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The Impact of Chronic Perceived Stress on Perceived Health Status and Symptom Experience in Pre- and Post-Menopausal Women



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# The Impact of Chronic Perceived Stress on Perceived Health Status and Symptom Experience in Pre- and Post-Menopausal Women

by

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DISSERTATION

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**Acknowledgements and Dedication**

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The Impact of Chronic Perceived Stress on Perceived Health Status and Symptom Experience in Pre- and Post-Menopausal Women

Holly J. Jones

## Abstract

Chronic stress has been recognized as a precursor to poor health outcomes and health disparity. The purpose of this dissertation research study was to evaluate the impact of chronic perceived stress on perceived health status and symptom experience in women before and after menopause. The theory of allostasis was used as the framework for this study and proposes that chronic perceived stress will result in symptom expression or illness if a person in unable to adapt effectively to a stressor(s). In an effort to fully explore this phenomenon, this study was comprised of two parts: 1) secondary analyses of retrospective data exploring symptom experience in a cohort of midlife women who participated in the UCSF Midlife Women's Health Study prior to menopause and, 2) mixed-methods analysis of current data exploring perceived stress and its long-term effects using a smaller sample of the women who participated in the parent study and are now post menopause.

Bladder and sleep symptoms were found to be prevalent in the sample. Reproductive status was a significant contributor to the variance in experiencing nocturia. Sleep quality and sleep hours were associated with several determinants of adverse health outcomes: perceived stress, body mass index, and race. Mixed methods analysis found perceived stress scores to be consistent over time in the subsample of African American women and six stress-related themes were identified.

Finally, multiple physiological, psychosocial, and demographic factors were investigated to determine their unique contributions to the variance in leukocyte telomere length. Telomere length is recognized as a measure of aging and chronic stress. Despite the small sample size, income, age, perceived stress, and diastolic blood pressure were noted to be influential to having shorter telomere length.

The combination of data from a cohort of contemporary women before and after menopause provided a better understanding of the stressors endured over time, symptom experience, coping strategies, and associations with genetic biomarkers. Results from this study should be used to identify vulnerable midlife women and formulate individualized care plans in an effort to decrease morbidity and health disparity.

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# The Impact of Chronic Perceived Stress on Perceived Health Status and Symptom Experience in Pre- and Post-Menopausal Women

Nursing Research Dissertation

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## Introduction

The purpose of this chapter is to familiarize the reader with the underlying motivation, theory, and knowledge that have supported this dissertation research proposal. I hope to communicate my heart-felt passion for a phenomenon of interest: the effect of chronic perceived stress on perceived health status and long-term health outcomes in midlife women. Perceived stress, especially when experienced over prolonged periods of time, contributes to health disparity and perpetuates a state of vulnerability for midlife women.

The doctoral research topic of interest has come from my experiences as a nurse practitioner (NP) working in an internal medicine office and in numerous volunteer settings. As a primary care provider, treatment of stress-related illness was common. After eliminating the likely physiological causes, I was often able to identify stress as the precursor to a particular illness or symptom expression. However, despite my knowledge of the patients and usual good rapport, I was less successful in guiding patients through self-management or elimination of the stressors in their lives. I often wondered whether the stressors they endured would adversely affect their long-term health conditions and functional status and, I worried that otherwise preventable illnesses would occur and result in debilitation. The differences in the appraisal of stressors and subsequent responses were remarkable from one individual to another; some patients were more susceptible to the effects of a stressor while others were more resilient in their style of coping.

Midlife women (women ages 40 to 60) appeared to be most affected by the stressors in their lives. It was not uncommon to discuss midlife issues with the women

under my care: empty nest syndrome, marital concerns, changes in employment, caring for grandchildren, or caring for an aging parent. In addition to midlife issues, aging is accompanied by physical changes, menopause, and an increased risk for disease and illness. African American women and other women of color often experience unique combinations of stressors in comparison to women of other races and ethnicities. Socioeconomic issues, racism, discrimination, or misogynistic practices often compounded the stressors encountered by diverse female populations. Symptoms management was futile without first identifying and addressing the prominent stressors in their lives.

When I chose to pursue a PhD, I contemplated multiple topics for my dissertation research such as diabetes, heart disease, and infectious disease, but I could not forget the midlife women and the difficulty that I encountered while caring for them. My desire was to bring new knowledge to the field and highlight phenomena observed in my practice. Through research, I hoped to enhance clinical decision-making and influence practice guidelines and protocols for improving patient care. The focus of my dissertation research is the effects of chronic perceived stress on perceived health status and on long-term health outcomes. The population of interest is midlife women. Midlife is a time of major life transition that has become increasingly more important as life expectancy continues to rise. In a sense, this time of change and maturity is a rite of passage and, our ability to successfully navigate the challenges may influence health outcomes and longevity.

During my doctoral studies I became familiar with several traditional approaches to stress theory (psychological, environmental, and biological) and their development.

Early stress research and observations focused on behavior and physical expressions such as heart rate, pupil dilation, and blood pressure. The effect of hormones such as cortisol and epinephrine on the central nervous system and other body organs were identified. Today, researchers utilize a combination of physiological and genetic markers to measure the effects of stress. Utilization of multiple stress measures can provide a more comprehensive approach to current stress research and its effects on the lives and well-being of individuals. Furthermore, the use of multiple measurement tools will allow for a well-balanced and informative dissertation research study on which to build a future body of research. I have proposed and conducted an ancillary study using data from a previous midlife women's health study. Using old and new responses to a perceived stress scale, anthropometrics, and biomarkers, a sample of midlife African American and European American women will be compared for similarities and differences.

**The Concept of Stress**

Stress is an abstract concept and yet most people can describe how it feels to be "under stress" or what comprises a stressful situation. Stress is not unlike the wind: invisible yet we feel it, we know it exists, we bend under its will, and are often powerless to its force. Researchers have documented the physiological effects of stress and can predict the body's response with great accuracy. Rises in cortisol and epinephrine levels, heart rate and blood pressure are typical responses. This response to stressful stimuli has been so well researched that cellular and systemic responses associated with chronic stress can also be predicted. Cardiovascular disease is a model example of the effects of chronic stress. Chronic stress results in sustained blood pressure elevations, inflammatory protein production, and cortisol levels that lead to vascular inflammation and the

development of intraluminal arterial plaque (Steptoe & Kivimaki, 2012). Plaque development within the arteries, also known as atherosclerosis, eventually occludes vessels and stops blood flow to critical heart tissue resulting in myocardial infarction.

Physical, psychological, or environmental stress can trigger the responses described above. Psychological stress has proven to be just as significant as physical or environmental stress. The link between mind and body has long been observed and is once again becoming a popular school of thought with recent focuses on "mindfulness" and other stress-reducing strategies. Hans Selye proposed the general adaptation syndrome in 1936 which described stress as "the non-specific response of the body" created by some stressor (Lazarus & Folkman, 1984, p. 15). Selye's colleagues recognized that physiological responses could be triggered by personal experiences and cognitive awareness. Stress and coping theory developed by Lazarus states that the bidirectional relationship between the environment and the person influences the cognitive appraisal of stressful stimuli (Folkman, Lazarus, Gruen, & DeLongis, 1986). This recognition that an individual's perception of a situation may influence their response was revolutionary.

Many health science disciplines, such as nursing, view stress according to its source: environmental, psychological/emotional, physical, or in terms of timing: acute, episodic or chronic. Basic scientists refer to stress in terms of its effects. Stress causes an imbalance within the body and the body's efforts become focused on restoring some level of acceptable balance and function (McEwen & Wingfield, 2003). Every cell, system and organ works with the same goal resulting in preservation of the organism. When balance is not maintained, the organism may become dysfunctional or die. Chronic perceived

stress does not elicit a 'flight-or-fight' response as if running from a vicious dog; its effects occur daily and persist over time. The epinephrine released in an episodic event such as escaping from an angry, snarling dog is beneficial and short lived. The heart rate elevates and vessels constrict to improve blood flow to the heart and lungs and facilitate a quick escape. The prolonged elevations of epinephrine in response to daily stressors such as living in a high-crime neighborhood are not beneficial over time; long-term constriction of blood vessels and blood pressure elevations result in disease.

For the purposes of this dissertation, the term *stress* will refer to occurrences that result in physiological imbalance via either a physiological or psychological response as defined by McEwen and Wingfield (2003). The terms *stressful stimuli* and *stressor* will be used interchangeably with the term stress. Stress may be perceived as psychological, environmental, physical, or social. The term *perceived stress* will be used throughout this paper but is considered interchangeable with the term *psychological stress*.

**Perceived Stress as a Precursor to Disease and Health Disparity**

Perceptions of stress are influenced by a multitude of factors. Aside from culture, gender, and ethnicity, stress perceptions and responses are also influenced by previous experience, current situation, and learned behavior. Therefore, although the physiologic stress response is predictable, the *human* response is quite variable and unpredictable. The appraisal and perceptions associated with the mind-body stress response add a level of uniqueness that maintains researchers' curiosity and promotes further study. Predicting which situations a person may perceive as stressful can be difficult despite cultural, family or gender norms.

Today, perceived stress is recognized as a precursor to poor health outcomes and increased risk of disease (Juster, McEwen, & Lupien, 2010; McEwen & Wingfield, 2003). The physiological pathways described above continue to be studied and multiple research studies have demonstrated a link between perceived stress, symptom expression, and disease progression (Cohen et al., 2013; Dirik & Karanci, 2010; Hobfoll, Johnson, Ennis, & Jackson, 2003; Mujahid, Diez Roux, Cooper, Shea, & Williams, 2011; Williams, Yan, Jackson, & Anderson, 1997). Perceived stress is an antecedent to illness and individuals who endure chronic stress are more vulnerable to its effects. This increased vulnerability is now the focus of research conducted in an effort to investigate health disparities in populations where the occurrence of significantly higher disease incidence, prevalence, morbidity, or mortality is found when compared to the general population (Health, 2009; Perry, Harp, & Oser, 2013). Despite medical, technological and pharmacological advances and improved access to quality healthcare, we continue to observe health disparities related to race, ethnicity, age and gender.

**Measures of Stress**

Measurement standards established among researchers have improved the ability to compare data between studies and thus contributed to the advancement of stress research. Stress markers have been recognized within the neuroendocrine, immune, metabolic, anthropometric, cardiac and respiratory systems and, current research includes genetic markers as well. Telomere length is a genetic marker that has quickly become accepted as a measure of aging and disease risk. Telomeres are protein strands located on the ends of chromosomes. Over time, as cells replicate, telomeres shorten; telomere shortening is associated with cellular age and senescence (Epel et al., 2004; Oeseburg et

al., 2010). Since the discovery of telomerase (an enzyme that synthesizes and regulates telomere activity) by Blackburn in 1985, research has ensued to explore the factors associated with telomere length (Blackburn, 1991). Oxidative and psychological stressors have since been shown to accelerate the rate of telomere shortening; therefore telomere length has also become a marker for long-term, chronic exposure to stress.

Self-report surveys and questionnaires have also been used to measure stress. Although subjective, these stress measures provide great insight into the individual's experience and perceptions. Multiple self-report tools have been developed over time and have been used in a variety of settings and populations including college students, pregnant women, soldiers of war, and midlife women (Anderson, Melby, Sievert, & Obermeyer, 2011; Creamer, Bell, & Failla, 2003; Jackson, Rowley, & Curry Owens, 2012; Rotem, Epstein, & Ehrenfeld, 2009). The Cohen's Perceived Stress Scale (PSS), the Impact of Events Scale (IES), and the Conservation of Resources Evaluation Tool (COR-E) are several tools used in the literature worldwide (Cohen, Kamarck, & Mermelstein, 1983; Creamer et al., 2003; Hobfoll, 1989). Each measurement tool has its benefits and downfalls; however, the PSS is considered a gold standard and is the tool against which most other measures are compared. The PSS was used in this dissertation research study.

The qualifying examination papers preceding this dissertation included an extensive literature review outlining what is known of telomeres in relation to gender, race, and stress; a theoretical critique outlining relevant social and physiological stress frameworks; and a measurement paper outlining the current and most commonly used tools to measure stress. The following is an overview of the literature and theory used to

support this research dissertation. The full research proposal approved by UCSF Committee on Human Research (CHR) is included as Appendix A.

**Telomere Length and Gender**

Research reveals distinct differences in telomere length for age and gender. For example, telomere length has been found to be inversely related to biological age; a finding that indicates a relationship between telomere length and longevity (Aviv, 2002). Most studies have found women to have longer telomere lengths when compared to men of the same age (Aviv, 2002; Barrett & Richardson, 2011; Benetos et al., 2001; Cherif, Tarry, Ozanne, & Hales, 2003; Seifarth, McGowan, & Milne, 2012; Stindl, 2004; Zhu et al., 2011) with few exceptions (Harris, Martin-Ruiz, von Zglinicki, Starr, & Deary, 2012). Interestingly, telomere length does not differ between genders at birth (Barrett & Richardson, 2011; Benetos et al., 2001; Oeseburg, de Boer, van Gilst, & van der Harst, 2010; Zhu et al., 2011). Between-gender differences in telomere length emerge in adolescence. Researchers have proposed that this difference may be associated with the reproductive hormone estrogen, but this view is somewhat controversial (Barrett & Richardson, 2011; Seifarth et al., 2012; Zhu et al., 2011).

In fact, it has been found that women who receive hormone replacement have longer telomeres than do women who do not (Barrett & Richardson, 2011; Lin et al., 2011). This finding would indicate a protective effect of estrogen and may partially explain why, in comparison to men, women tend to live longer (WHO, 2012) and why, after menopause, women are at higher risk for certain diseases (Aviv, 2002; Gray et al., 2014; Seifarth et al., 2012). For example, Raymond et al. (2014) conducted a study with a large sample of women and men of African descent to investigate the effects of gender,

menopause status, and telomere length on aortic stiffness. The researchers' findings suggested that, prior to menopause, gender is not a factor in shorter telomere length or in the development of aortic stiffness. However, their findings suggested that biological age as evidenced by telomere length was associated with aortic stiffness in women (Raymond, Norton, Woodiwiss, & Brooksbank, 2014).

**Telomere Length and Race/Ethnicity**

Race is another fixed characteristic that has been associated with telomere length and longevity. Unlike gender, race-based differences in telomere length have been noted at birth and in adulthood although controversy exists (Diez Roux et al., 2009; Hunt et al., 2008; Zhu et al., 2011). Most researchers have found that African American adults have longer telomere lengths in comparison to European American adults but at least one research group found the reverse (Diez Roux et al., 2009). The differences between races are puzzling, given that in comparison with other racial groups in the United States, African Americans often have poorer health-related outcomes and shorter life spans. One hypothesis to explain this phenomenon is that, in comparison with other racial groups, African Americans experience a faster rate of telomere length shortening (Rewak et al., 2014).

The relationship between telomere length and morbidity associated with chronic conditions such as heart disease and sleep disturbance have been studied (Fitzpatrick et al., 2011; Lee et al., 2014). Anthropometric differences, lifestyle (smoking, exercise, diet), socioeconomics, and environmental elements are the contributing factors most often investigated (Diaz, Mainous, Player, & Everett, 2010; Diez Roux et al., 2009;

Kroenke et al., 2012). The controversy highlights the inter-dependency and complexity of genetics, race, gender, age, lifestyle, longevity and long-term health outcomes.

**Utilization of Telomere Length in Stress Research & Women's Health**

Animal and human research has been conducted to investigate the effect of perceived stress on acute and long-term health outcomes. Animal species demonstrate accelerated telomere shortening with social or environmental stressors and disruption of their hierarchical norms (Cherif et al., 2003; Kikusui, Winslow, & Mori, 2006; McEwen & Wingfield, 2003, 2010). People who endure trauma at an early age have also been shown to have shorter telomere length than those who do not experience childhood trauma or adversity (Drury et al., 2012; Humphreys et al., 2012; Kananen et al., 2010). In addition, telomere length has been linked to discrimination and socioeconomic status (Carroll, Diez Roux, Fitzpatrick, & Seeman, 2013; Carroll, Diez-Roux, Adler, & Seeman, 2013; Chae et al., 2014; Woo, Suen, Leung, Tang, & Ebrahim, 2009).

In general, current research supports the detrimental effects of perceived stress on telomere length, health status and general well-being (Beach, Lei, Brody, Yu, & Philibert, 2014; Epel et al., 2004; Juster et al., 2010; Prather et al., 2014; Puterman et al., 2010). Telomere length is a tangible measure of stress that has become acceptable among researchers in a variety of disciplines. Researchers in women's health have used telomere length to explain differences in health care outcomes in comparison to men and also to explore gender-specific issues (Barrett & Richardson, 2011; Groer, 2010; Raymond et al., 2014). African American women in particular have been proposed as vulnerable to the effects of perceived stress (Geronimus, 1992, 2001; Geronimus, Hicken, Keene, & Bound, 2006; Groer, 2010). Telomere research has been useful in highlighting

differences that may place African American women at a greater risk for poor health outcomes (Geronimus et al., 2006). African American women may be even more vulnerable to stress during midlife given the changes that commonly occur during this time in their life course (empty nest syndrome, caring for aging parents, employment transitions, menopause).

Social capital, education, lower socioeconomic status, adversity, and social status have all been associated with elevated stress levels and shorter telomere length (Adler et al., 2013; Drury et al., 2012; Epel et al., 2004; Kananen et al., 2010; Muennig, Cohen, Palmer, & Zhu, 2013; Woo et al., 2009). In comparison with men, women have been found to report higher levels of stress (Cohen et al., 1983), and at least one study suggests that the rate at which telomeres shorten in women may be affected by stress-reducing lifestyle practices such as meditation (Hoge et al., 2013). The significance of these findings becomes great as longevity increases; factors related to aging, health maintenance, and eliminating health disparities are relevant and warrant further study.

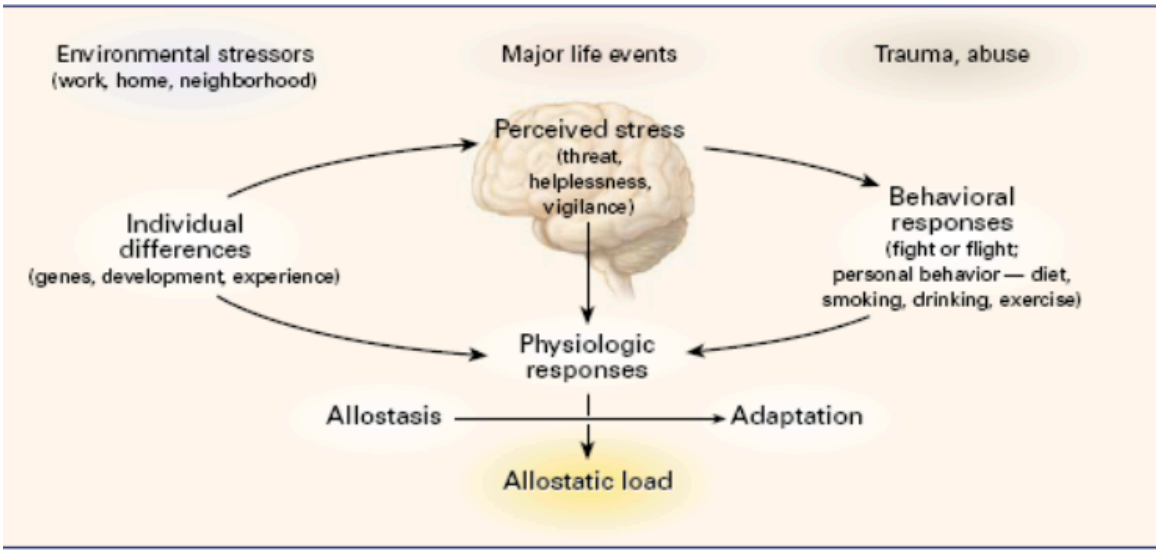
**The Theory of Allostasis**

The qualifying theory paper preceding this dissertation outlined the evolution of stress theory starting with the father of modern stress theory, Hans Selye, and his General Adaptation Syndrome' in 1936, followed by Richard Lazarus' idea of "cognitive appraisal" in the 1960's (Folkman, Lazarus, Gruen, & DeLongis, 1986; Selye, 1950). These concepts were essential to Steven Hobfoll's theory of conservation of resources and measurement tool of the same name. Dr. Hobfoll's ideas emerged in the late 1980s and created a more personal and objective view of stress using 74 resource items (Hobfoll, 1989). During this same period of time, Arline Geronimus developed a

conceptual framework that she called “weathering”. This conceptual framework focuses on the cumulative effects of socioeconomic disadvantage for African American women and utilizes the environmental and psychological aspects of stress to predict physiological outcomes and health disparity (Geronimus, 1992). Thus it is clear that stress theory has developed beyond its narrow focus of “flight-or-fight” response to encompass a broad array of societal and health issues that are of interest to persons of multiple disciplinary backgrounds.

The theory of allostasis is yet one more step towards the advancement and modernization of stress research. Developed by Sterling and Eyer in 1988, the theory of allostasis is based on the concepts of allostasis, allostatic load, and allostatic overload (Groer, 2010). These concepts in the framework present health as a state of physiological balance that can be upset by stress, resulting in illness (refer to Figure 1). *Allostasis* refers to the process of maintaining stability within the body and focuses on the changes necessary to adapt to environmental demands and stressors (Juster et al., 2010; McEwen & Wingfield, 2010). *Allostatic load* refers to cumulative stress. The concept of allostatic load is key to understanding allostasis because it helps to explain how chronic stress can lead to *allostatic overload*, disease, and senescence (Groer, 2010).

Figure 1. The allostatic load model (Juster et al., 2009).




Perceived stress is central to the theory of allostasis and has been shown to trigger stress hormones and other physiological stress responses. Often, these stress responses are measured using biomarkers (for example: cortisol, noradrenalin, cholesterol, glycosylated hemoglobin) and can be quantified into an *allostatic score*. The allostatic score provides an objective measurement of the allostatic load, allowing us to compare the effects of chronic stress (refer to Table1). Recent advances in aging, oncological, and cardiovascular research have been based on the theoretical framework of allostasis using allostatic scores. The integration of telomere length measurement into stress research provides yet another level of objectivity to a phenomenon that is generally considered subjective.

This dissertation research study is grounded in the theory of allostasis and its framework. The theory of allostasis will be used to investigate the hypothesis that high levels of perceived stress in African American midlife women can contribute to health disparity and differences in perceived health status in comparison to European American women of similar age, background, and perceived stress levels. Chapters 2 and 3 of this dissertation will describe clinical and demographic characteristics of a sample of midlife African American and European American women who were previously followed for up to 5 years as part of a UCSF Midlife Women's Health Study and were re-contacted for participation in this dissertation research. Descriptive statistics were used to analyze the differences in bladder and sleep symptoms experienced by these women. These two prevalent clinical symptoms are typically associated with women and aging. These symptoms have also been associated with lower perceived health status and lower quality of life in the literature, therefore allowing a more in depth understanding of the health status of this sample of women (Coyne et al., 2013; Coyne et al., 2014; Holm-Larsen, 2014; Kupelian et al., 2012; Tang et al., 2014; Zammit et al., 2010).

Chapter 4 is a qualitative analysis that explores the unique stressors experienced before and after menopause by 15 African American women from this cohort. Using conceptual analysis, themes and concepts will be identified from the women's written responses to open-ended questions. At least one study has identified race-based differences in perceived stress (Vines, Ta, Esserman, & Baird, 2009) and it is important for this research to establish a deeper understanding of the participants.

Chapter 5 follows and will focus on the differences in perceived stress and telomere length within this entire sample of midlife women. In addition to telomere

length, the PSS-10 and physiological biomarkers will be will be used to illustrate the effect of chronic perceived stress and the association with current perceived health status. Each chapter is written to convey the story of these women in relation to their stress levels (allostatic load) across midlife and its effects on their lives. Finally, chapter 6 will summarize the findings, discuss the relevance of the dissertation research, and propose opportunities for future research.

Table 1. Primary mediators, secondary outcomes, and tertiary outcomes in allostasis theory (McEwen & Seeman, 2009).

| PRIMARY MEDIATORS | SECONDARY OUTCOMES | TERTIARY OUTCOMES |
|---|---|---|
| Chemical messengers that are released as a part of allostasis | Integrated processes that reflect the cumulative outcome from primary effects in a tissue/organ specific manner in response to primary mediators | The actual diseases or disorders that result from allostatic load; predicted from the extreme values for secondary outcomes and the primary mediators |
| Cortisol<br>Noradrenalin<br>Epinephrine<br>DHEA | Waist-hip ratio<br>Blood pressure<br>Glycosylated hemoglobin<br>Cholesterol/HDL ratio<br>HDL cholesterol<br>Common cold | Cardiovascular disease<br>Decreased physical capacity<br>Severe cognitive decline<br>Cancer<br>Telomere length<br>Telomerase activity |

**References**


Adler, N., Pantell, M. S., O'Donovan, A., Blackburn, E., Cawthon, R., Koster, A., . . . Epel, E. (2013). Educational attainment and late life telomere length in the Health, Aging and Body Composition Study. *Brain Behav Immun, 27*(1), 15-21. doi: 10.1016/j.bbi.2012.08.014

Anderson, D., Melby, M. K., Sievert, L. L., & Obermeyer, C. M. (2011). Methods used in cross-cultural comparisons of psychological symptoms and their determinants. *Maturitas, 70*(2), 120-126. doi: 10.1016/j.maturitas.2011.07.014

Aviv, A. (2002). Telomeres, sex, reactive oxygen species, and human cardiovascular aging. *J Mol Med (Berl), 80*(11), 689-695. doi: 10.1007/s00109-002-0377-8

Barrett, E. L., & Richardson, D. S. (2011). Sex differences in telomeres and lifespan. *Aging Cell, 10*(6), 913-921. doi: 10.1111/j.1474-9726.2011.00741.x

Beach, S. R., Lei, M. K., Brody, G. H., Yu, T., & Philibert, R. A. (2014). Nonsupportive parenting affects telomere length in young adulthood among African Americans: Mediation through substance use. *J Fam Psychol, 28*(6), 967-972. doi: 10.1037/fam0000039

Benetos, A., Okuda, K., Lajemi, M., Kimura, M., Thomas, F., Skurnick, J., . . . Aviv, A. (2001). Telomere length as an indicator of biological aging: the gender effect and relation with pulse pressure and pulse wave velocity. *Hypertension, 37*(2 Pt 2), 381-385.

