Past Reproductive Events and Finger Digit Ratio as Predictors of Symptom Severity, Psychological Distress, and Medical Treatment-Seeking During the Perimenopausal Period

Suzanne Stone, M.A.

Submitted in partial fulfillment

of the degree of

Doctor of Philosophy in Clinical Psychology

May 16, 2011

Supervisor: Dr. Dwight Mazmanian

Second Reader: Dr. Kirsten Oinonen

Internal/External Examiner: Dr. Michel Bédard

Internal/Internal Examiner: Dr. Amanda Maranzan

External Examiner: Dr. Leora Swartzman

Acknowledgements

I would first like to thank my supervisor, Dr. Mazmanian, for the all of the knowledge and support he has provided to me over the past 6 years. This dissertation would not be complete without Dr. Mazmanian's knack for creativity, problem solving, and encouragement to get everything done months before the official deadlines. I would also like to thank Dr. Oinonen for her ongoing feedback on this project over the years and for her genuine interest in hormonal research and women's health – the information I learned from her inspired many of the ideas contained within this research study. Thank you to my research assistants for this project, Katelyn Gomes and Ashley Clarkson; you both provided me with invaluable assistance with data collection, and it is greatly appreciated. This project would not have been possible without support from the Canadian Institute for Health Research. I would like to thank both Sabreena Bola and Julie Riendeau for their friendship and encouragement over the past 6 years. I could not have asked for two better people to experience the ups and downs of graduate school with. Thank you for providing me with both the motivation to get through the tough times and for always providing a listening ear. I would like to thank my mom and dad for their unwavering support and encouragement as I embarked on a seemingly never-ending academic career. They fostered both my love of reading and learning. I want to thank my sisters, Jessica and Christy, as well as my close friends from Port Perry, Waterloo, and Thunder Bay for being my biggest cheerleaders! And lastly, I would like to thank Christopher Anderson, for always being there for me, for always helping me see the positive side of things, and for always making me laugh.

Abstract

Researchers have found that reproductive events in which levels of estrogen increase or decrease can influence the emergence of psychological distress in some women, and it has been proposed that some women may be more sensitive to hormonal changes across the lifespan (Brace & McCauley, 1997; Deecher et al., 2008). Further, finger digit ratio (2D:4D) may serve as a measure of prenatal hormonal exposure (Manning, 2008), and may be able to identify women who are sensitive to particular hormone changes. Two hundred and ninety perimenopausal and postmenopausal women completed a series of questionnaires pertaining to their menopausal symptoms as well as the severity of both physical and emotional symptoms experienced during past reproductive events (i.e., PMS, pregnancy, postpartum, and during oral contraceptive use). Of these 290 participants, 100 completed a second portion of the study in which their finger digit ratio was measured. Results partially supported the hypotheses. Mood symptoms experienced during past reproductive events were predictive of mood symptoms during menopause. Negative affect experienced prior to menstruation and during the postpartum period served as the best predictors of menopausal mood symptoms. The severity of some physical symptoms experienced during past reproductive events did predict the severity of menopausal physical symptoms. Some symptoms experienced prior to menstruation (i.e., pain, lack of concentration, water retention) and physical symptoms experienced during pregnancy were the best predictors of menopausal physical symptoms. Women who sought HRT during their menopausal transition did not have more severe past reproductive symptoms than those who did not seek HRT. Finger-digit ratio was significantly associated with some menopausal symptoms, although the relationship was not in the predicted direction. Limitations of the current study are reviewed along with suggestions for future research.

Table of Contents

List of Tables

Past Reproductive Events as Predictors of Symptom Severity, Psychological Distress, and Medical Treatment-Seeking During the Perimenopausal Period

Menopause is a time of significant physical change, which is often accompanied by varying degrees of emotional adjustment. Although the endocrinology of the menopausal period is relatively well understood, there is still some question regarding the relationship between menopausal symptoms and symptoms experienced during other times of hormonal change. The majority of menopausal symptom research has focused on depressive symptoms and how they may be related to mood change during the premenstrual period and/or during the postpartum period. Research investigating the possible link between physical symptoms across reproductive events needs to be further developed. Further, finger digit ratio research is a relatively new and exciting field that could be integrated into menopausal research. This research project will examine both of these areas. In order to understand the menopausal experience and its effects on the individual it is important to review the definition of menopause, the history of menopausal research, the evolutionary theories that have emerged regarding menopause, and the endocrinology of the menopause experience.

The term "menopause" is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity (World Health Organization [WHO], 1981). However, natural menopause cannot be confirmed until 12 months of amenorrhea have passed in the absence of any pathological or physical cause that would terminate menstruation (North American Menopause Society, 2006). The term premenopause refers to the entire reproductive period prior to menopause, and postmenopause is the time frame occurring after the final menstruation (WHO, 1981). Perimenopause includes the time when menstrual cycles become

variable and continues for a year after the final menstrual period (WHO, 1981). This term is often used in conjunction with the term "menopausal transition".

The cessation of menstruation typically occurs between the ages of 40 to 58, with an average age of 51 (North American Menopause Society, 2006). The mean commencement of the perimenopausal transition is 47.5 years, with irregular menses continuing for approximately 4 years until the final menstrual period (McKinlay, 1996). However, the menopausal experience is highly variable between individuals. For some women, menses may cease prior to the age of 40, which is considered premature menopause (North American Menopause Society, 2006). Some factors that are associated with an earlier age at menopause include current smoking, lower education, lower socioeconomic status, and undernourishment (Speroff & Fritz, 2005).

Menopause is considered to be "induced" when the cessation of menstruation can be attributed to the surgical removal of both ovaries (with or without hysterectomy) or iatrogenic ablation of ovarian function due to chemotherapy or radiation (WHO, 1981). If only one ovary is removed, the individual will not experience induced menopause, nor will she experience symptoms if she undergoes a hysterectomy and the ovaries are not removed.

History of Menopause Research

Historically, menopause has been a topic of curiosity, although it was rarely discussed in the social realm. It has only been in the past few decades that researchers have systematically studied the menopausal process and its symptoms. The term "menopause" was derived from the Greek words "men" (meaning "month") and "pauses" (meaning "cessation") (Utian, 1997). In the 4th century B.C., Aristotle and many other philosophers in classical Greece and Rome cited the age of menopause to occur between 40 and 50 years of age. By the 7th century A.D., writers were in accord that the minimum age for menopause was 35, the average age was 50 and the

maximum age was 60 (Amundson & Diers, 1970). In the 19th and 20th centuries, menopause was considered a negative state associated with physical and mental illness, and was often characterized by "hysteria" and other neuroses (Banks, 2002). Treatments at this time were aimed at alleviating psychological symptoms or curing the "diseases" that were thought to be tied to the menopausal transition. Some of these treatments included mineral baths, cannabis, opium, lead and mercurial purges, or blood-letting (Banks, 2002).

The treatment of menopausal symptoms has become gradually more scientific, and in 1896, three reports were published on the topic of hormone replacement therapy (HRT) (Utian, 1997). These treatments used ovarian tissue to alleviate menopausal symptoms, and encouraged the development of other preparations such as ovarian, placental, and urinary extracts (Banks, 2002). These treatments were the precursors to modern HRT, and remained popular for 50 years. Estrone, estriol, estradiol, and progesterone were all identified and isolated in the 1920s and 1930s, which lead to clinical trials and the prescription of hormones for disordered ovarian function, menopausal conditions, infertility, schizophrenia, melancholia, and dermatitis, among other disorders (Banks, 2002). The use of hormone replacement therapy became widespread in the 1960s for the treatment of menopausal symptoms. HRT was promoted as a way to preserve femininity and stave off the death of womanhood (Swartzman & Leiblum, 1987). The use of HRT was estimated to have increased by 240 percent between 1962 and 1967, and continued to rise until the late 1970s (Banks, 2002). However, its use sharply declined in the 1980s due to its association with endometrial cancer. Since that time, HRT has become increasingly controversial as it has also been associated with breast cancer, coronary heart disease, stroke, and pulmonary embolism (Writing Group for the Women's Health Initiative, 2002). Despite this controversy, HRT remains a popular treatment due to increased availability and demand, as well

as efficacy for treating menopausal symptoms. In recent years, it has become increasingly acceptable to discuss the menopausal transition, a topic once considered to be unmentionable. This can be demonstrated through the wealth of information in books, on the internet, and in the media for women experiencing menopausal symptoms.

Menopausal Theories

Reproductive cessation has been documented in both human and non-human female primates, lions, and a number of other mammals (Packer, Tartar, & Collins, 1998). Thus, human females and some other mammalian females live for an extended period of time after their ability to reproduce ceases. This is not true for all species, nor is it true for human males who can retain their fertility until they are approximately 94 years old (Silber, 1991). The menopausal transition is particularly noteworthy for humans because it serves as a significant outlier in normal reproductive progression. Given that the life expectancy for females is 77.4 years (Statistics Canada, 2008), women are living an average of 26 years after their ability to reproduce ceases (i.e., one-third of their lives). Menopause seems to contradict the traditional evolutionary belief that natural selection favours processes that maximize the number of offspring. Ultimately, the cessation of reproduction would seem to interfere with this maximization.

By-Product Hypotheses

There are two general categories into which many theories of menopause fall: by-product hypotheses and adaptive hypotheses (Kuhle, 2007). By-product hypotheses posit that menopause is a result of other changes or occurrences that take place over time; it is not necessarily beneficial (Kuhle, 2007). The first by-product hypothesis is the "lifespan artifact" theory, which posits that women experience menopause because they are living longer due to medical advances and associated decreases in mortality rates (Sherman, 1998). Ultimately,

menopause occurs because the lifespan has increased in mammals with a finite number of eggs (Austad, 1994). During the second trimester, the ovaries in the human fetus have 7 million ovarian follicles that have the potential to become eggs. When the infant is born, this number is reduced to 40,000, and about 400 develop into eggs and are shed during the female's lifetime (Baker & Bellis, 1995). These eggs deplete throughout the lifespan, and eventually menopause occurs when few eggs are left. In other words, the number of years that women are living is increasing, but the number of eggs that a female produces cannot be changed - it is fixed at birth.

The second by-product hypothesis is the lifespan biological model. The lifespan biological model differs from the lifespan artifact hypothesis because it emphasizes that human egg cells are genetically programmed to live for a given period of time, rather than just "wearing out" over time (Derry, 2006). Theorists that support this model explain that different cell types in the body live for different amounts of time. For example, red blood cells live for months, while brain cells survive through the lifespan of the individual (Derry, 2006). Ultimately, menopause occurs because female egg cells are genetically pre-programmed to survive for approximately 50 years. The self-destruction of these cells accelerates in a woman's 30s and continues until she is approximately 50 years old (Derry, 2006).

The third by-product hypothesis states that menopause developed as a result of an increase in men's lifespan. This "patriarch hypothesis" posits that the longevity of women was influenced by a "longevity allele" that was not located on the Y chromosome (Kuhle, 2007). Consequently, female longevity increased and introduced menopause due to female egg depletion (Kuhle, 2007).

Adaptive Hypotheses

These hypotheses view menopause as a positively selected event during human evolution because it served an adaptive purpose (Pavard, Metcalf, & Heyer, 2008). The first of these is the "mother" hypothesis, which states that it is more advantageous for women to stop reproducing after a certain age because offspring are highly dependent on their mothers and the risk of death linked to reproduction increases the chances that mothers will not survive to care for their new or existing offspring (Pavard et al., 2008). Menopause is advantageous because it provides an opportunity for women to stop reproducing in order to ensure the survival of their offspring. This hypothesis is supported by the increasing maternal mortality rate as women age, as well as the extreme dependency of young children (Pavard et al., 2008).

Similarly, the "grandmother" hypothesis stresses the importance of the cessation of reproduction in favour of caring for offspring. However, this hypothesis stresses the importance of a woman increasing her daughter's fertility through food-sharing and other forms of support (Pavard et al., 2008). After an offspring is born, a mother must devote an increased amount of energy in order to care for a newborn, and may neglect other dependents. Menopause allows a mammal to stop reproducing and focus their attention on their already-present offspring and the children of their offspring (Alvarez, 2000). Again, menopause is an opportunity to increase the chances that a woman's genes will continue to be passed on.

A complement to the "grandmother" hypothesis is the "absent father" hypothesis. This theory posits that increased maternal age and reduced paternal investment led to the evolution of menopause (Kuhle, 2007). These theorists explain that reduced paternal investment resulted from men's preference for younger mates, as they have a higher reproductive value (Kuhle, 2007). Consequently, males would leave middle-aged females in order to reproduce with

younger females. Reduced paternal investment would have also occurred due to the tendency of men to die several years before women (Kuhle, 2007). Due to these two factors, men were unable to care for their offspring, and women who had ceased reproduction were better able to become the primary caregivers for their children, as they did not need to attend to a newborn.

Another adaptive evolutionary hypothesis states that menopause occurs to protect the gene pool from the increase of birth defects with maternal age (Sherman, 1998). Therefore, mammals have evolved to stop reproducing after a certain age in order to keep genetic defects out of the population. Joseph and colleagues (2005) found that older maternal age was associated with higher rates of preterm birth, perinatal mortality, and fetal-growth restriction (see also Cleary-Goldman et al., 2005). Further, stillbirth rates increase from 2 percent (for young women) to 8 percent for women over the age of 45 (Pavard et al., 2008). In addition to birth complications, genetic defects in offspring become more prevalent as maternal age increases. For example, the frequency of infants born with Down's syndrome compared to normal births increases from 1/1400 for women between the ages of 20 to 24 to 1/350 for women who are 35 years of age (Hook, Cross, & Schreinemachers, 1983).

Despite the ability of the above theories to explain why menopause may occur, a singular unifying theory has yet to be developed.

Menopausal Endocrinology

After menarche and prior to the menopausal transition, women experience hormonal fluctuations according to a 28-day cyclic pattern. In a regular menstrual cycle, ovarian estrogen determines the cyclic pattern of both Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH). Around the midpoint of the cycle, high levels of estrogen allow the walls of the uterus to thicken and signal to the pituitary gland to release both FSH and LH. Typically,

estrogen levels peak at day 12, and FSH and LH levels tend to peak at day 13 (Coulam, 1986). After these hormones are released, ovulation occurs. During perimenopause, hormone levels change significantly.

Natural menopause occurs because oocytes (eggs) in the ovary disappear over time and the few remaining oocytes do not respond to gonadotropins such as LH and FSH. Because the ovarian follicles become unresponsive, the pituitary gland is stimulated to produce increasing amounts of FSH (Soares, Prouty, Born, & Steiner, 2005). Although there is evidence that estrogen levels increase early in the perimenopausal period (Prior, 1998), these levels drop off significantly throughout the course of the menopausal transition. Overall, both estrone (E1) and estradiol (E2) levels decrease, and there is a shift from E2 to E1 being the dominant estrogen at the time of menopause (Overlie, Moen, Morkrid, Skjæraasen, & Holte, 1999). After menopause, E1 is formed almost exclusively by the aromatization of androstenedione by the adrenal glands as well as by the adipose tissue and muscle (Norman & Litwach, 1997). Further, inhibins, (gonadal peptides produced in the ovarian granulosa cells) also decrease during the menopausal transition. As estrogen and inhibin levels decrease, cyclic intervals begin to shorten and ovulation becomes unpredictable (Soares et al., 2005).

Proposed Stages of Menopause

Prior (1998) developed 5 hypothesized phases of the perimenopausal transition in order to integrate findings from previous studies and develop a framework to account for general temporal changes. Phase A is hypothesized to last between 2 to 6 months and is a time of regular ovulatory cycles (Prior, 1998). However, it is a time of increased symptoms prior to menses such as breast tenderness, mood swings, and water retention (Prior, 1998). Women may also begin to experience vasomotor flushes (VMS) and heavy menstruation during this time period.

Hormonal characteristics include high levels of estradiol, normal FSH levels, and low inhibin levels (Prior, 1998).

Phase B is hypothesized to last between 2 to 6 months and is a time of regular menstruation although ovulatory disturbances commence (Prior, 1998). Menstrual flow tends to increase during this time, and there is an increase in PMS symptoms. FSH levels begin to increase during the follicular phase, estradiol levels are high and inhibin is low (Prior, 1998).

Phase C is postulated to be the onset of the perimenopausal transition and lasts for approximately 1 or 2 years (Prior, 1998). Ovarian cycles become irregular during this time, which is associated with unpredictable menstrual flow. Women tend to experience VMS more often, especially during the waking hours (Prior, 1998). Hormonally, estradiol levels can become quite high, but may also be normal or quite low in some women. Further, FSH levels tend to be elevated while inhibin remains low.

Phase D occurs when menstrual periods become infrequent and persistent VMS appear (Prior, 1998). This time frame is hypothesized to last for approximately 1 to 2 years, and is associated with infrequent ovulation (i.e., less than 50 percent of the time). Menstrual symptoms include spotting which may alternate with heavy menstrual flow (Prior, 1998). Estradiol levels tend to be normal, but may fluctuate intermittently and become elevated. FSH and LH levels are consistently elevated during this phase, and inhibin levels are low (Prior, 1998).

Finally, phase E occurs with the final menstrual period, and includes the year following this event (Prior, 1998). Typically, women experience fewer PMS symptoms during this time, but do experience an increased intensity of VMS. Estradiol and inhibin levels are low during this period, while FSH and LH levels remain high (Prior, 1998).

Another system has been developed by the North American Menopause Society (Soules et al., 2001). This staging system consists of 8 separate stages of reproduction, and considers menstrual cyclicity, endocrinology, symptoms, and fertility (Soules et al., 2001). Stages -5 to -3 represent stages of early to late reproductive fertility, where hormone levels are normal and menstrual cycles are relatively regular (Soules et al., 2001). Stage -2 is the early perimenopausal transition in which women experience variable cycle length (i.e., greater than 7 days different than normal). Stage -1 is considered to be the late perimenopausal period in which women experience greater than or equal to two skipped cycles (compared to their regular cycle length) and an interval of amenorrhea lasting greater than or equal to 60 days (Soules et al., 2001). During both of these stages, FSH levels are elevated. Stage 0 is the point in time when women experience their final menstrual period, while stage +1 is broken into substages: +1A, which is a period of time up until 12 months following the final menstrual period, and +1B, which is a time period between 12 months and 4 years following the final menstrual period (Soules et al., 2001). Finally, stage +2 is the late postmenopausal period that occurs 4 years following the final menstrual period until the individual's death (Soules et al., 2001).

It is important to note that the above phases are hypothetical, and the physiological and hormonal experiences vary greatly between and within women. Progression through these phases may not be linear for some women, and many may not experience all of the physiological changes outlined above.

Androgens

In contrast to the sharp decline of estrogens during the menopausal transition, androgens tend to decline steadily throughout the reproductive years and into the post-reproductive period. This is due to an age-related decline in adrenal androgen production as well as a loss of the

midcycle increase in ovarian testosterone secretion in the late reproductive years (Davis, 2001). The major androgens include testosterone, androstenedione, and dehydroepiandrosterone (DHEA). In a cross-sectional study, Davison, Bell, Donath, Montalo, and Davis (2005) studied the changes in androgen levels in women over time and found a mean decrease of 55 percent between their 18 to 24 age group and their 65 to 75 age group. More specifically, they found that mean free testosterone declined by 49 percent, DHEA declined by 77 percent, and androstenedione declined by 64 percent (Davison et al., 2005). Further, testosterone production decreases by approximately 25 percent after the final menstrual period (Speroff & Fritz, 2005). Sex hormone-binding globulin (SHBG), a carrier protein for the estrogens and androgens, affects the bioavailability of these hormones. Specifically, estrogens and androgens that are bound to SHBG are not available to tissues for use. SHBG levels tend to remain constant during the menopausal transition, which further decreases the amount of free testosterone at this time (Burger, Dudley, Cui, Dennerstein, & Hopper, 2000; Davison et al., 2005; Morley & Perry, 2003).

Women who have undergone surgical menopause tend to have even lower androgen levels after surgery than women experiencing natural menopause. After surgery, women experience a sharp decline in both testosterone and androsterone (Davis, 1999). After adjusting for age, both total and bioavailable testosterone levels are reduced by 40 percent after surgery when compared to women who have gone through natural menopause (Laughlin, Barrett-Connor, Kritz-Silverstein, & von Mühlen, 2000).

Physical and Psychological Symptoms of Menopause

Physical Symptoms

Typically, the first physical sign of menopause that women experience is irregular menses, which occurs when both the amount and duration of menstrual flow decrease, eventually tapering to spotting and cessation (Smith & Judd, 1994). More specifically, as women approach their final menstrual period, their ovarian cycles become increasingly variable in length, whereby the mean ovarian cycle typically increases to approximately 35 days (Taffe & Dennerstein, 2002). This is ultimately caused by erratic hormone production in the ovaries and less frequent ovulation. Approximately 90 percent of women experience 4 to 8 years of menstrual irregularity before they experience their last menstrual period (North American Menopause Society, 2006). It is important to note that the cessation of menstruation varies between women, but typically each woman will notice that a change has occurred before the final menstrual period.

Although many physical symptoms have been associated with menopause, there has been ongoing research to determine which symptoms associated with menopause are actually caused by the changing hormonal levels of the menopausal transition. There seems to be a growing consensus that vasomotor symptoms (VMS) and vulvovaginal symptoms are specifically related to hormonal changes in menopause (Dennerstein, Dudley, Hopper, Guthrie, & Burger, 2000; Kuh, Wadsworth, & Hardy, 1997; Utian, 1972).

VMS refer to hot flashes, hot flushes, and night sweats, which occur when a woman experiences a spontaneous sensation of warmth on the neck, chest, and/or face, often resulting in perspiration or feelings of weakness (Nelson, 2008). The terms "hot flush" and "hot flash" are often used interchangeably, although "hot flush" refers to a sensation of heat, while "hot flash" is a term used to describe the sensation of heat, followed by episodes of sweating and often a chill

(Nelson, 2008). Hot flashes are considered to be the most common menopausal symptom, as approximately 75 percent of women suffer from hot flashes at some point during the menopausal transition (Smith & Judd, 1994). Further, they last for an average of four minutes and can occur from one to two times per hour to one to two times per week, depending on the individual (Smith & Judd, 1994). Typically, women continue to experience hot flashes anywhere from 0.5 to 5.0 years after natural menopause, but these hot flashes may last longer for a number of women (Bachmann, 1999). Eventually, hot flashes are said to subside because the reduction in gonadal hormones results in the down regulation of hormone receptors in the hypothalamus (Bachmann, 1999).

The cause of hot flashes is still not fully known, although it has been determined that hot flashes are associated with declining levels of estradiol and increasing FSH levels (Guthrie, Dennerstein, Hopper, & Burger, 1996; Øverlie, Moen, Holte, & Finset, 2002). As a result, it has been postulated these decreased estradiol levels lead to decreased endorphin levels in the hypothalamus, which then increase the release of norepinephrine and serotonin (5HT). Consequently, these neurotransmitters lower the thermoregulatory set point which activates heat-loss responses such as sweating and increased blood flow (Nelson, 2008; Øverlie et al., 2002). It is important to note that hot flashes are not simply caused by low estradiol levels. As mentioned previously, women experience intermittent times of high levels of estradiol, and it is likely that hot flashes occur as these levels rapidly decrease, or are withdrawn quickly (Prior, 1998). Further, stress is likely involved in the experience of hot flashes. For example, experimental research has shown that women put in stressful situations experienced more hot flashes than those in a non stressful situation (Swartzman, Edelberg, & Kemmann, 1990).

Vulvovaginal symptoms are also specifically associated with the menopausal transition, which are tied to decreases in estradiol. Decreases in estradiol often cause vaginal tissue to become thin and dry, with less elasticity (North American Menopause Society, 2006). Vaginal lubrication also decreases due to a reduction in vaginal secretions. Finally, the pH balance of the vagina typically increases, disrupting the healthy acidic environment and increasing the likelihood of vaginal infections (North American Menopause Society, 2006).

Other symptoms are associated with menopause but may be secondary to hormonal changes during the menopause or may be influenced by both hormonal and non-hormonal factors. They could also be related to general aging, stressors experienced during this time period, and general lifestyle factors. Sexual complaints are common and include painful intercourse, loss of libido, decreased vaginal lubrication, and potential reactive sexual dysfunction of the woman's partner (Sarrel, Dobay, & Wiita, 1998). Many of these complaints result from the vaginal dryness discussed above. However, loss of libido may also be related to declining testosterone levels, as it is related to testosterone deficiency in women of all ages (Morley & Perry, 2003).

Another common menopausal symptom is insomnia due to night sweats, the night-time equivalent of hot flashes. Sleep may be frequently disrupted by uncomfortable sweating, which may lead to various cognitive and affective problems including irritability and memory loss (Smith & Judd, 1994). Night sweats and hot flashes are not the sole contributors to poor sleep patterns during menopause, however, as higher anxiety levels, higher depression levels, and lower levels of estradiol have also been associated with poor menopausal sleep patterns (Hollander et al., 2001).

Although not necessarily caused by the menopausal transition, up to 30 percent of women experience urinary incontinence during mid-life (North American Menopause Society, 2006). Those who experience urinary incontinence may feel the need to urinate more often, may experience painful urination, or may experience the need to get out of bed several times per night to urinate (North American Menopause Society, 2006).

Other common physical symptoms include thinning and loss of elasticity of the skin, changes in patterns of body hair, and a redistribution of body weight. Typically, skin loses collagen and elasticity with age, which results in wrinkling and sagging. Skin can also become dry and flaky during this time. These changes are particularly evident in the areas that are exposed to light, such as the face, neck, and hands (Smith & Judd, 1994). Women experiencing menopause may also notice changes in patterns of their body hair. Typically, there is a loss of pubic hair, as well as a loss of hair on the upper lip, chin and cheeks. However, there may be an increase in coarse, terminal hair on the upper lip due to the imbalance of androgen to estrogen that occurs during the menopausal transition (Smith & Judd, 1994). In terms of body weight, women experiencing menopause typically notice an increased distribution of fat over the hips and abdomen (North American Menopause Society, 2006).

Psychological Symptoms

In general, it is believed that the perimenopausal transition is related to an increased number of depressive symptoms for many women (Burt, Altshuler, & Rasgon, 1998). However, it is difficult to compare results across studies because they differ in terms of research design and symptom rating scales, as well as other problems including retrospective reporting, and the failure to consider the impact of culture on symptoms (Robinson, 2001). In their review, Burt and colleagues (1998) found that the majority of the cross-sectional and longitudinal studies they

investigated found an increase in depressive symptoms that coincided with the perimenopausal transition. Further research has found that the menopausal transition is strongly associated with increased risk of depressed mood, even for women who have never had a history of depression (Cohen, Soares, Vitonis, Otto, & Harlow, 2006; Freeman, Sammel, Lin, & Nelson, 2006).

Although there seems to be a consensus that depressive symptoms are more prevalent during the perimenopausal transition, it is unclear whether these symptoms are a result of hormonal changes or are secondary to other menopausal symptoms. Currently, there are three competing theories which try to explain why depressive symptoms are common in menopausal women.

The first theory is neurobiological, and posits that depressive symptoms are directly related to the hormonal changes that occur during the menopausal transition. Changes in estradiol, progesterone, FSH, and LH all have the potential to change neurotransmitter activity in the body (Robinson, 2001). Despite the many hormonal changes that occur during this time, this theory focuses mainly on the withdrawal of estradiol. Prior to the menopausal transition, estradiol can increase the level of 5HT in the body by inhibiting monoamine oxidase activity, making more binding sites available for 5HT by displacing tryptophan from albumin binding sites, and can enhance the transport of 5HT (Studd & Panay, 2004). Therefore, withdrawal of estrogen may help explain increased depressive symptoms as reduced levels of 5HT are associated with depressive symptomatology (Studd & Panay, 2004). This theory may also help to explain depressive symptoms during other reproductive events that involve a decrease in estradiol levels such as postnatal depression and symptoms of premenstrual syndrome (PMS).

Second, the "domino theory" suggests that the development of depressive symptoms is secondary to other menopausal symptoms. This theory acknowledges that depressive symptoms

are a result of changing estradiol levels, but are caused by the VMS that are tied to estradiol withdrawal (Rasgon, Shelton, & Halbreich, 2005). Therefore, estrogen has an indirect effect on depressive symptoms. For example, estrogen can cause night sweats, which often leads to sleep deprivation, which can lead to decreased concentration, irritability, and dysphoria (Burt et al., 1998).

Third, the "psychosocial theory" posits that depressive symptoms are related to other lifestyle changes that are common during this time period. As women age, many role and relationship changes occur including loss of fertility, children leaving or returning home, loss of friends or relatives due to illness, and decreased physical health (Robinson, 2001). Further, women may have to care for elderly parents during this time as well. Consequently, these changes and others may lead to feelings of helplessness and lowered self-esteem which may account for the development of depressive symptoms (Robinson, 2001).

Although there is no consensus as to why depressive symptoms develop during the perimenopausal period, there are many agreed-upon risk factors that may contribute to the development of a mood disorder during this time. Experiencing early menopause or a longer menopausal transition can lead to depression, as can undergoing surgical menopause (Feld, Halbreich, & Karkun, 2005). Other factors include a history of depression, stressful life events, marital concerns, unhealthy lifestyle, lower educational level, negative attitudes toward menopause and aging, prior PMS symptoms, and the presence of VMS (Feld et al., 2005).

Differences in Symptom Experience for Natural versus Surgical Menopause

Although the number, frequency, and severity of menopausal symptoms vary between women, there is a tendency for women who undergo surgical menopause to experience more frequent and severe symptoms than those who go through a natural menopause transition (North

American Menopause Society, 2006). For example, the percentage of women reporting severe symptoms is significantly greater (90 percent) than women who experience natural menopause (50 percent) (Oldenhave et al., 1993). Other symptoms such as angina, migraine, urinary tract symptoms, sexual dysfunction, and depression have been found to be more severe in women experiencing oophorectomy (Sarrel, 2002). Due to these symptoms, women who experience surgical menopause may have a greater need to seek treatment than those who experience a natural menopausal transition (North American Menopause Society, 2006).

