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# Women Who Continue Hormone Replacement Therapy Despite Findings from the Women's Health Initiative

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# WOMEN WHO CONTINUE HORMONE REPLACEMENT THERAPY DESPITE FINDINGS FROM THE WOMEN'S HEALTH INITIATIVE

by

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## Abstract

Since the results of the Women's Health Initiative (WHI) study were published in 2002, millions of women and their healthcare practitioners have had to re-examine decisions about the use of hormone replacement therapy. This level one descriptive study explored the characteristics of menopausal women who could not tolerate estrogen withdrawal and continued taking hormone replacement therapy despite findings of risk published in the Women's Health Initiative. The sample included the medical records of 1,195 patients in a single-physician OB-GYN practice in northeast Florida. All records of women with a birth date in 1954 or prior and a visit to the practice for gynecological care between July 2002 and March 1, 2004 were reviewed to collect data about demographics, past medical history, and hormone replacement therapy (HRT) use.

A significant portion of women (77.2%) had discontinued HRT. Of the women remaining on HRT, 54.7% changed either the dose or type of hormones taken. Only 59.5% of these women remained on the same estrogen dose both before and after the WHI results were published in 2002. Interestingly, there were 29 women (4%) who initiated HRT use after July 2002. The women who remained on HRT after WHI were more likely to be younger, Caucasian (72.7%), non-smokers (82.3%), and taking medication for other conditions (68.5%). The older the woman, the less likely she was to have continued HRT. Younger women were more likely to have changed HRT drug and/or dose post-WHI.

# CHAPTER 1

## INTRODUCTION

What are the characteristics of menopausal women who continue hormone replacement therapy (HRT) despite the warnings published from the Women's Health Initiative Study (WHI) and why is it important? In 2003, an estimated 30 million women in the United States were either going through the process of menopause or had already completed it. An anticipated 6 million more women will reach menopause over the next decade, doubling the number of women over age 50 by the year 2020 (Theroux & Taylor, 2003). Before the results of WHI were published in July 2002, it is estimated that 6 million women were taking hormone replacement therapy. By May 2003, only an estimated 2.7 million were taking HRT. Within a year, millions of women stopped using HRT and many more did not start due to the findings published by WHI (Goldstein, 2004; Hersh, Stefanick, & Stafford, 2004). The women who continued HRT despite the risks did so primarily to reduce menopausal symptoms and maintain quality of life (Hays, 2003; Rymer, Wilson, & Ballard, 2003; Woodward, 2005).

Advanced registered nurse practitioners (ARNP) and other health care providers offering care to women must have an understanding about the perimenopausal and menopausal periods, and knowledge about the health risks, health promotion, and counseling needs of this group of women. The average age of menopause today is 51.4 years and a healthy 50 year-old has a life expectancy of 91 years (Goldstein, 2004).

Three-fourths of women report vasomotor symptoms at menopause and one-fourth of all menopausal women seek treatment for menopausal symptoms (Poindexter & Wysocki, 2004). Since modern women live as many as one-third of their years in the post-menopausal state (Poindexter & Wysocki, 2004), health care practitioners are obligated to identify patients at risk, and promote health, effective decision-making, and quality of life in this large segment of the population.

*Purpose*

The purpose of this study was to describe the characteristics of menopausal women who either remain on HRT or restart HRT after a trial discontinuation subsequent to the WHI results published in July 2002. If the population of women who cannot tolerate withdrawal from estrogen can be identified, a population at increased risk for adverse health events such as myocardial infarction, stroke, venous thromboembolism, dementia, and breast cancer could be recognized and health care interventions initiated to prevent these complications (Breslau, 2003; Grady, 2003; Hays, 2003). Non-hormonal therapy and lifestyle change methods of dealing with the symptoms of menopause could be researched and prescribed, reducing risk and improving the quality of life for many women.

The research question examined in this study is: What are the characteristics of women who chose to remain on, begin or restart hormone replacement therapy after the results of the WHI were made public?

*Definitions*

Several terms are defined theoretically and operationally for the purposes of this study. Menopause is theoretically defined as absence of menstrual periods for one year

following the loss of ovarian function (National Cancer Institute, 2005). Systemic declines in estrogen production from the ovaries during menopause have a huge impact on estrogen receptive tissues. The thermoregulatory center in the brain becomes unstable causing hot flashes. Sleep disturbances, palpitations, vaginal dryness, and thinning of the vaginal mucosa are other changes associated with the climacteric (Liu, 2004). Operationally, a woman is considered menopausal if she is so identified by the physician in the medical record.

Hormone replacement therapy is defined theoretically and operationally as any formulation of estrogen with or without progestin taken by any delivery route including oral, transdermal, injectable, vaginal rings, vaginal tablets, or vaginal cream (Liu, 2004).

