# Effect of Physical Activity on Menopausal Symptoms in Non-Vigorously Active Postmenopausal Women

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By

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## Abstract

Menopause is the time in a woman's life when regular menstrual periods cease, due to a natural change in sex hormones, which may be accompanied by unwelcome symptoms. **PURPOSE**: To determine whether physical activity is associated with a reduction in menopausal symptoms (hot flashes, insomnia, numbness, fatigue, headaches, psychological symptoms, urogenital symptoms and physical symptoms). Providing that symptom differences among activity levels exist, a secondary purpose was to suggest an adequate level of physical activity for relief of menopausal symptoms. **METHODS**: Women (n=401) who were not taking hormone replacement therapy completed two questionnaires based on a 7-day recall of an average week: the Leisure-Time Exercise Questionnaire (Godin & Shephard, 1985) and the Menopausal Index (St. Germain, Peterson, Robinson, & Alekel, 2001). Women were divided into quintiles according to their physical activity scores (1=least active, 5=most active) and compared for menopausal symptoms using first a MANCOVA with covariate percent fat, as this was the only covariate that had significant group mean differences. Secondly a MANOVA with the appropriate post-hoc analysis was conducted. **RESULTS**: The mean (SD) age of the participants was 58.2 (6.3), the mean years postmenopausal was 6.7 (6.0), the mean percent body fat was 37.4 (5.6) %, and 16.5% had a previous hysterectomy. Univariate tests did not identify significant group differences for hysterectomy (p=0.774) or time since menopause (p=0.440); however, there were significant group differences for percent body fat (p=0). The MANCOVA was not significant between physical activity groups with percent fat as a covariate (Wilks' Lamda p = 0.126). The MANOVA indicated a significant group main effect of physical activity on menopausal symptoms

(Wilks' Lamda p = 0.034). Of the 8 symptoms under review there were significant group differences for fatigue (p=0.05), and physical symptoms (p=0.004). The post-hoc analyses identified that two least active groups reported above average fatigue occurrence whereas the three most active groups reported below average fatigue occurrence. Group 2 had significantly more physical symptom complaints than groups 4 & 5. Of the three symptoms comprising physical symptoms, there were significant differences for weight gain (p=0.004) but not for breast tenderness (p=0.742) or aches and pains (p=0.175). Groups 1 & 2 reported significantly higher frequency of weight gain than groups 4 & 5. **CONCLUSION**: Any indirect effect of physical activity on menopausal symptoms is most likely through the alteration of body composition. Women with lower percent body fat report less weight gain and fatigue. There was no significant relationship between physical activity levels and reporting of hot flashes/night sweats, insomnia, limb numbness, headache, psychological symptoms or urogenital symptoms. A randomized controlled clinical trial would likely determine the relationship between higher activity levels and symptom reduction. For future research it is recommended that groups be matched based on percent body fat prior to randomization and that a greater amount of physical activity be prescribed.

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# CHAPTER 1

## 1.1 Introduction

According to the Society of Obstetricians and Gynecologists of Canada (2006), the average age of menopause is 51 years. Year 2011 is when the first generation of baby-boomers will reach the age of 65. From 2011 until the year 2031 Canada's population will rapidly age and it is predicted that by 2031, 25% of Canada's population will be 65 years or older (Statistics Canada, 2005); thus, there will be a considerable number of menopausal women. The rising number of women dealing with menopausal symptoms could result in many women living with a decrease in quality of life; therefore, educating women on ways to cope with menopause would be beneficial.

Menopause is the time in a woman's life when regular menstrual periods cease, due to a natural change in sex hormones. A woman is considered to be postmenopausal after she has gone twelve consecutive months without menstruating.

Up to 75% of American women will experience unwelcome menopausal symptoms such as hot flashes during the menopausal transition (Avis, Crawford, & McKinley, 1997). Other symptoms may include: insomnia (Owens & Mathews, 1998), limb numbness, fatigue (Oldenhave, Jaszmann, Haspels, & Everaerd, 1993), headache (Oldenhave et al., 1993), psychological complaints (Asbury, Chandrruangphen, & Collins, 2006), urogenital complaints (Dennerstein, Randolph, Taffe, Dudley, & Burger, 2002) and physical complaints (Haines, Xing, Park, Holinka, & Ausmanase, 2005). One of the most common menopausal symptoms is hot flashes or night sweats that result from a sudden surge of heat throughout the body that may cause profuse sweating. Hot flashes are often referred to as vasomotor symptoms because of the dilation of blood vessels.

Fortunately, for most women menopausal symptoms such as hot flashes will abate within 6 months to 2 years (Kronenberg, 1990). Up to 85% of women will experience hot flashes for more than a year (Kletsky & Borenstein, 1987) whereas only 20% will experience symptoms for 10-20 years (Berg, Gottwall, Hammar, & Lindgren, 1988).

The menopausal transition may also be associated with irritability, tension, fatigue, headaches, muscle/joint pain and sometimes depression (Oldenhave et al., 1993). Sleep tends to be disrupted by night sweats (Hunter & Liao, 1996), and disrupted sleep can alter daily activities, which may lead to fatigue, irritability, and decreased quality of life (Greendale & Sowers, 1997).

Some longer-term outcomes of this hormonal change include urogenital symptoms (Modelska & Cummings, 2003). Urogenital symptoms can include vaginal dryness, uncomfortable intercourse, reduction in sexual desire or libido and urinary incontinence. Vaginal atrophy occurs as estrogen levels drop which results in the thinning of the vaginal epithelium, which may result in vaginal dryness, itching and/or burning (Willhite & O'Connell, 2001). An outcome of vaginal atrophy is that women may feel pain with intercourse, which can lead to avoidance of sexual activity and affect quality of life (Johnston et al., 2004). Vaginal dryness has been estimated to occur in 17% to 30% of postmenopausal women (Nelson et al., 2005) and 10% to 50% of postmenopausal women experience urinary incontinence (Larson, Collings, & Landgren, 1997). A community based survey with 16,065 pre to post menopausal women identified that urine leakage was more common among women with higher body mass index (BMI) and was not associated with age in late perimenopause or postmenopause (Gold et al., 2000). Nelson et al. (2005) conducted a literature review attempting to distinguish

between symptoms that were associated with the menopausal transition or simply of ageing. This literature review of 48 studies identified that urinary complaints were inconsistently associated with menopause.

Women who undergo surgical menopause (hysterectomy and/or oophectomy) experience a rapid drop in gonadal hormones and are more likely to have symptoms such as sexual dysfunction, psychological problems and more frequent and intense hot flashes (Kotz, Alexander, & Dennerstein, 2006; Sherwin & Gelfand, 1985). The occurrence of hot flashes has been reported at rates of up to 90% for women who undergo bilateral oophorectomy (Feldman, Voda, & Gronseth, 1985).