Hormone Replacement Therapy (HRT) For Menopausal Symptoms

Estrogen Replacement Therapy

There are two categories of estrogen replacement therapy: conventional hormone therapies (CHT) and bioidentical hormone therapies (BHT). Conventional hormone therapies consists of a mixture of estrogens (conjugated equine estrogens) that are derived from the urine of pregnant mares (Cirigliano, 2007). During the 1970s, researchers determined that treatment with conjugated equine estrogens significantly increased the incidence of endometrial cancer, and added synthetic progesterone (called progestin) to CHT treatment (Schwartz, 2002). Today, HRT treatment without progestin is not recommended for women with an intact uterus due to the risk of endometrial cancer, although women without a uterus can take estrogen without the combined progestin (Nelson, 2008). Bioidentical hormone therapies consists of hormones that are derived from a variety of sources such as plants, animals, or through synthetic production (Cirigliano, 2007). Unlike conjugated equine estrogens, they are molecularly identical to endogenous hormones (Cirigliano, 2007). Interest in BHT has increased since 2003, when the Women's Health Initiative (WHI) released findings describing significant side effects for CHT (Cirigliano, 2007). However, there is a lack of research investigating BHT, which raises

concerns about the potential dangers associated with this type of treatment (Cirigliano, 2007). Further research is needed.

Most efficacy and safety research for HRT has been conducted on conjugated equine estrogens with or without the addition of progestin. Numerous well-controlled research studies have demonstrated that short-term CHT is a highly efficacious treatment for VMS (MacLennan, Lester, & Moore, 2001; Nelson, 2004). Specifically, one study found that there was a mean significant reduction of 17 hot flushes per week for HRT compared to placebo, which is equivalent to a 77 percent reduction in hot flush frequency (MacLennan et al., 2001). There is also a great deal of evidence indicating that CHT is efficacious in alleviating sleep problems and problems with sexual functioning (Freedman, 2002). Further, some studies have found that CHT is beneficial for alleviating mood symptoms to some degree in perimenopausal women (Schmidt, Roca, Bloch, & Rubinow, 1997; Soares, Almeida, Joffe, & Cohen, 2004), although there are still some conflicting results (Burt et al., 1998). It is important to note that some research has demonstrated that the addition of progestin to estrogen therapy may blunt the positive effects of estrogen on mood symptoms in menopausal women (Freedman, 2002). Conventional hormone therapies also have other benefits including stabilizing bone mass and reducing fracture rates in women with osteoporosis (Rousseau, 2001).

Androgen Replacement Therapy

Many studies have investigated whether adding testosterone to traditional CHT therapy is beneficial for women who do not respond to estrogen and progestins alone. Some studies have found that the addition of testosterone to CHT can increase sexual activity, arousal, satisfaction, and/or the frequency of orgasm in women (Burger, Hailes, Nelson, & Menelaus, 1987; Davis,

McCloud, Stauss, & Burger, 1996; De Paula, Soares, Haidar, De Lima, & Baracat, 2007; Sarrel, Dobay, & Witta, 1998; Shifren et al., 2000).

Other studies have found that the addition of androgens to CHT can improve physical symptoms for perimenopausal women. Simon and colleagues (1996) found that women who were treated with a combined androgen-estrogen treatment had a greater reduction in somatic symptoms than those who were treated with estrogen replacement therapy. Further, Burger and colleagues (1984) demonstrated a benefit of androgen therapy for reducing VMS in women who had previously been unresponsive to estrogen therapy. Ultimately, interest in adding testosterone to CHT is growing due to an emerging consensus that androgens can help women who are not responding to traditional HRT.

Alternative Therapies for Menopause

The use of phytoestrogens has increased in popularity amongst perimenopausal women for the treatment of VMS. Phytoestrogens are plant-derived molecules that possess estrogen-like activity, or are metabolized into compounds that possess estrogen-like activity (Speroff, 2005). They are found in certain foods such as legumes, soybeans, vegetables, and cereals (Amato & Marcus, 2003). It is believed that phytoestrogens act as selective estrogen receptor modulators (SERMs) as they act as receptor agonists on some tissues but act as receptor antagonists on other tissues (Amato & Marcus, 2003). They seem to have a greater affinity for estrogen receptor-beta receptors than for estrogen receptor-alpha receptors, although this affinity is still only 35 percent that of estradiol (Speroff, 2005). Although some studies have demonstrated efficacy for the consumption of soy products to reduce VMS, other studies have not found a beneficial effect (Albertazzi, 2005; Amato & Marcus, 2003). Therefore, no firm conclusions can be made.

A variety of herbal supplements are also used to treat menopausal symptoms. One of the most popular is black cohosh, a plant indigenous to eastern North America (Albertazzi, 2005). Other commonly used herbal supplements include dong quai, ginseng, and chaste tree for the treatment of menopausal symptoms (Warren, Shortle, & Dominguez, 2002). The few efficacy trials that have been conducted for these supplements are inconclusive (Amato & Marcus, 2003; Warren, Shortle, & Dominguez, 2002; Wylie-Rosett, 2005). However, one systematic review has concluded that the research evidence supporting black cohosh is the most promising, and studies investigating red clover suggest that it may be helpful in reducing VMS for those with severe menopausal symptoms (Huntley & Ernst, 2003).

Finally, selective serotonin reuptake inhibitors (SSRIs) have also been investigated as a treatment strategy to reduce VMS. It is thought that SSRIs may be efficacious in reducing VMS because serum levels of serotonin are lower in postmenopausal women due to estrogen withdrawal (Albertazzi, 2005). It is hypothesized that hot flashes are related to a decrease in circulating estrogen, which causes an upregulation of the $5HT_{2A}$ receptor in the hypothalamus. A rise in serotonin levels through SSRIs can decrease hot flashes due to a down-regulation of these serotonin receptors (Albertazzi, 2005; Nelson, 2008). However, findings are inconclusive as to whether SSRIs can help reduce the frequency and severity of hot flashes (Nelson, 2008).

Risks of Hormone Replacement Therapy

Despite the benefits of estrogen replacement therapy, there are quite a few drawbacks associated with it as well. As previously mentioned, research studies found that conjugated equine estrogen increased the incidence of endometrial cancer in the 1970s. In 2002, the Women's Health Initiative (WHI) prematurely stopped a trial of estrogen plus progestin versus placebo due to adverse side effects that exceeded health benefits (Writing Group for the

Women's Health Initiative, 2002). Ultimately, they found that long-term HRT use led to increased risk of breast cancer, cardiovascular disease, and stroke (Writing Group for the Women's Health Initiative, 2002). Many other epidemiological studies have suggested a relationship with HRT and breast cancer, such that the risk of breast cancer for each year of HRT use increases by 2.3 percent (Collaborative Group on Hormonal Factors in Breast Cancer, 1997). After the cessation of the WHI trial, prescriptions for HRT diminished rapidly (Lindh-Åstrand, Brynhildsen, Hoffmann, Liffner, & Hammar, 2007).

Side effects of androgen replacement therapy include hirsutism (the growth of terminal hairs in the androgen-sensitive areas of the body), acne, and virilization (Braunstein, 2007). However, these side effects depend on the dose and duration of the androgen replacement therapy (Braunstein, 2007). Other possible risks may include increased incidence of heart disease or breast cancer, although the available evidence is not conclusive at this time (Braunstein, 2007).

Little is known about the long-term side effects of herbal supplements and phytoestrogens. Potential side effects may include rash or gastrointestinal problems (Wylie-Rosett, 2005). Although these side effects appear to be minimal, little is known about how these supplements affect the body because they are not regulated like other prescription medications (Albertazzi, 2005).

Use of HRT During the Perimenopausal Period

Past research has demonstrated that physical symptoms, women's attitudes toward the menopausal transition and HRT, as well as health status are important factors influencing the decision to seek HRT. For example, research has demonstrated that women who start HRT tend to report more frequent hot flashes, night sweats, mood swings, irritability, and sleep problems

prior to their HRT initiation (Bosworth et al., 2005). Also, women who initiate HRT do so to relieve some of these somatic and psychological symptoms, increase well-being, and prevent disease (Collins & Landgren, 1997). However, women's attitudes toward HRT and the menopausal transition are also important predictors of treatment seeking during the menopausal transition. Breheny and Stephens (2001) found that a positive attitude toward HRT and a negative attitude toward menopause significantly predicted HRT use, over and above age and health variables. A further study by Fisher, Sand, Lewis, and Boroditsky (2000) suggests that women who intend to take HRT during the perimenopausal period perceive greater health benefits and social support than women who do not intend to take HRT. They also found that these women did not differ in terms of perceived side effects when compared to women who did not intend to take HRT (Fisher et al., 2000). These authors suggest that women's perceived health benefits may be underestimated in the media, while perceived negative side effects may be overestimated (Fisher et al., 2000).

Lastly, women's health status may be another important predictor of HRT use during the perimenopausal period. For example, women who are at high risk for osteoporosis may choose to start HRT, while those at high risk for breast cancer may avoid HRT due to the cancer-related risks (Schapira, Gilligan, McAuliffe, & Nattinger, 2004).

Reproductive Events Across the Lifespan

Puberty

Hormonal changes. Typically, puberty in females begins between the ages of 9 and 10 due to a gradually increasing release of the gonadotropins, LH and FSH (Norman & Litwack, 1997). During this transition, bursts of LH and FSH occur during sleep, which results in an increased sensitivity of the ovaries to FSH and LH. Increased FSH promotes the growth of the

ovarian follicles, which then mature and produce estrogen (Katchadourian, 1977). There is also an increased production of adrenal androgens during puberty, which is often referred to as "adrenarche" (Speroff & Fritz, 2005). During this period, the growth of pubic and axillary hair occurs. Typically, adrenarche precedes the rise in estrogens and the growth spurt that occurs in early puberty by approximately 2 years (Speroff & Fritz, 2005).

Physical changes and psychological issues. For girls, puberty is a time of major physical change, and for many, psychological issues such as depression. Girls experience a growth spurt that begins between the ages of 10 to 15, but typically reaches a peak at the age of 12 and ends by age 14 (Katchadourian, 1977). Accompanying this growth spurt is a lengthening and thickening of the bones and changes in fat deposition. Typically, the first sign of puberty is breast development, followed by the appearance of pubic hair (Katchadourian, 1977). Other changes include growth of the external and internal sex organs, bone growth, and menarche. Many studies have indicated that the onset of menarche is primarily genetic, as specific polymorphisms of the estrogen receptor-alpha gene have been associated with a difference in the age of menarche (Speroff & Fritz, 2005). Following the first menstrual period, menstrual cycles are anovulatory, irregular, and usually heavy. This period of anovulation typically lasts for 12 to 18 months after the onsent of the first menstrual period, but can last for up to 4 years after menarche (Speroff & Fritz, 2005).

Increases in androgens lead to the growth of pubic and axillary hair and development of the clitoris (Katchadourian, 1997). Many adolescents experience acne at this time, which is likely caused by an androgen imbalance which can cause hyper-secretion of the sebaceous glands in the skin (Schwartz, 2002). Androgens seem to be the likely cause of acne because it typically appears during hyperandrogenic states (i.e., puberty and prior to menstruation)

(Olutunmbi, Paley, & English, 2008). However, the majority of people who experience acne do recover from the condition after puberty terminates, suggesting that it is caused by androgen changes or androgen imbalance rather than high androgen levels per se (Katchadourian, 1977).

Although the ratio of girls to boys who suffer from depression is approximately equal prior to puberty, there is a sharp shift in this ratio during mid-puberty. During this time, the gender proportion of depression shifts to a 2:1 female to male ratio (Kessler, McGonagle, Nelson, Hughes, Swartz, & Blazer, 1994; Kessler & Walters, 1998; Lewinsohn et al., 1998). Although there are many competing hypotheses as to why this shift may occur, one explanation focuses on the shift in hormones during the pubertal period. However, the direct impact of pubertal hormones on mood is still inconclusive (Steiner, Dunn, & Born, 2003). Some researchers have suggested that negative mood during puberty could be a result of higher levels of testosterone and cortisol, lower levels of dehydroepiandrosterone sulphate (DHEA-S), and/or rapidly increasing estradiol levels (Somerset, Newport, Ragan, & Stowe, 2006).

Menstruation

Hormonal changes. The menstrual cycle can be divided into the preovulatory (i.e., follicular) and postovulatory (i.e., luteal) phases. During the follicular phase, the ovarian follicle matures and the initiation of the maturation of the uterine endometrium occurs (Norman & Litwack, 1997). During the luteal phase, the corpus luteum grows and develops and the uterus lining is shed in the absence of initiation of pregnancy (Norman & Litwack, 1997). The time frame for the luteal phase remains relatively constant at 13 plus or minus 1 day (Norman & Litwack, 1997). Estrogen and progesterone levels are the lowest during menstruation. During the follicular phase, FSH levels increase which initiates the maturation of several ovarian follicles and stimulates the initial secretion of estrogen by the follicles (Halbreich & Monacelli,

2004). At the midpoint of the cycle, the high level of estrogen produced by the follicles initiates a LH surge by the pituitary which triggers ovulation, promotes formation of the corpus luteum, and stimulates the corpus luteum to produce estrogen and progesterone (Halbreich & Monacelli, 2004). If pregnancy is not initiated, the corpus luteum deteriorates and progesterone and estrogen levels decline. It is at this time that menstruation occurs (i.e., the start of the follicular phase).

Physical and psychological symptoms. The number and severity of physical and psychological symptoms vary between individuals. However, epidemiological studies have found that approximately 80 to 90 percent of menstruating women report at least one premenstrual symptom (Johnson, 2004). Approximately 10 to 20 percent of menstruating women have moderate symptoms, and 3 to 8 percent have severe symptoms that result in significant impairment (Johnson, 2004). Premenstrual Dysphoric Disorder (PMDD) is the most severe form of PMS, which consists of a greater intensity of symptoms, and symptoms that interfere with occupational or social functioning (Clayton, 2008).

Although definitions of premenstrual syndrome (PMS) vary, it includes physical, behavioural, and emotional symptoms that occur during the luteal phase of the menstrual cycle (Clayton, 2008). Specifically, symptoms tend to worsen 6 days before menstruation and peak approximately 2 days before the menstrual period (Yonkers, O'Brien, & Eriksson, 2008). Physical symptoms include breast tenderness, aches, headaches, and bloating. Behavioural symptoms may include sleep disturbance, appetite change, poor concentration, decreased interest, and social withdrawal. Finally, emotional symptoms may include irritability, mood swings, anxiety or tension, and depressive symptoms (Clayton, 2008).

Currently, the etiology of PMS symptoms is unknown, although it is suggested that fluctuations in estrogen and progesterone are partially responsible (Clayton, 2008). Since estrogen levels interact with many regulatory systems (i.e., reproductive, brain, hormonal, cardiovascular), it is possible that fluctuations in estrogen levels may induce fluctuations in activity of these systems and lead to many symptoms (Halbreich & Monacelli, 2004). For example, estrogen and progesterone interact with the reninangiotensin aldosterone system, which influences fluid and electrolyte balance (Halbreich & Monacelli, 2004). It is possible that fluctuations in estrogen stimulate this system which may lead to bloating and water retention (Halbreich & Monacelli, 2004). In addition to regulatory systems, estrogen influences neurotransmitters responsible for mood change, such as serotonin, noradrenaline, gamma-aminobutyric acid (GABA), dopamine, and acetylcholine (Halbreich, & Monacelli, 2004). This may explain some of the emotional symptoms experienced during the premenstrual phase.

Studies have demonstrated that symptoms may be related to luteal estrogen levels. Women who have higher luteal phase estrogen levels showed more severe symptoms than those who had lower luteal phase estrogen (Seippel & Bäckström, 1998). Further, another study found that increased estradiol levels during the luteal phase were related to more severe symptoms when compared with cycles in the same individuals with lower luteal phase estrogen levels (Hammarbäck, Damber, & Bäckström, 1989).

Other studies have implicated an imbalance of estrogen and progesterone. Some researchers have suggested that the irritability experienced during PMS may be related to a dominance of estrogen or susceptibility to estrogen around the premenstrual phase (Clare, 1985). Further, studies have shown that severe PMS is associated with significantly increased levels of estradiol and decreased levels of progesterone (Andrzej & Diana, 2006). Related to these

findings, a study conducted by Clayton, Keller, Leslie, and Evans (2006) suggested an association between increased sensitivity of 5HT receptors and elevated estradiol levels in the late luteal phase. Consequently, increased 5HT may alter the balance between estradiol and progesterone and lead to some premenstrual symptoms (Clayton, 2008).

Lastly, Kiesner (2009) suggests that the experience of physical symptoms indicates sensitivity to hormonal change. This study investigated whether physical symptoms experienced during the premenstrual period were related to depressive PMS symptoms. They found that physical symptoms explained 30 percent of the variance in depressive symptoms, and each of the physical symptoms investigated were independent of each other (Kiesner, 2009). Kiesner believes these results may suggest that women with few physical symptoms during the PMS period are generally not reactive to hormonal fluctuations, while those women who do have many physical symptoms are more reactive to these fluctuations. They state that this reactivity may be general, including both physical and depressive symptoms.

It is important to note that research has demonstrated that those who suffer from moderate to severe PMS tend to have levels of estrogen and progesterone within the normal limits, suggesting that these women may have a heightened sensitivity to hormonal changes during the menstrual cycle (Clayton, 2008).

Pregnancy

Pregnancy is another event in a woman's life that is associated with significant hormonal changes. The following sections will discuss the hormonal and physical changes that occur during pregnancy and during the postpartum period.

Hormonal changes. Both progesterone and estrogen increase during pregnancy. During pregnancy, progesterone ensures that the pregnancy state is promoted and sustained (Mesiano &

Jaffe, 2004). By the third trimester, studies have indicated that progesterone increases to 10 times the highest levels experienced during the menstrual cycle (Bloch, Daly, & Rubinow, 2003). Estrogen levels also increase during pregnancy, with estradiol levels increasing 50 times the highest levels experienced during the menstrual cycle (Bloch, Daly, & Rubinow, 2003). Moreover, there is a shift from estradiol to estriol as being the dominant circulating estrogen (Mesiano & Jaffe, 2004). In the final weeks of pregnancy, estrogen and progesterone levels rise in preparation for delivery. It is thought that progesterone and estrogen levels remain high during labour and delivery, but the body's responsiveness to these hormones changes, thus inducing labour (Mesiano & Jaffe, 2004). Specifically, the body's responsiveness to progesterone decreases and the body's responsiveness to estrogen increases.

However, during the postpartum period, hormone levels change drastically. Approximately 1 to 3 days after birth, estradiol levels reach early follicular levels, while estriol and estrone levels decline more steadily (Bloch, Daly, & Rubinow, 2003). For progesterone, follicular levels are reached between days 3 and 7 postpartum, and ovulation resumes between 4 and 12 weeks in non-nursing mothers (Bloch, Daly, & Rubinow, 2003).

Testosterone levels also change during pregnancy. In general, testosterone and androstenedione levels are increased during pregnancy due to a decrease in the metabolic clearing rate of these hormones (Bammann, Coulam, & Jiang, 1980). However, testosterone production increases after week 28 of pregnancy, which further elevates these hormone levels (Bammann, Coulam, & Jiang, 1980). Contrary to testosterone and androstenedione, the metabolic clearing rate for DHEA increases, decreasing these hormone levels in the body during pregnancy (Bloch, Daly, & Rubinow, 2003).

Physical and psychological symptoms. The significant hormonal change that occurs during pregnancy is associated with many physical and psychological symptoms. During the first trimester, nausea and vomiting are particularly common (Baron, Ramirez, & Richter, 1993). Between 50 and 90 percent of women experience nausea during pregnancy, while vomiting occurs in 25 to 50 percent of pregnant women (Striegel-Moore, Goldman, Garvin, & Rodin, 1996). Although the causes of nausea and vomiting during pregnancy are not fully understood, increases in chorionic gonadotropin, progesterone, and/or estradiol levels have been suggested (Baron, Ramirez, & Richter, 1993). Another common gastrointestinal complaint is heartburn, which occurs in approximately 30 to 50 percent of all pregnancies (Baron, Ramirez, & Richter, 1993). Research studies have suggested that increases in progesterone and estradiol can lead to a decrease in lower esophageal sphincter function, which leads to heartburn (Baron, Ramirez, & Richter, 1993). Many women also experience bloating and constipation during pregnancy, which is associated with increased levels of progesterone (Baron, Ramirez, & Richter, 1993). Other physical symptoms include fatigue, breast tenderness, increased heart-rate, frequent urination, hemorrhoids, and increased food cravings (Brown, 2007).

Some women experience depressive symptoms during pregnancy and in the postpartum period. Some research suggests that the rate of depression is similar during pregnancy and the postpartum period, although much of the research is focused on postpartum depression (Glover & Kammerer, 2004). Postpartum depression varies in severity from the "post-partum blues" to postpartum psychosis. Approximately 50 percent of women who have recently given birth suffer from the postpartum blues, which may include crying more easily or increased irritability (Miller, 2002). The onset of these blues typically occurs 3 to 5 days after delivery, and can last for several days to several weeks, but does not impair the individual's functioning (Miller, 2002).

Postpartum non-psychotic depression affects 10 to 20 percent of women and can include feelings of inadequacy, sleep and appetite changes, and problems with concentration (Miller, 2002). Postpartum psychotic depression occurs in 1 in 500 to 1 in 1,000 births and includes delusions and/or hallucinations (Glover & Kammerer, 2004).

Researchers have suggested that the rapid hormonal change after delivery is responsible for mood changes during pregnancy and the postpartum period. Bloch, Daly, and Rubinow (2003) outline the three circumstances that may have an effect on mood during this time, which include hormonal changes during pregnancy, the prolonged hypogonadal state following delivery, and the resumption of regular ovarian function. They argue that each of these three periods of drastic hormonal change can induce depressive symptoms in women who may be sensitive to hormonal change (Bloch, Daly, & Rubinow, 2003). Indeed, some research has suggested that changes in both estrogen and progesterone during these times can lead to depressive symptoms (Feksi, Harris, Walker, Riad-Fahmy & Newcombe, 1984; Harris, Lovett, Newcombe, Read, Walker, & Riad-Fahmy, 1994; O'Hara, Schlechte, Lewis, & Varner, 1991). One study suggests that it may not be low hormone levels that lead to depressive symptoms, but that some women may be more prone to depressive symptoms due to potential hormonal fluctuation sensitivity (Bloch, Schmidt, Danaceau, Murphy, Nieman, & Rubinow, 2000). Further supporting this is research that suggests that women who suffer from PMS or experience mood symptoms as a result of oral contraceptive use are more likely to experience post-partum depression (Bloch, Rotenberg, Koren, & Klein, 2005).

Although much of the literature has focused on the influence of hormonal change on postpartum depression, it is important to note that the significant hormonal change that occurs

during this period may also be responsible for the significant physical symptoms that occur as well (i.e., headaches, vaginal dryness, breast changes, etc.).

Hormonal Contraceptive Use

Hormonal changes. Hormonal contraceptives can be classified into combination, estrogen-only contraceptives, or progestin-only contraceptives. Combination hormonal contraceptives use both estrogen and progestin and can be further classified into monophasic, biphasic, or triphasic combinations (Frye, 2006). Monophasic combinations deliver a constant concentration of estrogen and progestin, while triphasic combinations deliver an overall low dose of both estrogen and progestin, although estrogen levels increase or remain constant at midcycle while progestin levels increase (Frye, 2006). Biphasic combinations deliver a low dose of estrogen with an increasing concentration of progestin, although they are uncommonly used (Frye, 2006). Progestin-only formulations are uncommon in an oral form, and are usually injected or implanted (i.e., Depo-Provera or Norplant) (Frye, 2006).

Hormonal contraceptives have a variety of effects on the hypothalamic-pituitary-ovarian axis, leading to a cessation of ovulation. Estrogen prevents the release of FSH and keeps the ovaries inactive, while progestin suppresses ovulation, suppresses the midcycle peaks of LH and FSH, increases the thickness of the cervical mucus, decreases sperm motility, and inhibits the development of the uterine lining (Frye, 2006). It is important to note that different types of hormonal contraceptives lead to some or all of the abovementioned contraceptive effects.

Hormonal contraceptives affect androgen levels as well. Overall, research has demonstrated that oral contraceptives reduce the levels of total testosterone, free testosterone, and/or DHEA-S (Graham, Bancroft, Doll, Greco, & Tanner, 2007; Greco, Graham, Bancroft, Tanner, & Doll, 2007). This is due to the reduced production of testosterone by the ovaries and

an increase in SHBG, which decreases free testosterone available for use by the body (Graham et al., 2007).

Physical and psychological side effects. Hormonal contraceptive use is associated with a number of physical and psychological side effects that often lead to discontinuation. Rosenberg and Waugh (1998) conducted a prospective study evaluating why women discontinued their use of oral contraceptives and found the primary reason was the side effects that were experienced. These included bleeding irregularities, nausea, weight gain, mood changes, breast tenderness, and headaches. Another study by Sanders, Graham, Bass, and Bancroft (2001) found that emotional and sexual side effects (i.e., decreased frequency of sexual thoughts, decreased psychosexual arousability) were also important predictors of oral contraceptive discontinuation. Some research has indicated that these sexual side effects may be associated with the decrease in androgen levels that accompany hormonal contraceptive use for some women who may be more sensitive to testosterone changes (Graham et al., 2007; Greco et al., 2007).

A review by Oinonen and Mazmanian (2002) discussed the psychological impact of oral contraceptives. Overall, those who are taking oral contraceptives tend to experience less variability in affect across the menstrual cycle than women who are not taking oral contraceptives (Jarva & Oinonen, 2007; Oinonen & Mazmanian, 2002). Women taking oral contraceptives also tend to experience less negative affect during the menstrual phase of their cycle (Oinonen & Mazmanian, 2002). Further, some factors may increase the risk of negative mood changes for women who are taking oral contraceptives. These include a history of depression and other symptoms of psychological distress, premenstrual mood symptoms prior to

oral contraceptive use, dysmenorrhea, a history of pregnancy-related mood symptoms, and being in the postpartum period (Oinonen & Mazmanian, 2002).

Mood Change Across Reproductive Events

There have been a number of studies investigating the depressive symptoms across reproductive events, although most compare only two of these events. The first of these studies, conducted by Sugawara, Toda, Shima, Mukai, Salakura and Kitamura (1997) investigated the relationship between premenstrual mood changes and maternal mental health in the perinatal period. They carried out their study in a prospective format evaluating the participants' mood throughout pregnancy and at different points in the postpartum period. They found that previous premenstrual irritability was correlated with depression during pregnancy and the postpartum period (Sugawara et al., 1997).

Further, Bloch and colleagues (2005) investigated risk factors that are associated with the development of postpartum mood disorders. In this study, the authors found that PMDD, mood symptoms experienced during the first 2 to 4 days postpartum, a past history of depression, and mood symptoms during past oral contraceptive use were all significant risk factors for postpartum depression (Bloch et al., 2005). A second study by Bloch, Rotenberg, Koren, and Klein (2006) investigated risk factors for very early postpartum depressive symptoms. They assessed present mood symptoms in women who had given birth 1 to 3 days prior. They found that a past history of postpartum depression, past depressive episodes, a family history of affective disorders, past PMDD, and mood symptoms during the third trimester of pregnancy were all significantly associated with postpartum depressive symptoms (Bloch et al., 2006). However, one study by Haywood, Slade, and King (2007) did not find an association between postnatal distress and premenstrual symptoms. This work differed from the previously

mentioned studies because it examined whether postnatal depressive symptoms predicted premenstrual distress, not vice versa. Also this study focused on premenstrual distress rather than a history of PMDD, which may have weakened the association between the variables.

There have been a few studies that have included the perimenopausal transition when examining the relationship between mood changes across reproductive events. The first of these studies was conducted by Stewart and Boydell (1993), who investigated whether women who reported high psychological distress during menopause report more psychological distress associated with past reproductive events. These authors compared women who reported high distress during menopause to women who experienced little distress during this time period. They were compared on their reports of previous psychiatric diagnoses/treatment, distress related to oral-contraceptive use, the premenstrual period, or distress associated with pregnancy (Stewart & Boydell, 1993). The authors found that women who had high psychological distress during the perimenopausal period also reported a history of psychological distress associated with the premenstrual period, associated with the use of oral contraceptives, and following delivery (Stewart & Boydell, 1993).

The second study in this area, by Woods and Mitchell (1996), examined the patterns of past depressed mood in perimenopausal women. This study compared four groups of women: those who had an emerging depressed mood during the menopausal transition, those who had an absence of a depressed mood, those with a consistent depressed mood, and those with a resolving depressed mood during this time (Woods & Mitchell, 1996). Among other factors, they found that women who had a history of PMS or postpartum blues were more likely to have emerging depressive symptoms or were consistently depressed. They also found that postpartum blues and

PMS history were more prevalent among women who were chronically depressed compared with those who had resolving depressive symptoms (Woods & Mitchell, 1996).

A third study by Gregory, Masand, and Yohai (2000) studied the correlations between mood change in various reproductive events. This study found a significant correlation between premenstrual and perimenopausal mood ratings, as well as another significant correlation between postpartum and perimenopausal mood ratings (Gregory et al., 2000).

Another correlational study was conducted by Becker, Orr, Weizman, Kotler, and Pines (2007). These authors asked women who were attending a menopause clinic to rate their current mood as well as their mood during different stages of the reproductive cycle. They found that depressed mood during the menopausal transition was significantly correlated with depressed mood during the premenstrual period. However, they did not find a significant association between depressed mood in the perimenopause and emotional difficulties in the postpartum period (Becker et al., 2007).