*Theoretical Framework*

The theoretical framework for this research was the midrange theory of reasoned action and planned behavior by Icek Ajzen and Martin Fishbein. Originally written in 1967 as the theory of reasoned action, it was updated in 1988 to counter criticisms that it did not address social influences (Ajzen, 1991; Fishbein & Ajzen, 1975). The theory was developed to, "provide a useful framework for predicting and understanding social behavior in general and health behavior in particular" (Werner, 2004, p.126). According to this theory, individuals are rational and able to process information and can use information to make reasonable behavioral decisions. The key components for reasoned action in women making decisions on whether or not to use HRT are identified by Azjen and Fishbein as knowledge, behavioral beliefs, normative beliefs, and control beliefs. Knowledge is the primary factor in this model, followed by attitudes towards the decision to be made, subjective norms of the community, and beliefs regarding ability to influence

outcome (Ajzen, 1991; Fishbein & Ajzen). Information concerning the risks, benefits, and alternatives to HRT are vital knowledge for women making treatment decisions. Cultural attitudes and norms towards menopause and feelings of self determination affect women's ability to make informed decisions on treatment of menopausal symptoms.

Fishbein and Ajzen assert that intention to perform a behavior is a major determinant of planned behavior and three factors determine intention: attitude, subjective norm, and perceived behavioral control. Attitude is defined as the degree of positive or negative feelings the individual has about performing a behavior. Subjective norm is defined as the individual's perceived ideas about how significant others and society feel about a specific behavior. Perceived behavioral control refers to the individual's beliefs about the extent to which they have the resources or opportunity to perform the specific behavior (Werner, 2004).

The theory of reasoned action and planned behavior is applicable to this study as millions of women struggle to decide if hormone replacement therapy for reduction of menopausal symptoms is worth the risks publicized by the WHI study. Self-efficacy, knowledge, and support are vital to women as they make informed healthcare choices (Wilhelm, 2002).

# CHAPTER 2

# REVIEW OF LITERATURE

This chapter provides an overview of the state of knowledge from current literature concerning menopause, hormone replacement therapy, the results of the WHI study, and its impact on women's healthcare. Alternatives to hormone replacement therapy and areas for further research are also presented.

## *Menopause*

Menopause is defined as absence of menstruation for one year following the loss of ovarian function (National Cancer Institute, 2005). Menopause is a normal transition from the reproductive stage to the non-reproductive stage of a woman's life. During menopause, there is a loss of ovarian follicular activity resulting in increases of follicle stimulating hormone and lutenizing hormone, decreases of estrogen and progesterone, and a cessation of menstruation (George, 2002). As women age, the decreased levels of estrogen present during perimenopause and menopause can cause a variety of symptoms and potentially serious health problems.

Qualitative studies of menopause reveal that no two women experience menopause in the same way (George, 2002; Wilhelm, 2003). Subjective symptoms of menopause include vaginal dryness, dysparunia, pain on urination, and urinary frequency and incontinence (Bertero, 2003).

Vasomotor symptoms, commonly called "hot flashes," are one of the hallmark symptoms of menopause. While the cause of vasomotor instability is uncertain, the literature reports that up to seventy-five percent of women over age 45 experience hot flashes (Bertero, 2003; Guttuso, Kurlan, McDermott, & Kieburtz, 2003). Eighty-five percent of women who experience hot flashes are symptomatic for more than one year and 25% to 50% report symptoms for up to five years (Fitzpatrick & Santen, 2002).

Hot flashes and sweating that occur at night are commonly labeled night sweats and are physiologically the same phenomenon (North American Menopause Society, 2004). Night sweats are often disruptive to sleep and frequent awakening has been linked to mild depression, changes in attention span and memory, irritability, fatigue, and decreased quality of life (Fitzpatrick & Santen, 2002; Liu, 2004).

Other reported symptoms of menopause believed to be caused by decreased hormone levels include increased perspiration, chills, palpitations, forgetfulness, insomnia, difficulty concentrating, mood alterations, early awakening, and breast soreness (Barnabei, 2002; Dennerstein, 2000; Dormire, 2003; George, 2002).

Accelerated bone loss leading to osteopenia and osteoporosis is a potentially serious complication of menopause. The link between estrogen depletion and bone loss has been recognized for over sixty years (Fitzpatrick, 2004). Osteopenia is a thinning of bone tissue which unchecked progresses to osteoporosis or a substantial loss of bone mass. The fractures that occur with minimal trauma in osteoporotic women have a significant effect on mortality and morbidity (Love). Peak bone mass is usually achieved at age 20 and maintained until age 35. Dual energy x-ray absorptiometry (DEXA) scans are a diagnostic tool used to measure bone density as compared to peak bone mass.

Scores are reported as T scores, which represent standard deviations from the norm. A T score of –2.5 or greater is diagnostic for osteoporosis (Love, 2004). One in four postmenopausal women is diagnosed with osteoporosis and an additional one in three has osteopenia, making it of great concern to healthcare professionals.

Menopause is a, "normal transition that occurs in all women" (Pearson, 2002, p.1). While some women become menopausal with little difficulty, other women have symptoms that disrupt their lives. Discomfort from hot flashes is the most common reason women seek HRT and these vasomotor symptoms have been shown to have a significant negative impact on quality of life (Barton, Loprinzi, & Waner-Roedler, 2001).