There is an increase in BMI with age, or more particularly body fat, with the peak BMI occurring between ages 50 and 59 (Kuczmarski, Flegal, Campbell, & Johnson, 1994). This is important to note since the timing coincides with post menopause. The relationship between BMI and vasomotor symptoms is unclear. Some research has shown that higher BMI is related to increased symptom reporting whereas others have shown the opposite, and others have found no relationship between BMI and menopausal symptoms (Schwingl, Hulka, & Harlow, 1994; Ivarsson, Spetz, & Hammar, 1998; Gold et al., 2006; Longcope, 1979; Erlik, Meldrum, & Judd, 1982; Gold et al., 2000, Chiechi et al., 1997; Freeman et al., 2001; and Mirzaiinjmabadi, Anderson, & Barnes, 2006).

At one time the leading treatment for menopause-related symptoms was hormone replacement therapy (HRT). Hormone replacement therapy is effective in the management of hot flashes; however, it has been suggested that it may pose a higher risk for breast cancer (Goodman et al., 1997; Collaborative Group on Hormonal Factors in Breast Cancer, 1997). Li and Holm (2003) found that the combination of HRT and

exercise was more effective than HRT or exercise alone for reducing vasomotor symptoms.

Physical activity has repeatedly been shown to have many health benefits in various populations including those in the menopause transition. The Canadian physical activity guide for older adults recommends getting at least 30-60 minutes of moderate intensity of physical activity on most days (PHAC, 2007). The Centre for Disease Control and Prevention suggests a minimum of 60 minutes per day to prevent weight gain (CDCP, 2007). In menopausal and postmenopausal age women, studies have shown that exercise has beneficial effects on mood (Slaven & Lee 1997), quality of life (Villaverde-Gutierrez et al., 2006), body composition (Sternfeld, Bhat, Wang, Sharp, & Quesenberry, 2005), strength, balance (Aloia, McGowan, Vaswani, Ross, & Cohn, 1991), aerobic fitness (Bloomfeld et al., 1993) and menopausal symptoms (McMillan & Mark, 2004; Slaven & Lee, 1997; Villaverde-Gutierrez et al., 2006; Li & Holm, 2003; Carmody, Crawford, & Churchill, 2006). The purpose of this research project was to determine whether reports of higher levels of physical activity are associated with reduced reporting of menopausal symptoms in a very specific population of non-vigorously active postmenopausal women, who were not taking hormone replacement therapy. Exercise has many positive health benefits and may be an inexpensive treatment for relief of menopausal symptoms. This study is unique in that it has very tight inclusion criteria, and possible confounding variables were considered including: years since last menstrual period, hysterectomy and percent body fat. The exclusion of women who were very physically active narrows the activity levels between groups allowing for a closer

prediction on the amount of physical activity necessary for the relief of menopausal symptoms.

### 1.2 Review of the Literature

Results from a number of cross-sectional studies have suggested that physical activity is beneficial for improving some menopausal symptoms but not others (Gold et al., 2000; Progetto Menopausa Italia Study Group, 2005, Ivarsson et al., 1998; Stadberg, Mattisson, & Milsom, 2000; Guthrie, Dennerstein, Taffe, Lehert, & Burger, 2005). The age range of women studied in the current menopausal literature is wide, ranging from the mid 30's into the 60's. The sample populations among studies are also largely variable, making it difficult to compare findings between studies. There are many cross-sectional studies and few clinical trials therefore it is difficult to derive any cause-effect relationship between higher activity levels and reduced symptoms. The measurement of activity levels and menopausal symptoms has been tested with various tools, making it difficult to compare studies against one another. Some studies failed to control for important co-factors (i.e. time since menopause, HRT, hysterectomies) that may affect the presence of menopausal symptoms. A weakness of most studies that did find an effect of physical activity is that they do not define the amount of physical activity required to relieve symptoms; therefore, an exercise prescription for inactive women is difficult to derive from these studies.

Results from the most current study on the relationship between physical activity and menopausal symptoms showed that high levels of physical activity are related to reduced stress but not vasomotor symptoms (Nelson, Sammel, Freeman, Lin, Gracia, &

Schmitz, 2007). The required amount of activity required to reduce stress was translated into walking 4.0 mph for 1.5 hours, 5 times per week. Nelson et al. (2007) suggested that maintaining or increasing physical activity during the menopausal transitional and during postmenopause may assist in reducing a variety of psychological symptoms, including anxiety, stress, and depression. During the course of this non-randomized prospective observational study spanning over an 8-year period, participants (N= 380, ages 35-47 at intake) completed self-reported questionnaires on depression, anxiety, stress and physical activity. A weakness of this study is that activity reports were only taken every second year and there were large fluctuations in activity levels between assessment periods. The authors were concerned with the accuracy of using physical activity reports at one assessment to predict symptoms in the next assessment period.

The Progetto Menopausa Italia Study Group (2005) conducted a large study on menopausal symptoms and activity levels. It was a cross-sectional study with a sample size of 66,501 women. They found that women attending menopausal treatment clinics, who performed regular exercise, experienced less frequent depression, headache, urinary leakage, irritability, hot flashes/night sweats, forgetfulness and difficulty to sleep. A relationship between activity levels and BMI was identified where women who did minimal physical activity had a higher BMI than women who performed regular physical activity. This study accounted for HRT use, presence of hysterectomy and menopausal status, however is not representative of an average Italian population. All women sampled in this study were seeking advice for menopause-related problems therefore may have had higher symptom complaints or may have been more health conscious than the average population.

Another large cross-sectional study by Gold et al. (2000) sampled 12,425 women of multiple ethnicities. The researchers found that women with BMI over 32 kg/m$^2$ had a higher prevalence of hot flashes/night sweats, urine leakage, vaginal dryness, sleep difficulty, stiff/soreness and forgetfulness than women with a BMI less than 19 kg/m$^2$. In this study, physical activity was assessed with a single question about activity levels relative to other women of similar age; finding significant differences in symptom reporting among women who did much less or much more physical activity than women of similar age. The differences between those who did much less versus those who did much more was as follows: hot flashes/night sweats 52.5% vs 32.6%, urine leakage 29.8% vs 13.6%, vaginal dryness 21.6% vs 11.9%, sleep difficulty 60.8% vs 31.2%, stiff/soreness 73.1% vs 46.8%, and forgetfulness 56.9% vs 33.5%.

In 2006, Mirzaiinjmabadi et al. examined the relationship between exercise and BMI on menopausal symptoms of 886 women between the ages of 45-60. Results from this cross-sectional study showed that exercise was effective in relieving psychological symptoms, tiredness, headache and limb numbness however identified no relationship between exercise and vasomotor symptoms or sexual symptoms. The researchers found no relationship between BMI and menopausal symptoms. Strength of this study is that confounding variables such as HRT use, menopausal status, education and smoking status were accounted for. Ivarsson et al. (1998) in a cross-sectional study of 793 postmenopausal women found that only 4.8% of women who exercised more than 2 hours per week reported severe vasomotor symptoms, whereas 14-16% of inactive women reported severe vasomotor symptoms. This study initially divided women into 3 activity levels based on self-reports; however the researchers chose to collapse the non-

exercising and the intermediate group comparing 84 exercisers against 256 non-exercisers. They found that it was not the type of activity that differentiated symptom reporting, but the intensity of activity.