Richards, Rubinow, Daly, and Schmidt (2006) examined the relationship between premenstrual symptoms and perimenopausal depression. This study compared the premenstrual symptoms of depressed and non-depressed perimenopausal women. They found that women with perimenopausal depression were significantly more likely to meet the criteria for PMDD than were perimenopausal women who were not suffering from depression (Richards et al., 2006).

Payne and colleagues (2007) investigated the association between reproductive mood symptoms in menopausal women with Major Depressive Disorder. They found that PMS mood symptoms predicted postpartum and postmenopausal mood symptoms, and concluded that reproductive mood symptoms tend to co-occur in individuals with Major Depressive Disorder

(Payne et al., 2007). However, a similar study conducted by Steinberg and colleagues (2008) found that neither premenstrual dysphoria nor postpartum depression were significant predictors of perimenopausal depression.

Most recently, Flores-Ramos, Heinze, and Silvestri-Tomassoni (2010) found evidence of a link in mood variability across reproductive events. They found that menopausal women who were suffering from depression were significantly more likely to have suffered from PMDD and postpartum depression in the past, compared to those who were not depressed during the menopausal transition.

Although the methodologies of these studies differ, together the majority of studies suggest that there is a link between depressed mood across reproductive events, up to and including the menopausal transition. It is also important to note that not all women experiencing a reproductive event will experience depressive symptoms; these studies show that there may be a subgroup of women who are more sensitive to hormonal change, and therefore more likely to experience depressive symptoms while experiencing a reproductive event.

It is very difficult to determine the relationship between reproductive events and mood changes, as many hormones change simultaneously during these events, and the metabolism of circulating steroid hormones is very complex (Altemus, 2010). For example, circulating hormone levels may differ in various parts of the brain or even within specific cells, due to metabolic differences (Altemus, 2010). Despite these challenges, there are a number of theories that attempt to explain why some women may be more sensitive to changes in hormone levels.

Reproductive Mood Change Theories

The first of these theories states that mood change may be due to low estrogen levels during reproductive events (Arpels, 1996). This hypothesis posits that brain center dysfunction

may occur when estrogen levels fall below the minimum brain estrogen requirement (Arpels, 1996). Estrogen affects more than 400 bodily functions, many of which can influence mood, especially neurotransmitters like norepinephrine, 5HT, dopamine, and acetylcholine (Douma, Husband, O'Donnell, Barwin, & Woodend, 2005). Importantly, estrogen acts as a 5HT agonist by increasing the number of 5HT receptor binding sites, increases 5HT synthesis and uptake, which ultimately mimics the effect of antidepressant medication (Steiner et al., 2003). It has been shown that there may be sex differences in the serotonergic system, as women appear to be at a higher risk than men for developing depressive symptoms in response to low levels of serotonin (see Payne, Palmer, & Joffe, 2009 for a review).

A related theory suggests that chronic exposure to and/or withdrawal from high levels of estrogen and/or progesterone can influence the function of GABA receptors, which can lead to depressive mood symptoms during the premenstrual phase (Poromaa, Smith, & Gulinello, 2003).

Douma and colleagues outline several lines of evidence that support the hypothesis that depressed mood can be affected by estrogen fluctuation, decline, and/or deficit. First, the ratio of females to males experiencing depressive symptoms increases after puberty (when estrogen levels change) and levels off after the menopausal transition (when estrogen levels are steady and low) (Douma et al., 2005). Second, there is a pattern of mood disturbance that occurs during significant hormonal transition (Douma et al., 2005). Third, there is relative stability of mood when estrogen levels are stable (i.e., during pregnancy) (Douma et al., 2005). Fourth, some studies have shown that there is a greater incidence of dysphoria with triphasic versus monophasic OCs, which corresponds to greater estrogen fluctuation (Douma et al., 2005). Finally, studies have shown that estrogen can be successfully used throughout the lifespan to

relieve mood disturbance and augment antidepressant treatment (Douma et al., 2005; Payne et al., 2009).

However, this theory cannot account for the mood disturbance that occurs when estrogen levels rise, such as the transition into puberty or during pregnancy. Further, hormone levels differ with each reproductive event, and it is not likely that it is the absolute levels of estrogen that lead to depressive symptoms, but the dramatic hormonal fluctuations (Soares & Zitek, 2008). One theory that can help explain these issues was put forth by Deecher, Andree, Sloan, and Schechter (2008). These authors suggest that due to constant hormonal fluctuation, the female brain must develop flexible and responsive mechanisms to maintain functional homeostasis (Deecher et al., 2008). The female brain can develop these flexible and responsive mechanisms by "resetting" or "adapting" to the changes in hormone levels (Deecher et al., 2008). They argue that certain women may not be able to compensate for unpredictable estrogen fluctuations and therefore have a reduced capacity to maintain this functional homeostasis. As a result, they are more likely to develop mood symptoms during periods of fluctuating estrogen and progesterone (Deecher et al., 2008). Further, they suggest that depressive symptoms decrease in the postmenopausal period because hormone levels are not fluctuating (i.e., not simply because they are low).

At the present time, one unifying theory does not exist to explain mood change during various reproductive events. However, the theory by Deecher and colleagues (2008) helps to expand upon the popular hypoestrogenic theory, and fills in some of the gaps that cannot be explained by it.

Physical Symptom Severity Across Reproductive Events

There is considerably less research on whether there is a relationship between the number and severity of physical symptoms experienced during each reproductive event. There is research to show that women experience some of the same symptoms across reproductive events, although there are very few studies that have actually investigated whether there is a relationship between physical symptoms experienced at various reproductive events.

Research has found that hot flashes are not solely experienced by menopausal women. For example, there are reports of women experiencing hot flashes both during pregnancy and during the postpartum period (Kronenberg, 1990). Casper, Graves, and Reid (1987) report that 72 percent of their sample experienced sweats and chills prior to menstruation. Other studies indicate that between 15 to 25 percent of premenopausal women report experiencing hot flashes (Speroff & Fritz, 2005). Hahn, Wong, and Reid (1998) compared the presence of hot flashes in three groups: women with confirmed PMS symptoms (i.e., PMS symptoms were experienced solely in the luteal phase), women who had chronic menstrual-cycle related symptoms (i.e., PMS symptoms were experienced across the reproductive cycle) and women without menstrual cycle-related symptoms. They found that approximately 83 percent of women in the PMS group had experienced chills and sweats related to the menstrual cycle, 81 percent of the women in the chronic menstrual-cycle related symptoms had experienced these symptoms, while only 43 percent of women in the control group had experienced chills and sweats related to their menstrual cycle (Hahn et al., 1998). Further, 63 percent of women in the PMS group reported waking up at night due to chills and sweats, which is a common symptom in menopausal women (Hahn et al., 1998).

Other similarities between reproductive events have been found as well. A study by Barrett, Pendry, Peacock, Victor, Thakar, and Manyonda (1999) investigated women's sexuality and physical symptoms experienced after childbirth. They found that 39 percent of their sample experienced vaginal dryness in the 3 month period after delivery (Barrett et al., 1999). This is a common symptom of women who are going through the perimenopausal transition, and may be due to declining or fluctuating levels of estrogen.

Headaches are also experienced during times of hormonal fluctuations, such as during the menstrual cycle and the perimenopause. A study by Wang, Fuh, Lu, Juang, and Wang (2003) found that perimenopausal women who had previously suffered from PMS symptoms were more likely to experience migraine headaches than women who did not have a history of PMS. This suggests that there may be a relationship between physical PMS symptoms and migraine during the perimenopausal transition.

Despite the similarities in symptoms across reproductive events, there are very few studies investigating whether women who suffer from more severe and/or frequent symptoms during past reproductive events are more likely to experience more severe symptoms during the perimenopausal period. Hunter (1992) investigated the relationship between premenstrual symptoms and vasomotor symptoms and found that a history of premenstrual tension and having vasomotor symptoms prior to menstruation explained 37 percent of the variation in reporting vasomotor symptoms during the menopausal period. Although these authors used a published scale to measure menopausal symptoms, it is unclear how extensively they assessed for premenstrual symptoms, as they did not use a validated scale for this portion of the study.

Three studies have looked at how PMS is related to a broader range of menopausal symptoms. Leidy (1996) found significant correlations between headaches experienced during

PMS and headaches at menopause, between menstrual cramps and menopausal hot flashes, and menstrual leg cramps and hot flashes. This study also found that the frequency of menstrual cramps was a significant factor predicting hot flash frequency in menopause. However, these authors used only 5 physical menstrual symptoms and 1 emotional symptom, which may not adequately capture the entire PMS experience for some women. Their list of menopausal symptoms was more extensive with 11 items, although they focused solely on the frequency of the symptoms experienced rather than their perceived severity.

Further, Morse, Dudley, and Dennerstein (1998) found that past premenstrual complaints were significantly associated with skeletal, digestive, and respiratory symptoms experienced during menopause. However, they found that premenstrual complaints did not contribute significantly to vasomotor symptoms experienced in the menopausal period.

Binfa and colleagues (2004) investigated what psychosocial factors potentially influence the experience of menopausal symptoms. They found that a history of premenstrual symptoms was a significant predictor of menopausal symptoms, especially vasomotor symptoms and physical symptoms in general (Binfa et al., 2004). However, their PMS symptoms focused more on emotional symptoms than physical symptoms, which might also be an important predictor.

Finally, Freeman, Sammel, Rinaudo, and Sheng (2004) found that women who suffered from PMS were five times more likely to report hot flashes during the menopausal period, and were significantly more likely to report decreased libido, depressed mood and/or poor sleep. However, this study classified participants as experiencing PMS (yes/no) based on irritability, mood swings, and emotional distress and did not include other physical symptoms that may be experienced. Therefore, the link that was found was between emotional symptoms experienced at PMS and menopausal symptoms rather than the link between physical symptoms experienced

at each time period. Freeman and colleagues (2004) also only assessed four menopausal symptoms: hot flushes (yes/no), depressed mood, decreased libido (yes/no), and poor sleep (yes/no). This type of measurement excludes many of the symptoms experienced during the menopausal transition and focuses solely on whether the symptom was ever experienced, rather than actual intensity of the symptom.

Although the link between the experience of physical symptoms throughout the lifespan is less extensively studied than mood change across reproductive events, these studies suggest that there is a link between physical symptoms experienced during PMS and menopause. Although there are not as many theories about why this may be occurring, some researchers have attempted to explain their findings. For example, Hunter (1993) suggests that women who experience vasomotor symptoms prior to menopause may have a less stable thermoregulatory system, or may be more sensitive to hormonal changes which may explain why vasomotor symptoms during each time period are so strongly linked. This theory parallels many of the theories that have been suggested for reproductive mood change (discussed above).

Despite the links that have been found between physical symptoms experienced across reproductive events, these studies have concentrated solely on PMS and menopausal symptoms and have ignored other important times of reproductive change such as pregnancy, the postpartum period, and during oral contraceptive use. Further research is needed to determine the relationship of menopausal symptoms to these other times of hormonal change. It may be possible that symptoms experienced during these times of fluctuation also have an impact on menopausal symptoms.

Second to Fourth Digit Ratio

Research investigating the ratio between the length of the 2nd and 4th digits (2D:4D) and various health issues has increased substantially over the past decade. Researchers have found that 2D:4D has a sexually dimorphic pattern, such that males tend to have a lower 2D:4D ratio than females (Manning, Scutt, Wilson, & Lewis-Jones, 1998). Further, researchers have demonstrated that lower 2D:4D is associated with higher levels of fetal testosterone compared to fetal estrogen while higher 2D:4D is associated with higher fetal estrogen levels compared to fetal testosterone, independent of sex (Lutchmaya, Baron-Cohen, Raggatt, Knickmeyer, & Manning, 2004). That is, men tend to have shorter second digits compared to fourth digits, while women tend to have longer or equal length second digits when compared to fourth digits. It has been hypothesized that the ring finger is more sensitive to the effects of testosterone, while the pointer finger is more sensitive to the effects of estrogen, explaining why men tend to have longer ring fingers compared to pointer fingers, and females have longer pointer fingers compared to ring fingers (Manning, 2008). Finger digit ratio is established as early as 14 weeks of gestation and studies have shown it to remain stable throughout the lifespan (Galas, Broek, Van Dongen,& Wijnaendts, 2010; Malas, Dogan, Evcil, & Desdicioglu, 2006; Manning, 2008). Typically, sex differences in 2D:4D are expressed more strongly in the right hand rather than the left hand, indicating that digit growth on the right hand may be more sensitive to androgen exposure (Manning, 2008).

Although there are general differences between males and females, there are also 2D:4D differences between individuals which are hypothesized to be partly due to the amount of androgen and/or estrogen that they are exposed to in the womb (Lutchmaya et al., 2004). For example, a woman who was exposed to a greater amount of androgen in the womb is likely to

have a lower 2D:4D compared to another woman who was not exposed to higher levels of androgens.

Past research has linked lower 2D:4D to traits commonly associated with males, such as aggression and sensation-seeking (Hampson, Ellis, & Tenk, 2008), as well as left hand preference (Manning, Trivers, Thornhill, & Singh, 2000). Other research has associated higher 2D:4D with traits commonly associated with females, such as high verbal fluency and emotional sensitivity (Manning, 2008).

While many researchers suggest that digit ratio is related to prenatal androgen and/or estrogen exposure, the sensitivity of hormonal receptors may also influence 2D:4D. Manning, Bundred, Newton, and Flanagan (2003) investigated the relationship between 2D:4D and androgen receptor sensitivity. They examined the association between 2D:4D and the number of CAG repeats on the androgen receptor gene. They found that individuals with a higher number of CAG repeats were more likely to be insensitive to the effects of testosterone, while those who had a lower number were more sensitive to the effects of testosterone (Manning et al., 2003). They found a positive correlation between number of CAG repeats and 2D:4D, indicating that those with a lower 2D:4D are more sensitive to testosterone, and those with a higher 2D:4D are more insensitive to testosterone (Manning et al., 2003). The authors point out that although an association was found, the amount of prenatal testosterone, the amount of prenatal estrogen, and the sensitivity of the estrogen receptor are also likely important factors in determining one's finger digit ratio (Manning et al., 2003).

Androgen-Related Health Problems

Finger digit ratio research has also investigated the relationship between finger ratios and hormone-related health problems. For example, Brown, Hines, Fane, and Breedlove (2002)

have demonstrated that males and females with Congenital Adrenal Hyperplasia (i.e., a disorder associated with an excess of androgen exposure in the womb) have significantly lower 2D:4D than those without this condition, suggesting that androgen exposure in the womb affects finger ratios.

One study by Cattrall, Vollenhoven, and Weston (2005) investigated finger ratios in women suffering from Polycystic Ovarian Syndrome (PCOS), another androgen-related hormonal disorder. Polycystic Ovarian Syndrome is a condition that affects approximately 10 percent of the population and causes the ovaries to produce excess androgens, interfering with egg production and release (The Canadian Women's Health Network, 2007). These researchers found that women with PCOS had significantly lower 2D:4D than women who did not suffer from PCOS, which suggests higher androgen exposure in the womb.

Further, a study by Berenbaum, Bryk, Nowak, Quigley and Moffat (2009) examined finger digit ratios in women with complete androgen insensitivity syndrome (CAIS). This is a disorder in which individuals are born with an XY karyotype, but have dysfunctional androgen receptors, resulting in no androgen exposure while in the womb. Ultimately, these individuals are genetically male, but have female external genitalia and are raised as females. This study found that individuals with CAIS had significantly higher finger digit ratios than men, indicating that androgen exposure is involved in 2D:4D (Berenbaum et al., 2009). However, they argue that this relationship is modest, as there was no significant difference in 2D:4D for those with CAIS and typical women. These authors argue that it is to be expected that typical women would have a lower 2D:4D due to some androgen exposure in the womb (Berenbaum et al., 2009). These results may indicate that androgen is not the sole contributor to variability in 2D:4D. Other hormones (i.e., estrogen) may also influence the length of the digits. For

example, there may have been variability in 2D:4D between women with CAIS and typical women due to the varying amounts of estrogen that they were exposed to in utero.

Another study investigated the relationship between digit ratio and age at menarche (Matchock, 2008). In general, androgens are related to later age of menarche and more anovulatory cycles in women (Matchock, 2008). Research has found that delayed menarche was associated with lower finger digit ratio on the right hand, indicating that the relationship between 2D:4D and health is manifested in "healthy" populations as well as those who are suffering from androgen-related disorders such as PCOS or Congenital Adrenal Hyperplasia (Matchock, 2008).

Lastly, Oinonen (2009) investigated the relationship between 2D:4D and oral contraceptive side effects related to decreased androgen levels. This study found that adverse oral contraceptive side effects were experienced by women with lower 2D:4D. The author suggests that prenatal androgen exposure and possible androgen sensitivity may play a role in the experience of oral contraceptive side effects.

It has been suggested that some women may be more sensitive to changes in androgen levels, and that women who are suffering from frequent and/or severe androgen-related menopausal symptoms (i.e., loss of sexual interest, sexual dysfunction) may have lower finger digit ratios than those who do not experience these symptoms to the same degree. This study will be investigating this potential relationship, as no studies to date have looked at the connection between 2D:4D and menopausal symptoms.

Estrogen-Related Hormonal Health Problems

There are also a few studies suggesting that estrogen-related hormonal health problems are linked to higher 2D:4D. Estrogen is linked to breast cancer, as many breast tumours depend on estrogen for their growth, and various research studies have indicated that approximately 50

to 80 percent of breast tumours have estrogen receptors (Manning, 2008). Further, it has been suggested that high concentrations of estrogen in the womb can increase the risk for breast cancer later on in life (Trichopoulos, 1990). Manning and Leinster (2001) investigated whether 2D:4D was related to breast cancer and found higher 2D:4D (i.e., higher exposure to estrogen in utero) was associated with earlier presentation of breast cancer. This finding indirectly supports the hypothesis that higher exposure to estrogen in the womb can predispose women to breast cancer.

Another study has investigated the relationship between 2D:4D and human papillomavirus (HPV), another health problem related to estrogen exposure (Brabin, Roberts, Farzaneh, Fairbrother, & Kitchener, 2008). These researchers found that women who developed cervical intraepithelial neoplasia (i.e., abnormal cervical cells that have the likelihood to develop into cervical cancer) were more likely to have a higher 2D:4D compared to HPV negative women (Brabin et al., 2008). The authors conclude that lower androgen exposure and/or higher estrogen exposure in the utero may predispose women to develop persistent HPV infection and increased risk of cervical intraepithelial neoplasia (Brabin et al., 2008).

Although not necessarily a hormonal health problem, one study has investigated finger ratios and depression, which is believed to be influenced somewhat by estrogen. Bailey and Hurd (2005) investigated whether depression in men was associated with finger length ratios and found that men with higher depression scores had higher finger digit ratios than men with lower depression scores. These authors suggest that depression is associated with lower prenatal testosterone and/or higher estrogen levels in utero.

No studies to date have investigated the potential association between 2D:4D and menopausal symptoms. Since past research has suggested that women with a higher 2D:4D may

be more susceptible to estrogen-related health problems (Brabin et. al., 2008; Manning & Leinster, 2001), it is possible that they may be more sensitive to the effects of fluctuating estrogen. Therefore, it could be possible that women suffering from severe estrogen-related menopausal symptoms (i.e., vasomotor and vulvovaginal symptoms) may be more sensitive to the declining levels of estrogen during the perimenopausal period, which could be related to androgen and/or estrogen exposure in utero (i.e., women with higher 2D:4D may be more sensitive to estrogen withdrawal and more likely to experience more severe and/or frequent vasomotor and vulvovaginal symptoms).

The Present Study

The primary purpose of the present study was to investigate how past reproductive events may be related to the severity of physical and psychological perimenopausal symptoms. Previous research demonstrates that there is a relationship between mood symptoms during past reproductive events and mood symptoms during the perimenopause (Gregory et al., 2000; Richards et al., 2006; Stewart & Boydell, 1993; Woods & Mitchell, 1996), although most studies focus on periods of estrogen decline, and do not investigate times of estrogen increase (i.e., pregnancy). It is important to look at periods of estrogen increase and decrease, as new theories posit that it is fluctuation in estrogen levels that may be responsible for mood changes, not solely the absolute level of estrogen (Deecher, 2008)

Further, there are very few studies investigating the relationship between physical symptoms across reproductive events. The studies that do exist concentrate solely on the relationship between premenstrual symptoms and menopausal symptoms and omit other times of hormonal change such as during pregnancy and oral contraceptive use (Freeman et al., 2004; Hunter, 1993; Leidy, 1996; Morse et al., 1998). Further knowledge is needed to determine if

women who experience more frequent and/or severe physical symptoms during other reproductive events are more likely to experience more severe menopausal symptoms.

A second purpose of this study was to determine if hormonal sensitivity to androgens and/or estrogen (measured through finger digit ratio) is related to the frequency and severity of perimenopausal symptoms. Past research has suggested that certain women may be more sensitive to androgen and estrogen changes, which may influence the severity of psychological symptoms experienced across reproductive events (Deecher et al., 2008; Douma et al., 2005). Although not explicitly stated by these theorists, hormonal sensitivity likely affects physical symptoms as well. Finger digit ratio serves as a non-invasive and inexpensive indicator of androgen and/or estrogen exposure in utero as well as a measure of androgen sensitivity (Manning, 2008; Manning et al., 2003), and 2D:4D could also be a non-invasive measure of estrogen sensitivity (Manning, 2008). Therefore, women with a lower 2D:4D may be more sensitive to androgen changes during the lifespan and may be more affected by androgen-related menopausal symptoms (i.e., loss of sexual interest), while women with a higher 2D:4D may be more sensitive to estrogen changes during the lifespan and may be more affected by estrogen-related menopausal symptoms during the perimenopausal period (i.e., VMS and vulvovaginal symptoms). This study was conducted, in part, to explore these possibilities.

Finally, the third purpose of this study was to investigate whether women who have experienced more severe or frequent physical and psychological symptoms during past reproductive events are more likely to seek HRT than women who did not experience severe physical and psychological symptoms during past reproductive events. As previously mentioned, both attitudes toward the menopausal transition and HRT, as well as symptom severity are all important predictors of HRT use during the menopausal period. This study was

conducted to determine whether women who have experienced more frequent and/or severe physical and psychological symptoms during the perimenopausal period would be more willing to seek HRT treatment because they may be more likely to experience bothersome physical and psychological symptoms during the perimenopausal period.

Hypotheses

1) Women who experience more depressive symptoms during the menopausal transition will be more likely to have had a history of distress associated with other reproductive events (i.e., the premenstrual period, during pregnancy, the postpartum period, puberty, and during oral contraceptive use).
2) Women who experience more severe physical symptoms during the menopausal transition will have experienced more severe physical symptoms during times of hormonal fluctuation (i.e., the premenstrual period, during pregnancy, the postpartum period, and during oral contraceptive use)
3) Women who sought HRT during their menopausal transition will have experienced more severe physical and/or psychological symptoms during other times of hormonal fluctuation (i.e., the premenstrual period, during pregnancy, the postpartum period, puberty, and during oral contraceptive use).
4) Women with a lower (masculinized) 2D:4D will have more severe androgen-related menopausal symptoms due to increased sensitivity to androgen changes (i.e., loss of libido, ability to become sexually aroused).
5) Women with a higher (feminized) 2D:4D will have more estrogen-related menopausal symptoms due to increased sensitivity to estrogen changes (i.e.,VMS and vulvovaginal symptoms.

All of the above analyses will be conducted using women who have experienced natural menopause rather than surgical menopause.

The following exploratory hypothesis will use data from those who underwent oophorectomy to determine the effect of significant and abrupt hormonal decline following surgery.

Exploratory Hypothesis:

6) For women experiencing surgical menopause, there will be a significant relationship between finger digit ratio and the severity of menopausal symptoms experienced. Specifically, higher (feminized) 2D:4D will be significantly related to the severity of estrogen-related menopausal symptoms, and lower (masculinized) 2D:4D will be significantly related to the severity of androgen-related symptoms. It is predicted that this will occur due to the abrupt hormonal change that occurs following oophorectomy and the possibility that finger digit ratio indicates potential androgen and/or estrogen sensitivity.

Method

Participants

Two hundred and ninety women who had started the menopausal transition were recruited to participate in this study. Participants were recruited in a number of different ways, including: newspaper advertisements, flyers, pamphlets, Lakehead University Communication Bulletins, health-related websites, Facebook advertising, and word-of-mouth. All recruitment materials specified that participants must be in the menopausal transition or postmenopausal (i.e., must have variable menstrual cycle lengths that are at least 7 days shorter or longer than usual).

Of the 290 participants who completed the series of questionnaires, 100 completed the second portion of the study.

Participants were excluded from the main analyses if they had experienced surgically-induced menopause (n = 20). However, the latter group was examined in the exploratory analysis. All other participants were included in the analyses, as they were all undergoing the menopausal transition or in the postmenopausal phase. Demographic variables for both those undergoing natural and surgical menopause can be found in Table 1.

In total, 270 participants were included in the main analyses. The women ranged in age from 39 to 65 years (M = 51.8, SD = 4.63). The mean age at which menopause began was 46.5 years (SD = 4.7). Approximately 68 % of participants were either married or living in common-law relationships, 20 % were divorced or separated, 3 % were widowed, and 8 % were single. The majority of participants self-identified as Caucasian (86.7 %), followed by First Nations (5.2 %), European (4.1 %), Middle Eastern (0.7%), Asian (0.4%), and Hispanic (0.4 %). Approximately 74 % of participants were currently employed, 19 % were unemployed, and 6 % were retired. Approximately 24 % of participants had obtained their undergraduate degree as the highest level of achieved education, 20 % had received a college diploma, and 16 % had received a high school diploma. In terms of reproductive history, the average age of menarche was 13.2 years (SD = 8.27, Mode = 13), and the average number of pregnancies was 2.7 (SD = 1.75, Mode = 2).

Measures

General Information Questionnaire. In order to obtain demographic information and reproductive information not covered in the other measures (e.g., number of pregnancies,

Table 1

Demographics – Means, Standard Deviations, and Raw Frequencies (N= 290)

Variable	Type of menopause	
	Natural (n = 270)	Surgically-induced (n = 20)
	Means and standard deviations	
Age (Years)	M = 51.79 (SD = 4.63)	M = 53.63 (SD = 5.68)
Age at menopause (Years)[a]	M = 46.49 (SD = 4.68)	M = 46.14 (SD = 3.52)
	Raw frequencies (percent)	
Marital Status		
Married/Common-law	183 (67.8 %)	14 (70.0 %)
Divorced/Separated	55 (20.4 %)	2 (10.0 %)
Single	21 (7.8 %)	2 (10.0 %)
Widowed	8 (3.0 %)	1 (5.0 %)
Ethnicity		
Caucasian/White	234 (86.7 %)	17 (85.0 %)
African-Canadian	-	1 (5.0 %)
First Nations	14 (5.2 %)	1 (5.0 %)
Hispanic/Latin	1 (0.4 %)	-
Asian	1 (0.4 %)	-
Middle Eastern	2 (0.7 %)	-
European	11 (4.1 %)	1 (5.0 %)
Other	7 (2.6 %)	-
Employment		
Employed	201 (74.4 %)	10 (50.0 %)
Retired	16 (5.9 %)	5 (25.0 %)
Unemployed	52 (19.3 %)	5 (25.0 %)
Education		
Elementary school	-	1 (5.0 %)
Some high school	9 (3.3 %)	1 (5.0 %)
High school diploma	44 (16.3 %)	3 (15.0 %)
Some college	39 (14.4 %)	3 (15.0 %)
College diploma	54 (20.0 %)	3 (15.0 %)
Some university	43 (15.9 %)	3 (15.0 %)
Undergraduate degree	64 (23.7 %)	5 (25.0 %)
Master's degree	15 (5.6 %)	1 (5.0 %)
Doctorate degree	2 (0.7 %)	-

Table 1 (continued)	Natural (n = 270)	Surgically-Induced (n = 20)
Menopausal stage [b,c]		
Early menopause	56 (20.7 %)	-
Late menopause	44 (16.3 %)	1 (5.0%)
Early Postmenopause	25 (9.3 %)	1 (5.0%)
Postmenopause	66 (24.4 %)	8 (40.0 %)
Late Postmenopause	72 (26.7 %)	9 (45.0%)
Past Pregnancy		
Yes	242 (89.6 %)	17 (85.0 %)
No	28 (10.4 %)	3 (15.0 %)
Past use of oral contraceptives		
Yes	242 (89.6 %)	18 (90.0 %)
No	26 (9.6 %)	2 (10.0 %)

Note. This table contains missing data due to unanswered items

[a] Women were asked to provide the age at which their variable cycles became irregular (i.e., at least 7 days shorter or longer than their usual cycle length)

[b] Some women could not identify their menopausal stage due to hysterectomy

[c] These stages were created using the guidelines set by the North American Menopause Society (Soules et al., 2001)

miscarriages, age at menarche, menstrual regularity), a General Information Questionnaire was created, and can be found in Appendix A. This questionnaire also asks about the use of HRT, antidepressant medication, and other alternative treatments for symptoms during the menopausal transition. Further, this questionnaire also inquires about participants' sex drive prior to menopause. In order to obtain this information, items from the Sex Drive Questionnaire were used (SDQ; Ostovich & Sabini, 2004). The SDQ is a brief 4-item questionnaire measuring a woman's sex drive, but does not inquire about sexual activities requiring a partner, which can confound measurement of "true" sex drive (Ostovich & Sabini, 2004). For example, women may have a high sex drive but may not have a sexual partner, or may have a high sex drive but have a partner with a low sex drive and therefore not participate in sexual activity. The SDQ has a Cronbach's alpha of .82, and a test-retest reliability of .90 (Ostovich & Sabini, 2004).