*Treatment of Menopausal Symptoms Using Hormone Replacement Therapy*

In 2000, Premarin, a conjugated equine estrogen hormone replacement therapy, was the second most prescribed drug in the United States (Rymer, Wilson, & Ballard, 2003). In 2002, 6 of the top 100 selling prescriptions were products containing ethinyl estradiol or conjugated equine estrogens (Ruggiero & Likis, 2002). Prior to the published results of the WHI study in July 2002, HRT was the routinely prescribed standard of care for menopausal women. A survey of postmenopausal women aged 50-75 conducted in 1995 found that approximately 38% of survey responders reported HRT use (Nelson, 2002/2005)

Hormone replacement therapy includes any formulation of an estrogen compound with or without progestin. Estrogen is either derived from the urine of pregnant mares (Premarin), or synthetically derived from plant sources (Cenestin) (National Institutes of Health [NIH], 2003). Estrogen products currently available in the United States include oral synthetic (Cenestin), oral equine (Premarin), oral micronized

estradiol (Estrace, Gynodial), oral esterfied (Menest), oral estropipate (Ogen, Orth-Est), transdermal (Estraderm, Vivelle, Climara), transdermal estrogel gel (EstroGel), injectable estradiol valerate in oil (Delestrogen), injectable estradiol cypionate in oil (Depo-Estradiol), vaginal tablets (Vagifem), vaginal creams (Estrace, Premarin, Ogen) and vaginal rings (Estring, Femring) (Liu, 2004). Unopposed estrogen use in women with intact uteri has been shown to increase the risk of endometrial hyperplasia and endometrial cancer (U.S. Preventative Services Task Force, 2002). Combined estrogen-progesterone therapy reduces the development of endometrial hyperplasia, and cyclical use of combined therapy reduces the risk of endometrial cancer to a rate similar to that of women not using hormone therapy (Humphries & Gill, 2003).

Purported benefits of HRT included the reduction of vasomotor symptoms, cardiovascular system protection, prevention of vaginal and urinary tract atrophy, maintenance of bone density, and protection against memory loss, irritability, and depression (Rousseau, 2001). Clinical studies have shown that estrogen is effective in preventing bone loss associated with menopause (Fitzpatrick, 2004; Humphries & Gill, 2003; Women's Health, 2004) however, Raloxifene (Evista), bisphosphonates such as alendronate (Fosamax), and parathormone are alternatives to estrogen for treatment of bone loss which are effective and have low risk (Love, 2004).

*The Heart and Estrogen/Progestin Replacement Study I.* The first large randomized placebo-controlled study to examine estrogen use and secondary prevention of coronary artery disease was The Heart and Estrogen/Progestin Replacement Study (HERS-I), funded by Wyeth-Ayerst Laboratories and published in 1998 (NIH, 1998). HERS-I considered 2,763 postmenopausal women with an average age of 67.

Participants were randomly assigned to an estrogen/progestin combination or a placebo and treated for approximately 4 years (Furberg, 2002).

Contradicting years of observational studies, HERS-I demonstrated no cardio-protective benefits from HRT. Women in the treatment arm with heart disease found estrogen and progestin use did not prevent further heart attacks or death from coronary heart disease despite the positive effects of treatment on lipoproteins (NIH, 1998). The study was criticized as too short, the conclusions generally were unheeded, and the results did not change HRT prescribing habits.

*The Heart and Estrogen/Progestin Replacement Study II.* To counter criticisms of the HERS-I study, open label observational follow-up of 93% of the surviving women was carried out with consent for an additional 2.7 years. HRT was prescribed to study participants at the personal physician's discretion. In the treatment group, patient usage of HRT declined from 81% in the first year to 45% in the sixth year. In the placebo group, hormone usage increased from 0% in the first year to 8% in the sixth year. The Heart and Estrogen/Progestin Replacement Study II (HERS-II) analyzed data from the total 6.8 years and again demonstrated no cardiac benefits from HRT (Hulley et al., 2002), foreshadowing the findings of the WHI which were published within days of HERS-II.

*The Women's Health Initiative Study.* The Women's Health Initiative, sponsored by the NIH, was an ambitious, multicenter placebo-controlled study of the effects of HRT on 16,608 healthy postmenopausal women aged 50-79 (Beattie, 2003). There were two arms of the study. The first included women with an intact uterus who received either

combination estrogen-progesterone therapy or a placebo. The second arm examined unopposed estrogens effects on healthy women with prior hysterectomies (Liu, 2004).

WHI was established in 1991 to examine, "the most common causes of death, disability, and impaired quality of life in postmenopausal women" (Brucker & Youngkin, 2002, p. 411). The goal was prevention of the major causes of morbidity and mortality in women such as heart disease, cancers of the breast and colon, and osteoporosis. Volunteers had varied backgrounds and demographics. The double blind study was designed to assign women randomly to an estrogen/progestin group and a placebo group. Participants were assessed every 6 months and had yearly mammogram and breast exams (National Institutes of Health [NIH], 2002). On July 9, 2002, the Data and Safety Monitoring Board of the Women's Health Initiative unexpectedly ended the combined hormone therapy arm of the WHI study three years early, citing increased risks for breast cancer, pulmonary embolisms, strokes, cardiac events, and dementia, with only a slight benefit of decreased fractures and colorectal cancers (Hormone Replacement, 2002). Use of HRT plummeted in the wake of HERS-II and the WHI results. The NIH further shocked health care providers when the second arm of WHI, the trial of conjugated equine estrogen (Premarin) alone in women with hysterectomies, was terminated on March 2, 2004, one year prior to its planned completion due to an increased risk of stroke in participants (NIH, 2004).

The WHI study is limited by the timing of initiation of estrogen and the use of only one oral preparation of HRT (0.625mg/d conjugated equine estrogen either alone or in combination with 2.5mg/d medroxyprogesterone acetate or Prempro). It has however,

had a radical impact on recommendations by health care providers to postmenopausal women concerning HRT.