Stadberg et al. (2000) (N=4,504) investigated factors associated with climacteric symptoms and the use of HRT. They randomly mailed out a survey to Swedish women between the ages of 42-62 years. This cross-sectional study identified a correlation between lower levels of vasomotor symptoms and regular exercise. The researchers reported that 69% of 54 year olds experienced hot flashes, and that 50% of 62 year olds were still experiencing vasomotor symptoms. Fifty two percent of the 4,504 women reported sleeping problems and 37% reported decreased libido. Although this study included information on associations between physical activity and menopausal symptoms, its primary purpose was not to examine the effects of exercise on symptoms but to identify all factors associated with symptoms and the use of HRT.

Guthrie et al. (2005) (N=381) investigated factors associated with the presence, severity, and frequency of hot flashes, reporting similar findings to Stadberg et al. (2000) where women who did less than average amounts of exercise were more likely to report bothersome hot flashes. They also reported that as women grew further from menopause, hot flashes became less of a problem. This 9-year prospective observational study did not find an association between BMI and hot flashes. Menopause status, age, exercise level, and smoking status all contributed to the experience of bothersome hot flashes. The sampled population had better self-rated health and exercise habits than reported by the general Australian population

Slaven and Lee (1997) conducted two cross-sectional studies. The first study included 220 women who were pre, peri or postmenopausal comparing exercisers to non-exercisers. Results showed that exercisers report fewer symptoms than non-exercisers and that exercising menopausal women experience less menopausal distress than sedentary menopausal women. The second study (N=47) found enhancements in mood regardless of menopausal status and reduction in reported menopausal symptoms (depressed mood, memory, concentration, anxiety, sexual dysfunction, sleep problems, irritability, head ache and depression) immediately following an aerobic fitness class when compared to non-exercisers. Although exercisers reported fewer somatic symptoms than non-exercisers there were no significant difference in reports of vasomotor symptoms between exercisers and non-exercisers.

Li et al. (2003) in a population based survey of 6,917 Swedish women between the ages of 50 and 64 identified that vigorous physical activity was associated with less vaginal dryness and lower intensity flashes. Weight gain and a BMI ranging from 25 to 29.9, were associated with a higher incidence of hot flashes. It was reported that weight gain increased the risk of hot flashes by 30% to 38%. Li et al. (2003) suggested that menopausal symptoms might commence earlier and be of longer duration in obese women. Although associations were made between physical activity and menopausal symptoms, physical activity was not identified as an independent factor for reducing menopausal symptoms.

These cross-sectional studies identified associations between higher activity levels and a reduction of hot flashes (Li et al., 2003; Ivarsson et al., 1998; Guthrie et al., 2005; Stadberg et al., 2000; Progetto Menopausa Italia Study Group, 2005), vaginal dryness (Li

et al., 2003), tiredness, headache, limb numbness (Mirzaiinjmabadi et al., 2006), psychologically-related symptoms (Nelson et al., 2007; Slaven & Lee, 1997; Progetto Menopausa Italia Study Group, 2005; Mirzaiinjmabadi et al., 2006) and some reported no change in vasomotor symptoms (Nelson et al., 2007, Slaven & Lee, 1997; Mirzaiinjmabadi et al., 2006). Li et al. (2003) identified that PA was not an independent factor for reducing menopausal symptoms and the menopausal literature often examines differences in BMI and its associations with menopausal symptoms. Some studies have identified that weight gain and elevated BMI are associated with higher incidence of vasomotor symptoms (Li et al., 2003; Gold et al., 2000) whereas others have reported no association between BMI and vasomotor symptoms (Guthrie et al., 2005; Mirzaiinjmabadi et al., 2006).

### *1.2.1 Clinical Trials*

The following studies describe exercise interventions and whether exercise had an effect on menopausal symptoms. The strongest evidence for an effect of exercise on menopausal symptoms can be derived from intervention studies.

Aiello et al. (2004) conducted a randomized clinical trial looking at the effect of moderate intensity exercise on the frequency and severity of menopausal symptoms in postmenopausal women. The average age of the participants was 61 years; all women were overweight and were not taking HRT. Half of the women (N=87) completed cardiovascular training such as walking, aerobics or cycling 5 days per week for a total of 225 minutes weekly for 12 months. The control group (N=86) performed stretching exercises. Their findings showed no differences in menopausal symptoms between the

stretching and cardiovascular training groups. A small number of the study participants in the cardiovascular intervention actually reported an increase in frequency and severity of some menopausal symptoms, but some showed a reduction in memory problems (Aiello et al. 2004). Since the average age of menopause is 51 years (Obstetricians and Gynecologists of Canada, 2006) and most women only experience hot flashes for 6 months to 2 years, (Kronenberg 1990) it is likely that many of the women studied would no longer experience symptoms; therefore it might be difficult to see a relationship with physical activity.

Elavsky and McAuley (2007) conducted a randomized clinical trial with 164 sedentary women ages 42-58 years on the effects of a 4-month walking (3 times per week) or yoga (2 times per week) intervention on mental health and menopause related quality of life (QOL), including sleep quality. The two exercise groups were compared to a control group who did not change their inactive behaviors. The results identified reduced vasomotor symptom reporting in both of the exercise groups, with a greater effect for the women in the walking group versus women in the yoga group. The control group demonstrated very little change in vasomotor symptoms indicating that the effect for the exercise groups was not due to passage of time. Within the same sample, both the walking and yoga interventions were found to be ineffective for improvements in sleep quality. Elavsky and McAuley (2007) stated that their study lacked sufficient power and that research with larger samples was warranted. The questionnaire used in that study was very long which may have affected the way in which participants responded. A shorter, yet detailed and precise questionnaire may be less of a burden for participants to complete and reduce the number of statistical tests required for analysis.

Villaverde-Gutierrez et al. (2006) examined the effects of physical exercise on QOL in 48 menopausal women between the ages of 55 and 72 years with a quasi-experimental analytical design. Half of the women acted as controls and the other half were assigned to an activity group that included cardiovascular training, stretching, strength and relaxation exercise 2 times per week for one year. Women in the exercise group showed an improvement in menopausal symptoms and health related QOL, whereas the symptoms and health related QOL of those in the control group worsened. This study reported a decrease in menopausal symptoms from 50% to 37.5% using the Kupperman-Blatt Menopausal Index as their measurement tool (the study in this thesis used a modified version of this index). However they failed to mention which symptoms were examined and which showed the most dramatic decrease.

Two of the three clinical trials identified that regular exercise reduces menopausal symptoms including vasomotor symptoms but not sleep problems (Elavsky & McAuley, 2007) and improves QOL (Villaverde-Gutierrez et al., 2006). However one of the three trials contradicted these finding showing no association between regular exercise and symptom reduction (Aiello et al., 2004). Therefore more research in the area of exercise and menopausal symptoms is needed. See appendix G for the literature review grid table.

