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An exploration of women's current hormone discontinuation experiences, influences, decisions, and alternatives

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An exploration of women's current hormone discontinuation experiences, influences, decisions, and alternatives

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Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor of Philosophy

The University of Texas at Austin

August 2007

Dedication

First and foremost this work is dedicated to the women who have participated in this study, former patients, friends, and colleagues for sharing their experiences with me.

I also dedicate this to my parents, Margaret M. Kupferer and the late Richard A. Kupferer Sr., and my loving children, Meghan Elizabeth and Matthew Travis Gregg, who have unconditionally and lovingly accepted and supported me in my personal, educational and professional endeavors.

Acknowledgements

I would like to begin by acknowledging Dr. Patricia Carter, whose enthusiastic encouragement along with Dr. Gayle Timmerman gave me the confidence to return to school and to follow my dreams. Dr. Carter's support and mentorship has been an integral part of my success here at the University.

I would also like to acknowledge Dean Dolores Sands for the Dean's Scholar Award I received which consisted of two sources, the "Kathryn Gurley Brown Scholarship" and the "Lee Hage and Joseph D. Jamail Endowed Scholarship in Nursing". As a working single mom with two children, I do not believe I could have made it through the doctoral program without this generous support. Words cannot describe the gratitude I have for generosity and thoughtfulness of all of the individuals involved in the provision of these scholarships.

I would also like to thank Dr. Lorraine Walker who was my original Program Advisor in Women's Health. Dr. Walker's encouragement and mentorship is very much appreciated. Dr. Walker so graciously introduced me to Dr. Sharon Dormire when she joined the faculty because of her vast experience and expertise in my area interest, menopause and vasomotor symptoms. I offer my utmost thanks to Dr. Sharon Dormire for so graciously stepping in as my mentor and Advisor and Dissertation Chair just as she was joining the faculty here at the University. Her calm demeanor and vast expertise in menopause has been invaluable.

I would also like to offer my heartfelt appreciation to Drs. Gayle Timmerman, Eun-OK Im, Heather Becker and Nancy J. Smith, the members of my dissertation committee for all of their time, patience and unending support during my dissertation process.

Special thanks goes out to my brother Edward Kupferer and his wife Patsy, sons Edward and Gregory for their help in getting the questionnaires sent out. I would also like to thank my work colleagues, especially Dr. Nancy Alexander, Debra Mitchiner and Carrie Murray for all their support and encouragement especially through the most trying of times. I would like to acknowledge Jake Knorr for study recruitment suggestions and support.

I must once again acknowledge all of the women who shared their experiences with me for this study. An overwhelming amount of women, those who were not eligible to participate in the study sent letters of thank you, encouragement and support for my work.

And last but not least, I want to acknowledge Sandra Benavides-Vaello, a fellow doctoral student, friend and confidant. Since our "crash" meeting on the first day of the doctoral program Sandy's warm wit, positive attitude, compassion and unconditional friendship has made this journey bearable and actually quite delightful. Thank you, Sandy.

An exploration of women's current hormone discontinuation experiences, influences, decisions, and alternatives

Publication No._____

Elizabeth Mary Kupferer, Ph.D.

The University of Texas at Austin, 2007

Supervisor: Sharon Dormire

ABSTRACT

Findings released from recent pivotal clinical trials on hormone therapy (HT) benefits and risks have stimulated a growing trend towards lower doses and earlier discontinuation of HT for menopausal women. Yet, there is little knowledge regarding women's personal experiences with the resultant earlier and possibly abrupt withdrawal of HT. The purpose of this study was to explore postmenopausal women's vasomotor symptom experiences after discontinuing HT.

The data for this study was collected from menopausal women who discontinued HT. The study questionnaire was created through an extensive review of the literature as well as an expert panel review. The questionnaire was also piloted with a small group of women prior to its use in this study.

Data analysis consisted of descriptive analysis with means and standard deviations and/or frequency distributions with percentages for demographic data, health behaviors, factors influencing HT decisions, use of CAM and perceived efficacy. Chi-square analysis, Spearman Rho correlation, and logistic regression analysis were conducted for contextual factors and vasomotor symptom experiences. A McNemar test

was performed to assess within group differences for vasomotor symptoms experiences pre and post HT.

Questionnaires were received from 563 menopausal women throughout the United States. This study revealed that 80% of participants experienced vasomotor symptoms after discontinuing HT. The most common predictors which accounted for only 13% of variance in the occurrence of vasomotor symptoms were younger age, type of menopause and the occurrence of vasomotor symptoms prior to initiation of HT.

Of the 563 women participating in the study, less than half reported the use of CAM to treat reemerging vasomotor symptoms. For the most part, less than half of the women felt their treatment choices were helpful in relieving their reemerging vasomotor symptoms

Because a woman's experience of menopause can be highly individualized, an adaptation of Bronfenbrenner's ecological theory was used guide this exploratory study. The study findings supported the usefulness of the adaptation of Bronfenbrenner's ecological theory as a model through which to view the vasomotor experiences of menopausal women who have discontinued HT.

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Chapter One: Introduction and Theoretical Framework

OVERVIEW

Natural menopause is a universal biologic event for all women who live long enough and have not experienced some type of pathology or medical/surgical intervention altering the natural process. Menopause can be viewed from two different perspectives, the biomedical perspective, in which menopause is viewed as a disease state characterized by estrogen deficiency or from a developmental perspective in which menopause is considered a natural part of a woman's life but experienced differently by women of varying backgrounds.

The biomedical paradigm began in the 1930's with the development of an etiologic theoretical framework for female sexual functioning introduced by researchers in the field of sex endocrinology and the discovery of sex hormones (Formanek, 1990). The medicalization of menopause emerged along with the introduction of diethylstilbestrol (DES) a synthetic estrogen introduced in 1941 to treat menopausal symptoms. At this time estrogen was approved by the US Food and Drug Administration (FDA) specifically for treatment of vasomotor symptoms (i.e.: hot flashes, night sweats) and urogenital atrophy brought about by declining endogenous estrogen levels experienced during menopause (Formanek, 1990; Rousseau, 2001). Vasomotor symptoms were and still are the most common symptom for which menopausal women seek relief from (Lobo, Kelsey & Marcus, 2000; Speroff & Fritz, 2005). Many women have indeed benefited from estrogen therapy to relieve symptoms experienced during menopause.

The use of estrogen has waxed and waned over the years in response to various historical events. A popular text published in the 1966, "Feminine Forever" by R. A.

Wilson heralded the news to lay women that menopause was a deficiency disease state and they should not have to suffer the consequences related to the decline in endogenous estrogen levels. Wilson (1966) believed that exogenous estrogen could be taken to 'cure' menopause and keep women forever vibrant and healthy. At this time estrogen was beginning to be prescribed as a hormone replacement therapy (HRT) by a few clinicians for menopause symptoms as well as other purported health benefits that were outside the prescribing guidelines (off label) set by the FDA in 1942. Note, to provide consistency of terms, from this point on HRT will be referred to as hormone therapy (HT) as is now currently recommended (FDA, 2003; Sturdee & MacLennan, 2003).

This trend of increasing HT use quickly declined in the 1970s because of the emergence of endometrial cancer. Endometrial cancer was found to be associated with the use of estrogen that was unopposed by a progestational agent (Antunes, 1979; Kaunitz, 1980). Soon after, with the addition of a progestational agent to the HT regimen to oppose the proliferative effects of estrogen on the endometrial tissue of the uterus, protecting it from endometrial cancer, HT use again began to rise once more (Rousseau, 2001; Genazzani, 2002).

The basic biomedical tenets with regard to the phenomenon of menopause as a deficiency disease and its treatment remained remarkably similar throughout the next few decades. In the 1980s and 90s, HT not only was recommended for vasomotor symptoms it became a panacea for the maintenance of a menopausal woman's health. During this time there was yet again a rise in the use of HT, especially in off label prescribing of HT for health promotion and disease prevention. During this time epidemiologic evidence began to emerge supporting the use of estrogen to reduce the risk chronic and other medical conditions such as osteoporosis, coronary heart disease (CHD), colon cancer and cognitive decline, of which CHD was the most prominent (Pinn, 2005; Rousseau, 2001).

In recent years evidenced based medicine (EBM) has emerged in which clinical practice is to be guided by high level clinical research. High level research should include the gold standard of a randomized, placebo controlled clinical trial, powered sufficiently to yield the most accurate findings. For HT, there are a few benefits that are clearly supported by EBM. These benefits include the relief of vasomotor (Nelson, 2004) and urogenital symptoms (Willhite & O'Connell, 2001) as well as the role of HT in the prevention of osteoporosis (Keating, Manassiev, & Stevenson, 2000). Although randomized, placebo controlled trials were lacking at this time, there were epidemiologic data and empirical evidence that provided some evidence that HT may indeed reduce the risk of heart disease in women (Bush, 1990; Derby, 2000; Grady, et al., 1992; Psaty, Heckbert & Atkins, 1994; Sidney, Petitti & Quesenberry, 1997; Stampfer & Colditz,1991)

The most common risks of HT known today were well known at that time as well. These known risks that were associated with the use of HT included an increased risk of venous thrombembolic events (VTE) and arterial strokes. Endometrial cancer was a known risk, but there was clear clinical evidence indicating that estrogen when opposed by a progestational agent not only decreased the risk of endometrial cancer, but indeed reduced the risk lower than that of a woman who did not take HT at all (Genazzani, 2002; Speroff & Fritz, 2005). Clinical trials and epidemiologic data with regard to breast cancer risk associated with HT demonstrated conflicting results with a trend towards only a mild increased risk for women who were at higher risk for breast cancer (Genazzani, 2002; Speroff & Fritz, 2005)

Recently, released findings from three recent key clinical trials on the effects of HT, the Heart and Estrogen/progestin Replacement Study (HERS) (Hulley, et al 1998), the follow-up non-cardiovascular disease outcomes during 6.8 years of hormone therapy:

the Heart and Estrogen/progestin Replacement Study follow-up (HERS II) (Grady, et al., 2002), and the Women's Health Initiative (WHI) (Rossouw, et al, 2002) have provided evidence based clinical guidance for health care providers with regard to the risks and benefits with the administration of exogenous hormones. The findings from these pivotal clinical trials, although controversial, have nudged the motion of the pendulum back toward the view of menopause as a natural life event experienced uniquely by each woman. For now routine use of HT for varied health conditions has turned to a more judicious individualized treatment approach for women. In response to this new data and to provide guidance for clinicians, an independent panel prepared and released the National Institute of Health (NIH) consensus statement on the "Management of Menopause-related Symptoms" in March of 2005. This report provides a review of the literature of EBM for the management of menopause symptoms as well as a recommendation to demedicalize menopause (National Institute of Health [NIH], 2005). The U.S. Food and Drug Administration (FDA) also recommends that estrogens should only be prescribed for the treatment of menopausal vasomotor and urogenital symptoms at the lowest possible dose for the shortest time possible (U.S. Food and Drug Administration (2004).

In response to these historical events/pivotal clinical trials clinical practice patterns now reflect that there has been a decrease in new prescriptions for hormones as well as a noted decrease in the dosage of current prescriptions for hormone therapy. (Blümel, et al., 2004; Hersh, Stefanick & Stafford, 2004). Although, there is documentation of a growing trend towards earlier discontinue hormone therapy there is little information about how this trend will affect women's menopausal experiences. Given that HT was once considered very beneficial for women and that they would likely continue with therapy for most of their postmenopausal life, information is lacking about

women's personal experiences related to withdrawal of HT with this abrupt change in clinical practice patterns. Thus, future research studies are needed to explore, assess and articulate the experiences of diverse groups of menopausal women who have chosen to discontinue hormone therapy.

PURPOSE

The primary purpose of this study was to explore postmenopausal women's vasomotor symptom experiences after discontinuing HT. The influence of contextual factors (i.e.: weight, smoking, ethnicity, and type of menopause) on the vasomotor experiences of post-hormone therapy postmenopausal women was examined and compared with factors that have been associated with vasomotor symptom experiences prior to initiation of hormone therapy. The factors that influenced discontinuation of hormone therapy were also explored. In addition, this study assessed the use of alternative medical treatments and complementary and alternative medicine (CAM) therapies women have undertaken specifically to treat vasomotor symptoms as well the women's perceived effectiveness of these therapies.

BACKGROUND AND SIGNIFICANCE

Life expectancy has increased dramatically over the past 100 years, and currently the average life expectancy at birth is 77 years of age in the United States. In addition to the increase in life expectancy, the population of older Americans has grown as well. In fact the youngest members of the seventy-five million American baby boomers born between 1946 and 1964 are now over the age of 40 (National Center for Health Statistics, Data Warehouse on Trends in Health and Aging).

It is estimated that in July 2004, there were 32,759,100 women who fell between 40 to 54 years of age (U.S. Census Bureau, Population Division, 2004). The average age

of natural menopause in the United States is between 50-52 years old (Speroff & Fritz, 2005), thus a substantial number of women have or will begin to experience menopause. Women experiencing menopause with the increased life expectancy in the last century, will live over a third of their lives postmenopause.

Clearly, the experiences of a population cohort this large cannot be ignored. For many women, menopausal vasomotor symptoms can impact their perception of health and influence the types of health behaviors they will adopt. Health behaviors may include the use of non hormonal alternative medications (i.e.: antidepressants and antiepileptics) as well as CAM therapies such as acupuncture, yoga, and the use of botanicals and dietary supplements to reduce vasomotor symptoms associated with menopause. Illuminating the needs of this large group of women will provide valuable information that will help to guide future research in evaluating the safety and efficacy of alternative therapies.

Vasomotor Symptoms

The term vasomotor symptoms describes a collection of menopausal symptoms such hot flashes, hot flushes and night sweats. A hot flash or hot flush is a sudden feeling of warmth and often a breakout of sweating usually confined to the chest, neck, face and head (Freedman, 1998, 2001; Speroff & Fritz, 2005). There is an intense feeling of heat that often initiates in the chest area and spreads to the face head and neck. When hot flashes occur at night, the breakout of profuse sweating which is often referred to as night sweats can disrupt sleep patterns (Friedman, 2001; Speroff & Fritz, 2005). Although many women may progress through menopausal transition without any difficulty, the majority of women will experience vasomotor symptoms. It is estimated that approximately 60 to 85% of women experience hot flashes during the peri- and postmenopause. (Feldman, Voda & Gronseth, 1985; Kronenberg, F., 1994; McKinlay,

Brambrilla, & Posner, 1992; Neugarten & Kraines, 1965; Stearns, et al., 2002). For women who have had surgical menopause, the number of women experiencing vasomotor symptoms is much higher at nearly 90% (Chakravarti, Collins, Newton, Orom & Studd, 1977; Feldman, Voda, & Gronseth, 1985). Studies have found that between 30 and 60% of women will report that symptoms are severe enough to disrupt activities of daily life, interfere with restful sleep and warrant treatment (Gold, et al, 2000; Freedman & Roehrs, 2004; Fuh, Wang, Lee, Lu, & Juang, 2003; Oldenhave, Jaszmann, Haspells & Everserd, 1993). It has been shown in various studies that women who have hot flashes will continue to have symptoms for an average of 1-2 years, up to 4-5 years or longer in some women (Kronenberg, 1994; Speroff & Fritz, 2005). Culture and ethnicity have been shown to play a part in the symptom reporting and experience (Avis, et al, 2001; Beyene, 1989; Lock & Kaufert, 2001), as well as lifestyle and demographic factors (Gold, et al, 2000; Randolph, et al., 2003) and even weight (Randolph, et al., 2003).

Despite the fact that vasomotor symptoms are very common among women, the etiology of vasomotor symptoms is still not clearly understood. Nor, are hot flashes exclusively experienced by menopausal women, men can experience them as well. Conditions other than menopause can also produce flushing such as emotional flushing, exposure to heat, alcohol or monosodium glutamate consumption, carcinoid syndrome, systemic mast cell disease, pheochromocytoma, medullary carcinoma of the thyroid, pancreatic islet-cell tumors, renal cell carcinoma, hypertension, hyperthyroidism, neurological flushing, and spinal cord injury (Wilkin, 1981).

Hot flashes associated with menopause were originally thought to be related simply to the drop in endogenous estrogen during menopause. This theory is supported in part by the overwhelming evidence showing that treatment with exogenous estrogens will almost always relieve hot flashes (MacLennan, Broadbent, Lester, S., & Moore, 2004).

Understanding these etiologies have led to additional clinical trials to investigate alternative treatment modalities to relieve menopausal symptoms. This is an important area of research as more women discontinue estrogen therapies in light of recent historical events. It is unknown whether vasomotor symptoms experienced after discontinuation of HT are in fact the same as those experienced prior to hormone initiation.

Hormone Therapy Discontinuation Experiences

Recent historical studies have provided more evidenced-based information about HT risks and benefits. Contrary to expectations, these studies did not provide evidence to support the use of HT for prevention of some chronic health conditions. These studies have initiated a trend towards a shorter period of use of HT for the treatment of vasomotor symptoms. Driven by this new evidence more women will likely personally opt out or will be guided by their health care providers to stop HT earlier than originally planned. At present, little is known about the potential symptom experiences of menopausal women with earlier and possibly abrupt discontinuation of HT. Only three studies were located that assessed the experiences of women after the discontinuation of HT. Two of the studies were published post WHI study and one prior.

In the one study published prior to the release of WHI findings, the researchers (Hammar, et al., 1999) assessed whether vasomotor symptoms might be induced specifically in menopausal women who had *never* previously experienced vasomotor symptoms when they were given HT for 14 weeks, and then abruptly taken off. Forty menopausal women, who had reported that they had *no* history of vasomotor symptoms, were *not* on HT and were not at an increase risk for thrombembolic events or malignant diseases were included in the study. Women who had a hysterectomy were excluded from this study. The women were randomized to either a treatment group (17β-estradiol

50μ/day for 12 weeks, followed by a progesterone withdrawal on weeks 13 and 14) or to the placebo group. Thirty eight women completed the study. The researchers found that there was no report of vasomotor symptoms in the either the treatment or placebo group after the 14 week trial. This study suggests that the abrupt withdrawal of estrogen does not trigger vasomotor symptoms. These findings although only apply to those women who had not previously experienced vasomotor symptoms. The authors did not report demographic information on race/ethnicity or socioeconomic status.

Grady, Ettinger, Tosteson, Pressman, & Macer (2003) published the first study after the release of data from WHI study, investigators. The primary purpose of this study was to identify certain characteristics in women that would make it more difficult to discontinue HT. The authors surveyed a random sample (N=377) from a large health plan database, the Kaiser Foundation Health Plan. Through phone interviews with trained interviewers, the authors found that approximately 26% (N=97) of the women who had attempted discontinuation of HT had difficulty in doing so because of withdrawal symptoms and resumed the use of HT. Contextual factors identified that were most highly associated with the inability to stop HT were hysterectomy and duration of hormone use of over 10 years. The authors found no significant association of symptoms with contextual factors of age, ethnicity, education, BMI and smoking.

Grady and colleagues (2003) also found that tapering off of HT was no more affective than stopping abruptly in preventing the occurrence of vasomotor symptoms, although data on the specific method of tapering was not collected. The participants in this study were primarily White (77%) and well educated with 43% having earned a basic college degree or better.

In a cross-sectional survey Ockene and colleagues (2005) explored the menopause symptom experiences of women who had recently participated in the estrogen and

progestin treatment arm of the WHI study. The study survey was sent approximately 8-12 months after the study was stopped to women who were still on HT prior to the discontinuation of the WHI study. All women who were on study drug (HT) when the WHI study was stopped were instructed to discontinue it. The authors reported that the respondents compared to the non-respondents of this survey were more likely to be White, older, married, with a high school education or better.

The authors found that the strongest determinant of occurrence of vasomotor symptoms after discontinuation of HT was the presence of vasomotor symptoms at baseline even after adjusting for age, BMI, alcohol and tobacco use. Other adjusted contextual factors that increased the likelihood of vasomotor symptoms included HT use before the study and current smoking. Similar to the findings of Hammar, et al (2003), the authors also found that women who did not have vasomotor symptoms prior to treatment were less likely to experience vasomotor symptoms even after abrupt withdrawal of HT.

Those participants who resumed HT on their own were asked why they did so. The most common reasons for restarting HT was for the relief of vasomotor symptoms, to feel better, and on the advice of their personal clinician. Of those participants who did not resume therapy, the authors explored lifestyle and medical management modalities that were undertaken for symptom relief. Fifty percent of the women reported the use of at least one management strategy. The most common management strategy was the use of lifestyle changes such as drinking more fluids. The participants in this study were primarily White (87%), well educated with nearly 37% with a basic college degree or better. Less than 5% did not finish high school in this sample (Ockene, et al., 2005).

Collectively these studies illustrate the varied experiences of menopausal women who were directed to discontinue HT. In 2 of the studies (Hammar, et al, 1999; Ockene,

et al, 2005) the women were clearly instructed to discontinue HT, whereas in the study by Grady, et al (2003) the women shared a variety of reasons for why they discontinued. Yet, more information about discontinuation experiences is needed about the women who are *not* typically represented in clinical trials (i.e.: Hammar, et al., 1999; Ockene, et al., 2005) or within a Health Maintenance Organization group (Grady, et al., 2003).

The current study builds upon these aforementioned studies through a retrospective exploration of postmenopausal women's vasomotor symptom experiences after discontinuing HT. The women in this study stopped HT on their own for a variety of reasons but were not asked to discontinue HT as part the study requirement (i.e. Hammar, et al, 1999; Ockene, et al., 2005). Similar to Ockene, et al, (2005) this study also assessed the use alternative medical treatments and complementary and alternative medicine (CAM) therapies women have undertaken specifically to treat vasomotor symptoms as well the women's perceived effectiveness of these therapies.

RESEARCH AIMS

1. To identify factors menopausal women report that influenced their decisions to discontinue HT.
2. To explore the vasomotor symptom occurrences in menopausal women who have discontinued hormone therapy.
3. To explore the relationship between contextual factors and vasomotor symptoms after the discontinuation of hormone therapy.
4. To identify alternative treatments that women have undertaken to treat menopause symptoms and their perceived efficacy.

THEORETICAL FRAMEWORK

Menopause is a term used to describe the end of a woman's fertile years which is signaled by the cessation of menstruation. In Western cultures, the predominant menopause discourse arises from the biomedical model and is considered a pathological condition. The universality of the reproductive senescence among aging women lends itself to the belief that the menopausal experience is universal in all women. Over the last few decades, as has been discussed earlier in this proposal, menopausal discourse continues to be a biomedical construct despite the trend towards use of HT only for the treatment of vasomotor symptoms.

Each woman experiences menopause through the lens of her personal experiences and interactions with others. An adaptation of Bronfenbrenner's ecological theory serves as a useful model for viewing these varied menopause experiences (Bronfenbrenner, 1979, 1986). There is no universal characterization of menopause and a woman's experiences are affected by all aspects of her life. Any theoretical framework used to guide culturally sensitive research exploring women's experiences during withdrawal from HT must be able to provide a multidimensional structure. Human Ecology is an interdisciplinary applied field that utilizes a holistic approach to solving problems and enhancing human potential within the context of family, home, community and state. An ecological theoretical framework emerging from the study of human developmental ecology can help to assess the multidimensional aspects of individual health and well being of the individual within the context their environment. Through this holistic assessment of the individual there is an opportunity to develop health promotion, education and disease prevention interventions within the individual and the community to achieve sustainable positive health behavior (Bent, 2003; Bronfenbrenner, 1979, 1986; Bronfenbrenner & Ceci, 1994; Cohen, Schribner & Farley, 2000; Dan, 1994; Elliott,

Taylor, Cameron & Schabas, 1998; Formanek, 1990; Green, Richard & Potvin, 1996, Gryzwacz & Fuqua, 2000; Karpati, Galea, Awerbuch & Levins, 2002; Richard, Potvin, Kishchuk, Prlic & Green, 1996; Stokols, 1996, 2000). In addition, findings from research that is conducted within an ecological framework can serve as catalysts and provide support for changes in community-specific health care practices as well as the initiation of pertinent health policies at various governmental levels which have the potential to positively impact health outcomes (Green, et al., 1996; Richard, et al., 1996; Ruffing-Rahal, 1989, 1993, 1998; Stokols, 1996, 2000).