Menopause Specific Quality of Life Questionnaire (MENQUOL). In order to measure the menopausal symptom severity during the menopausal transition, a modified version of the Menopause Specific Quality of Life Questionnaire (MENQUOL) was used, and can be found in Appendix B (Hilditch et al., 1996). The MENQOL was developed in 1996 to assess the vasomotor, psychosocial, physical, and sexual symptoms commonly experienced in the menopausal transition. The MENQUOL is a 29-item self-report measure tapping 4 domains: physical, vasomotor, psychosocial, and sexual symptoms. Participants are asked to rate the degree to which they are/were bothered by a number of menopausal symptoms. Symptoms are rated on a 7-point Likert scale ranging from "Not at all bothered by the symptom" (0) to "Extremely bothered by the symptom" (6). The total score for each subscale was calculated by taking the average score across all of the items in the subscale.

Participants who are currently experiencing menopause were asked to report on their current symptom experiences, while those who were postmenopausal were asked to report on their experiences prior to their final menstrual period. All participants were asked to indicate the severity of their symptoms prior to receiving HRT. Forty percent of the women in the sample were perimenopausal, while 60 percent were post menopausal. Of those who were perimenopausal, 15 percent had received HRT while 85 percent had not. Of those who were postmenopausal, 24 percent had received HRT while 76 percent had not. In past studies, test-retest reliability coefficients ranged from .81 for the psychosocial domain to .85 for the vasomotor domain (Zöllner, Aquadro, & Schaefer, 2005). Further, this measure demonstrates good construct validity (Hilditch et al., 1996).

Menstrual Distress Questionnaire (MDQ). A modified version of the Menstrual Distress Questionnaire (MDQ; Moos, 1986) was used to assess the severity of premenstrual symptoms. The MDQ is a 48-item self-report measure designed to assess the severity of symptoms experienced during and prior to menstruation, and can be found in Appendix C. The items of the MDQ were unchanged, although the instructions were modified. Participants were asked to retrospectively report on the severity of their PMS symptoms prior to the menopausal transition (i.e., before their menstrual periods became irregular). This questionnaire taps 7 domains: pain, concentration, behavioural change, autonomic reactions, water retention, negative affect, and arousal (Moos, 1986). Each of the items are rated on a 5-point scale ranging from "No experience of the symptom" (0) to "Present, Severe" (4). The total score from each subscale was calculated by summing the items for each subscale. Moos (1986) reports subscale internal consistencies of the MDQ ranging from .64 for the control scale to .94 for the negative affect scale.

Pregnancy Experiences Questionnaire (PEQ). The Pregnancy Experiences Questionnaire was created for this project in order to measure the various symptoms women experience while pregnant. This measure can be found in Appendix D. Items for this measure were generated through researching common symptoms cited in pregnancy education books, online discussion forums, and in gynaecological reference materials. A pool of 48 items was created, with an additional open ended question asking about any medical illness or complications that may have arose during pregnancy. Each item is rated on a 7-point scale ranging from "Large Decrease in the Symptom" (-3) to "Large Increase in the Symptom" (3). Those who did not experience a change in the symptom would endorse "No Noticeable Change" (0). Two subscales were created by asking 2 independent raters to indicate whether each item was a physical or emotional symptom. Two scores were calculated for this measure: one for an increase in negative symptoms and one for a decrease in negative symptoms. To look at an increase in negative symptoms, "Large Decrease in the Symptom" (-3), "Moderate Decrease in the Symptom" (-2), and "Mild Decrease in the Symptom" (-1) were re-coded to 0. For this sample, the internal consistency of the total physical subscale was .92 while the internal consistency of the total emotional subscale was .91. To look at a decrease in negative symptoms, "Large Increase in the Symptom" (3), "Moderate Increase in the Symptom" (2), and "Mild Increase in the Symptom" (1) were re-coded to 0. With the newly recoded scale, the internal consistency of the total physical subscale was (.97) while the internal consistency of the total emotional subscale was (.95).

Postpartum Physical Symptoms Questionnaire (PPSQ). A Postpartum Physical Symptoms Questionnaire was created in order to assess the severity of physical symptoms experienced after pregnancy. This measure can be found in Appendix E. A pool of 18 items was

generated through symptoms discussed in pregnancy education books, online discussion forums, and gynaecological reference materials. Participants were asked to note the change they experienced in each of the symptoms compared to their usual experience when they were not pregnant. Each item is rated on a 7-point scale ranging from "Large Decrease in the Symptom" (-3) to "Large Increase in the Symptom" (3). Those who did not experience a change in the symptom would endorse "No Noticeable Change" (0). Two scores were calculated for this measure: one for an increase in negative symptoms and one for a decrease in negative symptoms. To look at an increase in negative symptoms, "Large Decrease in the Symptom" (-3), "Moderate Decrease in the Symptom" (-2), and "Mild Decrease in the Symptom" (-1) were re-coded to 0. The internal consistency of the total scores of this measure was .86 for this sample. To look at a decrease in negative symptoms, "Large Increase in the Symptom" (3), "Moderate Increase in the Symptom" (2), and "Mild Increase in the Symptom" (1) were re-coded to 0. With the newly recoded scale, the internal consistency of the total PPSQ was .95.

Edinburgh Postnatal Depression Scale (EPDS). A modified version of the Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1989) was used to detect possible past postpartum depression, and can be found in Appendix F. The EPDS is a 10-item measure measuring various depressive symptoms in women who have given birth. Responses for each item are rated on a 4-point scale, although the scale differs for each item. The items on the original measure were unchanged, although the instructions were modified for this project. If participants had given birth in the past, they were asked to respond to the items on this scale in a retrospective manner. When used prospectively, the sensitivity of this measure is approximately 86 percent, while the specificity is approximately 78 percent (Cox et al., 1989). The internal

consistency of this measure is .87 (Spek, Nyklíček, Cuijpers, & Pop, 2008). The score from this measure was calculated by summing all items.

Oral Contraceptive Side Effects Questionnaire. A modified version of the Oral Contraceptive Side Effects Questionnaire was used to measure mood and physical symptoms experienced while women were taking hormonal contraceptives. This questionnaire can be found in Appendix G. The Oral Contraceptives Side Effects Questionnaire was developed by Bird and Oinonen (2009) to determine the severity of physical, emotional and sexual side effects of oral contraceptives. Although the original scale consists of 83 items, 22 items with the highest internal consistency and/or theoretical relevance were used in order to create a short form of the original scale. The original questionnaire has three subscales (physical, emotional/cognitive, sexual/libido), which are all represented in the short-form version of the questionnaire. The participant was asked to rate whether they experienced each side effect while taking oral contraceptives. Each item is rated on a 7 point scale ranging from "Yes, Large Decrease" (-3) to "Yes, Large Increase" (3). If there was no change experienced, the participant was asked to circle "No Change" (0). All items in the sexual/libido category were reverse coded before running the statistical analyses. Two scores were calculated for this measure: one for an increase in negative symptoms and one for a decrease in negative symptoms. To look at an increase in negative symptoms, "Large Decrease in the Symptom" (-3), "Moderate Decrease in the Symptom" (-2), and "Mild Decrease in the Symptom" (-1) were re-coded to 0. For this sample, the internal consistency of the total physical side effects scale was .70, the internal consistency of the total emotional side effects scale was .90, and the internal consistency of the total sexual side effects scale was .89. To look at a decrease in negative symptoms, "Large Increase in the Symptom" (3), "Moderate Increase in the Symptom" (2), and "Mild Increase in the Symptom"

(1) were re-coded to 0. With the newly recoded scale, the internal consistency of the total physical side effects scale was (.75), the internal consistency of the total emotional side effects scale was (.92), and the internal consistency of the total sexual side effects scale was (.88).

Neuroticism. The neuroticism subscale from the NEO Five Factor Inventory (NEO-FFI; Costa & McCrae, 1992) was included as a general measure of maladjustment and emotional distress. We have included this measure to explore the relationship between reporting menopausal complaints and neuroticism. This scale includes 12 items and can be found in Appendix H. Costa and McCrae (1992) report the internal consistency of the measure to be .92 and describe its excellent convergent and divergent validity. The total score for this measure was calculated by summing all items.

Infrequency. Eight items were included from the infrequency scale of the Personality Research Form (PRF; Jackson, 1984). In the PRF, a high number of positive responses to the infrequency items indicate poor comprehension, carelessness, confusion, or passive non-compliance (Jackson, 1984). This measure is included as a response style measure to detect non-purposeful responding. All unlikely responses to the items are scored as a 1, while all likely answers are scored as a 0. This scale is totalled by summing up the items, and any participant who scores above 4 should be examined for non-purposeful responding (Jackson, 1984).

Procedure

Ethical clearance for this study was obtained from Lakehead University's Senate Research Ethics Board and the Psychology Research Ethics Board. All recruitment materials contained a link to a secure website which contained a cover letter, consent form, each of the measures, and a debriefing form.

Before filling out the questionnaires, interested women read a cover letter in which they were told that they would be participating in a study to identify how physical and emotional symptoms experienced during the reproductive lifespan may affect the symptoms experienced during the menopausal transition. This cover letter can be found in Appendix I. They were then required to read the consent form found in Appendix J and provide their consent if they were interested in participating. It was outlined that participation in the study was voluntary, that subjects could withdraw from the study at any time without penalty, and that all data would remain anonymous and confidential. After giving their consent, participants filled out the General Information Questionnaire, MQUOL, MDQ, PEQ, PPSQ, EPDS, Oral Contraceptives Side Effects Questionnaire, NEO-FFI Neuroticism subscale, and the infrequency measures from the PRF. Participants who lived in the Thunder Bay area were asked if they were interested in participating in a second portion of the study in which they would receive 20 dollars to come to Lakehead University and have their hands scanned onto a desktop computer. After participants completed the questionnaires, they read the debriefing form found in Appendix K. This form explained the nature of the study and reiterated confidentiality. In addition, participants were given some recommended reading as well as contact information for any questions they may have.

Those women who indicated an interest in participating in the second portion of the study were contacted shortly after they completed the questionnaires online. These women visited the Health, Hormones, and Behaviour Lab at Lakehead University in order to have their hands scanned. These participants read and signed a second consent form, which is found in Appendix L. A line was drawn along the base of the crease of their second and fourth digits on both their left and right hands to help facilitate measurement, and all jewellery worn on these fingers were

removed. In cases where a band of creases existed on the hand, the most basal crease was used (i.e., the crease that was furthest from the finger tip and closest to the palm). Their hands were then scanned using a Hewlett Packard Scanjet G3010 and saved onto the laboratory desktop computer. Participants were verbally debriefed and told that the researchers would be measuring their finger digit length in order to determine if there was a relationship between finger digit ratio and menopausal symptoms. They then received 20 dollars for their participation.

Their second and fourth digits were each measured twice using Screen Calipers, a computer program that utilizes on-screen digital calipers for measurement, allowing measurement to 0.01 mm (available at http://www.iconico.com/caliper/). This method of measurement was chosen because past research has demonstrated that measuring finger digit length from a scanner seems to be more reliable than using digital callipers or a ruler (Kemper & & Schwerdtfeger, 2009), and serves as the "gold standard" technique. Both the right and left hands were measured in millimetres from the tip on the finger to the basal crease, which is a measurement that demonstrates a high level of test-retest reliability (Manning et al., 2000). Finger digit ratio was calculated by dividing the second digit by the fourth digit. After measurement, two 2D:4D scores were obtained for each participant's hand. The mean measurements for the right and left hands were used in data analyses.

Statistical Analyses

Since many of our questionnaires measure symptom change in both directions (i.e., increase or decrease in negative symptoms), the influence of both were separately analyzed for Hypotheses 1, 2, and 3. Related to the main hypotheses, the effect of increased negative symptoms during past reproductive events were examined and the PEQ, PPSQ, and the Oral Contraceptive Side Effects Questionnaire were re-coded. The "Large Decrease" (-3), "Moderate

Decrease" (-2), and "Mild Decrease" (-1) options were re-coded to (0) so that only increases in negative symptoms were examined. As a supplementary analysis for each of these hypotheses, the influence of a decrease in negative symptoms during past reproductive events was also examined. The PEQ, PPSQ, and the Oral Contraceptive Side Effects Questionnaire were re-coded in order to examine these relationships. The "Mild Increase" (1), "Moderate Increase" (2), and "Large Increase" (3) options were re-coded to (0) so only the decreases in negative symptoms were examined.

For the main analyses, stepwise multiple regression analyses were conducted to test the association between menopausal depressive symptoms and past depressive symptoms (Hypothesis 1) as well as the association between menopausal physical symptoms and past physical symptoms experienced during other reproductive events (Hypothesis 2).

A number of multiple regression analyses were conducted to test Hypothesis 2. Since the MQUOL has subscales for both physical symptoms and vasomotor symptoms (which could also be considered physical symptoms), the hypothesis was first tested by aggregating these two subscales into a composite physical symptom subscale. Next, multiple regression analyses were conducted to test the predictors (i.e., the physical symptom and vasomotor subscales) separately.

Discriminant function analyses were conducted to determine whether women who had sought HRT had experienced more severe physical and/or psychological symptoms during times of hormonal fluctuation (Hypothesis 3). Three separate discriminant function analyses were conducted: one with both physical symptom and emotional variables entered into the equation, one with just physical symptom variables entered into the equation, and one with just emotional variables entered into the equation.

The associations between 2D:4D and androgen-related and estrogen-related menopausal symptoms (Hypotheses 4 and 5) were tested using Pearson product-moment correlations. The association between 2D:4D and menopausal symptoms for women who have experienced surgical menopause (Hypothesis 6) were also examined using Pearson product-moment correlations. However, this hypothesis was also tested using a nonparametric test of correlation (Kendall's Tau), as the distributions for the specific items of interest were negatively skewed. Further, only 10 women who had undergone ovarian surgery also had their 2D:4D measured.

Results

Data Screening

Prior to data analyses, the raw data for all variables were examined for the presence of obvious errors and univariate outliers. Any values exceeding three standard deviations above or below the mean were replaced with the (*M* +/- 3*SD)* value. In total, 31 values were identified and replaced with a value representing 3 standard deviations above or below the mean. Specifically, one score was changed from the MDQ autonomic subscale, one score was changed from the MDQ concentration subscale, one score was changed for the MDQ behavioural change subscale, one score was changed for the MDQ arousal subscale, six scores were changed for the PEQ physical symptom subscale, four scores were changed for the PEQ emotional symptom subscale, five scores were changed for the PPSQ, one score was changed for the EPDS, two scores were changed for the physical subscale of the Oral Contraceptive Side Effects Questionnaire, five scores were changed for the emotional subscale of the Oral Contraceptive Side Effects Questionnaire, and four scores were changed for the sexual subscale of the Oral Contraceptive Side Effects Questionnaire.

Prior to each analysis, multivariate outliers were detected using Mahalanobis Distance and were eliminated from the analyses, as recommended by Tabachnick and Fidell (2007). Five multivariate outliers were eliminated from the data analyses of Hypothesis 1, and there were no multivariate outliers for Hypothesis 2. Three multivariate outliers were eliminated from the data analyses for Hypothesis 3. An analysis of these multivariate outliers revealed that these participants scored higher than the other participants on the emotional subscale of the Oral Contraceptive Side Effects Questionnaire ($M = 13.50$, $SD = 6.35$ vs. $M = 1.40$, $SD = 2.50$) but scored lower on the emotional subscale of the PEQ ($M = 3.00$, $SD = 4.76$ vs. $M = 4.24$, $SD = 4.84$).

Data were also evaluated for violations of normality, linearity, and homoscedasticity using histograms and bivariate scatter plots as outlined by Tabachnick and Fidell (2007). With a large sample size (i.e., over 200 cases), Tabachnick and Fidell (2007) recommend looking at the distribution of the sample to determine normality rather than using formal inference tests of skewness and kurtosis. This is because a variable with statistically significant skewness often does not deviate enough from normality to make a significant difference with the results. Upon examination of the histograms and bivariate scatter plots, it was found that the variables were generally normally distributed and those that were not did not deviate enough from normality to impact the results. The scores for these variables were not transformed to avoid increased difficulty in interpretation of the transformed variables. Multicollinearity was also assessed and no variables had correlations that exceeded .90.

A missing value analysis revealed that all variables were missing less than 2 % of the values. Each subject's missing value on a given variable was replaced with that subjects' mean

item score for that variable, as suggested by Tabachnik and Fidell (2007). Table 2 displays the means and standard deviations of the raw scores for each of the variables.

Finally, we examined the infrequency scores to determine whether any participants had endorsed over 4 items, resulting in an invalid questionnaire. However, no questionnaires were invalidated as no participants endorsed over 4 infrequency items.

Internal Consistency and Reliability of the Measures

Cronbach's alpha coefficients were calculated for all measures and their corresponding subscales. The internal consistencies, means, and standard deviations of all subscales can be found in Table 2. The internal consistencies of the majority of subscales fell in the moderate to high range, although the MDQ Water Retention ($\alpha = .63$) and Autonomic Reaction ($\alpha = .61$) subscales did not perform as well.

Examination of Bivariate Associations Between Variables

Initial analyses examined the relationship between all variables of interest. The correlations between all reproductive variables were examined and can be found in Table 3. Most of the reproductive variables were positively correlated and significant, with the exception of the OC side effects variable. The highest correlations were between the MDQ concentration subscale and the MDQ behaviour subscale ($r = .74, p < .01$), the MDQ concentration subscale, and the MDQ negative affect subscale ($r = .72, p < .01$), and the MDQ negative affect subscale and the MDQ behaviour subscale ($r = .68, p < .01$). The PEQ physical subscale and the PPSQ total scale were also highly correlated ($r = .62, p < .01$).

Next, correlations between all menopausal symptom variables were examined and can be found in Table 4. These variables were all significantly correlated in a positive direction. The highest correlations were between the MQUOL psychosocial subscale and the MQUOL physical

Table 2

Scale Means, Standard Deviations, and Internal Consistencies[a] *(N = 270)*

Scale	*N*	Means	Standard Deviations	Internal Consistency
MQUOL				
Vasomotor	284	3.73	1.88	.88
Psychosocial	283	2.93	1.59	.91
Physical	279	3.03	1.38	.93
Sexual	278	3.03	2.01	.87
MDQ				
Pain	280	9.00	5.45	.79
Water retention	278	5.60	3.19	.63
Autonomic reactions	277	2.93	3.10	.61
Negative affect	279	11.94	8.10	.92
Concentration	279	7.84	7.15	.87
Behavioural change	279	4.89	4.76	.84
Arousal	280	5.12	3.96	.74
PEQ				
Physical	233	26.99	14.79	.89
Emotional	236	4.35	4.97	.88
PPSQ	225	9.23	6.37	.77
EPDS	230	9.38	6.02	.87
Oral Contraceptives Questionnaire				
Physical	232	3.09	3.33	.73
Emotional	231	1.61	3.29	.90
Sexual	228	0.81	2.43	.89
NEO Five Factor Inventory – Neuroticism	255	34.42	10.05	.90
Infrequency Scale	265	0.11	0.37	.23

Note. MQUOL = Menopause Quality of Life Questionnaire, MDQ = Menstrual Distress Questionnaire, PEQ = Pregnancy Experiences Questionnaire, PPSQ = Postpartum Physical Symptoms Questionnaire, EPDS = Edinburgh Postnatal Depression Scale.

Table 3

Table 3: *Correlation Matrix for Reproductive Variables*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15.
1. MDQ Pain	-														
2. MDQ Water Retention	.58**	-													
3. MDQ Autonomic	.56**	.29**	-												
4. MDQ Negative Affect	.61**	.50**	.45**	-											
5. MDQ Concentration	.54**	.42**	.53**	.72**	-										
6. MDQ Behaviour	.57**	.39**	.49**	.68**	.74**	-									
7. MDQ Arousal	.25**	.10	.32**	.27**	.33**	.27**	-								
8. PEQ Physical	.37**	.37**	.22**	.34**	.34**	.31**	.10	-							
9. PEQ Emotional	.32**	.19	.15*	.42**	.45**	.38**	.07	.56**	-						
10. PPSQ Total	.26**	.26**	.20**	.25**	.27**	.29**	.13	.62**	.37**	-					
11. EPDS Total	.28**	.26**	.28**	.45**	.36**	.36**	.15*	.40**	.42**	.49**	-				
12. OC Physical	.30**	.30**	.24**	.15*	.13	.15*	.08	.28**	.06	.30**	.18*	-			
13. OC Emotional	.19**	.24**	.17*	.26**	.18*	.27**	.00	.25**	.17*	.20**	.24**	.54**	-		
14. OC Sexual	.01	.15	.07	.09	.10	.09	.06	.14	-.01	.06	.13	.18*	.17*	-	
15. Puberty Mood Change	.22**	.21**	.04	.24**	.08	.13*	.07	.26**	.30**	.25**	.33**	.09	.15*	.13	-

Note. * $p < .05$, ** $p < .01$

Table 4

Correlation Matrix for Menopausal Symptom Variables

	MQUOL Vasomotor	MQUOL Psychosocial	MQUOL Physical	MQUOL Sex
1. MQUOL Vasomotor	-			
2. MQUOL Psychosocial	.38**	-		
3. MQUOL Physical	.45**	.68**	-	
4. MQUOL Sex	.26**	.36**	.51*	-

Note. * $p < .05$, ** $p < .01$

subscale ($r = .68, p < .01$), as well as the MQUOL physical subscale and the MQUOL sexual subscale ($r = .51, p < .01$).

Finally, the correlations between each reproductive variable and menopausal symptom variable were examined and can be found in Table 5. Again, most of the variables were positively correlated, although not all were significant. OC sexual side effects did not correlate with any of the menopausal symptom variables. The highest correlations were between the MQUOL psychosocial subscale and the MDQ negative affect subscale ($r = .63, p < .01$), the MQUOL psychosocial subscale and the MDQ behaviour subscale ($r = .52, p < .01$), and the MQUOL physical subscale and the MDQ pain subscale ($r = .52, p < .01$). In order to minimize the influence of shared variance and determine the best reproductive predictors of various menopausal symptoms, multiple regression analyses were conducted to investigate Hypotheses 1 and 2.

Main Analyses

Hypothesis 1. A forward entry multiple regression analysis was used to determine the best predictors of menopausal depressive symptoms. For this analysis, the MQUOL psychosocial subscale served as the dependent variable, while the MDQ negative affect subscale, PEQ emotional subscale, EPDS total score, mood change at puberty, and Oral Contraceptive Side Effects emotional subscale were entered as predictors. Panel 1 of Table 6 displays the standardized regression coefficients (ß), R, adjusted R^2, and R^2 change statistics. Two variables emerged as unique predictors of menopausal depressive symptoms: the MDQ negative affect subscale, adjusted $R^2 = .38$, $F(1, 168) = 103.11, p < .001$, and the total score from the EPDS, adjusted $R^2 = .40$, $F(2, 167) = 57.13, p < .001$. Together, they accounted for 40.6 % of the variance in menopause depressive symptoms (R^2 value). Individually, the MDQ negative affect

Table 5

Bivariate Correlations Between Reproductive Variables and Menopausal Symptom Variables

	MQUOL Vasomotor	MQUOL Psychosocial	MQUOL Physical	MQUOL Sex
MDQ Pain	.25**	.38**	.52**	.26**
MDQ Water Retention	.25**	.37**	.47**	.26**
MDQ Autonomic	.32**	.27**	.39**	.20**
MDQ Negative Affect	.15*	.63**	.45**	.20**
MDQ Concentration	.15*	.50**	.45**	.13
MDQ Behaviour	.13	.52**	.40**	.14*
MDQ Arousal	.14*	.14*	.22**	.12
PEQ Physical	.11	.27**	.37**	.09
PEQ Emotional	.03	.40**	.31**	.07
PPSQ Total	.19**	.24**	.33**	.07
EPDS Total	.09	.40**	.26**	.07
OC Physical	.20**	.05	.25**	.16*
OC Emotional	.01	.16*	.15*	.08
OC Sexual	.06	.04	-.00	.04
Puberty Mood	.06	.23**	.18**	.10

Note. * $p < .05$, ** $p < .01$

subscale accounted for 38.0 % of the variance, while the EPDS accounted for an additional 2.6 % (R^2 change values).

As a supplementary analysis, the influence of a decrease in negative symptoms was examined using re-coded values for the PEQ, PPSQ, and the Oral Contraceptive Side Effects Questionnaire. However, all significant predictors remained the same, and the re-coded values did not affect the results.

Hypothesis 2. A series of forward entry multiple regression analyses were used to determine the best predictors of menopausal physical symptoms. First, a composite score consisting of both the physical and vasomotor subscales was used as the dependent variable, with the MDQ subscales, PEQ physical symptom subscale, PPSQ scale, and the physical symptom subscale from the Oral Contraceptive Side Effects Questionnaire acting as the predictors. Panel 2a of Table 6 displays the standardized regression coefficients (ß), R, adjusted R^2, and R^2 change statistics. Three variables emerged as unique predictors of the composite menopausal physical symptoms scale: the MDQ pain subscale, adjusted $R^2 = .18$, $F(1, 176) = 39.67$, $p < .01$, the MDQ autonomic subscale, adjusted $R^2 = .28$, $F(2, 175) = 26.97$, $p < .01$, and the MDQ water retention subscale, adjusted $R^2 = .26$, $F(3, 174) = 21.75$, $p < .01$. Together, these variables accounted for 27.3 % of the variance (R^2 value). Individually, the MDQ pain subscale accounted for 18.4 %, while the MDQ autonomic subscale accounted for an additional 5.2 %, and the MDQ water retention scale accounted for an additional 3.7 % (R^2 change values).

A second forward entry multiple regression was used with the MQUOL physical symptom subscale as the dependent variable. The MDQ subscales, PEQ physical symptom subscale, PPSQ scale, and the physical symptom subscale from the Oral Contraceptive Side Effects Questionnaire were used as the predictors. Panel 2b of Table 6 displays the standardized

Table 6

Summary of Regression Analyses for Hypothesis 1 and Hypothesis 2 (N = 270)[a]

Variable	*R*	Adjusted R^2	R^2 Change	*ß*
Panel 1: Hypothesis 1				
MDQ Negative Affect	.62	.38	.38**	.53**
EPDS Total	.64	.40	.03**	.18**
Panel 2a: Hypothesis 2, Composite Physical Symptom Score as DV				
MDQ Pain	.43	.18	.18**	.13
MDQ Autonomic	.49	.23	.05*	.28**
MDQ Water Retention	.52	.26	.04*	.24**
Panel 2b: Hypothesis 2, MQUOL Physical Symptom Score as DV				
MDQ Pain	.53	.27	.28**	.23**
MDQ Concentration	.58	.33	.07**	.24**
PEQ Physical Symptoms	.61	.36	.03**	.17**
MDQ Water Retention	.63	.38	.02*	.18*
Panel 2c: Hypothesis 2, MQUOL Vasomotor Score as DV				
MDQ Autonomic	.33	.11	.11**	.28**
MDQ Water Retention	.37	.13	.03*	.17*

Note. MQUOL = Menopause Quality of Life Questionnaire, MDQ = Menstrual Distress Questionnaire, PEQ = Pregnancy Experiences Questionnaire, PPSQ = Postpartum Physical Symptoms Questionnaire, EPDS = Edinburgh Postnatal Depression Scale

[a] Some participants' scores were not used in these analyses due to pairwise deletion (i.e., if a participant was never pregnant, they did not have scores on pregnancy measures and were omitted from those analyses)

* $p < .05$, ** $p < .01$

regression coefficients (ß), R, adjusted R^2, and R^2 change statistics. Four variables emerged as unique predictors of physical symptoms experienced during menopause: the MDQ pain subscale, adjusted $R^2 = .27$, $F(1, 176) = 67.32$, $p < .01$, the MDQ concentration subscale, adjusted $R^2 = .34$, $F(2, 175) = 45.31$, $p < .01$, the PEQ physical symptom subscale, adjusted $R^2 = .36$, $F(3, 174) = 34.59$, $p < .01$, and the MDQ water retention subscale, adjusted $R^2 = .38$, $F(4, 173) = 28.09$, $p < .01$. Together, these variables accounted for 39.34% of the variance (R^2 value). Individually, the MDQ pain subscale accounted for 27.7 %, while the MDQ concentration subscale accounted for an additional 6.5 %, the PEQ physical symptom subscale accounted for an additional 3.2 %, and the MDQ water retention subscale accounted for an additional 2.0 % (R^2 change values).

Finally, the MQUOL vasomotor symptom subscale was used as the dependent variable. The MDQ subscales, PEQ physical symptom subscale, PPSQ scale, and the physical symptom subscale of the Oral Contraceptives Side Effects Questionnaire were used as the predictors. Panel 2c of Table 6 displays the standardized regression coefficients (ß), R, adjusted R^2, and R^2 change statistics. Two variables emerged as unique predictors of vasomotor symptoms experienced during menopause: the MDQ autonomic subscale, adjusted $R^2 = .11$, $F(1, 168) = 20.92$, $p < .01$, and the MDQ water retention subscale, adjusted $R^2 = .12$, $F(2, 167) = 12.82$, $p < .01$. Together, these variables accounted for 13.7 % of the variance (R^2 value). Individually, the MDQ autonomic subscale accounted for 11.0 % of the variance, while the MDQ water retention subscale accounted for an additional 2.7 % (R^2 change values).

As a supplementary analysis, the influence of a decrease in negative symptoms was examined using re-coded values for the PEQ, PPSQ, and the Oral Contraceptive Side Effects Questionnaire. All significant predictors remained the same except for the second regression

equation. The PEQ physical symptom variable was no longer a unique predictor of physical symptoms during menopause.