Blackburn, E. H. (1991). Structure and function of telomeres. *Nature, 350*(6319), 569-573. doi: 10.1038/350569a0

Carroll, J. E., Diez Roux, A. V., Fitzpatrick, A. L., & Seeman, T. (2013). Low social support is associated with shorter leukocyte telomere length in late life: multi-ethnic study of atherosclerosis. *Psychosom Med, 75*(2), 171-177. doi: 10.1097/PSY.0b013e31828233bf

Carroll, J. E., Diez-Roux, A. V., Adler, N. E., & Seeman, T. E. (2013). Socioeconomic factors and leukocyte telomere length in a multi-ethnic sample: findings from the multi-ethnic study of atherosclerosis (MESA). *Brain Behav Immun, 28*, 108-114. doi: 10.1016/j.bbi.2012.10.024

Chae, D. H., Nuru-Jeter, A. M., Adler, N. E., Brody, G. H., Lin, J., Blackburn, E. H., & Epel, E. S. (2014). Discrimination, racial bias, and telomere length in african-american men. *Am J Prev Med, 46*(2), 103-111. doi: 10.1016/j.amepre.2013.10.020

Cherif, H., Tarry, J. L., Ozanne, S. E., & Hales, C. N. (2003). Ageing and telomeres: a study into organ- and gender-specific telomere shortening. *Nucleic Acids Res, 31*(5), 1576-1583.

Cohen, S., Janicki-Deverts, D., Turner, R. B., Marsland, A. L., Casselbrant, M. L., Li-Korotky, H. S., . . . Doyle, W. J. (2013). Childhood socioeconomic status, telomere length, and susceptibility to upper respiratory infection. *Brain Behav Immun, 34*, 31-38. doi: 10.1016/j.bbi.2013.06.009

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *J Health Soc Behav, 24*(4), 385-396.

Coyne, K. S., Sexton, C. C., Bell, J. A., Thompson, C. L., Dmochowski, R., Bavendam, T., . . . Quentin Clemens, J. (2013). The prevalence of lower urinary tract

symptoms (LUTS) and overactive bladder (OAB) by racial/ethnic group and age: results from OAB-POLL. *Neurourol Urodyn, 32*(3), 230-237. doi: 10.1002/nau.22295
Coyne, K. S., Wein, A., Nicholson, S., Kvasz, M., Chen, C. I., & Milsom, I. (2014). Economic burden of urgency urinary incontinence in the United States: a systematic review. *J Manag Care Pharm, 20*(2), 130-140.
Creamer, M., Bell, R., & Failla, S. (2003). Psychometric properties of the Impact of Event Scale - Revised. *Behav Res Ther, 41*(12), 1489-1496.
Diaz, V. A., Mainous, A. G., Player, M. S., & Everett, C. J. (2010). Telomere length and adiposity in a racially diverse sample. *Int J Obes (Lond), 34*(2), 261-265. doi: 10.1038/ijo.2009.198
Diez Roux, A. V., Ranjit, N., Jenny, N. S., Shea, S., Cushman, M., Fitzpatrick, A., & Seeman, T. (2009). Race/ethnicity and telomere length in the Multi-Ethnic Study of Atherosclerosis. *Aging Cell, 8*(3), 251-257. doi: 10.1111/j.1474-9726.2009.00470.x
Dirik, G., & Karanci, A. N. (2010). Psychological distress in rheumatoid arthritis patients: an evaluation within the conservation of resources theory. *Psychol Health, 25*(5), 617-632. doi: 10.1080/08870440902721818
Drury, S. S., Theall, K., Gleason, M. M., Smyke, A. T., De Vivo, I., Wong, J. Y., . . . Nelson, C. A. (2012). Telomere length and early severe social deprivation: linking early adversity and cellular aging. *Mol Psychiatry, 17*(7), 719-727. doi: 10.1038/mp.2011.53
Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proc Natl Acad Sci U S A, 101*(49), 17312-17315. doi: 10.1073/pnas.0407162101
Fitzpatrick, A. L., Kronmal, R. A., Kimura, M., Gardner, J. P., Psaty, B. M., Jenny, N. S., . . . Aviv, A. (2011). Leukocyte telomere length and mortality in the Cardiovascular Health Study. *J Gerontol A Biol Sci Med Sci, 66*(4), 421-429. doi: 10.1093/gerona/glq224
Folkman, S., Lazarus, R. S., Gruen, R. J., & DeLongis, A. (1986). Appraisal, coping, health status, and psychological symptoms. *J Pers Soc Psychol, 50*(3), 571-579.
Geronimus, A. T. (1992). The weathering hypothesis and the health of African-American women and infants: evidence and speculations. *Ethn Dis, 2*(3), 207-221.
Geronimus, A. T. (2001). Understanding and eliminating racial inequalities in women's health in the United States: the role of the weathering conceptual framework. *J Am Med Womens Assoc, 56*(4), 133-136, 149-150.
Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health, 96*(5), 826-833. doi: 10.2105/ajph.2004.060749
Gray, K. E., Schiff, M. A., Fitzpatrick, A. L., Kimura, M., Aviv, A., & Starr, J. R. (2014). Leukocyte telomere length and age at menopause. *Epidemiology, 25*(1), 139-146. doi: 10.1097/ede.0000000000000017
Groer, M. T. W. s. H. R. G. a. t. U. o. S. F. C. o. N. (2010). Allostasis: A Model For Women's Health *The Psychoneuroimmunology of Chronic Disease*. Washington, DC: Amerian Psychological Association.

Harris, S. E., Martin-Ruiz, C., von Zglinicki, T., Starr, J. M., & Deary, I. J. (2012). Telomere length and aging biomarkers in 70-year-olds: the Lothian Birth Cohort 1936. *Neurobiol Aging, 33*(7), 1486 e1483-1488. doi: 10.1016/j.neurobiolaging.2010.11.013

Health, N. I. o. (2009). *NIH health disparities strategic plan and budget years 2009-2013*. Washington DC.

Hobfoll, S. E. (1989). Conservation of resources. A new attempt at conceptualizing stress. *Am Psychol, 44*(3), 513-524.

Hobfoll, S. E., Johnson, R. J., Ennis, N., & Jackson, A. P. (2003). Resource loss, resource gain, and emotional outcomes among inner city women. *J Pers Soc Psychol, 84*(3), 632-643.

Hoge, E. A., Chen, M. M., Orr, E., Metcalf, C. A., Fischer, L. E., Pollack, M. H., . . . Simon, N. M. (2013). Loving-Kindness Meditation practice associated with longer telomeres in women. *Brain Behav Immun, 32*, 159-163. doi: 10.1016/j.bbi.2013.04.005

Holm-Larsen, T. (2014). The economic impact of nocturia. *Neurourol Urodyn, 33 Suppl 1*, S10-14. doi: 10.1002/nau.22593

Humphreys, J., Epel, E. S., Cooper, B. A., Lin, J., Blackburn, E. H., & Lee, K. A. (2012). Telomere shortening in formerly abused and never abused women. *Biol Res Nurs, 14*(2), 115-123. doi: 10.1177/1099800411398479

Hunt, S. C., Chen, W., Gardner, J. P., Kimura, M., Srinivasan, S. R., Eckfeldt, J. H., . . . Aviv, A. (2008). Leukocyte telomeres are longer in African Americans than in whites: the National Heart, Lung, and Blood Institute Family Heart Study and the Bogalusa Heart Study. *Aging Cell, 7*(4), 451-458. doi: 10.1111/j.1474-9726.2008.00397.x

Jackson, F. M., Rowley, D. L., & Curry Owens, T. (2012). Contextualized stress, global stress, and depression in well-educated, pregnant, African-American women. *Womens Health Issues, 22*(3), e329-336. doi: 10.1016/j.whi.2012.01.003

Juster, R. P., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. [Review]. *Neurosci Biobehav Rev, 35*(1), 2-16. doi: 10.1016/j.neubiorev.2009.10.002

Kananen, L., Surakka, I., Pirkola, S., Suvisaari, J., Lonnqvist, J., Peltonen, L., . . . Hovatta, I. (2010). Childhood adversities are associated with shorter telomere length at adult age both in individuals with an anxiety disorder and controls. *PLoS One, 5*(5), e10826. doi: 10.1371/journal.pone.0010826

Kikusui, T., Winslow, J. T., & Mori, Y. (2006). Social buffering: relief from stress and anxiety. *Philos Trans R Soc Lond B Biol Sci, 361*(1476), 2215-2228. doi: 10.1098/rstb.2006.1941

Kroenke, C. H., Pletcher, M. J., Lin, J., Blackburn, E., Adler, N., Matthews, K., & Epel, E. (2012). Telomerase, telomere length, and coronary artery calcium in black and white men in the CARDIA study. *Atherosclerosis, 220*(2), 506-512. doi: 10.1016/j.atherosclerosis.2011.10.041

Kupelian, V., Wei, J. T., O'Leary, M. P., Norgaard, J. P., Rosen, R. C., & McKinlay, J. B. (2012). Nocturia and quality of life: results from the Boston area community health survey. *Eur Urol, 61*(1), 78-84. doi: 10.1016/j.eururo.2011.05.065

Lazarus, R. S., & Folkman, S. (1984). *Stress, Appraisal, and Coping*. New York, NY: Springer Publishing Company.
Lee, K. A., Gay, C., Humphreys, J., Portillo, C. J., Pullinger, C. R., & Aouizerat, B. E. (2014). Telomere length is associated with sleep duration but not sleep quality in adults with human immunodeficiency virus. *Sleep, 37*(1), 157-166. doi: 10.5665/sleep.3328
Lin, J., Kroenke, C. H., Epel, E., Kenna, H. A., Wolkowitz, O. M., Blackburn, E., & Rasgon, N. L. (2011). Greater endogenous estrogen exposure is associated with longer telomeres in postmenopausal women at risk for cognitive decline. *Brain Res, 1379*, 224-231. doi: 10.1016/j.brainres.2010.10.033
McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. [Article]. *Hormones and Behavior, 43*(1), 2-15. doi: 10.1016/s0018-506x(02)00024-7
McEwen, B. S., & Wingfield, J. C. (2010). What is in a name? Integrating homeostasis, allostasis and stress. *Horm Behav, 57*(2), 105-111. doi: 10.1016/j.yhbeh.2009.09.011
Muennig, P., Cohen, A. K., Palmer, A., & Zhu, W. (2013). The relationship between five different measures of structural social capital, medical examination outcomes, and mortality. *Soc Sci Med, 85*, 18-26. doi: 10.1016/j.socscimed.2013.02.007
Mujahid, M. S., Diez Roux, A. V., Cooper, R. C., Shea, S., & Williams, D. R. (2011). Neighborhood stressors and race/ethnic differences in hypertension prevalence (the Multi-Ethnic Study of Atherosclerosis). *Am J Hypertens, 24*(2), 187-193. doi: 10.1038/ajh.2010.200
Oeseburg, H., de Boer, R. A., van Gilst, W. H., & van der Harst, P. (2010). Telomere biology in healthy aging and disease. [Research Support, Non-U.S. Gov't
Review]. *Pflugers Arch, 459*(2), 259-268. doi: 10.1007/s00424-009-0728-1
Perry, B. L., Harp, K. L., & Oser, C. B. (2013). Racial and Gender Discrimination in the Stress Process: Implications for African American Women's Health and Well-Being. *Sociol Perspect, 56*(1), 25-48.
Prather, A. A., Gurfein, B., Moran, P., Daubenmier, J., Acree, M., Bacchetti, P., . . . Epel, E. S. (2014). Tired telomeres: Poor global sleep quality, perceived stress, and telomere length in immune cell subsets in obese men and women. *Brain Behav Immun*. doi: 10.1016/j.bbi.2014.12.011
Puterman, E., Lin, J., Blackburn, E., O'Donovan, A., Adler, N., & Epel, E. (2010). The power of exercise: buffering the effect of chronic stress on telomere length. *PLoS One, 5*(5), e10837. doi: 10.1371/journal.pone.0010837
Raymond, A. R., Norton, G. R., Woodiwiss, A. J., & Brooksbank, R. L. (2014). Impact of Gender and Menopausal Status on Relationships Between Biological Aging, as Indexed by Telomere Length, and Aortic Stiffness. *Am J Hypertens*. doi: 10.1093/ajh/hpu212
Rewak, M., Buka, S., Prescott, J., De Vivo, I., Loucks, E. B., Kawachi, I., . . . Kubzansky, L. D. (2014). Race-related health disparities and biological aging: does rate of telomere shortening differ across blacks and whites? *Biol Psychol, 99*, 92-99. doi: 10.1016/j.biopsycho.2014.03.007

Rotem, M., Epstein, L., & Ehrenfeld, M. (2009). Does the conservation of resources motivate middle-aged women to perform physical activity? *West J Nurs Res, 31*(8), 999-1013. doi: 10.1177/0193945909340909

Seifarth, J. E., McGowan, C. L., & Milne, K. J. (2012). Sex and life expectancy. *Gend Med, 9*(6), 390-401. doi: 10.1016/j.genm.2012.10.001

Selye, H. (1950). Stress and teh general adaptation syndrome. *British Medical Journal*, 1383-1392.

Steptoe, A., & Kivimaki, M. (2012). Stress and cardiovascular disease. [Research Support, Non-U.S. Gov't

Review]. *Nat Rev Cardiol, 9*(6), 360-370. doi: 10.1038/nrcardio.2012.45

Stindl, R. (2004). Tying it all together: telomeres, sexual size dimorphism and the gender gap in life expectancy. *Med Hypotheses, 62*(1), 151-154.

Tang, D. H., Colayco, D. C., Khalaf, K. M., Piercy, J., Patel, V., Globe, D., & Ginsberg, D. (2014). Impact of urinary incontinence on healthcare resource utilization, health-related quality of life and productivity in patients with overactive bladder. *BJU Int, 113*(3), 484-491. doi: 10.1111/bju.12505

Vines, A. I., Ta, M., Esserman, D., & Baird, D. D. (2009). A comparison of the occurrence and perceived stress of major life events in black and white women. *Women Health, 49*(5), 368-380. doi: 10.1080/03630240903238743

WHO. (2012). Global Health Observatory Data Repository, 2014, from http://apps.who.int/gho/data/node.main.688

Williams, D. R., Yan, Y., Jackson, J. S., & Anderson, N. B. (1997). Racial Differences in Physical and Mental Health: Socio-economic Status, Stress and Discrimination. *J Health Psychol, 2*(3), 335-351. doi: 10.1177/135910539700200305

Woo, J., Suen, E. W., Leung, J. C., Tang, N. L., & Ebrahim, S. (2009). Older men with higher self-rated socioeconomic status have shorter telomeres. *Age Ageing, 38*(5), 553-558. doi: 10.1093/ageing/afp098

Zammit, G. K., Joish, V. N., Kong, M. C., Balkrishnan, R., Lerner, D., & Rosekind, M. (2010). Impact of nighttime awakenings on worker productivity and performance. *J Occup Environ Med, 52*(5), 513-518. doi: 10.1097/JOM.0b013e3181d8db23

Zhu, H., Wang, X., Gutin, B., Davis, C. L., Keeton, D., Thomas, J., . . . Dong, Y. (2011). Leukocyte telomere length in healthy Caucasian and African-American adolescents: relationships with race, sex, adiposity, adipokines, and physical activity. *J Pediatr, 158*(2), 215-220. doi: 10.1016/j.jpeds.2010.08.007

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Chapter 2

# Bladder Symptoms in the Early Menopausal Transition

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**Abstract**

*Purpose:* Bladder symptoms are common in women and result in use of healthcare resources and poor quality of life. Bladder symptoms have been linked to age and menopause, but controversy exists in the literature. This paper examines factors associated with bladder symptoms in late pre-menopausal and peri-menopausal women.

*Methods:* We analyzed data from a prospective cohort study of midlife women (mean age 48, range 44- 54 years) in northern California. The sample consisted of 158 late pre-menopausal and peri-menopausal women with complete data on bladder symptoms. Assessments included: anthropometrics, menstrual cycle lengths and symptoms, urine samples for follicular stimulating hormone level, and self-reported health perception and depressive symptoms. Analyses included descriptive statistics, group comparisons, and linear regression.

*Results:* The most common bladder symptoms were nocturia (72%) and urinary incontinence (50%). Incontinence was less prevalent in African American women compared to European Americans and Latinas ($p$=0.001) and more prevalent in late pre-menopausal than in peri-menopause ($p$=0.017). Compared to peri-menopausal women, women in late pre-menopause stage had more daytime urinary frequency (p=0.020) and nocturia ($p$=0.046). Higher BMI ($p$<0.001) also contributed to the variance in nighttime urinary frequency after controlling for age, race, and menopause status.

*Conclusion:* Bladder symptoms were associated with menopause stage, not chronological age. Women in late pre-menopause experienced more urinary frequency and incontinence compared to peri-menopausal women. The higher prevalence of nocturia in late stage pre-menopausal women is unclear and warrants further study.

*Keywords:* bladder symptoms, pre-menopause, peri-menopause, urinary frequency, nocturia, urinary incontinence, menopause stage, age, ethnicity, BMI

## Introduction

Over half of women will experience bladder symptoms at some time over the course of their lives, and bladder problems are common for women regardless of age or menopause status (Cardozo & Robinson, 2002; Lin, Ng, Chen, Hu, & Chen, 2005). Bladder symptoms such as incontinence, urgency, or frequency are commonly associated with a lower quality of life and increased use of healthcare resources (Coyne, Sexton, et al., 2013; Coyne et al., 2014; Holm-Larsen, 2014; Kupelian et al., 2012; Tang et al., 2014). Bladder symptoms may be due to age-related autonomic denervation, decreased bladder muscle tone or increased bladder muscle fatigue (Chen, Chen, Hu, Lin, & Lin, 2003). Parity and medical conditions such as diabetes, obesity, and depression are associated with prevalence and incidence of bladder symptoms (Gopal et al., 2008; Hsu et al., 2015; Link, Steers, Kusek, & McKinlay, 2011; Maserejian et al., 2014; Rortveit, Hannestad, Daltveit, & Hunskaar, 2001; Weiss, 2012). Racial and gender differences in bladder symptoms, specifically symptoms of overactive bladder such as incontinence or urgency have also been reported (Coyne, Margolis, Kopp, & Kaplan, 2012; Coyne, Sexton, et al., 2013; Hsu et al., 2015).

The menopause transition is also associated with increased urinary complaints linked to the drastic reduction in endogenous estrogens, yet the literature remains unclear as to whether age or menopause stage has a greater effect on bladder symptoms (Chen et al., 2003; Lin et al., 2005; Mac Bride, Rhodes, & Shuster, 2010; Portman & Gass, 2014; Robinson, Toozs-Hobson, & Cardozo, 2013). Many of these factors are interrelated and may depend on inherent personal characteristics, health conditions, or life-style situations. Therefore, the purpose of this paper is to describe factors associated with

bladder symptoms in late stage pre-menopausal and peri-menopausal women. Data from a San Francisco cohort of midlife women is used to describe the experience of bladder and urinary symptoms by age, menopause stage and ethnicity.

Based on the Symptom Management Theory (SMT), we hypothesized that age, menopause stage, race/ethnicity, and childbirth history would account for significant variance in the frequency and severity of bladder symptoms for midlife women. SMT has is based on three central concepts: symptom experience, symptom management strategies, and symptom status outcomes (Humphreys et al., 2014). Symptom experience is central to the theory and SMT recognizes the importance of person, environment, and situation in treating and managing symptoms (Humphreys et al., 2014). SMT proposes consideration of multiple factors for essential evaluation of symptoms, effective intervention, and improved symptom outcomes.

## Methods

### Design and Participants

This cross-sectional research was conducted within a prospective cohort study of midlife women in the San Francisco Bay Area who participated in the University of California San Francisco (UCSF) Midlife Women's Health Study. Persons between the ages of 40 to 60 are generally considered to be in midlife. Eligible participants were community-dwelling women between 40 and 50 years of age who reported still experiencing regular menstrual periods and denied using hormone replacement therapy in the past 12 months. Women who self-identified as having major health problems or who were taking hormone therapy at initiation of the study were excluded (Choi, Guiterrez, Gilliss, & Lee, 2012). The parent cohort study was conducted over 7 years with

assessments every 6 months through one year post-hysterectomy, one-year post-initiating hormone therapy, or one year after the last menstrual period (Gilliss et al., 2001). Assessments of bladder symptoms were added to the last three years of the study (years 5-7).

At baseline, there were 347 women in the study and attrition during the first two years was less than 10%. This sub-study of bladder symptoms is focused on the 158 participants who provided complete data for bladder symptoms. Details of recruitment and protocol were previously reported (Choi et al., 2012; Gilliss et al., 2001). The UCSF Committee on Human Research (CHR) approved the parent study and all participants provided informed consent prior to data collection.

Measures

Bladder symptoms such as day and nighttime urinary frequency, urinary incontinence, and urinary tract infections were assessed using self-report questionnaire measures adapted from other epidemiologic women's health studies focusing on urinary tract function (Bradley et al., 2011; Fitzgerald et al., 2006; Hannestad, Rortveit, Sandvik, & Hunskaar, 2000; Sandvik et al., 1995). Specifically, daytime and nighttime urinary frequency were assessed by asking women to report the number of times per day and the number of times per night that they urinated, on average, in the past week. Women were considered to have nocturia if they reported awakening at least once per night on average to void (Abrams et al., 2002).

Urinary incontinence was assessed by asking the women if they had leaked even a small amount of urine in the past 6 months, with responses ranged from none to every day. Women were considered to have clinically significant urinary incontinence if they

reported leakage occurring at least once per week on average therefore, the urinary incontinence variable was dichotomized (0 = less than once per week, 1= greater than once per week or daily) for accurate categorical representation. Those who reported incontinence were asked to identify whether their incontinence was related to activity (cough, sneeze, lifting), to a sudden urge to urinate but inability to get to the bathroom soon enough, or some other reason. Urinary tract infection was assessed using the question: "How many times have you been told that you had a urinary tract infection in the past 6 months?"

Other participant characteristics assessed by self-report included age, race/ethnicity (African American, Latina, or European American), education (ranging less than high school equivalent to college graduate), income (ranging less than $31,000 to over $81,000), perceived health status (rated from 1= excellent to 5 = poor) and parity (number of live births). Current use of diuretic medications was assessed with a yes or no response.

As part of the parent study, women underwent measurement of urine for assaying follicular stimulating hormone (FSH), measurement of weight and height to calculate body mass index (BMI), and measurement of waist and hip circumferences to determine waist-to-hip ratio (WHR). Menopause status was coded as either 'pre-menopause' or 'peri-menopause' using a combination of menstrual regularity, vasomotor symptoms, and FSH trends based on STRAW (Stages of Reproductive Aging Workshop) criteria that provide a comprehensive characterization of hormonal and physiological changes associated with menopause stages in order to standardize clinical and research nomenclature (Harlow et al., 2012) (refer to Figure 1). The determination of reproductive

stage and the criteria used was previously documented for this sample of women (Nosek et al., 2010).

Depressive symptoms were assessed using the 20-item Center for Epidemiologic Studies Depression (CES-D) Scale that asks participants to self-rate 20 symptoms on frequency of occurrence from 0 (not during the past week) to 3 (5-7 days in the past week). Scores range from 0-60 and scores of 16 or higher indicate risk for clinical depression and need for clinical follow up. The items were internally consistent in this sample (Cronbach alpha coefficient = 0.92).

[Figure 1. about here]

**Statistical Analysis**

Descriptive statistics were used to describe demographic and bladder characteristics by race/ethnicity and by menopause stage. Pearson correlation coefficients (*r*) or Spearman's *rho* were used to examine relationships between continuous variables and Chi square to evaluate categorical associations. Independent t-tests and analysis of variance (ANOVA) were conducted to evaluate mean differences in characteristics between racial/ethnic and menopausal stage groups. A linear regression model was used to evaluate independent associations between participant characteristics and nocturia, focusing on characteristics reported in the literature to have the potential to influence bladder symptoms: age, race/ethnicity, income, menopausal status, BMI, depressive symptoms, parity, medication usage, urinary incontinence, major illness, and perceived general health status. Finally, a logistic regression was used to evaluate the impact of the

same variables on incontinence. All analyses were performed using SPSS version 22.0 software.

**Results**

Demographic and Clinical Characteristics

The mean age (± SD) of the 158 participants was 48.1 (± 2.2) years, with 72 being pre-menopausal and 86 peri-menopausal. Over 60% of the women evaluated their health as 'very good' or 'excellent'. Approximately 8% reported having had a urinary tract infection (UTI) in the past 6 months and there was no significant difference by menopausal stage or race/ethnicity. As seen in Table 1, only 6% (n=10) of the women reported taking a diuretic, and the rate was significantly higher in African American women ($\chi^2 = 13.7$, $p = .001$).