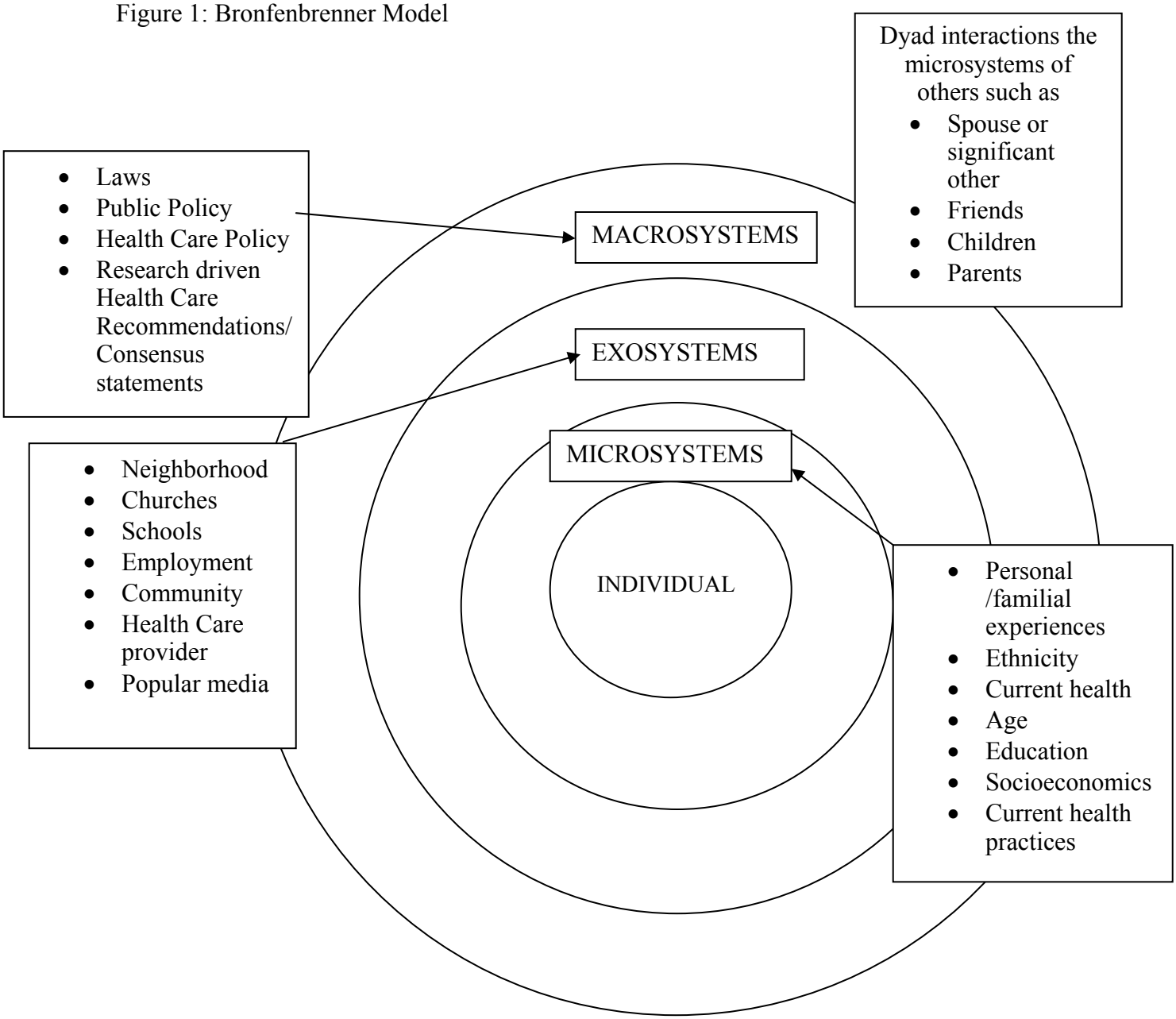
The developmental human ecological theoretical framework/model offered by Urie Bronfenbrenner (Bronfenbrenner, 1979) builds upon the work of Kurt Lewin who has suggested that in order to change behavior, the environment must be changed as well (in Bronfenbrenner, 1979). Bronfenbrenner's (1979, 1986) writings on the ecological approach to human development include the interaction between an individual and the social and physical environment.

Bronfenbrenner (1979) asserts that the ecological framework of human development involves the interaction of the individual, changes in their immediate environment as well as a larger environment beyond the immediate environment within which the individual is located. The individual is not a fixed entity within the environment, but is a dynamic force that has impact on the environment within which the individual resides as well. The environment in turn also affects the individual in a process of "mutual accommodation" (Bronfenbrenner, 1979, p.22)

The ecological model consists of progressively enlarging spheres representing individual and social systems (see figure 1) (Bronfenbrenner, 1979). The central sphere, the microsystem, represents the systems and characteristics that compose an individual *Microsystems* consist of an individual's genetic make up (ethnicity, race, age at

menopause), personal characteristics (weight, height, general health, smoking, alcohol or drug use) as well as a place or setting where individual is engaged in close face-to-face interactions with others, such as the home, extended family, work or school settings. Interrelations among microsystems are called *mesosystems*. The mesosystem, the next larger sphere encompassing the microsystem, provides positive ties among the microsystems benefiting the individual. *Mesosystems* are those settings in which the individual interacts in more than one setting either alone or through linkage of a third party and/or by the "intersetting" of knowledge through written communications such as pamphlets and books. The mesosystem could include social networks, clubs, churches, neighborhood and other peer groups. Additional systems include *exosystems* (i.e., influential external contexts, such as spouse's work settings or personal work settings, health care provider or clinic). And, finally, *macrosystems* (i.e., broader cultural and historical influences such as consensus statements following the WHI and HERS trials) in which all the other systems are embedded (Bronfenbrenner, 1979).

Figure 1: Bronfenbrenner Model



Ecological Model as a Guide for Women's Health Research

Given the vast differences of women's menopausal experiences, the ecological framework was chosen to help guide this research. McBride and McBride (1981) set forth seven criteria that should be embraced in theoretical frameworks used to guide women's health research. These criteria include: 1) that women be included as subjects in research; 2) that socio-cultural factors that impact health should be included in the investigation, 3) investigations should include how women are treated within the health care system (i.e. HT prescribing practices, acknowledgement of menopausal vasomotor symptoms, chronic disease risk recognition and prevention); 4) should acknowledge that male behavior is not necessarily the norm for women; 5) acknowledges that women's health concerns merit serious investigation (i.e. vasomotor symptoms); 6) should investigate all women's issues, not just reproductive concerns; and finally 7) appreciate that women's transitions should be seen as normal as opposed to as a pathological process .

Andrist and MacPherson (2001) outlined common valuable characteristics important for research for women's health. Characteristics include that the 1) research is grounded in the lived experience of the woman; 2) the researcher is in relation with the subject; 3) there is reflexivity and finally 4) that the research is useful and valuable to women.

Timmerman (1999) discusses theoretical underpinnings that provide a guide for women's health research studies that utilize quantitative measures. Timmerman (1999) addresses the importance of describing the lived experience of women in context, the acknowledgement and identification of possible personal biases of the researcher and its impact on the investigation, the importance of health as the focus of research with the avoidance of transforming normal processes into disease processes and finally, providing

feedback to the participants as well as making the process of study involvement convenient for the participants.

Clearly, an ecological theoretical framework resonates strongly with basic principles of women's health research. Women's health research provides a holistic approach that is *for* women, and in addition includes women in the intervention process. From this ecological viewpoint, women's health issues are not separated from the social, political and economic forces in society that impact health and health decisions.

Sociocultural and socioeconomic influences

American women represent multiple cultures that are alternatively defined by race, ethnicity, gender, age, religion, occupational status, SES and family background. How women interact in society is influenced by their diverse backgrounds. As Bronfenbrenner (1979) suggested individuals are influenced by the cultural expectations, perceptions and beliefs of the community and culture of which they are a part. Bronfenbrenner's ecological model provides a framework that enables researchers to assess the impact of culture and provides a broader picture of women's health and developmental transitions (i.e.; menarche, puberty, and menopause). The model incorporates personal experiences of women as a source of knowledge and insight about the connection between the individual and the environment. This acknowledgement enables women's health researchers' ways in which to analyze the differences within and between cultural groups as well as how the groups are constructed and sustained in various environmental contexts. In addition economically disadvantaged women's perceptions and experiences of menopause have largely been ignored in the assessment of menopause, especially in biomedical research. As mentioned previously, economically disadvantaged individuals often have poorer health outcomes

According to Bronfenbrenner (1979) "an ecological transition occurs whenever a person's position in the ecological environment is altered as a result of a change in role, setting or both" (p.26). For women, the transition into midlife or their post reproductive lives is signaled by the cessation of menses and reproductive senescence. This menopausal transition, occurring most commonly during midlife can be considered an ecological transition. Bronfenbrenner (1979) notes that ecological transition is often alteration of both biological and environmental factors thus representing the process of "mutual accommodation" (p. 27), the basic tenet of ecology of human development. Transitions occur throughout the life span and are often wonderful times to address health behaviors in the context of health promotion and age related disease prevention. Developmental transitions (i.e.: puberty, adolescence, menopause, retirement) represent opportunities, which encourage the transformation of the physical, mental and social self (Schulenberg et al., 1997). Ecological transitions typically involve changes at the individual, microsystem and mesosystem levels. The links between microsystems prior to transition (i.e., focus on the care of others such as the growing family, reproductive health care needs) and then post transition microsystems (i.e., empty nest, focus on self and health behaviors in the post reproductive phase, aging parents, etc.) can be considered mesosystems as well, suggesting the importance of contextual influences on successful adaptation during transitions (Bronfenbrenner, 1979).

For most women, natural menopause occurs at a time in life when role transitions are also occurring (growing children, empty nest, financial hardships related to putting children through college, aging parents, etc.), but not all women are going through these processes (i.e. surgical menopause, premature menopause, late childbearing). The ecological framework helps to facilitate the understanding of the individual's experience of this transition. The onset of menopause with or without significant symptoms may lead

some women to interact with the health care system if available and accessible to them, therefore this time of transition can provide an open opportunity for health care providers to educate women on ways to enhance well being and promote health as they age and work through the menopausal transition.

The health and well being of menopausal women should not be viewed as a single dimension such as a state of estrogen deficiency. Health and well being of women can be enhanced by an ecological perspective that is able to assess the multiple dimensionalities of the woman, her family, extended family, community and her environmental interactions with respect to adoption of personal health behaviors related to symptoms experience during the transition of menopause. Through ecologically oriented research aging issues are also viewed as public health issues that can lead to the identification of the value of health promotion and disease prevention at a national level. An enhanced focus on health promotion is an integral part of preserving independence and reducing long-term care needs among aging women as well as reducing escalating health care costs.

DEFINITIONS

Perimenopause

According to the World Health Organization (WHO) and the International Menopause Society (IMS) the term perimenopause is the appropriate term to describe the period immediately prior to menopause and including the first year following menopause (Council of Affiliated Menopause Societies (CAMS), 2004).

Menopause

Menopause (natural menopause occurring without pathology or medical intervention) is defined as the permanent cessation of menstruation resulting from the

loss of ovarian follicular activity. Because there is no clear biological marker, the diagnosis of natural menopause is made retrospectively after 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause (CAMS, 2004). This retrospective nature of diagnosing menopause and the overlapping of period of what is termed perimenopause provides insight into why the terms can be used interchangeably. Hereto forward the terms perimenopause and menopause may be used interchangeable based on the source information.

Menopausal Aged Women

The mean age of menopause in the United States and most of the industrialized world is approximately 51.3 years with a range from 44-55 years of age (Speroff& Fritz, 2005; Zacur, Appling, Freedman & Montgomery-Rice, 2002). Women, particularly those who live in underdeveloped countries may experience menopause at a younger age, such as the early or mid fourth decade of life (Beyene, 1989; Zacur, Appling, Freedman & Montgomery-Rice, 2002). Perimenopausal symptoms can appear in women approximately 6-10 years before the onset of menopause. Therefore the term menopausal aged women will reflect women between the ages of 40-55 years of age (Love, 2003; Zacur, Appling, Freedman & Montgomery-Rice, 2002).

Hormone Therapy

For the purposes of this study, HT is defined as the use of the sex hormones, estrogen and/or progesterone during menopause. There are several acronyms in menopause and hormone replacement literature which relate to HT, such as estrogen therapy (ET), combined estrogen-progesterone therapy (EPT), to name a few. Within this text the term HT shall encompass all types HT whether combined estrogen/progestin/testosterone or estrogen alone.

Vasomotor Symptoms

Vasomotor symptoms describe a collection of menopausal phenomena including hot flashes or hot flushes and night sweats. A hot flash or hot flush is a sudden feeling of warmth and often a breakout of sweating usually confined to the chest, neck, face and head. There is an intense feeling of heat that often initiates in the chest area and spreads to the face head and neck. When hot flashes occur at night, they are often accompanied by night sweats which can disrupt sleep patterns (Freedman, 2001, 2002c, 2005; Speroff & Fritz, 2005), within in this text the terms vasomotor symptoms or hot flashes may be used interchangeably.

Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) defines Complementary and Alternative Medicine (CAM) as a "group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine (NCCAM, 2005) pg.1".

Complementary and Alternative Medicine are not synonymous; complementary medicine utilized along with conventional medicine, such as the term complementary suggests. Complementary simply means to balance or harmonize with (NCCAM, 2005). For example, utilizing meditation to relax and reduce vasomotor symptoms along with HT.

Alternative medicine on the other hand is when modalities are used in place of or instead conventional medicine (NCCAM, 2005). An example of an alternative therapy may include the use of homeopathic medicine or meditation to reduce vasomotor symptoms instead of medical treatment with hormones or other prescribed drugs.

The NCCAM breaks down CAM into five categories; the first is alternative medicine, which may include modalities such as homeopathic medicine and naturopathic

medicine. The second is that of mind-body intervention which includes meditation, prayer, or therapies that use creative outlets such as art, music, or dance. Third are biologically based "natural" therapies such as herbs, foods, and vitamins. Fourth are manipulative and body-based methods such as chiropractics or and massage. And lastly, the fifth category is labeled energy therapies, which would include biofield therapies such as Reiki, and Therapeutic Touch or bioelectromagnetic based therapies using electromagnetic fields (NCCAM, 2005).

Macrosystems

Macrosystems consist of broad cultural and historical influences of which all the other systems are embedded within (Bronfenbrenner, 1979). Macrosystems are operationalized for this study as pivotal clinical trials influencing menopause symptom management modalities (i.e.: HERSI & II and WHI). Macrosystems also include the subsequent consensus statements aimed at guiding clinical practice that closely followed the publication of the WHI findings (see figure1& 2. also see appendix 1, section 4: what influenced your decision to stop taking HT).

Exosystems/Mesosystems

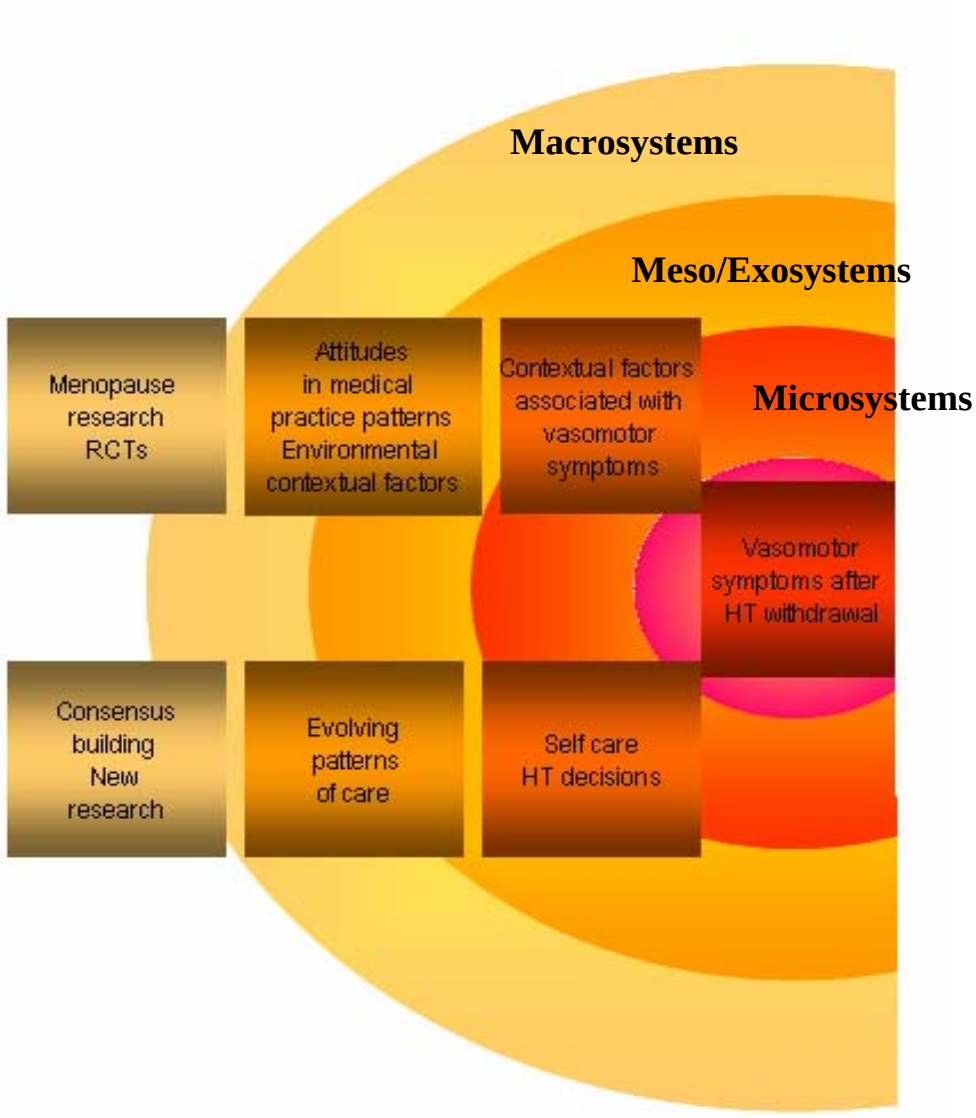
Mesosystems are those settings in which the individual interacts in more than one setting either alone or through linkage of a third party and/or by the "intersetting" of knowledge through written communications such as pamphlets and books. Mesosystems are actually interrelations among microsystems described in the next paragraph. This level also includes exosystems which include influential external contexts such as a woman's work, school or church settings or that of her family and close acquaintances. The mesosystem and exosystems is operationalized in this study as the influences of health care provider, pharmacist, husband, life partner, coworkers of friends a well as

popular media such as written word, television and Internet (see figure 1&2, also see appendix 1, section 4: what influenced your decision to stop taking HT).

Microsystems

Microsystems consist of an individual's genetic make up as well as a place or setting where individual is engaged in close face-to-face interactions with others, such as the home, extended family, work or school settings. Microsystems are operationalized in the questionnaire as contextual factors that may influence menopause experiences as follows: 1) ethnicity, 2) income 3) education 4) age, 5) length of time post menopause, 6) body mass index (height and weight), 7) type of menopause, 8) presence of hot flashes prior to HT use 9) severity of current hot flashes, 10) length of HT use, 11) smoking, and 12) alcohol consumption as well as 13) geographical location (see figure 1&2; also see appendix 1, section 2: hormone demographics &section 3: menopause history).

Figure 2: Dissertation Model



SUMMARY

Adequate studies exist that have assessed diverse groups of menopausal aged women with respect to the actual use or nonuse of HT, including use in low income women (Appling, Allen & Bellatoni, 1999; Appling, et al., 2000; Bartman & Moy, 1998), African American women (Holmes-Rovner, et al., 1996) and Hispanic women (Longworth, 2003).Yet there is little information available on women who are withdrawing from HT. The recent historical events have led to an increase in the number of women who are now choosing to discontinue or not begin hormone therapy (HT) at all (Hersh, Setanick & Stafford, 2004). There is a dearth of information about the menopausal experiences of women who have never used or have discontinued HT. Thus there is a great need for research to investigate the experiences of women who are discontinuing therapy. It is also important to understand the contextual factors associated with those experiences in order to identify women who may experience difficulties with withdrawal from hormones. Many women have chosen to treat their symptoms with alternatives therefore it is imperative that we start to explore the use of alternative medical treatments and CAM therapies as well as women's perceptions of effectiveness so that further studies can be designed to assess risks, benefits, safety and efficacy of these therapies.

The ecological model is a complex and abstract theoretical framework that elucidates the interconnectedness of the person and the environment. Although the theory lacks parsimony, the basic tenets of the theoretical framework are in a sense very intuitive within a nursing science perspective. Regardless of the abstract nature, acknowledgement of the interconnectedness between systems of the individual

(microsystems, mesosystems, exosystems and macrosystems) can play in integral role women's health research.

The ecological framework provides a useful guide to assess factors that may influence a woman's experience of menopause and adoption of health behaviors to manage symptoms, if indeed symptoms occur. The ecological model described by Bronfenbrenner (1979) provides a theoretical framework that can be used to guide research with women regarding their experiences of menopause. The model is useful in providing a framework for a research design that can help to elucidate what the experience of menopause after discontinuation of HT will look like through this multifaceted lens. The model will help define the macro-environmental and societal factors (i.e.; culture, religion, spirituality, family, community, historical events, health care trends) that affect the care of menopausal aged women, especially those that are experiencing vasomotor symptoms. An ecological model also includes biological factors (health risks such as urogenital atrophy, cardiovascular disease, osteoporosis) associated with menopause that vary within a cultural context. The findings of research driven by an ecological perspective will lead to identification of individual contextual factors associated with menopausal symptoms so that women at risk for return of symptoms can be appropriately counseled and assisted through the transition of with drawing from hormones. It will also lead to an understanding of the types of CAM that women accept, use and perceive as useful so that these modalities can be identified and studied further to ensure safety and efficacy.

Chapter Two: Review of the Literature

ETIOLOGY OF VASOMOTOR SYMPTOMS

Research has shown that vasomotor symptoms in menopausal women are in part related to a decrease in endogenous estrogen levels as they occur when estrogen levels drop and are readily relieved by HT (Freedman, & Blacker, 2002; Kasuga, 2004; Weiss, 2002). Vasomotor symptoms are far more complex than previously thought and the underlying mechanisms behind them are poorly understood. Several theories have emerged over the years and understanding these mechanisms is extremely important in the development of alternative methods to relieve symptoms. These theories are included in this review because they provide an understanding of the etiologic factors that drives current research and uses of alternative treatments for vasomotor symptoms. It is important to note that while these theories provide some understanding of vasomotor symptoms with the onset of menopause, it is unknown if these same theories would apply to vasomotor symptoms occurring after the discontinuation of hormone therapy.