*Recommendations for Hormone Replacement Therapy since WHI*

"The WHI is considered the most statistically valid study of HRT use in healthy postmenopausal women" (Voelker, 2002, p.2395) however there is some controversy concerning the implications for the care of menopausal women. There is also controversy regarding the methodology, since the average age of study participants was 63 (ACOG, 2004), and 74.4% of these women had never used estrogen and had been estrogen depleted for an average of 10 years (Chlebowski, n. d.). The American College of Obstetrics and Gynecology (ACOG) assembled an expert panel in 2002, which issued guidelines in 2004 for the use of HRT in the wake of the WHI results (ACOG Task Force, 2004).

ACOG stressed that each woman individually with her health care provider must evaluate use of hormone replacement therapy for risks and benefits. The second guideline stated that HRT be used for management of menopausal symptoms only and not as a preventative for chronic disease. The recommendations continued with a statement that HRT use should be evaluated periodically and at least annually, the lowest dose for the least amount of time should be used, and alternative therapies considered. Current users of HRT are advised to taper doses toward discontinuation of HRT (Hersh & Stafford, 2004). Women desiring long term hormone replacement therapy for general well-being must be counseled about the risks as WHI data concluded after four years of continuous HRT, diagnosis rates of invasive breast cancer significantly increased (ACOG, 2002). The North American Menopause Society recommendations echo ACOG

guidelines (Utian, 2004) as do the guidelines from the National Association of Nurse Practitioners in Women's Health (Wysocki, Alexander, Schnare, Moore, & Freeman, 2003).

*Alternative Therapies to HRT for Relief of Perimenopausal and Menopausal Symptoms*

As clinicians inform postmenopausal women about the risks and benefits of HRT, a discussion of alternative treatments for symptoms and chronic disease prevention is necessary. "The use of alternative therapies for menopausal symptoms is common, and women who use them generally find them to be beneficial" (Newton, 2002, p. 18). Alternative therapies must be matched to symptoms and treatment goals and include lifestyle changes, alternative health care, herbal and nutritional supplements, and other prescription medications.

*Lifestyle changes.* Lifestyle changes are suggested as the first alternative to HRT by the North American Menopause Society (Utian, 2004). Exercise and weight loss are advocated for perimenopausal women since fit women experience up to 50% less hot flashes than do sedentary women. Furthermore, a high body mass index is associated with more severe and more frequent vasomotor symptoms. Smoking and stress are also correlated with increased vasomotor symptoms (Kirn, 2004). Relaxation techniques and deep breathing are effective methods to help control menopausal symptoms. Lower air temperature, use of fans, avoidance of hot beverages and foods, and layered clothing are other suggestions (Kirn, 2004). Low fat diet, blood pressure control, and exercise are suggested for prevention of heart disease (Grimes & Lobo, 2002). Increased dietary intake of vitamin D and calcium in addition to weight bearing exercises are recommended for prevention of osteoporosis (Morley, 2004).

*Alternative health care.* Acupuncture has been used for relief of menopausal symptoms by 10% of women using alternative therapies. Visits to homeopathic or naturopathic physicians, chiropractors, massage therapists, and herbalists are also reported as somewhat to very helpful by women surveyed (Newton, 2002).

*Herbal and nutritional supplements.* Herbal and nutritional supplements are increasingly popular; however there are no randomized controlled studies that indicate efficacy in these products (Kim, 2004). Vitamin E, black cohash, red clover, and dong quai are the most widely used herbal and nutritional supplements for menopausal symptoms. Clinical trials have shown either no effectiveness or conflicting results, and the correct dosage and duration of treatment are in dispute, but as there is little potential for harm, these products may remain an option for women (ACOG, 2004; Hackley & Rousseau, 2004; Newton, 2002).

*Phytoestrogens.* Phytoestrogens are plant-derived non-steroidal compounds that that either have estrogenic activity or are metabolized in substances with estrogenic activity. Isoflavinoids, lignans, and coumestans comprise the three main groups of phytoestrogens (Krebs, Ensrud, MacDonald, & Wilt, 2004). While phytoestrogens are present in over 300 varieties of plants, legumes and particularly soybeans are rich in phytoestrogens. There is no evidence dietary soy intake reduces menopausal symptoms of hot flashes and night sweats and placebo-controlled trials on the clinical effects of phytoestrogens have been similar to placebo (Speroff, 2005).

*Prescription medications.* Other prescription medications for menopausal symptoms and chronic disease prevention are available. Progestin only regimes such as depo-medroxyprgesterone acetate, megestrol acetate, and topical progesterone creams

have reduced the frequency and severity of hot flashes 80-90% in studies (Hackley & Rousseau, 2004). Clonidine has been shown minimally more effective than placebo however adverse effects including insomnia are problematic (Hackley & Rousseau, 2004). Selective serotonin reuptake inhibitors (Effexor, Prozac, and Paxil) have proven effective at reduction of vasomotor symptoms in short term randomized trials and may be of interest in women unable or unwilling to take HRT for disruptive menopausal symptoms (ACOG, 2004 ; Evans et al., 2005 ; Hackley & Rousseau, 2004). Vaginal and genito-urinary tract symptoms may be relieved with use of topical estrogen creams, vaginal rings, or tablets. The use of lubricants may alleviate dysparunia. Urinary incontinence, urgency, and frequency may be relieved with tolterodine (Detrol), bladder training, and vaginal estrogen preparations (Hackley & Rousseau, 2004).