[Table 1. About here]

Bladder Symptoms by Race/Ethnicity and Other Socio-demographic Characteristics

The most prevalent bladder symptom (73.2%) was nocturia reported at least once per night by participants in this sample. Frequency of nocturia was associated with BMI (*rho* = 0.293, $p < .001$) and diuretic use (*rho* = 0.166, $p = .039$). The African American group had a higher frequency of nocturia, but this difference was not statistically significant and there was no race/ethnic difference in the prevalence of nocturia.

There was a significant difference in daytime urinary frequency between the three race/ethnicity groups ($p = 0.001$), with European American women reporting the highest daytime frequency (Table 2). Daytime urinary frequency was not significantly associated

with age, BMI, parity, depressive symptoms, or diuretic use. Only 42 (26.8%) women reported no nocturia in the past week.

Urinary incontinence was the second most common bladder symptom with 50% reporting that they had incontinence one or more times per month. Urinary incontinence was unrelated to age, BMI, parity, depressive symptoms, or diuretic use. This bladder symptom was significantly associated with race/ethnicity ($\chi^2 = 12.87$, $p = 0.001$); only 27% of African American women reported incontinence compared to 61% of European Americans and 56% of Latinas. Of the 78 participants who reported urinary incontinence, 42% reported urgency incontinence and 75% reported leakage related to activity (stress incontinence).

[Table 2. About here]

Bladder symptoms by menopausal stage

Nocturia, UTI, diuretics, and hormone use were not significantly associated with menopause stage. Peri-menopausal women had a higher BMI (29.50 ± 7.17) compared to women who were late pre-menopausal (28.18 ± 7.45). Menopause stage was associated with experiencing daytime urinary frequency ($t = 2.61$, $p = 0.010$); late pre-menopausal women were more likely to report both daytime and nighttime frequency in comparison to peri-menopausal women. Late pre-menopausal women were also significantly more likely to report urinary incontinence ($t = 2.28$, $p = 0.024$), although differences between types of incontinence (urgency or stress) were not significant.

[Table 3. About here]

Linear Regression

Given the high prevalence of nocturia and urinary incontinence within this sample, linear regression analyses were used to examine potential factors and interactions that could account for these two bladder symptoms. Variables in the models included: age, race (dummy coded), income, education, depressive symptoms, diuretic use, perceived general health status, major health problem in the past year, number of live births, menopausal stage, and BMI. As seen in Table 4, the model for nocturia was significant ($R^2 = .274$, $p = .002$). While controlling for age, income, education, parity, depressive symptoms, health status, and diuretic use, BMI ($p<0,001$) and premenopausal stage ($p=0.002$) had significant contributions to the overall model. Parity and income approached significance ($p = 0.065$ and 0.066 respectively).

[Table 4. About here]

As seen in Table 5, the model for frequency of urinary incontinence was not significant. However, being of African American race was a significant contributor to the model. The African American women in the sample were less likely to report symptoms of incontinence even after controlling for diuretic use and BMI as well as age, income, education, parity, depressive symptoms, and health status.

[Table 5. About here]

**Discussion**

In describing the bladder symptom experience for this female cohort of midlife women, we were able to show that the two most prevalent bladder symptoms were nocturia and urinary incontinence. Due to the prevalence of these bladder symptoms, it is reasonable to conclude that these women will continue to experience symptoms to some extent in the post-menopause reproductive stage (Blumel et al., 2012; Cardozo & Robinson, 2002; Chen et al., 2003; Hannestad et al., 2000). Although this sample of women was healthy when originally recruited, it is possible that developing medical conditions may have contributed to the bladder symptoms.

Rather than parity or age, BMI was the most significant contributor to variance in experiencing nocturia. This finding was not surprising, as obesity and weight gain have been identified as risk factors in bladder symptom occurrence (Chen et al., 2003; Coyne, Wein, et al., 2013). In addition, BMI has also been shown to influence menopause status and menopause stage was a significant contributor in the regression model (Santoro & Chervenak, 2004; Santoro et al., 2004; Thurston, Santoro, & Matthews, 2011).

Although we hypothesized that menopause stage would be a factor in bladder symptoms, it was surprising that women in the late pre-menopause stage reported a greater occurrence of nocturia, daytime urination, and urinary incontinence when compared to women of the same age who were in the peri-menopausal stage. The reasons for higher prevalence of bladder-related symptoms in the late pre-menopausal stage remain unclear, as current literature would suggest that bladder symptoms are more strongly associated with older age or peri-menopause stage.

Our findings support the hypothesis that menopause stage would account for significant variance in bladder symptoms, specifically frequency of nocturia and incontinence. Age, and parity were not significant factors and therefore not consistent with our hypothesis. Parity neared significance while controlling for other variables and parity has been associated with increased risk of bladder symptoms in the literature (Handa, Pierce, Munoz, & Blomquist, 2014; Palma et al., 2013). Race was the only significant contributor to the regression model for experience of incontinence, but the overall model was not significant with all 12 variables in the model. There is a paucity of literature to support this finding and the clinical significance is unclear (Fultz, Herzog, Raghunathan, Wallace, & Diokno, 1999; Townsend, Curhan, Resnick, & Grodstein, 2011). However, the model is reflective of the noted significant clinical differences within our sample.

Income neared significance in our model for nocturia and often serves as a proxy for socioeconomic status. The relevance of this variable is unclear but may reflect differences in health care access or risk of co-morbid conditions associated with bladder symptom occurrence.

Age was not a significant contributor in the prevalence of nocturia for these women, nor was it correlated with daytime urinary frequency or incontinence. However, there was a very narrow age range and little variance in age across the sample. The similarity in chronological age proved fortuitous as it allowed us to see the profound effect of biological age (menopause stage) rather than chronological age. Biological age is highly variable, and can be influenced by multiple factors such as genetics, health status, race and environmental stressors.

Using Symptom Management Theory as a foundation for this analysis, we explored multiple salient factors associated with bladder and urinary symptoms. These factors should be considered in developing and testing interventions to manage the bladder symptom experience and improve quality of life for women in any reproductive stage. Symptom management outcomes will be determined by our ability to further deconstruct the bladder symptom problems for the individual woman and tailor appropriate interventions.

**Study Limitations**

Our study design has several limitations that may influence the conclusions. Given the sample size and demographics of the sample, findings cannot be generalized to all midlife women. Data used for this secondary analysis were collected in Phase II of the original study and some participants were already excluded after 12 consecutive months of no menstrual periods, 12 months of hormone replacement therapy, or hysterectomy. Thus, our results are limited to only late pre- and peri-menopausal women. Demographic and health data were collected every 6 months over time (Phase 1, Times 1-7 and Phase II, Times 8-11), but the bladder symptom questionnaire was included only in Phase II (Times 8-11). Bladder symptom data over a longer time frame and earlier in the pre-menopausal Phase I time points may have enhanced this analysis by providing insight into the onset and timing of symptoms in conjunction with the onset and timing of transitions in menopause stage.

**Conclusions/Recommendations**

Women are at risk of bladder symptoms due to natural aging and menopause. Bladder symptoms, such as nocturia and urinary incontinence are associated with

significant morbidity and lower quality of life. BMI and late pre-menopause status were the most significant factors associated with the experience of nighttime urination in our sample of midlife women. Further research is needed to determine why late pre-menopausal women may experience more bladder symptoms than peri-menopausal women, and how menopause status may impact the severity and progression of bladder symptoms. While differences between pre- and post-menopausal symptoms have been more extensively researched, differences in symptom experiences for late pre- and early peri-menopausal stages are less clear. In addition, it is unclear why the African American subsample, with higher BMI and more prevalent diuretic use, experienced less incontinence in comparison to the European American and Latina women.

Further research about differences in urinary symptom experience between pre- and peri-menopausal stages and between more race/ethnicity groups of women would enhance our understanding and potentially decrease associated long-term morbidity and improve quality of life for all women across midlife.

**References**


Abrams, P., Cardozo, L., Fall, M., Griffiths, D., Rosier, P., Ulmsten, U., . . . Wein, A. (2002). The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn, 21*(2), 167-178.

Blumel, J. E., Chedraui, P., Baron, G., Belzares, E., Bencosme, A., Calle, A., . . . Vallejo, M. S. (2012). Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study. *Climacteric, 15*(6), 542-551. doi: 10.3109/13697137.2012.658462

Bradley, C. S., Brown, J. S., Van Den Eeden, S. K., Schembri, M., Ragins, A., & Thom, D. H. (2011). Urinary incontinence self-report questions: reproducibility and agreement with bladder diary. *Int Urogynecol J, 22*(12), 1565-1571. doi: 10.1007/s00192-011-1503-3

Cardozo, L., & Robinson, D. (2002). Special considerations in premenopausal and postmenopausal women with symptoms of overactive bladder. *Urology, 60*(5 Suppl 1), 64-71; discussion 71.

Chen, Y. C., Chen, G. D., Hu, S. W., Lin, T. L., & Lin, L. Y. (2003). Is the occurrence of storage and voiding dysfunction affected by menopausal transition or associated with the normal aging process? *Menopause, 10*(3), 203-208.

Choi, J., Guiterrez, Y., Gilliss, C., & Lee, K. A. (2012). Physical activity, weight, and waist circumference in midlife women. *Health Care Women Int, 33*(12), 1086-1095. doi: 10.1080/07399332.2012.673658

Coyne, K. S., Margolis, M. K., Kopp, Z. S., & Kaplan, S. A. (2012). Racial differences in the prevalence of overactive bladder in the United States from the epidemiology of LUTS (EpiLUTS) study. *Urology, 79*(1), 95-101. doi: 10.1016/j.urology.2011.09.010

Coyne, K. S., Sexton, C. C., Bell, J. A., Thompson, C. L., Dmochowski, R., Bavendam, T., . . . Quentin Clemens, J. (2013). The prevalence of lower urinary tract symptoms (LUTS) and overactive bladder (OAB) by racial/ethnic group and age: results from OAB-POLL. *Neurourol Urodyn, 32*(3), 230-237. doi: 10.1002/nau.22295

Coyne, K. S., Wein, A., Nicholson, S., Kvasz, M., Chen, C. I., & Milsom, I. (2013). Comorbidities and personal burden of urgency urinary incontinence: a systematic review. *Int J Clin Pract, 67*(10), 1015-1033. doi: 10.1111/ijcp.12164

Coyne, K. S., Wein, A., Nicholson, S., Kvasz, M., Chen, C. I., & Milsom, I. (2014). Economic burden of urgency urinary incontinence in the United States: a systematic review. *J Manag Care Pharm, 20*(2), 130-140.

Fitzgerald, M. P., Thom, D. H., Wassel-Fyr, C., Subak, L., Brubaker, L., Van Den Eeden, S. K., & Brown, J. S. (2006). Childhood urinary symptoms predict adult overactive bladder symptoms. *J Urol, 175*(3 Pt 1), 989-993. doi: 10.1016/s0022-5347(05)00416-7

Fultz, N. H., Herzog, A. R., Raghunathan, T. E., Wallace, R. B., & Diokno, A. C. (1999). Prevalence and severity of urinary incontinence in older African American and Caucasian women. *J Gerontol A Biol Sci Med Sci, 54*(6), M299-303.

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., & Murrell, N. (2001). Recruitment and retention of healthy minority women into community-

based longitudinal research. *J Womens Health Gend Based Med, 10*(1), 77-85. doi: 10.1089/152460901750067142
Gopal, M., Sammel, M. D., Pien, G., Gracia, C., Freeman, E. W., Lin, H., & Arya, L. (2008). Investigating the associations between nocturia and sleep disorders in perimenopausal women. *J Urol, 180*(5), 2063-2067. doi: 10.1016/j.juro.2008.07.050
Handa, V. L., Pierce, C. B., Munoz, A., & Blomquist, J. L. (2014). Longitudinal changes in overactive bladder and stress incontinence among parous women. *Neurourol Urodyn*. doi: 10.1002/nau.22583
Hannestad, Y. S., Rortveit, G., Sandvik, H., & Hunskaar, S. (2000). A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trondelag. *J Clin Epidemiol, 53*(11), 1150-1157.
Harlow, S. D., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W., . . . de Villiers, T. J. (2012). Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab, 97*(4), 1159-1168. doi: 10.1210/jc.2011-3362
Holm-Larsen, T. (2014). The economic impact of nocturia. *Neurourol Urodyn, 33 Suppl 1*, S10-14. doi: 10.1002/nau.22593
Hsu, A., Nakagawa, S., Walter, L. C., Van Den Eeden, S. K., Brown, J. S., Thom, D. H., . . . Huang, A. J. (2015). The burden of nocturia among middle-aged and older women. *Obstet Gynecol, 125*(1), 35-43. doi: 10.1097/aog.0000000000000600
Humphreys, J., Janson, S., Donesky, D., Dracup, K., Lee, K. A., Puntillo, K., . . . the University of California, S. F. U. S. o. N. S. t. M. F. G. (2014). Theory of Symptom Management. In M. J. Smith & P. R. Liehr (Eds.), *Middle Range Theory for Nursing* (3rd ed., pp. 141-164). New York: Springer Publishing Company.
Kupelian, V., Wei, J. T., O'Leary, M. P., Norgaard, J. P., Rosen, R. C., & McKinlay, J. B. (2012). Nocturia and quality of life: results from the Boston area community health survey. *Eur Urol, 61*(1), 78-84. doi: 10.1016/j.eururo.2011.05.065
Lin, T. L., Ng, S. C., Chen, Y. C., Hu, S. W., & Chen, G. D. (2005). What affects the occurrence of nocturia more: menopause or age? *Maturitas, 50*(2), 71-77. doi: 10.1016/j.maturitas.2004.03.017
Link, C. L., Steers, W. D., Kusek, J. W., & McKinlay, J. B. (2011). The association of adiposity and overactive bladder appears to differ by gender: results from the Boston Area Community Health survey. *J Urol, 185*(3), 955-963. doi: 10.1016/j.juro.2010.10.048
Mac Bride, M. B., Rhodes, D. J., & Shuster, L. T. (2010). Vulvovaginal atrophy. *Mayo Clin Proc, 85*(1), 87-94. doi: 10.4065/mcp.2009.0413
Maserejian, N. N., Chen, S., Chiu, G. R., Araujo, A. B., Kupelian, V., Hall, S. A., & McKinlay, J. B. (2014). Treatment status and progression or regression of lower urinary tract symptoms in a general adult population sample. *J Urol, 191*(1), 107-113. doi: 10.1016/j.juro.2013.07.005
Nosek, M., Kennedy, H. P., Beyene, Y., Taylor, D., Gilliss, C., & Lee, K. (2010). The effects of perceived stress and attitudes toward menopause and aging on

symptoms of menopause. *J Midwifery Womens Health, 55*(4), 328-334. doi: 10.1016/j.jmwh.2009.09.005

Palma, T., Raimondi, M., Souto, S., Fozzatti, C., Palma, P., & Riccetto, C. (2013). Prospective study of prevalence of overactive bladder symptoms and child-bearing in women of reproductive age. *J Obstet Gynaecol Res, 39*(8), 1324-1329. doi: 10.1111/jog.12063

Portman, D. J., & Gass, M. L. (2014). Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas, 79*(3), 349-354. doi: 10.1016/j.maturitas.2014.07.013

Robinson, D., Toozs-Hobson, P., & Cardozo, L. (2013). The effect of hormones on the lower urinary tract. *Menopause Int, 19*(4), 155-162. doi: 10.1177/1754045313511398

Rortveit, G., Hannestad, Y. S., Daltveit, A. K., & Hunskaar, S. (2001). Age- and type-dependent effects of parity on urinary incontinence: the Norwegian EPINCONT study. *Obstet Gynecol, 98*(6), 1004-1010.

Sandvik, H., Hunskaar, S., Vanvik, A., Bratt, H., Seim, A., & Hermstad, R. (1995). Diagnostic classification of female urinary incontinence: an epidemiological survey corrected for validity. *J Clin Epidemiol, 48*(3), 339-343.

Santoro, N., & Chervenak, J. L. (2004). The menopause transition. [Review]. *Endocrinol Metab Clin North Am, 33*(4), 627-636. doi: 10.1016/j.ecl.2004.07.002

Santoro, N., Lasley, B., McConnell, D., Allsworth, J., Crawford, S., Gold, E. B., . . . Weiss, G. (2004). Body size and ethnicity are associated with menstrual cycle alterations in women in the early menopausal transition: The Study of Women's Health across the Nation (SWAN) Daily Hormone Study. [Comparative Study Multicenter Study Research Support, U.S. Gov't, P.H.S.]. *J Clin Endocrinol Metab, 89*(6), 2622-2631. doi: 10.1210/jc.2003-031578

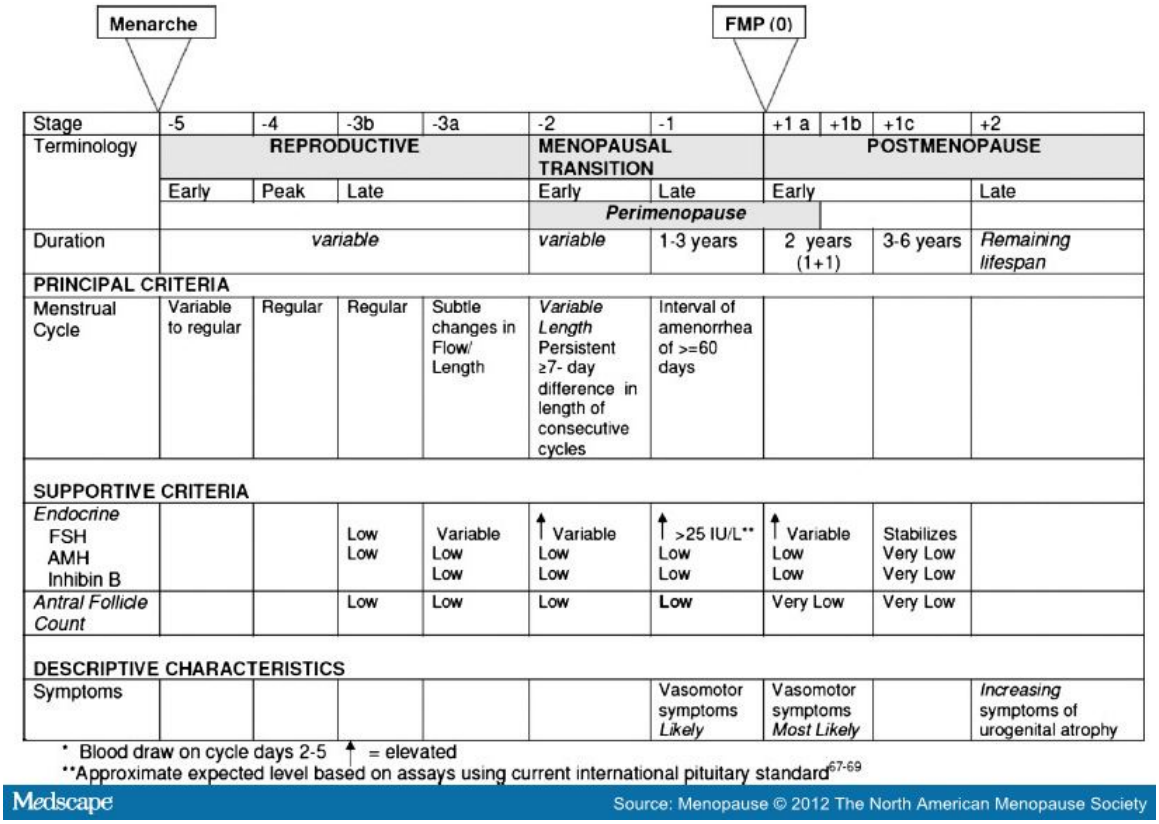
Tang, D. H., Colayco, D. C., Khalaf, K. M., Piercy, J., Patel, V., Globe, D., & Ginsberg, D. (2014). Impact of urinary incontinence on healthcare resource utilization, health-related quality of life and productivity in patients with overactive bladder. *BJU Int, 113*(3), 484-491. doi: 10.1111/bju.12505

Thurston, R. C., Santoro, N., & Matthews, K. A. (2011). Adiposity and hot flashes in midlife women: a modifying role of age. *J Clin Endocrinol Metab, 96*(10), E1588-1595. doi: 10.1210/jc.2011-1082

Townsend, M. K., Curhan, G. C., Resnick, N. M., & Grodstein, F. (2011). Original research: rates of remission, improvement, and progression of urinary incontinence in Asian, Black, and White women. *Am J Nurs, 111*(4), 26-33; quiz 34-25. doi: 10.1097/01.NAJ.0000396551.56254.8f

Weiss, J. P. (2012). Nocturia: focus on etiology and consequences. *Rev Urol, 14*(3-4), 48-55.

Figure 1. Stages of Reproductive Aging Workshop Criteria (STRAW)




| Stage | -5 | -4 | -3b | -3a | -2 | -1 | +1 a | +1b | +1c | +2 |
|---|---|---|---|---|---|---|---|---|---|---|
| Terminology | **REPRODUCTIVE** | | | | **MENOPAUSAL TRANSITION** | | **POSTMENOPAUSE** | | | |
| | Early | Peak | Late | | Early | Late | Early | | | Late |
| | | | | | ***Perimenopause*** | | | | | |
| Duration | *variable* | | | | *variable* | 1-3 years | 2 years (1+1) | | 3-6 years | *Remaining lifespan* |
| **PRINCIPAL CRITERIA** | | | | | | | | | | |
| Menstrual Cycle | Variable to regular | Regular | Regular | Subtle changes in Flow/ Length | *Variable Length* Persistent ≥7- day difference in length of consecutive cycles | Interval of amenorrhea of >=60 days | | | | |
| **SUPPORTIVE CRITERIA** | | | | | | | | | | |
| *Endocrine*<br>FSH<br>AMH<br>Inhibin B | | | Low<br>Low | Variable<br>Low<br>Low | ↑ Variable<br>Low<br>Low | ↑ >25 IU/L**<br>Low<br>Low | ↑ Variable<br>Low<br>Low | | Stabilizes<br>Very Low<br>Very Low | |
| *Antral Follicle Count* | | | Low | Low | Low | **Low** | Very Low | | Very Low | |
| **DESCRIPTIVE CHARACTERISTICS** | | | | | | | | | | |
| Symptoms | | | | | | Vasomotor symptoms *Likely* | Vasomotor symptoms *Most Likely* | | | *Increasing* symptoms of urogenital atrophy |

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

Medscape Source: Menopause © 2012 The North American Menopause Society

Table 1. Demographic and Clinical Characteristics (N (%) or mean ± standard deviation)

| Characteristics | African American n = 46 | Mexico/Central American n = 41 | European American n = 71 | Overall sample N = 158 |
|---|---|---|---|---|
| Age (yrs) | 48.02 ± 2.24 | 48.01 ± 2.61 | 48.04 ± 1.94 | 48.05 ± 2.20 |
| FSH[1] (IU/DL) | 3.27 ± 5.01 | 1.38 ± 1.98 | 1.33 ± 1.75 | 1.75 ± 2.87* |
| BMI | 30.54 ± 7.49 | 28.95 ± 5.89 | 27.05 ± 6.06 | 28.41 ± 6.43* |
| CES-D depressive symptoms (0-60) | 10.85 ±10.50 | 9.26 ± 9.66 | 11.62 ± 9.15 | 10.82 ± 9.92 |
| Parity | | | | |
| 0 live births | 16 (32) | 14 (27) | 30 (41) | 60 (35)* |
| 1-2 live births | 25 (57) | 15 (40) | 31 (45) | 71 (47) |
| 3 or more live births | 5 (11) | 12 (33) | 10 (14) | 27 (18) |
| Education | | | | |
| < high school | 2 (4.4) | 4 (9.7) | 0 | 6 (3.8)* |
| High school or GED | 1 (2.1) | 6 (14.6) | 0 | 7 (4.4) |
| Some college | 19 (41.3) | 13 (31.7) | 12 (16.9) | 44 (27.8) |
| College graduate | 24 (52.2) | 18 (43.9) | 59 (83.1) | 101 (64.0) |
| Marital Status | | | | |
| Married | 17 (37.0) | 21 (51.2) | 42 (59.1) | 80 (50.6)* |
| Living with partner | 4 (8.7) | 4 (9.8) | 14 (19.7) | 22 (14.0) |
| Single/Divorced | 24 (52.1) | 15 (36.6) | 14 (19.8) | 53 (33.5) |
| Widowed | 1 (2.2) | 1 (2.4) | 1 (1.4) | 3 (1.9) |
| Income | | | | |
| < $ 30,999 | 8 (18.7) | 10 (25.0) | 2 (2.8) | 20 (13.0)* |
| $31 – 50,999 | 7 (16.3) | 10 (25.0) | 10 (14.0) | 27 (17.5) |
| $51 – 80,999 | 13 (30.2) | 10 (25.0) | 13 (18.2) | 36 (23.4) |
| > $ 81,000 | 15 (34.9) | 10 (25.0) | 46 (64.8) | 71 (46.1) |
| | 3 missing | 1 missing | | |
| Take a diuretic | 8 (17.4) | 0 | 2 (2.8) | 10 (6.3)* |
| Perceives general health as 'excellent' (1) or 'very good' (2) | 21 (45.7) | 24 (58.5) | 47 (69.1) | 92 (59.0)* |
| Major health problem in the past year | 11 (23.9) | 15 (21.1) | 11 (26.8) | 37 (23.4) |