Hypothesis 3. A number of discriminant function analyses were conducted to determine whether the severity of physical and emotional symptoms experienced during past reproductive events predicts whether women sought HRT. First, a discriminant function analysis was conducted using both the physical and emotional symptom variables as predictors of seeking HRT. Specifically, predictor variables included the MDQ subscales, the emotional and physical subscales of the PEQ, the PPSQ total score, the EPDS total score, and the physical, emotional, and sexual subscales from the Oral Contraceptives Side Effects Questionnaire. These variables were entered simultaneously. The function did not significantly discriminate between groups, $\lambda = .89, X^2\ (14) = 16.67, p = .27$, accounting for only 6.7 % of the variance between the two groups. Using this discriminant function, approximately 77 % of participants were correctly classified into their respective groups, whereas 67 % would be correctly classified by chance alone.

Next, two separate discriminant function analyses were conducted for physical symptoms and emotional symptoms. For the analysis involving physical symptoms, the MDQ subscales, the PEQ physical symptom subscale, the PPSQ total score, and the physical symptom subscale from the Oral Contraceptive Side Effects Questionnaire were used as predictors and were entered simultaneously. The function did not significantly discriminate between those who sought HRT and those who did not, $\lambda = .93, X^2\ (9) = 10.66, p = .30$, accounting for 7.0 % of the variance between groups. Using this discriminant function, approximately 78 % of participants were correctly classified into their respective groups, whereas 66 % would be correctly classified by chance alone.

For the analysis involving emotional symptoms, the MDQ negative affect subscale, the PEQ emotional subscale, the EPDS total score, and the emotional subscale from the Oral Contraceptive Side Effects Questionnaire were used as predictors and entered simultaneously. Similarly, the function did not significantly discriminate between those who sought HRT and those who did not , $\lambda = .97$, X^2 (4) = 4.16, $p = .38$, accounting for only 2.6 % of the variance between groups. Using this discriminant function, approximately 80 % of participants were correctly classified into their respective groups, whereas 67 percent would be correctly classified by chance alone.

Since not all participants in this study had given birth or taken oral contraceptives in the past, the sample size for each analysis was reduced. Ninety-three participants (32 % of the sample) were omitted from these analyses because they had not completed the various pregnancy questionnaires and/or the Oral Contraceptive Side Effects Questionnaire. Further analyses were conducted to determine whether the above findings were affected by a reduction in statistical power due to the loss of participants. In order to determine whether past pregnancy was related to seeking HRT during menopause a new variable was created distinguishing those who had given birth in the past (1) and those who had not (0). A discriminant function analysis was conducted with the new pregnancy variable replacing the pregnancy questionnaires (PEQ physical and emotional subscales, PPSQ total score, EPDS total score). The MDQ subscales and Oral Contraceptive Side Effect Questionnaire subscales were still included in this analysis. Therefore, this analysis investigated whether ever being pregnant was a predictor of seeking HRT without losing as many participants. For this analysis, the number of missing participants was reduced to 69 (24 % of the sample). However, the function did not significantly

discriminate between groups, $\lambda = .94$, X^2 (11) = 13.12, $p = .29$, accounting for approximately 6 % of the variance between the two groups.

In order to determine whether past OC use was related to seeking HRT during menopause a new variable was created distinguishing those who had used oral contraceptives the past (1) and those who had not (0). A discriminant function analysis was conducted with the new oral contraceptive variable replacing the subscales from the Oral Contraceptive Side Effects Questionnaire. The MDQ and PEQ subscales were still included in this analysis, as were the total scores from the PPSQ and the EPDS. Therefore, this analysis investigated whether ever taking oral contraceptives was a predictor of seeking HRT without losing as many participants. For this analysis, the number of missing participants was reduced to 80 (28 % of the sample). However, the function did not significantly discriminate between groups, $\lambda = .95$, X^2 (12) = 11.01, $p = .53$, accounting for 5.3 % of the variance between the two groups.

An alternate analysis was conducted to investigate a related question – whether past reproductive variables can predict who actually received HRT. This variable was also tested because there are numerous patient and physician factors that may influence whether a woman actually receives HRT, despite whether she had originally sought it or not (i.e., risk for breast cancer, prevention of osteoporosis). The variables included in this analysis were the MDQ subscales, the PEQ physical and emotional subscales, the PPSQ total, the EPDS, and the Oral Contraceptive Side Effect Questionnaire subscales. The function that emerged from this analysis was also not significant, $\lambda = .87$, X^2 (14) = 23.32, $p = .06$, accounting for 12.3 % of the variance between the two groups.

Hypothesis 4. Pearson product-moment correlations were used to determine whether finger digit ratio is related to androgen-related menopausal symptoms. Left 2D:4D was

significantly associated with decrease in sexual desire ($r = .24, p < .05$) and avoiding intimacy ($r = .23, p < 0.05$). That is, increased (feminized) 2D:4D was associated with a decrease in sexual desire and avoiding intimacy during menopause. The correlations between right and left 2D:4D and androgen-related symptoms can be found at the top of Table 7.

Hypothesis 5. Pearson product-moment correlations were used to determine whether finger digit ratio is related to estrogen-related menopausal symptoms. However, 2D:4D was not significantly associated with any estrogen-related menopausal symptoms. The correlations between right and left 2D:4D and estrogen-related symptoms can be found at the bottom of Table 7.

Hypothesis 6. Pearson product-moment correlations were used to determine whether finger digit ratio is related to menopausal symptoms in women who have undergone ovarian surgery. Right 2D:4D was significantly associated with vaginal dryness during intercourse ($r = .81, p < .01$) and decrease in sexual desire ($r = .65, p < .01$). Left 2D:4D was significantly associated with hot flashes ($r = .70, p < .05$) and vaginal dryness during intercourse ($r = .77, p < .01$). Correlations between right and left 2D:4D and menopausal symptoms can be found in Table 8.

Bivariate scatter plots were also examined to ensure that the above correlations were not unduly influenced by outliers due to the small sample size for this analysis ($n = 10$). Each scatter plot was divided into quadrants drawn along the means for the two variables. For both the left 2D:4D and vaginal dryness scatter plot and the right 2D:4D and vaginal dryness scatter plot, all data points fell in the appropriate quadrant (i.e., those with the lowest finger digit ratio all fell below the mean for vaginal dryness during intercourse, and vice versa). All but one data point fell in the appropriate quadrants for the left 2D:4D and decrease in hot flashes scatter plot,

Table 7

Summary of Pearson Product-Moment Correlations for 2D:4D and Menopausal Symptoms (n = 90)

Menopausal Symptom	Mean Right 2D:4D	Mean Left 2D:4D
Androgen-related Symptoms:		
Decrease in sexual desire	.09	.24*
Vaginal Dryness during intercourse	.11	.19
Avoiding intimacy	.05	.23*
Estrogen-related Symptoms:		
Hot flashes or flushes	.06	.08
Night sweats	-.03	-.03
Sweating	.02	-.02

* $p < .05$, ** $p < .01$

Table 8

Summary of Pearson Product-Moment Correlations for 2D:4D and Menopausal Symptoms for Women Who Have Experienced Ovarian Surgery (n = 10)

Menopausal Symptom	Mean Right 2D:4D	Mean Left 2D:4D
Androgen-related Symptoms		
Decrease in sexual desire	.65*	.58
Vaginal Dryness during intercourse	.81**	.77**
Avoiding intimacy	.57	.56
Estrogen-related Symptoms		
Hot flashes or flushes	.52**	.70**
Night sweats	.14	.06
Sweating	.03	.07

* $p < .05$, ** $p < .01$

and all but two data points fell in the appropriate quadrant for the right 2D:4D and decrease in sexual desire scatter plot.

Because some of the distributions for these particular items were skewed for the 10 participants who were included in this analysis, Kendall's tau correlations were conducted. This nonparametric test was chosen, as Field (2009) recommends using this method of nonparametric correlation with a small data set and a large number of tied ranks. Right 2D:4D was significantly associated with decrease in sexual desire ($r = .56, p < .05$), vaginal dryness during intercourse ($r = .84, p < .01$), and avoiding intimacy ($r = .69, p < .05$). Left 2D:4D was significantly associated with hot flashes or flushes ($r = .55, p < .05$), vaginal dryness during intercourse ($r = .69, p < .05$). Kendall's Tau correlations between right and left 2D:4D and menopausal symptoms can be found in Table 9.

Supplementary Analyses

Hypothesis 1, 2, and 3. As discussed above, Hypotheses 1, 2, and 3 were each re-analyzed using re-coded versions PEQ, PPSQ, and the Oral Contraceptives Side Effects Questionnaire. Rather than investigating participants' reports of an increase in negative symptoms on these scales, this supplementary analysis investigated a decrease in negative symptoms and how they may relate to menopausal symptoms. However, only one multiple regression equation was affected by the re-coded scales. When predicting physical symptoms experienced during menopause, the PEQ physical symptoms variable was no longer a significant predictor.

NEO-FFI and Symptom Variables. The total neuroticism NEO-FFI scores were correlated with all symptom variables to determine whether neuroticism is related to symptom

Table 9

Summary of Kendall's Tau for 2D:4D and Menopausal Symptoms for Women Who Have Experienced Ovarian Surgery (n = 10)

Menopausal Symptom	Mean Right 2D:4D	Mean Left 2D:4D
Decrease in sexual desire	.56*	.51
Vaginal Dryness during intercourse	.69*	.69*
Avoiding intimacy	.53	.53
Hot flashes or flushes	.43	.55*
Night sweats	.18	.13
Sweating	.02	-.02

Note. * $p < .05$, ** $p < .01$

reporting. The neuroticism scores were significantly correlated with 16 out of 18 symptom variables. These correlations are presented in Table 10.

Discussion

The primary aim of this study was to investigate predictors of more severe physical and/or psychological symptoms associated with menopause, including symptoms associated with past reproductive events and physical markers such as finger digit ratio. A secondary aim of this study was to investigate the possible differences between women who sought HRT versus those who did not. The main findings of this study indicate that there is a link between mood symptoms experienced at menopause and during other reproductive events, with negative affect experienced prior to menstruation and post partum mood symptoms emerging as the most important predictors of negative affect experienced during menopause. Second, past physical symptoms experienced during reproductive events do predict the physical symptoms experienced in menopause, with many symptoms associated with PMS acting as the most important predictors. Third, past symptoms associated with reproductive events do not seem to predict whether a woman will seek HRT during the perimenopausal period. And finally, 2D:4D does not seem to be related to estrogen-related menopausal symptoms, although there are some associations with androgen-related menopausal symptoms. For those women who underwent surgical menopause, the association between 2D:4D and both androgen and estrogen-related menopausal symptoms was present. Each of the hypotheses will be further discussed in turn.

Bivariate Association Between Variables

As a preliminary analysis, the correlations between all variables were examined. Although examining the correlations between variables does present the problem of overlapping variance, this preliminary analysis illustrated that most of the variables of interest were, in fact,

Table 10

Correlations between the NEO – FFI Neuroticism Scale and the Symptom Subscales (N = 290)

Variable Name	NEO-FFI Neuroticism
MQUOL Vasomotor	.21**
MQUOL Psych	.60**
MQUOL Sex	.22**
MDQ Pain	.34**
MDQ Water Retention	.29**
MDQ Autonomic	.33**
MDQ Negative Affect	.57**
MDQ Concentration	.46**
MDQ Behaviour	.51**
MDQ Arousal	.15*
PEQ Physical Symptoms	.28**
PEQ Emotional Symptoms	.40**
PPSQ Total	.19*
EPDS Total	.49**
OC Physical Symptoms	.13
OC Emotional Symptoms	.16**
OC Sexual Symptoms	.10

Note. * $p < .05$, ** $p < .01$

significantly associated with each other and this association was in the expected direction. When examining the correlations between the past reproductive variables and the menopausal symptom variables, it was determined that most of the variables were significantly correlated with each other in a positive direction. That is, a higher severity of symptoms during the reproductive event was associated with a higher severity of menopausal symptoms.

In terms of Hypothesis 1, all of the mood variables associated with past reproductive events were positively correlated with mood symptoms experienced at menopause. This illustrates that there is indeed a relationship between menopausal mood symptoms and mood symptoms experienced during puberty, PMS, pregnancy, the postpartum period, and/or OC use.

For Hypothesis 2, all but one of the past physical symptom variables were significantly associated with physical symptoms associated with the menopausal transition. Sexual side effects resulting from OC use was not correlated with physical symptoms experienced at menopause. This could be due to differing causes for sexual side effects during these reproductive events. For example, research has pointed to elevated sex hormone binding globulin levels leading to decreased testosterone as a potential cause for sexual side effects during oral contraceptive use (Panzer et al., 2006). However, sexual side effects during menopause may be caused by decreasing estrogen levels (Graziottin, 2000).

Other than this variable, symptoms associated with PMS, pregnancy, the postpartum period, and physical side effects of OC use were all associated with physical symptoms experienced during menopause. Finally, correlations between vasomotor symptoms experienced during menopause and past physical reproductive symptoms revealed that most premenstrual symptoms (excluding behaviour change), postpartum physical symptoms, and physical side effects of OC use are associated with vasomotor symptoms in menopause.

It is important to note the potential influence of response bias, should it exist in this study. It is possible that the participants may have understood the underlying research question although it was not explicitly stated. Further, women suffering from a more severe menopausal transition might have endorsed more severe symptoms during past reproductive events if they allowed their recent menopausal symptoms to cloud their recollection of the severity of past reproductive events. However, response bias or memory bias could influence the results in both directions (i.e., the over reporting of past/present symptoms as well under reporting past/present symptoms). Therefore, these biases, if present, may be in either direction, and may not systematically influence the results.

Hypothesis 1

For Hypothesis 1, it was predicted that women who experience more depressive symptoms during the menopausal transition will be more likely to have had a history of distress associated with other reproductive events (i.e., the premenstrual period, during pregnancy, the postpartum period, puberty, and during oral contraceptive use). This hypothesis was supported. As discussed above, each of the mood-related reproductive variables were significantly correlated with negative affect during the menopausal period. Of these variables, negative affect experienced in the premenstrual period and negative mood experienced postnatally were the best predictors of negative mood during menopause, as they accounted for the largest portion of unique variance. Our findings were analogous to past studies that have found that negative mood experienced in the premenstrual period and/or during the postpartum period predicted mood symptoms in menopause (Flores-Ramos, et al., 2010; Gregory, et al., 2000; Payne et al., 2007).

However, our findings partially contradict Becker and colleagues (2007) who found that negative mood experienced during PMS was a predictor of menopausal mood symptoms, but not negative mood experienced after pregnancy. Our findings also contradict Steinberg and colleagues (2008) who found no association between premenstrual mood symptoms, postpartum mood symptoms, and depressive symptoms experienced during the menopause. These differences may be due to differing criteria between these studies and this study, or due to the measurement of mood symptoms. For example, Becker and colleagues (2007) used a visual analogue scale to retrospectively measure mood during PMS and postpartum. This study used a more detailed method of measurement, using comprehensive scales to capture the experiences of women during this time. Using this method of measurement may have more accurately captured the relationship between these two variables.

The participants in Steinberg and colleagues' (2008) study were menopausal women who were diagnosed with either minor or major depression at the time of the study, and they focused on premenstrual depression and postpartum depression, rather than depressive symptoms and negative mood experiences. Focusing on mood symptoms in general rather than strict criteria for depressive episodes may explain the conflicting finding between our study and Steinberg and colleagues' (2008).

Although the majority of past studies seem to support a link between menopausal mood symptoms and depressive symptoms during times of estrogen decline, there was a dearth of research related to times of hormonal fluctuations in which estrogen levels increase. This study found that symptoms experienced during times of estrogen increase (i.e., puberty, pregnancy, the use of oral contraceptives) are significantly associated with menopausal mood symptoms. However, these variables do not account for the largest portion of the variance, and therefore do

not emerge as significant when compared to symptoms associated with estrogen decline (i.e., premenstrual symptoms, postpartum mood change). Past research has suggested that negative mood does indeed occur during times of estrogen increase (Glover et al., 2004; Kessler & Walters, 1998; Lewinsohn et al., 1998; Sugawara et al., 1997), and current theories have suggested that it is not only times of estrogen decline that may lead to depressive symptoms, but that some women may not be able to compensate for fluctuations in estrogen (Deecher et al., 2008). The results of this study support these findings, although variables associated with estrogen decline seem to be better predictors of negative affect experienced during menopause.

Mood change during pregnancy may not be the best predictor of menopausal mood symptoms because estrogen levels change in a steady manner during pregnancy, and do not include rapid and unpredictable fluctuations. Therefore, it may be that women who experience negative mood symptoms tied to reproductive events have trouble adapting to changes in hormonal levels when there are unpredictable declines in estrogen, rather than steady increases. The hormonal changes that occur during both the premenstrual period and the postpartum period are analogous to the changes that occur during menopause. Therefore, it is reasonable that these reproductive events would be so closely associated. It is unclear as to why oral contraceptive use was not a unique predictor, as it is associated with some hormonal fluctuations.

Alternately, mood change during pregnancy and oral contraceptive use may not be unique predictors of menopausal symptoms because the measures might not have been sensitive enough to pick up any the effects of these variables. This may be due to the fact that both the PEQ and Oral Contraceptives Side Effects Questionnaire were newly created for the purposes of this study. However, the significant correlation between mood symptoms experienced during pregnancy, during OC use, and menopause indicate that there is indeed a relationship between

these variables, although these variables did not necessarily emerge as unique predictors of menopausal mood symptoms.

The results of this study support the notion that depressive symptoms during reproductive events are linked, and that negative symptoms experienced prior to menstruation and negative mood experienced during the postpartum period are the best emotional reproductive predictors of negative affect during the menopausal transition. However, it is hard to make firm conclusions due to the correlational nature of the analyses used and the complexity of the simultaneous hormonal changes that are occurring during each of the reproductive events. Ultimately, a prospective study could help clarify these relationships.

Hypothesis 2

For Hypothesis 2, it was predicted that women who experience more severe physical symptoms during the menopausal transition will have experienced more severe physical symptoms during times of hormonal fluctuation (i.e., the premenstrual period, during pregnancy, the postpartum period, and during oral contraceptive use). This hypothesis was partially supported. As discussed above, all but one of the past physical symptom variables were significantly associated with physical symptoms associated with the menopausal transition. Finally, correlations between vasomotor symptoms experienced during menopause and past physical reproductive symptoms revealed that most premenstrual symptoms (excluding behaviour change), postpartum physical symptoms, and physical side effects of OC use are associated with vasomotor symptoms in menopause.

When considering the best (or unique) predictors of menopausal physical and vasomotor symptoms, all unique predictors were associated with the premenstrual period. Pain, water retention, and autonomic symptoms experienced during the premenstrual phase were all unique predictors of menopausal symptoms. When only the physical symptom subscale from the

MQUOL was considered, autonomic symptoms were no longer a unique contributor, but symptoms experienced during pregnancy did emerge as a unique predictor. Finally, when vasomotor symptoms from the MQUOL were considered, autonomic symptoms and water retention experienced during PMS were the only unique predictors. Therefore, the best predictors of menopausal physical symptoms change depending on what symptoms are being considered.

The results of this study are analogous to past studies that have indicated that there is an association between PMS symptoms and symptoms experienced during menopause (Binfa et al., 2004; Freeman et al., 2004; Hunter, 1992; Leidy, 1996; Morse et al., 1998). It seems that there is a consistent association between PMS and menopausal symptoms despite differing methodologies and psychometric measures. This association may exist due to similarities in hormonal changes during both PMS and the menopausal transition. PMS symptoms are typically experienced during the luteal phase, when both estrogen and progesterone levels decline. The similarity between PMS symptoms and menopausal symptoms suggests that some women may be more susceptible to physical symptoms when hormone levels decline.

It seems as though physical symptoms experienced prior to menstruation and during pregnancy are the best predictors of physical menopausal symptoms. Although physical symptoms experienced during the postpartum period were correlated with menopausal symptoms, it was not a unique predictor of physical menopausal symptoms, despite the drastic estrogen drop that occurs after birth. This finding is surprising as the decline in estrogen that occurs during the postpartum period is analogous to the decline in estrogen that occurs during the menopausal transition.

This study lends further support to Hunter's (1993) theory that women who experience vasomotor symptoms prior to menopause may be more sensitive to hormonal changes. This study found that hot flashes and other autonomic symptoms experienced prior to menopause were significantly related to the severity of hot flashes experienced during menopause. This theory could be extended to other symptoms experienced during the premenstrual period such as water retention, cramping, and concentration problems, as significant associations with these variables were found as well. Further, these results lend support to Deecher and colleagues' (2008) theory that it is times of reproductive change, not necessarily declines in hormone levels, that trigger hormonal sensitivity in some women.

The results for Hypothesis 2 should be interpreted with some caution, as other variables are involved in the experience of menopausal symptoms. We found that past reproductive variables accounted for between 13 and 39 percent of the variance in the severity of menopausal symptoms (for vasomotor and physical symptoms respectively). Research has shown that other factors such as health status, stress, attitudes toward aging and menopause, health behaviours, and sociodemographic variables can all influence both the frequency and severity of menopausal symptoms (Dennerstein, 1996).

The present findings suggest that a history of premenstrual symptoms (i.e., pain, lack of concentration, water retention) and physical symptoms experienced during pregnancy were the best predictors of overall menopausal symptoms. Further, a history of autonomic symptoms and water retention prior to menstruation were the best predictors of vasomotor symptoms experienced during menopause.

Hypothesis 3

For Hypothesis 3, it was predicted that women who sought HRT during their menopausal transition will have experienced more severe physical and/or psychological symptoms during

times of hormonal fluctuation (i.e., during the premenstrual period, pregnancy, the postpartum period, puberty, and oral contraceptive use). This hypothesis was not supported. Neither emotional nor physical symptoms experienced during past reproductive events predicted whether or not women sought HRT during the menopausal transition. Our results suggest that women who seek HRT do not have significantly more severe symptoms associated with past reproductive events when compared to women who did not seek HRT. This finding is surprising as past research has indicated that women who have more severe menopausal symptoms are more likely to seek HRT (Bosworth et al., 2005), and we found that the severity of menopausal symptoms is significantly related to the severity of some past reproductive symptoms (see Hypotheses 1 and 2). It would be expected that there would be a relationship between past reproductive symptoms and HRT seeking, although our results suggest that both groups (HRT seeking vs. not) are essentially the same with respect to the severity of past reproductive symptoms.

Hypothesis 4 and Hypothesis 5

It was predicted in Hypothesis 4 that women with a lower (masculinized) 2D:4D will have more severe androgen-related menopausal symptoms due to increased androgen sensitivity. These androgen-related symptoms included loss of libido, and ability to become sexually aroused during the menopausal transition. This hypothesis was not supported, as the opposite was found. The results indicate that left 2D:4D is positively correlated with a decrease in sexual desire and avoiding intimacy, suggesting that women with a higher (feminized) 2D:4D suffer from more severe androgen-related menopausal symptoms. These results are difficult to interpret, as sexual desire consists of a complex interaction of physiological, psychological, and biochemical processes. Androgens are said to be responsible for the decrease in libido that can occur as women age, although Graziottin (2000) argues that the decrease in estrogen that occurs

during menopause has a substantial impact on one's sexual desire. This author states that estrogens prime the central nervous system as well as the sensory organs (including the skin) that are the key receptors for external sexual stimuli. She also states that the interplay between estrogens and the dopaminergic system is a key process that determines the appetitive side of sexual behaviour (Graziottin, 2000). Thus, it is possible that women who have a higher (feminized) 2D:4D may be more sensitive to the effects of estrogen on sexual desire, and may experience more severe sexual symptoms during the menopausal transition as a result.

Further, the decrease in estrogen that occurs during this time may affect the psychological aspects of sexual desire, as women may feel less feminine as they enter the menopausal transition. The menopausal transition is a concrete representation of the fact that reproduction can no longer occur. At this time, women may lose their sexual identity or sensuality, which may decrease the quality of their sexual relationships and ultimately lead to decreased libido (Graziottin, 2000). Again, it may be possible that women with a higher (feminized) 2D:4D are more sensitive to the effects of estrogen on sexual desire, and may be more affected by the psychological aspects associated with sexual desire as well. Further, Csathó and colleagues (2003) have found 2D:4D to be associated with sex role identity, such that participants with a lower 2D:4D showed masculinized sex role identity scores. Although not explicitly mentioned in the study, it is likely that higher 2D:4D scores were associated with a more feminine sex role identity. It is possible that 2D:4D is related to women's perceptions of femininity, which may ultimately affect their feelings toward sexual activity as they age.

It was predicted in Hypothesis 5 that women with a higher (feminized) 2D:4D will have more severe estrogen-related menopausal symptoms due to increased estrogen sensitivity. These estrogen-related menopausal symptoms included vasomotor and vulvovaginal symptoms. This

hypothesis was not supported, as no relationship between 2D:4D and estrogen-related menopausal symptoms was found. There could be a number of reasons why no relationship was found.

One possible reason is that 2D:4D may not be indicative of estrogen sensitivity. Originally, 2D:4D research emerged as an indicator of androgen exposure in utero, and has only recently expanded to include other studies investigating personality, health status, athletic ability, among other variables (Manning 2008). The effect of estrogen in the formation of 2D:4D is still relatively unknown. Most studies to date focus on how 2D:4D is related to estrogen-related health problems and make only indirect conclusions about how 2D:4D may be related to estrogen receptor sensitivity (Brabin et al., 2008; Manning & Leinster, 2001). Further research is needed to determine how the ratio of estrogen to testosterone in utero may affect 2D:4D and whether there is a relationship between 2D:4D and estrogen receptor sensitivity.

However, a relationship may exist between 2D:4D and estrogen-related menopausal symptoms and this study may have had insufficient power to detect a significant relationship. Voracek (2008) argues that many of the 2D:4D studies that have been conducted to date have an effect size of 0.50 or less. An analysis conducted using GPower suggests a sample size of 134 participants to detect a medium effect size of 0.3. For the finger digit portion of the study, we had 100 participants which may have been too few participants to pick up on a smaller effect size, should it exist.

Although not directly related to the above hypotheses, one interesting finding from this study was that both the left and right mean finger digit ratio was below 1.0. Past research has shown that the average digit ratio for white Caucasian females is approximately 1.0, while the average digit ratio for white Caucasian males is approximately 0.98 (Manning, 2008). In the first

of two studies conducted by Oinonen (2009) using mush younger participants sampled from the same community as the present study, the mean 2D:4D of the right hand was 0.995 and the mean 2D:4D of the left hand was 0.998. In the second study, both the left and right hands had a mean 2D:4D of 0.99 (Oinonen, 2009). For our sample, mean left 2D:4D was 0.97 (*SD* = .03) and mean right 2D:4D was 0.98 (*SD* = .04). There are a few past studies that might help explain why our sample may have a lower than average digit ratio.

First, Mayhew, Gillam, McDonald and Ebling (2007) found that 2D:4D fluctuated during the menstrual cycle, and suggest that 2D:4D may be dependent on circulating hormone levels. They found that 2D:4D values increased in the pre-ovulatory period and decreased prior to menstruation. These authors suggest that the increase in 2D:4D may occur at the level of the bone and/or the soft tissues when the estrogen level is highest in the menstrual cycle, as osteoblasts (cells responsible for bone formation) and osteoclasts (cells responsible for removal of bone tissue) both have estrogen receptors (Mayhew et al., 2007). However, there is some disagreement as to whether 2D:4D is related to circulating hormone concentrations (Hönekopp, Bartholdt, Beier, & Liebert, 2007). If 2D:4D does change with circulating estrogen levels, our sample may have lower 2D:4D because they are menopausal women whose estrogen is declining or postmenopausal women whose estrogen has already substantially declined. Unfortunately, it is hard to determine whether declining estrogen levels may be affecting 2D:4D without a longitudinal within-subject study. However, this research is not currently available as 2D:4D is a relatively new line of research.

Second, Van Dongan (2009) found that 2D:4D decreased significantly with age in females. Although this study had a narrow age range (18-26), they found that the older women in the study tended to have a masculinzed 2D:4D whereas the younger women had a more

feminized 2D:4D. The author argues that these changes are not likely due to the effects of the menstrual cycle, as the changes were much larger than what would be expected based on Mayhew and colleagues' (2007) findings (Van Dongan, 2009). However, this study is cross-sectional, and these results could be due to a cohort effect. It is difficult to tell without a longitudinal study whether finger digit length does, in fact, decrease with age. If finger digit ratio does decrease with age, it could be due to changing hormone levels, as discussed above. Also, if finger digit ratio decreases with age, it might explain why our sample had a lower mean 2D:4D, as they were middle-aged women over the age of 40. If this is true, it is unclear as to how this would have affected the results of the present study. Since the current study only correlated menopausal symptoms (as opposed to past reproductive symptoms) with 2D:4D, the possibility that 2D:4D decreases with age should not have had much of an effect. Relationships between 2D:4D of postmenopausal women and their menopausal symptoms may be inaccurate if 2D:4D continues to decline after the conclusion of the menopausal transition. Further research is needed to determine if 2D:4D does, in fact, decrease with age.

Third, past research has suggested that 2D:4D decreases at higher latitudes, although the reason for this association is still unknown. It is suggested that 2D:4D is highest at intermediate latitudes and lowest at the equator and high latitudes (Manning, 2008). Some researchers suggest that this relationship may exist due to differences in temperature, sunlight, day-length patterns, and/or genetic differences among populations (Helle & Laaksonen, 2009). Recently, a study by Helle and Laaksonen (2009) supported the notion that 2D:4D decreases with higher latitudes. They investigated the finger digit ratios of women from Finland and found that women's 2D:4D decreased by 0.0022 per one degree increase in latitude (Helle & Laaksonen,

2009). Although Finland is at a much higher latitude than Thunder Bay, these results may explain why our sample had a lower mean 2D:4D than the average female.