The subsequent sections in this review of literature examine each of the menopausal symptoms from the above-mentioned Kupperman-Blatt Menopausal Index and the possible effect that physical activity may have on these symptoms.

## 1.3 Effect of exercise on individual menopausal symptoms

### *1.3.1 Hot flashes and Night Sweats*

Exercise may play a role in the reduction of hot flashes and night sweats (Hammer, Berg, & Lindgren, 1990). Hot flashes or night sweats are often referred to as vasomotor symptoms because the hormonal change that occurs in menopausal women interrupts the norepinephrine and dopamine neurotransmitter balance, which leads to vasomotor instability (Ostrzenski, 1999). It is thought that hot flashes originate from the hypothalamus and are associated with a decline in estrogen levels (Speroff et al., 1999). As estrogen levels decrease in postmenopausal women, there is also a reduction in hypothalamic opioids, such as beta-endorphins (Hammar, Hammar-Henriksson, Frisk, Rickenlund, & Wyon, 2000). Reduction of beta-endorphins causes dysfunction of the body's thermoregulatory centre, which has been postulated to be the cause of hot flashes (Shanafelt, Barton, Adjei, & Loprinzi, 2002). Since postmenopausal women have lower beta-endorphin concentrations than fertile women (Nappi et al., 1990), and since exercise increases beta-endorphin release in the central nervous system and in the peripheries (Schwartz & Kindermann, 1992; Andersson & Lundeberg, 1995), exercise may help to stabilize thermoregulation (Ivarsson et al., 1998; Hammer et al., 1990). This could explain the reduced frequency and intensity of hot flashes with increased physical activity. It is also possible that women who exercise regularly are accustomed to and comfortable with the feeling of being hot and sweaty; therefore they report hot flashes to be less intense (Ivarsson et al., 1998).

Body Mass Index has been related to vasomotor symptoms in some studies but not all (Schwingl et al., 1994; Mirzaiinjmabadi et al., 2006; Ivarsson et al., 1998; Gold et

al., 2006, Guthrie et al., 2005). Some data suggests that heavier women report fewer hot flashes resulting from a fat-related increase in circulating estrone (Longcope, 1979; Erlik et al., 1982; Schwingl et al., 1994); whereas others such as Gold et al. (2000) found that hot flashes or night sweats were reported more frequently in women with a BMI greater than 27 $kg/m^2$. Conversely, others have reported no difference between hot flash frequencies in women with high and low BMI (Ivarsson et al., 1998; Mirzaiinjmabadi et al., 2006). Gold et al. (2006) found that those with excessive body mass had more vasomotor symptoms. Chiechi et al. (1997) and Freeman et al. (2001) also found that heavier women reported more hot flashes because they had more insulation and therefore a narrower thermoneutral zone. A thermoneutral zone is the range of ambient temperatures where one does not have to actively regulate body temperature through raising or slowing metabolism. Body mass index increases with age, peaking between 50 and 59 years (Kuczmarski et al., 1994). Exercise may help in the maintenance of optimal body composition, body fat distribution, and slow weight gain (Sternfeld et al., 2005). The effects of physical activity for relieving hot flashes may therefore be through its effects on body composition. This will be determined by considering percent body fat as a confounding variable in the analysis of the relationship of physical activity with menopausal symptoms.

### *1.3.2 Headache*

Similarly to hot flashes or night sweats, headaches during menopause may be triggered by fluctuations in estrogen levels (Marcus, 1994). Since exercise has been shown to result in a temporary increase of cortical blood flow and an increase of beta-

endorphin release (Oleson, 1971) it may dull or numb headache pain. Tension headaches are more commonly reported among sedentary individuals, in which exercise may be a viable preventative treatment (Steiner, Fontebasso, & Del Brutto, 2002). Tension headaches are often related to muscle tightness in the neck or prolonged periods in one position and stretching and relaxation exercise may reduce their occurrence. Many studies with menopausal women have found associations between higher activity reports and fewer headaches (Li, Holm, Gulanick, Lanuza, & Penckofer, 1998; Mirzaiinjmabadi et al., 2006; Progetto Menopausa Italia Study Group, 2005; Slaven & Lee, 1997).

### *1.3.3 Sleep Problems*

Up to 40% to 60% of perimenopausal and postmenopausal women experience sleep disturbance (Nelson et al., 2005), including symptoms such as waking too early, difficulty falling asleep and difficulty staying asleep. Despite the strong link of increase sleep problems being reported around the time of menopause, it is inconsistently reported as being associated with the menopausal transition (Nelson et al., 2005). Sleep disturbance is a common symptom of depression. Exercise may have an antidepressant and anti-anxiety effect thus may promote sleep (Youngstedt & Freelove-Charton, 2005). From another perspective, women with poor sleep quality may be more prone to depression; therefore, would report more frequent or severe menopausal symptoms, and as a result, may also participate in less physical activity (Elavsky & McAuley, 2007). Owens and Mathews (1998) found that women with higher waist to hip ratios reported higher frequency of difficulty falling asleep. They also found that women with disturbed sleep have a higher occurrence of joint pain. Studies with older adults have shown that

exercise may have a beneficial effect on sleep (Driver & Taylor, 2000) by increasing the duration of slow wave sleep (Youngstedt, O'Connor, & Dishman, 1997). It has been found that for postmenopausal women, 4 exercise sessions per week for 4 months reduced time to fall asleep by nearly half and increased sleep duration by nearly an hour (King, Oman, Brassington, Bliwise, & Haskell, 1997). Exercise may also have a beneficial effect on sleep by reducing anxiety and boosting mood state (O'Connor, Raglin, & Martinsen, 2000). A literature review by Youngstedt and Freelove-Charton (2005) proposed mechanisms by which exercise could promote sleep that included: anxiety reduction, antidepressant effects, thermogenic effect and circadian phase-shifting effect. Studies with menopausal women identified that higher activity levels reduced difficulty falling asleep (Progetto Menopausa Italia Study Group, 2005), and reduced sleep problems (Slaven & Lee, 1997) however one study reported that exercise failed to improve sleep quality (Elavsky & McAuley, 2007). Another study found that postmenopausal women who do regular morning exercise have less trouble falling asleep (Tworoger et al., 2003). This study consisted of a year-long intervention where participants either did moderate intensity exercise or low intensity stretching, finding that increased fitness is associated with improved sleep, and that evening exercisers had more difficulty falling asleep.

### *1.3.4 Fatigue*

Sleep deprivation is associated with increased fatigue and low energy levels. Inactivity induces muscular catabolism, which may negatively affect performance; therefore, more effort is required to carry out daily activities (Dimeo, Rumberger & Keul,

1998). An aerobic training program can break this cycle of lack of exercise, impaired performance, and easy fatigability (Dimeo et al., 1998). Fatigue can be associated with night sweats (Oldenhave et al., 1993), as sleep may be interrupted leading to fatigue. Mirzaiinjmabadi et al. (2006) found a positive relationship between exercise and reduced tiredness in postmenopausal women.