FSH[1] levels < 0.2 are consistent with post-menopause

*The 3 groups differed significantly *($F_{[2, 157]} > 3.0$, $p < .05$)*

Table 2. Bladder Symptoms by Race/Ethnicity

| Participant Characteristics | African American n = 46 | Mexico/Central American n = 41 | European American n = 71 | Total sample n = 158 |
|---|---|---|---|---|
| | **N (%)** | **N (%)** | **N (%)** | **N (%)** |
| Urinary infection (UTI) past 6 months | 2 (4.5) | 6 (16.2) | 5 (7.2) | 13 (8.2) |
| Incontinence frequency past 6 months | | | | |
| none | 22 (48) | 12 (29) | 11 (15) | 45 (28.5) |
| about once/month | 16 (35) | 17 (42) | 36 (51) | 69 (43.7) |
| about once/week | 6 (13) | 9 (22) | 19 (27) | 34 (21.5) |
| every day | 2 (4) | 3 (7) | 5 (7) | 10 (6.3) |
| Incontinence last week (yes) | 12 (26.1) | 23 (56.1) | 43 (60.6) | 78 (49.4)* |
| Urge incontinence | 8 (72.7) | 15 (35.7) | 9 (39.1) | 32 (20.2) |
| and/or Stress incontinence | 9 (75.0) | 18 (78.3) | 31 (73.8) | 58 (37.0) |
| **Urinary Frequency** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Day time (number/day) | 5.10 ± 1.95 | 5.66 ± 1.86 | 6.54 ± 2.11 | 5.86 ± 2.03* |
| Night time (number/night) | 1.26 ± 0.98 | 1.07 ± 1.13 | 1.04 ± 0.99 | 1.11 ± 1.03 |

*The 3 groups differed significantly $(F_{[2, 157]} > 5.0, p < .01)$

Table 3. Bladder Symptoms by Menopause Stage (N = 158)

| Bladder symptoms | Late Pre-menopause (n = 72) | Peri-menopause (n = 86) |
|---|---|---|
| | **N (%)** | **N (%)** |
| Urinary Tract Infection (UTI) in the past 6 months (yes) | 6 (8.5) | 7 (8.3) |
| Incontinence frequency past 6 months | | |
| none | 12 (17) | 33 (38) |
| about once/month | 38 (53) | 31 (36) |
| about once/week | 17 (23) | 17 (20) |
| every day | 5 (7) | 5 (6) |
| Incontinent last week (yes) | 43 (59.7) | 35 (40.7)* |
| Stress incontinence | 31 | 28 |
| and/or Urge incontinence | 18 | 15 |
| **Urinary Frequency** | **Mean ± SD** | **Mean ± SD** |
| Day time (number/day) | 6.31 ± 2.17 | 5.48 ± 1.84* |
| Night time (number/night) | 1.26 ± 1.03 | 0.99 ± 1.01** |

*The 2 groups differed significantly ($F_{[1, 157]} > 5.0$, $p \leq .01$)

** The 2 groups were not significantly different ($F_{[1,157]} = 2.85$, $p = .093$)

Table 4. Linear Regression Summary for Frequency of Nocturia Past Week

| Nocturia N=158 | | | | |
|---|---|---|---|---|
| Explained Variance ($R^2$) | | .276 | | P < .002 |
| **Characteristics** | **Beta** | **t (p-value)** | **Partial** | **Part** |
| Age | -.048 | -.578 (NS) | -.052 | -.045 |
| Race/ethnicity | | | | |
| Black (yes) | -.046 | -.489 (NS) | -.044 | -.038 |
| Latina (yes) | -.137 | -1.414 (NS) | -.128 | -.109 |
| Income | -.172 | -1.853/ .066 | -.166 | -.143 |
| Education | -.021 | -.225 (NS) | -.020 | -.017 |
| Menopause Status | - .255 | -3.086 (.003) | -.270 | -.238 |
| Diuretic Use | .087 | .993 (NS) | .090 | .077 |
| Number of Live Births | .156 | 1.865 (.065) | .167 | .144 |
| CES-D (depressive symptoms) | .055 | .624 (NS) | .057 | .048 |
| Perceived General Health Status | -.077 | -.848 (NS) | -.077 | -.065 |
| Body Mass Index (BMI) | .320 | 3.652 (<.001) | .315 | .282 |
| Major health Problem in the Past Year | -.105 | -1.269 (NS) | -.115 | -.098 |

NS = not statistically significant, p>.20

Table 5. Logistic Regression Summary Table for Experiencing Incontinence

| Incontinence N=158 | | | |
|---|---|---|---|
| Explained Variance $\chi^2 = 9.535$ , $p = .657$ | | | |
| **Characteristics** | **Beta** | ***Wald* (*p*-value)** | **Exp(B)** |
| Age | -.117 | .252 (NS) | .889 |
| Race/ethnicity | | | |
| African American (1=yes) | .981 | .147 (NS) | 2.667 |
| European American (1=yes) | -.482 | .385 (NS) | .618 |
| Income | -.015 | .148 (NS) | .986 |
| Education | .074 | .695 (NS) | 1.077 |
| Menopause Status | -.170 | .694 (NS) | .844 |
| Diuretic Use | -.183 | .853 (NS) | .833 |
| Number of Live Births | -.124 | .430 (NS) | .883 |
| CES-D (depressive symptoms) | -.006 | .777 (NS) | .994 |
| Perceived General Health Status | .085 | .755 (NS) | 1.089 |
| Body Mass Index (BMI) | .027 | .381 (NS) | 1.027 |
| Major health problem past year | -.388 | .430 (NS) | .678 |

NS = not statistically significant (p > .10)

Chapter 3

# Bladder Symptoms Associated with Sleep Quality in Midlife Women

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**Abstract**

*Background:* Sleep disturbances are associated with significant morbidity and increased healthcare costs in the United States. Sleep disturbance increases with age and has been linked to health problems such as nocturia. Nocturia is defined as awakening 1 or more times per night to void and has been noted to increase with age.

*Purpose:* To describe demographic and clinical differences in the experience of nocturia for late pre-menopausal women and evaluate variance in sleep quality and sleep hours.

*Methods:* A secondary analysis was performed using 72 (16 African American, 21 Latina, 35 European American) late pre-menopausal participants from the UCSF Women's Health Study. In addition to demographic and clinical data, the participants completed a general health survey, the Pittsburgh Sleep Quality Index (PSQI), and a bladder symptoms questionnaire. Descriptive and comparative analyses were performed on this small subsample to identify characteristics associated with nocturia. Linear regressions were conducted to explain the variance in both sleep quality and sleep hours.

*Results:* The women in this sample had a mean age of 47.5 and experienced poor sleep quality evidenced by PSQI scores (5.29±2.89). European women reported significantly greater sleep hours ($F=3.81$, $p=0.027$). Nocturia was correlated with BMI (r-.429, $p<0.001$). Neither linear regression was statistically significant while controlling for age, ethnicity (dummy coded), education, nocturia, diuretic use, general health status, and BMI. However, there were significant contributors within each model. Perceived general health status ($B=.266$, $p=.039$) was a significant contributor within the model for sleep quality and nocturia neared significance ($B=.255$, $p=.088$). Being African American was a significant contributor within the model for sleep hours ($B=-.292$, $p=.049$).

*Conclusions:* sleep disturbance remains a significant health problem in the U.S. and is associated with considerable health care costs and utilization. Identification of key factors such as perceived health status, race, or nocturia that influence the occurrence of sleep disturbance might prove helpful in prevention tactics and decreasing morbidity.

## Introduction

Sleep disturbance accounts for significant morbidity in the United States and around the world (Eriksen, Natvig, & Bruusgaard, 2001; Salo et al., 2010; Zammit et al., 2010). Disturbed sleep may result from specific sleep problems (e.g. insomnia, sleep apnea) or other health problems (e.g. urinary frequency, restless leg syndrome) ((NSF), 2015). Some of the cost attributed to sleep disturbance stems from healthcare utilization, pharmaceuticals (prescribed or over-the-counter), and lost productivity (Hillman & Lack, 2013). Sleep disturbance and its associated symptoms have been linked to poor quality of life and an increased risk of depression or other psychiatric diagnoses (Kloss, Tweedy, & Gilrain, 2004; Reid et al., 2006; Thase, 1998; Wallander, Johansson, Ruigomez, Garcia Rodriguez, & Jones, 2007).

Sleep problems increase with age and women are more likely than men to report complaints about their sleep (Krishnan & Collop, 2006; Maculano Esteves, Ackel-D'elia, Tufik, & De Mello, 2014). According to the National Sleep Foundation (NSF, 2003) sleep disturbance in the form of nighttime awakenings is the most prevalent complaint. Nighttime awakenings are a risk factor for excessive daytime sleepiness, poor daytime functioning, accidents and errors at work, mood disturbance, and other conditions that can affect quality of life (Zammit et al., 2010). Women have been shown to experience an increase in sleep disturbances with transition to menopause (Brown, Gallicchio, Flaws, & Tracy, 2009). However, there is debate as to whether sleep-related symptoms in midlife are due more in part to normal aging processes, the hormonal changes that accompany menopause, or the psycho-social stressors prominent during midlife (Freeman, Sammel, Gross, & Pien, 2014).

Recent studies have explored differences in sleep throughout the reproductive phases of pre-, peri-, and post-menopause (de Zambotti, Colrain, & Baker, 2015; Kravitz et al., 2003; Kravitz et al., 2008) but few have explored the differences occurring in late pre-menopause. Therefore, the objectives of this study were to: 1) describe demographic and clinical differences in the experience of nocturia for late pre-menopausal women and 2) describe the variance in sleep quality and sleep hours associated with nocturia.

**Design and Sample**

UCSF Midlife Women's Health Study

The multiethnic sample used in this current secondary analysis consisted of late pre-menopausal women from the San Francisco Bay area who were participants in the University of California San Francisco (UCSF) Midlife Women's Health Study originally recruited if they were between 40 and 50 years of age and still experiencing menstrual periods. The study was conducted over 3-5 years with assessments every 6 months (Gilliss et al., 2001). Data for this secondary analysis were taken from the last year of the parent study when there were 158 participants available for analysis. The details of recruitment and protocol have been previously reported (Choi, Guiterrez, Gilliss, & Lee, 2012; Gilliss et al., 2001).

The subsample from the parent study included 72 (16 African American, 21 Latina, and 35 European Americans) late pre-menopausal women who completed the bladder symptom checklist during Phase 2 of the parent study. This subsample of women had previously been identified as having a greater occurrence of nocturia in comparison to their peri-menopausal cohort of similar age and demographic. Therefore, it was

proposed that they might also experience sleep disturbance and poor sleep quality due to bladder symptoms.

Methods

Participant data included self-report questionnaires, demographics and anthropometrics. Physiological data included: urine samples for assaying follicular stimulating hormone (FSH), weight and height for calculations of body mass (BMI) and waist and hip circumferences to calculate waist-hip ratio (WHR). Estimation of menopause status (late pre-menopause or peri-menopause) using FSH levels and menstrual cycle regularity was based on the Stages of Reproductive Aging Workshop (STRAW) criteria whose recommendations standardize clinical and research nomenclature for the reproductive stages (Harlow et al., 2012).

Self-report questionnaires included a bladder symptom survey, the Pittsburgh Sleep Quality Index (PSQI), and a general perceived health status survey. Bladder symptoms such as day and nighttime urinary frequency, urinary incontinence, and urinary tract infections were assessed using self-report questionnaire measures adapted from other epidemiologic women's health studies focusing on urinary tract function (Bradley et al., 2011; Fitzgerald et al., 2006; Hannestad, Rortveit, Sandvik, & Hunskaar, 2000; Sandvik et al., 1995). Urinary tract infection and urinary incontinence were referenced over the previous 6 months while daytime urinary frequency were referenced over the previous week. Nocturia was dichotomized as either no nocturia (0) or having nocturia (1) at least once per night on average (Abrams et al., 2002). Nocturia-related nighttime awakenings were categorized on rated scale (0 = not at all, 3 = three or more times per week).

*Pittsburgh Sleep Quality Index (PSQI):* The PSQI is a self-report assessment instrument that distinguishes between 'good' and 'poor' sleep quality over the past month. The instrument measures 7 components of sleep (sleep quality, sleep duration, sleep latency, daytime dysfunction, sleep disturbance, use of sleep medications and habitual sleep efficiency) based on 19 items referencing the previous 1-month time period (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Scores range 0 – 21 and above 5 is indicative of poor sleep quality. Item 3 from the PSQI was used to assess the number of sleep hours per participant. Cronbach alpha in the parent sample was 0.718.

*General Perceived Health Status:* The participants were asked to classify their health as 'excellent', 'very good', 'good', 'fair' and 'poor'. Responses were coded from 1 to 5 (1=excellent, 5 =poor). This is a general perceived health item from the SF-36. The SF-36 is a health survey tool that has been highly validated in construct, criterion, and content.

**Statistical Analysis**

A secondary analysis was conducted using descriptive statistics, independent t tests, one-way analysis of variance, or Chi Square analyses. In accordance with our objectives, variable analyses were performed to test the associations between bladder symptoms of nocturia and sleep variables that included sleep quality and sleep duration. A linear regression model was used to evaluate the variance in sleep quality while controlling for race (dummy coded), age, income, bladder symptoms, BMI and, perceived general health status. A second linear regression was conducted to evaluate the variance in sleep hours using the same criteria. All analyses were performed using SPSS version 22.0 software.

**Results**

Demographic and Clinical Characteristics

The mean age for this subsample of 72 late pre-menopausal women was 47.5 (SD=2.34) years. Demographic characteristics are shown in Table 1. Race-based differences were noted in marital status ($\chi^2 = 20.05$, $p = 0.01$) and education ($\chi^2 = 24.60$, $p = 0.006$). European American women reported higher levels of education and were more likely to be married or partnered.

The women were similar in most clinical characteristics (Table2). However using one-way analysis of variance, there was a statistically significant difference in mean sleep hours (F=3.81, p=0.027) based on race; European American women reported a higher mean number of sleep hours per night compared to African American and Latin American women. Although not statistically significant, European American women scored lower on the general health perception survey in comparison to the African American and Latina women indicating a higher perception of their overall health.

[Place Tables 1 & 2 about here]

Bladder symptoms were common within this subsample with 73% reporting nocturia at least once per night, and 50% reporting urinary incontinence at least once per week. Although African American women reported a higher mean occurrence of nocturia, there were no significant race differences for nocturia. Additionally, urinary incontinence was not significantly different by race and there was minimal use of diuretics or estrogen.

Nocturia and Sleep Quality

The late pre-menopausal women in this sample had a mean PSQI score of 5.29 (SD=2.89) indicating poor sleep quality. Sleep quality was not significant between the race groups. There was not a significant correlation between nocturia and sleep quality. However, nocturia was significantly correlated with BMI (r-.429, $p<0.001$). Although not statistically significant (F=2.68, p=0.076), African American women in this subsample had greater mean BMI in comparison to European and Latin American women.

Nocturia and Sleep Duration

As indicated in Table 2, hours of sleep were significantly associated with race. African American women reported the fewest number of sleep hours and a higher mean number of nocturia-related awakenings. European American women reported a greater number of sleep hours. Sleep hours were not correlated with nocturia, race, or BMI.

Predictors of Sleep Quality and Quantity

In accordance with our second objective, a linear regression model was created to evaluate the association between chosen predictor variables and sleep quality (mean total PSQI scores). Variables included in the regression were age, ethnicity (dummy coded), education, nocturia, diuretic use, general health status, and BMI. As shown in Table 3, this model was not significant for variance in sleep quality. Within the model, perceived general health status was significantly associated with sleep quality (B=.266, p=.039) and nocturia neared significance (B=.255, p=.088).

A linear regression was performed using the same variables to evaluate the predictive relationship for hours of sleep. As shown in Table 4, this model also was not

significant for variance in sleep hours. However race, specifically being African American, was a significant predictor of the number of sleep hours within the model (B= -.292, p=.049). Perceived general health was not a significant predictor (B=-.216, p=.095).

[Place Tables 3 and 4 here]

**Discussion**

Our multiethnic sample of late pre-menopausal midlife women experienced poor sleep quality. Although these women reported significantly more bladder symptoms associated with nocturia when compared to peri-menopausal women of similar age and background, this symptom did not account for poor sleep quality or fewer sleep hours within our regression models.

The only significant variable in the regression model for poor sleep quality was perceived general health status; those women who reported poor perceived general health status were more likely to report poor sleep quality. This outcome suggests there are multiple factors that contribute to poor sleep quality. Health conditions such as nocturia may contribute to poor perceived health and in our analysis nocturia neared significance in the linear regression model developed to explain the variance in poor sleep quality.

The only significant variable in the regression model to explain variance in sleep hours was being African American. The African American women in this subsample demonstrated greater risk profiles for poor sleep quality and fewer sleep hours with higher BMI, lower perceived general health scores, and higher FSH levels. BMI has been

associated with sleep duration in past research (Appelhans et al., 2013; Parvaneh, Poh, Hajifaraji, & Ismail, 2014). The women in this subsample were overweight with a mean BMI of 28. BMI is associated with multiple medical problems (eg. sleep apnea) known to result in nighttime awakenings and in poor sleep quality. The African American women in our sample had the highest average BMI and the fewest sleep hours compared to the other two races. Our findings were consistent with the findings of at least one article where African American women scored higher on the PSQI and reported shorter sleep hours (Hall et al., 2009). The sample in the study by Hall et al. (2009) consisted of mostly peri-menopausal women with some post-menopausal women whereas the women in our analysis were in late pre-menopause.

Sleep quality was found to be independent of menopause status in the Hall et al. sample. This finding is in conflict with other studies that associate sleep quality and sleep disturbance with menopause status (Kravitz et al., 2003; Kravitz et al., 2008; Xu & Lang, 2014). We eliminated the effects of menopause status by focusing on late pre-menopausal women who were similar in age. In that way, we were able to identify correlations and trends suggesting the underlying influence of perceived health status, nocturia, and race.

**Conclusions**

Nocturia, sleep disturbance, and poor sleep quality were prevalent in our sample of late pre-menopausal women. Although nocturia was significantly correlated with BMI, this variable only neared significance in the regression for variance associated with sleep quality. Our study findings were consistent with the current literature and illustrate both the relevance and extent of poor sleep quality prior to the transition to menopause for

women who are of different ethnic backgrounds, who experience nocturia, and who are overweight or obese.

**Recommendations**

Further study is recommended to explore the relationships between late pre-menopause and nocturia-related sleep disturbances. Although multifactorial, sleep disturbances that arise during the late pre-menopausal stage may be more amenable to intervention. It has been shown that sleep disturbance increases with the transition to menopause and therefore early intervention during late pre-menopause stage may be important. Recognition of the influence of race, BMI, perceived health status, and nocturia may support timely prevention and decrease morbidity.

**Study limitations**

The cross-sectional nature of this secondary analysis and small sample size limit the ability to generalize our results to all midlife women. Menopause symptoms such as night sweats and hot flashes were not assessed in this analysis and therefore could not be assessed in relation to sleep quality. It is likely that nighttime awakenings due to night sweats may have contributed to poor sleep quality although menopause status was controlled for in our analyses.

The women recruited for the parent study were in good health when recruited for participation, yet this secondary analysis does not take into account any health problems that may have developed over the course of the study. Newly diagnosed conditions may contribute to sleep disturbance or the perception of poor sleep quality.

**References**


(NSF), N. S. F. (2015). Sleep Problems and Disorders, from http://sleepfoundation.org/sleep-disorders-problems

Abrams, P., Cardozo, L., Fall, M., Griffiths, D., Rosier, P., Ulmsten, U., . . . Wein, A. (2002). The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn, 21*(2), 167-178.

Appelhans, B. M., Janssen, I., Cursio, J. F., Matthews, K. A., Hall, M., Gold, E. B., . . . Kravitz, H. M. (2013). Sleep duration and weight change in midlife women: the SWAN sleep study. *Obesity (Silver Spring), 21*(1), 77-84. doi: 10.1002/oby.20251

Bradley, C. S., Brown, J. S., Van Den Eeden, S. K., Schembri, M., Ragins, A., & Thom, D. H. (2011). Urinary incontinence self-report questions: reproducibility and agreement with bladder diary. *Int Urogynecol J, 22*(12), 1565-1571. doi: 10.1007/s00192-011-1503-3

Brown, J. P., Gallicchio, L., Flaws, J. A., & Tracy, J. K. (2009). Relations among menopausal symptoms, sleep disturbance and depressive symptoms in midlife. *Maturitas, 62*(2), 184-189. doi: 10.1016/j.maturitas.2008.11.019

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 Res, 28*(2), 193-213.

Choi, J., Guiterrez, Y., Gilliss, C., & Lee, K. A. (2012). Physical activity, weight, and waist circumference in midlife women. *Health Care Women Int, 33*(12), 1086-1095. doi: 10.1080/07399332.2012.673658

de Zambotti, M., Colrain, I. M., & Baker, F. C. (2015). Interaction between reproductive hormones and physiological sleep in women. *J Clin Endocrinol Metab*, jc20143892. doi: 10.1210/jc.2014-3892

Eriksen, W., Natvig, B., & Bruusgaard, D. (2001). Sleep problems: a predictor of long-term work disability? A four-year prospective study. *Scand J Public Health, 29*(1), 23-31.

Fitzgerald, M. P., Thom, D. H., Wassel-Fyr, C., Subak, L., Brubaker, L., Van Den Eeden, S. K., & Brown, J. S. (2006). Childhood urinary symptoms predict adult overactive bladder symptoms. *J Urol, 175*(3 Pt 1), 989-993. doi: 10.1016/s0022-5347(05)00416-7

Freeman, E. W., Sammel, M. D., Gross, S. A., & Pien, G. W. (2014). Poor sleep in relation to natural menopause: a population-based 14-year follow-up of midlife women. *Menopause*. doi: 10.1097/gme.0000000000000392

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., & Murrell, N. (2001). Recruitment and retention of healthy minority women into community-based longitudinal research. *J Womens Health Gend Based Med, 10*(1), 77-85. doi: 10.1089/152460901750067142

Hall, M. H., Matthews, K. A., Kravitz, H. M., Gold, E. B., Buysse, D. J., Bromberger, J. T., . . . Sowers, M. (2009). Race and financial strain are independent correlates of sleep in midlife women: the SWAN sleep study. *Sleep, 32*(1), 73-82.