Osteopenia and osteoporosis can be treated with alendronate, raloxifene, and parathyroid hormone. All of theses prescription medications have been shown to increase bone density and reduce fractures in postmenopausal women (Love, 2004.).

Gabapentin, approved in 1994 for seizure therapy, is currently being studied for use in reduction of vasomotor symptoms in postmenopausal women. A randomized, double blind, placebo-controlled study of 59 postmenopausal women demonstrated a 54% decrease in hot flashes with low dose therapy over placebo. The authors propose further study which is merited (Guttuso, Kurlan, McDermott, & Kieburtz, 2003).

Tibolone is a synthetic steroid promoted by the manufacturer, Organon, as having "tissue-specific" hormonal effects thereby increasing safety over estrogen-based drugs. Prescribed for relief of hot flashes, to protect from bone loss, and to improve vaginal tissue, tibolone is unavailable in the United States. While tibolone is used in 70 countries

other than the U.S., The Lancet (August 9, 2003) reported United Kingdom's Million Women Study demonstrated an increased risk of breast cancer for women taking hormone therapies including tibolone (Robb-Nicholson, 2004).

*Women's Responses to HERS-I, HERS-II, and WHI*

With the publication of the results of HERS-I in 1998 followed by HERS-II and WHI results within days of each other in 2002, an estimated 65% of women using HRT abruptly discontinued it. Reports published two years later showed that 1 in 4 women who discontinued HRT because of WHI findings restarted hormone therapy to relieve menopausal symptoms (ACOG, 2004).

*Conclusions*

The results of HERS-I, HERS-II and WHI dramatically changed women's healthcare. No longer were women being told HRT was the panacea for aging. Long held ideas about the benefits of estrogen were proved false and millions of women abruptly discontinued its use. In the wake of WHI, some women refused to discontinue HRT despite the increased risk for significant health problems. Research related to the characteristics of women unwilling or unable to stop HRT may assist in identifying a patient group at risk for the complications of HRT and lead to prevention of these problems.

# CHAPTER 3

# METHODOLOGY

The purpose of this research was to describe the characteristics of postmenopausal women who chose to remain on, begin, or restart hormone replacement therapy after the results of the WHI were made public in July 2002. A retrospective chart review of medical records in a single-physician OB-GYN practice in northeast Florida provided the data for this level one descriptive study.

## *Sample*

A total non-probability convenience sample of every medical record that met the inclusion criteria was examined. Inclusion criteria for this study were the medical records of patients with a birth date in 1954 or earlier who were scheduled for gynecological care subsequent to July 2002 (the date of the cessation of the first arm of the WHI). A computer search on March 1, 2004 revealed approximately 1800 medical records that met the inclusion criteria.

A total of 1,783 charts were reviewed. Of these, 301 were noted as "no show" for the scheduled office visit, 19 had significant missing data, and 268 were seen for a non-gynecological appointment. The total number of charts for which data were analyzed, therefore was 1,195.

*Setting*

The population in the northeast Florida area where the practice is located is 90.0% white, 7.7% black or African-American, 1.5% Hispanic, and 0.5% Asian (U.S. Census Bureau, 2006). The median family household income is $49,845. Forty one percent of the population of Nassau County is age 45 and older (Nassau County Economic Development Board, 2004). An investigation of 100 randomly chosen medical records at the practice site on April 11, 2004, showed a close match with the demographic data of the county.

*Data Collection Procedure*

Every medical record that met the inclusion criteria was reviewed by the primary investigator. Data collection for this study took place from June 2004 to January 2005. No identifying data were collected. Patients were considered menopausal with a diagnosis of menopause on the chart.

*Instrument*

Data concerning the characteristics of menopausal women were collected using a data sheet developed for the research (See Appendix A). Demographic data included age, gravida and para, natural or surgical menopausal status, age at menopause, race, and marital status. Medical history included current weight, recent weight loss or gain, blood pressure, smoking status, other medical diagnoses, current medications, gynecological surgeries, mammogram BiRADS classification, and DEXA scan results. Current and previous hormone therapy, menopausal symptoms reported, and treatment for menopausal symptoms which were documented in the medical record were examined.

*Protection of Human Subjects*

This research was reviewed by the Institutional Review Board at the University of North Florida and granted approval as Exempt/Category 4 (See Appendix B). The chart review recorded no identifying data, and the data sheets were shredded once the information was tabulated, entered into a spreadsheet, and verification of accuracy was accomplished.

# CHAPTER 4

# RESULTS

A descriptive analysis of the data was conducted. This chapter summarizes the data regarding the characteristics of menopausal women who either continued, began, or restarted hormone replacement therapy during the two years after the publication of results from the WHI.

*Demographic Data*

A total of 1,195 charts was reviewed. The mean age of the patients was 61.36 at the time of data collection. Most of the women were Caucasian (82.7%), married (76.5%), and multiparous (81.3%) (see Table 4.1). The vast majority (92.2%) were menopausal (see Table 4.2). Menopause was surgical in 29.3% of women, with total abdominal hysterectomy and bilateral salpingo-oopherectomy performed 60.4% of the time. The majority of surgeries (60.3%) were performed for menometrorrhagia.