### *1.3.5 Limb numbness*

Limb numbness or a feeling of pins and needles in the limbs can be associated with poor blood circulation. It is commonly accepted that exercise increases cardiac output and vasodilation, which increases blood circulation to get oxygen to the working muscles. One might guess that performing regular exercise such as walking or swimming may increase blood circulation and reduce limb numbness. A community-based study of women (mean age = 64.9) with back and leg pain identified that women with limb numbness participated in less physical activity (Vogt, Lauerman, Chirumbole, & Kuller, 2002). Although this study related exercise to a reduction in limb numbness, this was not a study concerning menopausal symptoms. Limb numbness is not described as a symptom in the menopausal literature; it may be more related to ageing or to inactivity. One study with postmenopausal women did report fewer incidence of limb numbness among exercisers when compared to non-exercisers (Mirzaiinjmabadi et al., 2006).

### *1.3.6 Psychological Symptoms*

Up to 50% of women attending menopause clinics report psychological complaints during the menopausal transition (Hay, Bancroft, & Johnstone, 1994).

Physical activity influences neurotransmitter release, which plays a major role in depressive symptoms (Juarbe, Guti´errez, Gilliss & Lee, 2006). Vance, Wadley, Ball, Roenker & Rizzo (2005) found that physical activity boosts cognitive function by promoting social interaction in older adults. They also found that participating in more physical activity predicted larger social networks, which can increase brain stimulation, thus indirectly lower depressive symptoms. Elavsky and McAuley (2007) found that exercisers had enhanced mood and improved menopause-related quality of life. Moderate-intensity exercise can stimulate a positive change in psychological health and quality of life among healthy postmenopausal women. However, in order to sustain this improved psychological health, exercise participation must be maintained in previously inactive postmenopausal women (Asbury et al., 2006). Other researchers have also identified positive correlations between exercise and reduced psychological symptoms during menopause (Mirzaiinjmabadi et al., 2006; Nelson et al., 2007; Progetto Menopausa Italia Study Group, 2005; Slaven & Lee, 1997). A literature review by Dunn, Trivedi, and O'Neal (2001) identified that both moderate and vigorous exercise can reduce symptoms of depression.

### *1.3.7 Physical Symptoms*

Physical symptoms such as breast tenderness are specifically related to the hormonal changes during the menopausal transition; however, there is no research on whether exercise reduces the frequency of breast tenderness in postmenopausal women. Another physical symptom is aches and pains in the muscles and joints. A study conducted with 1028 postmenopausal women found that 86% of women reported body or

joint aches and pains (Haines et al., 2005). Myer et al. (1999) found a 54% reduction in aches and pains in a group of men and women between 40-97 years who participated in a community exercise program. One might speculate that aches and pains are reduced by the exercise induced beta-endorphin release, or it could be that since exercise reduces depressive symptoms (Vance et al., 2005) women are less likely to complain of body aches and pains.

Another physical symptom associated with menopause is weight gain. Physical activity may provide a low-risk way of preventing weight gain and promoting maintenance of weight loss in overweight and obese women (Pronk & Wing, 1994). Sedentary postmenopausal women who exercised for approximately 3 hours a week for a year lost 4.2% of total body fat while maintaining their usual diet (Irwin et al., 2003). Sternfeld et al. (2005) determined that exercise is beneficial for maintaining optimal body composition in postmenopausal women.

### *1.3.8 Urogenital Symptoms*

Menopause is associated with a decline in sexual activity (Stadberg et al., 2000). Dennerstein et al. (2002) found that 42% of women in the early menopausal transition reported sexual dysfunction, compared with an alarming 88% of postmenopausal women. It is not clear how physical activity affects sexual health although; since physical activity improves fitness levels it may improve sexual health (Li et al., 1998). Physical activity has been shown to slow the rate of aging (Dziura, de Leon, Kasl & DiPietro, 2003), and may reduce weight gain therefore it may reduce sexual dysfunction by maintaining positive body image and sense of well-being. Ojanlatva et al. (2006) found that women

aged 42 to 46 (premenopausal age) who participated in strenuous exercise had more positive orgasmic experiences. However this study did not report increase positive orgasmic experiences in strenuous exercising women ages 52 to 56 (postmenopausal age). Slaven and Lee (1997) indicated that menopausal women reported less sexual dysfunction immediately following an aerobic exercise class. Li et al. (2003) found lower reports of vaginal dryness in exercising postmenopausal women. Conversely Mirzaiinjmabadi et al. (2006) found no association between exercise and sexual problems.

Urinary stress incontinence is another commonly reported urogenital symptom and can occur as a result of vaginal atrophy and weakened muscles. The Progetto Menopausa Italia Study Group (2005) identified that regular exercise is associated with reduced reporting of urinary leakage.

### *1.3.9 Co-Factors*

Time since menopause, hysterectomy and percent body fat were selected as possible co-factors in the study in this thesis because they are all thought to affect the frequency of menopausal symptoms. Time since menopause is a factor since most women will only experience menopausal symptoms such as hot flashes for 6 months to 2 years (Kronenberg, 1990). Only 20% will experience symptoms for 10-20 years (Berg et al., 1988). Hysterectomy is thought to be a factor since surgical menopause has been associated with greater frequency of hot flashes, sexual dysfunction, and psychological problems (Sherwin & Gelfand, 1985; Kotz et al., 2006). Hot flashes have been reported at rates of up to 90% for women who have both ovaries removed (Feldman et al., 1985). As

the ovaries are the primary producer of estrogen, the removal of these hormone-producing glands causes an instant decrease in circulating estrogen. As for percent body fat, some say that heavier women report fewer hot flashes (Longcope, 1979; Erlik et al., 1982; Schwingl et al., 1994); whereas others found that hot flashes or night sweats were reported more frequently in heavier women (Gold et al., 2000; Chiechi et al., 1997; Freeman et al., 2001; Li et al., 2003). Some have reported no difference between hot flash frequencies in women with high and low BMI (Ivarsson et al., 1998; Mirzaiinjmabadi et al. 2006; Guthrie et al., 2005).

### *1.3.10 Summary*

There is evidence both supporting and refuting the effects of exercise on menopausal symptoms. Some studies suggest that higher activity levels reduce the number of vasomotor symptoms (Progetto Menopausa Italia Study Group, 2005; Stadberg et al., 2000; Guthrie et al., 2005; Li et al., 2003; Elavsky & McAuley, 2007) whereas others do not (Nelson et al., 2007; Mirzaiinjmabadi et al., 2006). Exercise has also been shown to reduce sleep problems (Progetto Menopausa Italia Study Group, 2005; Slaven & Lee, 1997; Elavsky & McAuley, 2007), limb numbness and tiredness (Mirzaiinjmabadi et al., 2006), headache (Progetto Menopausa Italia Study Group, 2005; Mirzaiinjmabadi et al., 2006; Slaven & Lee, 1997) psychological problems (Mirzaiinjmabadi et al., 2006; Slaven & Lee, 1997; Nelson et al., 2007; Progetto Menopausa Italia Study Group, 2005) and urogenital symptoms (Progetto Menopausa Italia Study Group, 2005; Slaven & Lee, 1997; Li et al., 2003).

