-D compared to women scoring <16. Chronic illness was reported by 30.8% African Americans compared to 26.4% European Americans and 15.8% Latinas. Research and clinical implications were identified.

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CHAPTER 1: INTRODUCTION

In over two decades of experience as a psychiatric consultation liaison clinical nurse specialist in inpatient clinical settings and over ten years as a faculty member in schools of nursing, I observed that chronic illness, depression and insomnia were frequently comorbid but there was little recognition of the co-occurrence and almost no evidence-based treatment of depression and sleep disturbance except the administration of drugs. My clinical practice efforts were directed to improving the situation.

Relationships between insomnia, mental disorders, and organic diseases are complex with limited epidemiological studies actually exploring the relationships among the three in the general population. Insomnia is a common sleep problem and a symptom managed by nurses. Depression and depressive symptoms are ubiquitous. This observation and my recognition of my need for science training directed me to the doctoral program. In the doctoral program, I discovered few studies exploring these complex comorbities. I learned that the term secondary insomnia frequently was used to catalog comorbid depression-insomnia or physical disease-insomnia to differentiate it from primary insomnia, which does not co-occur with mental or physical disorders. Most studies break the concepts into dyads, such as insomnia comorbid with a chronic physical illness or depression comorbid with a chronic physical illness or depression and comorbid insomnia. For example, Scott et al. (2007) explored mental-physical comorbidity worldwide, specifically focused on comorbid depression-anxiety co-occurring with physical conditions as well as non-comorbid depression and non-comorbid anxiety with physical conditions. Sleep disturbance was not explored as a comorbid factor.

Sleep disturbance often is viewed as a symptom of mental disorder rather than a risk for poor health outcomes on its own. Ohayon (2006) recently addressed this problem

in an editorial, commenting that mind and body medicine often run parallel non-intersecting paths.   For the patient, who is the sum of mind-body interactions, addressing only part of the problem poses risks for health outcomes. Ohayon (2006) illustrated his points with two Venn diagrams based on his epidemiological research showing the close interrelationships between mental disorders, sleep disturbances, especially insomnia, and organic diseases. His editorial was exciting to me because at that time, I was using a Venn diagram to illustrate my thoughts about co-occurring depression, insomnia and chronic diseases and was frustrated with the lack of attention to their co-occurrence in most of the literature.

My return to the doctoral program at UCSF was inspired by Dr. Kathryn Lee's presentation about her program of research on sleep and women. She agreed to be my research mentor and dissertation chair. I discovered, of course, how complex the study of the triad of comorbid depression, insomnia and chronic illness could be. Dr. Lee shared with me her database from the Midlife Women's Health Study, a longitudinal study of diverse midlife women's biobehavioral changes during menopausal transition funded by the National Institute of Nursing Research and the Office of Women's Health at the National Institutes of Health. My eyes opened to the issues related to the lack of research findings to guide women's health care. Using the Midlife Women's Health Study database, I have been able to study depressive symptoms, sleep quality, and health problems/chronic illness in diverse midlife women under the guidance of Dr. Lee.

This dissertation is organized into three manuscripts. The first paper (Chapter 2) presents a theoretical nursing perspective of sleep and insomnia and provides a critical appraisal of four key sleep theories and nursing concepts. Then proposed is a model of

insomnia focused on the symptom experience of insomnia linking mechanisms of insomnia with symptom management and outcomes. The purpose of the model is to enhance nurses's knowledge of insomnia and provide a base for intervention for insomnia. This manuscript will be submitted to a nursing journal. The second manuscript (Chapter 3) presents results of the study of predictors of depressive symptoms and patterns over time in ethnically diverse midlife women in the premenopausal late reproductive stage. The study identified a significant model of predictors of both higher and lower scores on the Center for Epidemiologic Studies-Depression (CES-D) scale used to measure depressive symptoms. This paper will be submitted to a psychiatric journal. The third and final paper (Chapter 4) presents the results of the study of the relationship between depressive symptoms and chronic illness in the broadest sense as well as hypertension as a specific type of chronic illness and the most prevalent in this sample of midlife women. Significant associations were found between ethnicity and chronic illness, between depressive symptoms and chronic illness, and between depressive symptoms and hypertension. This manuscript will be submitted to a psychiatric journal. The final paper is followed by a synthesis of findings and discussion of clinical and policy implications and directions for future research (Chapter 5).

References

Ohayon, M. M. (2006). Interlacing sleep, pain, mental disorders and organic diseases. *Journal of Psychiatric Research, 40*(8), 677-679.

Scott, K. M., Bruffaerts, R., Tsang, A., Ormel, J., Alonso, J., Angermeyer, M. C., et al. (2007). Depression-anxiety relationships with chronic physical conditions: Results from the world mental health surveys. *Journal of Affective Disorders, 103*(1-3), 113-120.

CHAPTER 2: A THEORETICAL NURSING PERSPECTIVE OF SLEEP AND

INSOMNIA

Abstract

Insomnia is a common sleep problem and a symptom managed by nurses. This paper proposes a theoretical nursing perspective of sleep and insomnia influenced by four key sleep theories and nursing concepts. Four theoretical sleep perspectives were critically appraised: The Conceptual Framework for Understanding Human Responses in Impaired Sleep, The Two Process Model of Sleep Regulation, The Spielman Model of Chronic Insomnia: Predisposing, Precipitating and Perpetuating Factors and The Neurocognitive Model of Insomnia.   The proposed model focuses on the symptom experience of insomnia linking mechanisms of insomnia with symptom management and outcomes.

Introduction

Insomnia is the most common of all sleep problems, with about one-third of the population age 15 and older reporting insomnia symptoms (Ancoli-Israel, 2006; Ohayon, 2002; Ohayon & Roth, 2001; Ohayon, Zulley, Guilleminault, Smirne, & Priest, 2001). However, neither health care providers nor the general public are well informed about what it is or how it is best managed (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006; Edinger & Means, 2005). The association between sleep and health is well documented and its importance is recognized in nursing (Berger et al., 2005; Lee et al., 2004; Ohayon, 2006; Zee & Turek, 2006). Nevertheless, nursing as a discipline has been slow to apply knowledge about sleep to clinical practice.

Active theory development continues in the areas of sleep regulation and insomnia (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006), reflecting the need to better understand a multidetermined phenomenon (Perlis, Smith, & Pigeon, 2005). Evidence links insomnia with a hyperarousal/stress syndrome (Stepanski & Rybarczyk, 2006), and with other physical and mental disorders, and requires theories that consider insomnia in the context of comorbities. Following a brief description of normal sleep and a discussion of insomnia, this paper will critically appraise four theoretical perspectives that address this complexity and explain potential mechanisms for insomnia. On the basis of these appraisals, a new symptom-focused model of insomnia will be proposed for the discipline of nursing that incorporates key mechanisms of insomnia.

What is Insomnia?

Normal sleep changes across the lifespan, with differences between women and men, young and old, and individual variations in sleep patterns depending on psycho-

social and environmental situations in one's life. However, characteristics of healthy sleep span these differences. In healthy sleepers, falling asleep is a transition from wake to light sleep (stage 1) that occurs within 10-15 minutes after turning the lights out and intending to fall asleep. Awakenings during sleep can be very brief cortical arousals that are not perceived or long bouts of frustrating wakefulness during the night. Wakefulness, or transition from light sleep to wake, indicates an arousal accompanied by increased norepinephrine or catecholamine secretion. Deep sleep (slow wave sleep (SWS) or stage 3-4 sleep) occurs primarily during the first third of the night and is considered restorative sleep and is associated with bursts of growth hormone and somatomedin peptides necessary for cell growth and restoration (Schmid et al., 2008).

Numerous definitions of insomnia exist. Insomnia may be a symptom or a disorder and may include difficulty falling asleep, difficulty staying asleep, a final awakening much earlier than planned, or poor quality, non restorative sleep that is unsatisfying (Edinger & Means, 2005; Roth & Roehrs, 2003). Some definitions include daytime dysfunction as a more specific indicator of non-restorative sleep and still others specify frequency (3 or more times per week) or duration of more than one month (Ancoli-Israel, 2006; Edinger & Means, 2005). Primary chronic insomnia is defined as difficulty initiating or maintaining sleep for the past six months, with clinically significant distress and impaired function. Primary insomnia is not diagnosed if the insomnia is related to or coexisting with other sleep disorders, mental disorders, medication side effects, or a medical condition (Ohayon, 2002; Petit, Azad, Byszewski, Sarazan, & Power, 2003). Insomnia coexisting with another condition (previously called

secondary insomnia) is now termed comorbid insomnia (Buysse, Ancoli-Israel, Edinger,

Lichstein, & Morin, 2006).

Why is Insomnia Important?

Insomnia is both a sleep disorder in its own right and a symptom experienced as a

part of physical or mental health problems or a response to stress. Although common,

insomnia is poorly defined, under-recognized, and under-treated. In clinical practice,

insomnia may be treated as a minor complaint or ignored, but it nevertheless has a

negative impact on quality of life, mood, metabolism and immune function, behavior,

daytime physical and cognitive functioning, and is associated with elevated use of

healthcare resources (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006; Edinger

& Means, 2005).

About one third of the adult population reports insomnia symptoms, and

insomnia is more common among women, middle-aged and older adults, shift workers,

and people with medical or psychiatric disorders (Morin et al., 2006; Ohayon, 2002). Not

only is chronic insomnia prevalent in the general population, it is even more prevalent

and more persistent in people with chronic diseases (Ancoli-Israel, 2006). Illness

conditions that are commonly associated with sleep problems are postoperative recovery

and the chronic diseases of chronic pain, cancer, cardiovascular, pulmonary or renal

disease, depression and neurological disorders such as Alzheimer's Disease and

Parkinson's Disease (Lee et al., 2004; Parker, 2003; Redeker, 2000; Redeker, Ruggiero,

& Hedges, 2004). Highly relevant to clinical nursing practice, sleep is viewed by experts

in the field as having a bidirectional relationship with health (Ohayon, 2006; Zee &

Turek, 2006).

Nurses and other health care providers are likely to encounter insomnia and sleep loss among their patients with chronic illnesses and must be able to provide appropriate theory-guided and evidence-based management. This is particularly relevant to the care of the elderly, for whom insomnia is an important risk factor for falls and hip fractures (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006), both serious safety concerns. In a review of literature and consensus statement of recommendations for standard research measures of insomnia, the authors report that typical daytime impairments reported with insomnia are fatigue, problems with cognitive abilities, such as attention and memory, mood disturbances and reduced quality of life (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006).

Insomnia is not caused by aging per se (Foley, Monjan, Simonsick, Wallace, & Blazer, 1999; Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). More often, comorbid insomnia co-occurs with, or results from, a medical or psychiatric condition, such as arthritis or peptic ulcer disease, or psychiatric disorders such as anxiety and depression (Benca, Ancoli-Israel, & Moldofsky, 2004; Lichstein, Wilson, & Johnson, 2000; Petit, Azad, Byszewski, Sarazan, & Power, 2003). Insomnia may also result from environmental factors, drug side effects, or negative health behaviors (such as smoking, alcohol or caffeine use, and lack of physical activity during the day) (Petit, Azad, Byszewski, Sarazan, & Power, 2003). Treatment of insomnia has been shown to improve both performance and cognitive daytime function (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006).

Although environmental sleep disruption in hospital settings has been a focus of research (Redeker, 2000), Griffiths and Peerson (2005) found that the development of

chronic insomnia following hospitalization was not associated with hospital

environmental issues although it could be predicted by predisposing factors that included

dysfunctional behaviors, beliefs and attitudes about causes and consequence of disturbed

sleep. This finding supports the importance of nursing assessment of pre-hospital sleep

patterns (Lee & Ward, 2005). In twenty-four hour settings, nurses have the responsibility

to identify, enhance and extend nursing activities that promote good sleep and in any

setting, patient/family education about sleep given by nurses may affect sleep quality of

patients (Griffiths & Peerson, 2005). Knowledge of sleep physiology and theories

explaining sleep have implications for nursing practice in understanding human responses

during illness and for the timing of drug administration and interpretation of laboratory

values (Lee et al., 2004).

Nurses in any setting, from public health to intensive care, will come across the

consequences of poor sleep quality, calling for increased awareness about sleep

disturbances. In non hospitalized samples, environmental sources of stress and sleep loss

include traumatic experiences, stress and anxiety related to threats of violence, loud

traffic and neighborhood noises, and noisy bed partners (Lee et al., 2004). Many

common life events are associated with sleep problems (Lee et al., 2004; Redeker,

Ruggiero, & Hedges, 2004), such as exposure to new or stressful environments, rapid

time zone changes, pregnancy and postpartum, and menopause. Impaired sleep can

affect school performance in children and is associated with errors and workplace

accidents among adults. The most extreme effects of insomnia may be reports of

fatalities due to driving while sleepy (Lee et al., 2004; Ohayon & Roth, 2001). Because

many health care settings operate all day and all night, the need for awareness extends to

caregivers who must consider the possible impact of sleep problems on their own health and performance, especially when rotating shifts or working permanently at night (Lee et al., 2004).

Theoretical Approaches to Sleep and Insomnia in Health and Illness

The four theoretical perspectives discussed here are selected based on their importance in sleep science or their previous application to nursing. These four perspectives will be described briefly and critically assessed in terms of the following criteria: purpose or goal of the theory and whether it provides knowledge of order, disorder or control, identification and definition of important concepts, description of important relationships or linkages, whether the theory has been empirically or clinically validated and nursing implications, including advantages or disadvantages for nursing research or practice. In relation to theory evaluation, Meleis (2005) defined knowledge of order, knowledge of disorder and knowledge of control. Knowledge of order refers to the natural and normal state, regularities in phenomena in health. Knowledge of disorder refers to a context or disorder which is dealt with by nurses or other providers. Knowledge of control refers to prescription of a course of action, that if implemented could change the subsequent events in a desired way. Key concepts from the four theoretical perspectives on sleep or insomnia will be incorporated into a proposed conceptualization of sleep that focuses on the experience of the symptom of insomnia, and links mechanisms of insomnia with symptom management.

The Conceptual Framework for Understanding Human Responses in Impaired Sleep

The Conceptual Framework for Understanding Human Responses in Impaired Sleep (Lee et al., 2004) was developed by sleep experts in nursing to guide nursing

curricula. Because nursing is the discipline interested in human responses in health and illness, this framework places sleep problems in the context of health and illness. Within this framework, impaired sleep is seen as a potential health problem, with bio-psycho-social health consequences occurring in response to sleep loss conceptualized as either sleep deprivation or sleep disruption or both. Sleep deprivation refers to an inadequate amount of sleep primarily due to self-imposed restriction, lifestyle factors or work demands. Sleep disruption refers to fragmented sleep primarily due to health conditions or changes in health status. Sleep disruption and fragmentation at night can be related to health problems, stress or environmental alterations. Sleep loss places an individual at risk for poor health outcomes that include physiological, cognitive, behavioral, emotional or social responses.

This conceptual framework is a key part of the recommendations about sleep and chronobiology content in nursing education programs that was developed by consensus of the nurse experts in sleep (Lee et al., 2004). Although the framework organizes concepts important for understanding impaired sleep and focuses intentionally on nursing education, it does not specifically address insomnia as a form of impaired sleep. However, it does link impaired sleep to health outcomes and includes stress, although not mechanisms of arousal, as a precipitant of impaired sleep. The framework has not been clinically or empirically validated. Nevertheless, it is the first published framework with recommendations for nursing education and the concepts are important for understanding and managing sleep disturbances.

The Two Process Model of Sleep Regulation

The Two Process Model (TPM) of Sleep Regulation is the accepted global view

on the regulation of sleep timing (Beersma, 2002) based on relationships that are deduced

from laboratory studies of sleep and circadian rhythms (Borbely & Achermann, 2005). It

was developed by sleep neurophysiologists and is used to explain and predict normal

sleep timing and health related changes in sleep. It provides knowledge of order (the

normal state of sleep and regulation of sleep), knowledge of disorder (such as sleep

disorders and sleep in depression), and knowledge of control (sleep interventions based

on the model such as the use of sleep deprivation).

According to Borbely and Achermann (2005), the propensity to sleep is

determined by a sleep-wake balance or homeostatic process (S) that regulates sleep, and a

circadian process (C). The interaction of Process S and Process C determines optimal

timing of sleep and wake for a particular individual (Borbely & Achermann, 2005) (See

Figure 1). Homeostatic mechanisms increase the propensity to sleep when sleep has been

absent, and reduce sleep propensity when sleep has recently occurred. The TPM

delineates these healthy homeostatic mechanisms (Borbely, Achermann, Geering, &

Tobler, 2000). Process C modulates sleep with an internal clocklike mechanism and it is

independent of prior sleep and waking (Borbely & Achermann, 2005; Borbely,

Achermann, Geering, & Tobler, 2000). In the TPM, Process C is influenced by the time

of day and thought to be a result of the impact of the circadian pacemaker located in the

suprachiasmatic nuclei of the hypothalamus (Beersma, 2002).

Timing of sleep and changes in daytime vigilance are governed by the interaction

of Processes S and C. Rising homeostatic sleep pressure during waking is compensated

by the declining circadian sleep propensity. Rising circadian sleep propensity during

sleep counteracts the declining homeostatic sleep pressure, thereby maintaining sleep

(Borbely & Achermann, 2005; Borbely, Achermann, Geering, & Tobler, 2000).

The TPM has implications for nurses, nursing problems and nursing therapeutics

but these are not addressed in the model. Though the TPM has been used as a framework

for nursing research (Parker, Bliwise, & Rye, 2000; Redeker, Ruggiero, & Hedges,

2004), it was not included in the recent nursing education recommendations for sleep

content (Lee et al., 2004). The TPM is abstract rather than concrete and may be difficult

to grasp without a schematic (see Figure 1). The TPM does not include contextual or

environmental factors important to nursing, other than light exposure, a key signal from

the environment that maintains the 24-hour internal circadian clock.

The Spielman Model of Chronic Insomnia: Predisposing, Precipitating and Perpetuating

Factors

The Spielman Model of Chronic Insomnia: Predisposing, Precipitating and

Perpetuating Factors (Spielman Model) is a behavioral model that was developed by

psychologists with a focus on assessment and treatment planning (Spielman, Yang, &

Glovinsky, 2005). According to the Spielman model, sleep is a complex behavior

responsive to stimuli encountered during wakefulness. The Spielman model places less

emphasis on physiology and more on cognitive and physiologic stimuli that cause acute

and chronic insomnia. It specifies behavioral processes and therefore actions for

intervention. Perlis and colleagues (Perlis, Smith, & Pigeon, 2005) suggested that it is a

stress-diathesis model. Predisposing factors are the diathesis, preexisting vulnerabilities.

Acute insomnia occurs due to traits (predisposing factors) and life stresses (precipitating

factors). Chronic insomnia then is maintained by maladaptive behavioral coping

strategies (perpetuating factors) (Perlis, Smith, & Pigeon, 2005). Because sleep is subject

to the same processes of conditioning that govern waking behaviors, sleep can be

modified (Spielman, Caruso, & Glovinsky, 1987). Therefore, Spielman and Glovinsky

(1991) view insomnia as the end result of their key concepts of predisposing,

precipitating and perpetuating factors.

Predisposing factors, conditions that set the stage for insomnia, may be

overlooked. A wide range of biopsychosocial factors may predispose to insomnia.

Examples include consistently elevated cortisol levels, excessive worry or rumination, or

a sleep schedule incompatible with the bed partner's (Perlis, Smith, & Pigeon, 2005).

Factors such as physiologic and cognitive arousal, maladaptive behaviors, and specific

beliefs or attitudes may serve as predisposing or perpetuating factors in chronic insomnia

(Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006). These factors or traits are

relatively constant, and if they are not identified and dealt with, they may delay

improvement or result in relapse (Spielman & Glovinsky, 1991; Spielman, Nunes, &

Glovinsky, 1996).

Precipitating factors are the triggers of a bout of insomnia and are "flushed out by

the question, 'Why now?'" (Spielman & Glovinsky, 1991, p. 11). An example of a

precipitating factor could be a new diagnosis of a serious medical condition and the

initiation of treatment. Many precipitating factors can be anticipated by nurses working

with their unique patient populations and therefore health promotion or insomnia-

preventing measures can be instituted to avoid perpetuating chronic and severe forms of

insomnia.

Perpetuating factors are usually not present at the inception of insomnia but appear as a consequence of behavioral coping with the insomnia problem. Examples include excessive time in bed, irregular timing of going to sleep and getting up, unpredictability of sleep, anxiety over daytime deficits, expectations of a bad night, sleep fragmentation, maladaptive conditioning, and alcohol, caffeine or hypnotic use (Spielman & Glovinsky, 1991). The intensity of precipitating factors diminishes with time. As the intensity of the precipitating factors subside, the perpetuating factors increase in importance and are then sufficient to sustain insomnia (Spielman, Nunes, & Glovinsky, 1996).