Finally, the differences may be due to sampling error among different studies. As mentioned previously, other studies have found mean 2D:4D to be approximately 1.0 (Manning, 2008; Oinonen, 2009). However, another study from Lakehead University using a younger population (mean age) found a mean 2D:4D of 0.97 (Teatero, 2009). Like the present study, Teatero (2009) measured 2D:4D from hand scans using a desktop scanner. Oinonen's study (2009) used digital callipers to directly measure the finger lengths of the participants. Kemper and Schwerdtfeger (2008) have found that 2D:4D can differ depending on the type of measurement used. This may explain why the mean for the present study is lower than the means found in previous studies using different measurement techniques.

It is unclear as to whether any of the above findings may have affected the results of this study. Although a significant result was found for Hypothesis 4, it was in the opposite direction to what was expected. Moreover, a relationship between 2D:4D and estrogen-related symptoms was not found. Since 2D:4D research is relatively new and has some conflicting findings, it hard to pinpoint the relationship between testosterone and/or estrogen exposure in utero and menopausal symptoms.

Hypothesis 6

It was predicted in Hypothesis 6 that higher (feminized) 2D:4D would be significantly related to the severity of estrogen-related symptoms and lower (masculinized) 2D:4D would be related to the severity of androgen-related symptoms in women who had undergone surgical menopause. This hypothesis was partially supported. Higher 2D:4D was positively correlated with two estrogen-related symptoms: hot flashes and vaginal dryness during intercourse. Finger digit ratio was also significantly correlated with androgen-related menopausal symptoms,

although the results were in the opposite direction of what was expected. 2D:4D was positively correlated with a decrease in sexual desire and avoiding intimacy, indicating that women who have a higher (feminized) 2D:4D suffered from more severe androgen-related symptoms during the menopausal transition. Since a decrease in sexual desire is considered to be a symptom associated with androgen decline, one would expect that lower (masculinized) 2D:4D would be associated with decreases in sexual desire. As discussed in Hypothesis 4, these unexpected results might be explained by estrogen's role in sexual desire.

It is interesting that a feminized finger digit ratio is associated with more severe hot flashes and vaginal dryness, as they are both symptoms that are directly linked to declining estrogen levels (Dennerstein et al., 2000; Kuh et al., 1997; Utian, 1972). Further, this relationship was not found in women who did not experience surgical menopause (see Hypothesis 5). As previously mentioned, women who experience oophorectomy tend to experience significantly more severe menopausal symptoms due to the abrupt decline in both estrogen and testosterone (North American Menopause Society, 2006). It is possible that a relationship between estrogen-related menopausal symptoms and 2D:4D was found with this population due to the abrupt decrease in estrogen that occurs after surgical menopause. Women who have a feminized finger digit ratio may be more sensitive to dramatic changes in estradiol, and therefore experience more severe symptoms when estrogen levels dramatically drop.

It is important to note that recent research has called into question the validity of using 2D:4D as a simplistic retrospective biomarker of prenatal androgen exposure (Medland et al., 2010). This study identified a gene that was strongly associated with 2D:4D, which influences both height and time of menarche in girls. These authors concluded that the relationship between 2D:4D and androgen exposure is likely more complex than was originally thought, and using

2D:4D as a biomarker for prenatal androgen exposure may not be an accurate method of measurement (Medland et al., 2010).

Supplementary Analyses

For Hypotheses 1, 2, and 3 the questionnaires that measured both an increase and decrease in negative symptoms were re-coded and re-analyzed to measure decreases in negative symptoms. However, this did not have much of an effect on the results as the PEQ, PPSQ, and the Oral Contraceptive Side Effects Questionnaire were not unique predictors in many of the original analyses. Although re-coding these scales changed the meaning of the research question (i.e., is a reduction in symptoms predictive of more severe menopausal symptoms), it did not change the influence of these variables. One change that did occur was that the PEQ physical symptom variable was no longer a unique predictor of menopausal physical symptoms. This makes sense as many women likely experience an increase in negative symptoms during pregnancy rather than a decrease. Further, it seems unlikely that a decrease in negative symptoms would predict an increase in symptoms at another reproductive event. The majority of research on this topic area has focused solely on increased negative mood and/or physical symptoms across the reproductive life span rather than a decrease. This is likely due to insufficient information about a decrease in symptoms during past reproductive events.

A further supplementary analysis was conducted to determine what extent neuroticism is predictive of reproductive distress. The NEO-FFI Neuroticism Subscale was significantly correlated with 16 of the 18 reproductive variables. Of the significant correlations, all were in the positive direction; such that increased scores on the neuroticism subscale were associated with higher symptom intensities. It is possible that those who are high in neuroticism are more likely to report higher distress and symptoms than those who are lower in neuroticism.

Pertaining to this study, those who are higher in neuroticism may report more menopausal symptoms due to a general tendency to endorse negative symptoms. However, this relationship between neuroticism and reported symptoms should remain constant across the lifespan, as neuroticism is a stable and enduring personality trait (Costa & McCrae, 1992). Unfortunately, it is hard to tease apart the influence that neuroticism has on symptom reporting and the symptom experience, as personality is an important contributor to how events are experienced.

Strengths and Limitations

This study has some important strengths, but also has some limitations. One strength of this study is the use of comprehensive questionnaires to measure past reproductive symptoms. Although there is some research investigating how menopausal symptoms are related to past physical and psychological symptoms, many of these studies use single items to measure past symptoms as well as menopausal symptoms. This study uses a reliable and valid measure of menopausal symptoms that tapped many domains of the menopausal experience. Further, all past reproductive symptoms were assessed using scales with many items and, for the most part, more than one subscale. Further, most of the subscales had excellent psychometric properties with Cronbach's alpha values exceeding .70. Another important strength of this study is that it explores a previously untouched area of hormonal sensitivity research. Most of the 2D:4D research focuses solely on how 2D:4D is may be related to androgen sensitivity. This study adds to the androgen sensitivity research by focusing on menopause, while most other studies to date have focused on other hormonal health problems. In addition, this study investigates a new area of interest: how 2D:4D may be related to estrogen sensitivity and how that may affect symptom experience across the lifespan. To date, the relationship between 2D:4D and estrogen sensitivity

has been discussed (Manning, 2008; Manning & Leinster, 2001; Brabin et al., 2008), although there have been no direct studies in the area. Although there is much work to be done in this area, this study serves as a starting point in determining if such a relationship exists.

This study has some limitations as well. Since the research design is retrospective, our results may have been influenced by retrospective bias or memory issues. For some women, it may be difficult to remember specific symptoms related to pregnancy and PMS if these events happened a very long time ago. Although a prospective design would have been ideal, it would be very costly and time-consuming to follow participants from menarche to menopause. Instead, we tried to eliminate retrospective bias and help with memory by continually reminding the participant of the time period to which the scales were referring. Another limitation was that we had to create some measures, as there were no published scales assessing symptoms experienced during pregnancy and physical symptoms experienced in the postpartum period. However, these questionnaires performed very well. Each of the subscales had excellent reliability, all above .85. A further limitation was the sample size for the 2D:4D analyses. Since 2D:4D research is a developing field of research with some conflicting findings, it would have been beneficial to increase our sample size to increase power. This is especially true for the analyses investigating 2D:4D and surgical menopause. Unfortunately, very few people from our 2D:4D sample had undergone oophorectomy. Similarly, our main analyses likely suffered from a loss of power due to the issue that not all women who filled out the questionnaires had been pregnant in the past or had taken oral contraceptives. Therefore, not all women could complete all of the questionnaires. Finally, the results of this study are correlational in nature, as this was not an experimental study. Therefore, no causal conclusions from these results can be made. This

study can serve to elucidate the relationships between variables, but careful manipulation of these variables is needed to draw causal inferences.

Directions for Future Study

Although this study was able to shed light on some of the relationships between the psychological and physical experiences experienced across the lifespan, there are still some unanswered questions, and a number of new research questions have emerged. It would be advantageous to further investigate the relationship between physical symptoms experienced in the postpartum period and during menopause. Although the hormonal profiles of both events are similar (a drastic drop in estrogen levels) and this and other studies (Gregory et al., 2000; Stewart & Boydell, 1993; Woods & Mitchell, 1996) have found a relationship between mood symptoms at both periods, our results suggest that physical symptoms during the postpartum period are not a unique predictor of physical menopausal symptoms. However, a correlational analysis did indicate that there is a relationship between these two variables. It may be beneficial to investigate this relationship in a prospective manner in order to reduce any error or memory issues. Similarly, it would be valuable to further clarify all of the findings in this study by using a prospective research design, although this task may be difficult.

Moreover, future research could be conducted to clarify why the severity of menopausal symptoms is associated with the severity of past reproductive symptoms and HRT seeking is associated with the severity of menopausal symptoms, but no relationship exists between HRT seeking and the severity of past symptoms. It would be interesting to investigate whether there are mediating or moderating factors that affect this relationship. For example, stage at menopause, attitudes towards HRT and/or the menopausal transition, and natural versus surgical menopause may all impact this relationship in some way.

Finally, one finding from this study that warrants future research relates to the fact that the mean 2D:4D in this sample is below 1.0, suggesting an overall "masculinized" population. As discussed above, there are a number of possible explanations for this. Past research has been conducted investigating the relationship between 2D:4D and circulating hormone levels (Hönekopp, 2007; Mayhew, 2007), but it would be beneficial to extend this research by looking more closely at the relationship between 2D:4D and declining estrogen and testosterone levels. This could be done in a prospective manner whereby researchers measure 2D:4D and gather hormonal assays from the premenopausal to postmenpausal period.

Conclusion

Overall, the purpose of this study was to identify women who may be at greater risk of suffering from physical and psychological symptoms during the menopausal period by elucidating the relationship between symptoms experienced during past reproductive events and those experienced during the menopausal transition. This was attempted by investigating physical symptoms, psychological symptoms, the role of seeking HRT, and the potential role of 2D:4D.

In terms of examining physical and psychological symptoms, this study attempted to build on past research by being more inclusive by including all potential times of hormonal change and using more comprehensive measures in assessing past reproductive symptoms. In general, it would seem as though physical and psychological symptoms experienced prior to menstruation tend to have the strongest relationship with the severity of menopausal symptoms. Symptoms experienced during pregnancy and during the postpartum period are associated with menopausal symptoms as well. Psychological symptoms experienced during puberty and when taking oral contraceptives are related to mood symptoms in menopause, although they are not the "best" predictors of these symptoms. Overall, negative affect prior to menstruation and/or during the

postpartum period are the best predictors of emotional symptoms during menopause. Pain, lack of concentration, water retention experienced prior to menstruation and physical symptoms experienced during pregnancy are the best predictors of physical symptoms experienced during menopause. Autonomic symptoms and water retention experienced prior to menstruation are the best predictors of menopausal vasomotor symptoms. Further, it would seem that past physical and psychological symptom experiences do not predict whether a woman will seek HRT during the menopausal transition.

This study also attempted to shed light on the relationship between 2D:4D and hormonal sensitivity in women in order to help identify women who may be more likely to suffer from more severe menopausal symptoms. Although some relationships between 2D:4D and menopausal symptoms were found, they were contrary to what was predicted and further research is needed to clarify the relationship between 2D:4D, hormonal sensitivity, and estrogen decline. If such a relationship exists, 2D:4D may serve as a non-invasive measure of hormonal sensitivity and a potential indicator of more severe menopausal symptoms. Despite the mixed findings of this study, this line of research is promising and worthy of further investigation.

The menopausal transition is a significant reproductive event for women ranging in age from 40 to 60, and it is often accompanied by significant physical and emotional distress. Ultimately, it would be beneficial for women to prepare for a difficult menopausal transition before it occurs, by planning potential HRT with their doctor, or learning about the symptoms that they may experience. This study is a step in the direction of trying to help women identify how past reproductive experiences may or may not influence or be related to their experiences during menopause, in order to make the menopausal transition a more comfortable one.

References

Albertazzi, P. (2005). Alternatives to estrogen to manage hot flushes. *Gynecological Endocrinology, 20* (1), 13-21. doi: 10.1080/09513590400020799

Altemus, M. (2010). Hormone-specific psychiatric disorders: Do they exist? *Archives of Women's Mental Health, 13,* 25-26. doi: 10.1007/s00737-009-0123-0

Alvarez, H.P. (2000). Grandmother hypothesis and primate life histories. *American Journal of Physical Anthropology, 113* (3), 435-450. doi: 10.1002/1096-8644(200011)113:3<435::AID-AJPA11>3.0.CO;2-O

Amato, P., & Marcus, D.M. (2003). Review of alternative therapies for treatment of menopausal symptoms. *Climacteric, 6, 278-284.* doi: 10.1080/713605428.

Amundsen, D.W., & Diers, C.J. (1970). The age of menopause in classical Greece and Rome. *Human Biology, 42* (1), 79-86.

Andrzej, M., & Diana, J. (2006). Premenstrual syndrome: From etiology to treatment. *Maturitas, 55* (suppl.) 47-54. doi: 10.1016/j.maturitas.2006.06.016

Arpels, J.C. (1996). The female brain hypoestrogenic continuum from the premenstrual syndrome to menopause: A hypothesis and review of supporting data. *The Journal of Reproductive Medicine, 41* (9), 633-639.

Austad, S.N. (1994). Menopause: An evolutionary perspective. *Experimental Gerontology, 29,* (3/4), 255-263. doi: 10.1016/0531-5565(94)90005-1

Bachmann, G.A. (1999). Vasomotor flushes in menopausal women. *American Journal of Obstetrics and Gynecology, 180* (3), 312-316. doi: 10.1016/S0002-9378(99)70725-8

Bailey, A.A., & Hurd, P.L. (2005). Depression in men is associated with more feminine finger length ratios. *Personality and Individual Differences, 39,* 829-836. doi: 10.1016/j.paid.2004.12.017

Baker, R. R., & Bellis, M.A. (2005). *Human sperm competition: Copulation, masturbation, and infidelity*. New York: Chapman & Hall.

Bammann, B.L., Coulam, C.B., Jiang, N.S. (1980). Total and free testosterone during pregnancy. *American Journal of Obstetrics and Gynecology, 137* (3), 293-298.

Banks, E. (2002). From dog's testicles to mares' urine: The origins and contemporary use of hormonal therapy for the menopause. *Feminist Review, 72,* 2-25. Retrieved from http://www.jstor.org/stable/1395878

Baron, T.H., Ramirez, B., & Richter, J.E. (1993). Gastrointestinal motility disorders during pregnancy. *Annals of Internal Medicine, 118* (5), 366-375.

Barrett, G., Pendry, E., Peacock, J., Victor, C., Thakar, R., & Manyonda, I. (1999). Women's sexuality after childbirth: A pilot study. *Archives of Sexual Behaviour, 28* (2), 179-191.

Becker, D., Orr, A., Weizman, A., Kotler, M., & Pines, A. (2007). Depressed mood through women's reproductive cycle: Correlation to mood at menopause. *Climacteric, 10* (1), 46-50. doi: 10.1080/13697130601174374

Berebaum, S.A., Bryk, K.K., Nowak, N., Quigley, C.A., & Moffat, S. (2009). Fingers as a marker of prenatal androgen exposure. *Endocrinology, 150* (11), 5119-5124. doi: 10.1210/en.2009-0774

Binfa, L., Castelo-Branco, C., Blümel, J.E., Cancelo, M.J., Bonilla, H., Muñoz, I., Vergara, V. ...Rios, R.V. (2004). Influence of psycho-social factors on climacteric symptoms. *Maturitas, 48,* 425-431. doi: 10.1016/j.maturitas.2003.11.002

Bird, J., & Oinonen, K. (2009). A prospective study of the relationship between oral contraceptive use and eating disorder symptoms. Unpublished dissertation proposal, Lakehead University, Thunder Bay, Ontario, Canada.

Bloch, M., Daly, R.C., & Rubinow, D.R. (2003). Endocrine factors in the etiology of postpartum depression. *Comprehensive Psychiatry, 44* (3), 234-246. doi: 10.1053/comp.2003.50014

Bloch, M., Schmidt, P.J., Danaceau, M., Murphy, J., Nieman, L., & Rubinow, D.R. (2000). Effects of gonadal steroids in women with a history of postpartum depression. *American Journal of Psychiatry, 157,* 924-930. doi: 10.1176/appi.ajp.157.6.924

Bloch, M., Rotenberg, N., Koren, D., & Klein, E. (2005). Risk factors associated with the development of postpartum mood disorders. *Journal of Affective Disorders, 88,* 9-18. doi: 10.1016/j.jad.2005.04.007

Bloch, M., Rotenberg, N., Koren, D., Klein, E. (2006). Risk factors for early postpartum depressive symptoms. *General Hospital Psychiatry, 28*, 3-8. doi: 10.1016/j.genhosppsych.2005.08.006

Bosworth, H.B., Bastian, L.A., Grambow, S.C., McBride, C.M., Skinner, C.S., Fish, L., Rimer, B.K.,...Siegler, I.C. (2005). Initiation and discontinuation of hormone therapy for menopausal symptoms: Results from a community sample. *Journal of Behavioral Medicine, 28* (1), 105-114. doi: 10.1007/s10865-005-2721-2

Brabin, L., Roberts, S.A., Farzaneh, F., Fairbrother, E., & Kitchener, H.C. (2008). The second to fourth digit (2D:4D) in women with and without human papillomavirus and cervical dysplasia. *American Journal of Human Biology, 20,* 337-341. doi: 10.1002/ajhb.20731

Brace, M., & McCauley, E. (1997). Oestrogens and psychological well-being. *Annals of Internal Health Medicine, 29,* 283-290. doi: 10.3109/07853899708999349

Braunstein, G.D. (2007). Management of female sexual dysfunction in postmenopausal women by testosterone administration: Safety issues and controversies. *Journal of Sexual Medicine, 4,* 859-866. doi: 10.1111/j.1743-6109.2007.00516.x

Breheny, M., & Stephens, C. (2001). The importance of attitudes in predicting hormone replacement therapy use in mid-aged women in a New Zealand community sample. *Women and Health, 34* (1), 29-43. doi: 10.1300/J013v34n01_03

Brown, H.L. (2007). Normal Pregnancy. *The Merck Manuals: Online Home Edition.* Retrieved January 24, 2009 from http://www.merck.com/mmhe/sec22/ch257/ch257a.html.

Brown, W.M., Hines, M., Fane, B.A., & Breedlove, S.M. (2002). Masculinized finger length patterns in human males and females with congenital adrenal hyperplasia. *Hormones and Behavior, 42,* 380-386. doi: 10.1006/hbeh.2002.1830

Burger, H.G., Dudley, E.C., Cui, J., Dennerstein, L., & Hopper, J.L. (2000). A prospective longitudinal study of serum testosterone, dehydroepiandrosterone sulphate, and sex hormone-binding globulin levels through the menopause transition. *The Journal of Clinical Endocrinology and Metabolism, 85* (8), 2832-2838. doi: 10.1210/jc.85.8.2832

Burger, H.G., Hailes, J., Menelaus, M., Nelson, J., Hudson, B. & Balazs, N. (1984). The management of persistent menopausal symptoms with oestradiol-testosterone implants: Clinical, lipid, and hormonal results. *Maturitas, 6,* 351-358. doi: 10.1016/0378-5122(84)90008-2

Burger, H.G., Hailes, J., Nelson, J., Menelaus, M. (1987). Effect of combined implants of estradiol and testosterone on libido in postmenopausal women. *British Medical Journal, 294*, 936-937. doi: 10.1136/bmj.294.6577.936

Burt, V.K., Altshuler, L.L., & Rasgon, N. (1998). Depressive symptoms in the perimenopause: Prevalence, assessment, and guidelines for treatment. *Harvard Review of Psychiatry, 6,* 121-132. doi: 10.3109/10673229809000320

Canadian Women's Health Network (2007). *Polycystic Ovary Syndrome (PCOS).* Retrieved April 29th, 2009 from http://www.cwhn.ca/resources/faq/pcos.html.

Casper, R.F., Graves, G.R., & Reid, R.L. (1987). Objective measurement of hot flushes associated with the premenstrual syndrome. *Fertility and Sterility, 47* (2), 341-344.

Cattrell, F.R., Vollenhoven, B.J., & Weston, G.C. (2005). Anatomical evidence for in utero androgen exposure in women with polycystic ovary syndrome. *Fertility and Sterility, 84* (6), 1689-1692. doi: 10.1016/j.fertnstert.2005.05.061

Cirigliano, M. (2007). Bioidentical hormone therapy: A review of the evidence. *Journal of Women's Health, 16* (5), 600-631. doi: 10.1089/jwh.2006.0311

Clare, A.W. (1985). Hormones, behaviour and the menstrual cycle. *Journal of Psychosomatic Research, 29* (3), 225-233. doi: 10.1016/0022-3999(85)90049-2

Clayton, A.H. (2008). Symptoms related to the menstrual cycle: Diagnosis, prevalence, and treatment. *Journal of Psychiatric Practice, 14* (1), 13-21. doi: 10.1097/01.pra.0000308491.54885.f8

Clayton, A.H., Keller, A.E., Leslie, C., & Evans, W. (2006). Exploratory study of premenstrual symptoms and serotonin variability. *Archives of Women's Mental Health, 9,* 51-57. doi: 10.1007/s00737-005-0118-4

Cleary-Goldman, J., Malone, F.D., Vidaver, J., Ball, R.H., Nyberg, D.A., Comstock, C.H., Saade, G.R.,...D'Alton, M. (2005). Impact of maternal age on obstetric outcome. *Obstetrics and Gynecology, 105,* 983-990.

Cohen, L.S., Soares, C.N., Vitonis, A.F., Otto, M.W., & Harlow, B.L. (2006). Risk for new onset of depression during the menopausal transition. *Archives of General Psychiatry, 63,* 385-390. doi: 10.1001/archpsyc.63.4.385

Collaborative Group on Hormonal Factors in Breast Cancer (1997). Breast cancer and hormone replacement therapy: Collaborative reanalysis of data from 51 epidemiological studies involving 52, 705 women with breast cancer and 108, 411 women without breast cancer. *Lancet, 350,* 1047-1059.

Collins, A., & Landgren, B. (1997). Psychosocial factors associated with the use of hormonal replacement therapy in a longitudinal follow-up of Swedish women. *Maturitas, 28* (1), 1-9. doi: 10.1016/S0378-5122(97)00063-7

Costa, P.T., & McCrae, R.R. (1992). *Revised NEO personality inventory (NEO-PR) and NEO five-factor inventory (NEO-FFI): professional manual.* Odessa, FL: Psychological Assessment Resources.

Coulam, C. (1986). Cyclic ovarian function and its neuroendocrine control. In D.N. Danforth & J.R. Scott (Eds.), *Obstetrics & gynecology,* (pp. 120-133). Philadelphia: J.B. Lippincott Company.

Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression: Development of the 10-item Edinburgh postnatal depression scale. *British Journal of Psychiatry, 150,* 782-786. doi: 10.1192/bjp.150.6.782

Csathó, A., Osvàth, A., Bicsàk, E., Karàdi, K., Manning, J., & Kàllai, J. (2003). Sex role identity related to the ratio of second to fourth digit length in women. *Biological Psychology, 62,* 147-156. doi: 10.1016/S0301-0511(02)00127-8

Davis, S. (1999). Androgen replacement in women: A commentary. *The Journal of Clinical*

Endocrinology and Metabolism, 84 (6), 1886-1891. doi: 10.1210/jc.84.6.1886

Davis, S., McCloud, P., Strauss, B., Burger, H. (1996). Testosterone enhances estradiol's effects on postmenopausal bone density and sexuality. *Maturitas, 21,* 227-236.

Davis, S.R. (2001). An external perspective on the report of the International Consensus Development Conference on Female Sexual Dysfunction: More work to be done. *Journal of Sex and Marital Therapy, 27* (2), 131-133. doi: 10.1080/00926230152051789

Davison, S.L., Bell, R., Donath, S., Montalo, J.G., Davis, S.R. (2005). Androgen levels in adult females: Changes with age, menopause, and oophorectomy. *The Journal of Clinical Endocrinology and Metabolism, 90* (7), 3847-3853. doi: 10.1210/jc.2005-0212

Deecher, D., Andree, T.H., Sloan, D., & Schechter, L.E. (2008). From menarche to menopause: Exploring the underlying biology of depression in women experiencing hormonal changes. *Psychoneuroendocrinology, 33,* 3-17. doi: 10.1016/j.psyneuen.2007.10.006

Dennerstein, L. (1996). Well-being, symptoms, and the menopausal transition. *Maturitas, 23,* 147-157.

Dennerstein, L., Dudley, E.C., Hopper, J.L., Guthrie, J.R., & Burger, H.G. (2000). A prospective population-based study of menopausal symptoms. *Obstetrics and Gynecology, 96,* 351-358. doi: 10.1016/S0029-7844(00)00930-3

De Paula, F.J.F., Soares, J.M., Haidar, M.A., De Lima, G. R., & Baracat, E.C. (2007). The benefits of androgens combined with hormone replacement therapy regarding to patients with postmenopausal sexual symptoms. *Maturitas, 56,* 69-77. doi: 10.1016/j.maturitas.2006.06.005

Derry, P.S. (2006). A lifespan biological model of menopause. *Sex Roles, 54,* 393-399. doi: 10.1007/s11199-006-9008-0

Douma, S.L., Husband, C., O'Donnell, M.E., Barwin, B.E., & Woodend, A.K. (2005). Estrogen-

related mood disorders: Reproductive life cycle factors. *Advances in Nursing Science, 28* (4), 364-375.

Feksi, A., Harris, B., Walker, R.F., Riad-Fahmy, D., & Newcombe, R.G. (1984). "Maternity Blues" and hormone levels in saliva. *Journal of Affective Disorders, 6,* 801-806. doi: 10.1016/S0165-0327(84)80013-0

Feld, J., Halbreich, U., & Karkun, S. (2005). The association of perimenopausal mood disorders with other reproductive-related disorders. *CNS Spectrums, 10* (6), 461-470.

Field, A. (2009). *Discovering statistics using SPSS.* Washington, DC: Sage.

Fisher, W.A., Sand, M., Lewis, W., & Boroditsky, R. (2000). Canadian menopause study-I: Understanding women's intentions to utilise hormone replacement therapy. *Maturitas, 37,* 1 -14. doi: doi:10.1016/S0378-5122(00)00163-8

Flores-Ramos, M., Heinze, G., & Silvestri-Tomassoni, R. (2010). Association between depressive symptoms and reproductive variables in a group of perimenopausal women attending a menopause clinic in México City. *Archives of Women's Mental Health, 13,* 99-105. doi: 10.1007/s00737-009-0107-0

Freedman, M. (2002). Quality of life and menopause: The role of estrogen. *Journal of Women's Health, 11* (8), 703-718. doi: 10.1089/15409990260363661

Freeman, E.W., Sammel, M.D., Lin, H., & Nelson, D.B. (2006). Associations of hormones and menopausal status with depressed mood in women with no history of depression. *Archives of General Psychiatry, 63,* 375-382. doi: 10.1001/archpsyc.63.4.375

Freeman, E.W., Sammel, M.D., Rinaudo, P.J., & Sheng, L. (2004). Premenstrual syndrome as a predictor of menopausal symptoms. *The American College of Obstetrics and Gynecologists, 103* (5), 960-966. doi: 10.1097/01.AOG.00124804.81095.7f

Frye, C.A. (2006). An overview of oral contraceptives: Mechanisms of action and clinical use. *Neurology, 66* (suppl. 3), 29-36.

Galis, F., Ten Broek, C.M.A., Van Dongen, S., & Wijnaendts, L.C.D. (2010). Sexual dimorphism in the prenatal digit ratio (2D:4D). *Archives of Sex Behaviour, 39,* 57-62. doi: 10.1007/s10508-009-9485-7

Glover, V., & Kammerer, M. (2004). The biology and pathophysiology of peripartum psychiatric disorders. *Primary Psychiatry, 11,* 37-41.

Graham, C.A., Bancroft, J., Doll, H.A., Greco, T., & Tanner, A. (2007). Does oral contraceptive-induced reduction in free testosterone adversely affect the sexuality or mood of women? *Psychoneuroendocrinology, 32,* 246-255. doi: 10.1016/j.psyneuen.2006.12.011

Graziotinn, A. (2000). Libido: The biologic scenario. *Maturitas, 34* (suppl. 1), s9-s16.

Greco, T., Graham, C.A., Bancroft, J., Tanner, A., & Doll, H.A. (2007). The effects of oral contraceptives on androgen levels and their relevance to premenstrual mood and sexual interest: A comparison of two triphasic formulations containing norgestimate and either 35 or 25 μg of ethinyl estradiol. *Contraception, 76,* 8-17. doi: 10.1016/j.contraception.2007.04.002

Gregory, R.J., Masand, P.S., & Yohai, N.H. (2000). Depression across the reproductive life life cycle: Correlations between events. *The Primary Care Companion to the Journal of Clinical Psychiatry, 2* (4), 127-129. doi: 10.4088/PCC.v02n0404

Guthrie, J.R., Dennerstein, L., Hopper, J.L., & Burger, H.G. (1996). Hot flushes, menopausal status, and hormone levels in a population-based sample of mid-life women. *Obstetrics*

and Gynecology, 88 (3), 437-442. doi: 10.1097/01.GME.0000155200.80687.BE

Hahn, P.M., Wong, J., & Reid, R.L. (1998). Menopausal-like hot flashes reported in women of reproductive age. *Fertility and Sterility, 70* (5), 913-918. doi: 10.1016/S0015-0282(98)00281-7

Halbreich, U., & Monacelli, E. (2004). Some clues to the etiology of premenstrual syndrome/ premenstrual dysphoric disorder. *Primary Psychiatry, 11* (12), 33-40.