Thermoregulation Dysfunction

The predominant theory of vasomotor symptoms is that of a dysfunction in the central thermoregulatory center. Vasomotor symptoms occur as a way to dissipate heat when the core body temperature rises above a certain set point. The core body temperature rises, peripheral dilation occurs causing flushing followed by sweating and cooling of the body with sweat evaporation. Core body temperature (T_c) is regulated by the hypothalamus. In menopausal women, this dysfunction of the thermoregulatory center in essence is a narrowing of the temperature regulating zone in women susceptible to hot flashes. Thus even a small increase in temperature could trigger the heat loss mechanism

resulting in hot flashes (Freedman, 2001, 2002b, 2002c; Freedman & Krell, 1999). Freedman (1995; 2002a, 2002c, 2005) also found that the thermoregulation zone in menopausal women may be in fact narrowed on both sides, where even the low T_c threshold is increased resulting in an increased rate of shivering in women after a hot flash. It has been postulated that the narrowing of the thermoregulation zone is caused by elevated levels of norepinephrine.

Freedman and Subramanian (2005) explored the T_c variation, sweating thresholds, sweat rate controlling for serum estradiol and progesterone, and BMI in three groups of women. These groups consisted of 12 symptomatic menopausal women, 10 asymptomatic menopausal women and 12 women with normal menstrual cycles. The researchers found that symptomatic women had a narrower thermoregulation zone than asymptomatic women or non-menopausal women. The results remained the same even when controlling for serum hormone levels and BMI.

Neuroendocrine Pathways

Norepinephrine

Emerging research has shown that complex neuroendocrine pathways involving norepinephrine, estrogen, testosterone, serotonin and endorphins may also play a role in thermoregulation. Norepinephrine is increased just before and with hot flashes. Norepinephrine plays its role through Alpha-adrenergic receptors. Estrogens modulate the adrenergic receptors in many tissues including the hypothalamus (Casper & Yen, 1985; Freedman & Woodward, 1992; Freedman, Woodward, & Sabharwal, 1990).

Studies measuring norepinephrine and hot flash experience have been inconclusive with regard to the presence of brain norepinephrine during hot flashes because it is difficult to assess true brain levels (Freedman & Woodward, 1992;

Freedman, 2000). Freedman and Woodward therefore measured plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) which is the main metabolite of norepinephrine in the brain and its peripheral metabolite vanillylmandelic acid (VMA) as proxy measures for brain norepinephrine levels. The authors found that there were significantly higher levels of MHPG in the 13 symptomatic women compared to the 6 asymptomatic menopausal women indicating an increase in brain norepinephrine levels is associated with hot flashes. These findings are consistent with earlier studies with Clonidine, a α_2-adrenergic agonist to reduce central noradrenergic activation and thus hot flushes (Clayton, Bell & Pollard, 1974; Laufer, Erlik, Meldrum, & Judd, 1982).

Serotonin

Serotonin (5-HT) levels have been shown to be decreased in natural or surgically menopausal women. When estrogen is given the values have been shown to return to normal (Gonzales & Carillo, 1993). Low serum estrogen levels have been associated with high concentrations of the 5-HT_{2A} receptor subtype on platelets, thus it may play a key role in the occurrence of hot flushes. Basically, estrogen withdrawal decreases 5-HT in the blood stream which increases the 5-HT_{2A} receptors in the hypothalamus which is involved in thermoregulation as has been noted previously. Increases in 5-HT_{2A} receptors results in a change in the thermoregulation set point causing a need for heat dissipation as is seen in hot flashes. Blocking the 5-HT_{2A} receptors could result in reducing hot flashes. Treatment with a selective serotonin reuptake inhibitor activates the 5-HT_{2C} receptor which will in turn inhibit the 5-HT_{2A} receptors (Berendsen, 2000).

MACROSYSTEMS INFLUENCES

The literature review that follows is constructed according to the ecological framework of this study. The macrosystems within an ecological model consist of broad

cultural and historical influences in which all the other systems of the ecological framework are embedded (Bronfenbrenner, 1979). This section describes those historical events that have led to recommendations to changes in HT prescribing and utilization.

Pivotal Clinical Trials

Findings from the Heart and Estrogen/progestin Replacement Study (HERS) were published in the Journal of the American Medical Association (JAMA) in August of 1998. The trial was to provide clinical evidence to support epidemiologic data suggesting there were lower rates of coronary heart disease (CHD) in postmenopausal women who took estrogen than in women who did not (Derby, 2000; Grady, Rubin & Petitti, 1992; Hughes, 1990; Psaty, Heckbert & Atkins, 1994; Sidney, Petitti & Quesenberry, 1997; Stampfer & Colditz, 1991; Sullivan, et al., 1990). HERS was a randomized, blinded, placebo-controlled clinical trial designed as a secondary prevention trial for women with established coronary disease to determine if estrogen plus progestin therapy alters the risk for CHD events. This study included a total of 2763 women with coronary disease with an average age of 67 years. The women were randomly assigned to receive either 0.625 mg of conjugated equine estrogens (CEE) plus 2.5 mg of medroxyprogesterone acetate (MPA) or a placebo. The women in this first report of the HERS trial were followed for an average of 4 years. The primary outcome variables were the occurrence of nonfatal myocardial infarction (MI) or CHD death. No significant differences between groups were found for the primary outcomes of the trial. Despite the lack of differences between the groups with regard to the primary outcome variables, there was a statistically significant time trend, with more CHD events in the hormone group than in the placebo group in the first year followed by fewer events in the 4th and 5th years of the trial. Given the findings of no apparent cardiovascular benefits with regard to MI or CHD deaths in the treatment group versus placebo and the additional findings of an increase in CHD

events in the first year for the treatment group, the researcher group recommended that estrogen not be given for the purpose of secondary prevention of CHD. Interestingly, they also found that women who received the treatment did have a statistically lower low-density lipoprotein (LDL) cholesterol level and a higher high-density lipoprotein (HDL) cholesterol level compared with the placebo group. Therefore it was recommended that women already on treatment could continue, given the trend towards a decrease in CHD events in years 4 and 5 (Hulley, et al., 1998).

The Follow Up Heart and Estrogen/progestin Replacement Study II (HERS II) was designed to determine if the decrease in risk of nonfatal MI and CHD that was found in years 4 and5 of the HERS continued with the additional years of follow-up. HERS II followed up the HERS trial for an additional 2.7 years. HERS II was un-blinded and 93% of the original participants consented to continue with this follow up. HERS II was an open-label trial where hormone therapy was prescribed at participant's personal physicians' discretion. The primary outcomes remained the same as nonfatal myocardial infarction and CHD death. At the completion of the follow up the research group found that the lower rates of CHD events noted previously among women in the hormone group in the final years of HERS did not continue in the following years. Recommendations following this trial were again simply that postmenopausal hormone therapy should not be used to reduce risk for CHD events in women with preexisting CHD (Grady, et al., 2002).

The Women's Health Initiative (WHI) is a long-term national health study designed to provide information that will help in preventing heart disease, breast and colorectal cancer and osteoporosis in postmenopausal women. The WHI was sponsored by the National Heart, Lung, and Blood Institute (NHLBI) and is one of the largest clinical trials of women's health ever undertaken in the U.S. The WHI study has three

parts, which include the randomized clinical trial that will be discussed in the following text, an observational study and a community prevention study (www.WHI.org, 2005).

Findings from the Women's Health Initiative (WHI) clinical trial were published in JAMA in July 2002. The WHI was designed to assess the major health benefits and risks of conjugated equine estrogen (CEE), the most commonly used exogenous estrogen in the United States. Recruitment from several clinical sites occurred between 1993 and 1998. This was a randomized controlled primary prevention trial designed to last 8 ½ years. The WHI participants were randomly assigned either to the treatment group, which received CEE 0.625 mg/d, plus MPA, 2.5 mg/d or placebo. Similar to the HERS trials, the primary outcome was non-fatal MI or CHD death and invasive breast cancer was the primary adverse outcome. Unlike other trials, a global index was set up prior to the onset of the study so that if the risks outweighed the benefits, the trial would be stopped. The balance of risks and benefits included the 2 primary outcomes in addition to the occurrences of stroke, pulmonary embolism (PE), endometrial cancer, colorectal cancer, hip fracture, and death due to other causes (Rossouw, et al, 2002).

The WHI trial was stopped just after 5 years when the data and safety monitoring board recommended stopping the trial because the global index of risk versus benefit exceeded the previously set limit for invasive breast cancer adverse effect and the global index statistic supported risks exceeding benefits. The findings at this time revealed absolute risks per 10 000 person-years that were attributable to estrogen plus progestin were 7 more CHD events, 8 more strokes, 8 more PEs, and 8 more invasive breast cancers. As for absolute risk reductions per 10 000 person-years there were 6 fewer colorectal cancers and 5 fewer hip fractures. The authors concluded that the findings from this trial did not support the initiation of or the continuation of CEE/MPA for primary prevention of chronic diseases (Rossouw, et al, 2002).

Consensus Statements

The trials described previously have been hotly debated resulting in several organizations providing consensus statements to guide health care providers. The American College of Obstetrics and Gynecology (ACOG) states that it is important to understand that different forms of hormone therapy are associated with different risks. And those women without a history of cardiovascular disease (CVD) or breast cancer who are currently use hormone therapy, it is recommended that they use the lowest effective dose for the shortest possible duration. In addition, ACOG also recommends the use of selective serotonin re-update inhibitors (SSRI) for the relief of vasomotor symptoms. Finally, the recommendations state that hormone therapy should not be used solely for the purpose of osteoporosis prevention as there are other treatment modalities such as biphosphonates or selective estrogen receptor modulators (SERMS) that are also effective in treating and/or reducing this risk (American College of Obstetricians and Gynecologists, 2004)

The American Heart Association (AHA) states that there is no research to support that hormone therapy is beneficial for primary prevention of CVD. Thus hormone therapy should not be initiated for secondary prevention of CVD. Treatment or non-treatment in women currently on HT should be individualized based on the patients' history, preferences and proven noncoronary benefits and risks. In the event that a woman develops CVD or is to be immobilized, hormone therapy should be discontinued to reduce risk of VTE. (Burger & Teade, 2001; Mosca, et al., 2001).

The American Society of Reproductive Medicine (ASRM) recommends that treatment of patients during the menopausal transition should be based primarily on symptom experience (American Society of Reproductive Medicine [ASRM], 2005).

The National Institute of Health (NIH) consensus statement on the "Management of Menopause-related Symptoms" in March of 2005 recommends the hormone therapy is only indicated for the treatment of vasomotor symptoms and thus should be used only for that purpose at the lowest possible dose for the shortest period of time (The National Institute of Health, 2005).

The FDA also recommends that estrogens should only be prescribed for the treatment of menopausal and urogenital symptoms at the lowest possible dose for the shortest time possible (U.S. Food and Drug Administration, 2004).

The North American Menopause Society (NAMS) provides the most comprehensive position statement to guide clinical practice. NAMS recommends that for women who are experiencing only mild vasomotor symptoms use of nonprescription complementary alternative methods should be offered despite the lack of evidence to support the effectiveness of these methods. For women with severe symptoms, HT remains is recommended (North American Menopause Society, 2004 a,b,c,d).

MESOSYSTEMS/EXOSYSTEMS INFLUENCING VASOMOTOR SYMPTOM EXPERIENCES

Mesosystems are interrelations between microsystems of others. These mesosystems can include social networks, communities and peer groups or even health care clinics within which the dyad interacts. Exosystems represent influential contexts outside of the individual's microsystems but within the microsystems of an individuals parents', children's or a spouse's school, work, social or community settings. For the purpose of this study, exosystems and mesosystems described here are that of the health care providers' attitudes and prescribing habits as well as the attitudes of women in response to the macrosystems historical influences (i.e.: pivotal trials and resulting consensus statements). Mesosystems such as family members, alternative health care

providers, and lay literature have also led to interest in and use of alternative treatments for vasomotor symptoms as caution increases over HT use.

Trends in attitudes and vasomotor symptom management

In the wake of WHI, studies now emerging have found that clinical practice has changed in that there has been a decrease in new prescriptions for hormones as well as a noted decrease in the dosage if of current prescriptions for hormone therapy (Haas, Kaplan, Gerstenberger, & Kerlikowske, 2004; Hersh, et al., 2004; MacLennan, Taylor, & Wilson, 2004). In addition, studies that have also found a definite change in patients and health care provider attitudes towards hormone therapy in the wake of WHI. These studies have shown more caution in the weighing of benefits and risk with a trend towards decreasing the dosage of HT if therapy would continue as well as discontinuance of therapy (Blümel, et al., 2004; Bosworth, et al., 2005; Ekström, 2005; Haas, et al., 2004; Leung, Ling, & Tang, 2005; MacLennan, et al., 2004; Rolnick, Kopher, DeFor, & Kelley, 2005). Despite the knowledge of the growing trend to discontinue hormone therapy, information is lacking on how this trend will affect women's menopausal experiences.

Adoption of Complementary and Alternative Medicine trends

With more and more women discontinuing HT during this time, little is known about the changing attitudes and adoption of complementary alternative medicine (CAM) therapies especially in women who have discontinued HT. Prior to WHI several studies have explored the use of CAM.

Kaufert and colleagues (1998) found that nearly 80% of the menopausal women surveyed at health conference utilized CAM (herbs, yoga, TCM) to treat menopausal symptoms. Newton and colleagues (2002) conducted a telephone survey of over 800

hundred women aged 44-65 and found that 75% of the women use CAM and 22% utilized CAM specifically for menopausal symptoms. The women surveyed in these studies were predominantly White and well educated.

Factor-Litvak and colleagues (2001) conducted a pilot survey via phone interview of a more diverse group of 300 women (100 White, 100 African American, and 100 Hispanic) in New York City. The authors found that over 50% of the women used some type of CAM therapy and 40% had visited a CAM provider without any significant racial or ethnic differences.

Bair and colleagues (2002, 2005) examined the use of CAM among midlife women who participated in the Study of Women's Health Across Nations (SWAN). The SWAN, is a 10-year cohort study of over 3300 women from varied ethnicities including African American, Hispanic, Japanese, Chinese and Caucasian. The authors found that nearly half of the total participants utilized some type of CAM therapy. Consistent with other surveys, those who utilized CAM were more likely to be older, married, higher SES, and reported lower health status than nonusers. The authors also found no racial and ethnic differences.

Kronenburg and colleagues' (2006) study represents the most recent data related to the women's adoption of 11 domains of CAM (excluding only religion and spirituality) use across racial/ethnic groups. The authors found that CAM use was high across all ethnic and racial groups. The highest overall use of CAM occurred in non-Hispanic White and Chinese American women. Women in this group tended to use a wider variety of CAM modalities and visited a CAM provider more than other groups. The authors also found that Hispanic women tended to use herbs and Chinese American women used acupuncture more often than other groups. Although not specific to

menopause this exciting study illustrates the increased use of CAM by women in all ethnic and racial groups.

The survey research presented here has illustrated that essentially all cultural groups of women adopt CAM, except that there is less utilization in women of lower socioeconomic status. Consistently, the most significant predictive demographic factors of socioeconomic status were that of income and educational level. The cost of herbal supplements and CAM therapies can be significant and in most cases is not covered by prescription health plans or state subsidized health care plans if indeed they have any health care insurance coverage. Given the historical changes that have occurred, it is important to see how attitudes and adoption of CAM have changed in the post WHI period with regard to adoption of CAM modalities specifically for menopause symptoms.

A review of the lay menopause literature was performed to assist in developing the list of CAM therapies for the questionnaire used in this study. The review found, interestingly enough, that out of the 700 texts, only two were intended for Hispanic women, and only one of the texts was available in the Spanish language (Vera, 2003). Only two books were located that discussed experiences and recommendations of menopause for African American women (Porter & Gaston, 2001; Scott-Brown, 2003). This clearly reflects a lack of culturally sensitive informative texts that may leave many women without knowledge of available measures to enhance health and well-being and or treat menopausal/vasomotor symptoms during menopause.

MICROSYSTEMS INFLUENCING VASOMOTOR EXPERIENCES

Ethnicity and Race

The predominant biomedical perspective makes the assumption that menopause is a universal experience. Yet, although there is a biologic universality, it is becoming

increasingly clear that a woman's experience of menopause can be quite varied within the context of culture, ethnicity and community. Lock and Kaufert (2001) challenge the notion that the experience of menopause is universal and suggests that not all women are at equal risk for morbidity measures associated with menopause and women should be looked at in what she terms "local biologies", which include varied cultural, social and psychological experiences.

For example, Beyene (1989) found that Mayan women in a Yucatan village experienced menopause a few years earlier than Western women. In addition, these women did not have a concept of menopause as a disease state as Western women do. Beyene contends that this perception is possibly a factor in why these Mayan women do not experience symptoms related to menopause.

Lock and Kaufert (2001) note that Japanese women report far less symptoms than women from the US or Canada. In addition, these women did not appear to be equally at risk for the commonly expected morbidity of osteoporosis, heart disease or breast cancer. Beyene (1989) also found similar evidence with the Mayan women from the Yucatan as they too, did not appear affected by osteoporosis despite the early onset of menopause and lack of HT use.

Avis and colleagues (2001) looked at the menopause experience across five racial/ethnic groups, African American, Caucasian, Chinese, Hispanic and Japanese. After controlling for age, education, health and economic strain, they found that Caucasian women experienced more somatic symptoms. African American women reported more vasomotor symptoms. And finally, consistent with other studies they found that the group of Asian women reported fewest symptoms compared to all groups. Langenberg, Kjerulff and Stolley (1997) also found that Black women were more likely to experience hot flashes compared to White women. Miller and colleagues (2006) found

that although Black women had a higher risk for hot flashes it was related to other concurrent risk factors such as being a current smoker, lower estrogen levels and a, higher BMI than Caucasian women in their study.

Gold, et al (2006) in their study of women's health across the nation (SWAN) has followed large diverse group of menopausal women (n=16,065) from 1997 on. Women included in this study were White (n=1543), African American (n=930), Hispanic (n=284), Chinese (n=250) and Japanese women 9n281) from 7 different sites throughout the US. Gold and colleagues found conversely found that African American women in this study experienced less vasomotor symptoms when compared to white women (p=<.01).

In contrast, Schwingl, Hulka, Sioban and Harlow (1994) did not find differences between Black and White women. Schwingl they found that socioeconomic status was a significant predictor of higher hot flash occurrences, not race.

Family genetics or familial tendencies have also been suggested as predictive factors for menopausal transition experiences. Starpoli (1998) found that women whose mothers had experienced hot flashes also experienced them as well.

The studies reviewed here have suggested that ethnic and cultural differences may affect vasomotor symptom experience in women, although the results have are conflicting. This is not surprising when viewing menopause through an ecological framework given the multidimensional makeup of each individual woman.

Socioeconomic Status

Socioeconomic status has been shown to be related to vasomotor symptom experience in women. Socioeconomic status can be defined by proxy measures of income and education. Numerous studies have shown that lower educational status is associated with higher incidence of vasomotor symptoms (Chiechi, Fereri, Bianco, Berardesca &

Loizzi, 1997; Gold, et al., 2000; Li, et al, 2003; Neri, Demyttenaere & Fracchineeti, 1997; Schnatz, Banever, Greene, & Sullivan, 2005). Consistent with low educational status, lower income or poor employment is also associated with an increase in vasomotor symptom reporting symptoms (Chiechi, et al., 1997; Gold, et al., 2000: Li, et al., 2003; Neri, et al., 1997).

Body weight

Body weight has been found in some studies to increase vasomotor symptoms (Campagnoli, et al, 1981; Wilbur et, al 1998). Li and colleagues (2003) found that weight gain in menopausal women, among others factors were major risks for vasomotor complaints.

Using BMI as measurement level, later studies have shown that a higher BMI was associated with a higher incidence of hot flashes (Chiechi, et al, 1997; Gold, et al, 2000; Gold et al, 2006; Langenburg, 1997; Starpoli, 1998) Using Odds Ratios (OR), several studies found higher BMI was associated with increased prevalence of hot flashes. Wilbur et al (1998) found an adjusted OR of 1.09. Whiteman (2003) reported that a BMI of over 30 kg/m^2 was associated with an increased risk for hot flashes compared with those with a BMI less than 24.9 kg/m^2 (adjusted OR = 2.1, 95% CI 1.5, 3.0).

Starpoli, et al (1998) found no association between BMI and hot flashes. Conversely, two studies found that women with lower BMI were more likely to have hot flashes (Guthrie, et al, 1996; Schwingl, et al, 1994), although in one of these studies this factor was mediated by positive smoking status (Schwingl, 1994).

Smoking

Several studies have shown that hot flashes are increased in smokers (Avis, et al, 1997, Gold, et al, 2000; Kuh, Wadsworth & Hardy R., 1997; Starpoli, 1998; Whiteman,

2003). Avis calculated OR of increased frequency of hot flashes of 1.44 and 1.57 for bothersome nature of hot flashes. Kuh, et al. (1997) reported an OR of 1.6 for ever smokers and the prevalence of hot flashes. Starpoli (1998) reported an OR of 1.1 for current smokers with pack years < 40 and OR of 2.5 for pack years >40. Gold and colleagues (2000) found OR of 1.68 in current smokers who smoked over 20 cigarettes per day. Whitman and associates (2003) found that women who were current smokers were at an increased risk for hot flashes had an adjusted odds ratio OR of 1.9 and the risk of hot flashes increased as the amount of smoking increased.

One study failed to show an association with smoking and the experience of hot flashes (Gannon, Hansel & Goodwin. 1987) The authors reported from this small study with 10 women that stress and anxiety were related to hot flashes but not alcohol or smoking.

Type of Menopause

Langenburg (1997) found that HT was most commonly recommended for women who have had a hysterectomy/oophorectomy for noncancerous conditions. In addition, there is agreement that women who experience surgical menopause encounter more vasomotor symptoms than women who have not. Studies have shown that number of women in this group experiencing vasomotor symptoms reaches nearly 90% (Chakravarti, et al., 1977; Feldman, Voda, & Gronseth, 1985).

Kritz-Silverstein (2003) in a study with 1121 women aged 50-89 the authors found that the duration of estrogen use was longer for women who had a hysterectomy than women who experience natural menopause ($p < 0.001$). Interesting to note, that among current estrogen users, the authors reported that positive feelings were significantly higher in women who had a hysterectomy, with or without bilateral oophorectomy ($p < 0.01$) than in women with natural menopause. In the post WHI period

Bosworth and colleagues (2006) recently published their findings from a study looking at factors related to discontinuation and initiation of HT. The researchers found that women who underwent surgical menopause were less likely to discontinue HT as compared to those who experienced natural menopause.

A recent study also suggests that HT does not entirely eliminate vasomotor symptoms in pre-menopausal women who have undergone a total hysterectomy and bilaterally oophorectomy. This could lead to continued use and unsuccessfully discontinuing HT as well (Madalinska, et al., 2006). All of these studies *strongly* suggest that surgical menopause increases the risk for vasomotor symptoms.

Age/ Menopause status (years post menopause)

Gold and colleagues (2000) did not find age to be associated with vasomotor experiences. Two studies (Gold, et al, 2006; Li et al, 2003) found that the older a woman was the more likely they would have hot flashes, but these studies also included perimenopausal women, therefore it is not surprising that the older the woman the more likely hot flashes would occur as they near menopause. Gold et al, (2006) also found that the more years post menopause, the less likely they would experience hot flashes.

Symptom experience prior to onset of hormone therapy

Three studies have reported vasomotor experiences of women who are discontinuing HT, one before the release of WHI study findings (Hammar, et al, 1999) and two after (Grady, et al., 2003; Ockene, et al., 2005). These studies suggest occurrence of vasomotor symptoms prior to HT is a significant predictor of the experience of the occurrence of vasomotor symptoms after discontinuation of HT. These studies were discussed in great detail in chapter 1.