No studies have precisely defined the minimal level of physical activity that is required to reduce menopausal symptoms. With the study described in this thesis, women who reported doing vigorous activity were excluded. This provides a narrow range of physical activity levels, allowing for suggestion of the minimal level of activity required for reducing menopausal symptoms.

This research project will examine whether reports of higher levels of physical activity are associated with reduced reporting of menopausal symptoms in a population base that is very specific to non-vigorously active postmenopausal. According to Health Canada reports, 60% of older adults are inactive (Health Canada, 2003). Exercise has many positive health benefits and may be an inexpensive treatment for relief of menopausal symptoms. This study is unique in that it has very tight inclusion criteria, and when appropriate adjustments will be made for possible confounding variables such as years since last menstrual period, hysterectomy and percent body fat. The Menopausal Index used in this study is detailed and specific to the most common menopausal symptoms; yet it is precise and quick to complete making it more likely for women to respond with accuracy. Since little research has been conducted in the area of exercise and its effects on menopausal symptoms this thesis is exploratory in nature.

## 1.4 Statement of the Purpose

This thesis is based upon secondary data analysis from a data set for a clinical trial and it is a cross-sectional design. The main purpose was to determine whether physical activity was associated with a reduction in menopausal symptoms. Providing that a difference among groups exists, a secondary purpose was to suggest an adequate level of physical activity for relief of menopausal symptoms.

### *1.4.1 Hypotheses*

It was **hypothesized** that among this sample of inactive women, those who are the *most* physically active will have fewer menopausal symptoms than those who are the *least* physically active.

# CHAPTER 2 – METHODOLOGY

## 2.1 Research Design

A cross-sectional observational design was used to explore menopausal symptom variation between women with differing activity levels. One of the inclusion criteria was that women could not be currently participating in vigorous physical activity; therefore the levels of physical activity were similar among women. Five physical activity groups were derived by dividing women based on self-reported levels of participation in physical activity.

### *2.1.1 Participants*

Four hundred and one non-vigorously active postmenopausal women were recruited by newspaper ads and posters; and were required to meet the inclusion criteria *(Appendix A)*. All subjects were postmenopausal defined by no menstrual period for at least 12 consecutive months. Women who were less than 2 years postmenopausal, or who had hysterectomies and were unsure of their menopausal status, were assessed for follicle stimulating and leutinizing hormone to confirm menopausal status. Subjects were not taking hormone replacement therapy or selective estrogen receptor modulators within 12 months of recruitment. Subjects were not involved in vigorous exercise (such as running, high impact aerobic activities and/or weight training) at the time of recruitment. Additional exclusion criteria are outlined in Appendix A as these criteria were derived for a clinical trial that was determining the effects of an exercise and dietary intervention on bone mineral density. Baseline results from the clinical trial were used in this study (prior to the administration of exercise or dietary supplements) to examine the relationship

between activity levels and menopausal symptoms. The study was approved by the University of Saskatchewan's Biomedical Research Ethics Board *(Appendix B)*. Written informed consent *(Appendix B)* was obtained from all subjects prior to participation.

### *2.1.2 Sample Size*

The minimum sample size was calculated using the mean and standard deviation of hot flashes and night sweats from the St. Germaine (2001) article (the questionnaire we chose to use). These were the only 2 symptoms with means and SD reported.

The estimated mean (SD) for hot flash frequency from St-Germaine et al. (2001) showed their control group to have 32 hot flashes per week (SD= 5) and 9 night sweats per week (SD= 2). Elavsky and McAuley (2007) showed decreases in vasomotor symptoms for subjects in a walking exercise program to be 17% and 6% for control subjects. The expected change scores were used to calculate how different a physically active group might be from a control group for both hot flash frequency and night sweat frequency. Using the mean values from the St-Germaine et al. (2001) paper. The sample size calculations were done according the procedures of Elashoff (1999) as follows: The physical activity group expected hot flash frequency = 32 - (32 x 0.17) = 26.6 and the control group expected hot flash frequency = 32 - (32 x 0.06) = 30.1. Subjects were divided into quintiles based on their physical activity scores. Based on this division it would be expected that three "intermediate physically active" groups would fall somewhere in-between the "physically active" and "control" values calculated above; therefore, assuming the improvement in vasomotor symptoms is linear across the groups, the estimated hot flash frequency for the intermediate groups would be 27.5, 28.4, and

29.2 from most active to least active. Using these estimated means of 5 physical activity groups and the SD of 5, an alpha of 0.05 and a power of 80% it was estimated that 41 subjects per group (i.e. 205 subjects total) would be required for the study.

The same calculations were used for night sweats: The physical activity group night sweat frequency = 9 - (9 x 0.17) = 7.5 and the control group night sweat frequency = 9 - (9 x 0.06) = 8.5. Intermediately active groups would have a value between these two = 7.75, 8.0, and 8.25. Using these means and the SD of 2, an alpha of 0.05 and a power of 80% it was estimated that 78 subjects per group (i.e. 390 subjects total) would be required.

## 2.2 Measures

The primary measurement tools used included the Leisure-Time Exercise Questionnaire (Godin & Shephard, 1985) and the Menopausal Index (St. Germain et al., 2001). Both questionnaires are based on a 7-day recall of an average week. The third measurement tool used to assess body composition was dual energy X-Ray absorptiometry.

### *2.2.1 Leisure-Time Exercise Questionnaire (Godin & Shephard, 1985) (Appendix C)*

The Leisure-Time Exercise Questionnaire (LTEQ) is commonly used as an assessment tool for health and exercise related research. It was primarily developed and validated for an adult population. This self-administered questionnaire asks about the frequency of strenuous, moderate and mild intensity exercise activity performed for more than 15 minutes during free time of an average 7-day period. The intensity of activity is

weighted by anticipated metabolic equivalent (MET) values. The frequency of reported strenuous, moderate and mild intensity exercise sessions of more than 15 minutes are multiplied by 9, 5 and 3, respectively. The multiplied totals for respective intensities of exercise are then summed to provide an overall activity score. Test-retest reliability on the LTEQ with adults has been reported to be $r$=0.74 with a 2-week wait between re-testing, and $r$=0.62 with a month between re-testing (Godin & Shepard, 1985; Jacobs, Ainsworth, Hartman & Leon, 1993). The LTEQ significantly correlates with accelerometer motion scores ($r$=0.32), and to $VO_2$ Max ($r$= 0.56) (Jacobs et al., 1993). Sallis, Buono, Roby, Micale and Nelson (1993) compared the activity rating score to other activity measures showing significant correlation coefficients of $r$= 0.32 for the activity score and $r$=0.39 for the amount of calories burned per day. The LTEQ is comparable to other physical activity questionnaires for reliability but is one of the best for validity (Pereira et al., 1997). This questionnaire was also chosen because of its ease of administration and the fact that it takes only a minute to complete. Participants in this thesis were involved in a larger intervention study that included many other measures; therefore, this relatively short physical activity questionnaire was partly chosen to limit subject burden.