Hannestad, Y. S., Rortveit, G., Sandvik, H., & Hunskaar, S. (2000). A community-based epidemiological survey of female urinary incontinence: the Norwegian

EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trondelag. *J Clin Epidemiol, 53*(11), 1150-1157.
Harlow, S. D., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W., . . . de Villiers, T. J. (2012). Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab, 97*(4), 1159-1168. doi: 10.1210/jc.2011-3362
Hillman, D. R., & Lack, L. C. (2013). Public health implications of sleep loss: the community burden. *Med J Aust, 199*(8), S7-10.
Kloss, J. D., Tweedy, K., & Gilrain, K. (2004). Psychological factors associated with sleep disturbance among perimenopausal women. *Behav Sleep Med, 2*(4), 177-190. doi: 10.1207/s15402010bsm0204_1
Kravitz, H. M., Ganz, P. A., Bromberger, J., Powell, L. H., Sutton-Tyrrell, K., & Meyer, P. M. (2003). Sleep difficulty in women at midlife: a community survey of sleep and the menopausal transition. *Menopause, 10*(1), 19-28.
Kravitz, H. M., Zhao, X., Bromberger, J. T., Gold, E. B., Hall, M. H., Matthews, K. A., & Sowers, M. R. (2008). Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. *Sleep, 31*(7), 979-990.
Krishnan, V., & Collop, N. A. (2006). Gender differences in sleep disorders. *Curr Opin Pulm Med, 12*(6), 383-389. doi: 10.1097/01.mcp.0000245705.69440.6a
Maculano Esteves, A., Ackel-D'elia, C., Tufik, S., & De Mello, M. T. (2014). Sleep patterns and acute physical exercise: the effects of gender, sleep disturbances, type and time of physical exercise. *J Sports Med Phys Fitness, 54*(6), 809-815.
Parvaneh, K., Poh, B. K., Hajifaraji, M., & Ismail, M. N. (2014). Sleep deprivation is related to obesity and low intake of energy and carbohydrates among working Iranian adults: a cross sectional study. *Asia Pac J Clin Nutr, 23*(1), 84-90. doi: 10.6133/apjcn.2014.23.1.02
Reid, K. J., Martinovich, Z., Finkel, S., Statsinger, J., Golden, R., Harter, K., & Zee, P. C. (2006). Sleep: a marker of physical and mental health in the elderly. *Am J Geriatr Psychiatry, 14*(10), 860-866. doi: 10.1097/01.JGP.0000206164.56404.ba
Salo, P., Oksanen, T., Sivertsen, B., Hall, M., Pentti, J., Virtanen, M., . . . Kivimaki, M. (2010). Sleep disturbances as a predictor of cause-specific work disability and delayed return to work. *Sleep, 33*(10), 1323-1331.
Sandvik, H., Hunskaar, S., Vanvik, A., Bratt, H., Seim, A., & Hermstad, R. (1995). Diagnostic classification of female urinary incontinence: an epidemiological survey corrected for validity. *J Clin Epidemiol, 48*(3), 339-343.
Thase, M. E. (1998). Depression, sleep, and antidepressants. *J Clin Psychiatry, 59 Suppl 4*, 55-65.
Wallander, M. A., Johansson, S., Ruigomez, A., Garcia Rodriguez, L. A., & Jones, R. (2007). Morbidity associated with sleep disorders in primary care: a longitudinal cohort study. *Prim Care Companion J Clin Psychiatry, 9*(5), 338-345.
Xu, Q., & Lang, C. P. (2014). Examining the relationship between subjective sleep disturbance and menopause: a systematic review and meta-analysis. *Menopause*. doi: 10.1097/gme.0000000000000240
Zammit, G. K., Joish, V. N., Kong, M. C., Balkrishnan, R., Lerner, D., & Rosekind, M. (2010). Impact of nighttime awakenings on worker productivity and performance. *J Occup Environ Med, 52*(5), 513-518. doi: 10.1097/JOM.0b013e3181d8db23

Table 1. Demographic Characteristics by Ethnicity

| Participant Demographics | African American n = 16 | Latin American n = 21 | European American n = 35 |
|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Age | 47.5 ± 2.42 | 47.7 ± 2.80 | 47.34 ± 2.06 |
| | **n (%)** | **n (%)** | **n (%)** |
| Marital Status | | | |
| -Married | 8 (50.0) | 10 (47.6) | 18 (51.4)* |
| -Living with partner/significantly involved | 1 (6.3) | 1 (4.8) | 10 (28.6) |
| -Single/Divorced | 7 (43.8) | 9 (42.8) | 7 (20.0) |
| -Widowed | 0 | 1 (4.8) | 0 |
| Education | | | |
| - high school or less | 2 (12.6) | 4 (19.0) | 0 |
| - some college or grad | 12 (75.1) | 12 (57.1) | 20 (57.2) |
| - Professional degree | 2 (12.5) | 5 (23.8) | 15 (42.9)* |
| Income | | | |
| < $ 30,999 | 2 (12.6) | 3 (15.0) | 1 (2.9) |
| $31 – 50,999 | 3 (17.8) | 6 (30.0) | 8 (22.8) |
| $51 – 80,999 | 4 (25.1) | 6 (30.0) | 5 (14.3) |
| > $ 81,000 | 7 (43.8) | 5 (25.0) | 21 (60.0) |
| | | 1 missing | |

* $p \leq .05$

Table 2. Clinical Characteristics by Race

| | African American n = 16 | Latin American n = 21 | European American n = 35 |
|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | **Mean ± SD** |
| Hours of sleep | 6.42 ± 1.40 | 7.02 ± 1.03 | 7.32 ± 0.94* |
| Nocturia | 1.63 ± 1.20 | 1.00 ± 0.89 | 1.26 ± 1.01 |
| BMI | 31.52 ± 10.62 | 28.44 ± 5.77 | 26.41 ± 6.04 |
| PSQI score | 6.00 ± 2.97 | 5.67 ± 3.88 | 4.74 ± 2.01 |
| Follicle stimulating hormone (FSH) | .55 ± .41 | .50 ± .31 | .44 ± .31 |
| | **n (%)** | **n (%)** | **n (%)** |
| Estrogen use | 0 | 0 | 3 (8.6) |
| Diuretic use | 2 (12.5) | 0 | 1 (2.9) |
| Incontinence>1x/wk | 4 (25.1) | 7 (33.3) | 11 (31.4) |
| Perceives general health as 'excellent' or 'very good' | 11 (68.8) | 23 (67.7) | 11 (52.4) |

*$p \leq .05$

Table 3. Linear Regression Summary for Sleep Quality

| Sleep Quality (PSQI Total Scores) N=72 | | |
|---|---|---|
| Explained Variance: F = 1.71, *p* = .116 | | |
| **Characteristics** | **Beta** | **p-value** |
| Age | -.087 | .477 |
| White (dummy coded) | -.092 | .563 |
| Black (dummy coded) | .073 | .615 |
| Education | -.033 | .807 |
| Diuretic (YES) | -.230 | .120 |
| Nocturia | .250 | .088 |
| BMI | -.001 | .992 |
| General Health | .266 | .039* |

***** = statistically significant, p < .05

Table 4. Linear Regression Summary for Sleep Hours

| Sleep Hours N=72 | | |
|---|---|---|
| Explained Variance: F = 1.49, *p* = .182 | | |
| **Characteristics** | **Beta** | **p-value** |
| Age | -.052 | .677 |
| White (dummy coded) | .053 | .740 |
| Black (dummy coded) | -.292 | .049* |
| Education | -.007 | .959 |
| Diuretic Use | -.134 | .369 |
| Nocturia | .034 | .816 |
| BMI | -.017 | .908 |
| General Health | -.216 | .095 |

***** = statistically significant, p < .05

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Chapter 4

# "Feeling the need to Fix Everything" – A Qualitative Understanding of Midlife Sources of Stress and Support in African American Women

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**Abstract**

*Background:* African American women suffer from disproportionate adverse health outcomes in comparison to women of other ethnicities living in the United States. Midlife is often accompanied by a cacophony of change that adds to the stress endured by African American women. Stress is an integral part of individual's lives and chronic stress is recognized as an antecedent to illness and adverse health outcomes. Multiple factors can increase a person's vulnerability to the effects of stress but integral to any intervention is our appraisal and perception of the stressor. Therefore, it is essential to identify persons or populations who are vulnerable to stress and the unique stressors they encounter in order to facilitate effective and purposeful health interventions.

*Purpose:* To evaluate the changes in perceived stress from late pre-menopause to post-menopause and identify the most significant life stressors perceived by a cohort of African American women.

*Methods:* 15 African American women were recruited for participation in this mixed methods study. Participants were post-menopausal who had participated in The University of California San Francisco Midlife Women's Health Study prior to menopause when they were between the ages of 40 and 50. This study incorporates data from the parent study and current data to evaluate stress and coping styles in this cohort of women. Both quantitative and qualitative methods were used. Statistical analyses were conducted to compare perceived stress scores before and after menopause and across time. A content analysis was used to establish themes from written responses to open-ended questions about stress and coping styles.

*Results:* The women's perceived stress scores were noted to be consistent over time despite differences in the specific life stressors prevalent before and after menopause. Six themes were identified in their responses about stress: finances, caring for family members, relationships, personal health and aging, race and discrimination, and raising children. The women also provided insight into stress-relieving strategies and factors that increased their stress.

*Conclusions:* Stress is inherent in our lives. Although the types of stressors will undoubtedly change over time, the manner in which stress is perceived (coping styles) may remain consistent. Perception and adaptation to stress is influenced by genetics, personality, learned behaviors, and environment. Nurturing of effective coping strategies might be essential to health and over-all well being. Understanding the unique role that race/ethnicity and discrimination may play in the lives of African American women is essential in anticipating and recognizing the, often silent, need for acknowledgement and assistance. Nurses and health care providers may benefit from taking the time to hear their patients' stories in order to effectively guide them through midlife and beyond.

**Background & Significance**

Chronic perceived stress is a precursor to disease and symptom expression. Chronic perceived stress results in physiological changes that can make individuals more vulnerable to disease over time and, it has been proposed as a factor in health disparities (Carlson & Chamberlain, 2005; Janssen et al., 2012; Zhao et al., 2015). Health disparities, according to the Department of Health and Human Services, are defined as differences in health outcomes across population subgroups (Services & (HHS), 2014). Despite advances in medicine, health care, resources, and technology, health disparities persist in the United States and around the world. Psychosocial and environmental stressors, in addition to lifestyle choices, are factors that can influence health status and long-term health outcomes. Therefore the evaluation of how perceived stress may impact individuals during certain life stages is recommended during routine health care.

As life expectancy continues to increase, it is increasingly more important to examine midlife. Women, in particular, are more vulnerable to certain health problems during midlife as a result of normal aging and menopause (Seib, Whiteside, Humphreys, et al., 2014). Midlife is a time during which most health care providers implement preventive care plans and aggressively screening for potential health problems (eg. breast cancer, cardiac disease, osteoporosis). Preventive guidelines are based on generalized health risks and therefore, it is not surprising that, despite aggressive implementation of preventive screenings and preventive measures, health disparities persist. For example, African American women continue to suffer from higher breast cancer mortality rates despite standardized guidelines for screening, surveillance, and treatment ((CDC), 2014).

Other than in sociological and psychological research, limited focus has been given to co-existing environmental and social factors that may increase risk for acquiring certain health conditions. Women commonly endure a wide range of stressors and role changes during midlife including, but not limited to, raising grandchildren, empty nest syndrome, employment changes, or caring for an elderly parent (Seib, Whiteside, Lee, et al., 2014). A firm understanding of stressors commonly experienced among contemporary midlife African American women is necessary to mitigate health disparities and promote early intervention.

Therefore, the purpose of this mixed-methods study is to evaluate the changes in perceived stress from late pre-menopause to post menopause and to identify the most significant life stressors perceived in a cohort of African American women. The women recruited for this study took part in the UCSF Midlife Women's Health Study conducted from 1996 to 2005 and answered questions about stress and discrimination while still pre-menopausal (Choi, Guiterrez, Gilliss, & Lee, 2012; Gilliss et al., 2001). These participants were re-contacted post-menopause for participation in the current study.

**Theory**

This study is guided by the theory of allostasis. Allostasis is defined as "stability through change" and refers to adaptation that occurs in response to life stressors (Carlson & Chamberlain, 2005, p. 308). The concept of allostasis was developed by Sterling and Eyer to describe how social and environmental factors influence health disparities (Carlson & Chamberlain, 2005). Further development of the framework and theory of allostasis by McEwen and Wingfield (2003) allows for a deeper understanding of the effects of cumulative wear and tear on the body's systems in response to stressors and

repeated adaptation (Geronimus, Hicken, Keene, & Bound, 2006; McEwen & Wingfield, 2003). Failure to adapt and maintain internal balance leads to infection, illness, or symptom expression (McEwen, 2012).

The theory of allostasis uses a systematic framework to understand the long-term effects of stress. Symptom expression and adverse health outcomes may occur from continual exposure and adjustment to chronic stressors. Everyday social and psychological stressors such as discrimination and bias have been shown to affect health outcomes (Chae et al., 2014; Giurgescu et al., 2015). Identification of key stressors for specific population groups is a key step prior to exploration of outcomes; thereby providing a practical basis for future research and intervention.

**UCSF Women's Health Study**

The University of California San Francisco (UCSF) Midlife Women's Health Study consisted of a multicultural sample (European American, Latin American, and African American) of community-dwelling women living in the San Francisco Bay Area. Women included in the study were between 40 and 50 years of age and, still experiencing regular menstrual periods. Women who self-identified as having major health problems or who were taking hormone therapy at initiation of the study were excluded (Choi et al., 2012). Details of recruitment and protocol for the parent study were previously reported (Choi et al., 2012; Gilliss et al., 2001).

At baseline, there were 93 African American women in the parent study and attrition during the first two years was less than 10%. Health assessments were obtained every 6 months through one year post-hysterectomy, one-year post-initiating hormone therapy, or one year after the last menstrual period (Gilliss et al., 2001). Participants were

followed for up to 3 years in Phase 1 and an additional 2 years in Phase 2. The study concluded in 2005.

**Design and Participants**

This mixed methods study utilized self-report data obtained during Phase 1 and Phase 2 of the parent study and current data from a one-time update assessment. The UCSF Committee on Human Research (CHR) approved both the parent study and this ancillary study and informed consent was obtained prior to data collection.

The sample for this study consists of 15 African American participants from the parent study who gave permission to be re-contacted at a later date. Inclusion criteria for this study included the participants' completion of at least two time points in the parent study and be post menopause in the current study. The participants were recruited through mailings and follow up phone calls. The mailings included study information, a copy of the consent form, and questionnaires. Additional study details and questions were discussed by phone. Those who were deemed eligible for participation and who agreed to participate were asked bring it to the completed questionnaire to their scheduled in-person visit. Meetings with the researcher took place at the Clinical and Translational Science Institute (CTSI) Clinical Research Center located in the UCSF Medical Center.

**Data Analysis**

This study was designed to include both qualitative and quantitative data about perceived stress in a cohort of women across midlife (before and after menopause).

Quantitative statistical analysis: Descriptive analyses, repeated measures analysis of variance (ANOVA), and paired t-tests were used to compare clinical characteristics and perceived stress scores in pre- and post-menopause.

Qualitative content analysis: Content analysis allows examination of text data using a systematic process of coding and identification of themes (Hsieh & Shannon, 2005). A content analysis of responses to the open-ended questions was conducted (refer to Table 1). Open-ended questions were asked to facilitate detailed responses about stressors in the lives of the women, alleviating and aggravating factors, and management strategies. Written responses were read multiple times for clarity and understanding; key words and concepts were identified and categorized to identify themes.

[Place Table 1 about here]

**Measures**

Participation in this study required the completion of a self-report questionnaire booklet. Items in the questionnaire booklet included demographic questions, the Perceived Stress Scale (PSS-10), a discrimination survey, self-report of major health problems in the past year, and open-ended questions about stressors in their lives and personal management strategies.

*Perceived Stress Scale (PSS-10 item).* The 10-item version of the PSS (PSS-10) is a widely used self-report measure of perception of stress. The 10 items are rated on a scale of 0 – 4 with a maximum score of 40. Higher levels of stress correspond with higher scores. The PSS-10 has been validated in a variety of sample populations and languages. Due to its generality, results from the PSS cannot be attributed to any specific subculture of a population (Cohen, Kamarck, & Mermelstein, 1983). Cronbach alpha in Phase 1 of the parent sample was 0.88.

**Results**

Quantitative Analysis

The post-menopausal women in this sample had a mean age of 61 ± 1.36 (SD) and varied in education and income (refer to Table 2). The women were highly educated with a median income over $57,000. The mean PSS-10 score in our sample was 17 ± 6.74 (SD) in Phase 1 and 18.1 ± 6.17 (SD) currently. Current mean PSS-10 scores were correlated with education (r = -.350) and with income (r= -.501). All of the women reported experiencing discrimination due to race, social class, or gender. Four women reported sexual harassment in the past year.

Premenopausal and post-menopausal scores on the PSS-10 were highly correlated (r=.687). Repeated measures ANOVA indicated stability in mean pre-menopausal PSS-10 scores over 3 time points; within-subject differences were not significant (F = 1.09, p = .352). A paired t-test was performed comparing the mean PSS-10 scores pre-menopause to post-menopause and the difference was not significant (t = -.482, p = .638) (Table 3).

[Place table 2 about here]

Content Analysis

The participants in this sample reported a variety of stressors via written responses to the open-ended questions. The content analysis revealed six categories of stress before and after menopause: finances, caring for family members, relationships, personal health and aging, race and discrimination, and raising children. Finances and

caring for family members were the most prevalent themes. The identities of the participants were protected in the following analysis using pseudo-names.

**Finances.** The women overwhelmingly expressed concerns about finances. Prior to menopause, finance-related stress was attributed to child rearing, school, or other career goals. Single mothers were more concerned about the financial support of their children and providing a safe and nurturing environment. For example, Adele (age 62, PSS score 25) stated: *"[I] struggled to raise 2 children alone. Always working two jobs. But I persevered!"* Employment was an underlying concept noted within the responses. Employment represented independence, success, and the ability to provide for the family. The women in this cohort were, overall, well educated and with that came the added stress and responsibility related to their respective jobs. Carla (age 62, PSS score 16) shared her experience: *"[Stress included] discrimination on the job, [I was] passed over for promotion, [and there was a] lack of opportunities."*

After menopause, financial concerns were focused on securing retirement and health care costs as stated by Joan (age 62, PSS score 13): *"Primarily, I [have been] concerned about medical coverage…"* Retirement or changes in job status are common in midlife and are often associated with additional stress and life adjustments as expressed by Laura (age 61, PSS score 23): *"After menopause, the primary source of stress has been loss of working life, income, and career due to [work-related] injuries."* Some women also remained the primary source of financial support for their children, grandchildren, or extended family members despite a fixed or limited income as

expressed by Adele: *"My children did not make very good choices…I ended up raising my daughter's 3 sons..."*

**Caring for family members.** Many of the women were responsible for taking care of siblings or other family members early in their youth as did Adele*: " I experienced a great deal of stress being the oldest daughter with several siblings. I was an extension of my mother."* Post menopause, they assumed responsibility for elderly parents or ailing family members. Caring for grandchildren, children, or an aging parent is not uncommon in a matriarchal role but the added responsibility and daily demands can be overwhelming. Adele stated: *"I am currently helping with the care of my brother who has cancer. Stress seems to be a big part of my life."* and Bonnie (age 63, PSS score 25) shared: *"[I provide] care/support for an elderly parent [and] and close family member."*

**Relationships.** The women expressed that relationships also could be significant sources of stress. Before menopause many women alluded to the stress of romantic relationships, getting married, and making decisions as a couple. Yvonne (age 62, PSS score 22) stated: *"[Stress came with] partnering to raise children and fear for their long-term work."* Other comments spoke to the presence (or lack of) support received from spouses or significant others as with Inez (age 62, PSS score 22):*"[I experienced stress from] marital conflicts over parenting styles."* Post-menopause, the women also spoke to the importance of family dynamics and the likelihood of stress caused by conflict between family members.

**Personal health and aging.** Aging and health-related themes were prevalent among the women's responses about post-menopause. Midlife is often a time during which issues of health and mortality become more relevant. There are multiple social,

family, and personal circumstances that may complicate existing issues or magnify their importance. For example, Claudette (age 59, PSS score 16) noted*: "The empty nest was hard to deal with. Nobody to [fuss over] meant focusing on myself."* A wide variety of issues were noted among the women in this cohort as well as a wide variety of responses to the challenges they presented:

> *"[I experienced stress related to]…social isolation due to difficulty using the new technology, the physical and emotional effects of aging and being post menopausal…worried about finances and who will take care of me when I am very old."* (Laura)

**Racism, sexism, and discrimination.** Race and gender issues persist within the United States and around the world. Therefore, it is not a surprise that race and gender based discrimination were cited as sources of stress by the women in this sample. Social and environmental stressors such as these may persist throughout life and be affected by socioeconomic issues. Yvonne commented: *"I think race is the hidden in plain view stressor in USA life. I am Black and that has caused me stress working in a White world. Equal or perhaps worse is the fight to have my voice heard as a woman."* Women of color endure discrimination on many levels: race, ethnicity, gender, and age. The women in this cohort shared personal experiences and expressed concern for their children's future and well-being within a racist society. *"[My stress is made worse by] work environment, news of injustices for African Americans, [and concern for] the safety of [my] family."* (Alicia, age 58, PSS score 22)

**Raising children.** Intermingled within the issues of finances, relationships, and discrimination were the issues associated with raising children. Every aspect of their lives affected their ability to care for their children and provide them with opportunities for

success. This issue was prevalent despite socioeconomic status or situation. The heart-felt concerns written by Joan effectively summarized the inter-connectedness of every aspect of the lives of these women: *" I was a single parent...and I was concerned if I had died [while] my child was a minor, how she would be taken care of. I wonder[ed] as I was raising my daughter if the divorce would have lasting effects in her life."* Opal (age 62, PSS score 24) commented: *"[I experienced stress] as a mother of two bi-racial sons."*

**Stress Management.** The women were also asked to comment on their stress-relieving tactics as a part of the study. They generously provided insight into personal remedies for combating stress. "*Exercise", "praying", "taking time to participate in hobbies or activities"* they enjoy, and maintaining relationships were the most common ways to alleviate stress. Although their individual approaches varied, many expressed an understanding of the value of nurturing mind, body, and soul. For example, Joan stated: *" I am a result-oriented person and recognized that you are not in this world alone and must reach out to others to aid in positive outcomes,"* and Laura shared: *" I am in counseling weekly. I exercise and focus very hard on good nutrition and lifestyle choices. I also sing and do story-telling to give me spiritual and creative outlets to channel stress."*

Other comments included the following:

> *"[I am] engaged in outside activities with friends and co-workers...[I have] personal hobbies and am interested in the arts." (Bonnie)*
>
> *"Exercise, walk, write, make things." (Yvonne)*
>
> *"God. Prayer. Faith." (Claudette)*
>
> *"Educate yourself: I learned a lot from the first midlife study." (Carla)*

Activities or situations that worsen stress were shared as well and they were congruent with the strategies used to relieve their stress:

> *"My stress becomes worse when I lose my focus on God." (Jeanne, age 60, PSS 8)*
>
> *"Being tired or hungry, trying to appease others, not taking care of myself." (Yvonne)*
>
> *"Not getting the help you know you need" (Noel, age 60, PSS 19)*
>
> *"Feeling the need to fix everything." (Adele)*

**Discussion**

Our sample of 15 African American post-menopausal women had high-perceived stress as demonstrated by their PSS-10 scores however, these scores varied little from their pre-menopausal values. Sources of stress may have changed over time but their perceived level of stress did not. This sample of women was overwhelmingly affected by the personal demands in their lives. Family roles and responsibilities coupled with societal roles were recurring concepts. Many had assumed the role of matriarch and were caring for parents, children and/or extended family members despite having already raised their children. Race and gender played a part in their lives and was instrumental in their stress, particularly at work. Health issues were relevant post-menopause and the importance of maintaining good health was a recurring concept. Some women expressed that their health status played a role in their perceived level of stress.

Interpersonal relationships were valuable commodities in the lives of these women and these relationships were both a source of stress and stress relief. Interpersonal conflict resulted in great stress when the women felt they needed to "appease others" or when the relationship kept them from caring for "self" or resulted in

"limited time" and "not being heard". Exercise, diet, meditation, and prayer were common strategies used to reduce stress and cope with the feelings associated with stress.

The stability of the PSS-10 scores from pre- to post-menopause speaks to the continued high stress in this sample. That the scores were not higher in post menopause might speak to inherent personal characteristics or learned coping styles in this cohort. Personal characteristics influence our appraisal of stressors in our lives. The stressors verbalized by the women were not uncommon in comparison to other contemporary midlife women. The uniqueness of this cohort of women is noted in the simultaneous experience of discrimination and racism. Cultural differences in the form of matriarchal expectations and roles likely mediate and moderate the responses to stress. Race-based differences in the type of life experiences encountered and the level of perceived stress associated with a particular stressor have been documented (Vines, Ta, Esserman, & Baird, 2009).

**Strength and Limitations**

The strengths of this study include the use of comparative time points and the use of mixed methodology. Utilization of both qualitative and quantitative methods allowed for a deeper understanding of the experience of stress for this sample of women.

The nature of the qualitative data collection and analysis, however, limits our ability to draw forth an in-depth analysis of the themes or to formulate theory. The responses were written and, therefore, techniques to further explore thoughts expressed by these women or develop deeper concepts are not possible.

**Conclusions**

Stress remains a constant throughout life. The manner in which we conceptualize the stressors in our lives impacts our responses and overall ability to cope (Lazarus & Folkman, 1984). It is impossible to foresee the long-term effects of stress, however research suggests that coping styles and attitudes are instrumental in preventing adverse outcomes. If we take steps to modify the way we perceive the stressors in our lives, we may prevent adverse health outcomes, thereby decreasing disparity. The women in this study expressed proactive attitudes and recognized the benefits of relieving their stress.

Studies have shown promise in the use of stress-reducing strategies for some observed health disparities in African American women such as low birth weight and heart disease (Cooper, Thayer, & Waldstein, 2013; Jallo, Ruiz, Elswick, & French, 2014; Woods-Giscombe & Gaylord, 2014). Recognition of the uniqueness of the stressors encountered by midlife women and the key periods during which they may occur is paramount in this effort. Health care providers should take the time to address social and psychological issues in an effort to assist women in navigating through life's challenges. Acknowledgement and validation of a woman's experience is an intervention in itself and will help to build a strong provider-patient relationship. Open provider-patient communication will allow for recognition of problem stressors and facilitate effective interventions.

**References**


(CDC), C. f. D. a. P. (2014, August 27. 2014). U.S. Mortality Files, National Center for Health Statistics, from http://www.cdc.gov/cancer/breast/statistics/race.htm

Carlson, E. D., & Chamberlain, R. M. (2005). Allostatic load and health disparities: a theoretical orientation. *Res Nurs Health, 28*(4), 306-315. doi: 10.1002/nur.20084

Chae, D. H., Nuru-Jeter, A. M., Adler, N. E., Brody, G. H., Lin, J., Blackburn, E. H., & Epel, E. S. (2014). Discrimination, racial bias, and telomere length in african-american men. *Am J Prev Med, 46*(2), 103-111. doi: 10.1016/j.amepre.2013.10.020

Choi, J., Guiterrez, Y., Gilliss, C., & Lee, K. A. (2012). Physical activity, weight, and waist circumference in midlife women. *Health Care Women Int, 33*(12), 1086-1095. doi: 10.1080/07399332.2012.673658

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *J Health Soc Behav, 24*(4), 385-396.

Cooper, D. C., Thayer, J. F., & Waldstein, S. R. (2013). Coping with Racism: The Impact of Prayer on Cardiovascular Reactivity and Post-stress Recovery in African American Women. *Ann Behav Med*. doi: 10.1007/s12160-013-9540-4

Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health, 96*(5), 826-833. doi: 10.2105/ajph.2004.060749

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., & Murrell, N. (2001). Recruitment and retention of healthy minority women into community-based longitudinal research. *J Womens Health Gend Based Med, 10*(1), 77-85. doi: 10.1089/152460901750067142

Giurgescu, C., Misra, D. P., Sealy-Jefferson, S., Caldwell, C. H., Templin, T. N., Slaughter-Acey, J. C., & Osypuk, T. L. (2015). The impact of neighborhood quality, perceived stress, and social support on depressive symptoms during pregnancy in African American women. *Soc Sci Med, 130C*, 172-180. doi: 10.1016/j.socscimed.2015.02.006

Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qual Health Res, 15*(9), 1277-1288. doi: 10.1177/1049732305276687

Jallo, N., Ruiz, R. J., Elswick, R. K., Jr., & French, E. (2014). Guided imagery for stress and symptom management in pregnant african american women. *Evid Based Complement Alternat Med, 2014*, 840923. doi: 10.1155/2014/840923

Janssen, I., Powell, L. H., Jasielec, M. S., Matthews, K. A., Hollenberg, S. M., Sutton-Tyrrell, K., & Everson-Rose, S. A. (2012). Progression of coronary artery calcification in black and white women: do the stresses and rewards of multiple roles matter? *Ann Behav Med, 43*(1), 39-49. doi: 10.1007/s12160-011-9307-8

Lazarus, R. S., & Folkman, S. (1984). *Stress, Appraisal, and Coping*. New York, NY: Springer Publishing Company.