Geographical Distribution

As has been elucidated earlier the most predominant theory of vasomotor symptoms is that of a dysfunction in the central thermoregulatory center. Vasomotor symptoms occur as a way to dissipate heat when the core body temperature rises above a certain set point. Even small increases in temperature may trigger the heat loss mechanism resulting in hot flashes (Freedman, 1998, 2001, 2002a, 2002b, 2002c, 2005, Freedman & Blacker, 2002, Freedman & Dinsay, 2000, Freedman & Krell, 1999, Freedman, Norton, Woodward, & Cornélissen, 1995). Given this theoretical framework, it is possible that geographic location may play a part in the experience of hot flashes in women living in warmer climates or during warmer seasons. Sievert and Flanagan (2005) analyzed hot flash frequencies from 54 studies. They found that menopausal women in warmer temperatures actually had fewer hot flashes than women in colder climates. The authors suggest that perhaps women in these warmer climates be accustomed to the warmer climate and are less sensitive to increases in temperature.

Hormone therapy discontinuation type

Two of the discontinuation studies discussed earlier have suggested that how discontinuation occurs does not necessarily reduce the occurrence of vasomotor symptoms after discontinuation of HT (Grady, et al, 2003; Ockene, et al, 2005). Only one small prospective study (N=91), was found that was specifically designed to look at discontinuation method. The researchers recruited women from May 2001 to June 2003 that had been on HT for 3 years or more and desired to discontinue HT. The women opting to discontinue HT were randomized to one of two groups, either tapering discontinuation or abrupt cessation of HT (Haimov-Kochman, et al., 2006). The authors reported that tapering of HT did not reduce the return of HT, but instead only delayed the return. The authors did feel that although the outcomes were similar the tapering of HT

may help to decrease the estrogen dose to the lowest effective dose as is the current accepted recommendation. These studies were discussed in depth in chapter 1.

In summary, these studies provide evidence that microsystems such as ethnicity/race, socioeconomic status, body weight, smoking, type of menopause, age, symptom experiences at menopause onset, geographical and how HT is discontinued may be associated with the varied vasomotor symptom experiences in menopausal women. The studies results in general are conflicting with the strongest evidence related to type of menopause and the way in which HT is discontinued. Women with surgical menopause consistently have been shown to have more vasomotor symptoms than women who have progressed through natural menopause. The studies presented have also clearly shown that how HT is discontinued did not seem to have an impact on the return of vasomotor symptoms. These conflicting findings are not entirely surprising especially when viewing menopause through the lens of an ecological framework in which many factors affect women's experience of menopause.

MEDICAL TREATMENT FOR RELIEF OF VASOMTOR SYMPTOMS

Hormone Therapy (HT)

Estrogen

HT is has long been considered as one of the most efficacious therapies for the treatment of vasomotor symptoms. Given its long history a Cochrane Database summary was published in 2004. The report found that the effects of estrogen for relief of hot flashes were sustained in trials of three months to three years duration with very few reports of serious adverse events or intolerable side effects. In addition the report states that the effectiveness and short term safety of oral HT for the alleviation of hot flushes and night sweats has been well established in clinical trials performed in symptomatic

perimenopausal and menopausal women. In addition, the report states that the longer term safety issues were reported in the findings of WHI study. The report did not attempt to differentiate between oral HT products, combinations, doses or regimens. According to the Cochrane Review there are no implications for further research with regard to safety and efficacy within the context of relieving vasomotor symptoms. Future research was suggested with regard to dosing to see if lower doses are similar in efficacy than current doses (Maclennan, Broadbent, Lester, S., & Moore, 2004).

Progesterone

Few recent clinical trials were found on the use of progesterone to relieve symptoms. Two older trials were found that studied the use of medroxyprogesterone acetate (MPA) (Morrison, et al., 1980; Schiff, Tulchinisky, Cramer, & Ryan1980). One trial utilized intramuscular MPA dosing and did not find any statistically significant improvement of symptoms (Morrison, et al., 1980). The second trial was a double blind crossover study of 27 women receiving oral MPA or placebo (Schiff, et al., 1980). A double-blind crossover study was designed to compare the effects of placebo and MPA on vasomotor symptoms 27 postmenopausal women. Both the treatment group and the placebo group had a decrease in symptoms after four weeks of use, 34% versus 73.0% respectively. But, when the treatment group crossed over to the placebo group, they began to have symptoms. This research suggests that MPA alone can help to relieve vasomotor symptoms. Recently use of MPA has become under fire as it was the progesterone studied with estrogen in the WHI trial and it has been suggested it that it may have a potentiating affect on breast cancer risk.

Recently with the increase in use of botanicals, natural progesterone creams have been marketed to women purporting to improve vasomotor symptoms as well as alleviating a variety of other menopausal symptoms. In a double blinded, placebo

controlled trial, designed to assess the effectiveness of a progesterone cream on vasomotor symptoms Leonetti and colleagues (1999) randomly assigned 102 healthy menopausal aged women to one of two groups, a transdermal progesterone cream or placebo group. The researchers noted that 83% of the women in the treatment group noted subjective improvement in vasomotor symptoms compared to only 19% of the placebo group suggesting that progesterone cream may be effective in reducing vasomotor symptoms.

A second trial was also undertaken to determine the effectiveness of transdermal progesterone cream on vasomotor symptoms (Wren, Champion, Willetts, Manga, & Eden). Wren and colleagues (2003) performed a double-blind, randomized, placebo-controlled trial comparing the effect of a transdermal cream containing a progesterone (32 mg daily) with a placebo cream. The researchers randomly assigned eighty postmenopausal to one of two groups, one would receive the progesterone cream and the other group would receive the placebo. The Greene Climacteric Scale and the Menopause Quality of Life Questionnaire were used to measure symptom relief. The authors did not find any significant differences between groups with regard to vasomotor symptom reporting.

Androgens

No studies were found specifically designed to assess the effectiveness of using testosterone alone for the relief of vasomotor symptoms. All studies used combined estrogen/testosterone interventions.

Studies with testosterone often did not have vasomotor symptoms as the primary outcome, but instead the primary outcomes were primarily based on libido or sex drive (Lobo, Rosen, Yang, Block & van der Hoop 2003; Shifren, et al., 2000). In addition these studies were in essence confounded by the fact that testosterone was used in combination

with estrogen. Estrogen is known to relieve vasomotor symptoms. Adverse events such as lipid change, acne and hirsutism tend to be higher with the use of testosterone versus estrogen alone (Hickok, Toomey, & Speroff, 1993). Given the limited research available and the side effect profile, testosterone by itself may not be the best choice for reduction of symptoms.

The use of dehydroepiandrosterone (DHEA) as a dietary supplement to reduce the symptoms of aging and improve well-being has increased despite the lack of evidence to support the safety and efficacy of its use. DHEA, an androgenic steroid hormone, has been shown to have an age-related decline. Perimenopausal women have only approximately 50% of peak DHEA levels. DHEA has neurosteroidal properties, and by exerting anti-gamma aminobutyric acid (GABA) action it may act like an antidepressant (Arlt, 2004). Two studies were found that looked at the use of dehydroepiandrosterone (DHEA) supplementation to relieve the symptoms of menopause In a randomized, double-blind placebo-controlled trial with 60 perimenopausal women, Barnhart and colleagues (1999) found that supplementation with DHEA did not alleviate or improve menopausal symptoms. In addition, may have some adverse effects on endocrine and lipid profiles.

Stomati and group (1999) investigated the neuroendocrine and behavioral effects of three months of DHEAS supplementation in 22 postmenopausal women. The women were further broken down into three groups, the first group was treated with oral DHEAS (n = 8) the second treated with the same dose of oral DHEAS and transdermal estradiol (n = 8) (DHEAS) and the third with transdermal estradiol alone (n = 6). In the groups treated with DHEAS, mean basal serum DHEA, DHEAS, androstenedione, and testosterone levels significantly increased after treatment, while no changes were shown in the group receiving estradiol alone. Vasomotor symptoms showed improvement in all

groups as measured by the Kupperman index. This study, although lacks significant statistical power provides some support for therapeutic efficacy of the DHEAS on menopausal symptoms.

Given the conflicting results of these studies and the low power of the Stomati (1999) study, support is lacking with regard to effectiveness of DHEA to treat symptoms. Indeed, there may be adverse effects on lipid and endocrine parameters (Barnhart, 1999).

Antidepressants

As reported earlier, it has been postulated that hot flashes occur as a result of an alteration in the thermoregulatory set point in the hypothalamus following estrogen decreases. The exact mechanism of action by which venlafaxine or other antidepressants may ameliorate hot flashes has not been established; however, both norepinephrine and serotonin are thought to be involved in central thermoregulation. It is possible that antidepressant effects on these receptors may help reestablish the thermoregulatory set-point.

Clinical research studies have examined at the use of variety of antidepressant medications such as selective serotonin reuptake inhibitors (SSRI) such as paroxetine (Paxil®). Stearns, Beebe, Iyengar and Dube (2003) studied paroxetine in a double-blind, placebo-controlled trial. The researchers' randomly assigned 165 menopausal women, who were experiencing at least 2 to 3 daily hot flashes and had discontinued HT for at least 6 weeks to one of three groups. The three groups consisted of a placebo arm, and two intervention arms with different paroxetine doses 12.5 mg/d or 25.0 mg/d. The study participants were followed for six weeks, with the main outcome measure of a mean change from baseline to week 6 in the daily hot flash composite score The hot flashes composite score was determined by the severity of the hot flash (mild = 1, moderate = 2, severe = 3, very severe = 4) multiplied by the daily number of hot flashes experienced at

that severity level. The authors found an equal improvement in the composite score for both the treatment groups. This study provides support for use of paroxetine to relieve symptoms although the dosing it is inconclusive because both groups had an equal improvement.

Venlafaxine (Effexor®) is a selective norepinephrine reuptake inhibitor (SNRI) that has a slightly different mechanism of action from an SSRI. Evans, et al, (2005) conducted a 5-month study to assess the safety and efficacy of venlafaxine for the treatment of hot flushes in menopausal women. Sixty women (mean age 47.6 years) were randomly assigned to one of 3 treatment groups the placebo control group, venlafaxine 37.5mg/day group or venlafaxine 75mg/day group. Due to high withdrawals from the venlafaxine 75mg/day group voluntarily withdrew; the intervention groups were collapsed into one single group receiving 37.5mg/day for an additional 4 months. Compared to the baseline assessment week, after the third week, hot flushes increased in the control group by 11%, and decreased in the venlafaxine treatment group.

Grady-Weliky et al (2001) published a case report of 52-year-old women with a history of major depressive disorder, hysterectomy and a bilateral salpingo-oopherectomy. The patient was placed on venlafaxine XR at 75 mg/day and complained of a return of hot flashes 2 weeks after starting venlafaxine. After 7 weeks on venlafaxine XR at 75 mg/day she noted a reduction in frequency and severity of hot flashes. The venlafaxine XR dose was titrated up to 150 mg/day and the patient noted increased frequency of hot flashes. The frequency and severity of her hot flashes were subsequently reduced after staying on the venlafaxine at 150 mg/day for an unspecified amount of time. The case report provides another viewpoint with regard safety and control of symptoms.

In summary, utilizing paroxetine or venlafaxine for hot flashes relief is an off label use of both drugs. With either the SSRI or SNRI although there is some suggestion they may improve symptoms, there is limited high level research to support their effectiveness in the relief of vasomotor symptoms.

Other Medical Therapies

Clonidine

As described earlier norepinephrine has been indicated as part of the etiologic factors for hot flashes. The earliest study located was by Lindsay and Hart (1978). This was a double-blind crossover trial of Clonidine which failed to show any affect of the treatment on vasomotor symptoms. In a later study, Nagamani, and colleagues (1986) did find a significant effect with Clonidine in lowering symptoms in a randomized prospective double-blind study intended to evaluate the efficacy of transdermal Clonidine for the treatment of menopausal hot flashes. The authors found that a highly significant reduction in symptoms in patients receiving the Clonidine in that 80% reported fewer hot flashes; 73% a decrease in severity; and 67% a decrease in duration. Only 36% of the placebo group reported a reduction in hot flashes, 29% a decrease in severity; and 21%, shorter duration. Clonidine did not have a significant effect on lowering of blood pressure or pulse in this study.

Gabapentin

Given the neuroendocrine pathways etiologic factors the use the anticonvulsant gabapentin was looked at for the relief of hot flashes. Albertazzi and colleagues (2003) reported on an open case series of 11 postmenopausal women who agreed to take gabapentin on hot flushes for relief of vasomotor symptoms. The participants kept a daily diary of the frequency and severity of their vasomotor symptoms pre and post treatment

with gabapentin. Nine women completed the case series. In this case series gabapentin was found to be extremely effective in reducing hot flush activity. A significant reduction in symptoms was observed with a dose of 300 mg/day. In addition to an improvement in vasomotor symptoms measured by the Green Climacteric Scale the researchers also noted a statistically significant decrease in palpitations, panic attacks, muscle and joint pains and paresthesias. Given these findings and the fact that gabapentin was well tolerated the authors suggest that gabapentin could be a viable alternative for the treatment of hot flushes in women with contraindications to hormonal replacement therapy.

Gabapentin was studied further by Guttuso and colleagues (2003) in a randomized, double-blind, placebo-controlled trial was conducted with 59 postmenopausal women with severe vasomotor symptoms (7 or more hot flashes per day). Guttuso used a higher dose (900mg per day) than did Albertazzi (2003). Guttuso found that after 12 weeks, the intervention group treated with gabapentin 900 mg per day had a statistically significant over placebo of 45% reduction in hot flash frequency and a 54% reduction in hot flash composite score (frequency and severity combined into one score) from baseline, compared with 29% and 31% respectively, for placebo. This study reflected an improvement in symptoms with gabapentin.

The most recent study was conducted by Reddy and colleagues (2006). The authors found in a randomized placebo controlled trial with estrogen as a comparator that gabapentin was as effective as estrogen in reducing hot flashes. Both comparators significantly reduced hot flashes over the placebo arm. These studies suggest that gabapentin may be an efficacious non hormonal alternative for treating vasomotor symptoms.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Up to this point, the review of the literature was developed from clinical research databases reflecting women who under treatment in a clinical setting. Yet, women who present to their health care providers for care because of symptoms related to menopause transition impart only a limited view of all women's experiences of menopause. Many women, especially those who do not experience difficulties or elect not to embrace the biomedical paradigm of menopause may never seek help from a health care provider, thus their voices are lost if one only views the medical literature for answers.

One way in which to understand what women are actually experiencing and what they choose to do to promote health and reduce symptoms during this midlife transition is to review the lay literature. A review of popular self help books and websites can enlighten the researcher or health care provider's perspective of what the general public currently desires to know and what types of health behaviors that are being suggested to them. An informal internet search of "menopause" on each of the following internet book sites, Barnes&Noble.com, Amazon.com, Booksamillion.com and Alibris.com yielded over 3000 subject hits and nearly 700 book titles related to menopause. A cursory first look finds many titles discussing the "management" of menopause. Lyons and Griffin (2003) found a similar pattern in their review of 4 menopause self help books in England. The authors found that the much of literature embraced a medicalized viewpoint of menopause, in that menopause is considered a stressful event diagnosed by the medical professionals, yet the "management" of perimenopause/menopause falls upon shoulders of the women. An example of this is found in a book aptly titled Managing your Menopause, by Wolfe Utian and Ruth Jacobwitz (1992).

To shed light on the most current literature, an advance search was performed that was limited to current books published from 2002 forward, after the Women's Health

Initiative (WHI) study findings were introduced to the health care community and the public. The search yielded approximately 70 books on menopause. The books reflected the changing times in that many titles reflected information about "truths" of hormone replacement (Love, 2003; Seaman, 2003) as well the experiences of menopause/perimenopause including some with a humorous side (Grabowski & Cheeley, 2003; Hulem, 2003; Malucci, 1999; Sacks & Davis, 1995; Taylor & Sumrall, 1991). As expected numerous books are available that suggest alternatives to HT for treatment of vasomotor symptoms. These books provide suggestions on ways to improve health and wellbeing as women navigate through the menopause transition period with the use of herbals, natural estrogens, or an estrogen/phytoestrogen rich diet (Gillespie, 2003; Liew & Ojeda, 1999; Weed, 2003), exercise (Sherman-Wolin, 2007; Smith, K., 2002), yoga (Francina, 2003), mind/body (Benson, Kagan, & Kessel, 2004), homeopathy (Ikenzie & Akenzi, 1998; Lockie & Geddes, 1994; MacEoin, 1997), Ayurveda (Lonsdorf & Mishra, 2002), traditional Chinese medicine (TCM), which includes acupuncture (Lu & Shaplowsky, 2000; Wolfe, 1992, 1994), and spirituality (Boylan, 2000; Cherry & Cherry, 1999; Colbert, 2000; Leonetti, 2002; Sharan, 1994). The following section will provide a review of the various types available treatments identified in the lay literature contrasted with the available medical treatments within the context of current clinical research studies supporting or not supporting the effectiveness of these alternatives for their use in the treatment of menopausal vasomotor symptoms.

Alternative Medicine Systems

As documented earlier in this text NCCAM breaks down CAM into five categories; the first is Alternative medicine, which may include modalities such as homeopathic medicine and naturopathic medicine. The second is that of mind-body intervention which includes meditation, prayer, or therapies that use creative outlets such

as art, music, or dance. Third are biologically based "natural" therapies such as herbs, foods, and vitamins. Fourth are manipulative and body-based methods such as chiropractics or and massage. And lastly, the fifth category is labeled energy therapies, which would include biofield therapies such as Reiki, and Therapeutic Touch or bioelectromagnetic based therapies using electromagnetic fields (NCCAM, 2005). The review of the literature utilizes these categories in its organization.

Traditional Chinese Medicine (TCM)

Traditional Chinese Medicine (TCM) has been integral part of Chinese culture for centuries (Wolfe, 1993). Today TCM is finding its place as a compliment to Western medicine. TCM is a holistic process that includes a variety of approaches, including herbs, acupuncture and meditation to name a few. Typical TCM herbal use is done through a combination of *individualized* prescribed herbs and alternative practices. Clinical trials utilizing Dong Quai (*Angelica sinensis*) or Ginseng (*Panax ginseng*) each as a single herb have shown support for their effectiveness in treating perimenopausal symptoms (Kronenberg & Fugh-Berman; 2002) It is important to note here, clinical trials may likely not be able to measure effectiveness of TCM given its highly *individualized* treatment regimens. Davis and colleagues (2001) studied the effect of a single defined formula of Chinese medicinal herbs (CMH) in a study double blind randomized clinical trial that included 55 menopausal women from Australia. The authors found that the CMH formula was no better than placebo for the treatment of vasomotor symptoms in the women studied.

Acupuncture

Acupuncture is becoming more widely recognized and accepted in the United States. Acupuncture has to do with restoring the natural energy flow (Qi) through the

body. It is postulated that the disruption of Qi is responsible for diseases (National Institute of Health [NIH] Consensus Development Panel, 1998). Three studies were located that examined at the use of acupuncture with menopausal women. All three found a decrease in hot flashes, although statistical significance was reached in only two of the studies (Dong, et al, 2001; Huang, Yael, Chen, Schnyer, & Manber, 2006; Wyon, Lingren, Lundeberg & Hammar, 1995). The first was a randomized trial with the use of either electroacupuncture as the intervention group or shallow acupuncture needle insertion as the control group. These researchers found a significant decrease in the Kupperman index (a measure of vasomotor symptoms) in both groups, but no differences between groups (Wyon, et al., 1995). The second study (Dong, et al., 2001) was a small exploratory project that used classic manual acupuncture with a group of 11 menopausal women. Similar to Wyon, et al, Dong and colleagues (2001) found that classic acupuncture resulted in a statistically significant improvement in vasomotor symptoms for the women studied and the effect lasted up to three months post treatment (Dong, et al., 2001). Huang and associates evaluated 29 menopausal women in a prospective randomized placebo (sham) controlled trial and found that acupuncture significantly reduced nocturnal hot flashes and improved sleep quality.

These findings are very promising, yet, as with other types of CAM modalities such TCM, the study of this health practice is fraught with difficulties with regard to study design and the use of appropriate placebo controls such as “sham” acupuncture (NIH Consensus Development Panel, 1998).

Homeopathy

Homeopathy is an alternative medical system that originated in Germany in the 18th century. The "Law of Similars,” which is the basic principle of the therapy (Lockie & Geddies, 1994). Two studies were located that examined the use of homeopathy for

treatment of menopausal symptoms. The first was a pilot study from the United Kingdom. While no comparator or placebo group was included, the investigators found a decrease in hot flushes from baseline in the women using Homeopathy (Clover & Ratsey, 2002). Jacobs and colleagues (2005) conducted a small (N=83) placebo controlled, double blind clinical trial that examined two types of homeopathy for the treatment of menopausal symptoms in breast cancer survivors. The authors found that the treatment groups did not differ significantly from the placebo groups although there was a trend toward a decrease hot flashes in the treatment group.

Ayurveda

No clinical trials were found supporting the efficacy and safety of the use of Ayurveda for the treatment of menopausal symptoms. One lay text was located in the lay literature review (Lonsdorf & Mishra, 2002). Basically Ayurveda links menopause with aging. Aging is a 'Vata' predominant stage of life. Thus, the symptoms of menopause experienced by some women are similar to the symptoms seen when the Vata dosha rises and upsets the normal balance of the body. Vata-type menopausal symptoms tend to include depression, anxiety, and insomnia. Menopause may also manifest itself as a rise in the other two humors also. Women with Pitta-type symptoms are often angry and suffer hot flashes. Kapha type symptoms include listlessness, weight gain, and feelings of mental and physical heaviness. The type of treatment depends upon the dosha in which the woman's menopausal symptoms are manifesting.

As a note of caution, Saper and colleagues (2004) reported that 1 in 5 of Aryuvedic herbal medicine products (HMD) may contain harmful levels of lead, mercury and/or arsenic. The study findings were limited to a review of products sold within the Boston, Massachusetts area that had been produced in South Asia.

Mind-Body Interventions

Stress Reduction/Applied Relaxation

Reducing stress is important for both menopause and aging in terms decreasing risk of heart disease and other chronic diseases. Harvard University physician Herbert Benson developed and popularized a type of relaxation response that includes a simple meditation process that creates a sense of relaxation and stress reduction. Hoffman, Benson and Ans (1981) have suggested that behavioral relaxation techniques reduce sympathetic activity. Given the purported endocrine involvement associated with menopause and vasomotor symptoms it is possible that relaxation techniques that reduce sympathetic activity could improve vasomotor symptoms as well. Dr. Benson has recently co-authored a book called *Mind Over Menopause*, with Leslee Kagan, M.S., N.P., and Dr. Bruce Kessel for as a guide for women going through this transition. A MEDLINE search for additional references or clinical studies from specifically the above referenced authors did not yield any results, but there were two studies located that examined the use of applied relaxation (AR) that were specific to menopausal aged women.

The first Wijma, Melin, Nedstrand and Hammer (1997) published the results of a small pilot study including 6 women. In this study the researchers examined the relationship of mooed and vasomotor symptoms. They did not explore overall health. Participants were randomly assigned to a treatment or a control group. The intervention they used was a technique called applied relaxation (AR). Results indicated that this technique was able to lower vasomotor symptoms measured using the Kupperman Index but did not have an effect on mood scores.

The second study was a randomized trial in which 12 menopausal women were randomly assigned to AR and 9 women to oral estrogen over a 12 week period (Nestrand,

Wijma, Wyon, & Hammar, 2005). Nestrand and colleagues found that although women in the estrogen group noted a reduction in vasomotor symptoms more quickly than the AR group, 11 of the 12 women in the AR group had a dramatic improvement in vasomotor symptoms similar to the estrogen group. In addition, the vasomotor symptom improvement persisted at the 6 month follow up assessment. It is also important to note that both the estrogen and the AR group there was a statistically significant improvement over the placebo group. These two studies, although very small, begin to suggest that AR may help in the reduction of vasomotor symptoms, yet clearly, there is a need for larger more well designed studies in this area.