### *2.2.2 Menopausal Index (St. Germain et al., 2001) (Appendix D)*

The second measurement tool was the Menopausal Index (St. Germain et al., 2001). It considers frequency, duration and severity of various menopausal symptoms experienced during an average 7-day period. The symptoms under examination include hot flashes or night sweats, insomnia, limb numbness (pins and needles), fatigue and

headaches. It also includes a series of yes/no questions with sections on psychologically related areas (i.e. mood changes, depression, irritability, anxiety, and decrease concentration), urogenital symptoms (i.e. decreased sexual libido, vaginal dryness, uncomfortable intercourse, changes in urinary frequency), and physical symptoms (aches and pains in the back, muscles, and joints, breast tenderness, and weight gain).

The Menopausal Index (St. Germain et al., 2001) was modified from the Kuppermann-Blatt Menopausal index (Blatt, Wiesbader & Kuppermann, 1953), which originally included a checklist of 11 symptoms. St. Germain et al. (2001) added another 6 symptoms to capture the effects of vaginal atrophy. Reliability of the Kupperman-Blatt Menopausal index (Blatt et al., 1953) is $r$=0.68 (Sousa R.L., Sousa, E.S., Silva & Filizola, 2000). Similar to the LTEQ, this questionnaire was chosen because of its ease and time of administration, limiting subject burden.

### *2.2.3 Body Composition*

Body fat was assessed by dual X-ray absorptiometry whole body scans in array mode (Hologic Discovery). Participants lay supine on the X-ray bed, while the bed motioned up and down under the X-ray arm. The length of a full body scan is approximately 8 minutes. A reproducibility study was conducted on this machine measuring 18 women on two occasions, one week apart showing a coefficient of variation for fat mass of 3% (unpublished data. Chilibeck, 2003). Chilibeck (2003) previously validated this measure by comparing to air displacement plethysmography. The correlation between the two techniques for fat mass was 0.98 (Pinkoski et al., 2006).

## 2.3 Procedure

Upon successful screening following the use of the inclusion/exclusion checklist and signing the consent form (*Appendix B*) women completed a personal information form *(Appendix E)* including such details as date of birth, date of last menstrual period and whether or not they have had a hysterectomy. Women were given oral instructions on how to complete the questionnaires. Based on the scores of the LTEQ, women were placed into quintiles for amount of physical activity (groups 1-lowest to 5-highest) and these quintiles were examined for differences in menopausal symptoms. Dividing women into 5 groups distinguishes between those who are doing less or more than the recommended 30 to 60 minutes of moderate intensity physical activity on most days (PHAC, 2007). Using this daily exercise recommendation the weekly exercise duration for health benefits would fall between 3.5 to 7 hours of moderate intensity exercise per week. The lowest quintile (Group 1) in this study were considered to be the inactive women (performing about 30 minutes of moderate intensity physical activity per week), and the highest quintile (Group 5) were considered to be the most active (performing more than 2 hours of moderate intensity physical activity per week). The women with scores in between quintiles 1 and 5 were considered to be intermediately active groups (performing between 30 minutes to 2 hours of moderate intensity physical activity per week). Therefore only the women in the top fifth quintile in the study were doing enough leisure time physical activity to receive optimal health benefits. It can be assumed that since 15-minutes is the minimum duration that most leisure activity sessions reported on the questionnaire lasted slightly longer, possibly between 20 to 30 minutes. These

calculations are averaged and based on the minimum 15-minute sessions; therefore activity levels in each group may actually be slightly under reported.

The activity groups were derived based on scores from the Leisure-Time Exercise Questionnaire (Godin & Shephard, 1985). This questionnaire asks the frequency of strenuous, moderate and mild exercise lasting longer than 15 minutes during a 7-day period. Strenuous exercise is explained as activity that induces a rapid heartbeat with exercises including jogging, hockey, soccer, squash, basketball, cross-country skiing, judo, and vigorous cycling. Moderate exercise is explained as activity that is not exhausting and includes exercises such as fast walking, baseball, tennis, easy cycling, volleyball, easy swimming and folk dancing. Mild exercise is explained as requiring minimal effort and includes activities such as yoga, bowling, golf and easy walking. The participants were divided into quintiles according to their scores on the LTEQ. Group1 had LTEQ scores between 0-8, whereas group 5 had scores higher than 38.5. Table 1 reflects 5 activity levels and the number of sessions of exercise per week lasting longer than 15-minutes in duration at any of the 3 intensities that women completed to fall within the range of that activity group. Table 1 also represents the frequency of exercise sessions lasting longer than 15-minutes that should be performed throughout the week in order to match one of the five activity groups. This will indicate the approximate amount of physical activity women in this study performed and the difference among the five activity levels, considering that all women were non-vigorously active upon entering the study.

**Table 1.**

| Activity Group | LTEQ Score | # of exercise sessions/week lasting > 15 min | | |
|---|---|---|---|---|
| | | Mild | Moderate | Strenuous |
| 1 | 0-8 | ~ 3 | ~ 2 | ~1 |
| 2 | 9-18 | 3-6 | 2- 4 | 1-2 |
| 3 | 19-26 | 6-9 | 4-5 | 2-3 |
| 4 | 27-38 | 9- 13 | 5-8 | 3-4 |
| 5 | 38.5 + | >13 | >8 | >4 |

The menopausal index asks the frequency (number of times per week), severity (score of 0 to 3, where 0 is no symptoms and 3 is severe), and duration (minutes) of 1) hot flashes, 2) insomnia, 3) limb numbness, 4) fatigue and 5) headache. The insomnia section of the questionnaire also includes yes/no questions of whether women have difficulty falling asleep, difficulty staying asleep and waking too early in the morning. The final sections of the questionnaire includes yes/no questions for: 1) psychologically-related symptoms (i.e. mood changes, depression, irritability, anxiety, and decrease concentration), 2) urogenital symptoms (i.e. decreased sexual libido, vaginal dryness, uncomfortable intercourse, changes in urinary frequency), and 3) physical symptoms (aches and pains in the back, muscles, and joints, breast tenderness, and weight gain). Each of these final sections was scored for number of "yes" responses to each symptom, where each "yes" response increased the score by 1. The severity and frequency responses were converted into Z-scores, and then the mean of the two Z-scores for each symptom was calculated to determine an overall Z-score for the symptoms of hot flashes, limb numbness, fatigue, and headaches. For insomnia the overall Z-score was calculated by taking the mean of the Z-scores from frequency and severity and the mean of the Z-scores from the yes/no responses for difficulty falling asleep, difficulty staying asleep and waking too early in the morning. The two mean Z-scores were combined to make a total

mean Z-score for insomnia. The responses to duration for each symptom were often left unanswered therefore we did not have enough data to consider it as an accurate response. Other studies have excluded the duration question in their analysis since they also found that the responses were inconsistent or incomplete (St. Germain et al., 2001). Finally, the yes/no responses for sections on psychological, urogenital, and physical symptoms were summed then converted to mean Z-scores representing an overall score for each section.