A learning perspective suggests that sleep behavior can be regulated by stimulus conditions (Spielman, Caruso, & Glovinsky, 1987; Spielman & Glovinsky, 1991; Spielman, Yang, & Glovinsky, 2005). Some behavioral treatments dampen cognitive and physiological activation to permit sleep to occur. The cause and pathogenesis of a proportion of insomnia cases often remain unsettled, and a full understanding of insomnia is elusive because it is multifactoral. Sleep cannot be produced by force of will; cognitive activation and muscle tension can serve as obstacles to sleep onset and sleep maintenance as arousal takes precedence over sleep (Spielman, Caruso, & Glovinsky, 1987; Spielman & Glovinsky, 1991; Spielman, Yang, & Glovinsky, 2005). Whether or not an individual will sleep is dependent on 1) level of the physiological drive to sleep, 2) an opposing tendency to maintain alertness arising from cortical excitation or other physiological sources of arousal, and 3) an individual's characteristic level of responsiveness (Spielman, Caruso, & Glovinsky, 1987; Spielman & Glovinsky, 1991; Spielman, Yang, & Glovinsky, 2005). Although Spielman and colleagues did not

elaborate, they made an important contribution in the inclusion of cortical arousal. In addition, the Spielman model addresses aspects of Process S as noted above in "level of the physiological drive to sleep" but not Process C (circadian factors).

Griffiths and Peerson (2005) are nurse researchers who used the Spielman Model in their Australian study to identify risk factors for chronic insomnia for patients following hospitalization. Other nurse researchers have applied the Spielman model to identify the etiologies of sleep and circadian rhythm disturbances in persons with cancer (Lee, Cho, Miaskowski, & Dodd, 2004). Similar reviews in other specialties could be conducted to develop this framework for use in setting standards for clinical settings in regard to sleep. The Spielman model was not included in the recent nursing education recommendations for sleep content (Lee et al., 2004). The Spielman model is untested, undeveloped as a model to guide research, and intended to guide clinical assessment and behavioral treatment planning. It explains psychological mechanisms of the onset and maintenance of insomnia. Compelling evidence for its validity is the success of treatments based on the behavioral principles but the model has never been empirically evaluated (Perlis, Smith, & Pigeon, 2005). Although it is a model of chronic insomnia, it is also helpful in understanding acute insomnia. An advantage of the Spielman model for nursing research and practice is its focus on client, health problem, health, environment and therapeutics. It does not focus on knowledge of order but primarily provides knowledge of disorder (a behavioral perspective on how insomnia develops and is maintained) and knowledge of control (cognitive and behavioral interventions for insomnia). The three factors of the Spielman Model are clearly defined and would be a useful addition to a symptom-focused nursing model of insomnia.

In its current form the model is simple and clinically useful. Its research utility is limited by the fact that not all of the potential items in each set of factors are identified. This is because items are individualized to the particular patient's circumstances. This would logically lead to a tailored approach to intervention, but researchers would be challenged to identify the active ingredient among so many potential items. In addition, as Perlis and colleagues (Perlis, Smith, & Pigeon, 2005) pointed out, the Spielman Model is limited by absence of research-based physiological mechanisms, such as conditioned arousal, that contribute to the initiation and maintenance of insomnia. The predisposing, precipitating and perpetuating factors are incorporated in the proposed new model.

Neurocognitive Model of Insomnia

The Neurocognitive Model of Insomnia, first published in 1997, is focused on primary insomnia and originated in cognitive neuroscience and behaviorism. The purpose of the Neurocognitive Model is to guide research leading to knowledge development about insomnia and leading to testing novel treatment approaches. It continues to be further developed and tested by Perlis and colleagues (Drummond, Smith, Orff, Chengazi, & Perlis, 2004; Perlis, 2001; Perlis, Smith, Andrews, Orff, & Giles, 2001; Perlis, Smith, & Pigeon, 2005) and extends behavioral models such as the Spielman model. The authors suggest that insomnia is best characterized as a disorder of hyperarousal of the central nervous system (Drummond, Smith, Orff, Chengazi, & Perlis, 2004). Core to this model is the view that acute insomnia occurs in association with cognitive and behavioral factors, but chronic insomnia is a reversible central nervous system disorder that occurs in relation to behavioral factors as a result of classical conditioning.

Incorporating the role of behavioral factors, the Neurocognitive Model of

Insomnia (Perlis, Smith, & Pigeon, 2005) attempts to define arousal and how arousal may

interfere with sleep initiation and maintenance as well as the perception of sleep. The

model considers three intersecting dimensions of arousal (somatic, cognitive and cortical)

with a particular focus on measurement and consequences of cortical arousal. The

researchers argue that cortical arousal occurs as a result of classical conditioning. Perlis

and colleagues (2005) hypothesized that cortical arousal allows for abnormally enhanced

sensory and information processing and increased long-term memory formation; these

link with sleep state misperception around sleep onset, where the distinction between

sleep and wakefulness can be blurred even among trained sleep technicians. In sleep

state misperception, objective laboratory criteria for sleep is documented by a change in

cortical brain activity from an awake state, but is nevertheless perceived by the individual

as still being awake (Perlis, Smith, & Pigeon, 2005).

Hyperarousal has been identified with symptoms of mind racing with

preoccupations, anxiety, and worries when in bed and found to indicate a sleep or mental

disorder diagnosis (Ohayon & Roth, 2001). The Neurocognitive Model assumes that

insomnia is a disorder of hyperarousal. This view is supported by the research of

Vgontzas and colleagues (Vgontzas et al., 2001; Vgontzas & Chrousos, 2002; Vgontzas

et al., 1998) on sleep and the activity of the stress system, particularly the hypothalamic-

pituitary-adrenal (HPA) axis and the sympathetic system. Sleep, particularly deep sleep,

appears to have an inhibitory influence on the HPA axis and cortisol secretion whereas

activation of the stress system, including the HPA axis, can lead to arousal and

sleeplessness. The findings of Vgontzas and colleagues (2001) support the view that

insomnia is a disorder of hyperarousal present throughout the 24-hour day. As a result, Vgontzas and colleagues (2001) concluded that the pathophysiology of chronic insomnia is likely different than sleep loss and suggested that treatment should focus not on improvement of quality or quantity of sleep, but on reducing overall hyperarousal. However, this approach is not specified in the Neurocognitive Model (Perlis, Smith, & Pigeon, 2005).

According to Perlis and colleagues (Perlis, Smith, & Pigeon, 2005), the major strength of the Neurocognitive Model is that it is an integrated perspective on primary insomnia which allows for behavior, neuropsychological function, and neurobiological considerations to contribute to the etiology and pathogenesis of insomnia (Perlis, Smith, & Pigeon, 2005). The model was limited by the absence of important homeostatic and circadian influences on sleep (Perlis, Smith, & Pigeon, 2005). Sleep homeostasis is altered in primary insomnia and may interact with hyperarousal and circadian factors (Pigeon & Perlis, 2006).

In a later publication, Pigeon and Perlis (Pigeon & Perlis, 2006), identified three main contributors that underlie insomnia: hyperarousal, circadian dysrhythmia and homoeostatic dysregulation. They reviewed a large body of research, which was focused on hyperarousal as either an elevated basal level of arousal or as the failure to down-regulate nighttime arousal. They reviewed the evidence for physiologic, cognitive and cortical dimensions of hyperarousal, and evidence for circadian and homeostatic dysregulation in insomnia. The physiologic dimension is supported by studies showing that adults with primary insomnia manifest elevated heart rate, galvanic skin response, sympathetic arousal (heart rate variability) and an increase in HPA axis activity. Studies

supporting the cognitive arousal dimension demonstrate that adults with primary insomnia worry more in general and worry more specifically about their sleep and insomnia symptoms. The cortical arousal dimension is supported by evidence of increased amounts of high frequency EEG activity at or near sleep onset and during non-REM sleep that is associated with perception of lower sleep quality and experience of sleep state misperception (Pigeon & Perlis, 2006).

A review of a smaller but growing body of evidence suggests that chronobiologic or circadian abnormalities in the biological clock may be related to sleep initiation or maintenance problems in primary insomnia (Pigeon & Perlis, 2006). Initiation insomnia is associated with circadian phase delay, while early morning awakenings are associated with circadian phase advance of core body temperature rhythm. Circadian phase abnormalities are not thought to be the sole precipitant of insomnia (Pigeon & Perlis, 2006). Pigeon and Perlis (2006) suggest that circadian disturbances may be a consequence of compensatory strategies, such as changing one's sleep schedule, which individuals do to deal, effectively or ineffectively, with sleep loss. These changes may alter the timing of their exposure to daylight. Once altered, these types of phase shifts may perpetuate insomnia (Pigeon & Perlis, 2006).

Pigeon and Perlis (2006) also reviewed research in support of their proposition that sleep homeostasis is altered in insomnia. They suggested that homeostatic dysregulation may contribute to predisposition, precipitation and perpetuation of insomnia and that sleep homeostasis interacts not only with circadian factors but also with hyperarousal. They found limited empirical evidence for homeostatic dysregulation

related to onset, incidence or severity of insomnia, and delineated a research agenda that could address these lines of inquiry (Pigeon & Perlis, 2006).

Similar to the Spielman model, the Neurocognitive Model focuses on the client, health problem, health, environment, and therapeutics. The model provides little knowledge of order, but provides knowledge of disorder (physiological and behavioral mechanisms accounting for the development and maintenance of primary insomnia) and knowledge of control (direction for the development of interventions, especially cognitive behavioral interventions for insomnia). The Neurocognitive Model is complex, but that may be appropriate given that clinical reality is complex. Not all linkages are explained; although vulnerability to physical and psychiatric illness is placed in the model it is not explained at all. The Neurocognitive Model was developed most recently and thus is not included in recommendations for sleep content in nursing education (Lee et al., 2004).

To the extent that nurses deal with insomnia from a perspective of symptom management, and because they care for people who experience insomnia in the context of other medical or psychiatric disorders, not all aspects of the Neurocognitive model may have nursing practice implications. The model emphasizes objective laboratory measurement of arousal and high frequency cortical brain activity in people with primary insomnia. While these measurements may not be essential to nursing practice, the concepts of arousal and hyperarousal have substantial meaning for symptom management and are therefore incorporated in the proposed new model.

A New Model of Insomnia as Symptom Experience

The Theory of Symptom Management (TSM) (Dodd et al., 2001; Humphreys et al., In press, 2008) was used as the basis for a new model of insomnia. TSM is a middle-range theory, developed by the School of Nursing faculty at the University of California, San Francisco, and serves to guide symptom assessment and treatment in the practice setting as well as identifying questions and hypotheses for nursing research (Humphreys et al., In press, 2008). The overall context for the TSM is the discipline of nursing and the meta-paradigmatic nursing domains of person, environment, health and illness. The three key dimensions of the TSM are symptom experience, management strategies, and outcomes (Dodd et al., 2001; Humphreys et al., In press, 2008). Symptom experience involves the simultaneous interactions between perception, symptom evaluation and a response to the change in feeling. The response may be emotional or behavioral (Humphreys et al., In press, 2008). For example, if a woman is living with chronic pain, this pain symptom may include a response that involves frequent waking during the night. If the symptom is difficulty falling asleep, the response may be anxiety because of one's attitude toward the importance of a "good night's sleep" or daytime sleepiness and poor work performance.

The second dimension of the TSM is symptom management strategies that include efforts to prevent, postpone, or minimize the symptom experience using strategies specific to who delivers the intervention, what it is, what dose, where, to whom and when (Humphreys et al., In press, 2008). If someone experiences difficulty falling asleep and uses a self-care strategy of drinking alcohol to fall asleep, it may induce sleep but then create or precipitate another form of insomnia with frequent awakening, less

deep sleep, and more daytime sleepiness. The third key dimension of the TSM is symptom status outcomes. Clear and validated outcome measures are critical and include a change in symptom status, such as improved sleep quality, as well as better physical or mental function, not falling asleep during the day, or having more energy for personal interactions.

The three dimensions of TSM are influenced by the contextual variables of person, health and illness and environment. The health and illness domain is especially important to the study of insomnia comorbid with other chronic disorders which is a relatively new area in sleep science (Ancoli-Israel, 2006). TSM components overlap, with bidirectional relationships indicating that the dimensions and domains are in constant interaction (Henly, Kallas, Klatt, & Swenson, 2003). The TSM was designed to explain a broad variety of symptom experiences within an interventionist framework, and the example of sleep symptoms has been used to support the validity of the overall model (Dodd et al., 2001; Henly, Kallas, Klatt, & Swenson, 2003; Humphreys et al., In press, 2008). However, mechanisms producing symptoms have not been explicitly included as part of the TSM. Further description of the TSM is available elsewhere (Dodd et al., 2001; Humphreys et al., In press, 2008).

Key concepts for the proposed model (see Figure 2) of mechanisms of insomnia within the symptom experience dimension include predisposing factors, precipitating factors and perpetuating factors from the Spielman model, hyperarousal and stress system concepts from the research of Vgontzas and colleagues and hyperarousal and conditioned arousal from Perlis and colleagues' neurocognitive model as well as Process S (homeostatic sleep regulation) and Process C (circadian sleep regulation) from the TPM.

Definitions of the dimensions and domains of the TSM, which were discussed above, remain the same as in that theory.

Predisposing factors are traits within the person that set the stage for the experience of insomnia and co-occur with precipitating factors. A stressful event would be a precipitating factor, or trigger for a bout of acute insomnia, and that event may be from the domains of environment, person or health and illness, such as diagnosis of a serious physical illness or a planned medical procedure. The individual's perception of this experience may result in a cascade of the hypothalamic-pituitary-adrenal (HPA) system that leads to arousal and acute insomnia. As defined in the Neurocognitive Model, arousal includes three intersecting dimensions (somatic, cognitive and cortical). For example, the individual could perceive bodily and cognitive arousal, and cortical arousal would be evident from objective laboratory measurement of sleep-wake patterns. The individual then perceives the symptoms associated with insomnia, simultaneously evaluates that experience, and responds, all within the symptom experience dimension (from the TSM).

The proposed model of mechanisms leading to the insomnia symptom experience incorporates the concept of Process C (circadian regulation) and Process S (homeostatic sleep regulation) from the theory of sleep regulation. This two-process model has global acceptance by the sleep research community. Circadian dysrhythmia and homeostatic dysregulation of sleep are thought to contribute to insomnia (Pigeon & Perlis, 2006). Process C is included here as a potential predisposing factor because it is an internal neurobiological mechanism, independent of prior sleep and waking. Process S is included as a potential precipitating factor that is influenced by behavioral changes in

sleep and wake patterns from self-imposed restriction, lifestyle factors or work demands.

It may be that either process, once dysregulated and interacting with the other, could

affect the stress system cascade and lead to hyperarousal. In addition, either process once

dysregulated and interacting with hyperarousal, could be considered a perpetuating factor

in conditioned arousals and the development of chronic insomnia (Pigeon & Perlis,

2006).

To further elaborate on the proposed model of insomnia as symptom experience,

the previous discussion of the individual who perceives the symptoms associated with

insomnia and simultaneously evaluates and responds is continued here. If an adult's

inherent attitude toward sleep is one of low importance, there is likely to be no further

action; but if sleep is seen as very important, then a bout of even one night of insomnia

can be perceived as distressing and the individual may choose any one of several

potential management strategies. Many of these strategies, such as excessive time in bed,

irregular timing of going to sleep and getting up, caffeine late in the day, over-the-counter

sleep medication or alcohol, may be maladaptive and actually perpetuate the insomnia

through conditioning of cortical arousal, and result in chronic insomnia. This is

illustrated in the model in Figure 2 with the directional arrow of perpetuating factors

(from the management strategies dimension not included in Figure 2). These behaviors

then condition arousal, resulting in insomnia that is chronic. The model in Figure 2

implies an interaction over time within the symptom experience dimension and affected

by the mechanisms of predisposing factors, stress system cascade, precipitating and

perpetuating factors, arousal and conditioned arousal. The directional arrows show how

symptoms of acute insomnia when affected by the perpetuating factors can become chronic.

Combining the TSM and mechanisms of insomnia figuratively is complicated, as it would be with any theory of human behavior. To simplify the proposed model for parsimony and for the purposes of discussion, one figure is presented, specific to the symptom experience dimension and key mechanisms of insomnia.

This model of the symptom experience of insomnia has implications for practice as well as research. It points to aspects of the symptom experience, arousal and conditioned arousal; where management strategies could be instituted to prevent precipitating factors from leading to acute insomnia, prevent the transition from acute to chronic insomnia or to block perpetuating factors from conditioning chronic insomnia. The focus on potential conditioning of arousal in this model points to the use of behavioral methods for symptom assessment and management as well as management of overall arousal. Critical timing of nursing management strategies would be important for the prevention of conditioned arousal and chronic insomnia.

The predisposing, precipitating, and perpetuating factors should be assessed and identified before the clinical application of appropriate management strategies. If perpetuating factors are already in place and insomnia is chronic, then the appropriate management strategies would involve part or all of cognitive behavioral therapy for insomnia. As with other chronic medical conditions, both qualitative and quantitative research methods could be used to optimize the understanding and thus management strategies for both primary insomnia and insomnia that is comorbid with other chronic illnesses.

Summary

Current theoretical perspectives of the mechanisms explaining sleep and insomnia have been critiqued for their relevance for nursing practice and research. The theoretical perspectives include relevant content for nurses. Key concepts germane to nursing were identified and incorporated into a new model proposed for insomnia as a symptom experience. This new model extends the Theory of Symptom Management to include physiological and psychological mechanisms of acute and chronic insomnia in the symptom dimension to provide clearer guidance for the timing and choice of management strategies. Management strategies are beyond the scope of this paper but effective strategies would then have a role in improving sleep and reducing the outcomes of biopsychosocial morbidity associated with sleep loss.

References

Ancoli-Israel, S. (2006). The impact and prevalence of chronic insomnia and other sleep disturbances associated with chronic illness. *American Journal of Managed Care, 12*(8 Suppl), S221-229.

Beersma, D. G. M. (2002). Insomnia and the 2-process model of sleep regulation: Etiopathogenic considerations. *Primary Care Companion Journal of Clinical Psychiatry, 4 (suppl 1)*, 13-16.

Benca, R. M., Ancoli-Israel, S., & Moldofsky, H. (2004). Special considerations in insomnia diagnosis and management: Depressed, elderly, and chronic pain populations. *Journal of Clinical Psychiatry, 65 Suppl 8*, 26-35.

Berger, A., Parker, K., Young-McCaughan, S., Mallory, G., Barsevick, A., Beck, S., et al. (2005). Sleep wake disturbances in people with cancer and their caregivers: State of the science. *Oncology Nursing Forum, 32*(6), E98-E126.

Borbely, A., & Achermann, P. (2005). Sleep homeostasis and models of sleep regulation. In M. H. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (Fourth edition) . Philadelphia: Elsevier Saunders.

Borbely, A., Achermann, P., Geering, B., & Tobler, I. (2000). Processes underlying sleep regulation. In A. C. o. Neuropsychopharmacology (Ed.), *Psychopharmacology-- the fourth generation of progress*: American College of Neuropsychopharmacology.

Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Lichstein, K. L., & Morin, C. M. (2006). Recommendations for a standard research assessment of insomnia. *Sleep, 29*(9), 1155-1173.

Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E. S., Humphreys, J., et al. (2001). Advancing the science of symptom management. *Journal of Advanced Nursing, 33*(5), 668-676.

Drummond, S. P., Smith, M. T., Orff, H. J., Chengazi, V., & Perlis, M. L. (2004). Functional imaging of the sleeping brain: Review of findings and implications for the study of insomnia. *Sleep Medicine Reviews, 8*(3), 227-242.

Edinger, J. D., & Means, M. K. (2005). Overview of insomnia: Definitions, epidemiology, differential diagnosis, and assessment. In M. H. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (4th ed.). Philadelphia: Elsevier Saunders.

Foley, D. J., Monjan, A., Simonsick, E. M., Wallace, R. B., & Blazer, D. G. (1999). Incidence and remission of insomnia among elderly adults: An epidemiologic study of 6,800 persons over three years. *Sleep, 22 Suppl 2*, S366-372.

Griffiths, M. F., & Peerson, A. (2005). Risk factors for chronic insomnia following hospitalization. *Journal of Advanced Nursing, 49*(3), 245-253.

Henly, S. J., Kallas, K. D., Klatt, C. M., & Swenson, K. K. (2003). The notion of time in symptom experiences. *Nursing Research, 52*(6), 410-417.

Humphreys, J., Lee, K. A., Carrieri-Kohlman, V., Puntillo, K., Faucett, J., Janson, S., et al. (In press, 2008). A middle range theory of symptom management In M. J. Smith & P. R. Liehr (Eds.), *Middle range theory for nursing (2nd ed).* New York: Springer Publishing Company.

Lee, K. A., Cho, M., Miaskowski, C., & Dodd, M. (2004). Impaired sleep and rhythms in persons with cancer. *Sleep Medicine Reviews, 8*(3), 199-212.

Lee, K. A., Landis, C., Chasens, E. R., Dowling, G., Merritt, S., Parker, K. P., et al. (2004). Sleep and chronobiology: Recommendations for nursing education. *Nursing Outlook, 52*(3), 126-133.

Lee, K. A., & Ward, T. M. (2005). Critical components of a sleep assessment for clinical practice settings. *Issues in Mental Health Nursing, 26*(7), 739-750.

Lichstein, K. L., Wilson, N. M., & Johnson, C. T. (2000). Psychological treatment of secondary insomnia. *Psychology and Aging, 15*(2), 232-240.

Meleis, A. I. (2005). *Theoretical nursing: Development and progress* (3rd edition revised reprint ed.). Philadelphia: Lippincott Williams & Wilkins.