Biofeedback

Freedman and Woodward (1992) studied thirty-three women with frequent menopausal hot flushes who were randomly assigned to the treatment group who received eight sessions of training in paced respiration, muscle relaxation, or placebo group who underwent alpha-wave electroencephalographic biofeedback. The authors found a significant decrease in hot flushes in women who had the paced respiration, leading them to conclude that paced respiration training may be a useful treatment alternative for the reduction of hot flushes.

Yoga

Another relaxation practice that is becoming increasingly popular among all age groups is Yoga. Adams (2003) an OB/GYN nurse practitioner and a practicing yogini suggests that yoga could be highly effective for symptom relief in perimenopausal women. Adams believes that yoga is able to increase flexibility, decrease anxiety, depression and blood pressure. A general internet search found one website, www.hotflashyoga.com supporting the use of yoga to reduce hot flashes. A

MEDLINE/CINAHL literature search failed to find any references of randomized clinical trials directly looking at the impact of yoga on health in menopausal aged women. Again, as with the previously mentioned therapies, studying the varied types of Yoga available, the study design would be very difficult to develop.

Biologically Based Therapies

The intake of herbal/dietary supplements is becoming more common among women. Kam and colleagues (2002) found that within a group of women attending a health conference the majority of them had used herbal treatments for menopausal symptoms, of which the most common were soy, ginkgo biloba, and black cohosh.

Soy

Recent studies of Japanese and Chinese women who consume a soy-rich found that their risk of breast cancer, heart disease and experience of menopause related vasomotor symptoms were less than American women (Nagata 2001; Nagata, 1999). Given the growing awareness of the cultural disparity of the menopausal experience, researchers began to postulate that the typical Japanese diet high that is high in soy might play a part in this disparity (Adlecreutz, Hämäläinen, Gorbach & Goldin, 1992). These factors have played a part in the increase interest and use of soy supplements among women.

The lay literature has multiple titles touting the benefit of soy in the diet or as a dietary supplement (Love, 2002; Northrup, 2001; Seaman, 2003; Weed, 2002). Soy appears to be the most well studied dietary supplementation in terms of randomized, placebo controlled clinical studies. Studies on the effectiveness of soy in reducing vasomotor symptoms have shown conflicting results, whether soy foods (Albertazzi, et al., 1998; Burke, et, al., 2003; Dalais, et al., 1998; Lewis, et al., 2006; Knight, Howes,

Eden, & Lowes, 2001; Murkies, et al., 1995; St. Germaine, Peterson, Robinson, & Alekel, 2001; Van Patten, et al., 2002) or soy isoflavone supplements (Faure, Chantre, & Mares, 2002; Han, Soares, Haidar, de Lima, & Baracat, 2002; Penotti, et al., 2003; Quella, et al., 2000; Scambia, et al., 2000; Uplmalis, et al, 2000) are consumed. For those studies showing an improvement (Albertazzi et al, 1998; Faure, et al, 2002 Han, et al, 2002; Scambia, et al, 2000) in menopausal symptoms the effect has been only modest. Unfortunately, even though many of the aforementioned studies were well designed and placebo controlled the amount and type of soy used as the intervention in these studies was varied, so a true meta-analysis is not possible.

Beyond alleviating symptoms of menopause, evidence also exists to suggest that soy intake may have possible health protective effects on bones and the cardiovascular system (Jayagopal, et al., 2002; Lewis & Modlesky, 1998; Moeller, et al., 2003; Washburn, Burke, Morgan, & Anthony, 1999). In addition, Kritz-Silverstein and colleague's (2003) Soy and Postmenopausal Health In Aging (SOPHIA) study suggests that soy isoflavone supplementation has a favorable effect on cognitive function, particularly verbal memory, in menopausal women.

Black Cohosh

The next most common dietary supplement used is Black Cohosh (*Cimicifuga racemosa*). Black cohosh is normally used by women for menstrual cramping, anxiety, insomnia, as well as menopausal vasomotor symptoms (Weed, 2002). This herb has historical use, according to the ACOG Practice Bulletin (2001); black cohosh was the principal ingredient in the classic early turn of the 20th century product "Lydia Pinkham's Vegetable Compound," Black cohosh has been studied most commonly using the standardized branded product called Remifemin®. The studies provide mixed results with regard to its effectiveness. Five clinical trials did not show black cohosh to be any

more effective than placebo in contrast to an additional two clinical trials that did find significant improvement in menopausal symptoms, mainly hot flashes (North American Menopause Society (NAMS), 2004a; Kronenberg & Fugh-Berman, 2002). Evidence indicates that Black Cohosh does not contain estrogenic properties (Amato, Christophe, & Mellon, 2002) therefore the mechanism of action is not clearly understood.

Red Clover

Red clover (*Trifolium pretense*) contains multiple phytoestrogenic compounds and is available as an over the counter (OTC) dietary supplement under a variety of names, of which Promensil® is the most common. Clinical trials for the most part have not found red clover to be effective in relieving symptoms in menopausal women (Baber, Templeman, Morton, Kelly, & West, 1999; Knight, Howes & Eden, 1999; Tice, et al., 2003). Although, one study with red clover (Promensil®) did find a slight improvement in vasomotor symptoms (van de Weijer & Barentsen, 2002).

Evening Primrose Oil

Evening primrose oil (*Oenothera Biennis*) is another commonly used product by women (Northrup, 2002; Weed, 2002). It has been recommended for many years by health care providers for a variety of uses, such as reducing breast tenderness, premenstrual syndrome as well as menopausal symptoms (Kronenberg & Fugh-Berman, 2002). Evening primrose is rich in gamma linolenic acid (GLA) and is purported to contain anticoagulant substances (ACOG Practice Bulletin, 2001). One study was found by Chenoy and Colleagues (1994) that found no benefit in reducing vasomotor symptoms or sweating in menopausal women. In contrast, a study looking at premenstrual syndrome PMS), by Budeiri, Li Wan Po, & Dornan (1996) found no improvement with PMS symptoms, but a significant decrease in breast tenderness.

Vitamins/Calcium

Calcium and vitamin D are commonly accepted and recommended for perimenopausal women. Supplementation with calcium (approximately 1000 mg/day in divided doses) can reduce bone loss in premenopausal, perimenopausal and postmenopausal women, especially at sites that have a high cortical bone composition. Vitamin D supplementation slows bone loss and reduces fracture rates in late postmenopausal women (Lewis & Modlesky, 1998). As for symptom relief, menopausal symptoms can be very similar to PMS symptoms. Clinical trials have found that for women with PMS calcium supplementation can effectively alleviate mood and somatic symptoms (Thys-Jacob, 2000).

Manipulative and Body-Based Methods

Only one study was located discussing the use of manipulative therapies to relieve vasomotor symptoms. Cleary and Fox (1994) reported that women of menopausal age often suffer from some form of chronic joint dysfunction that could be relieved by treatment with cranial osteopathy combined with Fox's low force manipulation which reduces local irritations in the neurological system. Clearly and Fox postulated that given the relationship between the neurological and endocrine systems these manipulations may indeed reduce symptoms. After an initial pilot study, Clearly and Fox performed a placebo controlled trial with 30 participants. The placebo manipulation resembled the intervention manipulation of Fox's low force manipulation, but force was delivered to an adjacent joint. The researchers found a significant reduction in menopausal symptoms. Symptom questionnaires were collected via interviews prior to treatment and at week 15.

Energy Therapies

A single study was found investigating the use of reflexology to relieve symptoms of menopause (Williamson, White, Hart & Ernst, 2002). Williamson and colleagues randomized self selected participants to receive nine sessions of either reflexology or nonspecific foot massage (control) by four qualified reflexologists given over a period of 19 weeks. The outcome measures utilized for vasomotor symptoms were a visual analogue scale (VAS) for severity of hot flashes as well as diary for frequency of hot flashes and night sweats. The authors found no significant differences between the control group and the treatment groups receiving the actual reflexology intervention.

PHYSICAL ACTIVITY/EXERCISE

Exercise is well accepted as an integral part of a healthy lifestyle. Exercise can help reduce the risk of these chronic diseases for women of any age, but the benefits can be significant for menopausal aged women. Exercise helps to reduce the risk of heart disease by enhancing cardiovascular fitness and lowering cholesterol. In addition, exercise can help women maintain a healthy weight. Wildman and colleagues (2004) found that women enrolled in the Women's Health Lifestyle Project, a dietary and exercise intervention trial, experienced a slowing of menopause transition related atherosclerosis.

Exercise that includes weight bearing activities such as walking and weight training can improve bone health. Additionally, irrespective of changes in bone mineral density, physical activities that improve muscular strength, endurance, and balance may reduce fracture risk by reducing the risk of falling (Lewis & Modlesky, 1998).

With regard to menopausal symptoms, a study by Freedman and Krell (1999) found that strenuous physical activity could be a trigger for vasomotor symptoms in menopausal women. Gold and colleagues (2006) found no significant differences related

to vasomotor symptoms related to the level of physical activity the women undertake. In contrast evidence does exist that suggests that women who are physically active may actually experience less vasomotor symptoms than their inactive counterparts (Elavsky & McAuley, 2005; Hammar, Berg & Lindgren, 1990; Ivarson, Spetz & Hammar, 1998).

SUMMARY

The etiology of hot flashes is unclear, although emerging science has begun to see that the causes are multifaceted. Understanding the complex nature of the hot flashes and the recent change in HT recommendations has led to increasing amounts of research search for treatments for vasomotor symptoms. Although there is a call to demedicalize menopause, it is important to remember that the experience of menopause for some women can be quite bothersome. It is for these women that it is important to continue to strive to find ways in which to assist her through this transition.

The ecological framework provides a means to study the varied influences upon a woman's experience of menopause. The over arching macrosystems can affect the experience of menopause by influencing the current paradigm, be that biomedical or natural. In addition, high level clinical research often determines the safe practice patterns and attitudes of clinicians caring for women. Publication of guidelines of lay books, pamphlets and internet information influence women's perceptions and beliefs as well. Acknowledging these levels provides for a more robust evaluation of contextual factors related to women's menopausal experiences.

Chapter Three: Methods

DESIGN

In this descriptive study a retrospective, single cross sectional design was used to explore the vasomotor symptom experiences of postmenopausal women who have discontinued the use of HT. Historically, HT was prescribed for health promotion and chronic disease prevention and use was intended to continue for most of a women's postmenopausal life. However, as a result of several large clinical trials, perceptions regarding HT and HT use protocols now result in earlier discontinuation of HT. Given the rapidly changing standards of care for hormone therapy, little is known about how discontinuing HT influences women's vasomotor symptom experiences. This study enriches the literature regarding this by providing initial information to fill this void.

QUESTIONNAIRE DEVELOPMENT

Given the diversity of women experiencing menopause, it is important to explore differences and similarities in the menopause experience as well as the strategies women use to promote health during this midlife transition. In particular, differences in hot flashes emerge through cross-cultural studies. In order to capture this diversity a questionnaire was created through an extensive review of the literature on the etiology of hot flashes, cultural influences, and contextual factors associated with the experience of hot flashes in women which include 1) ethnicity, 2) socioeconomic status 3) age, 4) length of time post menopause, 5) body mass index (height and weight), 6) type of menopause, 7) presence of hot flashes prior to HT use 8) severity of current hot flashes, 9) length of HT use, 10) smoking, and 11) alcohol consumption as well as 12) geographical location.

The questionnaire was designed with 7 sections to make it more visibly appealing as well as to provide a clear delineation between the different areas of the questionnaire. The final questionnaire sections include an 1) introductory/cover letter that provides an overview of the study, investigator contact information and an informed consent followed by the data gathering sections on 2) demographic information 3) menopause history, 4) discontinuation influences, 5) discontinuation vasomotor experiences, 6) CAM use and perception and a 7) health behavior history (see appendix 1). In addition the pilot questionnaire had a final section with questions about readability and understandability, time to complete and any other comments.

Once the questionnaire was constructed, a group of experts involved in the care of menopausal women were asked to review it. This expert group consisted of 2 physicians (MD), 2 registered nurses (RN), and 5 advanced practice nurses (ANP), provided input on the general content and face validity of the questionnaire. The experts felt that the questionnaire was complete and did not have any additional items to add.

PILOT STUDY

Following expert panel review, the questionnaire was piloted to assess readability and comprehension in a sample of 10 menopausal volunteers. The primary goal of the pilot study was to gain the perspective of menopausal women with regard to ease of completion, readability and understandability of the questionnaire as a basis for revision, if needed.

Sample

The questionnaire was piloted with a volunteer sample of 10 women recruited via flyers or word of mouth. All volunteers were White with an average age of 55 years old with a range from 46 to 79 years. Four of the participants were married, 5 divorced and 1

widowed. The pilot group was very well educated with all women having at least completed some college credits. Eight of the participants had earned an Associates degree or better. Income was also high in this group with 50% of the group reporting a household income over $100,000 per year. The mean age at menopause onset in this group was 46.3 (SD 5.4). The earliest onset was age 35 and the oldest was 52. The majority of the participants (60%) experienced surgical menopause and 40% experienced natural menopause. This small group is of course too small to be representative of the all menopausal women, but it is very similar to the type of women who typically use HT. (Brennan, Crespo & Wactawski-Wende, 2004).

The intent of the pilot study was to test the instrument for ease of completion, readability and understandability. The questionnaire was created as a Microsoft Word (MS) document that was printed out as a hard copy. The questionnaire was also designed to be used via email in a protected MS Word format with check boxes, drop down selections and text entry spaces. Five of the participants requested and completed an email version of the questionnaire without problems. Two participants of the 5 participants who requested the email version had difficulty opening, saving and/or returning the questionnaire via email, so they subsequently requested a hard copy which was sent via postal mail. The problems encountered were related to type of email server (AOL versus MS Outlook) and a lack of computer literacy. The 5 participants who did not desire the email version requested the hard copy of the questionnaire. The questionnaire was sent out via postal mail and was promptly returned without problems.

The final section of the pilot questionnaire contained specific questions about the questionnaire's understandability and readability: 1) How long did it take you to complete the questionnaire, 2) Are any of the questions hard to understand or unclear, 3) Are there any words contained within the questionnaire that are difficult to understand, 4)

Are there any experiences you had that are not shown on the questionnaire and 5) Are there any items that you think are not necessary or should be removed from the questionnaire.

The participants indicated that it took an average of 11 minutes to complete the questionnaire with a range of 5 to 15 minutes. Two participants reported that the only term not clear to them was "Aryuvedic medicine" and one noted they were not familiar with the term "Homeopathy". One participant who had requested a hard copy after attempting to fill out an electronic version commented that the hard copy was less confusing and so much easier to fill out.

Conclusions

Participants of the pilot study did not report any difficulty in understanding the questionnaire. Although two participants did not understand the terms Aryuvedic Medicine and one did not understand Homeopathy, the terms were not changed because it would appear that if the participant is unfamiliar with the term then they have not utilized this alternative medicine system.

Given the difficulty of some women in completing an electronic version of the questionnaire, the drop down menus were removed and replaced with check boxes to provide a clear and easy to use hard copy version. For the larger study, the questionnaire was still offered electronically *but* participants were strongly encouraged to complete the hard copy version instead.

MAIN STUDY

Sample

A convenience nonprobablity sample of women was recruited from September 1, 2006 through December 31, 2006 to participate in this study. The population of interest

was menopausal women over the age of 40 who had recently discontinued or taken a break from the use of any type of prescribed HT. For this study a minimum sample size of 150 participants was needed based on the "rule of thumb". The rule of thumb indicates that there are at least 10 subjects per variable for correlation and logistic regression analysis (Knapp, 1988). There were initially 15 variables (contextual factors) for this study indicating that a minimum sample of 150 women was needed.

Eligible participants were menopausal females over the age of 40 living in the United States, previously on prescribed HT but having discontinued or taken a break from prescribed HT, having the ability to read, write and speak English, and willing to complete the survey. Participants were not eligible if they were not menopausal, never used or inconsistently used prescribed HT for less than three consecutive months prior to discontinuation. Returned questionnaires that were missing pertinent responses or large gaps of data were not included in the final analysis. Women who became menopausal as a result of cancer treatments were not included in the final analysis because it is known that cancer itself can also be a cause of hot flashes (Speroff & Fritz, 2005; Wilkin, 1981).

Study volunteers were recruited using a variety of strategies. The main method used was a mailing list, purchased from a marketing company. The mailing list was derived from a selection of women throughout the United States who had filled out a general information survey for the list owner. The survey was a pen and paper, non-internet based survey that the women had completed within the six months prior to purchase of the list for this study in the fall of 2006. The survey was not specific to menopause; it was a general information survey that gathered information such as survey respondent's demographics, purchasing preferences and health interests. The purchased list was narrowed to include only women who were over the age of 40 who had noted on the questionnaire that they had an interest in menopause. The available demographics of

the list revealed that the majority of the women (61%) were married, were between the ages of 45 and 64 years of age (83%) and had at least a high school education (61%). The sample was fairly well balanced for reported income with the majority of the women (57%) reporting an income falling between $30,000 and $99,000. Thirty percent of the sample was considered to be low income reporting an income of less than $30,000 per year. Race data was not collected by the list owner, but ethnicity data entered by at least 75% of the sample, revealed only 3% of the women reporting a Hispanic origin.

Additional participants were recruited through flyers and postcards placed with permission at several health care provider offices, a weight loss program, and a grocery store in Central Texas. In addition to providing flyers for offices of the women's health care provider colleagues who provide care for menopausal women, they were also given the actual questionnaire to distribute to patients who fit the criteria for the study. The questionnaires were in a packet that included a self addressed envelope. Furthermore, business cards with the study overview and contact information were created and carried by the primary investigator to be given out to women who fit the entry criteria when the opportunity arose.

The varieties of ways and settings for participant recruitment were chosen in hopes to promote recruitment of a more diverse sample of women than what is usually represented in studies related to menopause and HT. Women who present to their health care providers for treatment of menopause symptoms represent only a limited view of all women's experiences of menopause. Many women, especially those who may not experience difficulties or do not embrace the biomedical paradigm of menopause, may never seek help from a health care provider. Thus their voices would be lost in this study if participants were recruited only from health care provider clinics.

As described in the previous paragraphs, in this study a small proportion of participants self-selected and requested the study questionnaire to be sent to them and another small group were identified by a health care provider as fitting the criteria for the study and individually recruited for the study. However, the most of the participants were randomly selected from purchased mailing list and received an unsolicited questionnaire through the mail. Given the anonymity of the returned questionnaire it was impossible to identify which ones requested the questionnaire or answered and returned the unsolicited questionnaire.

A mailed questionnaire was chosen because of the many advantages: ease of administration, relatively low cost versus personal interviews, lack of interviewer bias, anonymity, and opportunity to access a larger amount of participants. These advantages are balanced with the acknowledged disadvantages including that the respondents may stop the questionnaire midway through, they cannot ask for clarification, there is no interviewer to probe for further explanations, respondents may represent extremes and there is a risk of non-response bias based on the individuals who did not return the questionnaire.

Additionally, mailed surveys traditionally have a low response rate. In fact, it has been reported that the response rate for mailed surveys is less than 20% (Bourque & Fielder, 1995). However, in this study the sampling method was very successful in reaching far more than the originally needed sample of 150 women. Six hundred and twenty eight women returned the questionnaire resulting in an overall response rate of 25%, which was better than expected.

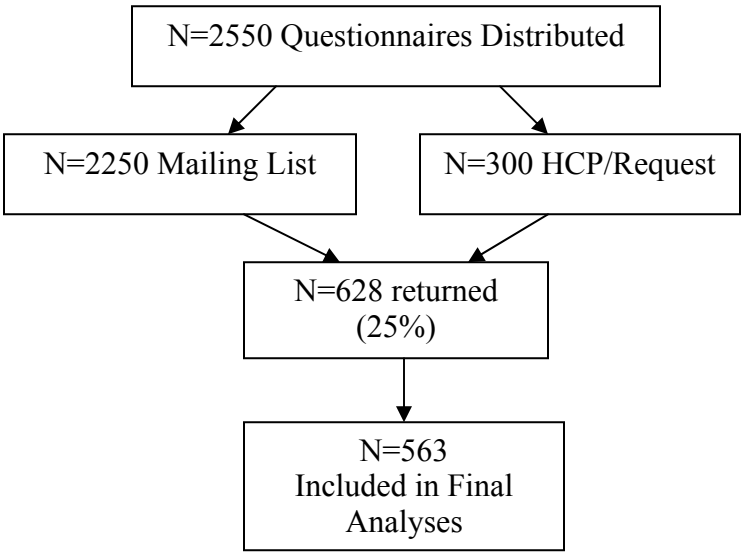
No monetary compensation was offered for the participation in the study, but the participants were offered an opportunity to be added to an email distribution list so that they can be informed of study findings. E-mail or mail notices of the completed study

will be sent to those women who have requested a report and who had provided their e-mail postal mail addresses to receive study findings information.

Sample Distribution

Twenty five hundred and fifty questionnaires were distributed to women throughout the US. Of those questionnaires, 2,250 were selected randomly from the purchased mailing list of 4,350 using an every other person method of selection. The remaining 300 questionnaires were either distributed by health care colleagues or requested by the participant. Twelve of the 2,550 questionnaires mailed were returned as undeliverable. From all sources, a total of 628 completed questionnaires were returned; 563 of these were usable. Fifty-one questionnaires were not usable because they either never started HT (N=35) or never stopped (N= 17) or had significant missing data (N=13) (see figure 3).

Figure 3: Questionnaire distribution



Data Collection

All women who volunteered for this study received the questionnaire via postal mail. The questionnaire was sent in a packet that contained the questionnaire and preaddressed and stamped return envelope in which to return the questionnaire. No electronic versions of the questionnaire were used in the main study.

Protection of Human Subjects

This study was approved on August 29, 2006 by The Office of Research Support and Compliance at the University of Texas at Austin, Institutional Review Board (IRB) (IRB approval-IRB protocol number #2006-05-0091). Procedures to protect the subjects were adhered to during the entire study period.

An overview of the study was incorporated in the questionnaire introduction. The over view included the title of the study, the general purpose, how and why the participant was selected, study procedures, and potential risks and procedures adopted to minimize those risks. The overview also provided information stating that participants do not have to answer all questions, and a statement describing the privacy and confidentiality of the participant's responses. The participants' name, addresses, and telephone number and/or email address was used only to contact them initially to mail or email the questionnaire to them. To provide anonymity the participant's name, address, email address, return envelopes and telephone number were shredded/deleted after the questionnaire was sent. Participants were also instructed that they could stop filling out the questionnaire at anytime or choose not to send it back without penalty if they chose to do so. Consent to participate was presumed by the participants' completion and return of the questionnaire.

All data collected during the course of the proposed study is stored in a locked file cabinet in the principal investigator's home office. Access is limited to the primary

investigator who is the only person who holds the key to the file cabinet. All personnel including the primary investigator participating in this research completed the Human Subjects Training established by the University's Office of Research Support and Compliance.

Data Analysis

Questionnaires were returned via US postal mail. Once the questionnaires were received they were opened, the envelope discarded and the questionnaire itself was labeled with an ID number by the primary investigator. The data from the questionnaire was entered into a Statistical Package for Social Sciences (SPSS, Inc, Chicago, IL) database created by the primary investigator. A coding sheet was used to assist in data entry. After data entry, the database was reviewed for accuracy by comparing the raw data and running frequencies on each variable to assess for any inaccuracies in data entry (outliers, missing values, etc). Specific methods of statistical analysis for demographic variables and the research questions are reported in the following sections.