Hammarbäck, S., Damber, J.E., & Bäckström, T. (1989). Relationship between symptom severity and hormone changes in women with premenstrual syndrome. *Journal of Endocrinology and Metabolism, 68,* 125-130. doi: 10.1210/jcem-68-1-125

Hampson, E., Ellis, C.L., & Tenk, C.M. (2008). On the relationship between 2D:4D and sex-dimorphic personality traits. *Archives of Sex Behavior, 37,* 133-144. doi: 10.1007/s10508-007-9263-3

Harris, B., Lovett, L., Newcombe, R.G., Read, G.F., Walker, R., & Riad-Fahmy, D. (1994). Maternity blues and major endocrine changes: Cardiff puerperal mood and hormone study II. *British Medical Journal, 308* (6934), 949-953. doi: 10.1016/0020-7292(94)90590-8

Haywood, A., Slade, P., & King, H. (2007). Is there evidence of an association between postnatal distress and premenstrual symptoms? *Journal of Afffective Disorders, 99,* 241-245. doi: 10.1016/j.jad.2006.08.024

Helle, S., & Laaksonen, T. (2009). Latitudinal gradient in 2D:4D. *Archives of Sex Behavior, 38,* 1-3. doi: 10.1007/s10508-008-9419-9

Hilditch, J.R., Lewis, J., Peter, A., van Maris, B., Ross, A., Franssen, E., Guyatt, G.H...Dunn, E. (1996). A menopause-specific quality of life questionnaire: Development and psychometric properties. *Maturitas, 24,* 161-165.

Hollander, L.E., Freeman, E.W., Sammel, M.D., Berlin, J.A., Grisso, J.A., & Battistini, M. (2001). Sleep quality, estradiol levels, and behavioral factors in late reproductive age. women. *Obstetrics and Gynecology, 98*, 391-397. doi: 10.1016/S0029-7844(01)01485-5

Hönekopp, J., Bartholdt, L., Beier, L., Liebert, A. (2007). Second to fourth digit length ratio (2D:4D) and adult sex hormone levels: New data and a meta-analytic review. *Psychoneuroendocrinology, 32,* 313-321. doi: 10.1016/j.psyneuen.2007.01.007

Hook, E.B., Cross, P.K. & Schreinemachers, D.M. (1983). Chromosomal abnormality rates at amniocentesis and in live-born infants. *Journal of the American Medical Association, 249*, 2034-2038. doi: 10.1001/jama.249.15.2034

Hunter, M.S. (1992). The South East England longitudinal study of the climacteric and postmenopause. *Maturitas, 14* (2), 117-126. doi: 10.1016/0378-5122(92)90004-N

Hunter, M.S. (1993). Predictors of menopausal symptoms: Psychosocial aspects. *Baillière's Clinical Endocrinology and Metabolism, 7* (1), 33-45. doi: 10.1016/S0950-351X(05)80269-1

Huntley, A.L., Ernst, E. (2003). A systematic review of herbal medicinal products for the treatment of menopausal symptoms. *Menopause: The Journal of the North American Menopause Society, 10* (5), 465-476. doi: 10.1097/01.GME.0000058147.24036.B0

Jackson, D.N. (1984). *Personality research form manual.* Port Huron, MI: Research Psychologist Press.

Jarva, J.A., & Oinonen, K.A. (2007). Do oral contraceptives act as mood stabilizers? Evidence of positive affect stabilization. *Archives of Women's Mental Health, 10* (5), 225-234. doi: 10.1007/s00737-007-0197-5

Johnson, S.R. (2004). The epidemiology of premenstrual syndrome. *Primary Psychiatry, 11* (12), 27-32.

Joseph, K.S., Allen, A.C., Dodds, L., Turner, L.A., Scott, H., & Liston, R. (2005).The perinatal effects of delayed childbearing. *Obstetrics and Gynecology, 105*, 1410-1418.

Katchadourian, H (1977). The biology of adolescence. San Francisco: W.H. Freeman and Company.

Kemper, C.J., & Schwerdtfeger, A. (2009). Comparing indirect methods of digit ratio (2D:4D) measurement. American Journal of Human Biology, *21*, 188-191. doi: 10.1002/ajhb.20843

Kessler, R.C., McGonagle, K.A., Nelson, C.B., Hughes, M., Swartz, M., & Blazer, D.G. (1994). Sex and depression in the National Comorbidity Survey II: Cohort effects. *Journal of Affective Disorders, 30* (1), 15-26. doi: 10.1016/0165-0327(94)90147-3

Kessler, R.C., & Walters, E.F. (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression and Anxiety, 7,* 3-14. doi: 10.1002/(SICI)1520-6394(1998)7:1<3::AID-DA2>3.0.CO;2-F

Kiesner, J. (2009). Physical characteristics of the menstrual cycle and premenstrual depressive symptoms. *Psychological Science, 20* (6), 763-770. doi: 10.1111/j.1467-9280.2009.02358.x

Kronenberg, F. (1990). Hot flashes: Epidemiology and physiology. In M. Flint, F. Kronenberg, & W. Utian (Eds.), *Multidisciplinary perspectives on menopause* (pp.52-85). New York: New York Academy of Sciences.

Kuh, D.H., Wadsworth, M., Hardy, R. (1997). Women's health in midlife: The influence of the menopause, social factors and health earlier in life. *British Journal of Obstetrics and Gynaecology, 104,* 923-933.

Kuhle, B.X. (2007). An evolutionary perspective on the origin and ontogeny of menopause. *Maturitas, 57*, 329-337. doi:10.1016/j.maturitas.2007.04.004

Laughlin, G.A., Barrett-Connor, E., Kritz-Silverstein, D., & von Mühlen, D. (2000). Hysterectomy, oophorectomy, and endogenous sex hormone levels in older women: The Rancho Bernardo study. *The Journal of Clinical Endocrinology and Metabolism, 85* (2), 645-651. Retrieved from www.jcem.endojournals.org

Leidy, L.E. (1996). Symptoms of menopause in relation to the timing of reproductive events and past menstrual experience. *American Journal of Human Biology, 8,* 761-769.

Lewinsohn, P.M., Rohde, P., & Seeley, J.R. (1998). Major depressive disorder in older adolescents: Prevalence, risk factors, and clinical implications. *Clinical Psychology Review, 18* (7), 765-794. doi: 10.1016/S0272-7358(98)00010-5

Lindh-Åstrand, L., Brynhildsen, J. Hoffmann, M., Liffner, S., & Hammar, M. (2007). Attitudes towards the menopause and hormone therapy over the turn of the century. *Maturitas, 56,* 12-20.

Lutchmaya, S., Baron-Cohen, S., Raggatt, P., Knickmeyer, R., & Manning, J.T. (2004). 2nd to 4th digit ratios, fetal testosterone and estradiol. *Early Human Development, 77,* 23-28. doi: 10.1016/j.earlhumdev.2003.12.002

MacLennan, A., Lester, S., & Moore, V. (2001). Oral estrogen replacement therapy versus placebo for hot flushes: A systematic review. *Climacteric, 4,* 58-74.

Malas, M.A., Dogan, S., Evcil, E.H., & Desdicioglu, K. (2006). Fetal development of the hand, digits and digit ratio (2D:4D). *Early Human Development, 82,* 469-475. doi: 10.1016/j.earlhumdev.2005.12.002

Manning, J. (2008). *The finger ratio. London: Faber and Faber.*

Manning, J.T., Bundred, P.E., Newton, D.J., & Flanagan, B.F. (2003). The second to fourth digit ratio and variation in the androgen receptor gene. *Evolution and Human Behaviour, 24,* 399-405. doi: 10.1016/S1090-5138(03)00052-7

Manning, J.T., & Leinster, S.J. (2001). The ratio of 2nd to 4th digit length and age at presentation of breast cancer: A link with prenatal oestrogen? *The Breast, 10,* 355-357. doi: 10.1054/brst.2001.0296

Manning, J.T., Scutt, D., Wilson, J., & Lewis-Jones, D.I. (1998). The ratio of 2nd to 4th digit length: A predictor of sperm numbers and concentrations of testosterone, lutenizing hormone and oestrogen. *Human Reproduction, 13* (11), 3000-3004. doi: 10.1093/humrep/13.11.3000

Manning, J.T., Trivers, R.L., Thornhill, R., & Singh, D. (2000). The 2nd to 4th digit ratio and asymmetry of hand performance in Jamaican children. *Laterality, 5,* 121-132.

Matchock, R.L. (2008). Low digit ratio (2D:4D) is associated with delayed menarche. *American Journal of Human Biology, 20,* 487-489. doi: 10.1002/ajhb.20763

Mayhew, T.M., Gillam, L., McDonald, R., & Ebling, F.J.P. (2007). Human 2D (index) and 4D (ring) digit lengths: their variation and relationships during the menstrual cycle. *Journal of Anatomy, 211,* 630-638. doi: 10.1111/j.1469-7580.2007.00801.x

McKinlay, S.J. (1996). The normal menopause transition: An overview. *Maturitas, 23,* 137-145. doi: 10.1016/0378-5122(95)00985-X

Medland, S.E., Zayats, T., Glaser, B., Nyholt, D.R., Gordon, S.D., Wright, M.J., Montgomery, G.W. ... Evans, D.M. (2010). A variant in LIN28B is associated with 2D:4D finger-length ratio, a putative retrospective biomarker of prenatal testosterone exposure. *The American Journal of Human Genetics, 86,* 519 – 525. doi: 10.1016/j.ajhg.2010.02.017.

Mesiano, S., & Jaffe, R.B. (2004). The endocrinology of human pregnancy and fetal-placental neuroendocrine development. In J.F. Strauss & R.L. Barbieri (Eds.), *Yen and Jaffe's reproductive endocrinology: Physiology, pathophysiology, and clinical management* (5th ed., pp. 327-366). Philadelphia, PA: Elsevier Saunders.

Miller, L.J. (2002). Postpartum depression. *Journal of the American Medical Association, 287* (6), 762-765. doi: 10.1001/jama.287.6.762

Moos, R.H. (1986). *Menstrual Distress Questionnaire Manual.* Los Angeles: Western Psychological Services.

Morley, J.E., & Perry, H.M. (2003). Androgens and women at the menopause and beyond. *Journal of Gerontology, 58* (5), 409-416.

Morse, C.A., Dudley, J., & Dennerstein, L. (1998). Relationships between premenstrual complaints and perimenopausal experiences. *Journal of Psychosomatic Obstetrics and Gynecology, 19,* 182-191. doi: 10.3109/01674829809025696

Nelson, H.D. (2004). Commonly used types of postmenopausal estrogen for treatment of hot flashes: Scientific review. *Journal of the American Medical Association, 291* (13), 1610-1620. doi: 10.1001/jama.291.13.1610

Nelson, H.D. (2008). Menopause. *The Lancet, 371,* 760-770.

Norman, A.W., & Litwack, G. (1997). Estrogens and progestins. In *Hormones* (2nd ed., pp.361-386). Toronto, ON: Academic Press. doi: 10.1016/B978-012521441-4/50014-6

North American Menopause Society (2006). *The menopause guidebook.* Retrieved November 19, 2008 from http://www.menopause.org/edumaterials/guidebook/guidebook.aspx.

O'Hara, M.W., Schlechte, J.A., Lewis, D.A., & Varner, M.W. (1991). Controlled prospective study of postpartum mood disorders: Psychological, environmental, and hormonal variables. *Journal of Abnormal Psychology, 100* (1), 63-73. doi: 10.1037/0021-843X.100.1.63

Oinonen, K.A. (2009). Putting a finger on potential predictors of oral contraceptive side effects: 2D:4D and middle-phalangeal hair. *Psychoneuroendocrinology, 34* (5), 713-726. doi: 10.1016/j.psyneuen.2008.11.009

Oinonen, K.A., & Mazmanian, D. (2002). To what extent do oral contraceptives influence mood and affect? *Journal of Affective Disorders, 70,* 229-240. doi: 10.1016/S0165-0327(01)00356-1

Oldenhave, A., Jaszmann, L.J.B., Everaerd, W.T., Haspels, A.A. (1993). Hysterectomized women with ovarian conservation report more severe climacteric complaints than do normal climacteric women of similar age. *American Journal of Obstetrics and Gynecology, 168,* 765-771.

Olutunmbi, Y., Paley, K., & English, J.C. (2008). Adolescent female acne: Etiology and management. *Journal of Pediatric and Adolescent Gynecology, 21,* 171-176. doi: 10.1016/j.jpag.2007.07.004

Ostovich, J.M., & Sabini, J. (2004). How are sociosexuality, sex drive, and lifetime number of sexual partners related? *Personality and Social Psychology Bulletin, 30* (10), 1255-1266. doi: 10.1177/0146167204264754

Øverlie, I., Moen, M.H., Holte, A., & Finset, A. (2002). Androgens and estrogens in relation to hot flushes during the menopausal transition. *Maturitas, 41,* 69-77. doi: 10.1016/S0378-5122(01)00256-0

Øverlie, I., Moen, M., Morkrid, L., Skjæraasen, J.S., & Holte, A. (1999). The endocrine transition around menopause: A five years prospective study with profiles of gonadtopines, estrogens, androgens, and SHBG among healthy women. *Activa Obstetricia Et Gynecologica Scandinavica, 78* (7), 642-647. doi: 10.1034/j.1600-0412.1999.780714.x

Packer, C., Tatar, M., & Collins, A. (1998). Reproductive cessation in female mammals. *Nature, 392*, 807-811.

Panzer, C., Wise, S., Fantina, G., Kang, D., Munarriz, R., Guay, A. ... Goldstein, I. (2006). Impact of oral contraceptives on sex hormone-binding globulin and androgen levels: a retrospective study in women with sexual dysfunction. *The Journal of Sexual Medicine, 3,* 104-113. doi: 10.1111/j.1743-6109.2005.00198.x

Pavard, S., Metcalf, J.E., & Heyer, E. (2008). Senescence of reproduction may explain adaptive menopause in humans: A test of the "mother" hypothesis. *American Journal of Physical Anthropology, 136,* 194-203. doi: 10.1002/ajpa.20794

Payne, J.L., Palmer, J.T., Jofee, H. (2009). A reproductive subtype of depression: Conceptualizing models and moving toward etiology. *Harvard Review of Psychiatry, 17* (2), 72-86. doi: 10.1080/10673220902899706

Payne, J.L., Roy, P.S., Murphy-Eberenz, K., Weismann, M.M., Swartz, K.L., McInnis, M.G., Nwulia, E. ... Potash, J.B. (2007). Reproductive cycle-associated mood symptoms in women with major depression and bipolar disorder. *Journal of Affective Disorders, 99,* 221-229. doi: 10.1016/j.jad.2006.08.013

Poromaa, I.S., Smith, S., & Gulinello, M. (2003). GABA receptors, progesterone and premenstrual dysphoric disorder. *Archives of Women's Mental Health, 6,* 23-41. doi: 10.1007/s00737-002-0147-1

Prior, J.C. (1998). Perimenopause: The complex endocrinology of the menopausal transition. *Endocrine Reviews, 19* (4), 397-428. doi: 10.1210/er.19.4.397

Rasgon, N., Shelton, S., & Halbreich, U. (2005). Perimenopausal mood disorders: Epidemiology and Phenomenology. *CNS Spectrums, 10* (6), 471-478.

Richards, M., Rubinow, D.R., Daly, R.C., & Schmidt, P.J. (2006). Premenstrual symptoms and perimenopausal depression. *American Journal of Psychiatry, 163,* 133-137. Retrieved from http://ajp.psychiatryonline.org

Robinson, G. (2001). Psychotic and mood disorders associated with the perimenopausal period: Epidemiology, aetiology, and management. *CNS Drugs, 15* (3), 175-184. doi: 10.2165/00023210-200115030-00002

Rosenberg, M.J., & Waugh, M.S. (1998). Oral contraceptive discontinuation: A prospective evaluation of frequency and reasons. *American Journal of Obstetrics and Gynecology, 179,* 577-582. doi: 10.1016/S0002-9378(98)70047-X

Rousseau, M.E. (2001). Evidence-based practice in women's health: Hormone therapy for women at menopause. *Journal of Midwifery and Women's Health, 46* (3), 167-180. doi: 10.1016/S1526-9523(01)00116-7

Sanders, S.A., Graham, C.A., Bass, J.L., & Bancroft, J. (2001). A prospective study of the effects of oral contraceptives on sexuality and well-being and their relationship to discontinuation. *Contraception, 64,* 51-58. doi: 10.1016/S0010-7824(01)00218-9

Sarrel, P.M. (2002). Androgen deficiency: Menopause and estrogen-related factors. *Fertility and Sterility, 77* (4), 63-67.

Sarrel, P.M., Dobay, B., Wiita, B. (1998). Estrogen and estrogen-androgen replacement in postmenopausal women dissatisfied with estrogen-only therapy: Sexual behaviour and neuroendocrine responses. *Journal of Reproductive Medicine, 43*, 847-856.

Schapira, M.M., Gilligan, M., McAuliffe, T.L., & Nattinger, A.B. (2004). Menopausal hormone therapy decisions: Insights from a multi-attribute model. *Patient Education and Counseling, 52,* 89-95. doi: 10.1016/S0738-3991(02)00266-5

Schmidt, P.J., Roca, C.A., Bloch, M., & Rubinow, D.R. (1997). The perimenopause and affective disorders. *Seminars in Reproductive Endocrinology, 15*, 91-100. doi: 10.1055/s-2008-1067971

Schwartz, E. (2002). *The hormone solution: Naturally alleviate symptoms of hormonal imbalance from adolescence through menopause.* New York: Warner Books.

Seippel, L., & Backström, T. (1998). Luteal phase estradiol relates to symptom severity between patients with premenstrual syndrome. *Journal of Endocrinology and Metabolism, 83* (6), 1988-1992.

Sherman, P.W. (1998). Animal behaviour: The evolution of menopause. *Nature,* 392, 759-761.

Shifren, J.L., Braunstein, G.D., Simon, J.A., Casson, P.R., Buster, J.E., Redmond, G.P. Burki, R.E.,...Daughtery, C.A. (2000). Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *The New England Journal of Medicine,*

343 (10), 682-688. doi: 10.1056/NEJM200009073431002

Silber, S.J. (1991). Effect of age on male fertility. *Seminars in Reproductive Endocrinology,* 9, (3). Retrieved November 19, 2008 from http://www.infertile.com/inthenew/sci/maleage.htm

Simon, J.A., Klaiber, E., Wiita, B., Yang, H.W., & Artis, A. (1996). Double-blind comparison of two doses of estrogen and estrogen-androgen therapy in naturally postmenopausal women: Neuroendocrine, psychological, and psychosomatic effects. *Fertility and Sterility, 66,*

Smith, K.E., & Judd, H.L. (1994). Menopause and postmenopause. In A.H. Decherney & M.L. Pernoll (Eds.), *Current obstetric and gynecologic diagnosis and treatment* (pp. 1030-1050). Toronto, ON: Prentice Hall of Canada, Inc.

Soares, C.N., Almeida, O.P., Joffe, H., & Cohen, L.S. (2004). Efficacy of estradiol for the treatment of depressive disorders in perimenopausal women: A double-blind, randomized, placebo-controlled trial. *Archives of General Psychitary, 58,* 529-534.

Soares, C.N., Prouty, J., Born, L., & Steiner, M. (2005). Treatment of menopause-related mood disturbances. *CNS Spectrums, 10* (6), 489-497.

Soares, C.N., & Zitek, B. (2008). Reproductive hormone sensitivity and risk for depression across the female life cycle: A continuum of vulnerability? *Journal of Psychiatry and Neuroscience, 33* (4), 331-343.

Somerset, W., Newport, D.J., Ragan, K., & Stowe, Z.N. (2006). Depressive disorders in women: From menarche to beyond the menopause. In C.L.M. Keyes & S.H. Goodman (Eds.), *Women and depression: A handbook for the social, behavioural, and biomedical sciences* (pp.62-88). New York: Cambridge University Press.

Soules, M.R., Sherman, S., Parrott, E., Rebar, R., Santoro, N., Utian, W., & Woods, N. (2001). Executive summary: Stages of reproductive aging workshop (STRAW). *Fertility and Sterility, 76* (5), 874-878.

Spek, V., Nyklíček, I., Cuijpers, P. & Pop, V. (2008). Internet administration of the Edinburgh Depression Scale. *Journal of Affective Disorders, 106,* 301-305. doi: 10.1016/j.jad.2007.07.003

Speroff, L. (2005). Alternative therapies for postmenopausal women. *International Journal of Fertility and Menopausal Studies, 50* (3), 101-114.

Speroff, L., & Fritz, M.A., (2005). Clinical gynecologic endocrinology and infertility. Philadelphia: Lippincott Williams & Wilkins.

Statistics Canada. (2008). *Deaths* (Catalogue no. 84F0211XIE). Ottawa, ON: Statistics Canada. Retrieved November 19, 2008 from http://www.statscan.ca.

Steinberg, E.M., Rubinow, D.R., Bartko, J.J., Fortinsky, P.M., Haq, N., Thompson, K. & Schmidt, P.J. (2008). A cross-sectional evaluation of perimenopausal depression. *Journal of Clinical Psychiatry, 69* (6), 973-980. doi: 10.4088/JCP.v69n0614

Steiner, M., Dunn, E., & Born, L. (2003). Hormones and mood: From menarche to menopause and beyond. *Journal of Affective Disorders, 74,* 67-83. doi: 10.1016 /S0165-0327(02)00432-9

Stewart, D.E., & Boydell, K.M. (1993). Psychologic distress during menopause: Associations across the reproductive life cycle. *International Journal of Psychiatry in Medicine, 23* (2), 157-162.

Striegel-Moore, R.H., Goldman, S.L., Garvin, V., & Rodin, J. (1996). A prospective study of somatic and emotional symptoms of pregnancy. *Psychology of Women Quarterly, 20,*

393-408. doi: 10.1111/j.1471-6402.1996.tb00307.x

Studd, J. & Panay, N. (2004). Hormones and depression in women. *Climacteric, 7,* 338-346. doi: 10.1016/S0020-7292(09)60327-1

Sugawara, M., Toda, M.A., Shima, S., Mukai, T., Sakakura, K., Kitamura, T. (1997). Premenstrual mood changes and maternal mental health in pregnancy and the postpartum period. *Journal of Clinical Psychology, 53* (3), 225-232. doi: 10.1002/(SICI)1097-4679(199704)53:3<225::AID-JCLP5>3.0.CO;2-Q

Swartzman, L.C., Edelberg, R., & Kemmann, E. (1990). Impact of stress on objectively recorded menopausal hot flushes and on flush report bias. *Health Psychology, 9*(5), 529-545. doi: 10.1037//0278-6133.9.5.529

Swartzman, L.C., & Leiblum, S.R. (1987). Changing perspectives on the menopause. *Journal of Psychosomatic Obstetrics and Gynaecology, 6,* 11-24. doi: 10.3109/01674828709023857

Tabachnick, B.G., & Fidell, L.S. (2007). *Using multivariate statistics* (5th ed.). Toronto: Allyn and Bacon.

Taffe, J.R., & Dennerstein, L. (2002). Menstrual patterns leading to the final menstrual period. *Menopause: The Journal of the North American Menopause Society,* 9 (1), 32-40. doi: 10.1097/00042192-200201000-00006

Trichopoulos, D. (1990). Hypothesis: Does breast cancer originate in utero? *The Lancet, 335* (8695), 939-940.

Utian, W.H. (1972). True clinical features of postmenopause and oophorectomy, and their response to oestrogen therapy. *South African Medical Journal, 46*, 732-737.

Utian, W.H. (1997). Menopause – A modern perspective from a controversial history.

Maturitas, 26, 73-82.

Van Dongen, S. (2009). Second to fourth digit ratio in relation to age, BMI and life history in a population of young adults: a set of unexpected results. *Journal of Negative Results: Ecology and Evolutionary Biology, 6,* 1-7.

Voracek, M., Offenmüller, D., & Dressler, S.G. (2008). Sex differences in directional asymmetry of digit length and its effects on sex differences in digit ratio (2D:4D). *Perceptual and Motor Skills, 107,* 576-586. doi: 10.2466/PMS.107.2.576-586

Wang, S.J., Fuh, J.L., Lu, S.R., Juang, K.D., Wang, P.H. (2002). Migraine prevalence during menopausal transition. *Headache, 43,* 470-478. doi: 10.1046/j.1526-4610.2003.03092.x

Warren, M.P., Shortle, B., Dominguez, J.E. (2002). Use of alternative therapies in menopause. *Best Practice and Research Clinical Obstetrics and Gynecology, 16* (3), 411-448. doi: 10.1053/beog.2002.0290

Woods, N.F., & Mitchell, E.S. (1996). Patterns of depressed mood in midlife women: Observations from the Seattle Midlife Women's Health Study. *Research in Nursing and Health, 19,* 111-123. doi: 10.1002/(SICI)1098-240X(199604)19:2<111::AID-NUR3>3.0.CO;2-P

World Health Organization Scientific Group. (1981). *Research on the menopause* (WHO Report Series 670). Geneva: World Health Organization.

Writing Group for the Women's Health Initiative. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. *Journal of the American Medical Association, 288* (3), 321-333.

Wylie-Rosett, J. (2005). Menopause, micronutrients, and hormone therapy. *American Journal of Clinical Nutrition, 81* (suppl.), 1223-1231.

Yonkers, K.A., O'Brien, P.M., & Eriksson, E. (2008). Premenstrual syndrome. *The Lancet, 371,* 1200-1210.

Zöllner, Y.F., Acquadro, C., & Schaefer, M. (2005). Literature review of instruments to assess health-related quality of life during and after menopause. *Quality of Life Research, 14,* 309-327. doi: 10.1007/s11136-004-0688-z

Appendix A: General Information Questionnaire

1) Month of Birth: _____ **2) Year of Birth:** _____

3) Height: _____ **4) Weight:** _____

5) Marital status:

Married/common-law	_____	Single	_____
Divorced/separated	_____	Widowed	_____

6) What is your ethnic background?

Caucasian/White	_____	Middle Eastern	_____
African-Canadian/Black	_____	East Indian	_____
Native-Canadian/Aboriginal	_____	European	_____
Hispanic/Latino	_____	Other (please specify)	_____
Asian	_____		

7) Are you currently employed? Yes _____ No _____ Retired _____

8) If you are employed, do you work: Full Time _____ Part Time _____

9) What is the highest level of education that you have achieved?

Some elementary school	_____	College diploma	_____
Elementary school	_____	Some university	_____
Some high school	_____	Undergraduate degree	_____
High school diploma	_____	Master's degree	_____
Some college	_____	Doctorate degree	_____

10) At what age did your menopausal transition begin (i.e., variable menstrual cycle length, at least 7 days different than normal)? _____

11) The following scale outlines different stages of the menopausal transition. Please circle the number that best corresponds where you <u>currently</u> fall on this continuum.

0	1	2	3	4
Early menopause	Late menopause	Early Postmenopause	Postmenopause	Late Postmenopause
(variable menstrual cycle length – at least 7 days different than normal)	(at least 2 skipped menstrual periods in a row)	(at least one year since your last menstrual period)	(1 to 4 years since your last menstrual period)	(over 4 years since your last menstrual period)

12) If you are currently postmenopausal (i.e., 12 months without a menstrual period), approximately how long did your menopausal transition last?

_____ years _____ months

13) Have you had surgery to have one or both of your ovaries removed?

No	_____
I don't know	_____
Yes, unknown number were taken out	_____
Yes, part of an ovary was taken out	_____
Yes, one was removed	_____
Yes, both were removed	_____

14) How many times have you been pregnant? _____

15) How many children have you given birth to in your lifetime? (as opposed to adopted or foster children)? _____

16) How many stillbirths have you had in your lifetime? _____

17) How many spontaneous miscarriages have you had in your lifetime? _____

18) How many tubal pregnancies have you had? _____

19) How many C-sections have you had? _____

20) If you have ever given birth, did you experience any type of negative mood change during the postpartum period?

Yes No Unsure

21) If yes, were you formally diagnosed with postpartum depression?

Yes No

22) If yes, did you receive any treatment for your negative mood change?

Yes No

23) How many different sexual partners have you had in your entire lifetime?_____

24) Prior to menopause, how often did you experience sexual desire?

Never	Less than once a month	About once a month	About once a week	Several times a week	Daily	Several times a day
0	1	2	3	4	5	6

25) Prior to menopause, how often did you orgasm in an average month?

Never	One to two times	About once per week	Several times a week	Daily	Several times a day
0	1	2	3	4	5

26) Prior to menopause, how often did you masturbate in an average month?

Never	One to two times	About once per week	Several times a week	Daily	Several times a day
0	1	2	3	4	5

27) How would you compare your current level of sex drive with the average person of your gender and age?

Very much lower						Very much higher
0	1	2	3	4	5	6

28) Prior to menopause, how would you rate your sex drive?

Absent	Very low	Somewhat low	Neutral	Somewhat high	Very high
0	1	2	3	4	5

29) Have you had a past episode of depression not associated with childbirth (prior to menopause)?

Yes No

30) If YES, how many depressive episodes? _____

31) If YES, at what age did the depressive episode(s) occur? _____

32) If YES, what kind of treatment did you receive? _____

33) Did you use anti-depressant medication prior to menopause?

Yes No

34) Did you ever take Hormone Replacement Medication prior to menopause (other than oral contraceptives)?

Yes No

35) Prior to your menopausal transition, did you have a tubal ligation (i.e. have your "tubes tied"?

Yes No

36) Prior to your menopausal transition, did you have any reproductive surgery? (i.e. Hysterectomy, cyst removal from your ovaries, etc.)

Yes No

37) Prior to your menopausal transition, did you have any surgery that would affect the endocrine system? (i.e., adrenal glands, pituitary gland, thyroid gland?)