Morin, C. M., Bootzin, R. R., Buysse, D. J., Edinger, J. D., Espie, C. A., & Lichstein, K. L. (2006). Psychological and behavioral treatment of insomnia: Update of the recent evidence (1998-2004). *Sleep, 29*(11), 1398-1414.

Ohayon, M. M. (2002). Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Medicine Reviews, 6*(2), 97-111.

Ohayon, M. M. (2006). Interlacing sleep, pain, mental disorders and organic diseases. *Journal of Psychiatric Research, 40*(8), 677-679.

Ohayon, M. M., Carskadon, M. A., Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. *Sleep, 27*(7), 1255-1273.

Ohayon, M. M., & Roth, T. (2001). What are the contributing factors for insomnia in the general population? *Journal of Psychosomatic Research, 51*(6), 745-755.

Ohayon, M. M., Zulley, J., Guilleminault, C., Smirne, S., & Priest, R. G. (2001). How

    age and daytime activities are related to insomnia in the general population:

    Consequences for older people. *Journal of the American Geriatrics Society,*

    49(4), 360-366.

Parker, K. P. (2003). Sleep disturbances in dialysis patients. *Sleep Medicine Reviews,*

    7(2), 131-143.

Parker, K. P., Bliwise, D. L., & Rye, D. B. (2000). Hemodialysis disrupts basic sleep

    regulatory mechanisms: Building hypotheses. *Nursing Research, 49*(6), 327-332.

Perlis, M. L. (2001). Response to "Do increases in beta EEG activity uniquely reflect

    insomnia?" (C. H. Bastein and M. H. Bonnet). *Sleep Medicine Reviews, 5*(5), 379-

    383.

Perlis, M. L., Smith, M. T., Andrews, P. J., Orff, H., & Giles, D. E. (2001). Beta/gamma

    EEG activity in patients with primary and secondary insomnia and good sleeper

    controls. *Sleep, 24*(1), 110-117.

Perlis, M. L., Smith, M. T., & Pigeon, W. R. (2005). Etiology and pathophysiology of

    insomnia. In M. H. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and*

    practice of sleep medicine (4th ed.). Philadelphia: Elsevier Saunders.

Petit, L., Azad, N., Byszewski, A., Sarazan, F. F., & Power, B. (2003). Non-

    pharmacological management of primary and secondary insomnia among older

    people: Review of assessment tools and treatments. *Age and Ageing, 32*(1), 19-25.

Pigeon, W. R., & Perlis, M. L. (2006). Sleep homeostasis in primary insomnia. *Sleep*

    Medicine Reviews, 10(4), 247-254.

Redeker, N. S. (2000). Sleep in acute care settings: An integrative review. *Journal of Nursing Scholarship, 32*(1), 31-38.

Redeker, N. S., Ruggiero, J. S., & Hedges, C. (2004). Sleep is related to physical function and emotional well-being after cardiac surgery. *Nursing Research, 53*(3), 154-162.

Roth, T., & Roehrs, T. (2003). Insomnia: Epidemiology, characteristics, and consequences. *Clinical Cornerstone, 5*(3), 5-15.

Schmid, D. A., Brunner, H., Lauer, C. J., Uhr, M., Yassouridis, A., Holsboer, F., et al. (2008). Acute cortisol administration increases sleep depth and growth hormone release in patients with major depression. *Journal of Psychiatric Research*.

Spielman, A. J., Caruso, L. S., & Glovinsky, P. B. (1987). A behavioral perspective on insomnia treatment. *Psychiatric Clinics of North America, 10*(4), 541-553.

Spielman, A. J., & Glovinsky, P. B. (1991). Introduction: The varied nature of insomnia. In P. J. Hauri (Ed.), *Case studies in insomnia* (pp. 1-15). New York, New York: Plenum Press.

Spielman, A. J., Nunes, J., & Glovinsky, P. B. (1996). Sleep disorders I: Insomnia. *Neurologic Clinics, 14*(3).

Spielman, A. J., Yang, C.-M., & Glovinsky, P. B. (2005). Assessment techniques for insomnia. In M. H. Kryger, T. Roth & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (4 ed.). Philadelphia: Elsevier Saunders.

Stepanski, E. J., & Rybarczyk, B. (2006). Emerging research on the treatment and etiology of secondary or comorbid insomnia. *Sleep Medicine Reviews, 10*(1), 7-18.

Vgontzas, A. N., Bixler, E. O., Lin, H. M., Prolo, P., Mastorakos, G., Vela-Bueno, A., et al. (2001). Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: Clinical implications. *Journal of Clinical Endocrinology and Metabolism, 86*(8), 3787-3794.

Vgontzas, A. N., & Chrousos, G. P. (2002). Sleep, the hypothalamic-pituitary-adrenal axis, and cytokines: Multiple interactions and disturbances in sleep disorders. *Endocrinology and Metabolism Clinics of North America, 31*(1), 15-36.

Vgontzas, A. N., Tsigos, C., Bixler, E. O., Stratakis, C. A., Zachman, K., Kales, A., et al. (1998). Chronic insomnia and activity of the stress system: A preliminary study. *Journal of Psychosomatic Research, 45*(1 Spec No), 21-31.

Zee, P. C., & Turek, F. W. (2006). Sleep and health: Everywhere and in both directions. *Archives of Internal Medicine, 166*(16), 1686-1688.

Figure 1 The Two-Process Model of Sleep Regulation

Sleep/Wake Cycle

S

C̄

Awake   Asleep   Awake   Asleep

7   23   7   23   7

Time of Day
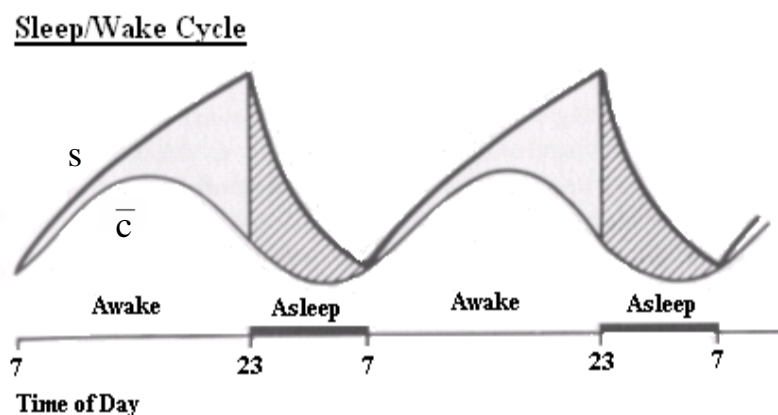
Sleep occurs as a result of the combined action of process S and process C. Process S (the

curve S) is dependent upon sleep/wake behavior and declines during sleep. Process C is

a circadian process, independent of sleeping and waking, governed by the circadian

rhythm of the "internal clock". The curve C represents the negative function and can be

considered a wake-up threshold that is modulated by a circadian rhythm.   "Sleep

pressure" is measured by the interval between the curves S and C.

Adapted from Berger, A., Parker, K., Young-McCaughan, S., Mallory, G., Barsevick, A.,

Beck, S., et al. (2005). Sleep wake disturbances in people with cancer and their

caregivers: State of the science. *Oncology Nursing Forum, 32*(6), E98-E126.

Figure 2 Minarik Model of Mechanisms Leading to the Insomnia Symptom Experience
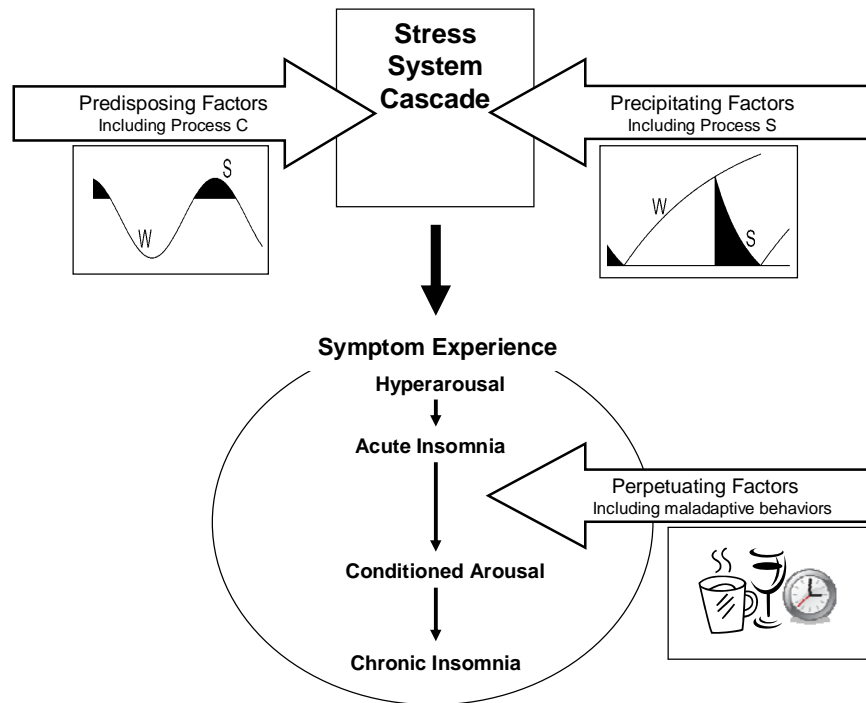
Mechanisms include psychological and physiological mechanisms, the predisposing, precipitating and perpetuating factors, and the stress system cascade, hyperarousal and conditioned arousal.

Process C is included among potential predisposing factors and Process S is included among potential precipitating factors. Perpetuating factors include maladaptive behaviors, such as caffeine and alcohol use and sleep schedule changes, used to deal with insomnia.   S = sleep; W =wake

CHAPTER 3: PREDICTORS OF DEPRESSIVE SYMPTOMS IN DIVERSE MIDLIFE

WOMEN: A LONGITUDINAL STUDY

Abstract

Background: The predictors of first onset depressive symptoms in midlife women are not well studied longitudinally and there is controversy about the association of the menopausal transition with depressive symptoms.

Objective: To describe depressive symptoms in ethnically diverse premenopausal women in the late reproductive stage and patterns of depressive symptoms across time as a function of fixed demographic factors as well as biological and social factors that vary over time.

Design: Longitudinal observational prospective cohort of the University of California, San Francisco Midlife Women's Health Study.

Setting: Community-based sample from the San Francisco Bay area.

Participants: Healthy sample of 347 regularly menstruating 40 to 50-year-old African American, European American and Latina women.

Main Outcome Measures: Participants completed the Center for Epidemiologic Studies-Depression (CES-D) scale every 6 months for 36 months.

Results: Using negative binomial regression analysis, the final model was significant ($X_{LR}^2 = 349.57$, df = 8, p < .0001). Significant predictors of increased average CES-D scores were poor sleep quality (IRR=1.3, $p < .001$, (95% CI 1.224, 1.391), presence of chronic illness at 30 months (IRR=1.2, $p=.007$, (95% CI 1.051, 1.363), high BMI (IRR=1.011, $p=.021$(95% CI 1.051, 1.363), and the interaction of poor sleep quality with time (IRR=1.005, $p=.005$ (95% CI 1.001, 1.007). Significant predictors of decreased average CES-D scores were time (IRR= .998, $p=.020$ (95% CI .995, .9995), having a partner (IRR=.851, $p = .002$, (95% CI .768, .941), positive social support from

relationships (IRR=.981, *p*<.001, (95% CI .977, .985). and the interaction of BMI with time (IRR =.9996, *p*=.042, (95% CI .999, .9999). Time, having a partner, positive social support from interpersonal relationships and the interaction between BMI and time were protective factors.

Conclusions: These data about the association and timing of depressive symptoms with time-varying poor sleep quality, partner status, quality of relationships and BMI, and chronic illness may suggest modifiable risk factors for depressive symptoms in midlife women. The development of preventive intervention strategies for poor sleep quality and BMI could delay or abort full clinical episodes of depression in women and thereby contribute to the improvement of public mental health. This study contributes to the literature about the potential vulnerability of women prior to menopause for depressive symptoms and may lead to the development of appropriately timed interventions for women that involve improving BMI, sleep patterns, and support from family and social networks.

Introduction

Depression is a major issue for women because of their increasing numbers, their higher proportion in the United States (US) population and their role as caregivers (McGuire, Strine, Vachirasudlekha, Mokdad, & Anderson, 2008). More common in women than men at a risk ratio of about 2:1, depression risk increases with age through midlife and is the leading cause of disease-related disability among women worldwide (Kessler, 2003; McGuire, Strine, Vachirasudlekha, Mokdad, & Anderson, 2008). Between the 1950s and the 1990s, there has been a five-fold increase in the lifetime prevalence of depression in the US (Kessler, 2003). In recent studies, depression prevalence was found to be higher in women than in men (Bonnet et al., 2005; Ohayon, 2007a). Prevalence of depression in women varied from a one month prevalence of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) major depressive disorder of 5.8% in women in the general population of New York and California (Ohayon, 2007a), 12% in postmenopausal women with coronary disease measured with the Hospital Anxiety and Depression Scale (Ruo et al., 2006), and 8% to 29% in a review of studies that used the Center for Epidemiologic Studies-Depression Scale (CES-D) with late reproductive stage premenopausal women (Woods & Mitchell, 2005) and 24% using the CES-D in 727 middle-aged women in the Study of Women's Health Across the Nation (SWAN). Higher risk of first onset, which emerges in puberty is thought to be responsible for the higher prevalence of depression in women (Kessler, 2003) although a recent study found differential persistence in older women compared to men (Barry, Allore, Guo, Bruce, & Gill, 2008). Other developmental experiences related to changes

in sex hormones were not found to be a significant influence on major depression (Kessler, 2003).

The predictors of first onset episodes of major depressive disorder in midlife women are not well studied and there is controversy about the association of the menopausal transition with depressive symptoms and depression diagnoses (Bromberger, 2006; Bromberger et al., 2008; Freeman, Sammel, Lin, & Nelson, 2006). The majority of women do not experience high severity of depressed mood during the menopausal transition (Bromberger et al., 2003; Woods, Mariella, & Mitchell, 2006). Recent studies provided evidence that menopausal stage is associated with increased risk of depressive symptoms or depression (Bromberger, 2006; Bromberger et al., 2007; Freeman, Sammel, Lin, & Nelson, 2006; Kravitz, Janssen, Lotrich, Kado, & Bromberger, 2006; Maartens, Knottnerus, & Pop, 2002) but other studies did not find this association (Kuh, Hardy, Rodgers, & Wadsworth, 2002; Vesco, Haney, Humphrey, Fu, & Nelson, 2007; Woods, Mariella, & Mitchell, 2006; Woods et al., 2007). In addition to hormonal reproductive status, history of depressed mood or depression (Bromberger et al., 2008; Bromberger et al., 2005; Kessler, 2003), stressful life events (Bromberger et al., 2007; Kessler, 2003; Kuh, Hardy, Rodgers, & Wadsworth, 2002), socioeconomic status (Ohayon, 2007a), smoking (Freeman, Sammel, Lin, & Nelson, 2006; Ohayon, 2007a; Ruo et al., 2006), self-perception of poor health and health problems (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004; Bromberger et al., 2005; Ohayon, 2007a; Ruo et al., 2006) and obesity (Scott et al., 2008; Simon et al., 2006) may play significant roles in women's depression or depressive symptoms. Sources of stress for midlife women can include poor sleep resulting from vasomotor symptoms of menopause and primary sleep disorders, low

social support and partner relationships (Alexander et al., 2007; Freedman & Roehrs, 2007).

Racial or ethnic differences in the prevalence of depression or depressive symptoms have been found in studies of midlife women (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004; Bromberger et al., 2007; Freeman et al., 2001; Kravitz, Janssen, Lotrich, Kado, & Bromberger, 2006; Ohayon, 2007a; Ruo et al., 2006). In SWAN, racial differences were attenuated after adjustment for socioeconomic factors (including education, employment status, marital status and level of difficulty paying for essential needs) (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004).

The aim of this study was to describe depressive symptoms in ethnically diverse premenopausal women in the late reproductive stage and patterns of depressive symptoms across time as a function of fixed demographic factors as well as biological and social factors that vary over time. Specific hypotheses were: 1) there will be a change in frequency of depressive symptoms over time, 2) frequency of depressive symptoms will change over time as a function of potential risk factors that include ethnicity, menopausal status, income and enough money to pay for essential needs, and education, body mass index (BMI), smoking, chronic illness, partner status, social support from interpersonal relationships, and quality of sleep, and 3) time-varying factors such as BMI, menopausal hormone status and quality of sleep and relationships will be more significant in predicting the pattern of depressive symptoms than more fixed factors such as ethnicity, education or income or it could be stated that time-varying factors such as BMI, menopausal hormone status and quality of sleep and social support from

relationships will be significant in the final model and have a larger effect size than fixed factors.

Methods

Participants and Settings

This study was an analysis of data collected from a healthy, community-based sample of regularly menstruating 40 to 50-year-old women as part of the Midlife Women's Health Study, a five year descriptive longitudinal study begun in 1996 to describe changes in biopsychosocial health factors of midlife women during menopausal transition. Inclusion criteria were still regularly menstruating in the past year, English-speaking, self identified as either African American, European American or of Mexican or Central American heritage, and having lived in the US for at least 20 years to control for level of acculturation. Potential participants with a history of major health problems and specified prescription medications (for example, hormones and antidepressants) were excluded. The primary study was approved by the University of California, San Francisco Committee on Human Research and all participants gave written informed consent. This analysis involved no participant contact and approval was renewed annually for the purpose of analyses and manuscript writing. The original San Francisco Bay Area sample included 347 women, self-identified as African American (n=91), European American (n= 161) and Mexican or Central American (Latina) (n=95) recruited through strategies such as placing advertisements in newspapers, posting flyers in public places and visiting community-based support and social groups with culturally specific memberships. Detailed descriptions of the population-based individualized recruitment and retention strategies and the first year retention results are available elsewhere (Gilliss,

et al. 2001). Questionnaires and biometric measurements were completed during face-to-face visits in the participant's home or at the off-campus research site every 6 months for 3-5 years or until twelve months after the last menstrual period, one year after hormone replacement, or one year after having had a hysterectomy.

Instruments

Every six months, depressive symptoms were measured with the Center for Epidemiologic Studies-Depression Scale (CES-D) (Radloff, 1977). This well-established 20 item self-report scale measures frequency of symptoms in the past week from 0 (none) to 3 (5-7 days). The CES-D was developed to assess depressive symptoms in the general population and its reliability and validity are acceptable (Blank, Gruman, & Robison, 2004; Fountoulakis et al., 2007; Haringsma, Engels, Beekman, & Spinhoven, 2004; Husaini, Neff, & Stone, 1979; Radloff & Locke, 1986; Radloff & Teri, 1986; Shafer, 2006; Thomas, Jones, Scarinci, Mehan, & Brantley, 2001; Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977). In this study, CES-D scores were used as a continuous variable (0-60). For this sample, the Cronbach alpha for the three ethnic groups was .92 for African American participants, .89 for European Americans and .89 for Latina participants.

Sociodemographic data, including partner status, income and having enough money for essential needs, current employment, and education were updated every 12 months with an investigator-designed demographic questionnaire. Current smoking was asked at the baseline visit. Health perception was assessed every 6 months with an item from the Medical Outcomes Study Short Form (Stewart & Ware, 1992) that asks about

current health in general (excellent, very good, good, fair or poor). Higher score

indicates poorer perceived health.

Biological measures collected at each 6-month visit included a first morning urine

sample for follicle-stimulating hormone (FSH), blood pressure measures, and weight and

height. BMI was calculated as height (cm^2) x weight (kg^2). Scales calibrated with

standard weights each week were taken into the home or used at the research site. Heights

were measured with stadiometers. Low FSH values and continued regular menstrual

cycles indicated premenopausal status (Garcia et al., 2005). Urine samples were frozen

and shipped to Esoterix Inc (Calabasas Hills, CA) for FSH assay.

At 30 months, the sixth data collection time point, participants were queried about

the onset of chronic illnesses. They were asked "Has a doctor or nurse ever told you that

you had any of these problems?" and presented with a list of twelve health problems with

yes/no forced choice boxes.   These twelve problems had been exclusions in screening for

eligibility for the study: heart attack, stroke, psychiatric illness, kidney disease (renal

dialysis), cancer, Type I diabetes-insulin, Type II diabetes, diabetes in pregnancy, high

blood pressure, gall bladder disease, ulcers (stomach or intestinal) and thyroid disorder.

They were in the same order as the original exclusion criteria on the telephone screening

questionnaire. The total number of endorsed chronic illnesses could range from 0 to 12,

the distribution was skewed and the total was correlated ($rho = .302$, $p < .01$) with

participant's response at T6 on the 5-point General Health Perception Scale. For this

analysis, chronic illness was then dichotomized as either present or absent. At 30 months,

the group with one or more chronic illnesses scored higher (unpaired t (231) = 4.76, p <

.001) (2.80 $\pm$ .88) compared to the group with no chronic illness (2.23 $\pm$ .88). Higher

score indicates perception of poorer health.

The 15-item Pittsburgh Sleep Quality Index (PSQI) was used at each data

collection time to measure self-reported sleep quality over the past month (Buysse,

Reynolds, Monk, Berman, & Kupfer, 1989; Devine, Hakim, & Green, 2005). The PSQI

global score was found in previous research to correlate with the CES-D question about

sleep restlessness (r>0.69, p<0.001) (Carpenter & Andrykowski, 1998). Because items in

the PSQI (enthusiasm to get things done) overlap with items in the CES-D (getting going

during the day and feeling that everything was an effort), the single PSQI item about

sleep quality (During the past month, how would you rate your sleep quality overall?)

was used for the analysis, with the four possible responses (very good, fairly good, fairly

bad, very bad). The correlation between this single item and the PSQI global sleep

quality score was .72 (p < .001). The correlation between this single item and the CES-D

score was .48 (p < .01).