Demographics

Variables included in the demographic data analysis were categorical, ordinal and interval. Frequency distributions and percentages were run on the following categorical and ordinal demographic variables: 1) current age, 2) age at menopause, 3) years post menopause, 4) ethnicity/race, 5) BMI range, 6)geographical location, 7) marital status, 8) education, 9) income and 10) type of menopause. A descriptive analysis with means and standard deviations (SD) also was completed on the following demographic interval level variables: 1) current age, 2) age at menopause, 3) years post menopause 4) BMI. Frequencies were also run for the aforementioned interval level variables as they were collapsed into ordinal level data for Chi-square analysis (χ^2). Ethnicity/race was collapsed

into 3 categories of Black, White and other because of the limited sample of Asian, Hispanic, American Indian and other race/ethnicities.

Health Behaviors

Frequency distributions and percentages of the pertinent health behaviors that may have some influence on the experience of vasomotor symptoms were calculated. The health behaviors were: 1) type of exercise, 2) smoking and 3) alcohol use. A descriptive analysis with means and standard deviations (SD) also was completed for pack years of smoking and number of alcoholic drinks per week.

Research aim 1: Factors influencing discontinuation of HT

To identify factors menopausal women report that influenced their decisions to discontinue HT.

Frequency distributions with percentages were completed for 1) reasons women gave for why discontinued HT, 2) familiarity with WHI, and 3) whether WHI influenced decision to stop HT.

Research aim 2: Vasomotor symptom occurrences

To explore the vasomotor symptom occurrences in menopausal women who have discontinued hormone therapy.

In addition to demographics, vasomotor symptom occurrences of participating menopausal women before and after discontinuation of HT were explored. Frequency distributions were run for the 1) occurrence of vasomotor symptoms prior to start of HT, 2) the occurrence of vasomotor symptoms immediately after discontinuation of HT, 3) continued vasomotor symptoms after discontinuation and 4) resolution of vasomotor symptoms after discontinuation without any intervention, 5) the severity of vasomotor

symptoms immediately after discontinuation and 6) the severity of vasomotor symptoms that continued to occur after discontinuation.

A descriptive analysis was performed with the range, mean and standard deviation (SD) on 1) frequency per day of vasomotor symptoms occurring immediately after discontinuation and 2) the frequency per day of continued vasomotor symptoms and 3) time in months that it took for resolution of vasomotor symptoms without any intervention.

A McNemar test was performed to assess if the participants vasomotor symptom occurrences prior to the use of HT differed from the vasomotor symptom occurrence after HT was discontinued.

Frequency distributions with percentages were completed for the participants who 1) restarted HT after they had discontinued, 2) indicated that they restarted because of vasomotor symptoms and 3) whether symptoms were either partially or full resolved after restarting therapy.

Research aim 3: Contextual factors and vasomotor symptoms

To explore the relationship between contextual factors and vasomotor symptoms after the discontinuation of hormone therapy

The dependent variable is the *presence of* or *lack of* vasomotor symptoms (hot flashes and/or night sweats). Contextual factors that have previously been reported in the literature to have a possible effect on the occurrence of vasomotor symptoms represent the independent variables of which the majority are categorical/ordinal data with the exception of age, number of years post menopause and BMI. The independent variables include 1) current age, 2)ethnicity/race 3) education, 4) income, 5) geographical location, 6) BMI, 7)type of menopause, 8) age at menopause, 9) years post menopause, 10) the

presence of vasomotor symptoms (hot flashes/night sweats) prior to initial HT use 11) how HT was discontinued, 12) exercise and 13) smoking and 14) alcohol intake.

Chi-square (χ^2) analysis was used to determine any statistically significant relationships to the dependent variable, the occurrence of vasomotor symptoms after the discontinuation of HT with the independent variables of ethnicity/race, education, income, geographical location, type of menopause, the presence of vasomotor symptoms prior to initial HT use, how HT was discontinued, exercise behaviors, smoking and alcohol intake. A Cramer's V can be used for any size of contingency table and was run on all variables to assess the strength of the relationships. The Phi coefficient (φ) is appropriate only for a 2x2 table and is listed for variables of type of menopause, the presence of vasomotor symptoms prior to initial HT use, how HT was discontinued, smoking and alcohol intake. The Phi coefficient and Cramer's V statistical values were identical, therefore for ease of reading, only the Cramer's V was listed for all variables. Spearman's Rho was run for the interval level variables of current age, age at menopause, years post menopause and BMI.

Following the initial Chi-square ($\chi^{2)}$ and correlations, a binary logistic regression analysis was performed. The dependent variable was "*the presence* or *absence of* vasomotor symptoms after discontinuation of HT". This variable was entered into the regression model as categorical, with (1) yes had vasomotor symptoms or (0) no, did not have vasomotor symptoms after discontinuing HT.

Based in part on the literature and the findings from the χ^2 and correlations 8 independent variables were chosen to be entered into the regression model. The independent variables in the model that were ordinal were converted to categorical variables as appropriate for logistic regression. Each variable was dummy coded into two response sets (0, 1). The following non-interval level data were dummy coded and

entered into the regression model as categorical variables: 1) education (high school education/less or college degree), 2) type of menopause (natural or hysterectomy), 3) how HT was discontinued (weaned or stopped suddenly), 4) vasomotor symptoms prior to starting HT (yes or no), 5) smoking (smokes or does not smoke), 6) alcohol intake (drinks alcohol or does not). Interval level data entered into the model included 7) current age and 8) BMI

Variables that were not entered into the regression model included 1) the number of years post menopause given the redundancy of the data, as years post menopause, equals current age minus age at menopause. The sample was predominantly White (89%) and the majority of the participants exercised (90%), therefore exercise and race/ethnicity were not included in the model because of the severe unequal split of the data responses. Lastly, income was not included because of a large amount of missing data with nearly 13% of the participants failing to comment on their income.

Type of menopause was collapsed into either natural menopause or surgical menopause. Medically induced menopause was not included given the sample size and the fact that causes of medically induced menopause such as cancer or the medical intervention itself may unduly influence vasomotor symptom experiences.

Research Aim 4: Complementary and Alternative Medicine

To identify alternative treatments that women have undertaken to treat menopause symptoms and their perceived efficacy.

Frequency distributions with percentages were used to explore what types of alternative medical treatments and complementary and alternative medicine (CAM) therapies the participants had undertaken to treat their vasomotor symptoms. Frequency distributions with percentages were also utilized to the participants perceived the efficacy of their chosen method.

Chapter Four: Results

DATA ANALYSIS

Demographics

This was not a population based survey and is not to be considered a nationally representative sample. However, questionnaires were received from women in every State in the United States except Hawaii. The geographical locations were consistent with the United States (US) census configurations, which breaks the US into 4 Regions (Northeast, Midwest, South and West). Over 98% of participants (N=554) listed their geographical location. Frequency distributions revealed a fairly evenly distributed sample from each region of the US, with 23.8 % from the Northeast (N=132), 26.7% the Midwest (N=148), 31.6% the South (N=175), and 17.9% from the West (N=99) (See table 1).

Study participants were primarily White (89.3%, N= 503), followed by 7.8% Black (N=44), 1.2% Hispanic (N=7), 1.1% Native American (N=6), 0.4% Asian (N=2) and 0.2% multiracial (N=1) (see table 1). The mean age of participants was 58 years with a range from 40 to 82 years of age. Eligible participants who provided their weight and height (N=538) were included in the BMI calculation. Participants had an average BMI of 29.5, ranging from 16.99 to 57.76 (see table 2).

The majority of the participants (61.5%) were married, followed by 16.2% who were divorced, 8.3% that were widowed, 7.5% that were single, 3.9% who reported partnered relationship and 2.7% who were separated. Of the participants who reported their educational status (N=560), nearly 68% (N=380) held only a high school diploma or less. Eight percent of those women had a GED or did not complete high school.

Approximately 23% of the women completed an undergraduate degree and 9.2% had completed a graduate degree (see table 1).

For the purposes of this study the low income cut point was chosen to reflect the US Department of Health and Human Services (DHHS) low-income description which is described as an individual whose family's taxable income for the preceding year did not exceed 150 percent of the poverty level amount. The 2006 poverty level was set at $20,000 for a family of 4 (US Department of Health and Human Services, 2006). Using a family unit of 4 as the US average, the low income cut point for this study was women who reported a total family income of less that $30,000 which is 150% of the poverty level for a family of 4.

Household income information was the most frequent question that women failed to answer, with 72 of 563 women declining to comment on their income. Analysis revealed that for participants who reported their household income, 40.7% were considered to be low income as described previously with a total household income of $30,000 or less. Slightly greater than 36% of the participants fell into a middle income range between $30,001 and $60,000. Fourteen and a half percent of the participants fell into the middle upper income range reporting income between $60,001 and $80,000 and in the upper income range, 8.4% reported an income of $90,001 or above (See table 1).

Table 1: Demographic information (categorical and ordinal)

Characteristic	*N (%)*	*Familiar with WHI*	*VMS prior to using HT*	*VMS after HT discontinued*	*Restarted HT*	*Used alternative and/or CAM*
Current Age[1]						
40-50 years old	59 (10.6%)	9 (15%)	43 (72.9%)	55 (93.2%)	12 (20.3%)	33 (55.9%)
51-60 years old	298 (53.8%)	64 (21.5%)	231 (77.5%)	250 (83.9%)	44 (14.8%)	147 (49.3%)
61 years old or over	197 (35.6%)	42 (21.3%)	143 (72.5%)	141 (71.6%)	23 (11.7%)	70 (35.5%)
Age at Menopause[2]						
39 years old or under	103 (18.5%)	18 (17.5%)	68 (66.0%)	91 (88.3%)	18 (17.5%)	58 (56.3%)
40-50	344 (53.8%)	73 (21.2%)	264 (76.7%)	277 (80.5%)	51 (14.8%)	144 (41.9%)
51-60 or older	110 (19.8%)	26 (23.6%)	86 (78.2%)	81 (73.6%)	11 (10.0%)	48 (43.6%)
Years Postmenopause[3]						
1 year or less	7 (1.3%)	0 (0%)	5 (71.4%)	6 (85.7%)	1 (14.3%)	4 (57.1%)
More than 1 year to 5 years	77 (14.1%)	21 (27.3%)	65 (84.4%)	70 (90.9%)	14 (18.2%)	48 (62.3%)
More than 5 years to 10 years	145 (26.5%)	32 (22.1%)	115 (79.3%)	111 (76.6%)	16 (11.0%)	60 (41.4%)
More than 10 to 20 years	216 (39.4%)	46 (21.3%)	160 (74.1%)	172 (79.6%)	32 (14.8%)	92 (42.6%)
More than 20 years	103 (18.8%)	16 (15.5%)	67 (65.0%)	83 (80.6%)	16 (15.2%)	44 (42.7%)
Ethnicity/Race						
Black	44 (7.8%)	9 (20.5%)	34 (77.3%)	41 (93.2%)	2 (4.5%)	21 (47.7%)
White	503 (89.3%)	107 (21.3%)	379 (75.3%)	401 (79.7%)	78 (15.5%)	227 (45.1%)
Other	16 (2.8%)	1 (6.3%)	10 (62.5%)	11 (68.8%)	0 (0%)	4 (25.0%)
Asian 2(0.4%)						
Hispanic 7(1.2%)						
Native American 6 (1.1%)						
Mixed 1 (0.2%)						
BMI ranges[4]						
Underweight (<18.5)	16 (3.1%)		12 (75.0%)	12 (75.0%)	2 (12.5%)	11 (68.8%)
Normal range (18.5-24.9)	138 (27.1%)		105 (76.1%)	112 (81.2%)	30 (21.7%)	72 (52.2%)
Overweight (25-29.9)	152 (29.8%)		115 (75.7%)	127 (83.6%)	21 (13.8%)	69 (45.4%)
Obese (>30)	204 (40.0%)		155 (76.0%)	160 (78.4%)	17 (8.3%)	79 (38.7%)

Characteristic	*N (%)*	*Familiar with WHI*	*VMS prior to using HT*	*VMS after HT discontinued*	*Restarted HT*	*Used alternative and/or CAM*
Region[5]						
Northeast	132(23.8%)	30 (22.7%)	101 (76.5%)	106 (80.3%)	18 (13.6%)	57 (43.2%)
Midwest	148(26.7%)	33 (22.3%)	108 (73.0%)	121 (81.8%)	23 (15.5%)	75 (50.7%)
South	175(31.6%)	26 (14.9%)	134 (76.6%)	144 (82.3%)	24 (13.7%)	77 (44.0%)
West	99(17.9%)	25 (25.3%)	73 (73.7%)	75 (75.8%)	15 (15.2%)	41 (41.4%)
Marital Status						
Single	42(7.5%)					
Partnered	22(3.9%)					
Married	346(61.5%)					
Separated	15(2.7%)					
Divorced	91 (16.2%)					
Widowed	47(8.3%)					
Highest level of Education[6]						
HS Diploma (or less)	380 (67.9%)	48 (12.6%)	291 (76.6%)	304 (80.0%)	53 (13.9%)	172 (45.3%)
Undergraduate Degree	128 (22.9%)	36 (28.1%)	92 (71.9%)	108 (84.4%)	21 (16.4%)	57 (44.5%)
Graduate Degree	52 (9.2%)	*32 (61.5%)	37 (71.2%)	38 (73.1%)	6 (11.5%)	23 (44.2%)
Family income[7]						
<$30,000 (low income)	200(40.7%)	24 (12.0%)	151 (75.5%)	156 (78.0%)	20 (10.0%)	86 (43.0%)
$30,001-$60,000 (middle income)	179(36.5%)	36 (20.1%)	144 (80.4%)	150 (83.8%)	26 (14.5%)	83 (46.4%)
$60,001-$90,000 (middle/upper)	71(14.5%)	*26 (36.6%)	50 (70.4%)	58 (81.7%)	15 (21.1%)	32 (45.1%)
>$90,001 (high income)	41(8.4%)	*14 (34.1%)	27 (65.9%)	31 (75.6%)	9 (22.0%)	19 (46.3%)
Type of menopause[8]						
Natural	358(63.9%)	81 (22.6%)	293 (81.8%)	275 (76.8%)	44 (12.3%)	154 (43.0%)
Surgical	193(34.5%)	35 (18.1%)	120 (62.2%)	167 (86.5%)	34 (17.6%)	90 (46.6%)
Medical	9(1.6%)	1 (11.1%)	7 (77.8%)	8 (88.9%)	1 (11.0%)	6 (66.7%)

[1]Missing data for current age for 9 participants, posted percentages represent valid responses only
[2]Missing data for age at menopause for 15 participants, posted percentages represent valid responses only
[3]Missing data for years post menopause for 15 participants, posted percentages represent valid responses only
[4]Missing data for years post menopause for 15 participants, posted percentages represent valid responses only
[5]Missing data for geographical location for 5 participants, posted percentages represent valid responses only
[6]Missing data for educational level on 3 participants, percentages represent valid responses only
[7]Missing data for income for 72 participants, percentages represent valid responses only
[8]Missing data on type of menopause for 3 participants, percentages represent valid responses only

The mean age for the onset of menopause of the participants was 45 years of age. The earliest onset was age 20 and the oldest was 61. The mean years post menopause for the participants was approximately 14 years with a range from less than a year up to 45 years (see table 2). Five hundred and sixty women reported the type of menopause they experienced, the majority of them (63.6%) experienced natural menopause (N=358), 34.3% experienced surgical menopause (N=193) and 1.6% reporting medically induced menopause (N=9). (See table 1). According to the Center for Disease Control (CDC) July 2002 Morbidity and Mortality Weekly Report (MMWR) from 1994 through 1999, one in every nine women aged 35-45 years had a hysterectomy. The respondents to this study had a 3 times higher rate of hysterectomy than what is reflected in this report.

Table 2: Demographic information (interval)

Characteristic	***Minimum***	***Maximum***	***Mean***	***Std Deviation***
Current Age[1]	40	82	58.74	6.99
Age at menopause[2]	20	61	44.99	7.56
Years post menopause[3]	0	45	13.69	8.18
Body Mass Index (BMI)[4]	16.99	57.16	29.55	7.35

[1]Missing data for current age on 9 participants, posted statistics represent valid responses only
[2]Missing data for age at menopause on 6 participants, posted statistics represent valid responses only
[3]Missing data for years post menopause on 15 participants, posted statistics represent valid responses only
[4]Missing data on BM on 25 participants, posted statistics represent valid responses only

Health behaviors assessed included exercise, smoking habits and alcohol intake. Surprisingly, 10% of the participants reported that they did not exercise at all. Just over 50% of the women reported exercising mildly which was described as climbing stairs, walking 3 blocks, golf). Eighteen percent of the women listed their exercise as moderate (30 minutes of vigorous activity less than 4 times per week and 20.6% women reported vigorous activity for at least 30 minutes more than 4 times per week (see table 3). Eighty

percent of the women reported that they did not smoke (see table 3), conversely 20% of women reported smoking with an average of 32 pack years (see table 4). Pack years is calculated by the number of packs per day x the number of years smoked. Nearly 42% of women reported no alcohol intake at all, while 58% of women (see table 3) reported an average intake of approximately 3 drinks per week (see table 4), primarily wine (77.2%), followed by beer (13.5%) and hard liquor (8.8%).

Table 3: Health Behaviors (categorical, ordinal)

Characteristic	***N (%)***	***Vasomotor symptoms***
Exercise[1]		
No exercise	60 (10.8%)	47 (78.3%)
Mild exercise	279 (50.1%)	223 (79.9%)
Occasional vigorous exercise	101 (18.1%)	81 (80.2%)
Regular vigorous exercise	115 (20.6%)	94 (81.7%)
Smoker[2]		
Yes	107 (19.3%)	89 (84.0%)
No	449 (80.8%)	356 (79.3%)
Alcohol use[3]		
Yes	232 (41.9%)	194 (83.6%)
No	322 (58.1%)	250 (77.6%)

[1]Missing data on type of exercise for 7 participants, percentages represent valid responses only
[2]Missing data on smoking for 7 participants, percentages represent valid responses only
[3]Missing data on alcohol use for 9 participants, percentages represent valid responses only

Table 4: Health behaviors (interval)

Characteristic	***Minimum***	***Maximum***	***Mean***	***Std Deviation***
Smoking pack years	0	132	32.54	23.76
Alcohol (drinks/week)	0	24	3.24	3.71

Research aim 1: Factors influencing discontinuation of HT

To identify factors menopausal women report that influenced their decisions to discontinue HT.

Participants were asked to select all the factors that influenced their decision to discontinue HT. Forty one percent of the respondents indicated that they stopped HT because of the information they received about HT (see table 5). The majority of the women indicated that their primary source of this information was in the form of written publication (21.3%), followed by television (14%) and internet (6.2%).

The second most common reason women (33.2%) selected was because their health care provider recommended that they discontinue (see table 5). Participants reported several reasons why their health care provider recommended discontinuation. Some health care providers recommended because of certain health conditions such as hypertension, headaches, leg pains or swelling. Some of the participants discontinued HT when they had an extended hospitalizations or surgery, and others were stopped via their healthcare provider's suggestion because of a family history of breast cancer. Many of the participants reported that their health care provider suggested the discontinuation of HT because of new information about HT. The reported new information that the included comments such as a suggested link to an increase risk of breast cancer, an increased cardiovascular risk and stroke, no benefit for cardiovascular disease, and that the newly recommended shorter length of use of HT than previously recommended. In addition many of the participants reported that their health care provider recommended they discontinue HT without any providing any specific reason to do so.

The third most common response that nearly 25% of women indicated was a reason they discontinued was because they were afraid of the increased risk of breast cancer. Following this many women reported that they simply stopped HT to test how

they would feel off of HT (19.9%). A similar number of women also reported that they feared the occurrence of a blood clot or stroke (19.4%). Fourteen percent of women reported that they discontinued HT because of non-life threatening side effects such as breast tenderness, irregular bleeding, swelling in the extremities, heart palpitations, nausea, weight gain, polyps, dizziness and mood swings. Thirteen percent of the participants stopped HT after experiencing a serious life threatening side effect such as a thrombembolic event, stroke, cancer or heart attack. The less common reasons for discontinuation were the cost of the prescription (8.5%), to try another type of treatment (5.7%), no specific reason (5.3%), friend or coworker suggested (3.2%), husband or life partner recommended (2.5%), HT did not relieve symptoms (1.8%), pharmacist recommended (<1%), and felt that they had been on HT too long (<1%) (See table 5).

Table 5: Reasons for discontinuation of HT

Reasons for discontinuation of HT	***N (%)***
Because of recent information obtained via:	234 (41.5%)
written publication	*120 (21.3%)*
television	*79 (14%)*
internet	*35 (6.2%)*
Health care provider recommended	187 (33.2%)
Afraid of the risk of breast cancer	140 (24.9%)
Stopped on own to see how felt off of HT	112 (19.9%)
Afraid of the risk of blood clot or stroke	109 (19.4%)
Side effects	79 (14.1%)
Serious life threatening side effects	73 (13%)
Because of the cost of the prescription	45 (8.5%)
To try another type of treatment	32 (5.7%)
Stopped on own for no particular reason	30 (5.3%)
Friend or coworker recommended	18 (3.2%)
Husband or life partner recommended	14 (2.5%)
No relief of symptoms	10 (1.8%)
Pharmacist recommended	5 (0.9%)
Felt was on HT too long	5(0.9%)

Despite the high percentage of women who discontinued HT based on information they read or received from their health care provider (see table 5), only 20% (N=117) of the participants indicated that they were actually familiar with a study specifically called the Women's Health Initiative (WHI). Of those women that were familiar with the study and had discontinued HT in the year 2002 or after (N=111), only 40% of them indicated that the findings did influence their decision to discontinue HT. Women who were aware of the WHI were statistically significantly (χ^2) more likely to

have an income above $60,000 and had completed a graduate degree than the women who indicated they were not familiar with the study (see table 1).

Research aim 2: Vasomotor symptom occurrences

To explore the vasomotor symptom occurrences in menopausal women who have discontinued hormone therapy.

Seventy five percent of the study participants reported the occurrence of vasomotor symptoms *prior* to the initial start of HT. In contrast, 80% reported the occurrence of vasomotor symptoms *after* discontinuation of HT. The women who experienced vasomotor symptoms immediately after discontinuation reported upon the severity of their symptoms, of which 21.1% stated their symptoms were mild, 32.7% moderate, and 23.2% were reported as severe (see table 7). The frequency of vasomotor symptoms occurring immediately after discontinuation ranged from less than 1 to a maximum of 30 vasomotor symptoms per day with a average frequency of approximately 5 per day (see table 7).

Table 6: Vasomotor experiences (categorical, ordinal)

Vasomotor Symptoms (VMS)		***N (%)***
Experienced VMS *before* started HT		423 (75.1%)
Experienced VMS *immediately* after discontinued HT		453 (80.5%)
Severity of VMS *immediately* after discontinuation	Severe	131 (23.2%)
	Moderate	184 (32.7%)
	Mild	119 (21.1%)
Continued to have VMS after discontinuation		320 (56.8%)
Severity of *continued* VMS	Severe	39 (6.9%)
	Moderate	105(18.7%)
	Mild	138 (24.5%)
VMS resolved without any intervention		215(38.2%)

Thirty eight percent of the participants reported that their vasomotor symptoms resolved spontaneously without any intervention. For those women whose symptoms had resolved the time frame ranged from immediately upon discontinuation up to 2 ½ years with an average resolution time of approximately 5 months. Almost 57% of the participants continued to have vasomotor symptoms. A closer look at the symptoms of this women demonstrated that the vasomotor symptoms decreased over time. The percent of women having severe symptoms immediately after discontinuation decreased from 23.2% to 6.9%, and moderate symptoms went from 32.7% to 18.9% (see table 6). The range of the frequency of symptoms remained similar at 0 to 30 per day although the average decreased from 5 to 3 per day (see table 7).