Sixty four percent of women whose records were reviewed reported other medical diagnoses and 71.1% reported taking medications other than HRT. The top four medical diagnoses that included pharmacologic management were hypertension (23.6%), thyroid dysfunction (14.5%), osteoporosis (11.7%), and depression (11.7%). Smoking at some time in the past was reported by 19.8% of women and current smoking was reported by 17.7%. Caffeine intake was reported by 71.4% of women. Bone density results were tabulated from DEXA scans with approximately one-third of women with

Table 4.1
*Demographic Characteristics of Sample*

| Characteristic | n | % |
|---|---|---|
| Race (n = 1,169) | | |
| Caucasian | 967 | 82.7% |
| African American | 162 | 13.9% |
| Other | 40 | 3.4% |
| Marital Status (n = 1,164) | | |
| Married | 890 | 76.5% |
| Single | 52 | 4.5% |
| Divorced/Separated | 103 | 8.8% |
| Widowed | 119 | 10.2% |
| Parity (n = 1,182) | | |
| Nullipara | 99 | 8.4 |
| Primipara | 122 | 10.3 |
| Multipara | 804 | 68 |
| Grand Multipara | 157 | 13.3 |

Table 4.2
*Initiating Events for Menopause (n= 1195)*

| Menopausal Status | n | % |
|---|---|---|
| Non-menopausal | 93 | 7.8% |
| Natural Menopause | 649 | 54.3% |
| Surgical Menopause | 453 | 37.9% |
| Menometrorrhagia (n = 273) | | |
| Ovarian Mass (n = 28) | | |
| Fibroid Uterus (n = 50) | | |
| Diagnosis Not Listed (n = 101) | | |
| Cancer (n = 1) | | |

osteoporosis, one-third with osteopenia, and one-third with normal bone density (see Table 4.3)

The average time on HRT for the sample as a whole was 8.3 years (range = 0 to 46). Seven hundred-thirty of the 1,195 women on whom charts were reviewed (61.1%) had been on hormone replacement therapy prior to the release of the WHI results in July 2002. Four hundred-forty-three of the women on whom charts were reviewed (37.1%) were on hormone replacement therapy at the time of data collection (See Figure 4.1).

Table 4.3
*Bone Density DEXA Scan Results (n = 129)*

| | n | % |
|---|---|---|
| Osteoporosis (T score -2.5 or less) | 46 | 35.7% |
| Osteopenia (T score -1.0 to -2.4) | 44 | 34.1% |
| Normal bone density (T score > -1.0) | 39 | 30.2% |

Of the women for whom both pre and post WHI data on HRT use were available (n= 724), 254 discontinued HRT after July 2002. Of the 75 women remaining on HRT, 41 changed either the dose or type of hormones taken (see Figure 4.2). Only 59.5% of women taking HRT after July 2002 remained on the same estrogen dose both before and after WHI results were published (See Figure 4.3). Interestingly, there were 29 women (4%) who initiated HRT use after July 2002.

Figure 4.1 Overall Effect of WHI on HRT Use

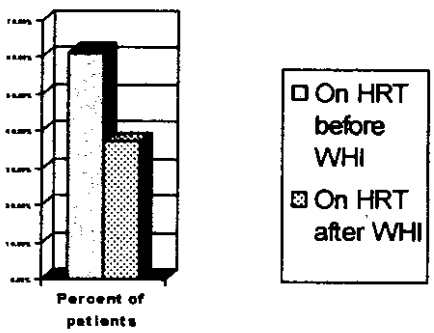



Figure 4.2 Effect of WHI Results on HRT Use

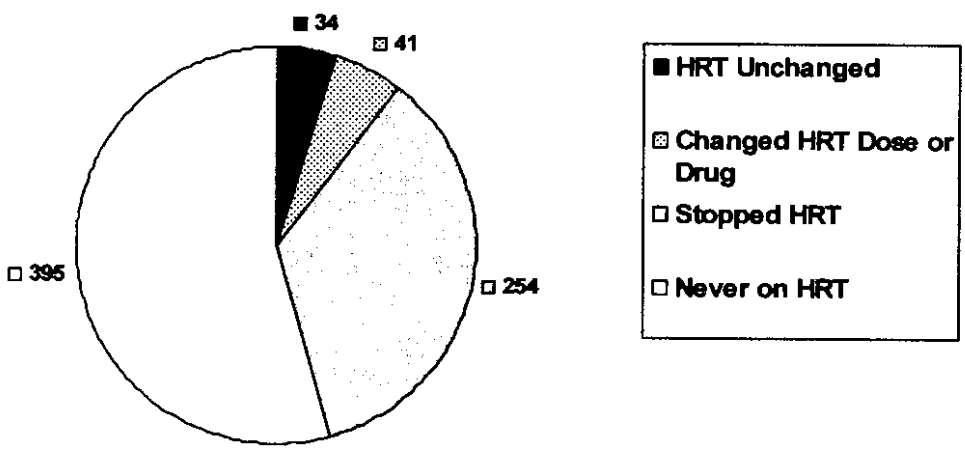
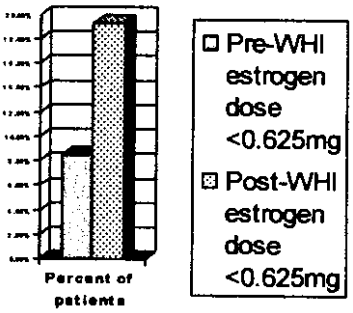


Figure 4.3 Overall Effect of WHI on Estrogen Dose




The women who remained on HRT after WHI were more likely to be younger, Caucasian, and married (See table 4.4), non-smokers (82.3%), and taking medications for other conditions (68.5%). The older the woman, the less likely she was to have continued HRT. Younger women were more likely to have changed HRT drug and/or dose post-WHI.