The type and quality of the participant's social support from partner, family and

friends was assessed every 6 months using the Interpersonal Relationships Inventory

(IPRI) subscale for social support (Tilden, Hirsch & Nelson, 1994). This 13 item subscale

has established test-retest reliability (.91) and internal consistency (Cronbach alpha = .82-

.90) in multiple samples. It assesses perceptions (11 items with a 5-point Likert-type

scale ranging from strongly disagree to strongly agree) and enactment (2 items on a 5-

point Likert-type scale ranging from never to very often) of helping behaviors by persons

with whom one is engaged in relationships that are informal or non-contractual. Total

score ranges from 13-65.

These data were collected over five years. Missing data in the later years were due to subsequent exclusion criteria when participants reached one year without menstrual cycles, after a hysterectomy or after starting hormone therapy. With missing data over time, a multilevel regression approach is preferred thus cases with missing values are not excluded from the analysis. CES-D scores were strongly right-skewed in this non-clinical healthy sample, therefore a regression method that does not assume normality is warranted. CES-D score is the sum of the number of items endorsed, and with positive skewness, they have a Poisson-like distribution (Gardner, 1995; Hutchinson & Holtman, 2005) However, these data have strong overdispersion, meaning that the variance is greater than the mean. The Poisson distribution is characterized as having the variance equal to the mean. The generalization of the Poisson distribution is the negative binomial distribution, for which the mean and variance are not assumed to be equal. Therefore, multilevel negative binomial regression was employed to examine change in CES-D scores, to accommodate missing data and the strongly right-skewed, overdispersed distribution (Hilbe, 2007; Long & Freese, 2006). STATA xtnbreg Version 10 (StataCorp, 2007) was used to perform the multilevel negative binomial analyses with a natural log link. Time was measured as months and was "centered" at baseline, so the intercept for all models would represent predicted initial status. To improve interpretation of the contributions of the quantitative predictors in each model, grand mean centering was used (Cohen, Cohen, West, & Aiken, 2003). For predictors that changed over time, grand mean centering was computed ignoring time. Descriptive statistics and frequency distributions were used to describe the sample. Significance was determined with alpha =

0.05 for the complete model and to assess significance of individual predictors. A large number of potential predictors were considered for this exploratory study. As a preliminary screen for predictors to be included in the model building analyses, predictors that correlated with CES-D scores > .15 were selected for inclusion in the initial models. This strategy insures that predictors were not included with trivial associations based solely on statistical significance for this reasonably large sample. Data for 7 time points over 36 months were used in the regression model.

Predictors screened with $r > .15$ analyses for inclusion in the initial models were age, Latina (dummy variable), African-American (dummy variable), current employment, diastolic and systolic blood pressure, hemoglobin, waist/hip ratio, waist measure, BMI, weight, income, education, menopausal status, partner status, chronic illness at T6, social support subscale from the Interpersonal Relationships Index, Pittsburgh Sleep Quality Index global score and the single item about sleep quality from the Pittsburgh Sleep Quality Index (See Table 2). Variables that were screened and met the $r > .15$ criterion and selected for the negative binomial regression model-building analysis were BMI, income, education, menopausal status, partner status, chronic illness at T6 and the single item about sleep quality from the Pittsburgh Sleep Quality Index. Binary variables that were not correlated but were entered into initial models were current smoking at T1 and having enough money to pay for essential needs.

<div align="center">Results</div>

<div align="center">*Sample characteristics*</div>

The demographic characteristics and CES-D mean scores and frequencies are presented in Table 1. The sample profile reflects the demographics of California women

at the time the data were collected (Gilliss et al., 2001; Kennedy, Taylor, & Lee, 2005).

Most of the women were well-educated and employed for pay. Only 6% identified

themselves at US poverty level and nearly half had a household income before taxes

greater than or equal to $51, 000 per year. European American women (64%) and

Mexican/ Central American women (62%) were more likely to be partnered than African

American women (41%). African American women (76%) and Mexican/ Central

American women (74%) were more likely to have children than were European

American women (59%). Most (77%) were non-smokers. There were no ethnic

differences in mean CES-D total scores but African American women had a significantly

higher proportion (41%) scoring $\geq$ 16 on the CES-D compared to 26% for each of the

other ethnic groups.

Development of Models of Predictors of Depressive Symptom Scores

Hosmer and Lemeshow (2000) recommend that models be developed in

exploratory research by first entering all candidate predictors simultaneously in a model,

then sequentially simplifying the model by removing predictors that do not meet the

researcher's criterion for significance. Although Hosmer & Lemeshow recommended the

use of a liberal alpha to avoid loss of information from multicollinear predictors, in the

present study, the alpha for testing significance for individual predictors was held at .05,

because the sample size was large enough to ensure adequate power for the tests of the

predictors. Predictors were evaluated as possible predictors by evaluating their

correlations with CES-D at 0.15 (see Table 2).

Following the identification of predictors that met the initial criterion of $r > .15$,

the variables were entered into a model in two steps – a "main effects" model, and a

model testing the cross-level (time by predictor) interaction for each predictor using Stata 10 (StataCorp, 2007). Following Hosmer & Lemeshow, the predictor with the weakest association was identified and removed from the model, if it was not significant at alpha = .05. A second model was then tested, leaving out the identified predictor, and the remaining predictors were again evaluated for significance. Again, the predictors were evaluated, and another predictor was identified and removed, and this process continued until all predictors and cross-level interactions met the criterion for significance. Note that the exception to this was that if a predictor was not significant as a "main effect" but the cross-level interaction with time was significant, the "main effect" was retained in the model, as recommended by Hox (2002). This final model is shown in Table 3.

The unconditional model (Model 1) tested the effect of time to predict depressive symptom score (see Table 3). The incident rate ratio (IRR) was .9969, $p < .01$ (95% CI .9946, .9991). For each month, there was a minor but statistically significant average decline in average CES-D scores of 4/1000 of a point. Overall, for the 36 months of the study, the average CES-D score fell nearly one-half point.

Ethnicity, age, income, current smoking, employment status and menopausal status were not associated with CES-D scores at T1 or over time and were removed from the model. Education level and having enough money for essential needs were non-significant and were removed from the final model. The interactions of time with chronic illness, education, partner status, income, quality of social support from relationships and BMI were non-significant. Therefore, they were removed from the final model. The final model (See Table 3) included time (as measured in months), partner status, presence of a chronic illness at 30 months, sleep quality, quality of social support from relationships,

and BMI. Only two interaction terms (time-by-sleep quality and time-by-BMI) were significant and remained in this final model. With centered predictors, the regression equation characterizes the average case at the value of zero across the range of other predictors. Overall, the model significantly predicted the pattern of change in depressive symptom scores in midlife women over time ($X_{LR}^2 = 349.57$, df $= 8$, p $< .0001$).

For the final model, poor sleep quality, chronic illness at T6, high BMI, and the interaction of poor sleep quality with time significantly predicted increased depression scores over time. The IRR for sleep quality was 1.3, $p < .001$, (95% CI 1.224, 1.391). For each unit increase in sleep quality, CES-D scores were predicted to be 3-tenths of a point higher, on average, with all other variables centered at the mean. The IRR for chronic illness at T6 was 1.2, $p=.007$, (95% CI 1.051, 1.363), meaning that women with chronic illness were predicted to have CES-D scores two-tenths of a point higher than women without chronic illness, with all other variables centered at the mean. The IRR for BMI was 1.011, $p=.021$(95% CI 1.051, 1.363), indicating that a one-unit change in BMI was associated with a predicted CES-D score 1/100 of a point higher, with all other variables centered at the mean. The IRR for the interaction of poor sleep quality with time was 1.005, $p=.005$ (95% CI 1.001, 1.008). For a one-unit increase in sleep quality score at each month, there was a predicted increase in average CES-D scores of 5/1000 of a point, with all other variables centered at the mean.

For the final model, time (in months), partner status, quality of social support from relationships and the interaction of BMI with time significantly predicted decreased depression scores over time. In the final model, the IRR for time was .998, $p=.020$ (95% CI .995, .9995). For each month, there was a minor but statistically significant average

decline in CES-D scores of 2/1000 of a point, with all other variables centered at the mean. The IRR for partner status was .851, *p* = .002, (95% CI .768, .941). Participants with partners were predicted to have CES-D scores that were .15 points lower than participants without partners, with all other variables centered at the mean. The IRR for quality of social support from relationships was .981, *p*<.001, (95% CI .977, .985). For a one unit increase in quality of social support from relationships, the predicted decrease in CES-D score was 2/100s of a point, with all other variables centered at the mean. The IRR for the interaction of BMI with time was .9996, *p*=.042, (95% CI .999, .9999). For each one unit decrease in BMI over time, there was a significant average decrease in CES-D score of 4/10000 of a point per month or .0144 over the 36 months of the study for all other variables centered at the mean. A decrease in BMI of 7 units over 36 months would reduce the average CES-D score by 1 point.

Discussion

Depressive symptoms in this sample of premenopausal midlife women in the late reproductive stage were fairly stable over time, with an indication that CES-D scores would continue to decrease with time. The first hypothesis was supported—there was a change in frequency of depressive symptoms over time but the average decrease was very small. The incident rate ratio numbers are quite small but significant predictors of increased and decreased CES-D scores over time were identified. The finding that CES-D scores declined over time during the premenopausal late reproductive stage may be unexpected but is consistent with other findings that showed that depressive symptoms and depressive disorders were more likely during perimenopause than premenopause.

Studies over a longer period of time may be needed to elucidate what is actually happening and achieve more meaningful IRRs.

The second hypothesis was supported. The frequency of depressive symptoms changed over time as a function of identified risk factors. Predictors of increased average CES-D scores were poor sleep quality, presence of chronic illness at T6, high BMI, and the interaction of poor sleep quality with time. Predictors of decreased average CES-D scores were time, having a partner, positive social support from relationships and the interaction of BMI with time. Thus time, having a partner, positive social support from interpersonal relationships and the interaction between BMI and time were protective factors.

The third hypothesis was supported. Time-varying factors were significant in the final model predicting the patterns of depressive symptoms as noted above. There were no differences in CES-D scores by more fixed factors including ethnicity, education, and income and having enough money to pay for essential needs. Smoking at T1 was not a significant predictor and the time-varying factor menopausal hormone status was not a significant predictor in this sample.

In this study, the entire sample is women from diverse ethnic groups who were still menstruating when the study was initiated. There are fewer than 15 (Nelson et al., 2005; Vesco, Haney, Humphrey, Fu, & Nelson, 2007) published longitudinal studies of this type. The findings of this study differ from previous studies that have shown a relationship between depressive symptoms or diagnoses and hormonal changes of menopausal transition (Freeman et al, Bromberger et al) and support other studies that

found no significant relationship between menopausal hormone status and depressive symptoms (Woods, Mariella, & Mitchell, 2006).

The evidence for the relationship between depressed mood and the stages of the menopausal transition is inconsistent but the majority of women do not experience high severity of depressed mood during the menopausal transition (Bromberger et al., 2003; Woods, Mariella, & Mitchell, 2006). Woods and colleagues (Woods, Mariella, & Mitchell, 2002; , 2006) used cluster analysis to identify patterns of depressed mood during the menopausal transition but they did not include late reproductive stage premenopausal women. A recent publication from SWAN (Bromberger et al., 2007) reported that a change in menstrual status over time is associated with increased risk of high depressive symptoms and women with low CES-D at baseline may be at higher risk. The strongest predictor of depressive symptom scores was very stressful life events.

The menopausal transition can be seen as a time of vulnerability for mood problems along a continuum ranging from distress to higher depressive symptoms to minor depression and to major depression. Previously assumed based on clinical observations, then controversial based on epidemiological community studies with inconsistent results, new evidence supports an increased risk of depressive symptoms and depression during the menopausal transition compared to the premenopausal period for women both with and without prior depression history. Freeman and colleagues (2006) evaluated the association of the menopausal transition and reproductive hormone levels with depressed mood and new onset of depressive disorders in a longitudinal study with a community sample of women who were premenopausal at enrollment. In the depressed women subgroup, they found that hormone levels and menstrual cycles were

independently associated with high depressive symptoms (Freeman, 2006). The findings

of the study reported here are inconsistent with these findings. That may be due to a

shorter follow-up in this study and Freeman et al.'s focus on within-woman analysis of

multiple hormone levels.

Poor sleep quality showed the strongest effect on depressive symptoms, both as a

main effect and the interaction with time. Poor sleep quality is a known predictor of

depressed mood and has been found to be a precursor of first or recurrent depressive

episodes in multiple samples, independent of age (N. Breslau, Roth, Rosenthal, &

Andreski, 1996; Cuijpers, Beekman, Smit, & Deeg, 2006; Ford & Cooper-Patrick, 2001;

Johnson, Roth, & Breslau, 2006; Mallon, Broman, & Hetta, 2000; Ohayon, 2007b; Perlis

et al., 2006; Riemann & Voderholzer, 2003; Roberts, Shema, Kaplan, & Strawbridge,

2000).   In the Seattle Midlife Women's Health Study in which women were transitioning

from middle or late menopausal transition stage to post menopause, depressed mood was

correlated with sleep disruption yet early morning awakening, awakening during the

night and depressed mood were not related to hormonal status (Woods, Mariella, &

Mitchell, 2006).

Sleep disturbances are classically attributed to menopause (Alexander &

Dennerstein, 2007) and women report more insomnia than men but Ohayon (2007a; ,

2007b)emphasizes the importance of carefully evaluating sleep complaints and associated

disorders and not assuming sleep difficulties are a result of chronological age or

menopausal status. Sleep disturbances also are a symptom of depression. Results of

studies are mixed but good studies indicate that women have more sleep difficulty as they

transition through menopause, possibly due to vasomotor symptoms, compared to

premenopausal prevalence rates (not reported); sleep disturbance is experienced by 40 to 60 percent of perimenopausal or postmenopausal women (Nelson et al., 2005).

Neither ethnic differences nor socioeconomic factors were significant predictors of depressive symptom scores in this sample despite ethnic differences in the sample for education, household income before taxes and marital status, common indicators of socioeconomic status. These findings differ from the findings of Freeman, et al (2001) who found that depressive symptoms and depressive disorders were more prevalent in African American women than white women in the late reproductive years. In an early paper from SWAN, Bromberger et al.(2004) examined racial differences in depressive symptoms in a sample of 727 middle-aged women before and after adjustment for socio-economic, health-related, and psychosocial characteristics, using cross-sectional data from the baseline visit of SWAN. Twenty-four percent of the sample had depressive symptoms (CES-D score $\geq$ 16). African-American and Hispanic women had the highest incidence of CES-D score $\geq$ 16. Japanese and Chinese women had the lowest incidence. In SWAN, racial differences were attenuated after adjustment for socioeconomic factors (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004). Although in this sample, there were no ethnic differences in mean CES-D scores, African American women had a higher proportion of women who scored $\geq$ 16, indicating possible depressive disorder.

In contrast, lower lifetime risk for mood disorders and other "internalizing" psychiatric disorders was found among Hispanic and non Hispanic Black women and men, compared to non-Hispanic Whites, specifically in a younger cohort (born in 1958 or later) (J. Breslau et al., 2006, p. 64). Among minorities, lower risk was marked at lower educational levels. The pattern suggested protective childhood factors in the minority

groups studied (J. Breslau et al., 2006). However, in a study of men and women, chronicity of major depressive disorder was higher for Blacks than non-Hispanic whites and usually was untreated and more disabling (Williams et al., 2007).

Stressful events were not measured directly in this study. Findings show protective effects of receiving social support from interpersonal relationships and being partnered and the depressogenic effects of having chronic illness, a stressful situation for many women. Kuh et al.(2002), acknowledging the impact of recent life stress, found that women who were followed since birth in 1946 who experienced high psychological distress between 47 and 52 years of age had different life course trajectories than those with less distress. Those with more distress at midlife were more likely to come from families with divorced parents, to have high neuroticism or antisocial behavior as a teenager, and prior experiences of mental and physical health problems. These factors were accountable for the associations between adult sources of risk, such as interpersonal difficulties or poor socioeconomic circumstances, and psychological symptoms at midlife. They found no evidence that menopausal status had any effect on psychological symptoms except for women on hormone replacement therapy for whom there was a small additional risk. These authors (Kuh, Hardy, Rodgers, & Wadsworth, 2002) argued for consideration of features of women's life course trajectories that may mediate the associations between adult sources of risk, such as interpersonal difficulties or poor socioeconomic circumstances, and psychological symptoms at midlife.

In this study, BMI was a significant factor, having a depressogenic effect as a main effect but a protective effect as it declined over time. The depressogenic effect is consistent with other research. Obesity (defined by body mass index [BMI]) has been

found to be associated with mood disorders in women (Simon et al., 2006). Using data from 9125 women in the National Comorbidity Survey Replication (NCS-R), lifetime prevalence of mood disorder was higher in women with a BMI of $\geq$ 30 (26.6%) compared to women with BMI $<$ 30 (22.1%) (Simon et al., 2006). In contrast, in a New Zealand study with 12,992 participants, stronger associations were found between obesity and anxiety than between obesity and mood disorders (Scott, McGee, Wells, & Oakley Browne, 2008). Interventions that target obesity may benefit depressive symptoms.

This study has both strengths and limitations. The strengths include the large sample of community-based diverse midlife women initially studied prior to the onset of menopause and the longitudinal design with data collected over 3-5 years. However, because the women were respondents to flyers and talks in the community, the findings may not generalize to the wider community of women who may not volunteer in response to these recruitment strategies.

The CES-D is a self-report measure of depressive symptoms in the past week and as such is subject to recall bias. The CES-D does not discriminate depressive disorders. However, depressive symptoms that do not meet the threshold for a clinical diagnosis of major depression are still associated with significant impairments, both functional and psychosocial ((Kravitz, Janssen, Lotrich, Kado, & Bromberger, 2006). Additionally, the CES-D is frequently used in community-based studies of midlife women and thus allows for comparison of findings across studies (Vesco, Haney, Humphrey, Fu, & Nelson, 2007).

Conclusions

These data about the association and timing of depressive symptoms with time-varying poor sleep quality, partner status, quality of relationships and BMI, and chronic illness may suggest modifiable risk factors for depressive symptoms in midlife women. The development of preventive intervention strategies for poor sleep quality and BMI could delay or abort full clinical episodes of depression in women and thereby contribute to the improvement of public mental health. This study contributes to the literature about the potential vulnerability of women prior to menopause for depressive symptoms and may lead to the development of appropriately timed interventions for women that involve improving BMI, sleep patterns, and support from family and social networks.

References

Alexander, J. L., & Dennerstein, L. (2007). Series overview and introduction. *Expert Review Neurotherapeutics, 7*(11 Suppl), S3-6.

Alexander, J. L., Dennerstein, L., Woods, N. F., McEwen, B. S., Halbreich, U., Kotz, K., et al. (2007). Role of stressful life events and menopausal stage in wellbeing and health. *Expert Review Neurotherapeutics, 7*(11 Suppl), S93-113.

Barry, L. C., Allore, H. G., Guo, Z., Bruce, M. L., & Gill, T. M. (2008). Higher burden of depression among older women: The effect of onset, persistence, and mortality over time. *Archives of General Psychiatry, 65*(2), 172-178.

Blank, K., Gruman, C., & Robison, J. T. (2004). Case-finding for depression in elderly people: Balancing ease of administration with validity in varied treatment settings. *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 59*(4), 378-384.

Bonnet, F., Irving, K., Terra, J. L., Nony, P., Berthezene, F., & Moulin, P. (2005). Depressive symptoms are associated with unhealthy lifestyles in hypertensive patients with the metabolic syndrome. *Journal of Hypertension, 23*(3), 611-617.

Breslau, J., Aguilar-Gaxiola, S., Kendler, K. S., Su, M., Williams, D., & Kessler, R. C. (2006). Specifying race-ethnic differences in risk for psychiatric disorder in a USA national sample. *Psychological Medicine, 36*(1), 57-68.

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. *Biological Psychiatry, 39*(6), 411-418.

Bromberger, J. T. (2006). The menopausal transition increases the risk of depressive

    symptoms and depression diagnosis in women without a history of depression.

    Evidence Based Mental Health, 9(4), 110.

Bromberger, J. T., Assmann, S. F., Avis, N. E., Schocken, M., Kravitz, H. M., & Cordal,

    A. (2003). Persistent mood symptoms in a multiethnic community cohort of pre-

    and perimenopausal women. *American Journal of Epidemiology, 158*(4), 347-

    356.

Bromberger, J. T., Harlow, S., Avis, N., Kravitz, H. M., & Cordal, A. (2004).

    Racial/ethnic differences in the prevalence of depressive symptoms among

    middle-aged women: The study of women's health across the nation (swan).

    American Journal of Public Health, 94(8), 1378-1385.

Bromberger, J. T., Kravitz, H. M., Matthews, K., Youk, A., Brown, C., & Feng, W.

    (2008). Predictors of first lifetime episodes of major depression in midlife

    women. *Psychological Medicine*, 1-10.