Table 7: Vasomotor symptom frequencies/resolution (interval)

Vasomotor Symptoms	***Min***	***Max***	***Mean***	***Std Deviation***
Frequency/day of VMS immediately after discontinuation	0.5	30	4.96	4.807
Frequency/day of continued VMS con	0.5	30	3.41	3.488
Months to resolve VMS	0	354	4.99	24.071

As noted earlier, fewer women experienced vasomotor symptoms *prior* to HT initiation (N=423) than *after* discontinuation of HT (N=453). To determine if there was significant difference between vasomotor symptoms *prior* to and those immediately *after* discontinuation, a McNemar test was conducted. The test revealed that the occurrence of vasomotor symptoms *prior* to the initiation of HT was significantly different (<.05) than the occurrence of vasomotor symptoms *after* the discontinuation of HT.

Women who were Black, between the ages of 40-50, experienced menopause before age 40, were less than 5 years post menopause tended to report more vasomotor symptoms after discontinuation of HT than prior to their use of HT (See table 1).

Fourteen percent of the participants (N=82) restarted HT after they had discontinued. Of those women, approximately 80% (N=66) indicated that they restarted because of vasomotor symptoms. Ninety two percent (N=61) of the women who restarted HT because of vasomotor symptoms reported that their symptoms were either partially or full resolved after restarting therapy. Women who restarted HT were more likely to be White, between the ages of 40 and 50, less than 5 years post menopause onset, had at least a graduate degree, and experienced surgical menopause (See table 1).

Participants who had not restarted therapy were asked if they planned to do so in the future. They were given 4 response sets: 1) no, 2) yes, 3) not sure or 4) awaiting more information. The majority of the women (67%) indicated that they would not restart HT. Although, twelve percent of the women indicated they were not sure at this time and 5% reported that they were still awaiting more information before they made the decision to restart.

Research aim 3: Contextual factors and vasomotor symptoms

To explore the relationship between contextual factors and vasomotor symptoms after the discontinuation of hormone therapy

Chi-square analysis (χ^2) of categorical and ordinal level contextual factors of was conducted with the following variables: ethnicity/race, education, income, geographical location, menopause type, presence of vasomotor symptoms prior to initial HT use, how HT was discontinued, exercise behaviors, smoking and alcohol intake. Given the small number of participants of Asian, Hispanic, American Indian or other, ethnicity/race was collapsed into three categories of Black or White or Other (Asian, Hispanic, American

Indian or other). Education was collapsed into three categories high school education or less, undergraduate degree or graduate degree.

Chi-square analysis revealed that ethnicity (p=0.047), type of menopause (p=.019) and the presence of vasomotor symptoms prior to beginning HT initially (p=.000) were significantly related to the dependent variable, vasomotor symptom occurrence. For two of the variables, Cramer V's statistics revealed that the relationships were fairly weak for ethnicity (.104) and type of menopause (.119). However, vasomotor symptoms prior to HT initiation revealed a moderate association (.027). (see table 8).

Table 8: Relationship (χ^2) of ordinal level contextual variables and VMS

Characteristic	***Cramer's V***	***Significance***
Ethnicity	.104	.047
Education	.074	NS
Income	.074	NS
Geographic location	.059	NS
Type of menopause	.119	.019
VMS prior	.276	.000
How HT discontinued	.001	NS
Exercise	.027	NS
Smoking	.048	NS
Alcohol use	.074	NS

Correlations were run with a Spearman Rho test set at the .05 significance level for the interval level variables of current age, BMI, age at menopause and years post menopause. Analysis revealed a significant inverse relationship between the dependent variable (vasomotor symptoms post discontinuation), and the variables of current age and age at menopause. These results indicated that younger current age and younger age at menopause onset were statistically associated with a higher occurrence of vasomotor

symptoms after the discontinuation of HT, however the relationships for both variables were weak (see table 9).

Table 9: Relationship (Spearman Rho) of interval contextual factors and VMS

Characteristic	Spearman's Rho	Significance
Current Age	-.180	.000*
BMI	-.035	NS
Age at menopause	-.110	.009*
Years post menopause	-.059	NS

To assess further the combined influence of contextual factors on the independent variable of vasomotor symptom occurrence a logistic regression was performed. The dependent variable, vasomotor symptoms after discontinuation of HT was entered into the model as categorical, with yes (1), had vasomotor symptoms *or* no(0), did not have vasomotor symptoms after discontinuing HT. In order to conduct logistic regression analysis all ordinal independent variables were converted to categorical variables. The variables were dummy coded into two response sets (0, 1).

Based on findings in the literature and the results of χ^2 and Spearman Rho correlations the following independent variables appeared to be useful to the model and were entered into the regression model. Categorical variables included 1) education (high school education/less *or* college degree), 2) type of menopause (natural *or* hysterectomy), 3) how HT was discontinued (weaned *or* stopped suddenly), 4) vasomotor symptoms prior to HT (yes *or* no), 5) smoking (smokes *or* does not smoke), 6) alcohol intake (drinks alcohol *or* does not). The interval level variables entered into the model included 7) current age and 8) BMI

Variables not included in the model were 1) ethnicity/race, 2) income, 3) geographical location, 4) exercise, 5) age at menopause and 6) years post menopause.

Although variable of ethnicity/race has been shown in the literature to be associated with vasomotor symptom experiences and revealed significance in the initial $\chi 2$ it was not included because of the severe split in the data (89% White, 7.8% Black, and 2.8% other). The variable of exercise was not included in the model because of a bad split in the data as well, with the overwhelming majority of the women (90%) exercising versus no exercise (10%). Income was removed from the model because of a significant amount of missing data; this question was the most common question that went unanswered. Thirteen percent of the participants declined to enter a response for income. Finally, given the redundancy of the data, in that years post menopause equals current age minus age at menopause, only current age was entered into the model. In addition current age reporting ensures better accuracy in the data then a retrospective report of age at menopause.

Simple logistic regression model with all of the aforementioned variables entered into the model summary revealed a Cox and Snell R^2 statistic of 0.128 indicating that the combined independent variables accounted for only 13% of the total variance of vasomotor symptoms occurrence (table 10).

With a 0.5 criterion for statistical significance, three of the eight predictor variables entered into the model had a significant partial effect on the model, although the strength of the effect was relatively small. Those variables were the presence of vasomotor symptoms prior to initial start of HT (p=.000), type of menopause (p=.000), and current age (p=.001) (see table 10).

The presence of vasomotor symptoms prior to starting HT when all other variables were held constant had a negative B statistic and odds ratio of .179, indicating that if vasomotor symptoms were absent prior to the initial start of HT it is likely they will be absent after discontinuation of HT as well. Type of menopause had a positive B

statistic with an odds ratio 2.92 indicating that women who have had a hysterectomy are 3 times more likely to experience vasomotor symptoms after discontinuation of HT. For current age with all the other variables were held constant the regression model revealed a negative B statistic with an odds ratio of .942 suggesting that the older the current age of the woman, the less likely she would experience vasomotor symptoms after discontinuation of HT.

Table 10: Regression analysis: Contextual factors to predict presence of vasomotor symptoms

Predictor Variable	***B***	***Wald***	***Sig***	***Odds ratio***	***95% CI***	
					Lower	**Upper**
Educational level	.087	.110	NS	1.091	.651	1.828
Type of Menopause	1.07	13.76	.000	2.920	1.658	5.142
How HT was discontinued	-.002	.00	NS	.998	.589	1.693
VMS symptoms prior to HT	-1.71	43.07	.000	.179	.107	.300
Smoke	.10	.10	NS	1.11	.587	2.108
Alcohol intake	-.46	3.27	NS	.629	.381	1.039
Current age	-.06	11.38	.001	.942	.910	.975
BMI	-.02	1.38	NS	.981	.949	1.013

Research aim 4: Complimentary and Alternative Medicine

To identify alternative treatments that women have undertaken to treat menopause symptoms and their perceived efficacy.

Of the 563 study participants, less than half (N=252) reported the use of an alternative treatment to treat vasomotor symptoms. Women who were between the ages of 40-50, less than 5 years post menopause onset, and experienced medical menopause were more likely to utilize alternative treatments (see table 1).

Beginning with the most common choice of alternative methods used were 1) multivitamins and calcium (59.2%), 2) Black Cohosh (46.4%), 3) Soy supplements and food (42.4%), 4) antidepressants (32%), 5) meditation and relaxation (26%), 6) Evening

Primrose Oil (17.2%), 7) Other (15.1%), 8) blood pressure medications (13.7%), 9) Homeopathy (12.4%), 10) Red Clover (7.6%), 11) anti-seizure medications (8.4%), 12) bio-identical hormones (6.4%), 13) Traditional Chinese Medicine (2.8%), 14) Acupuncture (2.4%), 15) Aryuvedic Medicine (0.2%). In the "other" category note above, the use of Estroven, Flaxseed, or Progesterone cream was listed by 5 women. New Phase and St. Johnswort was listed by 2 women and the use of Bellergal, Colchicines, Echinacea, Estro-life, GNC Menopause, Phyto Prolief Arborne, and Valerian were reported by at least 1 woman (see table 11).

Table 11: Alternative Treatments for vasomotor symptoms

Alternative Treatment	*Utilized treatment N (%)*	*Perceived Efficacy N (%)*	
	Alternative Medicine Systems		
Acupuncture	6(2.4%)	Helped	3(50%)
		Did not Help	0(0.0%)
		Not sure	3(50%)
		Missing info 0	
Aryuvedic Medicine	1(0.4%)	Helped	1(100%)
		Did not Help	0(0.0%)
		Not sure	0(0.0%)
		Missing info 0	
Homeopathy	31(12.4%)	Helped	14(46.7%)
		Did not Help	13(43.3%)
		Not sure	3(10%)
		Missing info 1	
Traditional Chinese Medicine	7(2.8%)	Helped	4(57.1%)
		Did not Help	3(42.9%)
		Not sure	0(0.0%)
		Missing info 0	
	Biologically based therapies		
Black Cohosh	116(46.4%)	Helped	37(33.9%)
		Did not Help	53(48.6%)
		Not sure	19(17.4%)
		Missing info 7	
Evening Primrose Oil	43(17.2%)	Helped	15(38.5%)
		Did not Help	13(33.3%)
		Not sure	11(28.2%)
		Missing info 4	
Soy supplements/food	106(42.4%)	Helped	32(32%)
		Did not Help	45(45%)
		Not sure	23(23%)
		Missing info 6	

Alternative Treatment	*Utilized treatment N (%)*	*Perceived Efficacy N (%)*	
Red Clover	19(7.6%)	Helped	8(50%)
		Did not Help	6(37.5%)
		Not sure	2(12.5%)
		Missing info	3
Multivitamins/Calcium	148(59.2%)	Helped	34(25.2%)
		Did not Help	50(37%)
		Not sure	51(37.8%)
		Missing info	13
Other listed alternatives:	38(15.1%)	*Helped*	25(71.4%)
		Did not Help	7(20%)
		Not sure	3(8.6%)
		Missing info	3
Mind Body Methods			
Meditation/Relaxation	65(26%)	Helped	26(41.9%)
		Did not Help	19(30.6%)
		Not sure	17(27.4%)
		Missing info	3
Yoga	26(10%)	Helped	11(47.8%)
		Did not Help	6(26.1%)
		Not sure	6(26.1%)
		Missing info	3
Alternative Western Medical Treatments			
Antidepressants	80(32%)	Helped	43(55.1%)
		Did not Help	15(19.2%)
		Not sure	20(25.6%)
		Missing info	2
Antiseizure medications	21(8.4%)	Helped	4(19.1%)
		Did not Help	10(47.6%)
		Not sure	7(33.3%)
		Missing info	0
Blood pressure medications	34(13.7%)	Helped	12(35.2%)
		Did not Help	7(17.7%)
		Not sure	16(47.1%)
		Missing info	0

Women were asked to comment on whether the method helped, did not help or if they were unsure if it helped. Given the relatively small numbers of women using some of the methods, assessment of what was the most efficacious method of all is not feasible. There were 8 alternative therapies that were used by at least 30 women which were

multivitamins and calcium, Black Cohosh, Soy supplements and food, antidepressants, meditation and relaxation, evening primrose oil, Homeopathy and blood pressure medications. Of these the participants perceived antidepressants as one of the most efficacious method with 55% of the 80 women saying that it helped their symptoms, followed by Homeopathy (46.7%), meditation and relaxation (41.9%), evening primrose (38.5%), blood pressure medications (35.2%), Black Cohosh (33.9%), soy products (32%), and multivitamins and calcium (25.2%). (See table 11).

Of the methods less frequently identified, 21 women utilized anti-seizure medications, of those 21 women, only 4 (19.1%) women reported that they felt it helped, next was red clover which was used by 19 women, 8 (50%) of which felt it helped. Next was bio-identical hormones which were used by 16 women, of which 7 (43.7%) of them felt they helped. Seven women chose Traditional Chinese Medicine (TCM) and 4 (57.1%) of them felt TCM helped their symptoms. Six women tried Acupuncture and 3 (50%) of them felt it helped their symptoms. One woman reported using Aryuvedic Medicine and she reported that it helped her symptoms (see table 11).

Chapter Five: Discussion

This study contributes to the literature on HT discontinuation experiences of menopausal women. This study was not a population based sample nor was not ethically or racially diverse, yet, data was captured from a unique group of menopausal women. The women in this study were not a clinic based sample, and there was a lower educational and income status that are not usually a part of menopause and HT related studies.

Demographics

This was not a population based survey and is not to be considered a nationally representative sample. However, questionnaires were received from women in every State in the United States except Hawaii. Not all States were equally represented in the sample, although the women were fairly well equally distributed throughout the United States census defined regions (Northeast, Midwest, South and West). The participants were predominantly White, married and of lower socioeconomic status. Interestingly, the sampling procedure resulted in a sample which included women who are often not represented in menopause research. One unique aspect of this sample was that the majority of the participants reported their highest level of education being a high school diploma. Also, participants reported lower income levels than is usually recruited with nearly 40% of the sample reporting income of less than $30,000 per year. The lack of an ethnically and racially diverse sample that was representative of the US population was not totally unexpected. What was most impressive with this sample was the ability to capture a group of menopausal women with a lower educational and income status. Not only is it more likely that studies with menopausal women usually reflect a sample that is predominantly White and of higher socioeconomic status, the literature also tells us that

these same women are more likely to see a health care provider for menopause and to be prescribed and take HT (Brennan, Crespo& Wactawski-Wende, 2004).

RESEARCH AIM 2: VASOMOTOR SYMPTOM OCCURRENCES

Ockene and colleagues (2005) found that nearly half of the participants who had reported vasomotor symptoms at baseline also experienced vasomotor symptoms following discontinuing treatment and this had a great impact on whether a woman was able to stop HT successfully without unbearable symptoms. This study does provide some support for the Ockene findings (2005), yet the current study found that slightly more women experienced vasomotor symptoms *after* discontinuation of HT versus *prior* to initiation. A McNemar test comparing the two groups revealed that difference was statistically significant which may suggest the difference in the occurrence of vasomotor symptoms at menopause onset *prior* to HT use is perhaps a different phenomenon than the vasomotor symptoms experienced immediately *after* discontinuation of HT. It is also possible that this finding may be a result of a recall bias due to the fact that the vasomotor symptoms experienced before the start of HT occurred much further in the past than the current experiences of HT after recent discontinuation.

Participants who reported more vasomotor symptoms after discontinuation of HT than prior to their use of HT were more likely to be Black, between the age of 40-50, experienced menopause before age 40, and were less than 5 years post menopause. These findings related to current age, age at menopause and years post menopause is not surprising and rather intuitive, as it is known that vasomotor symptoms have been shown to decrease over time in most women (Speroff & Fritz, 2005). Women who experienced surgical menopause also reported a greater occurrence of vasomotor symptoms after discontinuation of HT than prior to. These findings are not surprising; research has shown that women who experience surgical menopause tend to have a higher incidence of

vasomotor symptoms and they are likely to be more severe (Chakravarti, et al., 1977; Feldman, Voda, & Gronseth, 1985; Speroff & Fritz, 2005). This is also consistent with studies looking at this after discontinuation of HT. Grady and colleagues (2003) found that the factors that were most highly associated with the inability to stop hormone therapy were hysterectomy and duration of hormone use of over 10 years.

Fourteen percent of the participants restarted HT after discontinuation. Of those women, approximately 80% (N=66) indicated that they restarted because of vasomotor symptoms. This finding is higher than what Ockene and colleague (2005) found in their study. They found that only 5% of the women in their study restarted HT with the primary reason to treat vasomotor symptoms. In contrast Grady and colleagues (2003) found that nearly 25% of the women in their study who had discontinued HT, restarted because of vasomotor symptoms.

RESEARCH AIM 3: CONTEXTUAL FACTORS AND VASOMOTOR SYMPTOMS

One primary purpose in this study was to explore the relationship between contextual factors and vasomotor symptoms after the discontinuation of hormone therapy. Initial analysis began with a $\chi 2$ and Spearman's Rho correlations to ascertain which factors, if any, were related to the occurrence of vasomotor symptoms after discontinuation of HT. Significant variables indicated in the initial analysis in addition to variables indicated from the literature review were entered into the logistic regression model. In the resulting model, the significant contextual factors associated with the reoccurrence of vasomotor symptoms after discontinuation of HT were the presence of vasomotor symptoms prior to initial start of HT (p=.000), type of menopause (p=.002), and current age (.001). With the exception of current age, these findings are quite consistent with other studies that have looked at HT discontinuation experiences.

Grady and colleagues (2003) identified characteristics in women that would make it more difficult for them to discontinue HT. Similar to the current study, the authors found that women who had had a hysterectomy were the least likely to successfully discontinue HT without recurrence of vasomotor symptoms. They also found no significant association of symptoms with contextual factors of age, ethnicity, education, BMI and smoking.

Ockene and colleagues (2005) explored menopause symptom experiences of women who had recently participated in the estrogen and progestin treatment arm of the WHI study. They found that the strongest determinant of vasomotor symptoms after discontinuation of HT was the presence of vasomotor symptoms at baseline even after adjusting for age, BMI, alcohol and tobacco use. Consistent with these findings, Grady, et al (2005) and Hammar, et al (2003), found that women who did not have vasomotor symptoms prior to treatment were less likely to experience vasomotor symptoms after withdrawal of HT. The current study found a similar relationship with the occurrence of vasomotor symptoms prior to HT. There was an increased likelihood of the occurrence of vasomotor symptoms after discontinuation of HT if there were vasomotor symptoms prior to the start of HT.

All three of the discontinuation studies (Grady, et al, 2003; Hammar, et al, 2003; Ockene, 2005) found that that tapering off of HT was no more affective then stopping abruptly in preventing the occurrence of vasomotor symptoms. The current study findings are consistent with these studies. The samples for both Grady et al (2003), and Ockene et al (2005) were predominantly White and had a higher educational status than the women in the current study.

In contrast, studies examining the varied vasomotor symptom experiences of women at menopause onset and *prior* to the initiation of HT have shown that

socioeconomic status, ethnicity/race, body weight, smoking, alcohol intake, type of menopause and years post menopause do influence symptom experiences. In the current study, lack of ethnic/racial diversity precluded examining group differences. However, no significant relationships were found with body weight (BMI), smoking or alcohol intake. Socioeconomic status was evaluated by proxy measure of educational status only and was non-significant. These findings contrast with factors identified as significant prior to initiation of HT. Further examination of these differences is needed.

RESEARCH AIM 4: COMPLEMENTARY AND ALTERNATIVE MEDICINE

Prior studies have shown that 50-80% of midlife women have utilized some type of CAM. (Bair, et al., 2005; Bair, et al., 2002; Factor-Litvak, et al., 2001; Kaufert, et al., Utian, 1998; Kronenberg & Fugh-Berman, 2002). These studies illustrated that many different cultural groups of women adopt CAM, yet women of lower socioeconomic status are less likely to use CAM.

Consistent with prior studies, the current study found that nearly half of the women reported the use of an alternative treatment to treat vasomotor symptoms. Women who were between the ages of 40-50, less than 5 years post menopause onset, and those who experienced medical menopause were more likely to utilize alternative treatments (see table 1). Although it is known that CAM therapies can be expensive, the current study did not find educational level or income to be a factor in the adoption of CAM.

The most common choices of CAM modalities were botanicals such as multivitamins and calcium, Black Cohosh and Soy supplements and/or soy foods. Other more commonly chosen CAM methods included meditation and relaxation. Although early research is beginning to emerge with regard to the usefulness and safety of alternative medical systems such as homeopathy, acupuncture, and TCM very few women listed these as an option that they had utilized.

Many women reported the use of antidepressants specifically taken to relieve vasomotor symptoms. In fact, those who utilized antidepressants perceived them to be one of the most efficacious methods. There were only 8 alternative therapies that were used by at least 30 women (multivitamins and calcium, Black Cohosh, Soy supplements and food, antidepressants, meditation and relaxation, evening primrose oil, Homeopathy and blood pressure medications). Given the vast amount of alternatives that can be used, and the small numbers for each method, it not possible to discern what is the most effective method. Further studies are needed in this area.

VALIDATION OF THE MODEL

The study findings support the usefulness of Bronfenbrenner's ecological theory as a model to view the vasomotor experiences of menopausal women who have discontinued HT. This study showed that there are many factors that influencing the occurrence of vasomotor symptoms after discontinuation HT.

Macrosystems are broad cultural and historical influences (Bronfenbrenner, 1979) which were operationalized for this study as pivotal clinical trials influencing menopause symptom management modalities (i.e.: HERS I & II and WHI) and the subsequent consensus statements from different organizations. The consensus statements provided evidence based clinical practice guidelines for health care providers who care for women. The findings in this study illustrated that indeed over 40% of the women reported that they discontinued HT because of clinical information that they had personally read, heard on the television or obtained from the internet. Additionally, women reported that they stopped HT based on their health care provider's recommendations. These findings indicate that these macrosystems do influence their decisions.

Mesosystems as described earlier are those settings in which the individual interacts in more than one setting either alone or through linkage of a third party. The

mesosystem and exosystems were operationalized in this study as the influences of friends, family or health care providers with regard to the menopause experience and management strategies for vasomotor symptoms. Thirty three percent of the participants discontinued HT because their health care provider recommended that they do so. Many women also stopped on the recommendations of their family, friends, coworkers and even pharmacists demonstrating that mesosystems also contributed to their decisions to stop HT.

Microsystems consist of an individual's genetic make up (ethnicity, race, age at menopause), personal characteristics (weight, height, general health, smoking, alcohol or drug use). Microsystems were operationalized in this study as the individual contextual factors previously identified (Research aim 1). As validated by the logistic regression model, some of the contextual factors played a significant role in the occurrence of vasomotor symptoms post discontinuation of HT.

Over a third of the women in this study used some type of alternative medical, or CAM therapy to treat their symptoms after discontinuation of HT. As more women seek out other alternatives for the relief of vasomotor symptoms, there will be an increase demand by women and clinicians for high level evidenced based clinical information about the safety and efficacy of these alternatives.

In response there is an increasing amount of studies designed to look the safety and efficacy of CAM methods such as acupuncture are appearing in the literature (Huang, et al., 2006), homeopathy (Jacobs, Herman, Heron, Olsen, & Vaughters, 2005), Aryuvedic (Saper, et al., 2004), biofeedback and relaxation (Nestrand, et al., 2005), and soy (Lewis, Nickell, Thompson, Szalai, Kiss, et al, 2006). In addition, various related clinical trials are in progress. Of 163 menopausal related clinical trials registered at http://www.clinicaltrials.gov/, 35 were investigating non-hormonal methods to reduce hot

flashes. Of these studies, there was one with homeopathy, two with mindful meditation and breathing, two new trials investigating the use of TCM herbs and at least two additional trials are underway with acupuncture. Biological agents being studied are DHEA and soy. One study is investigating the use of yoga for the treatment of hot flashes. Although there have been lay texts and websites indicating that yoga may be effective in reducing vasomotor symptoms, there were no randomized controlled trials that have been published testing yoga. The interest in these methods and new trials ensuing is very exciting for women and health care providers alike.