For women with an HRT history, 43.6% reported no symptoms off HRT, 29.1% reported symptoms when HRT was discontinued, and 27.2% were never off HRT. Of those who reported menopausal symptoms with the discontinuation of HRT, 36.5% took no medication to relieve symptoms while 31.1% reported restarting HRT. Additional treatments used for menopausal symptoms among those who discontinued HRT included sleeping pills for insomnia (9.8%), Vagifem (7.6%) and vaginal lubricants (4.8%) for vaginal dryness and dyspareunia, herbal supplements for general relief of symptoms, D & C for menometrorrhagia (1.9%), selective serotonin reuptake inhibitors (SSRIs) for depression (1.3%), and pessaries for urinary incontinence (0.6% ).

Table 4.4

*Comparison of Characteristics of Women by HRT Use Pre and Post WHI*

| | Pre WHI | | | | Post WHI | | | | Total Sample | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No HRT | | HRT | | No HRT | | HRT | | | |
| | n | % | n | % | n | % | n | % | n | % |
| Number of Women with HRT History | 431 | 56.7 | 329 | 43.3 | 708 | 61.5 | 443 | 38.5 | 1195 | 100 |
| Mean Age | 62.6 | | 62.1 | | 62.3 | | 60.6 | | 61.4 | |
| Race | | | | | | | | | | |
| Caucasian | 353 | 49.2 | 259 | 36.1 | 596 | 52.4 | 348 | 30.6 | 967 | 82.7 |
| African American | 52 | 7.2 | 32 | 4.5 | 75 | 6.6 | 80 | 7.0 | 162 | 13.9 |
| Other | 14 | 1.9 | 8 | 1.1 | 24 | 2.1 | 14 | 1.2 | 40 | 3.4 |
| Marital Status | | | | | | | | | | |
| Married | 312 | 46.6 | 190 | 28.4 | 521 | 46.0 | 345 | 30.5 | 890 | 76.5 |
| Single | 23 | 3.4 | 2 | 0.3 | 23 | 2.0 | 28 | 2.5 | 52 | 4.5 |
| Divorced/Separated | 37 | 5.5 | 21 | 3.1 | 66 | 5.8 | 35 | 3.1 | 103 | 8.8 |
| Widowed | 49 | 7.3 | 36 | 5.4 | 80 | 7.1 | 35 | 3.1 | 119 | 10.2 |

# CHAPTER 5

# DISCUSSION

## *Discussion of Findings*

The published findings of WHI radically changed healthcare for menopausal women, both nationally and in the study population. With significant numbers of women abruptly terminating HRT, menopausal symptoms again became an issue for many women. Of WHI participants, 63.3% report at least one moderate or severe symptom after discontinuing HRT. It is important to note that 40.5% of placebo group participants also report moderate to severe symptoms after placebo discontinuation (Petitti, 2005), suggesting that symptoms previously attributed to a lack of estrogen may in fact have other causes. This study found that younger, Caucasian, non-smoking women taking medications for other conditions were more likely to remain on HRT after WHI. Additionally, younger women in general were more likely to have changed HRT drug or dose post-WHI by lowering the estrogen dose to below 0.625mg. With information about menopause and HRT and counseling regarding the findings of WHI, one in four women nationally have resumed taking HRT for moderate to severe menopausal symptoms (ACOG, 2004). The increased numbers of women (37%) in this study who remained on HRT post-WHI might be attributable to this fairly homogeneous sample of predominately Caucasian, upper-middle-class women.

No published studies were found describing the characteristics of women who either continued HRT or resumed hormone therapy despite the substantial risks delineated in WHI. Currently, WHI's applicability to all postmenopausal women is coming under scrutiny. Francine Grodstein of Harvard University, in an article published in January, 2006, reports findings contradictory to WHI results. The results of her study found women beginning HRT near the start of menopause had a significantly (30%) lower risk of coronary heart disease (CHD) compared to menopausal women who had never taken HRT. In a subgroup of women similar demographically to WHI participants, no relationship was found between HRT use and CHD (Grodstein, Manson, & Stampfer, 2006).

Hormone therapy remains controversial and many questions remain unanswered. One thing experts agree on is HRT should be used for treating hot flashes and vaginal dryness at the lowest effective dose for the shortest amount time (ACOG, 2004; Woodward, 2005).

*Limitations*

Limitations of this study included missing pieces of data, the potential for error with patient self-reporting and staff assumptions in initial recording of data in the chart, and the utilization of a single facility for data collection.