Bromberger, J. T., Kravitz, H. M., Wei, H. L., Brown, C., Youk, A. O., Cordal, A., et al.

    (2005). History of depression and women's current health and functioning during

    midlife. *General Hospital Psychiatry, 27*(3), 200-208.

Bromberger, J. T., Matthews, K. A., Schott, L. L., Brockwell, S., Avis, N. E., Kravitz, H.

    M., et al. (2007). Depressive symptoms during the menopausal transition: The

    study of women's health across the nation (swan). *Journal of Affective Disorders,*

    103 (1-3), 267-272

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28*, 193-213.

Carpenter, J. S., & Andrykowski, M. A. (1998). Psychometric evaluation of the pittsburgh sleep quality index. *Journal of Psychosomatic Research, 45*(1 Spec No), 5-13.

Cohen, J., Cohen, P., West, S. G., & Aiken, L. S. (2003). *Applied multiple regression/correlation analysis for the behavioral sciences (3rd edition).* Mahwah, New Jersey: Lawrence Erlbaum Associates, Publishers.

Cuijpers, P., Beekman, A., Smit, F., & Deeg, D. (2006). Predicting the onset of major depressive disorder and dysthymia in older adults with subthreshold depression: A community based study. *International Journal of Geriatric Psychiatry, 21*(9), 811-818.

Devine, E. B., Hakim, Z., & Green, J. (2005). A systematic review of patient-reported outcome instruments measuring sleep dysfunction in adults. *Pharmacoeconomics, 23*(9), 889-912.

Ford, D. E., & Cooper-Patrick, L. (2001). Sleep disturbances and mood disorders: An epidemiologic perspective. *Depression and Anxiety, 14*(1), 3-6.

Fountoulakis, K. N., Bech, P., Panagiotidis, P., Siamouli, M., Kantartzis, S., Papadopoulou, A., et al. (2007). Comparison of depressive indices: Reliability, validity, relationship to anxiety and personality and the role of age and life events. *Journal of Affective Disorders, 97*(1-3), 187-195.

Freedman, R. R., & Roehrs, T. A. (2007). Sleep disturbance in menopause. *Menopause 14*(5), 826-829.

Freeman, E. W., Grisso, J. A., Berlin, J., Sammel, M., Garcia-Espana, B., & Hollander, L. (2001). Symptom reports from a cohort of african american and white women in the late reproductive years. *Menopause, 8*(1), 33-42.

Freeman, E. W., Sammel, M. D., Lin, H., & Nelson, D. B. (2006). Associations of hormones and menopausal status with depressed mood in women with no history of depression. *Archives of General Psychiatry, 63*(4), 375-382.

Gardner, W., Mulvey, E. P., & Shaw, E. C. . (1995). Regression analyses of counts and rates: Poisson, overdispersed poisson, and negative binomial models. . *Psychological Bulletin, 118*(3), 392-404.

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., et al. (2001). Recruitment and retention of healthy minority women into community-based longitudinal research. *Journal of Women's Health and Gender Based Medicine, 10*(1), 77-85.

Haringsma, R., Engels, G. I., Beekman, A. T., & Spinhoven, P. (2004). The criterion validity of the center for epidemiological studies depression scale (ces-d) in a sample of self-referred elders with depressive symptomatology. *International Journal of Geriatric Psychiatry, 19*(6), 558-563.

Hilbe, J. M. (2007). *Negative binomial regression*. New York, NY: Cambridge University Press.

Hosmer, D. W., & Lemeshow, S. (2000). *Applied logistic regression (2nd ed.)*. New York: Wiley.

Hox, J. (2002). *Multilevel analysis: Techniques and applications.* Mahwah, NJ: Lawrence Erlbaum Associates.

Husaini, B. A., Neff, J. A., & Stone, R. H. (1979). Psychiatric impairment in rural communities. *Journal of Community Psychology, 7*(2), 137-146.

Hutchinson, M. K., & Holtman, M. C. (2005). Analysis of count data using poisson regression. *Research in Nursing and Health, 28*(5), 408-418.

Johnson, E. O., Roth, T., & Breslau, N. (2006). The association of insomnia with anxiety disorders and depression: Exploration of the direction of risk. *Journal of Psychiatric Research, 40*(8), 700-708.

Kennedy, H. P., Taylor, D., & Lee, K. A. (2005). A study of midlife women's reasons for changing healthcare providers. *Journal of the American Academy of Nurse Practitioners, 17*(11), 480-486.

Kessler, R. C. (2003). Epidemiology of women and depression. *Journal of Affective Disorders, 74*(1), 5-13.

Kravitz, H. M., Janssen, I., Lotrich, F. E., Kado, D. M., & Bromberger, J. T. (2006). Sex steroid hormone gene polymorphisms and depressive symptoms in women at midlife. *American Journal of Medicine, 119*(9 Suppl 1), S87-93.

Kuh, D., Hardy, R., Rodgers, B., & Wadsworth, M. E. (2002). Lifetime risk factors for women's psychological distress in midlife. *Social Science and Medicine, 55*(11), 1957-1973.

Long, J. S., & Freese, J. (2006). *Regression models for categorical dependent variables using stata (2nd ed.)*. College Station, TX: Stata Press.

Maartens, L. W., Knottnerus, J. A., & Pop, V. J. (2002). Menopausal transition and
increased depressive symptomatology: A community based prospective study.
Maturitas, 42(3), 195-200.

Mallon, L., Broman, J. E., & Hetta, J. (2000). Relationship between insomnia,
depression, and mortality: A 12-year follow-up of older adults in the community.
International Psychogeriatrics, 12(3), 295-306.

McGuire, L. C., Strine, T. W., Vachirasudlekha, S., Mokdad, A. H., & Anderson, L. A.
(2008). The prevalence of depression in older U.S. women: 2006 Behavioral Risk
Factor Surveillance System. *Journal of Womens Health (Larchmont), 17*(4), 501-
507.

Nelson, H. D., Haney, E., Humphrey, L., Miller, J., Nedrow, A., Nicolaidis, C., et al.
(2005). *Management of menopause-related symptoms. Summary, evidence
report/technology assessment no. 120. (prepared by the Oregon Evidence-based
Practice Center, under Contract No. 290-02-0024.)*. Retrieved April 15, 2008
from www.ahrq.gov.

Ohayon, M. M. (2007a). Epidemiology of depression and its treatment in the general
population. *Journal of Psychiatric Research, 41*(3-4), 207-213.

Ohayon, M. M. (2007b). Insomnia: A ticking clock for depression? *Journal of
Psychiatric Research, 41*(11), 893-894.

Perlis, M. L., Smith, L. J., Lyness, J. M., Matteson, S. R., Pigeon, W. R., Jungquist, C.
R., et al. (2006). Insomnia as a risk factor for onset of depression in the elderly.
Behavioral Sleep Medicine, 4(2), 104-113.

Radloff, L. S., & Locke, B. Z. (1986). The Community Mental Health Assessment

 Survey and the CES-D scale. In M. M. Weissman, J. K. Myers & C. E. Ross

 (Eds.), *Community surveys of psychiatric disorders* (Vol. 4). New Brunswick,

 New Jersey: Rutgers University Press.

Radloff, L. S., & Teri, L. (1986). Use of the Center for Epidemiological Studies-

 Depression scale with older adults. *Clinical Gerontologist, 5*(1/2), 119-136.

Riemann, D., & Voderholzer, U. (2003). Primary insomnia: A risk factor to develop

 depression? *Journal of Affective Disorders, 76*(1-3), 255-259.

Roberts, R. E., Shema, S. J., Kaplan, G. A., & Strawbridge, W. J. (2000). Sleep

 complaints and depression in an aging cohort: A prospective perspective.

 American Journal of Psychiatry, 157(1), 81-88.

Ruo, B., Bertenthal, D., Sen, S., Bittner, V., Ireland, C. C., & Hlatky, M. A. (2006). Self-

 rated health among women with coronary disease: Depression is as important as

 recent cardiovascular events. *American Heart Journal, 152*(5), 921 e921-927.

Scott, K. M., Bruffaerts, R., Simon, G. E., Alonso, J., Angermeyer, M., de Girolamo, G.,

 et al. (2008). Obesity and mental disorders in the general population: Results from

 the world mental health surveys. *International Journal of Obesity (London),

 32*(1), 192-200.

Scott, K. M., McGee, M. A., Wells, J. E., & Oakley Browne, M. A. (2008). Obesity and

 mental disorders in the adult general population. *Journal of Psychosomatic

 Research, 64*(1), 97-105.

Shafer, A. B. (2006). Meta-analysis of the factor structures of four depression

    questionnaires: Beck, CES-D, Hamilton, and Zung. *Journal of Clinical*

    Psychology, 62(1), 123-146.

Simon, G. E., Von Korff, M., Saunders, K., Miglioretti, D. L., Crane, P. K., van Belle,

    G., et al. (2006). Association between obesity and psychiatric disorders in the US

    adult population. *Archives of General Psychiatry, 63*(7), 824-830.

StataCorp. (2007). Stata Statistical Software: Release 10. College Station, TX: StataCorp

    LP.

Thomas, J. L., Jones, G. N., Scarinci, I. C., Mehan, D. J., & Brantley, P. J. (2001). The

    utility of the CES-D as a depression screening measure among low-income

    women attending primary care clinics. The Center for Epidemiologic Studies-

    Depression. *International Journal of Psychiatry in Medicine, 31*(1), 25-40.

Vesco, K. K., Haney, E. M., Humphrey, L., Fu, R., & Nelson, H. D. (2007). Influence of

    menopause on mood: A systematic review of cohort studies. *Climacteric, 10*(6),

    448-465.

Weissman, M. M., Sholomskas, D., Pottenger, M., Prusoff, B. A., & Locke, B. Z. (1977).

    Assessing depressive symptoms in five psychiatric populations: A validation

    study. *American Journal of Epidemiology, 106*(3), 203-214.

Williams, D. R., Gonzalez, H. M., Neighbors, H., Nesse, R., Abelson, J. M., Sweetman,

    J., et al. (2007). Prevalence and distribution of major depressive disorder in

    African Americans, Caribbean blacks, and non-Hispanic whites: Results from the

    national survey of American life. *Archives of General Psychiatry, 64*(3), 305-315.

Woods, N. F., Mariella, A., & Mitchell, E. S. (2002). Patterns of depressed mood across

    the menopausal transition: Approaches to studying patterns in longitudinal data.

    Acta Obstetricia et Gynecologica Scandinavica, 81(7), 623-632.

Woods, N. F., Mariella, A., & Mitchell, E. S. (2006). Depressed mood symptoms during

    the menopausal transition: Observations from the Seattle Midlife Women's Health

    Study. *Climacteric, 9*(3), 195-203.

Woods, N. F., & Mitchell, E. S. (2005). Symptoms during the perimenopause:

    Prevalence, severity, trajectory, and significance in women's lives. *American*

    Journal of Medicine, 118 Suppl 12B, 14-24.

Woods, N. F., Smith-Dijulio, K., Percival, D. B., Tao, E. Y., Taylor, H. J., & Mitchell, E.

    S. (2007). Symptoms during the menopausal transition and early postmenopause

    and their relation to endocrine levels over time: Observations from the Seattle

    Midlife Women's Health Study. *Journal of Womens Health (Larchmont), 16*(5),

    667-677.

Table 1 Sample Characteristics at Baseline

Characteristic	Total Sample N=347	African American (AA) n=91 (26%)	European American (EA) n=161 (46%)	Latina (L) n=95 (27%)	Test statistic *p* value Group differences
	Mean (SD) n (%)	Mean (SD) n (%)	Mean (SD) n (%)	Mean (SD) n (%)	
Age (years)*	43.5 ($\pm$ 2.4)	43.2 ($\pm$ 2.5)	43.5 ($\pm$ 2.2)	43.6 ($\pm$ 2.5)	F = 5.6 p = .004 L > AA[a]
CES-D Total Score	12.5 ($\pm$ 9.98)	14.8 ($\pm$ 12.1)	11.6 ($\pm$ 8.8)	11.5 ($\pm$ 9.6)	NS
CES-D Score $\geq$ 16*	104 (30)	37 (41)	42 (26)	23 (26)	X^2 = 9.4 p = .009 AA > L[a] AA > EA[a]
Education ** High school or less Partial college College graduate Professional graduate degree	36 (10.5) 107 (31) 96 (28) 103 (30)	5 (5.7) 36 (41.4) 25 (28.7) 21 (24.1)	5 (3.1) 38 (23.8) 56 (35) 61(38)	26 (27.4) 33 (34.7) 15 (15.8) 21 (22)	F = 23.5 p < .001 AA > L[a]
Employed for pay Yes No	287 (86) 48 (14)	76 (87) 11 (12.6)	131 (84.5) 24 (15.5)	80 (86) 13 (14)	NS
Household income (before taxes) ** <$10, 999 $11, 000-$30, 999 $31, 000-$50, 999 $51,000-$80,999 >$81, 000	20 (5.9) 60 (17.7) 90 (26.5) 89 (19.3) 81 (24)	9 (10.5) 17 (19.7) 30 (34.9) 22 (25.6) 8 (9.3)	6 (3.8) 18 (11) 34 (21) 44 27.6) 58 (36)	5 (5.3) 25 (26.6) 26 (27.6) 23 (24.5) 15 (16)	F = 16.7 p < .001 EA > AA[a] EA > L[a]
Marital status* Married, permanently partnered Single, divorced, separated, widowed	197 (57) 146 (42.6)	36 (40.9) 2 (59)	102 (63.8) 58 (36.3)	59 (62) 36 (37.9)	X^2 = 12.6 p = .002 L > AA[a] EA > AA[a]
Children* Yes No	230 (67) 111 (32)	66 (75.9) 21 (24)	94 (58.8) 66 (41)	70 (74.5) 24 (25.5)	X^2 = 72.97 p < .001 L > EA[a] AA>EA[a]
Smoke now Yes No	37 (23) 124 (77)	15 (33) 30 (66.7)	15 (18.8) 65 (81)	7 (7) 88 (93)	NS

** p<.001; * *p*<.01; [a] *p* = 0.0167   (Totals may vary because of missing data)

Table 2 Pairwise Correlations with CES-D for Variable Selection

Variable	Correlations (r)		Number (n)	
	Time 1	Time 6	Time 1	Time 6
Age	-.04		342	
Dummy variable for ethnic = Latina	-.046			
Employed now	-.06		333	
Diastolic blood pressure	.08		340	
Hemoglobin	-.08			
Systolic blood pressure	.09		340	
Waist/hip ratio	.096		338	
Dummy variable for ethnic = African American	.11			
Waist measure	.16		341	
Weight	.18		342	
Body Mass Index (BMI)	.18	.24	342	224
Income	-.21	-.18	338	218
Education	-.22	-.04	340	220
Menopausal Status				
FSH (IU/DL) at T6	--	.13	--	214
premenopausal=0	.05	.22	343	225
Partnered (yes=1)	-.24	-.09	342	222
Chronic illness at T6 (yes=1)	--	.18	--	342
Social Support subscale from IPRI	- .46	-.39	343	233
PSQI #13	.48	.52	341	232
PSQI	.62	.43	342	219

FSH = follicle stimulating hormone in urine in international units per deciliter
IPRI = Interpersonal Relationships Inventory subscale for social support
PSQI #13 = Pittsburgh Sleep Quality Index single question asking about sleep quality
PSQI = Pittsburgh Sleep Quality Index

Table 3 Unconditional Model and Final Model: Depressive Symptoms Predicted from Time and Multiple Predictors

CES-D	IRR	Standard Error	z score	*p* value < .05	95% CI
Unconditional Model					
Time (month)	.997	.0011	-2.71	0.007	.995,.999
Final Model					
Time (month)	.997	.0012	-2.33	0.020	.995, .999
Chronic illness (presence)	1.197	.0792	2.72	0.007	1.052, 1.363
Sleep quality	1.305	.0424	8.20	<0.001	1.225, 1.391
Partnered	.851	.0441	-3.12	0.002	.768, .941
Social support from interpersonal relationships	.981	.0019	-9.74	<0.001	.977, .985
Body Mass Index (BMI)	1.016	.0050	2.32	0.021	1.002, 1.021
Month by sleep quality	1.005	.0017	2.79	0.005	1.001, 1.008
Month by BMI	.9996	.0002	-2.04	0.042	.999, .99999

CES-D= Center for Epidemiologic Studies-Depression; IRR=Incident rate ratio; CI=Confidence interval

CHAPTER 4: DEPRESSIVE SYMPTOMS AND CHRONIC PHYSICAL ILLNESS IN

MIDLIFE WOMEN: A LONGITUDINAL STUDY

Abstract

Objectives: To describe the relationship between depressive symptoms and physical illness in a cohort of ethnically diverse women in the late reproductive stage during the decade before menopause.

Methods: This study was conducted using data collected during a longitudinal observational community-based prospective study of the University of California, San Francisco Midlife Women's Health Study, to investigate changes in biobehavioral health factors associated with menopausal transition. The participants were 347 healthy regularly menstruating 40 to 50-year-old African American, European American and Latina women. Participants completed the Center for Epidemiologic Studies-Depression (CES-D) scale every 6 months for 30 months. Other variables included self-reported health conditions, self-reported chronic illness and self-reported hypertension. Groups were compared using t-tests, ANOVA, chi square and non-parametric Mann-Whitney U when appropriate.

Results: Prevalence of depressive symptoms in the total sample was 30% at study initiation and 26% at 30 months. Number of health conditions was significantly higher for women scoring $\geq$16 on CES-D compared to women scoring <16. There was a significant association between ethnicity and chronic illness; 30.8% of African Americans reported a chronic illness, compared to 26.4% of European Americans and 15.8% of Latinas. Slightly over half of the 60 women with CES-D scores $\geq$16 reported chronic illness (53%) whereas only 29% (50 of 174) who scored <16 (29%) reported a chronic illness. Self-reported hypertension (HTN) was correlated with blood pressure measures, and the self-reported HTN group had a mean CES-D score nearly twice as high

75

as the non-HTN group.

Conclusions: This study provides strong support for the association between depressive symptoms and chronic illness, particularly hypertension, in pre-menopausal late reproductive stage women. Depressive symptoms were stable for the sample as a whole at baseline and at 30 months, but significantly increased with consequent reports of chronic illness or hypertension. Health care providers may underestimate the health impact of depressive symptoms.

Introduction

Depression is the leading cause of disease-related disability among women worldwide, more common in women than men with risk ratios about 2:1 and risk increases with age through midlife (Bonnet et al., 2005; Kessler, 2003; Ohayon, 2007). In the United States (US) between the 1950s and the 1990s, there has been a five-fold increase in lifetime prevalence of depression (Kessler, 2003). Higher risk of first onset, which emerges in puberty, rather than differential persistence or recurrence, is thought to be responsible for the higher prevalence of depression in women (Kessler, 2003) although a recent study found differential persistence in older women (Barry, Allore, Guo, Bruce, & Gill, 2008). Other developmental experiences related to changes in sex hormones were not found to be a significant influence on major depression (Kessler, 2003). Gender differences in depression prevalence are not consistent across all US racial and ethnic groups (Kessler, 2003). Kessler (2003) suggested that investigating the joint effects of biological vulnerabilities and environmental provoking experiences will lead to understanding the higher rates of depression among women than men.

The evidence for depressed mood associated with stages of menopausal transition is inconsistent, but most research indicates that women do not experience a high severity in depressive symptoms during their menopausal years (Bromberger et al., 2003; Bromberger et al., 2007; Woods, Mariella, & Mitchell, 2002, 2006). Woods and colleagues (2006) used cluster analysis of longitudinal data to identify patterns of depressed mood through the menopausal transition, but the late premenopausal reproductive stage was not included. In recent findings from the Study of Women Across the Nation (SWAN), change in menstrual status over time was associated with increased

risk of depressive symptoms and women with initially low depressive symptoms may be at even higher risk (Bromberger et al., 2007). The strongest predictors of depressive symptom scores were very stressful life events rather than menopausal status or age.

The prevalence of depression in women is inconsistent across studies possibly reflecting different definitions, sampling and measures. Woods & Mitchell (2005) reviewed 98 longitudinal studies on symptoms during the perimenopause. In six studies that used the Center for Epidemiological Studies-Depression (CES-D) Scale, they found that depressive symptoms measured during the late reproductive stage ranged from 8% to 29%. Twenty-four percent of the baseline sample for the SWAN had depressive symptoms (score at or above 16 on the CES-D), with African-American and Hispanic women having the highest incidence and Japanese and Chinese women having the lowest incidence (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004). The prevalence of major depressive disorder was found to be 5.8% in the general population of New York and California samples of women using criteria from the Diagnostic and Statistical Manual of Mental Disroders, fourth edition (DSM IV) (Ohayon, 2007), 12% in postmenopausal women with coronary disease measured with an algorithm adapted from the CES-D (Ruo et al., 2006), and 13% of French women with hypertension and metabolic syndrome measured with the Hospital Anxiety and Depression Scale (Bonnet et al 2005).

Evidence is growing for significant comorbidity of mental disorders, especially mood disorders, and chronic physical conditions (Ortega, Feldman, Canino, Steinman, & Alegria, 2006; Scott et al., 2007). Research on the association between mental disorders and physical illness has been limited by the predominance of clinical population studies

compared to general population studies (Scott et al., 2007). The correlates of depression are not consistent across studies. Depression has been found to be more common in middle-age women and men (Ohayon, 2007) with a greater likelihood among non-White women (Ruo et al., 2006) who are current smokers (Ohayon, 2007; Ruo et al., 2006). Depression is also more likely to occur in women and those who are non-partnered, unemployed and without a high school diploma, as well as those who are obese or diagnosed with heart disease (Ohayon, 2007).