McEwen, B. S. (2012). Brain on stress: how the social environment gets under the skin. *Proc Natl Acad Sci U S A, 109 Suppl 2*, 17180-17185. doi: 10.1073/pnas.1121254109

McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. [Article]. *Hormones and Behavior, 43*(1), 2-15. doi: 10.1016/s0018-506x(02)00024-7

Seib, C., Whiteside, E., Humphreys, J., Lee, K., Thomas, P., Chopin, L., . . . Anderson, D. (2014). A longitudinal study of the impact of chronic psychological stress on health-related quality of life and clinical biomarkers: protocol for the Australian Healthy Aging of Women Study. *BMC Public Health, 14*(1), 9. doi: 10.1186/1471-2458-14-9

Seib, C., Whiteside, E., Lee, K., Humphreys, J., Tran, T. H., Chopin, L., & Anderson, D. (2014). Stress, lifestyle, and quality of life in midlife and older Australian women: results from the Stress and the Health of Women Study. *Womens Health Issues, 24*(1), e43-52. doi: 10.1016/j.whi.2013.11.004

Services, U. S. D. o. H. a. H., & (HHS). (2014, May 2014). Elimination of Health Diparities; National Prevention Strategy Retrieved April 3, 2015, from http://www.surgeongeneral.gov/initiatives/prevention/strategy/elimination-of-health-disparities.html

Vines, A. I., Ta, M., Esserman, D., & Baird, D. D. (2009). A comparison of the occurrence and perceived stress of major life events in black and white women. *Women Health, 49*(5), 368-380. doi: 10.1080/03630240903238743

Woods-Giscombe, C. L., & Gaylord, S. A. (2014). The Cultural Relevance of Mindfulness Meditation as a Health Intervention for African Americans: Implications for Reducing Stress-Related Health Disparities. *J Holist Nurs*. doi: 10.1177/0898010113519010

Zhao, Y., Kershaw, T., Ettinger, A. S., Higgins, C., Lu, M. C., & Chao, S. M. (2015). Association Between Life Event Stressors and Low Birth Weight in African American and White Populations: Findings from the 2007 and 2010 Los Angeles Mommy and Baby (LAMB) Surveys. *Matern Child Health J*. doi: 10.1007/s10995-015-1734-x

Table 1. Open-Ended Questions

1.Please comment on the primary source of stress that has been present through your life: a) **before** you had children or before menopause and b) **after** your children left home or after menopause.

2. Is there something more you would like to share about your experiences with stress in your life?

3. What do you do or think to relieve your stress?

4. What do you think makes your stress worse?

Table 2. Current Sample Demographics

| N =15 | Post menopause |
|---|---|
| | **Mean (SD)** |
| Age | 60.93 (1.49) |
| | **n (%)** |
| Education<br>-less than high school<br>-High school or GED<br>-Some college<br>-College graduate/ Professional degree | <br>1 (7.1)<br>1 (7.1)<br>2 (14.3)<br>10 (71.5) |
| Marital Status<br>-Married<br>-Living with partner/significantly involved<br>-Single/Divorced<br>-Widowed | <br>6 (42.9)<br>2 (14.3)<br><br>5 (35.7)<br>1 (7.1) |
| Income<br>< $ 30,999<br>$31 – 50,999<br>$51 – 80,999<br>> $ 81,000 | <br>3 (21.4)<br>1 (7.1)<br>2 (14.3)<br>7 (50.0)<br>1 missing |

Table 3. Individual PSS-10 Scores by Menopause Stage

| Participant | Mean PSS score (Time 4, 5, 6) Pre-menopause | Current PSS score Post-menopause |
|---|---|---|
| Claudette | 21 | 16 |
| Valerie | 9 | 10 |
| Laura | 29 | 23 |
| Carla | 15 | 16 |
| Yvonne | 29 | 22 |
| Adele | 21 | 25 |
| Bonnie | 10 | 8 |
| Anita | 19 | 22 |
| Inez | 5 | 15 |
| Camille | 14 | 28 |
| Joan | 14 | 13 |
| Alicia | 22 | 22 |
| Opal | 19 | 24 |
| Jeanne | 5 | 8 |
| Noel | -- | 19 |

Chapter 5

# The Impact of Chronic Perceived Stress on Leukocyte Telomere Length in Post-Menopausal Women

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**Abstract**

*Background:* Psychological stress is a known antecedent for adverse health outcomes and increased morbidity. Increased risk for poor health outcomes has been associated with telomere length; an accepted biological marker for aging and chronic stress. Women endure a variety of life stressors as they transition through midlife and we propose that previously identified clinical and socioeconomic determinants of health outcomes would be associated with shorter telomere length.
*Purpose:* The purpose of this pilot study was to evaluate the effects of chronic perceived stress on perceived general health status and leukocyte telomere length.
*Methods:* A sample of 39 African American and European American women who participated in the UCSF women's health study when they were pre-menopause, were re-contacted post-menopause for participation in the current study. Demographics, blood pressure measurement, and anthropometric measurements were obtained. Self-report scales included weekly exercise intensity, a discrimination survey, a perceived general health status scale, the Center for Epidemiologic Studies Depression Scale (CES-D), and the perceived stress scale (PSS-10). Peripheral whole blood samples were obtained to measure leukocyte telomere length (LTL). Demographic and comparative statistics were used to describe group differences. Three regression models were created to evaluate the variance in LTL based on demographics, clinical characteristics, and psychosocial factors.
*Results:* The overall sample had high-perceived stress (mean total PSS scores = 16) and a mean age of 61 years (SD = 1.83). African American women had significantly higher mean PSS-10 scores in comparison to European women ($t = -2.48$, $p < 0.018$). African American women were also noted to have comparatively higher body mass index and systolic and diastolic blood pressures. LTL was not significantly different between the groups but African American women had greater telomere lengths. The demographic linear regression model was significant ($F=3.25$, $p=.018$) and explained 24% of the variance in LTL. Income ($B = .748$, $p=0.006$) was identified as the only significant contributing variable within this model. The regression models accounting for clinical and psychosocial characteristics were not significant however age ($B = -.409$, $p = 0.014$ and $B = .400$, $p = 0.025$) was a significant contributor to telomere length in both models. Diastolic blood pressure ($B = -.351$, $p = 0.037$) and perceived stress ($B = -.501$, $p = .037$) were significant contributors within their respective models.
*Conclusions:* Our study results were consistent with the literature that suggests African American women have longer telomere lengths and higher perceived stress scores. The African American women in this study also demonstrated clinical characteristics commonly associated with chronic stress: high BMI and elevated blood pressures. Despite the small sample and cross-sectional nature of the study, the findings suggest that stress-reduction strategies and lifestyle interventions could prove useful during midlife to improve long-term health outcomes and decrease health disparities as income, elevated diastolic blood pressure, and perceived stress each uniquely contributed to LTL.

## Introduction

Stress is an unavoidable and persistent factor in our lives. Everyday individuals make conscious and unconscious reactionary decisions about the stressors in their lives. Regardless of the nature of the stressor, appraisal and responses are required to cope with these daily demands. The manner in which an individual responds to stress is determined, in part, by learned experience, inherent factors such as personality or genetics, and cultural or societal norms. Some individuals inherently deal with stress with few residual effects while others are not as well equipped to withstand the demands associated with a particular stressor.

Over time, stress can lead to physiological and psychological changes that increase a person's vulnerability to illness and disease. This process is best illustrated by the extensive research done on the development and progression of heart disease (Steptoe & Kivimaki, 2012). This extensive research into the relationship between stress and the development of heart disease has inspired similar research related to other disease processes and syndromes. Now, chronic stress is recognized as an antecedent to illness and new research has explored the types of stressors likely to trigger the observed adverse physiological responses. It is clear that health care professionals and communities recognize the importance of this research as evidenced by the resurgence of stress reduction strategies and the incorporation of "healthy living" components to multiple health care plans and incentive packages.

Despite extensive research, the mechanisms by which psychological/perceived stress results in physiological change remains largely unknown. The extent to which stress increases a person's (or group's) vulnerability to disease and poor health outcomes

remains unclear. Research is now focused on exploring the moderating and mediating effects of stress and its contribution to health disparities. It is clear that health disparities persist despite our best efforts, improved health care access, and technological and medical advances. Chronic perceived stress and its associated physiological changes may play a key role in increasing a person's risk for poor health outcomes. Genetic biomarkers such as leukocyte telomere length (LTL) have been used in recent literature as objective measures of the effects of subjective factors like perceived stress.

The purpose of this pilot study was to evaluate the effects of chronic perceived stress on perceived general health status and LTL. We compared prospective perceived stress levels in a sample of pre-menopausal women and their post-menopausal measure of LTL to test the hypothesis that race, age at menarche, age at menopause, current age, socioeconomic status, body mass index, perceived general health, and on-going perceived stress would be associated with shorter LTL.

**Theory**

This ancillary research analysis is based on the theory of allostasis. Allostasis is defined as "stability through change" and refers to adaptation that occurs in response to life stressors (Carlson & Chamberlain, 2005, p. 308). The concept of allostasis was developed by Sterling and Eyer to describe how social and environmental factors influence health disparities (Carlson & Chamberlain, 2005). Further development of the framework and theory of allostasis by McEwen and Wingfield (2003) allows us to understand the effects of cumulative wear and tear on the body's systems in response to repeated coping and adaptation to stress (Geronimus, Hicken, Keene, & Bound, 2006;

McEwen & Wingfield, 2003). Failure to adapt and maintain internal balance leads to infection, illness, or symptom expression (McEwen, 2012).

Symptom expression and adverse health outcomes result from continual exposure and adaptation to stressors. In response to chronic stressors, our bodies will sustain elevated levels of key enzymes and hormones that, over time, result in systemic changes. These metabolic and systemic changes can be measured and used to gauge the overall effect of stress on the body or allostatic load. Allostatic load refers to the cumulative burden of chronic stress and is measured using specific biomarkers or a combination of biomarker scores. One such marker is telomere length, a genetic marker for aging and chronic stress that will be used in this study as a proxy for adverse health outcomes.

**UCSF Women's Health Study**

The University of California San Francisco (UCSF) women's health study consisted of a multiethnic sample of community-dwelling women living in the San Francisco Bay Area. The women were between the ages of 40 and 50 and still experiencing regular menstrual periods. Women who self-identified as having major health problems or who were taking hormone therapy at initiation of the study were excluded (Choi, Guiterrez, Gilliss, & Lee, 2012). Details of recruitment and protocol were previously reported (Choi et al., 2012; Gilliss et al., 2001).

At baseline, there were 347 women in the study and attrition during the first two years was less than 10%. Health assessments were obtained every 6 months through one year post-hysterectomy, one-year post-initiating hormone therapy, or one year after the last menstrual period (Gilliss et al., 2001). Participants were followed for up to 3 years during Phase 1 and an additional 2 years in Phase 2. The study concluded in 2005.

**Study Design & Measures**

This study utilizes demographics and self-report questionnaires obtained during both the parent study and the current study. The questionnaires included perceived health status, a discrimination survey, the Center for Epidemiologic Studies Depression Scale (CES-D), and Cohen's perceived stress scale (PSS-10). Physiological measurements obtained during the current study included blood pressure, anthropometric measurements, and a blood sample for telomere measurement; a genetic marker associated with chronic stress and aging. Anthropometric measures included height, weight, waist and hip circumferences from which waist-hip ratio (WHR) and body mass index (BMI) were calculated. Standardized procedures for anthropometrics were identical to the prior study: a calibrated weight scale for weight and stadiometer for height. Height was obtained with shoes off and the participant standing against a stadiometer. Waist and hip circumferences were obtained using a tension tape and each measure was taken 3 times and averaged.

Inclusion criteria were previously established at the initial recruitment, but for this phase of the study, women must have completed at least two time points to be approached for consent to continue with this phase of the Midlife Women's Health Study. At least two prior time points, in addition to the current time point were necessary for adequate longitudinal data analysis.

**Covariates**

*Perceived Health Status.* The participants were asked to classify their health as 'excellent', 'very good', 'good', 'fair' and 'poor'. Responses were coded from 1 to 5 (1=excellent, 5 =poor). This is a general perceived health item from the SF-36. The SF-

36 is a health survey tool that has been highly validated in construct, criterion, and content.

*Center for Depressive Epidemiologic Studies Depression Scale (CES-D).* Depressive symptoms were assessed using the 20-item CES-D that asks participants to self-rate 20 symptoms on frequency of occurrence from 0 (not during the past week) to 3 (5-7 days in the past week). Scores range from 0-60 and a score of 16 or higher indicates risk for clinical depression and need for clinical follow up. The items were internally consistent in the parent sample (Cronbach alpha coefficient = 0.92).

*Cohen's Perceived Stress Scale (PSS-10 item).* The PSS is a widely used self-report instrument developed to measure the perception of stress. The 10 items are rated on a scale of 0 – 4 with a maximum score of 40. Higher levels of stress correspond with higher scores (scores greater than 20). The PSS has been validated in a variety of sample populations and languages. Due to its generality, results from the PSS cannot be attributed to any specific subculture of a population (PSS, 2013). Cronbach alpha in the parent sample was 0.88.

*Leukocyte telomere length (LTL).* Telomeres are genetic protein strands that cap the ends of chromosomes. As a cell ages, the length of the telomeres shortens. Over time, as the telomere shortens the cell (and its organism) is more susceptible to dysfunction and senescence and this process can be accelerated by stress (Chan & Blackburn, 2004). Research has yet to discover the exact pathways through which perceived stress results in accelerated telomere shortening, illness and vulnerability to disease. However, differences in aging and health status have been documented in response to life stress

(Epel et al., 2004) and a growing body of literature substantiates the use of telomere length as an objective marker for chronic stress.

Mean LTL was assessed by the UCSF Blackburn Lab using an adapted quantitative polymerase chain reaction method originally published by Cawthon (Cawthon, Smith, O'Brien, Sivatchenko, & Kerber, 2003; Lin et al., 2010). Total genomic DNA was purified using QIAamp® DNA blood Mini kit (QIAGEN, Cat#51106) from whole blood stored at -80 °C and quantified by measuring OD260. Telomere length is quantified as a ratio of telomeric product to single copy gene (T/S).

The telomere thermal cycling profile consists of: *Cycling for T(telomic) PCR: 96°C for 1 minute; denature at 96°C for 1 second, anneal/extend at 54°C for 60 seconds, with fluorescence data collection, 30 cycles. Cycling for S (single copy gene) PCR: PCR: 96°C for 1 minute; denature at 95°C for 15 seconds, anneal at 58°C for 1 second, extend at 72°C for 20 seconds, 8 cycles; followed by denature at 96°C for 1 second, anneal at 58°C for 1 second, extend at 72°C for 20 seconds, hold at 83°C for 5 seconds with data collection, 35 cycles.*

The primers for the telomere PCR are *tel1b* [5'-CGGTTT$(GTTTGG)_5$GTT-3'], used at a final concentration of 100 nM, and *tel2b* [5'-GGCTTG$(CCTTAC)_5$CCT-3'], used at a final concentration of 900 nM. The primers for the single-copy gene (human beta-globin) PCR are *hbg1* [5' GCTTCTGACACAACTGTGTTCACTAGC-3'], used at a final concentration of 300 nM, and *hbg2* [5'-CACCAACTTCATCCACGTTCACC-3'], used at a final concentration of 700 nM. The final reaction mix contains 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 200 mM each dNTP; 1% DMSO; 0.4x Syber Green I; 22 ng E. coli DNA per reaction; 0.4 Units of Platinum Taq DNA polymerase (Invitrogen Inc.) per

11 microliter reaction; 6 ng of genomic DNA. Tubes containing 26, 8.75, 2.9, 0.97, 0.324 and 0.108ng of a reference DNA (a pooled samples of leukocyte genomic DNA from 100 female donors ) are included in each PCR run so that the quantity of targeted templates in each research sample can be determined relative to the reference DNA sample by the standard curve method. The same reference DNA was used for all PCR runs.

To control for inter-assay variability, 8 control DNA samples are included in each run. In each batch, the T/S ratio of each control DNA is divided by the average T/S for the same DNA from 10 runs to get a normalizing factor. This is done for all 8 samples and the average normalizing factor for all 8 samples is used to correct the participant DNA samples to get the final T/S ratio. The T/S ratio for each sample was measured twice. When the duplicate T/S value and the initial value vary by more than 7%, the sample was run the third time and the two closest values were reported. The average CV for this study is 2.2%.

**Sample**

The sample for this pilot study consisted of 15 African American and 25 European American women all now post-menopause who participated in the prior study when pre-menopausal and had prospective measures of stress and anthropometrics. The UCSF Committee on Human Research (CHR) approved both the parent study and this ancillary pilot study and, informed consent was obtained prior to data collection. The participants were recruited for the current study through mailings and follow up phone calls. The mailings included study information, copy of consent form, and questionnaires. Additional study details and questions were discussed by phone. Those who agreed to participate were asked to complete the questionnaire and were scheduled for an in-person

visit at the UCSF Clinical Research Center during which the questionnaire would be collected and anthropometric measures and a blood sample would be obtained. Out of 40 participants, whole blood samples for LTL were collected from 39 (14 African American and 25 European American) of the 40 participants. One participant declined venipuncture and body measurements but completed all other study requirements.

**Statistical Analysis**

We performed descriptive and comparative statistical analyses (t-tests and chi square) to compare group characteristics by race/ethnicity and by menopause status. Repeated measure analysis of variance was used to evaluate the change in perceived stress scores over time. The sample was further categorized into high and low stress groups for comparison of LTL using independent t-test analysis. Regression analyses were performed to determine the variance in telomere length. Due to the small sample size, three different regressions were developed to capture variance associated with demographic characteristics, clinical characteristics, and social determinants.

**Results**

Demographics

This sample was similar demographically (refer to Table 1). The mean age for the sample was 61 years (SD = 1.83). There were no significant race-based differences for age, age at menarche, age at menopause, or age at first child. There were no significant race differences for level of education, income, marital status, general perceived health, or having a major health problem in the past year. Over half of the sample perceived their health as very good or excellent and only 20% reported having had a major health problem in the past year.

[Table 1. about here]

Clinical Characteristics

PSS scores were consistent over time for this sample of women. The mean total PSS score pre-menopause was 16 (SD 6.27) and this remained consistent for the subsample of post-menopausal women (16 ± 5.87) participating in this pilot study. Using the mean as a cutoff point, the sample was divided into high and low stress groups. The low-stress group had a mean PSS-10 score of 11 (SD=2.99) in comparison to the high-stress group with a mean PSS-10 score of 21 (SD=3.78) and this difference was significant ($t = -8.89$, $p < 0.001$). There was a significant difference in mean PSS scores by race ($t = -2.48$, $p = 0.018$) with African American women (18 ± 6.35) having higher PSS-10 scores in comparison to European American (14 ± 5.12) women in the sample. BMI ($p = .001$), mean systolic blood pressure ($p = .024$) and mean diastolic blood pressure ($p = .026$) were significantly different by race while WHR was not significant. Compared to European American women, African American women had higher BMI and perceived stress scores. Perceived stress scores were correlated with BMI ($r = .252$, $p = .117$).

Mean LTL for the total sample was 0.951 (SD = .147). Telomere length had a significant inverse relationship with age ($r = -.371$, $p = .020$) but telomere length was not significantly different by race. Neither age at menarche or age at menopause was related to telomere length in this sample.

[Table 2. about here]

Predictors of Leukocyte Telomere Length

A regression analysis was performed to evaluate the variance in LTL. Because of the small sample size, the first model tested the variance in LTL due to demographic variables of age, race, education, marital status, and annual income. The regression model was significant (F=3.25, p=.018) and accounted for approximately 24% of the variance in telomere length. Income was the only significant contributing variable in the model (B = .748, p=0.006).

The second regression model tested the variance in LTL due to age, age at menarche, age at menopause, BMI, waist-hip ratio, and systolic and diastolic blood pressure. This regression was not significant but age (B = -.410, p = .018) and diastolic blood pressure (B = -.350, p = .044) were significant within the model.

The third regression model tested the variance in LTL due to age, level of physical activity, general health perception, discrimination, frequency of depressive symptoms, and perceived stress. This model also was not significant. However age (B=-.400, P =.027) and mean PSS scores (B = -.501, p = .037) were significant predictors within the model.

[Table 3, 4, 5 about here]

**Discussion**

The women in our sample were similar in many demographic and clinical characteristics despite race. There were no statistically significant differences in demographic variables within this small sample. However, race-based differences were noted in the perception of stress. African American women had higher perceived levels of stress compared to European American women. Clinically, African American women had greater BMIs, and blood pressures.

There were no significant race-based differences in LTL however, consistent with the literature, African American women in this sample had longer LTL in comparison to the European American women. The current literature suggests that although African Americans may have longer telomeres, they demonstrate a faster rate of telomere length shortening over time (Rewak et al., 2014; Zhu et al., 2011).

As expected, age was a contributing factor in telomere length. However income minimized its effects in the regression model including demographics. This finding suggests that socioeconomic status may have a profound mediating effect over time. Low socioeconomic status has been linked to adverse health outcomes and increased risk for the development of certain health conditions (Carroll, Diez-Roux, Adler, & Seeman, 2013; Giurgescu et al., 2015; Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010)

Diastolic blood pressure was noted to be a significant contributor to variance in telomere length when controlling for other key clinical characteristics. Causation is unable to be determined in this study but this finding suggests a bidirectional relationship between blood pressure and chronic stress. Elevated diastolic blood pressure has been linked to perceived stress and chronically elevated diastolic blood pressure may result in

increased oxidative stress and shorter telomere length (Bhupatiraju et al., 2012; Rizvi, Raza, & Mahdi, 2014).

Finally, perceived stress was significantly related to LTL in our final model that included psychosocial factors as potential predictors. Given the considerable literature in support of the adverse effects of perceived stress on LTL, it is not surprising that this variable uniquely contributed to the variance in LTL (Carlson & Chamberlain, 2005; Chae et al., 2014; Epel et al., 2004; Giurgescu et al., 2015). Given the higher perceived stress scores, greater BMI and blood pressures, and income and education disparities observed for the African American women in the sample, shorter telomere length would be expected. The longer telomere length observed for these post-menopausal African American women is encouraging as it may indicate that interventions implemented during (and prior to) midlife may have potential for stabilizing the rate of telomere shortening and decreasing risk of co-morbid conditions or health-related complications. Recent literature suggests that stress-reducing strategies and certain life-style changes may be effective in maintaining telomere length and minimizing risk of adverse health outcomes (Hoge et al., 2013; Puterman et al., 2010; Takahashi et al., 2013).

**Limitations**

This study is limited by its cross-sectional design and small sample size. Telomere measurements over time and a larger sample could have improved the depth of this study and its statistical power.

**Conclusions**

Socioeconomic factors (income), age, blood pressure, and psychosocial factors (perceived stress) were influenced telomere length in this small sample of African

American and European American women. There were no significant differences in LTL between African American and European American women. Although the literature suggests that African Americans experience a more rapid decline in LTL over time, African Americans in this sample had a greater mean telomere length. As LTL has been shown to predict disease risk and morbidity, we propose that midlife may be an optimal time for intervention to slow the rate of decline and improve individual health outcomes. Stress-reduction strategies and anticipatory guidance during midlife could potentially impact the health status trajectory for these women during the menopause transition and beyond.

**Recommendations**

Our findings suggest that interventions during midlife have the potential to stabilize cumulative effects of stress over time. Further research to evaluate the effectiveness of preventive interventions such as stress-reduction strategies is recommended. Inclusion of multiple biomarkers measured over time could improve the depth of any future studies in pre- and post-menopausal women.