In the present study, women reported antidepressants were one of the most efficacious methods for treating vasomotor symptoms. Antidepressants are also increasingly included in clinical trials (Evans, et al., 2005). Emerging clinical trials are being designed to explore alternative doses of previously approved antidepressants tailored specifically for the treatment of hot flashes such a mirtazapine (Remeron®). Mirtazapine is classified as a noradrenergic and specific serotonergic antidepressant (Perez, et al., 2004). In addition, several studies are evaluating the effectiveness of the antiseizure medication, gabapentine with the most recent in 2006 (Reddy, et al., 2006). In fact, the pharmaceutical company, Depomed, Inc, has recently submitted an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) for Gabapentin GR$^{(TM)}$ for the treatment of postmenopausal hot flashes.

In summary, Bronfenbrenner (1979) asserts that the ecological framework of human development involves the interaction of the individual, changes in their immediate environment as well as a larger environment beyond the immediate environment within which the individual is located. The individual is not a fixed entity within the environment, but is a dynamic force that has impact on the environment within which the individual resides as well. Clearly the literature and the findings of this study have

illustrated this concept. The influence of pivotal trails and consensus statements has had an impact on health care provider practice patterns and women's decisions to discontinue HT earlier and possible abruptly. The appearance of vasomotor symptoms after discontinuation has resulted in the adoption of alternative methodologies to treat continuing vasomotor symptoms. With the increase in use of these therapies there is an increase demand for high level studies on safety and efficacy of these methods.

LIMITATIONS

The sample size for this study was adequate in numbers for the statistical tests used. However, it was nonprobablity convenience sample drawn from mailing list of which there was limited knowledge about the group of women. The sample does not include an adequate sample from each state, although the participants were fairly equally distributed throughout the 4 US census geographical regions. The sample was predominantly White and while it does not actually reflect the ethically and racial diverse US population it does reflect the population of women who typically use HT (Brennan, Crespo& Wactawski-Wende, 2004).

Generalizability of this study is limited and is dependent upon the depth and breadth of the population sample that was gathered. Findings only reflect those women who have taken a break from or discontinued hormone therapy and cannot be generalized to women who continue HT. To avoid selection bias every effort has been made to gather participants from various venues (doctor's offices, health clubs, malls, grocery stores, and churches). In addition, a variety of advertisements (word of mouth, written ads, flyers, business cards) were used to ensure that as many women as possible will be reached throughout the various regions of the US. Despite the efforts to attract a diverse population of women, the sample does not represent all women in the United States particularly with regard to race and socioeconomic status.

Recall bias is also a limitation of this study as a majority of the participants were well past menopause onset. Participants were asked to complete a questionnaire that reflected incidents that happened in the past. It is known that an individual's ability to recall the past is limited and recall bias can make the information less reliable. Although recall bias was considered important, in order to recruit an adequate sample, no restraints were placed on length of time since hormones were discontinued.

The questionnaire developed for this study was piloted in a group of 10 women in order to assess any biases within the format of the questions. From the pilot group responses there did not appear to be any questions that were ambiguous or leading. The participants reported that the terms with the exception of Aryuvedic medicine and Homeopathy were clear and familiar to them. The small sample size and lack of diversity of the participants of the pilot is another limitation with regard to questionnaire development.

There is no clear biological marker for menopause therefore the diagnosis of natural menopause is made retrospectively after 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause (CAMS, 2004). This retrospective nature of diagnosing menopause can be very confusing for women. In this study women were not given a specific definition for menopause and were self selected and using their own judgment regarding their menopausal status. Purposeful sampling of women who were over the age of 40 and had been prescribed HT from a health care provider for menopause may have helped to avoid recruitment of women who were not menopausal.

In summary although biases and limitations exist, this study was an exploratory study designed to assess trends and characteristics of women who have discontinued HT.

The findings have generated additional descriptive data that will provide a platform for future prospective studies.

IMPLICATIONS AND RECOMMENDATIONS

The results of this study suggest that a majority of menopausal women experience vasomotor symptoms after discontinuation of HT. Guided by an ecological framework this study identified contextual factors that were significantly associated with the occurrence of vasomotor symptoms after discontinuation of HT. This knowledge plays an integral part in helping health care providers to identify women who may find it more difficult to discontinue HT so that they can be appropriately counseled and assisted through the transition of withdrawing from hormones.

In this study, a small number of women restarted HT because of the vasomotor symptoms. It is important for health care providers to be aware that despite the recommendations for a shortened duration of HT there will be women who do not want to discontinue or desire to restart HT after a difficult discontinuation. Data also showed that many women do intend to make informed choices by gathering information for themselves as well as from their health care provider. This illustrates the importance of individualizing care, discussing the benefits and risks at a level that is appropriate the individual's health literacy level. Women should have the opportunity to weigh the benefits, risks and adverse events for themselves.

Nearly a third of the women opted to try an alternative medical or CAM therapy to manage vasomotor symptoms. This study provides an early glimpse into what types of CAM that women accept, use and perceive as helpful. As discussed earlier, the North American Menopause Society (NAMS) recommends that for women who are experiencing only mild vasomotor symptoms that a medical alternative or nonprescription CAM methods should be offered despite the lack of evidence to support

the effectiveness of these methods. (NAMS, 2004). Given these recommendations there will likely be an increase in the use of these modalities. From an ecological standpoint, not only are more randomized clinical trials needed to evaluate the safety and efficacy of these alternative methods, there is also a need for exploratory studies to look acceptance as well as possible cultural or socioeconomic barriers to their use.

Many of these emerging therapies such as over the counter botanicals, acupuncture, meditation, and yoga classes can be costly and may not be available in some areas or to all women. This opens up opportunities for the establishment of sustainable community based programs that can offer low or no cost CAM methodologies for menopausal women who may not have the resources or availability of these modalities in their areas. In addition, there is a need for community based awareness programs to educate women about menopause, HT, and the available alternatives for treatment of vasomotor symptoms.

Although this study has shown there are significant relationships between some contextual factors and the occurrence of vasomotor symptoms, they explain only small part of the variation of symptom experiences between women. There is a need for further studies investigating other emerging etiologic factors related to vasomotor symptoms such as diminished glucose availability (Dormire & Reame, 2003).

CONCLUSION

This study contributes to the literature on HT discontinuation experiences of menopausal women. What is unique about this study is that although it was not a population based sample and was not ethically or racially diverse, it was able to capture data from a group of menopausal women with a lower educational and income status that are not usually included in menopause and HT related studies.

The current study findings reveal that a large majority of menopausal women who were previously taking HT do experience vasomotor symptoms after discontinuation. These findings are consistent with other recent discontinuation studies (Grady, et al, 2003; Ockene, et al, 2005). The most common predictors of the occurrence of vasomotor symptoms were younger age, type of menopause and the occurrence of vasomotor symptoms prior to initiation of HT.

These study findings have also shown that many women undertook some type of alternative medical, or CAM therapy to treat their vasomotor symptoms after discontinuation of HT. As more women seek out other alternatives for the relief of vasomotor symptoms, there is an increase demand by women and clinicians for high level evidenced based clinical information about the safety and efficacy of these alternatives. I

Finally, the study findings clearly support the usefulness of an adaptation of Bronfenbrenner's ecological theory as a model through which to view the vasomotor experiences of menopausal women who have discontinued HT. This study showed that there are many factors influencing the decision to discontinue HT. Individual contextual factors were also identified that are associated with occurrence of vasomotor symptoms after discontinuation. Through this framework, this study opens up many opportunities for further studies in the areas of vasomotor treatment modalities safety and efficacy, exploration of women's acceptance of these new methods as well as the development of community outreach programs to educate women on menopause and alternative treatments.

Appendix

APPENDIX 1: QUESTIONNAIRE

COVER LETTER INTRODUCTION

Thank you for your interest in participating in this study. I am exploring the experiences of menopausal women who have taken prescription hormones (estrogen or estrogen plus progesterone) for menopause, but have either taken a break from or stopped taking them all together. Women who participate in this study should be over the age of 40, have previously been on "prescription" hormones (estrogen, progesterone or testosterone) for menopause, have taken that prescription for at least 3 months consistently, then have either taken a break from or stopped taking the hormones completely.

No information identifying you as an individual will be collected; therefore a consent form is not necessary. Below you will find an written overview of this study. Your completion and return of the questionnaire will be all that is needed to indicate your willingness to participate. Your name, address, and telephone number and/or email address will only be used to contact you initially to mail or email the questionnaire to you. The questionnaire will have an identification number but your personal information will not be connected in any way to that number. To provide anonymity your name, address, and telephone number will be shredded/deleted after the questionnaire is sent to you.

To participate in the study, please complete the attached questionnaire and return it via email at EMKupferer@aol.com or via postal mail in the supplied preaddressed and stamped envelope to:

Principal Investigator:
Elizabeth M. Kupferer MSN, RN-C
Women's Health Care Nurse Practitioner
Doctoral Candidate, School of Nursing University of Texas, Austin TX
2511 Trimmier Road, Suite 140, PMB 347
Killeen, TX 76542 Toll free number: 1-866-224-1161

I sincerely thank you for contributing your information to this exploratory study. Your time and effort will help to gain more knowledge about women's experiences with hormone therapy during these perplexing times of conflicting information with regard to hormone therapy use.

Sincerely,
Elizabeth M. Kupferer

Study Overview

Title of Research Study: "An exploration of Women's current Hormone discontinuation experiences, influences, decisions, and alternatives

Principal Investigator:	**Faculty Sponsor:**
Elizabeth M. Kupferer MSN, RN-C	Sharon Dormire, PhD, RN
Women's Health Care Nurse Practitioner	Assistant Professor
Doctoral Candidate, School of Nursing	School of Nursing
University of Texas, Austin TX	University of Texas, Austin TX
2511 Trimmier Road, Suite 140	1700 Red River Street
PMB 347	Austin, TX 78701-1499
Killeen, TX 76542	Campus Mail Code: DO100
512-567-6117 or 254-939-3318	512-471-7944

Funding source: No outside funding sources

What is the purpose of the study?

The primary goal of this project is explore the experiences of women who have discontinued hormone therapy as well as to investigate factors have influenced discontinuation. In addition, we will look at the use of alternative treatments and their perceived efficacy.

What is next if you decide to take part in this research study?

If you have received this study packet and are interested in participating you only need to review this document, read the cover letter, complete the questionnaire then return the questionnaire either via Email to **EMKupferer@aol.com** or return via postal mail in the supplied preaddressed, stamped envelope to the address listed above. Your consent to participate in this study will be noted by the completion and return of the questionnaire with your comments, no signature is necessary.

What are the possible discomforts and risks?

Your participation should not impose any psychological, social or legal risks to the participants. Potential drawbacks might include your being inconvenienced because of the time spent filling out the survey and returning them via mail. If you are upset by any of the questions please feel free to stop the survey. If you have any questions or comments please do not hesitated to contact Elizabeth Kupferer.

What are the potential benefits to you or others?

Although you will not likely directly benefit from participation in the study, but you will potentially benefit other menopausal women by allowing the researcher to gain insight regarding yours and other women's hormone discontinuation experiences. In addition, if you would like to be notified of the study results when completed, you should send an email to Elizabeth Kupferer at EMKupferer@aol.com to be added to a distribution list that will only be used for notification of the study results.

If you choose to take part in this study, will it cost you anything?

There will be no cost to you for being in this study.

Will you receive compensation for your participation in this study?

There is no compensation for your participation

What if you are injured because of the study?

No injury would result from the completion of a questionnaire.

If you do not want to take part in this study, what other options are available to you?

Participation in this study is entirely voluntary. It is entirely up to you if you want to participate in the study. You are free to refuse to be in the study by simply not filling out the questionnaire. If you decline to participate it will not influence current or future relationships with The University of Texas at Austin.

How can you withdraw from this research study and who should I call if I have questions?

If you do not wish to participate, simple discard the materials. You are free to withdraw your consent at any time without penalty or loss of benefits. If you have any additional questions about your rights as a research participant, please contact Lisa Leiden, PhD, Chair, The University of Texas at Austin Institutional Review Board for the Protection of Human Subjects at 512-232-4381.

How will your privacy and the confidentiality of your research records be protected?

Authorized persons from the University of Texas at Austin and Institutional Review Board have the legal right to review research records and will protect the confidentiality of those records to the extent permitted by law. Your research records will not be released without your consent unless required by law or court order. If the results of this research are published or presented at a scientific meeting your identity will NOT be disclosed. No names will be used on the surveys. ID numbers have been assigned to each individual questionnaire that is NOT linked to the actual participant. All identifying information will be deleted and/or shredded and will not be kept by the researcher. Access to the questionnaire is only allowed to the principal investigator, Elizabeth Kupferer.

Will the researcher benefit form your participation in this study?

Completion of this study will contribute to meeting doctoral degree requirements for the Elizabeth Kupferer, the principal investigator.

ELIGIBILITY CRITERIA

Are you menopausal? Have you gone through menopause?	☐Yes ☐No
Are you over the age of 40?	☐Yes ☐No
Have taken "prescription" for hormone therapy (i.e.: estrogen) for menopause previously?	☐Yes ☐No
Did you take those hormones consistently for at least 3 months in row?	☐Yes ☐No
Have you stopped or taken a break from prescription hormones?	☐Yes ☐No
Are you willing to complete and return the questionnaire via mail or email?	☐Yes ☐No

HORMONE DISCONTINUATION QUESTIONNAIRE

ID# (for office use only)	**Birth date: / Age:**
Where do you live?	City: _____ State: _____
Ethnicity/Race:	☐ Asian ☐ Black ☐ Hispanic ☐ White ☐ Other (list)
Marital status:	☐Single ☐ Partnered ☐ Married ☐ Separated ☐ Divorced ☐ Widowed
Education:	☐Some high school ☐General Education Degree (GED) ☐High school diploma ☐Some college ☐Associate Degree ☐Bachelors Degree ☐Masters Degree ☐Doctoral Degree
Income:	☐<$10,000 ☐$10,001-$20,000 ☐$20,001-$30,000 ☐$30,001-$40,000 ☐$40,001-$50,000 ☐$50,001-$60,000 ☐$60,001-$70,000 ☐$70,001-$80,000 ☐$80,001-$90,000 ☐$90,001-$100,000 ☐>$100,001
What is your height: _____ feet _____ inches	**What is your weight: _____ pounds**

MENOPAUSE HISTORY

At what age or what year did you go through menopause?	Age: _____ or Year:_____
What type of menopause?	☐ Natural ☐ Surgical (hysterectomy with removal of ovaries) ☐ Medical (i.e.: cancer treatments)
When did you begin hormone therapy?	Age: _____ or Year:_____
Why was hormone therapy prescribed for you? (check all that apply)	☐ To treat hot flashes/night sweats ☐ To reduce risk for heart disease ☐ To treat other menopausal symptoms ☐ To reduce risk of osteoporosis ☐ To treat/reduce vaginal dryness ☐ To reduce risk of colon cancer ☐ To treat bladder or urinary problems ☐ Other (please list): ☐ I am not sure why
Did you have hot flashes before you started hormone therapy?	☐ Yes ☐ No
Did you have night sweats before you started hormone therapy?	☐ Yes ☐No

HORMONE THERAPY DECISION INFLUENCES		
When did you discontinue hormone therapy?	Month: _____ Year: _____	
How did you discontinue hormone therapy?	☐ Stopped suddenly ☐ Weaned off slowly	
What type of hormone therapy were you on prior to stopping?	☐Premarin®(conjugated equine estrogen: [CEE]) ☐PremPro® (CEE/medroxyprogesterone) ☐PremPhase® (CEE/medroxyprogesterone) ☐Estrace®/Gynodiol® (estradiol) ☐Cenestin® (conjugated estrogen) ☐Ogen® (estropipate) ☐Activella® (estradiol/norethindrone) ☐FemHRT® (ethinyl estradiol/norethindrone) ☐ Vivelle®,Climara®, Estraderm®, Alora®, Esclim® (estrogen only patch)	☐Combipatch® (estradiol/norethindrone acetate) ☐FemRing® (vaginal ring) ☐Estring® vaginal ring or Premarin®/Estrace® vaginal creams (local estrogens) ☐Estratab®/Menest®(Esterifed estrogen) ☐Estratest® (estrogen with testosterone) ☐Topical estrogen gel/lotion (Estragel®, Estrasorb®) ☐Evista® (raloxifine) ☐Bio-identical hormones ☐Cannot remember ☐Other (please list):
What influenced your decision to stop taking hormone therapy? (check all that apply)	☐Side effects (bloating, headache, bleeding) ☐Serious life threatening side effect (stroke, cancer, blood clot) ☐Health care provider recommended without a specific reason ☐Health care provider recommended because of current health conditions such has high blood pressure, cardiovascular disease or other illnesses	☐Your husband or life partner recommended that you should stop ☐A friend or co-worker recommended that you stop ☐Your pharmacist recommended that you stop ☐Stopped because of the cost of your prescription ☐Stopped on your own because of recent information obtained from: ☐**internet** ☐**written publication** ☐**television ad** Please list what that info was about:	☐To try another type of treatment ☐Afraid of increased breast cancer risk ☐Afraid of blood clot or stroke ☐No particular reason, you just decided to stop on your own ☐Stopped on own, wanted to see how you would feel off hormones ☐Other (please list):
Are you familiar with a study called the Women's Health Initiative (WHI)?	☐ Yes ☐ No	
Did the study findings influence your decision to stop hormone therapy?	☐ Yes ☐ No ☐ I am not familiar with this study	
DISCONTINUATION EXPERIENCES		
Did you experience hot flashes after you stopped hormone therapy?	☐No ☐Yes: How many per day? _____How severe? ☐ Mild ☐ Moderate ☐ Severe	
Did you experience night sweats after you stopped hormone therapy?	☐No ☐Yes: How many per day? _____ How severe? ☐ Mild ☐ Moderate ☐ Severe	
Have your hot flashes resolved without restarting hormone therapy or alternative treatments?	☐No ☐Yes: Resolved within _____ months or _____days of stopping	
Are you still experiencing hot flashes?	☐No ☐Yes: How many per day? _____How severe? ☐ Mild ☐ Moderate ☐ Severe	
Are you still experiencing night sweats?	☐No ☐Yes: How many per day? _____ How severe? ☐ Mild ☐ Moderate ☐ Severe	
Have you restarted hormone therapy?	☐No ☐ Yes	
Did you restart hormone therapy because of hot flashes?	☐No ☐ Yes: Are hot flashes/night sweats now resolved? ☐ No ☐ Yes ☐Partially	

If you have not restarted hormone therapy, will you?	☐No ☐ Yes ☐ Not sure ☐ Awaiting more information
Have you used other alternative therapies or medications to treat hot flashes or night sweats?	☐No ☐ Yes (if you answered yes to the use of alternatives to treat your hot flashes or night sweats please complete the next section "Alternative menopause treatments used to treat hot flashes or night sweats")

ALTERNATIVE MENOPAUSE TREATMENTS USED TO TREAT HOT FLASHES OR NIGHT SWEATS		
ALTERNATIVE MEDICINE SYSTEMS		
Acupuncture	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Ayurveda	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Homeopathy	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Traditional Chinese Medicine (TCM)	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
BIOLOGICALLY BASED THERAPIES (DIETARY SUPPLEMENTS)		
Black Cohosh	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Evening primrose oil	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Soy	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Red clover	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Vitamins/Calcium	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Bio-identical hormones	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Other (list)	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
MIND BODY METHODS		
Meditation/Relaxation	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Yoga	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
OTHER MEDICAL TREATMENTS		
Prescription antidepressants (Prozac, Effexor, Paxil)	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Prescription antiseizure medication (Neurontin [*gabapentine*])	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure
Prescription blood pressure medication (Clonidine)	☐ Yes ☐ No	☐ Helped ☐ Did not help ☐ Not sure

HEALTH HABITS	
Exercise	☐ No exercise
	☐ Mild exercise (i.e., climb stairs, walk 3 blocks, golf)
	☐Occasional vigorous exercise (i.e., work or recreation, less than 4x/week for 30 min.)
	☐ Regular vigorous exercise (i.e., work or recreation 4x/week for 30 minutes)
Alcohol	Do you drink alcohol? ☐Yes ☐No If yes, what kind? ☐wine ☐beer ☐liquor How many drinks per week? _____
Tobacco	Do smoke cigarettes? ☐ Yes ☐ No How many packs per day? _____ How long have you smoked? _____ years

The questionnaire is complete
Thank you for participating
Please return the questionnaire in the enclosed preaddressed stamped envelope or via email to EMKupferer@aol.com

If you would like to be notified of the findings of the study, please send an email to EMKupferer@aol.com to be added to the distribution list.

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Vita

Elizabeth Kupferer was born April 17, 1958 in St. Louis, Missouri, to Margaret Mary Rasmussen Kupferer and Richard Anthony Kupferer. Elizabeth began her basic primary education in St. Louis within the Catholic grade school system. After moving to Houston Texas with her parents in 1974, Elizabeth earned her high school diploma in February 1976 from J. Frank Dobie High School of the Pasadena Independent School District in Houston, Texas. Following high school Elizabeth went directly to San Jacinto Junior College in Pasadena, Texas to study nursing and completed her Associate Degree in Nursing in 1978 at the age of 20. She received her Registered Nurse (RN) license in September of that same year. Beginning in May of 1978 Elizabeth worked as an RN in Labor and Delivery within the Sisters of Charity Health Care system at St. Joseph Hospital, in downtown Houston, TX.

Elizabeth continued within the Sisters Health Care System in Maternal Fetal Services with varied experience in women's health and progressive management roles up to the level of Director of Maternal Fetal Services. Elizabeth stayed within the Sisters' health care system up until 1996, and during this time she was married and gave birth to three beautiful children, Meghan Elizabeth Gregg, who is now 23, Anthony Paul Gregg who died shortly after he was born in 1985, and Matthew Travis Gregg who is now 20 and the father of Elizabeth's first grandchild, Graci Lynn Gregg.

Elizabeth returned to school during this time and completed her Bachelor's Degree in Science and Nursing at the University of Texas Medical Branch in Galveston Texas in 1990 and her Masters Degree in Science and Nursing in 1994, also at the University of Texas Medical Branch in Galveston. Elizabeth was licensed as a Women's Health Care Nurse Practitioner in September of 1994. Elizabeth worked as a Nurse

Practitioner in Houston, with Dr. George Kuhn from 1994 to 1996 and then moved to Austin Texas to join in with the Renaissance Women's Group at its inception until 2002.

While still employed with Renaissance Women's Group, Elizabeth had an opportunity to teach her first course in nursing, basic physical assessment in 2000. This wonderful opportunity was the catalyst for her to return to school to pursue a doctoral degree so that she could further her teaching career. When Elizabeth left Renaissance Women's Group, she began work with Organon Bio-Sciences USA, a Dutch owned company as a Women's Health Medical Science Manager where she is now currently employed. Elizabeth has gained a significant amount of knowledge through the development of reciprocal relationships with thought leaders in women's health, presenting scientific information to small and large groups, locally, nationally and internationally. In her current role she provides support investigator initiated research, has gained an understanding of the early development, and pre-launch, launch, and post launch activities of women's health care products in contraception, fertility and menopause at a national and international level.

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