More important than gross indicators of socioeconomic status (SES) commonly associated with depressive symptoms, health and psychosocial factors may be significant risk factors for depressive symptoms (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004). One or more stressful events, low social support and high perceived stress were psychosocial factors that increased the odds of CES-D scores of 16 or higher in the SWAN cross-sectional data at study initiation. Reporting fair/poor perceived health, one or more physical symptoms, vasomotor symptoms and anemia were health-related factors that increased the odds of CES-D scores of 16 or higher in the SWAN cross-sectional data at study initiation. In longitudinal data from SWAN, change in menopausal status across time, frequent vasomotor symptoms, low social support and very stressful life events predicted high depressive symptom score (Bromberger et al., 2007).

Depression is also strongly associated with hypertension (HTN) and cardiovascular disease (CVD) in men and women (Davis, Fujimoto, Juarez, Hodges, & Asam, 2008; Feresu, Zhang, Puumala, Ullrich, & Anderson, 2008). Women with persistent or new depression were more likely to report fair/poor health, and in those with coronary disease, a recurrent or new depression had an impact on perceived health with

comparable magnitude to that of recent angina, myocardial infarction, angioplasty, heart failure, or bypass surgery (Ruo et al., 2006).

Data about the association and timing of depressive symptoms associated with chronic illness may identify modifiable risk factors for depressive symptoms in midlife women, a group at risk for depression and disability from CVD. The aim of this study was to describe the relationship between depressive symptoms and physical health in late reproductive stage women during the decade before menopause. Specific hypotheses included: 1) Women who report a history of one or more health conditions at study initiation will have significantly higher depressive symptoms across time than women who reported no health conditions; 2) Women with higher depressive symptom scores at study initiation will report more health conditions at T1; 3) Women with higher depressive symptom scores will report significantly more chronic illnesses at T6, 30 months into the study; and 4) Women with a chronic illness or hypertension at T6 will have significantly higher depressive symptom scores across time than women without a chronic illness or hypertension.

Methods

Study participants

This was an analysis of data collected from a healthy, community-based sample of regularly menstruating midlife women between 40 and 50 years of age as part of the Midlife Women's Health Study, a five year longitudinal descriptive study begun in 1996 to describe changes in biopsychosocial health factors of midlife women during transition to menopause. Women with a history of major chronic health problems (e.g., heart attack, stroke, psychiatric illness, kidney disease or renal dialysis, cancer, Type I or Type

2 diabetes mellitus, or auto-immune disease) were initially excluded as were women

taking tranquilizers, antidepressants, sleeping pills, and estrogen or other hormone

therapy including birth control or hormone replacement. The original study was approved

by the University of California, San Francisco Committee on Human Research and all

participants gave written informed consent. The original sample from the San Francisco

Bay Area included self-identified European Americans (n=161), Mexican or Central

Americans (Latinas) (n=95) and African Americans (n=91). Details of the recruitment

and retention strategies and first-year retention results are available elsewhere (Gilliss et

al., 2001).

Study variables

Questionnaires were completed during face-to-face visits at the off-campus research

site or in the participant's home every 6 months for either 3-5 years or until twelve

months after one of the following occurred: 1) the last menstrual period, 2) a

hysterectomy or 3) taking hormones. Sociodemographic variables were collected with an

investigator-designed demographic questionnaire. Biological measures were collected at

each 6-month visit and included a urine sample for follicle-stimulating hormone (FSH) to

indicate premenopausal status, weight and height from which body mass index (BMI)

was calculated, and blood pressure (systolic and diastolic) measures.

Frequency of depressive symptoms was measured with the Center for Epidemiologic

Studies-Depression Scale (CES-D) (Radloff, 1977). This well-established 20-item self-

report measure asks about frequency of depressive symptoms in the past week from 0

(none) to 3 (5-7 days). Developed for epidemiologic studies of depressive symptoms in

the general population, the CES-D was intended to be used for screening and not

intended to be a diagnostic measure or a measure of general distress. It has acceptable

reliability and validity (Blank, Gruman, & Robison, 2004; Fountoulakis et al., 2007;

Haringsma, Engels, Beekman, & Spinhoven, 2004; Husaini, Neff, & Stone, 1979;

Radloff & Locke, 1986; Radloff & Teri, 1986; Shafer, 2006; Thomas, Jones, Scarinci,

Mehan, & Brantley, 2001; Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977).

It takes less than five minutes for most subjects to complete. In this study, CES-D score

was used as a continuous variable (0-60) and as a dichotomous variable with a cut point

of 16 and higher to indicate risk for depression.

Physical health problems were assessed at study initiation with an investigator-

designed checklist of 15 alphabetized conditions, labeled *Current and Past*

Medical/Health History, which asked "Do you now have, or have you ever had, any of

the following conditions?" with yes/no boxes and a fill-in blank for "other" (see Table 2).

The number of health conditions was summed for a potential range of 0-16. The single-

item measure of health perception from the Medical Outcomes Study Short Form was

used as an indicator of general health (Stewart & Ware, 1992). This item asks about

current health in general with 5 possible responses: "In general, would you say your

health is excellent, very good, good, fair or poor?" The number of endorsed conditions

was correlated ($r = .225, p < .001$) with the General Health Perception scale and women

with one or more health conditions had significantly poorer health perception than those

with no condition (Humphreys and Lee, in press).

At each subsequent 6-month data collection point, participants answered specific

questions about their health: "Have you ever had a major health problem?" "If yes, what

has been this problem?" and "are you still having this problem?" Responses to this set of

questions at T6 reflect 30 months since their initial response. Also at T6, participants were specifically asked "Has a doctor or nurse ever told you that you had any of these problems?" and presented with a list of 12 chronic illnesses with yes/no response options (Table 3). These were in the same order as the original exclusion criteria on the screening questionnaire prior to enrollment. The total number of endorsed chronic illnesses (range 0-4) was correlated ($rho = .304$, $p < .001$) with General Health Perception scores at T6.

Hypertension is included in the analysis as an example of a specific chronic illness common in women and the most common chronic illness reported by women in this sample. Participants who reported having hypertension at T6 were matched on ethnicity, age, partner status, income, education, children and smoking with participants who reported no hypertension. This resulted in 36 cases and 36 controls for a substudy analysis using a case-control design. Blood pressure (BP) was measured by trained data collectors at each 6-month data collection point; both systolic and diastolic BP measures were recorded at each time point.

Statistical Analysis

All analyses were conducted using SPSS version 14.0 (SPSS, Inc., Chicago). Descriptive statistics were used to summarize demographic characteristics as well as prevalence and frequency of physical health problems. CES-D scores and number of chronic illnesses were log transformed because both were highly skewed to the lower end of scores. Groups were compared using t-tests, ANOVA, chi square and non-parametric Mann-Whitney U when appropriate. All statistical tests were 2-tailed and $p \leq .05$ was considered statistically significant.

Results

Sample Characteristics

Characteristics of the convenience sample are detailed in Table 1 and reflect

California demographics at the time of data collection (Gilliss et al., 2001), Women self-

identified as either European American (46%), African American (26%) or Latina with

heritage from either Mexico or Central America (27%). Most were well-educated and

employed for pay. Only 6% were at poverty level. Most (77%) were non-smokers.

The CES-D was internally consistent (Cronbach alpha coefficient = .91 at T1).

There were no significant ethnic differences at study initiation or over time in mean CES-

D scores although the African American women had a higher proportion of CES-D

scores $\geq$ 16 (41%) compared to 26% for each of the other ethnic groups. There was no

relationship between FSH and CES-D scores at T6. Sample characteristics dichotomized

by CES-D scores $\geq$16 are shown in Table 1. There were significant differences between

the groups. Women scoring < 16 on the CES-D reported significantly higher education

and significantly higher household income.

Depressive Symptoms and Health Conditions at Study Initiation (T1)

Over 95% of participants reported a health condition at study initiation (T1). The

number of health conditions at T1 did not differ by ethnicity. The frequency distribution

for type of health condition at T1 is shown in Table 2 for health conditions reported by 50

or more women. The mean number of health conditions was 3.9 $\pm$ 2.14 (median = 4.0;

range 0-12). Health conditions not in Table 2 included a variety of conditions such as

chronic bronchitis or ear problems, reported by 1-32 women each. CES-D score at T1

was correlated with number of health conditions at T1 (*rho* = .199, *p* < .001). When the

328 women who reported one or more health conditions were compared to the 14 women who reported no health conditions at T1, there was no difference in CES-D scores, whether compared by unpaired t-test for mean difference in raw scores or log-transformed scores, or compared by Mann-Whitney U for median differences. Hypothesis 1 was not supported; repeated measures ANOVA showed no significant differences in CES-D scores (log transformed, mean, or median) over time or between health condition groups across time. However, the second hypothesis was supported when the sample was dichotomized by CES-D scores at T1; number of health conditions was significantly higher (t (340) =2.43, p = .016) for the 103 women scoring $\geq$16 (4.3 $\pm$ 2.17) compared to the 239 women who scored <16 (3.7 $\pm$ 2.11).

Depressive Symptoms, Health Problems and Chronic Illness at 30 Months (T6)

At T6, 29% of 233 women answered yes to the open-ended question, "Have you ever had a major health problem?" The problem was current for 20%. The frequency distribution of the types of reported health problems and types of chronic illnesses endorsed at T6 are shown in Table 3. There was a significant association (X^2(2) = 6.119, p = .047) between ethnicity and chronic illness; 30.8% of the African American women reported one or more chronic illnesses, compared to 26.4% of European American and 15.8% of Latina women. General Health Perception at T6 was significantly worse (unpaired t (231) = 4.76, p < .001) for the 82 women with one or more chronic illnesses (2.8$\pm$.88) compared to the 151 women with no chronic illness (2.2 $\pm$.88). At T6, the mean CES-D score for the total sample was 11.3 $\pm$ 9.66 with 174 (74%) women scoring <16 and 60 (26%) scoring $\geq$ 16.

Women who scored $\geq$16 on the CES-D at T1 had a significantly (t (97.3) = 3.33, p = .001) higher mean number of chronic illnesses at T6 (.74 $\pm$ .857) than women scoring <16 (.58 $\pm$ .636). This also was significantly different for median number of chronic illnesses (U = 4394.0, p < .001). This significant difference was confirmed with log transformed chronic illness T6 total scores (t (137.6) = 2.1, p = .033). These findings supported hypothesis #3. In addition, chi-square analysis compared T1 CES-D scores $\geq$16 and CES-D score <16 with presence of chronic illness at T6. A significant association was found (X^2(1) = 6.56, p = .010). Of the 104 women scoring $\geq$16 at T1, 34% reported one or more chronic illnesses at T6, of the 237 women who scored <16 on the CES-D at T1, 21% reported one or more chronic illnesses. These findings also supported hypothesis 3. The 59 women who scored $\geq$16 on the CES-D at T6 also had a significantly (t (229) = 3.16, p = .002) higher number of chronic illnesses (.71 $\pm$ .789) than 172 women scoring < 16 (.38 $\pm$ .669); the median difference in number of chronic illnesses between the two groups at T6 was also significant (U = 3797.0, p = .001). A significant association was found between chronic illness group and T6 CES-D group; slightly over half of the 60 women with CES-D scores $\geq$16 reported one or more chronic illness (53%) whereas only 50 of the 174 women who scored <16 (29%) reported one or more chronic illnesses (X^2(1) = 11.86, p = .001).

In support of the final hypothesis, women who reported one or more chronic illnesses at T6 had significantly higher CES-D scores than women who reported no chronic illness (see Table 4). The difference remained with log-transformed CES-D scores (t (190.9) = 5.04, p < .001) as well as median differences (Mann Whitney U = 3890.5, p < .001). Figure 1 illustrates the pattern of CES-D raw scores over time for the

women reporting one or more chronic illnesses at T6 compared with those reporting no

chronic illness. There was no significant within-subject change over time for either

group, but there was a significant between-group difference using either the raw CES-D

scores (F (1,200) = 25.1, p < .001) or log transformed scores (F (1, 210) =15.4, p < .001).

Depressive Symptoms and Hypertension

Blood pressure was measured at each of the six time points, with an intraclass

correlation coefficient (ICC) of .89. At T6, those who self-reported HTN had

significantly (p < .001) higher mean systolic (127.4+13.7 mmHg) and diastolic (83.1+9.1

mmHg) pressure compared to the non-HTN group (112.7+10.6, 73.4+7.9, respectively).

There was no significant change over time in diastolic pressure, while systolic pressure

varied significantly (F (5, 995) = 3.04, *p* = .010) between T3 and T6 (*p* = .03) as well as

T5 and T6 (*p* = .045).

There were significant CES-D group differences in both diastolic (F (1, 199) =

7.87, *p* = .006) and systolic (F (1, 199) = 12.13, *p* = .001) pressures. Women who scored

≥16 on the CES-D at initial T1 data collection point had higher blood pressure over time

compared to women who scored <16 at T1 who had lower and more stable blood

pressure over time.

Similar to the findings that support hypothesis #4 with dichotomized chronic

illness groups, the self-reported HTN group at T6 also had a mean CES-D score nearly

twice as high as the non-HTN group (t-test (t(68) = 3.2, *p* = .002) (Table 4). This

significance was also sustained using the log transformed CES-D scores (t (64.705) =

3.32, *p* = .001), and Mann-Whitney U raw scores (*U* = 343.5, *p* = .003). The association

between HTN group and CES-D group was not statistically significant (X^2(1) = 3.65, *p* =

.056). Figure 2 illustrates the pattern of CES-D raw scores over time by self-reported HTN group at T6. No significant group difference was found ($F (1,56) = 2.9$, $p = .097$) and group CES-D scores were similar at the initial visit. There was a group by time interaction; those with HTN at T6 had a significant increase in CES-D scores from T1 to T6 and those without HTN at T6 has a significant decrease in CES-D scores from T1 to T6 in repeated measures ANOVA with the log-transformed CES-D scores ($F (1) = 4.6$, $p = .036$).

Discussion

This study examined the relationship of depressive symptoms and physical illness in late reproductive stage women during the decade before menopause in a community-based non-clinical sample. Prevalence of depressive symptoms in the total sample was 30% at T1 and 26% at T6. These rates are consistent with a review of prior research reporting 8-37% prevalence in premenopausal women (Alexander, Dennerstein, Woods, Kotz et al., 2007). Findings are almost identical to the 24% rate reported in the SWAN study which used the CES-D to measure depressive symptoms among ethnically diverse women in the decade prior to menopause (Bromberger, Harlow, Avis, Kravitz, & Cordal, 2004). Few studies have examined diverse women over time in the decade prior to menopause. In this current study, the entire sample consists of women from diverse ethnic groups. There are fewer than 15 published longitudinal studies of this type and many do not include diverse ethnic groups (Vesco, Haney, Humphrey, Fu, & Nelson, 2007). These findings do not show an ethnic difference in mean depression scores but a higher proportion of African Americans scored ≥ 16 indicating possible depressive disorder.

The analyses supported three out of four hypotheses for this study. The first (that women who report a history of one or more health conditions at study initiation would have significantly higher depressive symptoms across time) was not supported. This may be due to the fact that only 4% of participants reported having no health condition, limiting statistical power to detect differences. The high number of healthy women (96%) reporting one or more health conditions, with a mean of 3.9 per woman, was surprising and may be indicative of variation in the meaning of healthy as well as types of health conditions that women cope with during midlife. Findings support the second hypothesis: that mean number of health conditions would differ between groups dichotomized on CES-D scores. Women with more depressive symptoms reported more health conditions.

The third hypothesis, that women with higher depressive symptom scores at study initiation would report more chronic illnesses at 30 months, was supported. Women who scored ≥ 16 on the CES-D at T1 had a higher mean number of chronic illnesses at T6 and a higher proportion of those women reported one or more chronic illness. HTN, thyroid disorder and psychiatric illness (primarily anxiety as defined by the participant) were the most frequently reported chronic illnesses. In addition, women who scored ≥ 16 on the CES-D at T6 had a higher mean number of chronic illnesses at T6 and a higher proportion of those women reported one or more chronic illness. Significant differences in numbers of chronic illness for groups dichotomized by CES-D score were found at T1 and T6. Depressive symptoms were associated with number of chronic illnesses as well as the presence or absence of a chronic illness.

The final hypothesis, that women with chronic illness or hypertension at 30 months would have significantly higher depressive symptom scores across time than others, was also supported. Figure 1 shows significant differences in raw CES-D scores for groups dichotomized by presence or absence of chronic illness. Findings for groups dichotomized by self-reported HTN also showed significant differences in CES-D scores. The Chi-square test was not significant ($p =.056$); the small number of HTN cases and controls may have limited the power to detect a statistically significant difference. Figure 2 illustrates the difference in depression scores over time by HTN group, showing that the CES-D scores at T1 were similar and that over time, the HTN group's CES-D scores increased while the non-HTN group's scores decreased. Results were similar for actual systolic and diastolic blood pressures, which are not shown here.

The three most frequently reported health conditions at T1 were allergies (including hay fever), headache or migraine and back problems. Our findings are consistent with the literature about prevalence of aches and pains among midlife women (Alexander, Dennerstein, Woods, Halbreich et al., 2007; Szoeke, Cicuttini, Guthrie, & Dennerstein, 2008). Allergies are not reported in other studies of symptoms and health conditions of midlife women (Alexander, Dennerstein, Woods, Halbreich et al., 2007; Woods & Mitchell, 2005) and may not be related to midlife in particular.

Results of studies of midlife women's depressive symptoms and physical disease comorbidities are sparse and women are understudied in regard to the links of depression and physical disease (Evans et al., 2005). Recognition is growing for the important role of depressive symptoms and disorders in the etiology, course and outcomes related to

chronic illness (Chapman, Perry, & Strine, 2005). These findings lend support to the studies demonstrating a link between depressive symptoms and chronic physical disease.

Chronic illnesses that are prevalent in older women may begin to manifest in premenopausal late reproductive stages prior to the onset of menopause. In this study, CES-D score showed a strong relationship with subsequent and current chronic illnesses. In explaining the worldwide association of depressive and anxiety disorders with chronic physical conditions, Scott and colleagues (2007) suggest that these relationships may be bidirectional involving a combination of biological and psychosocial mechanisms, either mental disorder leading to physical condition or a combination of internal and external factors conducive to both the experience of mental disorders and the occurrence of numbers of physical conditions. As explored in a subset of the SWAN sample, a common physiological pathway by which depressive symptoms impact health may involve modulation of immune function, including inflammation or proinflammatory cytokines (Cyranowski et al., 2007). From this perspective, recognition of and treatment of depressive symptoms may prevent or delay or reduce the severity of manifest chronic illnesses.

Where general medical services are separate from mental health services, recognition and adequate treatment of mental-physical comorbidity (Scott et al., 2007) is difficult in both sites and will require more focused attention. Further research is needed about the relationship between depressive symptoms and chronic illness in midlife women over time with the goal of improving knowledge of the determinants, consequences and treatment or care of the mental-physical comorbidity in this population (Scott et al., 2007).

Strengths of this study include the focus on diverse women at midlife initially studied prior to the onset of menopause, the longitudinal design with data collected over 3-5 years and attention to mental-physical comorbidity. The study also has limitations. Self report data has disadvantages because human beings are not precise observers of themselves (Fernandez-Ballesteros, 2004). Response bias and distortion can also be an issue. Self-report of depressive symptoms may not discriminate depression categories from general distress. As a self-report measure, the CES-D is subject to recall bias but the CES-D corrects for this by measuring the past week when people are more apt to recall accurately than over a longer period of time (Radloff & Teri, 1986). It is a measure of current depressive symptoms rather than a diagnosis of depressive disorder (Bromberger et al., 2007; Radloff & Teri, 1986). However, the CES-D is commonly used in community-based studies of women at midlife and allows for comparison of findings across studies (Vesco, Haney, Humphrey, Fu, & Nelson, 2007).

Physical health was measured using investigator-designed lists of common chronic health problems and the General Health Perception item from the SF-36. These measures did not permit examination of the full range of women's health problems. At T1, participants were asked about current or past health conditions. The questionnaire did not ask about whether the condition was past or current. For the chronic illnesses asked about at T6, participants were asked if they had ever been told by a doctor or a nurse that they had the condition. Medical records/clinician diagnosis of chronic health problems was not used. The self-report nature of the measure may be subject to bias, but research has shown correspondence between self-reported chronic conditions such as cardiovascular disease and diabetes mellitus, and medical record data (Kriegsman,

Penninx, van Eijk, Boeke, & Deeg, 1996; Scott et al., 2007). In addition, the presence of depressive symptoms did not appear to bias or overstate self-report of diagnosed physical conditions in a community-based sample (Kolk, Hanewald, Schagen, & Gijsbers van Wijk, 2002; Scott et al., 2007).

Repeated measures ANOVA in SPSS does not account for missing data, varied data collection times or the skewed distribution of CES-D scores and number of chronic illnesses at T6. Other analyses that meet statistical assumptions should be considered in future research with this type of non-clinical population of midlife women.