**References**


Bhupatiraju, C., Saini, D., Patkar, S., Deepak, P., Das, B., & Padma, T. (2012). Association of shorter telomere length with essential hypertension in Indian population. *Am J Hum Biol, 24*(4), 573-578. doi: 10.1002/ajhb.22264

Carlson, E. D., & Chamberlain, R. M. (2005). Allostatic load and health disparities: a theoretical orientation. *Res Nurs Health, 28*(4), 306-315. doi: 10.1002/nur.20084

Carroll, J. E., Diez-Roux, A. V., Adler, N. E., & Seeman, T. E. (2013). Socioeconomic factors and leukocyte telomere length in a multi-ethnic sample: findings from the multi-ethnic study of atherosclerosis (MESA). *Brain Behav Immun, 28*, 108-114. doi: 10.1016/j.bbi.2012.10.024

Cawthon, R. M., Smith, K. R., O'Brien, E., Sivatchenko, A., & Kerber, R. A. (2003). Association between telomere length in blood and mortality in people aged 60 years or older. *Lancet, 361*(9355), 393-395. doi: 10.1016/s0140-6736(03)12384-7

Chae, D. H., Nuru-Jeter, A. M., Adler, N. E., Brody, G. H., Lin, J., Blackburn, E. H., & Epel, E. S. (2014). Discrimination, racial bias, and telomere length in african-american men. *Am J Prev Med, 46*(2), 103-111. doi: 10.1016/j.amepre.2013.10.020

Chan, S. R., & Blackburn, E. H. (2004). Telomeres and telomerase. *Philos Trans R Soc Lond B Biol Sci, 359*(1441), 109-121. doi: 10.1098/rstb.2003.1370

Choi, J., Guiterrez, Y., Gilliss, C., & Lee, K. A. (2012). Physical activity, weight, and waist circumference in midlife women. *Health Care Women Int, 33*(12), 1086-1095. doi: 10.1080/07399332.2012.673658

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proc Natl Acad Sci U S A, 101*(49), 17312-17315. doi: 10.1073/pnas.0407162101

Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health, 96*(5), 826-833. doi: 10.2105/ajph.2004.060749

Gilliss, C. L., Lee, K. A., Gutierrez, Y., Taylor, D., Beyene, Y., Neuhaus, J., & Murrell, N. (2001). Recruitment and retention of healthy minority women into community-based longitudinal research. *J Womens Health Gend Based Med, 10*(1), 77-85. doi: 10.1089/152460901750067142

Giurgescu, C., Misra, D. P., Sealy-Jefferson, S., Caldwell, C. H., Templin, T. N., Slaughter-Acey, J. C., & Osypuk, T. L. (2015). The impact of neighborhood quality, perceived stress, and social support on depressive symptoms during pregnancy in African American women. *Soc Sci Med, 130C*, 172-180. doi: 10.1016/j.socscimed.2015.02.006

Hoge, E. A., Chen, M. M., Orr, E., Metcalf, C. A., Fischer, L. E., Pollack, M. H., . . . Simon, N. M. (2013). Loving-Kindness Meditation practice associated with longer telomeres in women. *Brain Behav Immun, 32*, 159-163. doi: 10.1016/j.bbi.2013.04.005

Lin, J., Epel, E., Cheon, J., Kroenke, C., Sinclair, E., Bigos, M., . . . Blackburn, E. (2010). Analyses and comparisons of telomerase activity and telomere length in human T and B cells: insights for epidemiology of telomere maintenance. *J Immunol Methods, 352*(1-2), 71-80. doi: 10.1016/j.jim.2009.09.012

McEwen, B. S. (2012). Brain on stress: how the social environment gets under the skin. *Proc Natl Acad Sci U S A, 109 Suppl 2*, 17180-17185. doi: 10.1073/pnas.1121254109

McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. [Article]. *Hormones and Behavior, 43*(1), 2-15. doi: 10.1016/s0018-506x(02)00024-7

Puterman, E., Lin, J., Blackburn, E., O'Donovan, A., Adler, N., & Epel, E. (2010). The power of exercise: buffering the effect of chronic stress on telomere length. *PLoS One, 5*(5), e10837. doi: 10.1371/journal.pone.0010837

Rewak, M., Buka, S., Prescott, J., De Vivo, I., Loucks, E. B., Kawachi, I., . . . Kubzansky, L. D. (2014). Race-related health disparities and biological aging: does rate of telomere shortening differ across blacks and whites? *Biol Psychol, 99*, 92-99. doi: 10.1016/j.biopsycho.2014.03.007

Rizvi, S., Raza, S. T., & Mahdi, F. (2014). Telomere length variations in aging and age-related diseases. *Curr Aging Sci, 7*(3), 161-167.

Seeman, T., Epel, E., Gruenewald, T., Karlamangla, A., & McEwen, B. S. (2010). Socio-economic differentials in peripheral biology: cumulative allostatic load. *Ann N Y Acad Sci, 1186*, 223-239. doi: 10.1111/j.1749-6632.2009.05341.x

Steptoe, A., & Kivimaki, M. (2012). Stress and cardiovascular disease. [Research Support, Non-U.S. Gov't

Review]. *Nat Rev Cardiol, 9*(6), 360-370. doi: 10.1038/nrcardio.2012.45

Takahashi, M., Miyashita, M., Park, J. H., Kawanishi, N., Bae, S. R., Nakamura, Y., . . . Suzuki, K. (2013). Low-volume exercise training and vitamin E supplementation attenuates oxidative stress in postmenopausal women. *J Nutr Sci Vitaminol (Tokyo), 59*(5), 375-383.

Zhu, H., Wang, X., Gutin, B., Davis, C. L., Keeton, D., Thomas, J., . . . Dong, Y. (2011). Leukocyte telomere length in healthy Caucasian and African-American adolescents: relationships with race, sex, adiposity, adipokines, and physical activity. *J Pediatr, 158*(2), 215-220. doi: 10.1016/j.jpeds.2010.08.007

Table 1. Demographic and Clinical Characteristics

| Demographic & Clinical Characteristics | African American n = 15 | European American n = 25 | Overall sample N = 40 |
|---|---|---|---|
| Age (yrs) | 60.93 ± 1.49 | 61.56 ± 1.98 | 61.33 ± 1.83 |
| Age at Menarche (yrs) | 13.14 ± 1.41 | 12.54 ± 1.62 | 12.75 ± 1.55 |
| Age at Menopause (yrs) | 50.71 ± 6.23 | 52.40 ± 3.67 | 51.78 ± 4.77 |
| Age at First Child (yrs) | 27.10 ± 7.97 | 28.25 ± 5.90 | 27.73 ± 6.76 |
| Education (%) | | | |
| < high school | 1 (7.1) | 0 | 1 (2.6) |
| High school or GED | 1 (7.1) | 1 (4) | 2 (5.1) |
| Some college | 2 (14.3) | 0 | 2 (5.1) |
| College graduate/ professional training | 10 (71.5) | 24 (96.0) | 34 (87.2) |
| Marital Status (%) | | | |
| Married | 6 (40.0) | 15 (60.0) | 21 (52.5) |
| Partnered | 2 (13.3) | 1 (4.0) | 3 (7.5) |
| Single/Divorced | 7 (46.7) | 9 (36.0) | 16 (40) |
| Widowed | 0 | 0 | 0 |
| Income (%) | | | |
| < $ 30,999 | 3 (23.1) | 1 (4.2) | 4 (10.8) |
| $31 – 50,999 | 1 (7.7) | 0 | 1 (2.7) |
| $51 – 80,999 | 2 (15.4) | 7 (29.2) | 9 (24.3) |
| > $ 81,000 | 7 (53.8) | 16 (66.7) | 23 (62.2) |
| | 2 missing | 1 missing | |
| Perceives general health as ‘excellent’ (1) or ‘very good’ (2) | 6 (40.0) | 14 (58.3) | 20 (51.3) |
| Major health problem in the past year | 2 (13.3) | 6 (24.0) | 8 (20.0) |

Table 2. Perceived Stress and Telomere Length (mean ± SD)

| Perceived Stress & Telomere Length | African American n = 14 | European American n = 25 | Overall sample N = 39 |
|---|---|---|---|
| Mean PSS scores | 18 ± 6.35 | 14 ± 5.12 | 16 ± 5.87 |
| Mean BMI | 33 ± 5.50 ** | 27 ± 4.39 | 29 ± 5.51 |
| Mean WHR | .86 ± .06 | .84 ± .05 | .848 ± .06 |
| Mean SBP | 137 ± 15.86* | 117 ± 29.18 | 125 ± 26.53 |
| Mean DBP | 75 ± 9.96 * | 67 ± 12.35 | 70 ± 12.16 |
| Telomere length | .971 ± .140 | .940 ± .152 | .95 ± .147 |

* p value ≤ .05 , ** p value ≤ .001

Table 3. Linear Regression Summary: LTL and Demographics

| Explained Model variance: R square = .243, F = 3.25, p = 0.018 | | Standardized Coefficients | | | Correlations | | |
|---|---|---|---|---|---|---|---|
| | | Beta | t | Sig. | Zero-order | Partial | Part |
| 1 | (Constant) | | 2.808 | .009 | | | |
| | Age | -.255 | -1.606 | .119 | -.371 | -.281 | -.236 |
| | ethnicity | -.150 | -.921 | .364 | -.102 | -.166 | -.135 |
| | Education | -.394 | -1.788 | .084 | .014 | -.310 | -.263 |
| | household income before taxes | .748 | 2.951 | .006 | .345 | .474 | .434 |
| | marital status now | .159 | .859 | .397 | -.071 | .155 | .126 |

Dependent Variable: Telomere Length

Table 4. Linear Regression Summary: LTL and Clinical Characteristics

| Explained Model Variance: R square= .124, F= 1.77, p= .130 | | Standardized Coefficients | | | Correlations | | |
|---|---|---|---|---|---|---|---|
| | | Beta | t | Sig. | Zero-order | Partial | Part |
| 1 | (Constant) | | 2.938 | .006 | | | |
| | Age | -.409 | -2.592 | .014 | -.371 | -.422 | -.394 |
| | waist/hip ratio | .202 | 1.095 | .282 | .169 | .193 | .166 |
| | systolic b/p | .087 | .511 | .613 | -.014 | .091 | .078 |
| | diastolic b/p | -.351 | -2.175 | .037 | -.259 | -.364 | -.330 |
| | body mass index | .118 | .622 | .538 | .077 | .111 | .094 |
| | Age at Menarche | .013 | .079 | .937 | .047 | .014 | .012 |
| | Age at Menopause | .002 | .011 | .992 | .032 | .002 | .002 |

a. Dependent Variable: Telomere Length

Table 5. Linear Regression Summary: LTL and Psychosocial Characteristics

| Explained Model Variance R square 0.118, F= 1.80, p= 0.132 | | Standardized Coefficients | | | Correlations | | |
|---|---|---|---|---|---|---|---|
| | | Beta | t | Sig. | Zero-order | Partial | Part |
| 1 | (Constant) | | 3.472 | .002 | | | |
| | Age | -.393 | -2.323 | .027 | -.371 | -.390 | -.364 |
| | cesd T8 | .284 | 1.326 | .195 | .134 | .235 | .207 |
| | Total PSS | -.501 | -2.186 | .037 | -.120 | -.371 | -.342 |
| | Regular activity once a week? | -.142 | -.836 | .410 | -.050 | -.151 | -.131 |
| | genhlth | .088 | .515 | .610 | -.028 | .094 | .081 |
| | TotalDiscrimination | .198 | 1.128 | .268 | .084 | .202 | .177 |

a. Dependent Variable: Telomere

# Chapter 6

# Doctoral Dissertation: Discussion and Implications

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**Discussion and Implications**

This research has emerged from years of clinical observation in office, acute care, and community settings. Stress-related symptoms such as anxiety, depression, and gastrointestinal problems were prominent yet women appeared more distressed and their symptoms more difficult to manage. Midlife women appeared to shoulder heavier burdens of stress and responsibility and yet there was little focus in managed health care to assist with the sometimes-overwhelming physical and psychological changes that occur during this critical life stage and transition. Even the vasomotor symptoms commonly associated with the menopause transition were more difficult to treat in women identified as experiencing stress-related symptoms. Certainly more could be done to prepare women for this inevitable life stage transition; improve their overall health and sense of well-being while decreasing morbidity. Further research was needed to evaluate the vulnerability of this particular subgroup of the American population that is so essential to the success of our society as a whole.

Life expectancy continues to rise and midlife is now truly that; a midlife transition where new beginnings and can take place and new goals can be realized. It is no longer unrealistic to plan to live into our $9^{th}$ or even $10^{th}$ decade but with age comes an inevitable risk of health decline and we are faced with the reality of our own mortality. Unfortunately, these health risks exist in unequal distribution and some persons and populations are more likely to develop certain health conditions, suffer more complications, and experience poorer health outcomes. Since modern medicine, improved healthcare access, and technology have failed to eliminate existing health

disparities, research is needed to identify subgroups of our population at risk of experiencing adverse health outcomes.

This dissertation study is comprised of four manuscripts intended to tell the story of a multiethnic cohort (African American, European American, and Latina) of midlife women from the San Francisco Bay Area before and after menopause. All women were participants in the UCSF Midlife Women's Health Study and had agreed to be re-contacted for future study participation. At the close of the study in 2005, there were 158 women remaining in the study, all of whom were pre-menopausal. The women were re-contacted in 2015 and 15 African American and 25 European American women with a mean age of 61 years agreed to participate in this current study.

Chapters 2 and 3 of this dissertation research use secondary analysis of data from the parent study to focus on symptom experience in the remaining sample of 158 women. Bladder and sleep symptoms were specifically chosen for evaluation as these symptoms have been shown to increase with age and are associated with midlife. Chapter 4 includes a qualitative content analysis of responses to open-ended questions intended to promote disclosure of unique life stressors before and after menopause, management strategies, and stress perception for the 15 African American women in the current sample. Finally, Chapter 5 includes a quantitative analysis of current data that attempts to bring the research full circle with an evaluation of the effects of multiple demographic, psychosocial and, clinical factors on leukocyte telomere length; a genetic biomarker acknowledged for its strong association with aging and chronic perceived stress. This final chapter provides a synthesis of the current research study, its findings, implications for future research and, potential clinical use.

Chapter 2 documented the results of a secondary analysis intended to provide insight into the experience of bladder symptoms in the remaining sample from the parent study. The sample was multi-racial and comprised of African American, Latina, and European American midlife women. Symptoms of nocturia and urinary incontinence were prevalent throughout the sample however there were distinct race-based differences. Being African American was associated with a higher frequency of nocturia compared to the Latina and European American women in the sample while being African American also appeared to be protective for experiencing urinary incontinence. Neither of these findings were statistically significant nor was causation able to be determined due to the retrospective methodology.

Interestingly, late pre-menopause stage was a significant factor in the experience of nocturia. Late pre-menopausal women in the cohort were more likely to experience nocturia than peri-menopausal women. Of those women who experienced nocturia, one-third reported awakening 3 or more times during the week to void. Although more research is needed, chapter 2 highlighted the importance of reproductive stage and race in the occurrence of nocturia and urinary incontinence during midlife. Due to the prevalence of nocturia (73%) and urinary incontinence (50%) in the sample, these bladder symptoms are likely to persist into post-menopause and be associated with significant morbidity.

As a result of the overwhelming incidence of nocturia experienced by the late pre-menopausal women in the sample, another secondary analysis was performed to evaluate the effect of nocturia and related factors on sleep quality and sleep disturbance. Sleep disturbance is associated with significant morbidity within the United States and nocturia-related sleep disturbance has been shown to increase with age. Chapter 3 is the

sister manuscript to Chapter 2 and provided details of the secondary analysis of sleep quality in the sample.

The sample consisted of the 72 pre-menopausal women had a mean score of 5.29 (SD=2.89) on the Pittsburg Sleep Quality Index (PSQI); this score is indicative of poor sleep quality. Although nocturia was associated with body mass index, it was not associated with sleep quality or sleep hours for the women in this sample. Race was not found to be associated with sleep quality but there were distinct race differences in sleep hours. European American women reported a greater number of sleep hours compared to the African American and Latina women in the sample. In contrast, the African American women reported the least number of sleep hours and were noted to have greater BMIs, a factor associated with nocturia.

Linear regression models created to evaluate the variance in sleep quality and sleep hours were not significant. However, perceived general health status was a significant contributing factor within the model evaluating variance in sleep quality and race was a significant contributing factor in the model evaluating variance in sleep hours. Overall, the findings highlighted race-based differences and the inter-relatedness of known risk factors for sleep disturbance. The African American women were more likely to be obese, report fewer sleep hours, and have higher FSH levels that may indicate potential for sleep disturbance related to vasomotor symptoms. In addition, significant differences were noted in education, an accepted proxy for socioeconomic status. All of the factors combined may potentially increase a person's risk for sleep disturbance as socioeconomic factors, vasomotor symptoms, bladder symptoms, and BMI have all been

reported in the literature as risk factors for sleep disturbance (Appelhans et al., 2013; Furtado et al., 2012; Hall et al., 2009; Kravitz et al., 2008).

Chapter 4 presented the findings from a mixed-methods study based on the subset of 15 African American women (mean age 61 ± 1.49) who agreed to participate in the current study. These women completed a self-report survey booklet that contained questionnaires about perceived stress and discrimination as well as open-ended questions. The open-ended questions were intended to illicit thoughtful responses about the unique stressors in their lives, perceptions of stress, and coping mechanisms before and after menopause.

For the quantitative portion of this study, the women's scores on the Perceived Stress Scale (PSS-10) were compared pre-menopause to post-menopause. Their scores were found to be consistent over time. Overall, this sample of African American women was found to be demographically similar and they most reported experiencing discrimination based upon race, social status, or gender. The qualitative portion of this study used content analysis to establish concepts and themes found within the written responses. Six themes were noted within the types of stress experienced by this subset of African American women: finances, caring for family members, relationships, personal health and aging, race and discrimination, and raising children. These themes remained prominent for these women from pre-menopause to post-menopause although the context within which they were experienced changed.

The women also provided insight into factors that worsened and improved their stress. Stress was worsened by a lack of control, not "having a voice", fatigue, hunger, and lack of exercise among others. Stress was improved through spiritual faith, exercise,

creative expression, and support from family and friends. Overall the stressors experienced by these contemporary African American women were not unlike the stressors experienced by most midlife women. However, the underlying thread that permeated their lives and likely enhanced their stress levels was discrimination, whether it pertained to their lives or the lives of their children and families. Therefore, despite the inability to further develop the concepts and themes presented in these written responses or to formulate theory, this qualitative analysis provided insight into the most relevant stressors in the lives of these African American women and set the stage for recognition and validation of unique stressors that may lend them more vulnerable to its effects. These stressors were noted across time and early intervention may prove beneficial in decreasing morbidity associated with its effects.

The qualitative aspects associated with the mixed-methods study outlined in Chapter 4 is a great preamble to Chapter 5 which described the findings of the final manuscript from this dissertation research. A quantitative research study was conducted using the entire sample of women who agreed to participate in this ancillary pilot study. Forty African American and European American women with a mean age of 61 years (SD = 1.83) took part. The women were compared based on race and perceived stress levels. There were no statistically significant demographic differences between the two race groups. The mean total PSS-10 score was 16 and this was established as the cutoff for high and low stress within the sample.

High stress was significantly associated with race; African American women had higher mean total PSS-10 scores in comparison the European American women in the sample. For the African American women higher mean total PSS-10 scores, higher BMIs,

and greater systolic and diastolic blood pressures were also found to be statistically significant in comparison to European American women.

As expected, mean leukocyte telomere length (LTL) was inversely associated with age but LTL was not associated with race, age at menarche, or age at menopause. Three regression models were created due to the small sample size to account for variance in LTL due to demographic characteristics, clinical characteristics, and psychosocial characteristics. The regression model used to account for unique contribution from demographic characteristics was the only statistically significant model and accounted for 24% of the variance in LTL. Income was the only significant variable in the model and its significance highlights the complexity of life stress and its long-term effects across time. Income represents security, social mobility, and support in a materialistic society and is often the source of much stress and "distress".

Although the remaining two regression models created to account for the variance in LTL contributed by clinical and psychosocial factors were not significant. Age was a statistically significant contributor to both models. This further validates the use of LTL as a biomarker for aging and also validates the findings within this study. Diastolic blood pressure was also a significant contributor to LTL while controlling for other clinical factors but this likely represents a bidirectional relationship between physiological stress and LTL and illustrates the concepts outlined within the theory of allostasis.

Finally, perceived stress scores significantly contributed to the regression model for variance in LTL while controlling for other psychosocial characteristics. As hoped, the chapters within this dissertation bring the research full-circle to the effects of chronic

perceived stress. Despite the fact that the overall model was not significant, perceived stress uniquely accounted for 34% of the variance in LTL.

Clinical Implications

There are multiple clinical implications to be taken from the results of this study. Chronic stress is detrimental to our health and has been shown to contribute to adverse health outcomes, disease incidence, and disease progression (Epel et al., 2004; Steptoe & Kivimaki, 2012). Bladder and sleep symptoms were prevalent in this cohort of women prior to menopause and although causation cannot be determined from this study, there were associations between perceived stress and accepted measures of stress such as BMI, socioeconomic status, and race. Midlife women were identified as a vulnerable population and clearly African American women were noted to be a more vulnerable subset within this population of women.

Nurses and other health care clinicians would do well to appreciate the effects of stress and assist their patients in navigating through stressful issues through education and appropriate resource referrals. Just as we provide anticipatory guidance from infancy to early adulthood, we should prepare women as they enter midlife and begin to transition to menopause. Recognition of relevant stressors and open discussion will facilitate the provider-patient relationship. Validation of the patients' stress and symptom experience is a valuable and powerful intervention. Incorporation of a screening tool to assist in anticipating the need for referrals and/or use of community or insurance-based resources is recommended.

Health Policy Implications

Although stress-relieving strategies such as "mindfulness" and meditation have seen resurgence in popularity, these methods and concepts are not yet shared equally at all socioeconomic levels. Access to and education about alternative treatments and lifestyle medicine is lacking. Health care providers should lobby for incorporation of such programs within their communities and the health management networks with whom they contract. In addition, providers should familiarize themselves with the resources available for efficient referral and patient education. Availability of health care services result from supply and demand and proven outcomes; none of which will occur without the investment of all members of the health care team to utilize these resources.

Directions for Future Research

Further analysis of the data obtained in this study is intended. Anthropometric data obtained before and after menopause will be compared for a more in-depth analysis of changes in waist-hip ratio and body mass index over time as these biomarkers have been determined to be responsive to stress and are indicative of an increased health risk for co-morbid conditions, health-related complications, and poor health outcomes.

Extension of this research to other vulnerable populations is needed. As our society continues increase in diversity, we will need to identify those stressors that make them more certain populations vulnerable. Early identification may prevent the occurrence of widening health disparities. Further validation of findings associated with chronic perceived stress through research will transcend financial obstacles and offer continued growth and acceptance of early screening and stress management strategies.

Finally, continued research in stress-related symptom experience and symptom expression will allow for expansion of this research into a variety of disciplines and

promote interdisciplinary collaboration. The research conducted in this dissertation is hoped to provide a springboard for continued research of stress-related illness, symptom experience, vulnerable populations, and health disparities.

**References**


Appelhans, B. M., Janssen, I., Cursio, J. F., Matthews, K. A., Hall, M., Gold, E. B., . . . Kravitz, H. M. (2013). Sleep duration and weight change in midlife women: the SWAN sleep study. *Obesity (Silver Spring), 21*(1), 77-84. doi: 10.1002/oby.20251

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proc Natl Acad Sci U S A, 101*(49), 17312-17315. doi: 10.1073/pnas.0407162101

Furtado, D., Hachul, H., Andersen, M. L., Castro, R. A., Girao, M. B., & Tufik, S. (2012). Nocturia x disturbed sleep: a review. *Int Urogynecol J, 23*(3), 255-267. doi: 10.1007/s00192-011-1525-x

Hall, M. H., Matthews, K. A., Kravitz, H. M., Gold, E. B., Buysse, D. J., Bromberger, J. T., . . . Sowers, M. (2009). Race and financial strain are independent correlates of sleep in midlife women: the SWAN sleep study. *Sleep, 32*(1), 73-82.

Kravitz, H. M., Zhao, X., Bromberger, J. T., Gold, E. B., Hall, M. H., Matthews, K. A., & Sowers, M. R. (2008). Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. *Sleep, 31*(7), 979-990.

Steptoe, A., & Kivimaki, M. (2012). Stress and cardiovascular disease. [Research Support, Non-U.S. Gov't

Review]. *Nat Rev Cardiol, 9*(6), 360-370. doi: 10.1038/nrcardio.2012.45

**Appendix 1.** Dissertation Proposal

Dissertation Proposal

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## Introduction

### Problem Statement

Gender and race-based health disparities remain a significant problem within the United States and around the world. Despite new knowledge of disease progression, risk factors, preventive strategies, disease management and genetics, health disparities remain for race, gender, and ethnicity. Society has failed to make strides in eliminating these disparities. Our knowledge has not translated into actionable plans that can be implemented effectively at individual, community, state, or national levels. We continue to see disproportionately poor outcomes in health and mortality statistics along race and gender lines. According to the Center for Disease Control and Prevention (CDC, 2010) statistics, life expectancy at birth for women in the United States is 81.0 years while it is only 76.2 years for men. The life expectancy of African American women is 3.3 years lower than European American women while African American men have a life expectancy that is 4.7 years lower than European American males (CDC, 2010).

Documentation of disparities is not enough to combat the problem as there remain factors at play that extend beyond race and sex. Multiple factors have been studied in the effort to better understand the complexity of the problem. Some researchers have chosen to focus on the influence of socioeconomic factors (Olsansky et al., 2012; Needham et al., 2013) while others investigate hormonal influences (Zhu et al., 2011), vitamin deficiencies (Zhu et al., 2012), life adversity and the chronicity of stressors (Drury et al., 2012). Olshansky et al. (2012) report life expectancy to be shorter for those who are the least educated. Their study found that US men and women with less than a twelfth grade education had life expectancies similar to men and women who lived in the 1950s and

1960s and when race was considered, “the results were even more striking” (Olsansky et al., 2012). This is discouraging news as global life expectancy continues to increase. The World Health Organization (WHO) estimates that life expectancy has increased by 8 hours every day over the past 20 years (Miles, 2013).