Yes No

38) Have you ever been diagnosed with Polycystic Ovarian Syndrome?
□

Yes No

39) Have you experienced any of the following prior to menopause:

Infrequent menstruation (fewer than 8 times per year) _____
Long, coarse hair on your face, chest, lower abdomen, back, or upper arms _____
Acne _____
Thinning/Loss of Hair _____
Infertility _____
Skin tags (usually found on the neck or armpit area) _____

40) Have you ever been diagnosed with breast cancer?

Yes No

41) Have you ever been diagnosed with ovarian cancer?

Yes No

42) Have you ever been diagnosed with endometriosis?

Yes No

43) Prior to menopause, did you often find it difficult to relax your vaginal muscles enough to permit intercourse or the insertion of a tampon (this condition is sometimes called vaginismus)?

Yes No

44) Prior to menopause, did you frequently find sexual intercourse to cause considerable discomfort and pain (this condition is sometimes called dyspareunia)?

Yes No

45) How old were you when you first started menstruating? _____

46) How old were you when your breasts started developing? _____

47) How old were you when you first noticed pubic hair growth? _____

48) I believe that going through puberty affected my mood: (Circle the best answer)

Very Negatively	Slightly Negatively	In no way at all	Slightly Positively	Very Positively
0	1	2	3	4

49) As a teenager and young adult, how did your acne/pimples compare to others your age? Please consider times when you were not on any oral contraceptives.

I had _____ acne/pimples compared to most girls my age (circle the appropriate number).

1	2	3	4	5
Significantly Less	Slightly Less	About the same	Slightly More	Significantly More

50) Prior to your menopausal transition, were your periods (check all that apply):

Regular	_____
Irregular	_____
Relatively short	_____
Relatively long	_____
Trouble-free	_____
Distressing and discomforting	_____

51) Prior to menopause, what was the average length of your menstrual cycle? Please consider times when you were not using hormonal contraceptives. Note: Most women have an approximate 28-day cycle (i.e., 28 days between the first day of their period and the day before their next period). _____ **days**

52) Have you ever used oral contraceptives in the past? Yes No

53) IF YES, how long did you continue to use oral contraceptives? _____

54) IF YES, I believe that using oral contraceptives affected my mood:

Very Negatively	Slightly Negatively	In no way at all	Slightly Positively	Very Positively
0	1	2	3	4

55) Prior to menopause, did you have any significant trouble with premenstrual distress (PMS)?

Yes No

56) In general, how would you rate the severity of your PMS symptoms?

No Symptoms	**Mild**	**Moderate**	**Severe**
0	1	2	3

57) Do you Smoke?

Yes No

58) Did you seek HRT treatment during your menopausal transition?

Yes No

59) Please indicate if you received any of the following treatments during your menopausal transitions? (check all that apply):

_____ Hormone Replacement Therapy (e.g., estrogen, progesterone, estradiol (common names include: Premarin, Cenestin, Estrace, Provera, Prempro, Activella). **This includes the use of Bioidentical Hormones.**

If yes, please specify: _____

_____ Androgen Replacement Therapy (i.e., testosterone patches, gel, skin implants, or pills) (Estratest, Andriol, Androderm, Androplex, Androgel).

If yes, please specify: _____

_____ Alternative Hormone Replacement Therapy (e.g., black cohosh, dong quai, ginseng, chaste tree)

If yes, please specify: _____

_____ Anti-depressant medication (examples include: Paxil, Effexor, Prozac, Celexa, Welbutrin, Trazodone, etc.)

If yes, please specify: _____

_____ Psychotherapy or Counselling (specifically for menopausal complaints)(examples include: Cognitive-Behavioural Therapy, marital therapy, supportive counselling, etc.). **Please do not include therapy for other issues occurring at that time (i.e., therapy specifically for divorce, anxiety, etc.)**

If yes, please specify: _____

Please circle on a scale of 1-7 the extent to which you agree with the following statements:

60) My menopausal transition caused me a significant amount of emotional and physical stress:

1	2	3	4	5	6	7
Strongly Disagree			Neutral			Strongly Agree

61) I was satisfied with my social life during my menopausal transition:

1	2	3	4	5	6	7
Strongly Disagree			Neutral			Strongly Agree

62) I was satisfied with my line of work during my menopausal transition:

1	2	3	4	5	6	7
Strongly Disagree			Neutral			Strongly Agree

63) I felt like I had a lot of familial support during my menopausal transition:

1	2	3	4	5	6	7
Strongly Disagree			Neutral			Strongly Agree

64) I was physically active during my menopausal transition:

1	2	3	4	5	6	7
Strongly Disagree			Neutral			Strongly Agree

For the following questions, please circle TRUE if the statement describes you AT **THE PRESENT TIME** and FALSE if it does not describe you **AT THE PRESENT TIME**.

65) I could easily count from one to twenty-five.	TRUE	FALSE
66) I have never talked to anyone by telephone.	TRUE	FALSE
67) I make all my own clothes and shoes.	TRUE	FALSE
68) Things with sugar usually taste sweet to me.	TRUE	FALSE
69) I have never had any hair on my head.	TRUE	FALSE

Appendix B: Menopause-Specific Quality of Life Questionnaire

Please fill out the following questionnaire about your menopausal symptoms. If you are currently experiencing menopause (**i.e., variable menstrual cycle length - at least 7 days different than normal**) , please report how much the following symptoms have bothered you thus far. If you have completed your menopausal transition (i.e., one year since your last menstrual period), please indicate how much each of the following symptoms bothered you **DURING** your menopausal transition (**from the time when your menstrual cycles became variable – at least 7 days different than normal**).

If you received Hormone Replacement Therapy for your menopausal symptoms, please report how bothered you were by the symptoms **PRIOR** to receiving Hormone Replacement Therapy.

	How much were you bothered by the symptom?
1. Hot flushes or flashes	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
2. Night sweats	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
3. Sweating	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
4. Being dissatisfied with my personal life	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
5. Feeling anxious or nervous	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
6. Experiencing poor memory	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
7. Accomplishing less than I used to	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
8. Feeling depressed, down, or blue	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
9. Being impatient with other people	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
10. Feelings of wanting to be alone	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
11. Flatulence (wind) or gas pains	**0 1 2 3 4 5 6** **Not at all bothered** **Extremely Bothered**
12. Aching in muscles and	**0 1 2 3 4 5 6**

joints	Not at all bothered Extremely Bothered
13. Feeling tired or worn out	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
14. Difficulty sleeping	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
15. Aches in back of neck or head	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
16. Decrease in physical strength	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
17. Decrease in stamina	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
18. Feeling a lack of energy	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
19. Drying skin	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
20. Weight gain	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
21. Increased facial hair	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
22. Changes in appearance, texture, or tone of your skin	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
23. Feeling bloated	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
24. Low backache	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
25. Frequent urination	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
26. Involuntary urination when laughing or coughing	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
27. Decrease in your sexual desire	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
28. Vaginal dryness during intercourse	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered
29. Avoiding intimacy	0 1 2 3 4 5 6 Not at all bothered Extremely Bothered

Appendix C: Menstrual Distress Questionnaire

The list below shows common symptoms and feelings associated with menstruation or the premenstrual period. Please estimate your experience during your menstrual and/or premenstrual phases **PRIOR** to your menopausal transition (i.e., **before your menstrual cycles became irregular – at least 7 days different than normal**). For each item, please decide whether you have "no experience of the symptom", or whether your experience was "present, mild", "present, moderate", or "present, severe", and circle the appropriate number. For each item, choose the best category that describes your overall experience **WHEN NOT USING HORMONAL CONTRACEPTIVES** (i.e., birth control pill, patch, ring, injection).

Symptom	No Experience of Symptom	Present, Mild	Present, Moderate	Present, Strong	Present, Severe
1. Muscle stiffness	0	1	2	3	4
2. Weight gain	0	1	2	3	4
3. Dizziness, faintness	0	1	2	3	4
4. Loneliness	0	1	2	3	4
5. Headache	0	1	2	3	4
6. Skin blemish or disorder	0	1	2	3	4
7. Cold sweats	0	1	2	3	4
8. Anxiety	0	1	2	3	4
9. Mood swings	0	1	2	3	4
10. Cramps	0	1	2	3	4
11. Painful or tender breasts	0	1	2	3	4
12. Nausea, vomiting	0	1	2	3	4
13. Crying	0	1	2	3	4
14. Backache	0	1	2	3	4
15. Swelling (breasts, abdomen)	0	1	2	3	4

	No Experience of Symptom	Present, Mild	Present, Moderate	Present, Strong	Present, Severe
16. Hot flashes	0	1	2	3	4
17. Irritability	0	1	2	3	4
18. Tension	0	1	2	3	4
19. Fatigue	0	1	2	3	4
20. Feeling sad or blue	0	1	2	3	4
21. General aches and pains	0	1	2	3	4
22. Restlessness	0	1	2	3	4
23. Insomnia	0	1	2	3	4
24. Poor school or work performance	0	1	2	3	4
25. Affectionate	0	1	2	3	4
26. Feelings of suffocation	0	1	2	3	4
27. Forgetfulness	0	1	2	3	4
28. Take naps, stay in bed	0	1	2	3	4
29. Orderliness	0	1	2	3	4
30. Chest pains	0	1	2	3	4
31. Confusion	0	1	2	3	4
32. Poor judgment	0	1	2	3	4
33. Stay at home	0	1	2	3	4
34. Excitement	0	1	2	3	4
35. Ringing in the ears	0	1	2	3	4

	No Experience of Symptom	Present, Mild	Present, Moderate	Present, Strong	Present, Severe
36. Difficulty concentrating	0	1	2	3	4
37. Avoid social activities	0	1	2	3	4
38. Feelings of well-being	0	1	2	3	4
39. Heart pounding	0	1	2	3	4
40. Distractible	0	1	2	3	4
41. Decreased efficiency	0	1	2	3	4
42. Bursts of energy, activity	0	1	2	3	4
43. Numbness, tingling	0	1	2	3	4
44. Minor accidents	0	1	2	3	4
45. Blind spots, fuzzy vision	0	1	2	3	4
46. Poor motor co-ordination	0	1	2	3	4

Appendix D: Pregnancy Experiences Questionnaire

If you have ever been pregnant, please fill out the following questionnaire. If you have had more than one child, and had different experiences during each pregnancy, please consider your **OVERALL** experience with pregnancy in general. Pregnancy is associated with many physical, emotional, and sexual changes that can be positive or negative. Please read the following list of experiences and indicate the extent and direction of the change you experienced. **If you did not experience the symptom, or if there was no change please circle 4 (No Noticeable Change).**

A	B	C	D	E	F	G
Large Decrease	Moderate Decrease	Mild Decrease	No Noticeable change	Mild Increase	Moderate Increase	Large Increase

Change In:	Amount and Direction of Change						
	Large Decrease	Moderate Decrease	Mild Decrease	No Noticeable Change	Mild Increase	Moderate Increase	Large Increase
1. Fatigue	A	B	C	D	E	F	G
2. Frequency of urination	A	B	C	D	E	F	G
3. Nausea	A	B	C	D	E	F	G
4. Vomiting	A	B	C	D	E	F	G
5. Heartburn	A	B	C	D	E	F	G
6. Indigestion	A	B	C	D	E	F	G
7. Flatulence	A	B	C	D	E	F	G
8. Bloating	A	B	C	D	E	F	G
9. Food aversions	A	B	C	D	E	F	G
10. Food cravings	A	B	C	D	E	F	G
11.Food intake	A	B	C	D	E	F	G
12. Tender/painful breasts	A	B	C	D	E	F	G
13. Irritability	A	B	C	D	E	F	G
14. Mood swings	A	B	C	D	E	F	G
15. Weepiness	A	B	C	D	E	F	G
16. Irrationality	A	B	C	D	E	F	G
17. Frustration	A	B	C	D	E	F	G
18. Depression	A	B	C	D	E	F	G
19. Headaches	A	B	C	D	E	F	G
20. Constipation	A	B	C	D	E	F	G
21. Feeling faint/dizzy	A	B	C	D	E	F	G
22. Appetite change	A	B	C	D	E	F	G
23. Nasal congestion	A	B	C	D	E	F	G
24. Swelling of ankles/feet	A	B	C	D	E	F	G
25. Varicose veins	A	B	C	D	E	F	G
26. Hemorrhoids	A	B	C	D	E	F	G
27. Concentration problems	A	B	C	D	E	F	G
28. Leg cramping	A	B	C	D	E	F	G

	Large Decrease	Moderate Decrease	Mild Decrease	No Noticeable Change	Mild Increase	Moderate Increase	Large Increase
29. Abdominal achiness	A	B	C	D	E	F	G
30. Backache	A	B	C	D	E	F	G
31. Change in cervical mucous	A	B	C	D	E	F	G
32. Clumsiness	A	B	C	D	E	F	G
33. Diarrhea	A	B	C	D	E	F	G
34. Forgetfulness	A	B	C	D	E	F	G
35. Bleeding gums	A	B	C	D	E	F	G
36. Change in energy	A	B	C	D	E	F	G
37. Change in sensitivity of smell	A	B	C	D	E	F	G
38. Insomnia	A	B	C	D	E	F	G
39. Pelvic discomfort/pressure	A	B	C	D	E	F	G
40. Restless Legs Syndrome	A	B	C	D	E	F	G
41. Shortness of breath	A	B	C	D	E	F	G
42. Tingling hands	A	B	C	D	E	F	G
43. Urinary incontinence	A	B	C	D	E	F	G
44. Vaginal dryness	A	B	C	D	E	F	G
45. Hot flashes	A	B	C	D	E	F	G
46. Change in sexual desire	A	B	C	D	E	F	G
47. Acne/pimples	A	B	C	D	E	F	G
48. Discoloration of skin	A	B	C	D	E	F	G

49. Did you develop any significant medical conditions or illnesses while you were pregnant? If yes, please specify:

_____

_____

_____

_____

_____

Appendix E: Postpartum Physical Symptoms Questionnaire

If you have ever given birth, please fill out the following questionnaire about your postpartum experiences. We are interested in the physical symptoms you may have experienced during the postpartum period **(i.e., up to 6 months after the birth of your child)**. If you have had more than one child, and had different experiences during each postpartum period, please consider your **OVERALL** experience with the postpartum period in general. The postpartum period is associated with many physical and emotional changes, which can be either positive or negative. Please indicate whether you experienced a change in any of the following symptoms (as compared to when you were not pregnant). Please read the following list of experiences and indicate the extent and direction of the change you experienced. **If you did not experience the symptom, or if there was no change please circle 4 (No Noticeable Change).**

A	B	C	D	E	F	G
Large Decrease	Moderate Decrease	Mild Decrease	No Noticeable change	Mild Increase	Moderate Increase	Large Increase

Change In:	Amount and Direction of Change						
	Large Decrease	Moderate Decrease	Mild Decrease	No Noticeable Change	Mild Increase	Moderate Increase	Large Increase
1. Fatigue/Exhaustion	A	B	C	D	E	F	G
2. Frequency of urination	A	B	C	D	E	F	G
3. Bloodshot eyes	A	B	C	D	E	F	G
4. Breast leakage	A	B	C	D	E	F	G
5. Heartburn	A	B	C	D	E	F	G
6. Insomnia	A	B	C	D	E	F	G
7. Hair loss	A	B	C	D	E	F	G
8. Sweating	A	B	C	D	E	F	G
9. Hot flashes	A	B	C	D	E	F	G
10. Vaginal dryness	A	B	C	D	E	F	G
11. Urinary incontinence	A	B	C	D	E	F	G
12. Appetite	A	B	C	D	E	F	G
13. Headaches	A	B	C	D	E	F	G
14. Backaches	A	B	C	D	E	F	G
15. Hemorrhoids	A	B	C	D	E	F	G
16. Inability to control bowel movements	A	B	C	D	E	F	G
17. Breast milk production	A	B	C	D	E	F	G
18. Uterine cramping	A	B	C	D	E	F	G

Appendix F: Edinburgh Postnatal Depression Scale

If you have previously given birth, please fill out the following measure, focusing on your feelings AFTER the birth of your child (**i.e., up to 6 months after the birth of your child**). Please place an "X" next to the response that best describes how you were feeling during this period. If you have given birth more than once please focus on your overall postnatal experience in general.

After the birth of my child:

1. **I was able to laugh and see the funny side of things**

_____ As much as I always could
_____ Not quite so much as I usually could
_____ Definitely not as much as I usually could
_____ Not at all

2. **I looked forward with enjoyment to things**

_____ As much as I always did
_____ Rather less than I usually did
_____ Definitely less than I usually did
_____ Hardly at all

3. **I blamed myself unnecessarily when things went wrong**

_____ Yes, most of the time
_____ Yes, some of the time
_____ Not very often
_____ No, never

4. **I felt anxious or worried for no good reason**

_____ No, not at all
_____ Hardly ever
_____ Yes, sometimes
_____ Yes, very often

5. **I felt scared or panicky for no good reason**

_____ Yes, quite a lot
_____ Yes, sometimes
_____ No, not much
_____ No, not at all

6. Things were getting on top of me

_____ Yes, most of the time I wasn't able to cope at all
_____ Yes, sometimes I wasn't able to cope as well as usual
_____ No, most of the time I coped quite well
_____ No, I coped as well as ever

7. I was so unhappy that I had difficulty sleeping

_____ Yes, most of the time
_____ Yes, some of the time
_____ Not very often
_____ No, not at all

8. I felt sad or miserable

_____ Yes, most of the time
_____ Yes, quite often
_____ Not very often
_____ No, not at all

9. I was so unhappy that I cried

_____ Yes, most of the time
_____ Yes, quite often
_____ Only occasionally
_____ No, never

10. The thought of harming myself occurred to me

_____ Yes, quite often
_____ Sometimes
_____ Hardly ever
_____ Never

Appendix G: Oral Contraceptives Questionnaire

Please fill out the following questionnaire if you have ever used oral contraceptives in the past. Some women who use oral contraceptives (birth control pills) experience side effects. Side effects are changes in physical, emotional, and sexual functioning that can be either *positive* or *negative*. We would like to learn about any changes that you have experienced due to oral contraceptives.

Please read the following list of side effects and choose either YES or NO to indicate whether you have experienced a change in the item as a result of using oral contraceptives. If you noticed any of these changes in yourself, only choose YES if your experience is due to oral contraceptive use and reflects a change from when you did not use oral contraceptives.

If you choose YES, please indicate the amount and direction of change as compared to when you did not use oral contraceptives:

A	B	C	D	E	F	G
Yes, Large Decrease	Yes, Moderate Decrease	Yes, Mild Decrease	No Change	Yes, Mild Increase	Yes, Moderate Increase	Yes, Large Increase

Side Effect	Yes, Large Decrease	Yes, Moderate Decrease	Yes, Mild Decrease	No Change	Yes, Mild Increase	Yes, Moderate Increase	Yes, Large Increase
1) Amount of menstrual bleeding (period)	A	B	C	D	E	F	G
2) Weight	A	B	C	D	E	F	G
3) Tiredness/fatigue	A	B	C	D	E	F	G
4) Appetite	A	B	C	D	E	F	G
5) Problems concentrating	A	B	C	D	E	F	G
6) Short-tempered	A	B	C	D	E	F	G
7) Irritability	A	B	C	D	E	F	G
8) Depression	A	B	C	D	E	F	G
9) Mood Instability	A	B	C	D	E	F	G
10) Feeling unsociable	A	B	C	D	E	F	G
11) Enjoyment of sex	A	B	C	D	E	F	G
12) Ability to become sexually aroused	A	B	C	D	E	F	G
13) Desire to masturbate	A	B	C	D	E	F	G
14) Sexual thoughts	A	B	C	D	E	F	G

	Yes, Large Decrease	Yes, Moderate Decrease	Yes, Mild Decrease	No Change	Yes, Mild Increase	Yes, Moderate Increase	Yes, Large Increase
15) Bloating/swelling	A	B	C	D	E	F	G
16) Headaches	A	B	C	D	E	F	G
17) Vaginal dryness	A	B	C	D	E	F	G
18) Disrupted sleep	A	B	C	D	E	F	G
19) Hot flashes/cold sweats	A	B	C	D	E	F	G
20) Sadness	A	B	C	D	E	F	G
21) Aggressive feelings	A	B	C	D	E	F	G
22) Desire for sex with others	A	B	C	D	E	F	G

23) I believe that oral contraceptives affected my mood and emotions:

1	2	3	4	5
Very Negatively	Slightly Negatively	In No Way At All	Slightly Positively	Very Positively

24) I believe that oral contraceptives affected my physical health:

1	2	3	4	5
Very Negatively	Slightly Negatively	In No Way At All	Slightly Positively	Very Positively

25) I believe that oral contraceptives have affected my sexual functioning (i.e., arousal, sex drive)

1	2	3	4	5
Very Negatively	Slightly Negatively	In No Way At All	Slightly Positively	Very Positively

Appendix H: NEO-FFI Scale

Please answer the following questions as they apply to you AT THE PRESENT TIME.

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1) I am not a worrier.	1	2	3	4	5
2) I often feel inferior to others.	1	2	3	4	5
3) When I'm under a great deal of stress, sometimes I feel like I'm going to pieces.	1	2	3	4	5
4) I rarely feel lonely or blue.	1	2	3	4	5
5) I often feel tense and jittery.	1	2	3	4	5
6) Sometimes I feel completely worthless.	1	2	3	4	5
7) I rarely feel anxious or nervous.	1	2	3	4	5
8) I often get angry at the way people treat me.	1	2	3	4	5
9) Too often, when things go wrong, I get discouraged and feel like giving up.	1	2	3	4	5
10) I am seldom sad or depressed.	1	2	3	4	5
11) I often feel helpless and want someone else to solve my problems.	1	2	3	4	5
12) At times I have been so ashamed I just wanted to hide.	1	2	3	4	5

For the following questions, please circle TRUE if the statement describes you **AT THE PRESENT TIME** and FALSE if it does not describe you **AT THE PRESENT TIME**.

49) I have never ridden in an automobile. TRUE FALSE

50) I try to get at least some sleep every night. TRUE FALSE

51) I have attended school at some time during my life. TRUE FALSE

Appendix I: Letter to Participants

Dear Potential Participant,

You are invited to participate in Lakehead University's Menopause Study. This study is being conducted by Ms. Suzanne Stone and Dr. Dwight Mazmanian, and will serve as Ms. Stone's doctoral dissertation. This research is being sponsored by the Canadian Institutes of Health Research (CIHR). The purpose of this study is to identify how physical and emotional symptoms experienced during reproductive events throughout the lifespan may affect the symptoms experienced during the menopausal transition.

Participation in this study will involve filling out a series of questionnaires (either online or in paper-and-pencil format), and should take approximately 35 to 40 minutes. You will be asked questions about past and present reproductive experiences such as menopause, pregnancy, and menstruation. After completing the questionnaires, you will be entered into a draw to win one of three 50 dollar gift certificates to a dining establishment (i.e., Montana's, Milestones, Kelsey's, Swiss Chalet, or Harvey's). If you live in the Thunder Bay area, you may be contacted to participate in a lab session, where you will receive 20 dollars for your participation.

Participation in this study is voluntary, and you may withdraw at any time without penalty. You may also choose to not answer a question if you do not feel comfortable doing so. The possible benefits of this study include: gaining an understanding of your own physical and mental health, learning more about the research process, contributing to women's health research, as well as the potential to win a 50 dollar gift certificate. The risks of this study are mild if any, but may include discomfort pertaining to answering personal questions.

All records of your participation will be kept in strict confidence and any reports of the study will not identify you as a participant. As per university requirements, all data will be stored for five years by Dr. Dwight Mazmanian and remain anonymous andÿÿonÿÿdential. We have asked for your nameÿÿnd contact information in order to possibly contact you for a lab session, as well as to enter you into the draw. However, your contact information is stored separately from your questionnaire responses, and there will be no way that your name can be connected to your responses.

If you have any questions or concerns about this study please contact Ms. Stone at menopause@lakeheadu.ca, or Dr. Mazmanian by phone at (807) 343-8257. If you would like to receive a summary of the findings by email once the study is complete, please send a request to menopause@lakeheadu.ca. This study has received ethics approval by the Lakehead University Research Ethics Board. Please feel free to contact Susan Wright (Research Ethics and Administration Officer) at (807) 343-8283 if you have any concerns.

Sincerely,

Suzanne Stone, M.A. (Doctoral Candidate)
Department of Psychology
Lakehead University
955 Oliver Road
Thunder Bay, ON, P7B 5E1
menopause@lakeheadu.ca

Dr. Dwight Mazmanian, Ph.D.
Department of Psychology
Lakehead University
955 Oliver Road
Thunder Bay, ON, P7B 5E1
dwight.mazmanian@lakeheadu.ca
(807) 343-8257

Appendix J: Menopause Study Consent Form A

Please read the following points about this study:

- Your participation is voluntary, you may refuse to participate in any part of the study, and you may withdraw from the study at any time without penalty.
- You may decline to answer any question
- Your participation in this study will involve the completion of several questionnaires that will take between 35 and 40 minutes.
- The purpose of this study is to identify how physical and emotional symptoms experienced during reproductive events throughout the lifespan may affect the symptoms experienced during the menopausal transition. Benefits of participating in this research include: gaining an understanding of your own physical and mental health, learning more about the research process, contributing to women's health research, as well as the potential to win a 50 dollar gift certificate.
- All of the data collected will remain strictly confidential, and will only be accessed by Suzanne Stone, Dr. Dwight Mazmanian, and members of Dr. Mazmanian's lab group who have been trained in research ethics.
- There will be no way that your name can be connected to your responses.
- As per university requirements, all data will be stored for five years by Dr. D. Mazmanian at Lakehead University.
- You may contact the researchers if you would like to receive a summary of the findings.

I have read and understood the consent form, and I agree to participate in this study under these conditions.

Name (please print): _____

Signature: _____

Date: _____

Email (if you reside in Thunder Bay): _____

Phone Number (if you reside in Thunder Bay): _____

- If you have any questions or concerns regarding this study please contact Suzanne Stone (menopause@lakeheadu.ca) or the supervisor of this study, Dr. Mazmanian (phone:343-8257, email: dwight.mazmanian@lakeheadu.ca). Other collaborators in the Menopause Research Group include Dr. Kirsten Oinonen (Associate Professor of Psychology at Lakehead University) and Dr. Verinder Sharma (Professor of Psychiatry and Professor of Obstetrics & Gynecology at the University of Western Ontario)

Appendix K: Debriefing Form

The purpose of this study is to determine how premenopausal physical and psychological symptoms may influence the physical and psychological symptoms experienced during the menopausal transition. For example, past research has demonstrated that there is a relationship between depressive symptoms experienced during the menopausal transition and feelings of depression during other reproductive events as well as more severe PMS symptoms (Steward & Boydell, 1993; Woods & Mitchell, 1996). However, there is a lack of research investigating how past reproductive events are related to physical menopausal symptoms (i.e., hot flashes). The purpose of this study is to investigate this question further.

Please be assured that all of your responses are coded to conceal your identity and that all data will remain anonymous.

Listed below are some related references which might be of interest to those who would like further information on the effect of physical and emotional symptoms of the menopause on menopausal attitudes and the decision to seek help during the menopausal transition.

If you wish to have a summary of the overall results of this study, please email Suzanne Stone at menopause@lakeheadu.ca requesting this information and a summary will be sent to you when all data has been collected and the project has been completed.

Thank you sincerely for taking the time to participate in this research.

Recommended Readings:

Stewart, D.E., & Boydell, K.M. (1993). Psychologic distress during menopause: Associations across the reproductive life cycle. *International Journal of Psychiatry in Medicine, 23* (2), 157-162.

Woods, N.F., & Mitchell, E.S. (1996). Patterns of depressed mood in midlife women: Observations from the Seattle Midlife Women's Health Study. *Research in Nursing and Health, 19,* 111-123.

If you have any questions or concerns regarding this study please contact Suzanne Stone (menopause@lakeheadu.ca) or the supervisor of this study, Dr. Mazmanian (phone: 343-8257, email: dwight.mazmanian@lakeheadu.ca).

Other collaborators in the Menopause Research Group include Dr. Kirsten Oinonen (Associate Professor of Psychology at Lakehead University) and Dr. Verinder Sharma (Professor of Psychiatry and Professor of Obstetrics & Gynecology at the University of Western Ontario)

Appendix L: Menopause Study Consent Form B

Please read the following points about this study:

- Your participation is voluntary, you may refuse to participate in any part of the study, and you may withdraw from the study at any time without penalty.
- Your participation in this study will involve scanning your hands onto desktop computer, so they can be measured by the researcher.
- The purpose of this study is to identify how physical and emotional symptoms experienced during reproductive events throughout the lifespan may affect the symptoms experienced during the menopausal transition. We are also looking at how finger digit length may be related to hormonal sensitivity.
- Benefits of participating in this research include: gaining an understanding of your own physical and mental health, learning more about the research process, contributing to women's health research, as well as earning 20 dollars for your participation.
- All of the data collected will remain strictly confidential, and will only be accessed by Suzanne Stone, Dr. Dwight Mazmanian, and members of Dr. Mazmanian's lab group who have been trained in research ethics.
- There will be no way that your name can be connected to your hand scan.
- As per university requirements, all data will be stored for five years by Dr. D. Mazmanian at Lakehead University.
- You may contact the researchers if you would like to receive a summary of the findings.

I have read and understood the consent form, and I agree to participate in this study under these conditions.

Name (please print): _____

Signature: _____

Date: _____

- If you have any questions or concerns regarding this study please contact Suzanne Stone (menopause@lakeheadu.ca) or the supervisor of this study, Dr. Mazmanian (phone:343-8257, email: dwight.mazmanian@lakeheadu.ca). Other collaborators in the Menopause Research Group include Dr. Kirsten Oinonen (Associate Professor of Psychology at Lakehead University) and Dr. Verinder Sharma (Professor of Psychiatry and Professor of Obstetrics & Gynecology at the University of Western Ontario)