Conclusion

Despite its limitations, this study provides strong support for the association between depressive symptoms and chronic illness. Depressive symptoms were stable for the sample as a whole at baseline and at 30 months, but significantly increased with consequent reports of chronic illness or hypertension and in relation to the number of chronic illnesses. The direction of the relationship cannot be confirmed, which is a pressing issue for future studies. Nevertheless, the fact that depression and chronic physical disease co-occur suggests the need to assess for this comorbidity in cases of depressive symptoms or physical disease that occur among this population and to identify points of preventive intervention for midlife women, at risk for depression, chronic illness, and disability. Management strategies for symptoms such as insomnia or disturbed sleep could delay or abort full clinical episodes of depression in women. This study contributes to the literature about the potential vulnerability of diverse women at mid life to co-morbid depression and may lead to the development of appropriately timed, ethnically relevant and gender-specific interventions for women.

The failure to identify ethnic differences in mean depression scores in this sample is puzzling since it is inconsistent with prior literature on depression. The relative homogeneity of this sample in social and economic terms may have masked ethnic difference that might have been detectable in a larger sample.   However, ethnically relevant interventions for women could help to reduce depression symptoms and physical-mental comorbidity overall.

These findings have implications for health care providers who may underestimate the health impact of depressive symptoms. When women report health conditions or are diagnosed with a new chronic condition, an assessment for depressive symptoms and depressive disorders is suggested. Women who present with depression may be at high risk for physical health conditions. Where general medical services are separate from mental health services, recognition and adequate treatment of comorbid depressive symptoms and chronic illness is difficult at both sites and will require more focused attention. Further research is needed about the relationship between depressive symptoms and chronic illness in women over time with the goal of improving knowledge of the mental-physical comorbidity (Scott et al., 2007). More research is needed about the temporal relationships between depressive symptoms and chronic illness prior to onset of menopause to better prevent or limit mental-physical comorbidity and its consequences for both midlife and older women.

References

Alexander, J. L., Dennerstein, L., Woods, N. F., Halbreich, U., Kotz, K., Richardson, G.,
et al. (2007). Arthralgias, bodily aches and pains and somatic complaints in
midlife women: Etiology, pathophysiology and differential diagnosis. *Expert
Review Neurotherapeutics, 7*(11 Suppl), S15-26.

Alexander, J. L., Dennerstein, L., Woods, N. F., Kotz, K., Halbreich, U., Burt, V., et al.
(2007). Neurobehavioral impact of menopause on mood. *Expert Review
Neurotherapeutics, 7*(11 Suppl), S81-91.

Barry, L. C., Allore, H. G., Guo, Z., Bruce, M. L., & Gill, T. M. (2008). Higher burden of
depression among older women: The effect of onset, persistence, and mortality
over time. *Archives of General Psychiatry, 65*(2), 172-178.

Blank, K., Gruman, C., & Robison, J. T. (2004). Case-finding for depression in elderly
people: Balancing ease of administration with validity in varied treatment
settings. *Journals of Gerontology. Series A, Biological Sciences and Medical
Sciences, 59*(4), 378-384.

Bonnet, F., Irving, K., Terra, J. L., Nony, P., Berthezene, F., & Moulin, P. (2005).
Depressive symptoms are associated with unhealthy lifestyles in hypertensive
patients with the metabolic syndrome. *Journal of Hypertension, 23*(3), 611-617.

Bromberger, J. T., Assmann, S. F., Avis, N. E., Schocken, M., Kravitz, H. M., & Cordal,
A. (2003). Persistent mood symptoms in a multiethnic community cohort of pre-
and perimenopausal women. *American Journal of Epidemiology, 158*(4), 347-
356.

Bromberger, J. T., Harlow, S., Avis, N., Kravitz, H. M., & Cordal, A. (2004).

    Racial/ethnic differences in the prevalence of depressive symptoms among

    middle-aged women: The study of women's health across the nation (swan).

    American Journal of Public Health, 94(8), 1378-1385.

Bromberger, J. T., Matthews, K. A., Schott, L. L., Brockwell, S., Avis, N. E., Kravitz, H.

    M., et al. (2007). Depressive symptoms during the menopausal transition: The

    study of women's health across the nation (swan). *Journal of Affective Disorders,*

    103 (1-3), 267-272

Chapman, D. P., Perry, G. S., & Strine, T. W. (2005). The vital link between chronic

    disease and depressive disorders. *Prevention of Chronic Disease, 2*(1), A14.

Cyranowski, J. M., Marsland, A. L., Bromberger, J. T., Whiteside, T. L., Chang, Y., &

    Matthews, K. A. (2007). Depressive symptoms and production of

    proinflammatory cytokines by peripheral blood mononuclear cells stimulated in

    vitro. *Brain, Behavior, and Immunity, 21*(2), 229-237.

Davis, J., Fujimoto, R. Y., Juarez, D. T., Hodges, K. A., & Asam, J. K. (2008). Major

    depression associated with rates of cardiovascular disease state transitions.

    American Journal of Managed Care, 14(3), 125-128.

Evans, D. L., Charney, D. S., Lewis, L., Golden, R. N., Gorman, J. M., Krishnan, K. R.,

    et al. (2005). Mood disorders in the medically ill: Scientific review and

    recommendations. *Biological Psychiatry, 58*(3), 175-189.

Feresu, S. A., Zhang, W., Puumala, S. E., Ullrich, F., & Anderson, J. R. (2008). The

    frequency and distribution of cardiovascular disease risk factors among nebraska

women enrolled in the wisewoman screening program. *Journal of Women's Health (Larchmont)*.

Fernandez-Ballesteros, R. (2004). Self-report questionnaires. In M. J. Hilsenroth & D. Segal (Eds.), *Comprehensive handbook of psychological assessment* (Vol. 2, pp. 194-221). New York: John Wiley & Sons.

Fountoulakis, K. N., Bech, P., Panagiotidis, P., Siamouli, M., Kantartzis, S., Papadopoulou, A., et al. (2007). Comparison of depressive indices: Reliability, validity, relationship to anxiety and personality and the role of age and life events. *Journal of Affective Disorders, 97*(1-3), 187-195.

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., et al. (2001). Recruitment and retention of healthy minority women into community-based longitudinal research. *Journal of Women's Health and Gender Based Medicine, 10*(1), 77-85.

Haringsma, R., Engels, G. I., Beekman, A. T., & Spinhoven, P. (2004). The criterion validity of the center for epidemiological studies depression scale (ces-d) in a sample of self-referred elders with depressive symptomatology. *International Journal of Geriatric Psychiatry, 19*(6), 558-563.

Husaini, B. A., Neff, J. A., & Stone, R. H. (1979). Psychiatric impairment in rural communities. *Journal of Community Psychology, 7*(2), 137-146.

Kessler, R. C. (2003). Epidemiology of women and depression. *Journal of Affective Disorders, 74*(1), 5-13.

Kolk, A. M., Hanewald, G. J., Schagen, S., & Gijsbers van Wijk, C. M. (2002). Predicting medically unexplained physical symptoms and health care utilization.

A symptom-perception approach. *Journal of Psychosomatic Research, 52*(1), 35-44.

Kriegsman, D. M., Penninx, B. W., van Eijk, J. T., Boeke, A. J., & Deeg, D. J. (1996). Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly. A study on the accuracy of patients' self-reports and on determinants of inaccuracy. *Journal of Clinical Epidemiology, 49*(12), 1407-1417.

Ohayon, M. M. (2007). Epidemiology of depression and its treatment in the general population. *Journal of Psychiatric Research, 41*(3-4), 207-213.

Ortega, A. N., Feldman, J. M., Canino, G., Steinman, K., & Alegria, M. (2006). Co-occurrence of mental and physical illness in us latinos. *Social Psychiatry and Psychiatric Epidemiology, 41*(12), 927-934.

Radloff, L. S., & Locke, B. Z. (1986). The Community Mental Health Assessment Survey and the CES-D scale. In M. M. Weissman, J. K. Myers & C. E. Ross (Eds.), *Community surveys of psychiatric disorders* (Vol. 4). New Brunswick, New Jersey: Rutgers University Press.

Radloff, L. S., & Teri, L. (1986). Use of the Center for Epidemiological Studies-Depression scale with older adults. *Clinical Gerontologist, 5*(1/2), 119-136.

Ruo, B., Bertenthal, D., Sen, S., Bittner, V., Ireland, C. C., & Hlatky, M. A. (2006). Self-rated health among women with coronary disease: Depression is as important as recent cardiovascular events. *American Heart Journal, 152*(5), 921 e921-927.

Scott, K. M., Bruffaerts, R., Tsang, A., Ormel, J., Alonso, J., Angermeyer, M. C., et al. (2007). Depression-anxiety relationships with chronic physical conditions:

Results from the world mental health surveys. *Journal of Affective Disorders, 103*(1-3), 113-120.

Shafer, A. B. (2006). Meta-analysis of the factor structures of four depression questionnaires: Beck, CES-D,, Hamilton, and Zung. *Journal of Clinical Psychology, 62*(1), 123-146.

Stewart, A. L., & Ware, J. E. (1992). *Measuring functioning and well-being: The medical outcomes study approach*. Durham and London: Duke University Press.

Szoeke, C. E., Cicuttini, F. M., Guthrie, J. R., & Dennerstein, L. (2008). The relationship of reports of aches and joint pains to the menopausal transition: A longitudinal study. *Climacteric, 11*(1), 55-62.

Thomas, J. L., Jones, G. N., Scarinci, I. C., Mehan, D. J., & Brantley, P. J. (2001). The utility of the CES-D as a depression screening measure among low-income women attending primary care clinics. The Center for Epidemiological Studies-Depression. *International Journal of Psychiatry in Medicine, 31*(1), 25-40.

Vesco, K. K., Haney, E. M., Humphrey, L., Fu, R., & Nelson, H. D. (2007). Influence of menopause on mood: A systematic review of cohort studies. *Climacteric, 10*(6), 448-465.

Weissman, M. M., Sholomskas, D., Pottenger, M., Prusoff, B. A., & Locke, B. Z. (1977). Assessing depressive symptoms in five psychiatric populations: A validation study. *American Journal of Epidemiology, 106*(3), 203-214.

Woods, N. F., Mariella, A., & Mitchell, E. S. (2002). Patterns of depressed mood across the menopausal transition: Approaches to studying patterns in longitudinal data. *Acta Obstetricia et Gynecologica Scandinavica, 81*(7), 623-632.

Woods, N. F., Mariella, A., & Mitchell, E. S. (2006). Depressed mood symptoms during

    the menopausal transition: Observations from the Seattle Midlife Women's Health

    Study. *Climacteric, 9*(3), 195-203.

Woods, N. F., & Mitchell, E. S. (2005). Symptoms during the perimenopause:

    Prevalence, severity, trajectory, and significance in women's lives. *American*

    Journal of Medicine, 118 Suppl 12B, 14-24.

Table 1 Sample Characteristics at Study Initiation

Sample Characteristics	Total sample N=347	CES-D < 16 N=239 (70%) Group 1	CES-D ≥16 N=104 (30%) Group 2	Test statistic, *p* values
Age (years) *mean (SD)*	43.5 ± 2.4	43.5 ± 2.4	43.4 ± 2.3	$t(340)$ = .146 p = .884
CES-D *mean (SD)*	12.5 ± 9.98	7.15 ± 4.56	24.7 ± 8.08	t (330.358) = 23.567 (log transformed CES-D), $p < .001$, 2 > 1

Education
  High school or less
  Partial college
  College graduate
  Professional graduate degree
	
	36 (10.5%)
	107 (31%)
	96 (28%)
	103 (30%)
		
		20 (8.3%)
		67 (28%)
		72 (30%)
		80 (33.5%)
			
			16 (15.9%)
			39 (38.6%)
			24 (23.8%)
			22 (21.8%)
				Z = 3.149, p = .002, 1 > 2

Employed for pay
  Yes
  No
	
	287 (86%)
	48 (14%)
		
		203 (86%)
		33 (14%)
			
			82 (84.5%)
			15 (15.5%)
				X^2 =.122, p = .727

Household income (before taxes)
  <$10, 999
  $11, 000-$30, 999
  $31, 000-$50, 999
  $51,000-$80,999
  >$81, 000
	
	20 (5.9%)
	60 (17.7%)
	90 (26.5%)
	89 (19.3%)
	81 (24%)
		
		13 (5.5%)
		38 (16%)
		57 (24%)
		66 (27.9%)
		63 (26.6%)
			
			7 (6.9%)
			22 (21.7%)
			33 (32.7%)
			21 (20.8%)
			18 (17.8%)
				Z = 3.149, p = .002 1 > 2

Marital status
  Married or permanently partnered
  Single, divorced, separated, widowed
	
	197 (57%)
	
	146(42.6%)
		
		145 (60.7%)
		
		94 (39.3%)
			
			51 (50%)
			
			51 (50%)
				X^2 = 3.330, p = .068

Children
  Yes
  No
	
	230 (67%)
	111 (32%)
		
		153 (64.3%)
		85 (35.7%)
			
			76 (74.5%)
			26 (25.5%)
				X^2 = 3.394, p = .065

Smoke now
  Yes
  No.
	
	37 (10.7%)
	310 (89.3%)
		
		24 (10%)
		215 (90%)
			
			13 (12.5%)
			91 (87.5%)
				X^2 =.455, p = .500

SD = standard deviation
(Totals may vary because of missing data)

Table 2 High Frequency Health Conditions Reported by 50 or More Women (n=344) at Study Initiation

Health Condition	n	%
No health conditions reported	14	4
One or more health condition	330	96
Allergies (including hay fever)	207	61
Headaches or migraines	192	56
Back problems	181	53
Hemorrhoids	136	40
Skin problems, psoriasis, eczema or dermatitis	127	37
Kidney, bladder or urinary problems	91	27
Varicose veins	83	24
Irritable bowel problems	71	21
Asthma	55	16
Arthritis	54	16

Table 3 Chronic Illnesses & Major Health Problems Reported at 30 Months (n = 243)

Chronic Illness (forced choice list)	n	%	Mean (SD)	Median, Range
Chronic illnesses at 30 months			.46 ± .723	.00, 0-4
No chronic illness at 30 months	260	75.4		
One or more chronic illnesses at 30 months	85	24.6		
High blood pressure	34	14.6		
Thyroid disorder	25	10.7		
Psychiatric illness	14	6.0		
Gall bladder disease	10	4.3		
Ulcers (stomach or intestinal)	7	3.0		
Cancer	7	2.9		
Type 11 diabetes	5	2.0		
Diabetes of pregnancy	5	2.0		
Stroke	4	1.6		
Kidney disease (renal dialysis)	2	0.8		
Type 1 Diabetes	0	0		
Major Health Problem (open-ended question)	**n**	**%**	**Mean (SD)**	**Median, range**
Health problems at 30 months			11.2 ± 7.63	0, 0-26
No health problems at 30 months	165	70.8		
One or more health problems at 30 months	68	29.0		
Pain	4	7.7		
Gynecological ("PID", postpartum hemorrhage, dysplasia, toxic shock)	4	7.7		
Muscle or joint problems	4	7.7		
Asthma	4	7.7		
Fibroids	4	7.7		
Eye problems	3	5.8		
Headache or migraine	3	5.8		

Table 4 Group Differences in Depressive Symptoms Score by Health Conditions,
Chronic Illness and Hypertension

| Grouping Variable	CES-D score (m, sd)	CES-D score Median, Range	Test statistic, *p* value
Health conditions at T1	*T1*	*T1*	
No health conditions	12.1 ± 9.69	10, 0-29	*Z* = - .093
One or more health conditions	12.4 ± 9.96	10, 0-53	*p* = .926
Chronic illness at T6	*T6*	*T6*	
No chronic illness	9.2 ± 8.3	7, 0-46	*Z*=-4.70
One or more chronic illness	15.3 ± 10.8	13, 0-57	*p* < .001
Hypertension at T6	*T6*	*T6*	
No hypertension	8.8 ± 7.76	6, 0-26	*Z*= -3.07
Hypertension	16.3 ± 11.60	14, 1-57	*p* =.002

CES-D = Center for Epidemiologic Studies-Depression

Figure 1 Depressive Symptom Scores over Time by Chronic Illness Group
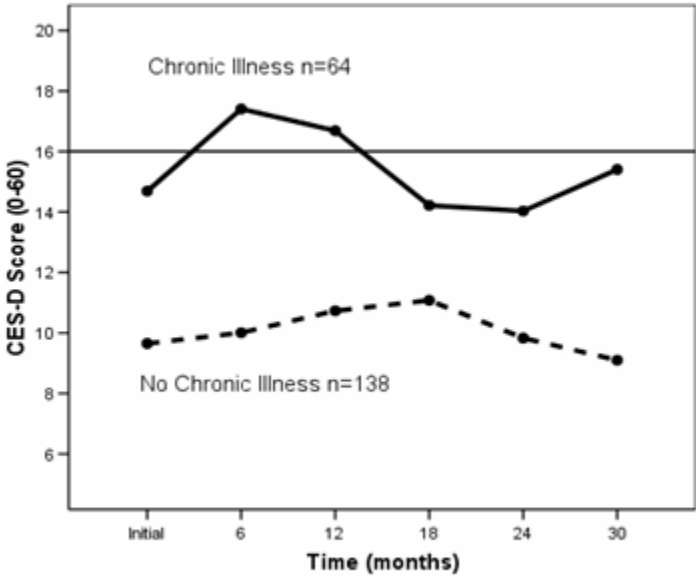
CES-D = Center for Epidemiologic Studies-Depression

Figure 2 Depressive Symptom Scores over Time by Hypertension Group
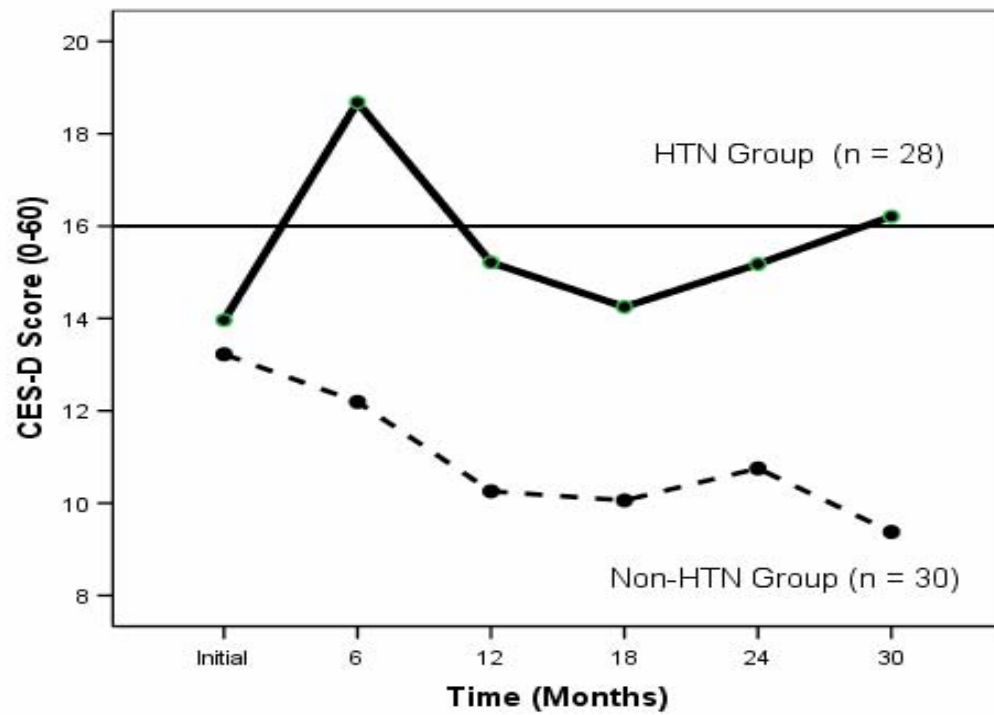
CES-D = Center for Epidemiologic Studies-Depression
HTN= Hypertension

CHAPTER 5: SYNTHESIS

This research stemmed from observations of the ubiquitous co-occurrence of depressive symptoms and chronic disease in the inpatient acute care setting, the realization that poor sleep quality was a major contributor to this problem and the recognition that research was needed. Three manuscripts are presented in this dissertation: a conceptual approach and two papers reporting study results. The research involved a community-based sample of 347 healthy, ethnically diverse, premenopausal women between 40-50 years of age. In this chapter, key observations from the three papers will be synthesized including clinical and health policy implications and directions for future research.

The first paper (chapter 2) presented a conceptual approach to insomnia. About one-third of the adult population experiences insomnia. It is more common among women, middle-aged and older adults, and people with chronic diseases (Ancoli-Israel, 2006; Morin et al., 2006; Ohayon, 2002). Sleep is essential to health, with experts suggesting a bidirectional relationship with health (Ohayon, 2006; Zee & Turek, 2006). Nurses are likely to encounter sleep disturbance among their patients with chronic illnesses and must be able to provide appropriate theory-guided and evidence-based management. In twenty-four hour settings, nurses have responsibility to identify and extend nursing interventions that promote good sleep and provide patient/family education about sleep that may affect patient's sleep quality. Nurses in any setting, from public health to intensive care, often encounter the consequences of poor sleep quality. This calls for increased awareness and knowledge about sleep disturbances. Because many health care settings operate all day and all night, the need for awareness extends to caregivers who must consider the possible impact of sleep problems on their own health

and performance, especially when rotating shifts or working permanently at night (Lee et al., 2004). Nurses deal with insomnia from a perspective of symptom management, and they care for people who experience insomnia in the context of other medical or psychiatric disorders. Four theoretical perspectives of the mechanisms explaining sleep and insomnia were critiqued for their relevance for nursing practice and research. Key concepts germane to nursing were identified and incorporated into a new model proposed for insomnia as a symptom experience. This new model extends the Theory of Symptom Management to include physiological and psychological mechanisms of acute and chronic insomnia in the symptom dimension to provide clearer guidance for the timing and choice of management strategies.