The original number of charts reviewed was 1,783 with 85 potential pieces of information retrieved from each chart. This voluminous amount of data was recorded by one researcher on a data collection sheet and then entered by the researcher and two assistants into an Excel spreadsheet allowing for the introduction of typographical errors. Missing data was frequently encountered and only 724 charts contained HRT data both

pre and post-WHI. Limiting the sample size by eliminating charts without pre and post-WHI hormone use data would have made for more manageable data collection, recording, and analysis.

The use of a retrospective chart review did not allow for the consistent initial recording of the data. Patients self reported much of the demographic data; however race was recorded by the medical assistant, nurse, or physician doing the initial assessment and may have differed from what the patient would have reported. Education levels were not recorded which may have affected the results. Patient interviews conducted from a script by one interviewer would have provided consistent and more complete data than the retrospective chart review undertaken for this study.

This study is further limited by the fact that all patients visited a single physician in a rural practice setting. Replication of these findings from several practices in urban, suburban and other rural settings would validate the findings.

*Implications for Further Study*

Further research is desperately needed in the area of HRT for post-menopausal women. Limitations in the sample used in WHI must be addressed so women and their health care providers can make informed choices about treatments for menopausal symptoms and chronic diseases. Studies of women initiating HRT at the time of menopause are required as this is the point when most women initiate hormone therapy. Reports of resumption of vasomotor symptoms upon discontinuation of HRT ("Study Shows HT May," September 2005) add additional problems to the issue. Further research into alternative treatments for vasomotor symptoms would be useful for women unwilling or unable to take HRT.

*Conclusions*

The premature end of the WHI study and findings of substantial risk with HRT changed long-standing practices with regard to the treatment of post-menopausal women. The literature reports that almost two years after the publication of the results of the WHI study, many women remain confused about the risks and benefits of hormone replacement therapy. Seventy-five percent of respondents to a survey published in the Journal of the American Medical Women's Association reported that they needed additional information about hormone replacement therapy and consequences (Breslau, 2003). Health care providers need to be current on the research and recommendations regarding HRT and the treatment of menopausal symptoms and counsel their postmenopausal patients appropriately. As Margaret Freda, editor of the *American Journal of Maternal Nursing* wrote, "If we believe in evidence-based practice, now is the time for us to read studies and practice accordingly, teaching our patients and helping them understand this issue. Our practice, as well as our collective mind-set about menopause needs to change." (Freda, 2003. p. 259).

The theory of reasoned action and planned behavior would assert that women must receive accurate information concerning the risks, benefits, and alternatives to HRT if they are to be empowered to make informed decisions about the treatment of their menopausal symptoms (Azjen and Fishbein, 1975). The results of the current study underscore that treatment decisions by both health care providers and the women for whom they care have been heavily influenced by the results of WHI.

As the numbers of postmenopausal women increase, the need for safe and effective therapies for symptoms and chronic diseases associated with menopause

becomes more pressing. Research on HRT other than conjugated equine estrogen and non-oral delivery systems needs to be conducted to see if the results mimic those of the WHI study. Studies on alternative treatment need to be undertaken to determine effectiveness, clarify dosage regimes, and define benefits and risks. Timing of HRT in relation to menopause needs to be examined. Women who cannot tolerate estrogen withdrawal need to be identified, counseled about risks and benefits of HRT, and offered alternatives to treat symptoms and preserve quality of life.

# APPENDIX A

## RESEARCH TOOL: CHARACTERISTICS OF MENOPAUSAL WOMEN

♦Demographic data

Age:_____(dob 1954 and earlier) G_____P_____

Menopausal?_____if surgically menopausal, list surgery:_____

Age at menopause:_____race:_____marital status:_____

BP:_____current weight:_____recent wt loss or gain?_____amt?_____

♦Hormone replacement therapy usage

Previous methods of birth control:_____

HRT currently?_____previously?_____type/dose:_____

Length of time on HRT:_____

Symptoms on discontinuation of HRT:_____

_____

Treatment for symptoms?_____

♦Past medical history

Any gyn surgeries? (list)_____

Other diseases (hypertension, heart disease, thyroid, diabetes, cancers):_____

Current Medications:_____

Smoke currently?_____in past?_____caffeine use?_____

T score_____Birads_____

# APPENDIX B

## INSTITUTIONAL REVIEW BOARD WAIVER

UNIVERSITY OF NORTH FLORIDA
ACADEMIC AFFAIRS
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Division of Sponsored Research and Training

**MEMORANDUM**

TO: Catherine Greenblum
College of Nursing

VIA: Kathaleen C. Bloom
College of Nursing

Signature Deleted

FROM: James Collom, Institutional Review Boar

DATE: May 12, 2004

RE: Review by the Institutional Review Board #04-084
"Characteristics of Menopausal Women Who Continue Hormone Replacement Therapy Despite the Findings of the Women's Health Initiative"

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This is to advise you that your project "Characteristics of Menopausal Women Who Continue Hormone Replacement Therapy Despite the Findings of the Women's Health Initiative" has been reviewed on behalf of the Institutional Review Board and has been declared exempt from further IRB review.

This approval applies to your project in the form and content as submitted to the IRB for review. Any variations or modifications to the approved protocol and/or informed consent forms as they relate to dealing with human subjects must be cleared with the IRB prior to implementing such changes.

If you have any questions or problems regarding your project or any other IRB issues, please contact this office at 620-2498.

sah

c: Dr. Li Loriz

Attachments

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# VITA

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