The health disparities that exist between racial groups are alarming. Statistics confirm that African Americans fair far worse than other racial groups as indicated by morbidity and mortality rates. Life expectancy for African Americans is lower than Whites due to higher death rates for heart disease, cancer, perinatal conditions, and stroke (Kochanek, Arias, & Anderson, 2013; CDC, 2010). These conditions represent well-researched areas for which standards of care, prevention and practice guidelines exist. Yet, the disparities remain. Factors related to low socioeconomic status such as inadequate access to healthcare, failing school systems, inner-city violence and unsafe neighborhoods contribute to the disparities and perpetuate the cycle. However when studies control for these factors, disparities persist (Olshansky et al., 2012). For example, African Americans with a college degree have a shorter life expectancy in comparison to Whites of comparable educational background (Olshansky et al., 2012).

The solution to this phenomenon has eluded researchers. The complexity of the human condition and the influence of health and socioeconomic factors are often underestimated. Poverty itself does not cause illness, nor does receiving instruction from incompetent teachers in poorly funded schools. But there is something, perhaps about the life circumstance surrounding poverty, poorly funded schools, inadequate access to health care and, exposure to inner city violence that places certain individuals in a more precarious state of health and increases their risk for certain health conditions.

The examination of *stress perception and stress adaptation* may provide a better understanding of the risk of health disparities. An individual's health status and longevity may be determined by differences in the perception, processing, response, and adjustment to stressful environmental stimuli. Stress, coping, and adaptation have been topics of study since the early 1900s. In 1936, Hans Selye proposed his General Adaptation Syndrome which described stress as a 'universal physiological set of reactions and processes' created by the effect of some stressor (Lazarus & Folkman, 1984). Selye's colleagues recognized that our physiological responses could be triggered by personal experiences and cognitive awareness. Today psychological stress is recognized as a risk factor for adverse health outcomes. A study of caregivers found chronic maternal stress to be positively associated with biomarkers of aging (telomere length), indicating an increased risk for accelerated aging and poor health outcomes (Epel et al., 2004). Studies such as this highlight the risks associated with stress and prompt further evaluation of coping strategies and adaptation.

Differences in stress perception and coping mechanisms are associated with gender, culture and ethnicity (Lazarus & Folkman, 1984; Folkman, Lazarus, Gruen, & DeLongis, 1986). Stress and coping theory states that there is a bidirectional relationship between the environment and the person that influences the cognitive appraisal of stressful stimuli (Folkman, Lazarus, Gruen, & DeLongis, 1986). Our communities, families, and situation provide continual feedback, molding our beliefs. This dynamic relationship is a concept deserving of evaluation in the exploration of disparities in health outcomes, morbidity, and mortality. Further research into the effects of perceived stress may provide inroads to improved health outcomes, thereby decreasing disparities.

The purpose of this ancillary study is to explore the relationship between perceived stress and perceived health status among midlife African American women compared to European American women. Within the context of Lazarus and Folkman's stress and coping framework, this dissertation has 4 specific aims.

**Specific Aims**

1. Compare perceived stress and perceived general health status assessed during late pre-menopausal years with their current perception assessed post-menopause.
2. Identify key factors that best predict current perceived stress and perceived general health status in African American postmenopausal women compared to European American women of the same age.
3. Identify potential biomarkers associated with the perceived stress and perceived general health.
4. Identify commonalities among the sources of stress in the lives of post-menopausal African American women.

**Impact**

Midlife is an important point in the life course of women, and screening for risks and planning preventive health promoting interventions is an important step towards eliminating health disparities among African American women. Some studies confirm that African Americans fair far worse than other ethnicities, as indicated by morbidity and mortality rates. For example, higher rates of heart disease, cancer, perinatal conditions, and stroke account for lower life expectancy in African Americans when compared to European Americans (Kochanek, Arias, & Anderson, 2013).

Transitions in midlife may be physical (such as menopause), social (employment status) or personal (role reversals, change in family situation or structure), all of which can be stressful. The stressors experienced during midlife may place more vulnerable women at an increased risk of health issues during this time. As socioeconomic status, education and health care access have not proven to fully account for disparities in healthcare and outcomes, research into the effects of culture, ethnicity, and race on stress perception may fill a gap in the knowledge of African American women's health disparities. Given the existing health disparities in this African American subculture of midlife women, it seems clear that this phenomenon needs to be further investigated.

Little attention has been directed towards the unique stressors and perceptions that exist for African American midlife women. This proposed study hopes to open a door to a deeper understanding and inspire future research. The impact of this study is potentially great in that the stress endured by African American women may be modifiable. It is important to know which stressors may be of the greatest significance in their lives and if changes in perceived stress levels over time lead to changes in health outcomes. The incorporation of biomarkers into this study will provide an opportunity for insight into tertiary outcomes associated with stress. Preventive strategies and public health initiatives may evolve.

**Background and significance**

The African American subculture has emerged through a legacy of slavery, civil rights, segregation, discrimination, and institutionalized racism. The culture that has emerged is grounded in family, pride, spirituality, and inner strength. The 'American experience' can be significantly different for individuals of different racial and ethnic

backgrounds. An individual's ideas and perceptions are influenced by personal (culture, genetics, family) and environmental factors (Lazarus & Folkman, 1984). Past research has documented differences between African Americans and European Americans in regards to their perceptions of health status, health care and discrimination.

The contextual background associated with environmental stressors may account for the differences in experience. Theoretically, stress responses are cultivated within our society and environment through learned behavior. For African Americans, cultural practices and beliefs such as spirituality have often evolved in the face of adversity. Roles and expectations may become complicated as individuals try to maintain family and cultural norms in the context of a prejudiced society that perpetuates stereotypes and oppressive practices through institutionalized racism. Maintaining multiple roles and continued vigilance increases odds of success within society but also contributes to a heightened level of stress.

African American women have emerged as the guardians of tradition, history and culture. It is often the matriarch who steadies and guides the family through crises and celebration. Midlife African American women naturally transition into multiple roles as they are looked to for their strength and experience. These roles exist at home and in the community and may encompass work, church, volunteer, and career-oriented duties. The roles are common among all women, but for African American women these roles are complicated by race, societal expectations, biases, stereotypes, and institutionalized discriminatory practices. Far too many African American women fulfill their roles within communities plagued by violence, poverty and inadequate resources. Therefore the

challenges presented by family, societal, and community roles are strongly influenced by the environment, culture, and community in which we live.

A recent study by Perry, Harp & Ose (2013) proposed that the current research literature is lacking in depth because most researchers do not take into account the importance of chronic stressors and psychological appraisal in the lives of African American women. Their study was based on a framework of 'intersectionality'. Using a sample of 204 low-income African American women, they explored how gender and race discrimination affected stress (Perry et al., 2013). The findings from this study indicate race and gender discrimination increase susceptibility to specific stressors, resulting in a greater propensity for poor health (Perry et al., 2013). The idea that African American women (and all women of color) face unique challenges and that cumulative stress from multiple sources may contribute to morbidity and mortality is not new (Crenshaw, 1991). However, few studies have incorporated measures of stress and aging to examine the unique influence associated with life stage, race and ethnic differences.

Telomere length coordinates with risk of poor health outcomes and accelerated aging (Epel et al., 2004). Telomeres are genetic protein strands that cap the ends of chromosomes. As a cell ages, the length of the telomeres shortens. Over time, as the telomere shortens the cell is more susceptible to dysfunction and senescence and this process can be accelerated by stress (Chan & Blackburn, 2004). Research has yet to discover the exact pathways through which perceived stress results in accelerated telomere shortening, illness and vulnerability to disease. However, differences in aging have been documented in response to life stress (Epel et al., 2004), sex (Barrett & Richardson, 2011; Seifarth et al., 2012), and race (Hunt et al., 2008; Zhu et al., 2011). A

growing body of literature substantiates the use of telomere length as a marker for biological aging.

The theory of allostasis developed by Sterling and Eyer allows us to understand the effects of cumulative wear and tear on the body's systems in response to stressors and repeated coping and adaptation (Geronimus et al., 2006). The failure to adapt and maintain internal balance may lead to infection, illness, or symptom expression. The theory of allostasis has been used to explain the progression and development of certain disease states. It has been a guiding force behind research in cancer and gastrointestinal disorders because cumulative stress, or *allostatic load,* is known to affect both the immune and endocrine systems (Groer et al., 2010).

In allostatic 'overload' chronic stressors trigger a hormonal response that can alter the metabolic state and increase appetite or impair fat metabolism (McEwen & Wingfield, 2003). Because an emergent-like event is not in progress, the hormones have a very different physiological effect over time. For example, the physical and psychological stress associated with a low socioeconomic status (SES) may trigger an increase in stress hormones that are linked to abdominal obesity and immune suppression. Allostatic overload is characterized by physiological changes that can be precursors to conditions commonly associated with SES: diabetes, obesity, heart disease, and immune disorders (McEwen & Wingfield, 2003). According to Groer et al. (2010) allostasis is a relevant theory in women's health issues because allostasis is cumulative over time, allostatic load influences physical morbidity, and allostatic load results from physical and social demands, genetics, and lifestyle choices. Incorporation of the theory

of allostasis and measurement of relevant biomarkers will add depth to this study of perceived stress and perceived health status (Refer to Table 1).

Table 1. Examples of biomarkers by type (Juster, McEwen, & Lupien, 2010).

| **TYPE** | **BIOMARKERS** |
|---|---|
| Neuroendocrine | Cortisol, Dehydroepiandrosterone, epinephrine, norepinephrine, dopamine, aldosterone |
| Immune | Interleukin-6, tumor necrosis factor-alpha, C-reactive protein, Insulin like growth factor-1, fibrinogen |
| Metabolic | High density lipoprotein cholesterol, Low density lipoprotein cholesterol, Triglycerides, Glycosylated hemoglobin, Glucose, Insulin, Albumin, Creatinine, Homocysteine |
| Cardiovascular and Respiratory | Systolic blood pressure, Diastolic blood pressure, Peak expiratory flow, Heart rate/pulse |
| Anthropometric | Waist-hip-ratio, Body mass index |

**Innovation**

This study is innovative in that it focuses on a vulnerable subgroup of the general population for which there is a paucity of research: midlife, post-menopausal African American women. This study will use multiple time-point data from the Midlife Women's Health Study that ended recruitment in 1998. The participants will be contacted to participate in this new study at a single time point, 14 to 20 years after initial enrollment. Most studies on midlife women have cross-sectional data. Few have longitudinal data and even fewer have focused on African American women. The cross-sectional data collected in this study will be combined with previously collected data, resulting in more saliency. The Midlife Women's Health Study findings will be enhanced through collection of follow up data at this single time point.

Anthropometric measurements such as body mass index and waist-hip-ratio have been accepted as physiological biomarkers indicative of poor health outcomes (Juster et al., 2010). These biomarkers along with telomere length have been linked to perceived stress and oxidative stress (McEwen & Wingfield, 2003). Using the measure of relative telomere length, it is possible to gain some insight into the cumulative effects of stressors on health status and the overall perceived health status and perceived health status.

Lastly, most studies have focused on African American women of lower socioeconomic status. The sample proposed for this dissertation study will be comprised of women who are mostly mid-to-higher socioeconomic status, therefore providing an opportunity to evaluate health outcomes with a much wider lens.

**Approach/ Research design and Methods**

**Study Design**

This will be an ancillary study using comparative time points and open-ended questions. Quantitative data will be analyzed and open-ended questions will be reviewed.

**Sample**

Former participants of the Midlife Women's Health Study included 90 African American and 160 European American women. In the original study, women were followed every 6 months for up to five years. It has been 14 years since concluding the final phase of that NIH-funded study. After obtaining approval from the UCSF Committee on Human Research (CHR), these women will be recruited through follow up mailings or phone calls. The sample will include African American and European American women with ages likely to range from 60 – 65 years. The desired sample size is 80 with equal numbers of African American and European American women. Due to

the strength of the longitudinal design and existing data from numerous time points, 80 women would provide adequate numbers for statistical analysis. This is expected to be about half of the original sample of African Americans (92 invited to get at least 40 women) and about 25% of the original sample of European Americans (160 invited to get at least 40 women).

Inclusion criteria were previously established at the initial recruitment, but for this phase of the study, women must have completed at least two time points to be approached for consent to continue with this phase of the Midlife Women's Health Study. At least two prior time points, in addition to the current time point, are necessary for adequate data analysis.

**Setting**

Follow up interviews and examinations will be held on the UCSF campus in a location amenable to privacy and convenience to the participants. The University of California San Francisco (UCSF) is recognized as a premier medical center in the United States. The UCSF main campus houses the School of Nursing (SON). The environment on the UCSF campus and within the SON promotes high standards for patient care and interaction. The faculty and staff in the SON are held in high regard for nursing research and collaboration with other disciplines.

**Measures**

The previous data collected consisted of self-report questionnaires, history and demographics, anthropometrics and vital signs. All pertinent measures will be repeated in addition to updating demographic and history data. The genetic marker of interest is telomere length and this measurement will be added to the current study.

Physiological variables to be measured include age, waist-hip ratio (WHR), height, weight and blood pressure. Standardized measurements for anthropometrics will include procedures identical to the prior study: a calibrated weight scale for weight and stadiometer for height. Height will be obtained with shoes off and the participant standing against a stadiometer. To obtain a waist-hip-ratio, waist and hip circumferences will be obtained using a tension tape measure of the waist at the level of the umbilicus and hip at the most prominent girth of the buttocks. Each measure will be taken 3 times and averaged. Telomere length will be measured using standardized techniques in an accredited lab.

Self-report questionnaires included: Cohen's Perceived Stress Scale (PSS 10); General Sleep Disturbance Scale (GSDS); Center for Epidemiologic Studies Depression Scale (CES-D); and self-report tools for current health conditions, exercise and lifestyle patterns, experiences of racism and discrimination and perceived health status. Open-ended questions will be included to allow the women to write comments and explain their written responses in further detail.

**Procedures**

Participants will be recruited using phone and mailings. All pertinent information about the study will be provided. In the case that the participant is contacted by phone, an appointment will be scheduled for consent and data collection following full disclosure of the study methods, terms, and goals. Those who respond to the mailings will be scheduled for consent and data collection if in agreement with the goals and terms of the study. Every effort will be made to answer all questions prior to having the participant

commit to an appointment and the study will be reviewed prior to consent signature at the time of the appointment.

Data collection will take place during one time point and will consist of self-report questionnaires, anthropometrics, and venipuncture. Standardized procedures exist and will be adhered to during the collection of anthropometric data and telomere measurements. As stated above, waist and hip circumferences, height and weight measures will be taken 3 times and averaged. Training in proper blood collection technique and anthropometric measurement will be provided per study protocol. Blood samples for telomere measurement will be submitted to an accredited and experienced lab.

The questionnaires will be administered in a comfortable setting that provides privacy, minimal distractions and adequate time. The Primary investigator and/or co-investigator will be available to answer questions and provide clarification if needed. The participants may return the questionnaires by mail if time constraints exist. There will be no intervention in this study. This is a descriptive study using data collection over time and current biomarker evaluation.

**Analysis Plan**

*Aim #1*: Compare perceived stress and perceived general health status assessed during late pre-menopausal years with their current perception assessed post-menopause. The analytical plan consists of descriptive statistics and measures of central tendency (means and standard deviations, percentages, etc.). Assuming data will be normally distributed, a two-way ANOVA (group and time) will be used to compare women by the two time

points and by race. If the data is not normally distributed, a Kruskall-Wallis test will be performed.

*Aim #2*: Identify key factors that best predict current perceived stress and perceived general health status in African American postmenopausal women compared to European American women of the same age. Relationships will be tested using scatterplots and correlation coefficients. Race will be dummy coded and all correlations that are > .20 will be used in a multiple regression model to predict current perceived health status. A multiple linear regression models will also be used to account for the variance in perceived stress scores from up to five potential independent variables/ predictors (age, race, education, BMI, WHR…).

*Aim #3:* Identify potential biomarkers associated with the perceived stress and perceived general health. Telomere length will be the biomarker of interest for this aim. The analytical plan will be to test the association of the biomarker, telomere length, with the variables perceived stress and perceived health.

*Aim #4*: Identify commonalities among the sources of stress in the lives of post-menopausal African American women. The fixed-response questions about discrimination and stress will be followed by open-ended questions to elicit the participant's views about factors in her life that she thinks contribute to her stress as well as interventions that have positively or negatively influenced her stress level. The responses will be reviewed for commonalities.

**Power analysis**

We propose a moderate to large effect size for the variable of perceived stress on symptoms and perceived health in this study. Using previous data from the Midlife Women's Health Study, we calculated an effect size of .44 for the item 'General health now', indicating moderate variation in the scores for African American and European American groups. Effect sizes associated with the items 'sleep quality' and 'fatigue' were of .26 and .30 respectively. Over time, these effects may be expected to increase with age. Using a power of .80 with a significance of 0.05 (Cohen, page 55), the minimum desired sample size would be 26 per group (African American and European American). The expected sample size is 40 per group.

This power analysis is further supported with the well-documented association between perceived/psychological stress, adverse health outcomes and telomere shortening. In the integrative literature review by Starkweather et al. (2014) the authors found chronic psychological stress, acute psychological stress, socioeconomic status and educational attainment to be associated with telomere shortening or the stimulation of inflammatory biomarkers and oxidative stress. Of the 284 articles that were reviewed, most involved women and the total sample sizes ranged from 22 to 4,441.

**Rigor**

External validity would be high as this study would be applicable to women of other races, ethnicities, and communities. The tools and measurements are valid and reliable in this population. Despite the novelty of telomere length, it is becoming more widely used to assess stress and aging, and therefore should not be a hindrance for other researchers to replicate the study. Internal validity is high in that the anthropometric

measurements are standardized. The survey tools have been validated in multiple settings and with a variety of populations. Due to the time lapse since these tools were previously administered and lack of intermittent contact with these women there may be substantial loss to follow-up. The direct questions should have minimal risk to validity as they will be self-report and rely on recounting personal experiences. Participant bias in their responses may be decreased due to familiarity and comfort with the process.

**Summary**

**Knowledge to be gained**

This study has the potential to increase knowledge about the effects of perceived stress and stressors experienced by midlife European American and African American women. Recent studies have found associations between environmental stressors and accelerated biological aging. The use of telomere length in this study may shed light on the importance of 'everyday' stressors obtained prospectively in the past and long-term implications. The focus on African American women, their roles and stressors is a unique approach to a population of women who persistently suffer from poor health outcomes in comparison to women of other ethnicities. Increased stress and poor health outcomes have been traditionally associated with lower socioeconomic status. On average this sample of African American women in the San Francisco Bay Area was highly educated compared to women in the general US population. Therefore, it will be an interesting contrast to the literature and add insight into the influence of SES factors within the context of race.

**Strengths of design/ methods**

The strengths of this ancillary study include longitudinal data with multiple time-points for collecting data that serve as true predictor variables, sound statistical analysis and innovative use of telomere length as a biological measure of aging and stress. The use of open-ended questions will provide insight into the women's responses that would otherwise be missed with survey tools alone.

Limitations to this study include the extended time lapse, possible missing data and risk of small sample size. The recruitment process is limited as contact information is outdated, thereby increasing the possibility of participant loss to follow up.

**References**


Albert, M. A., Cozier, Y., Ridker, P. M., Palmer, J. R., Glynn, R. J., Rose, L., . . . Rosenberg, L. (2010). Perceptions of race/ethnic discrimination in relation to mortality among Black women: results from the Black Women's Health Study. *Arch Intern Med, 170*(10), 896-904. doi: 10.1001/archinternmed.2010.116

Barrett, E. L., & Richardson, D. S. (2011). Sex differences in telomeres and lifespan. *Aging Cell, 10*(6), 913-921. doi: 10.1111/j.1474-9726.2011.00741.x

Centers for Disease Control (2010). Retrieved from http://www.cdc.gov/nchs/data/databriefs/db125.htm

Chan, S. R., & Blackburn, E. H. (2004). Telomeres and telomerase. *Philos Trans R Soc Lond B Biol Sci, 359*(1441), 109-121. doi: 10.1098/rstb.2003.1370

Crenshaw, K. (1991). Mapping the margins: intersectionality, identity politics, and violence against women of color. *Tanford Law Review,* 43:1241-79.

Drury, S. S., Theall, K., Gleason, M. M., Smyke, A. T., De Vivo, I., Wong, J. Y., . . . Nelson, C. A. (2012). Telomere length and early severe social deprivation: linking early adversity and cellular aging. *Mol Psychiatry, 17*(7), 719-727. doi: 10.1038/mp.2011.53

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proc Natl Acad Sci U S A, 101*(49), 17312-17315. doi: 10.1073/pnas.0407162101

Folkman, S., Lazarus, R. S., Gruen, R. J., & DeLongis, A. (1986). Appraisal, coping, health status, and psychological symptoms. *Journal of Personality and Social Psychology,* 50 (3), 571-579

Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health, 96*(5), 826-833. doi: 10.2105/ajph.2004.060749

Groer, M & The Women's Health Research Group at the University of South Florida College of Nursing. (2010). Allostasis: a model for women's health. In Kendall-Tackett, K. (Ed.). *The Psychoneuroimmunology of Chronic Disease.* Washington, DC: American Psychological Association.

Hines-Martin, V., Speck, B. J., Stetson, B., & Looney, S. W. (2009). Understanding systems and rhythms for minority recruitment in intervention research. *Res Nurs Health, 32*(6), 657-670. doi: 10.1002/nur.20355

Hunt, S. C., Chen, W., Gardner, J. P., Kimura, M., Srinivasan, S. R., Eckfeldt, J. H., . . . Aviv, A. (2008). Leukocyte telomeres are longer in African Americans than in whites: the National Heart, Lung, and Blood Institute Family Heart Study and the Bogalusa Heart Study. *Aging Cell, 7*(4), 451-458. doi: 10.1111/j.1474-9726.2008.00397.x

Juster, R. P., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. [Review]. *Neurosci Biobehav Rev, 35*(1), 2-16. doi: 10.1016/j.neubiorev.2009.10.002

Kochanek, K. D., Arias, E., & Anderson, R. N. (2013, July). How did cause of death contribute to racial differences in life expectancy in the United States in 2010? (National Center for Health Statistics Data Brief, No. 125). U.S. Department of Health and Human Services

Kwate, N. O., Valdimarsdottir, H. B., Guevarra, J. S., & Bovbjerg, D. H. (2003). Experiences of racist events are associated with negative health consequences for African American women. *J Natl Med Assoc, 95*(6), 450-460

Lazarus, R. S. & Folkman, S. (1984). *Stress, Appraisal, and Coping*. New York: Springer Publishing Company.

McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. [Article]. *Hormones and Behavior, 43*(1), 2-15. doi: 10.1016/s0018-506x(02)00024-7

Miles, T. (2013). Global life expectancy: life spans continue to lengthen around the world, WHO says. *The Huffington Post.* Retreived from http://www.huffingtonpost.com/2013/05/15/global-life-expectancy-span-world_n_3281211.html

National Association for the Advancement of Colored People (NAACP). (2014). Retrieved from http://www.naacp.org/pages/criminal-justice-fact-sheet

Olshansky, S. J., Antonucci, T., Berkman, L., Binstock, R. H., Boersch-Supan, A., Capiocco, J. T., Carnes, B. A., Carstensen, L. L., Fried, L. P., Goldman, D. P., Jackson, J., Kohli, M., Rother, J., Zheng, Y., & Rowe, J. (2012). Differences in Life expectancy due to race and educational differences are widening, and many may not catch up. Health Affairs, August, 31(8), 1803 – 1813.

Perry, B. L., Harp, K. L., & Oser, C. B. (2013). Racial and Gender Discrimination in the Stress Process: Implications for African American Women's Health and Well-Being. *Sociol Perspect, 56*(1), 25-48.

Starkweather, A. R., Alhaeeri, A. A., Montpetit, A., Brumelle, J., Filler, K., Montpetit, M., . . . Jackson-Cook, C. K. (2014). An integrative review of factors associated with telomere length and implications for biobehavioral research. *Nurs Res, 63*(1), 36-50. doi: 10.1097/nnr.0000000000000009

Zhu, H., Guo, D., Li, K., Pedersen-White, J., Stallmann-Jorgensen, I. S., Huang, Y., . . . Dong, Y. (2012). Increased telomerase activity and vitamin D supplementation in overweight African Americans. *Int J Obes (Lond), 36*(6), 805-809. doi: 10.1038/ijo.2011.197

Zhu, H., Wang, X., Gutin, B., Davis, C. L., Keeton, D., Thomas, J., . . . Dong, Y. (2011). Leukocyte telomere length in healthy Caucasian and African-American adolescents: relationships with race, sex, adiposity, adipokines, and physical activity. *J Pediatr, 158*(2), 215-220. doi: 10.1016/j.jpeds.2010.08.007

**Appendices**

Self-report surveys will include: Cohen's Perceived Stress Scale (PSS 10), General Sleep Disturbance Scale (GSDS), Center for Epidemiologic Studies Depression Scale (CES-D). In addition, self-report tools for current health conditions, exercise and lifestyle patterns, experiences of racism and discrimination and perceived health status are included.

Open-ended questions:

1. Please comment on the primary source of stress that has been present through your life: 1) before you had children or before menopause and 2) after your children left home or after menopause.
2. Is there something more you would like to share about your experiences with stress in your life?
3. What do you do or think to relieve your stress?
4. What do you think makes your stress worse?

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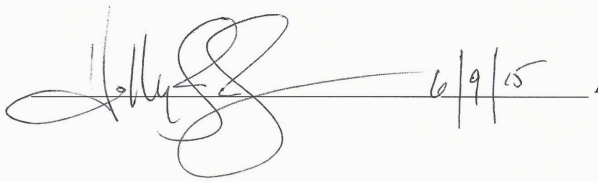

6/9/15 Author Signature Date