The purpose of the second paper (chapter 3) was to describe depressive symptoms in ethnically diverse premenopausal women in the late reproductive stage and patterns of depressive symptoms across time as a function of fixed demographic factors as well as biological and social factors that vary over time. The predictors of first onset depressive symptoms in midlife women are not well studied longitudinally and there is controversy about the association of the menopausal transition with depressive symptoms. Using negative binomial regression analysis, a significant model of predictors of high and low average CES-D scores was identified. Depressive symptoms in this sample of premenopausal midlife women in the late reproductive stage were fairly stable over time, with an indication that CES-D scores would continue to decrease with time. The finding that CES-D scores declined over time during the premenopausal late reproductive stage was unexpected given other research that showed that depressive symptoms and depressive disorders were more likely during perimenopause than pre-menopause.

Predictors of higher average CES-D scores during the 36-month time frame were poor sleep quality, presence of chronic illness at 30 months, high BMI, and the interaction of poor sleep quality with time. Time, having a partner, positive social support from interpersonal relationships, and the interaction between low BMI and time predicted lower average CES-D scores and were considered protective factors. There was no significant relationship between depressive symptoms and income, age, education, children or follicle stimulating hormone (FSH), the hormone that begins to increase as ovarian function declines. The findings of this study differ from previous research that has shown a relationship between depressive symptoms or diagnoses and hormonal changes of menopausal transition (Freeman, Sammel, Lin, & Nelson, 2006) and supports other research that found no significant relationship between menopausal hormone status and depressive symptoms (Woods, Mariella, & Mitchell, 2006). These findings are consistent with studies that show the majority of women do not experience high severity of depressed mood during the menopausal transition (Bromberger et al., 2003; Woods, Mariella, & Mitchell, 2006) and that life events are the strongest factor influencing depressed mood, rather than age or menopausal status.

In this sample of women from 40-50 years of age, poor sleep quality showed the strongest effect on depressive symptoms. Poor sleep quality is a known predictor of depressed mood and has been found to be a precursor of first or recurrent depressive episodes in multiple samples, independent of age (Breslau, Roth, Rosenthal, & Andreski, 1996; Cuijpers, Beekman, Smit, & Deeg, 2006; Ford & Cooper-Patrick, 2001; Johnson, Roth, & Breslau, 2006; Mallon, Broman, & Hetta, 2000; Ohayon, 2007b; Perlis et al., 2006; Riemann & Voderholzer, 2003; Roberts, Shema, Kaplan, & Strawbridge, 2000).

There is evidence that women have more sleep difficulty as they transition through menopause (Nelson et al., 2005). Sleep disturbances in women are classically attributed to menopause (Alexander & Dennerstein, 2007) and women report more insomnia than men, but Ohayon (2007a; 2007b) emphasized the importance of carefully evaluating sleep complaints and associated disorders and not assuming sleep difficulties result from chronological age or menopausal status.

Neither ethnic differences nor socioeconomic factors were significant predictors of depressive symptom scores in this sample of midlife women despite ethnic differences in the sample for education, household income before taxes, children and marital status, common indicators of socioeconomic status. The failure to identify ethnic differences is puzzling because it is inconsistent with prior literature on depression. The relative homogeneity of this sample in social and economic terms may have masked ethnic difference that might have been detectable in a larger sample. Although there were no ethnic differences in mean CES-D scores, a higher proportion of African American women scored $\geq$ 16 on the CES-D, indicating possible depressive disorder. This finding warrants more exploration.

The third paper (chapter 4) described the relationship between depressive symptoms and physical health in the same sample of midlife women. Prevalence of depressive symptoms in the total sample was 30% at study initiation and 26% at 30 months. Number of health conditions was significantly higher for women scoring $\geq$16 on CES-D compared to women scoring <16. There was a significant association between ethnicity and chronic illness; 30.8% of African Americans reported a chronic illness, compared to 26.4% of European Americans and 15.8% of Latinas. Slightly over half of

the 60 women with CES-D scores $\geq$16 reported chronic illness (53%) whereas only 29% (50 of 174) who scored <16 reported a chronic illness. The self-reported HTN group had a mean CES-D score nearly twice as high as the non-HTN group. This study provides strong support for the association between depressive symptoms and chronic illness, particularly hypertension, in pre-menopausal late reproductive stage women. Depressive symptoms were stable for the sample as a whole at baseline and at 30 months, but significantly increased with consequent reports of chronic illness or hypertension. The direction of the relationship between depressive symptoms and chronic illness could not be confirmed in this sample and should be a pressing issue for future studies.

<div align="center">Clinical Implications</div>

The model of the symptom experience of insomnia has implications for practice as well as research. It points to aspects of the symptom experience, arousal and conditioned arousal, where management strategies could be instituted to prevent precipitating factors from leading to acute insomnia, prevent the transition from acute to chronic insomnia by modifying perpetuating factors, and prevent conditioning of chronic insomnia (Perlis, Jungquist, Smith, & Posner, 2005). The focus on potential conditioning of arousal in this model suggests the use of cognitive behavioral methods for symptom assessment and management as well as management of overall arousal. Critical timing of nursing management strategies would be important for the prevention of conditioned arousal and chronic insomnia. To apply this model to clinical practice, nurses may need more training in appropriate cognitive behavioral methods applicable to sleep disturbance (Morin, 1993; Morin & Espie, 2003; Perlis, Jungquist, Smith, & Posner, 2005; Szuba, Kloss, & Dinges, 2003).

The predisposing, precipitating, and perpetuating factors relevant to each person should be assessed and identified to ensure appropriate application of management strategies. If perpetuating factors are already in place and insomnia is chronic, then the appropriate management strategies would involve part or all of evidence-based cognitive behavioral therapy for insomnia. Management strategies are beyond the scope of this dissertation but effective strategies would have a role in improving sleep and reducing the outcomes of biopsychosocial morbidity associated with sleep loss.

The finding showing that poor sleep quality has the strongest effect on high depression scores points to the importance of attending to improvement of sleep quality to prevent or delay depressive symptoms and consequences for women's health. Findings supporting the association of depressive symptoms and chronic physical disease add to a growing call for attention to this comorbidity. The fact that depression and chronic physical disease co-occur suggests the need to assess for this comorbidity in cases of depressive symptoms or physical disease among midlife women. The ability to identify points of preventive intervention should be a clinical imperative for this population at risk for depression, chronic illness and disability. Management strategies for symptoms such as insomnia or disturbed sleep could delay or abort full clinical episodes of depression in women. This study contributes to the literature about the potential vulnerability of diverse women at mid life for co-morbid depression, and identifies protective factors that may be enhanced by intervention. The development of appropriately timed, ethnically relevant and gender-specific interventions for women would help to reduce symptoms of depression and physical-mental comorbidity overall.

Findings have implications for health care providers and the health care of women. Health care providers may underestimate the health impact of depressive symptoms and ignore the impact of sleep quality. When women report health conditions or are diagnosed with a new chronic condition, an assessment for depressive symptoms and depressive disorders, as well as an assessment of sleep quality, is recommended. Women who present with depression may be at high risk for physical health conditions. Women with depressive symptoms also may be experiencing poor sleep quality. Where general medical services are separate from mental health services, recognition and adequate treatment of comorbid depressive symptoms and chronic illness is difficult at both sites and will require more focused attention.

<div align="center">Health Policy Implications</div>

The term health policy refers to authoritative decisions that are made within government, and within the private sector, that pertain to health and the pursuit of health (Block, 2008). Health policy can be addressed at national, state and local levels and in the private sector. The literature review for this dissertation revealed a gap in research to guide women's health care and the findings raise health policy issues that may be addressed appropriately at the national and state level and in the private sector at the level of health care delivery organizations.

It was not until the late 1980s and the 1990s that research on women's health expanded beyond traditional reproductive health and women were more widely included in research samples (Correa-de-Araujo, 2006; Sarto, 2008). Women and minorities continue to be underrepresented in published studies, outcomes generally are not reported by sex or racial or ethnic group and compliance is inadequate for the National Institutes

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of Health (NIH) guidelines for inclusion of women and minorities in research (Geller, Adams, & Carnes, 2006). Women's health care has been based primarily on studies of men and postmenopausal women (Correa-de-Araujo, 2006). The reports of this study of premenopausal women in the late reproductive stage, an understudied group, will contribute to filling the gap.

Generally, fixed factors such as gender, education, economic status, race and ethnicity are seen as predictors of health status with resultant policy implications for further research and for appropriate health care (Sarto, 2008). Similarly, in this study, a higher proportion of African American women reported higher depressive symptoms and presence of chronic illness and this finding warrants further investigation. However, ethnicity was not a predictor of depressive symptoms when other factors such as income and social support were in the model. The negative findings for socioeconomic factors are new. Time varying factors, such as partner status, social support, BMI, chronic illness and sleep quality predicted depressive symptoms more so than fixed factors, demonstrating the complexity of factors that influence mental and physical health in midlife women. The antecedents of the gender differences in health and the issues about the complex connections between biological and social processes underlying health are highlighted in a call for collaborative interdisciplinary science with biomedical and social science researchers working together (Bird & Rieker, 1999, 2002; Rieker & Bird, 2005). The findings of this study illustrate the importance of this integrated approach both for national policy about science and its funding and public health policy.

The fact that depression and chronic physical illness co-occur suggests the need to assess for this comorbidity in cases of depressive symptoms or physical disease that

occur among midlife women and to identify points of preventive intervention for midlife women, who are at risk for depression, chronic illness, and disability. Where general medical services are separate from mental health services, recognition and adequate treatment of comorbid depressive symptoms and chronic illness is difficult at both sites. In health care delivery organizations that include women's health clinics, care of comorbid mental-physical conditions may be facilitated for women. Effective treatments for depression in non-psychiatric settings have been reported but do not include results stratified by gender (Manber et al., 2008; Unutzer et al., 2002), leaving the question about effectiveness of the treatments for women unanswered. The question of whether subsyndromal depressive symptoms should be monitored or treated also is a matter of debate in the literature (Kessler, 2002).

<div align="center">Directions for Future Research</div>

There is more to be learned with these data from midlife women. An analysis to identify predictors of poor sleep quality over time and the relationship of sleep quality with chronic illness in midlife women is the next step in this research. Because BMI was found to be a significant predictor of depressive symptom scores, a future study with this sample will identify the differences between premenopausal women with high BMI and low BMI in patterns of sleep disturbance, patterns of depressive symptoms and reported diagnosis of onset of chronic illnesses. A further goal is to identify how depressive symptoms and sleep quality in this sample may together contribute to the development of chronic illness and in particular, hypertension. Complex comorbidities may be explored with these data from midlife women.

Additional analysis of the data from the women who scored $\geq$ 16 on the CES-D may reveal information about the most at-risk subgroup of the sample and identify which women more urgently need intervention. Another analysis may provide an avenue for exploring different CES-D cut-points for depressive symptoms in midlife women. Kessler (2002) reported a high prevalence of symptoms in epidemiological research using screening scales, such as the CES-D, and a relatively low prevalence of depressive disorder, suggesting that many people have symptoms that do not meet diagnostic criteria for major depressive disorder. Minor depression (also called subsyndromal or subthreshold depression) refers to symptoms that do not meet diagnostic criteria (Davidson et al., 2005), and has become increasingly important in research and clinical practice. For example, minimal increases in self-reported symptoms predicted the recurrence of acute coronary syndrome (Davidson, Rieckmann, & Rapp, 2005). Concerns have been raised about the scale's sensitivity and specificity in detecting depression particularly in older adults with comorbid medical illnesses (Davidson, Rieckmann, & Rapp, 2005). As a result, different cutpoints have been studied for the CES-D in different populations.

A related issue is the use of self-reports of symptoms rather than measures that provide depressive diagnoses. Self-reports have advantages: emphasis on the experience of depression, speed, economy, no need for professional observation. Self-reports are not only common measures for assessing treatment expectancy; they may be the best predictors of treatment outcome (Fernandez-Ballesteros, 2004). The CES-D is commonly used in studies of midlife women and allows for comparison of findings across studies and populations.

Further research is needed about the relationship between depressive symptoms and chronic illness in women over time with the goal of improving knowledge of the mental-physical comorbidity (Scott et al., 2007). More research is needed about temporal relationships between poor sleep quality, depressive symptoms and chronic illness prior to onset of menopause to better prevent or limit mental-physical comorbidity and its consequences for both midlife and older women. Clarity about the direction of the depressive symptoms—chronic illness relationship in midlife women is important and not answered by this research. It is not known whether this relationship is bidirectional as has been suggested. In many populations, it has been shown that poor sleep quality leads to depressive symptoms but this is not confirmed in midlife women

A future research goal is to design a study based on the model of insomnia presented in this dissertation, using cognitive-behavioral interventions for insomnia with depressive symptoms and sleep quality as outcomes or mediators or moderators of hypertension or other chronic disease in a clinic (such as cardiac or primary care) population of midlife and older women. This approach may include preventive interventions for women that involve improving BMI and enhancing support from family and social networks as identified in this research. Most important, and most complex, will be to develop studies that address mental-physical comorbidity.

References

Alexander, J. L., & Dennerstein, L. (2007). Series overview and introduction. *Expert Review Neurotherapeutics, 7*(11 Suppl), S3-6.

Ancoli-Israel, S. (2006). The impact and prevalence of chronic insomnia and other sleep disturbances associated with chronic illness. *American Journal of Managed Care, 12*(8 Suppl), S221-229.

Bird, C. E., & Rieker, P. P. (1999). Gender matters: An integrated model for understanding men's and women's health. *Social Science and Medicine, 48*(6), 745-755.

Bird, C. E., & Rieker, P. P. (2002). Integrating social and biological research to improve men's and women's health. *Womens Health Issues, 12*(3), 113-115.

Block, L. E. (2008). Health policy: What it is and how it works. In C. Harrington & C. L. Estes (Eds.), *Health policy: Crisis and reform in the U.S. health care delivery system* (5th ed.). Sudbury, MA.: Jones and Barlett Publishers.

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. *Biological Psychiatry, 39*(6), 411-418.

Bromberger, J. T., Assmann, S. F., Avis, N. E., Schocken, M., Kravitz, H. M., & Cordal, A. (2003). Persistent mood symptoms in a multiethnic community cohort of pre- and perimenopausal women. *American Journal of Epidemiology, 158*(4), 347-356.

Correa-de-Araujo, R. (2006). Serious gaps: How the lack of sex/gender-based research impairs health. *Journal of Women's Health, 15*(10), 1116-1122.

Cuijpers, P., Beekman, A., Smit, F., & Deeg, D. (2006). Predicting the onset of major

    depressive disorder and dysthymia in older adults with subthreshold depression: A

    community based study. *International Journal of Geriatric Psychiatry, 21*(9),

    811-818.

Davidson, K. W., Rieckmann, N., & Rapp, M. A. (2005). Definitions and distinctions

    among depressive syndromes and symptoms: Implications for a better

    understanding of the depression-cardiovascular disease association.

    Psychosomatic Medicine, 67 Suppl 1, S6-9.

Fernandez-Ballesteros, R. (2004). Self-report questionnaires. In M. J. Hilsenroth & D.

    Segal (Eds.), *Comprehensive handbook of psychological assessment* (Vol. 2, pp.

    194-221). New York: John Wiley & Sons.

Ford, D. E., & Cooper-Patrick, L. (2001). Sleep disturbances and mood disorders: An

    epidemiologic perspective. *Depression and Anxiety, 14*(1), 3-6.

Freeman, E. W., Sammel, M. D., Lin, H., & Nelson, D. B. (2006). Associations of

    hormones and menopausal status with depressed mood in women with no history

    of depression. *Archives of General Psychiatry, 63*(4), 375-382.

Geller, S. E., Adams, M. G., & Carnes, M. (2006). Adherence to federal guidelines for

    reporting of sex and race/ethnicity in clinical trials. *Journal of Womens Health

    (Larchmont), 15*(10), 1123-1131.

Johnson, E. O., Roth, T., & Breslau, N. (2006). The association of insomnia with anxiety

    disorders and depression: Exploration of the direction of risk. *Journal of

    Psychiatric Research, 40*(8), 700-708.

Kessler, R. C. (2002). Epidemiology of depression. In I. H. Gotlib & C. L. Hammen

 (Eds.), *Handbook of depression* (pp. 23-42). New York: The Guilford Press.

Lee, K. A., Landis, C., Chasens, E. R., Dowling, G., Merritt, S., Parker, K. P., et al.

 (2004). Sleep and chronobiology: Recommendations for nursing education.

 Nursing Outlook, 52(3), 126-133.

Mallon, L., Broman, J. E., & Hetta, J. (2000). Relationship between insomnia,

 depression, and mortality: A 12-year follow-up of older adults in the community.

 International Psychogeriatrics, 12(3), 295-306.

Manber, R., Edinger, J. D., Gress, J. L., San Pedro-Salcedo, M. G., Kuo, T. F., & Kalista,

 T. (2008). Cognitive behavioral therapy for insomnia enhances depression

 outcome in patients with comorbid major depressive disorder and insomnia.

 Sleep, 31(4), 489-495.

Morin, C. M. (1993). *Insomnia: Psychological assessment and management*. New York,

 New York: The Guilford Press.

Morin, C. M., Bootzin, R. R., Buysse, D. J., Edinger, J. D., Espie, C. A., & Lichstein, K.

 L. (2006). Psychological and behavioral treatment of insomnia: Update of the

 recent evidence (1998-2004). *Sleep, 29*(11), 1398-1414.

Morin, C. M., & Espie, C. A. (2003). *Insomnia: A clinical guide to assessment and

 treatment*. New York, New York: Kluwer Academic/Plenum Publishers.

Nelson, H. D., Haney, E., Humphrey, L., Miller, J., Nedrow, A., Nicolaidis, C., et al.

 (2005). *Management of menopause-related symptoms. Summary, evidence

 report/technology assessment no. 120. (prepared by the Oregon Evidence-based*

Practice Center, under Contract No. 290-02-0024.). Retrieved April 15, 2008 from www.ahrq.gov.

Ohayon, M. M. (2002). Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Medicine Reviews, 6*(2), 97-111.

Ohayon, M. M. (2006). Interlacing sleep, pain, mental disorders and organic diseases. *Journal of Psychiatric Research, 40*(8), 677-679.

Ohayon, M. M. (2007a). Epidemiology of depression and its treatment in the general population. *Journal of Psychiatric Research, 41*(3-4), 207-213.

Ohayon, M. M. (2007b). Insomnia: A ticking clock for depression? *Journal of Psychiatric Research, 41*(11), 893-894.

Perlis, M. L., Jungquist, C., Smith, M. T., & Posner, D. (2005). *Cognitive behavioral treatment of insomnia: A session-by-session guide*. New York, New York: Springer Science + Business Media, LLC.

Perlis, M. L., Smith, L. J., Lyness, J. M., Matteson, S. R., Pigeon, W. R., Jungquist, C. R., et al. (2006). Insomnia as a risk factor for onset of depression in the elderly. *Behavioral Sleep Medicine, 4*(2), 104-113.

Rieker, P. P., & Bird, C. E. (2005). Rethinking gender differences in health: Why we need to integrate social and biological perspectives. *Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 60 Spec No 2*, 40-47.

Riemann, D., & Voderholzer, U. (2003). Primary insomnia: A risk factor to develop depression? *Journal of Affective Disorders, 76*(1-3), 255-259.

Roberts, R. E., Shema, S. J., Kaplan, G. A., & Strawbridge, W. J. (2000). Sleep complaints and depression in an aging cohort: A prospective perspective. *American Journal of Psychiatry, 157*(1), 81-88.

Sarto, G. E. (2008). The gender gap: New challenges in women's health. In C. Harrington & C. L. Estes (Eds.), *Health policy: Crisis and reform in the U.S. health care delivery system* (5th ed.). Sudbury, MA.: Jones and Bartlett Publishers.

Scott, K. M., Bruffaerts, R., Tsang, A., Ormel, J., Alonso, J., Angermeyer, M. C., et al. (2007). Depression-anxiety relationships with chronic physical conditions: Results from the world mental health surveys. *Journal of Affective Disorders, 103*(1-3), 113-120.

Szuba, M. P., Kloss, J. D., & Dinges, D. F. (2003). *Insomnia: Principles and management*. New York, NY: Cambridge University Press.

Unutzer, J., Katon, W., Callahan, C. M., Williams, J. W., Jr., Hunkeler, E., Harpole, L., et al. (2002). Collaborative care management of late-life depression in the primary care setting: A randomized controlled trial. *Journal of American Medical Association, 288*(22), 2836-2845.

Woods, N. F., Mariella, A., & Mitchell, E. S. (2006). Depressed mood symptoms during the menopausal transition: Observations from the Seattle Midlife Women's Health Study. *Climacteric, 9*(3), 195-203.

Zee, P. C., & Turek, F. W. (2006). Sleep and health: Everywhere and in both directions. *Archives of Internal Medicine, 166*(16), 1686-1688.

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