### 2.4 Analysis

The analysis was conducted using SPSS version 14.0. Prior to any data analysis, the level of significance was preset at $p \leq 0.05$. This thesis was based upon secondary data analysis from a data set from a clinical trial. This was a cross-sectional study and was exploratory in nature.

First, a MANCOVA was conducted to determine whether higher activity levels have an independent effect on menopausal symptom reduction by including potential confounders that were different among the groups. Differences among the dependent variables were analyzed according to the independent variable of activity levels (i.e. there are 5 levels of the independent variable in the one-way MANCOVA).

Secondly, a one-way MANOVA was conducted looking for symptom differences among the 5 activity levels (significant if Wilks' Lamda $p \leq 0.05$). The dependent variables in the MANOVA were: Z-scores for hot flashes, insomnia, limb numbness, fatigue, headache, psychologically-related symptoms, urogenital symptoms and physical symptoms. Appropriate univariate tests were conducted. Post-hoc tests (Bonferroni) were

used to determine where the group differences existed for each significant menopausal symptom.

There is empirical evidence supporting that years post-menopause, hysterectomy (yes=1 or no=0), and percent body fat may have an effect on menopausal symptoms therefore may be potential confounding variables. The purpose of running both the MANOVA and the MANCOVA was to determine whether differences between physical activity levels are due to the potential confounding variable(s).

## CHAPTER 3 – RESULTS

The mean (SD) age of the participants was 58.2 (6.3) years, the mean years postmenopausal was 6.7 (6.0) years and the mean percent body fat was 37.4 (5.6) %. Of the 401 in the study, 16.5% had a previous hysterectomy. Other group characteristics can be seen in Table 2.

**Table 2.**

| PA Level | N | Mean Age | Mean Years Menopausal | Mean % Body Fat | Mean % with Hysterectomy |
|---|---|---|---|---|---|
| 1 | 82 | 56.7 (6.3) * | 6.6 (5.9) | 39.3 (4.6)*** | 21 |
| 2 | 80 | 57.3 (5.2) | 5.9 (4.9) | 38.3 (5.9)**** | 16 |
| 3 | 82 | 59.2 (7.5) | 7.1 (6.6) | 36.9 (4.9) | 17 |
| 4 | 80 | 60.1 (5.9)** | 7.5 (6.2) | 36.9 (5.7) | 14 |
| 5 | 77 | 58.0 (5.9) | 6.3 (6.2) | 35.6 (6.0) | 14 |
| **Total Mean** | 80.2 | 58.2 (6.3) | 6.7 (6.0) | 37.4 (5.6) | 16 |

* Significantly younger than PA level 3, ($p<0.05$).
** Significantly older than PA level 1, 2 & 5, ($p<0.05$).
*** Significantly higher than PA level 3, 4 & 5, ($p<0.05$).
**** Significantly higher than PA level 5, ($p<0.05$).

Results of the MANOVA indicated a significant group main effect of physical activity on menopausal symptoms {Wilks' Lamda $F(32,1436) = 1.510$, $p = 0.034$}. The overall multivariate effect size for the MANOVA was 0.03. Of the 8 symptoms under review there were significant group differences for physical symptoms {$F(4,396) = 3.844$, $p=0.004$}and fatigue {$F(4,396) = 2.341$, $p=0.05$}. The effect size for both physical symptoms and fatigue was 0.31. The post hoc analyses are displayed in Figures 1 and 3.

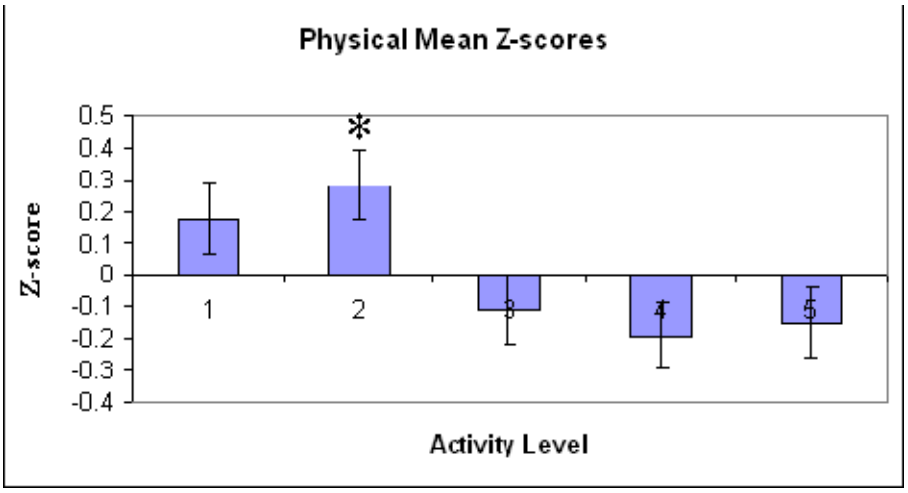


**Figure 1**. ∗ = Significantly more physical symptom complaints than groups 4 & 5
Error bars reflect Standard Error

Of the 3 symptoms comprising physical symptoms there was significant differences for reported weight gain {$F(4,396) = 3.902$, $p$=0.004} but not for breast tenderness {$F(4,396) = 0.491$, $p$=0.742} or aches and pains {$F(4,396) = 1.596$, $p$=0.175}. The effect size for weight gain was 0.32. Figure 2 shows the differences in reported weight gain among the 5 levels of physical activity.

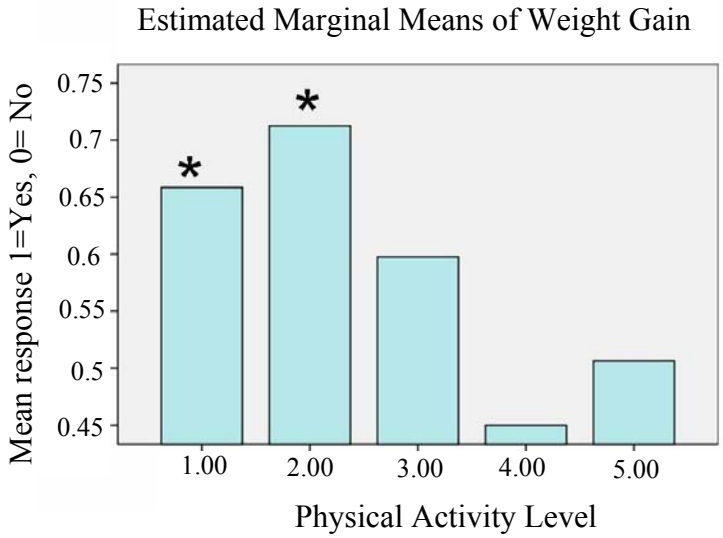


**Figure 2.**
∗ = Significantly more weight gain than groups 4 & 5.

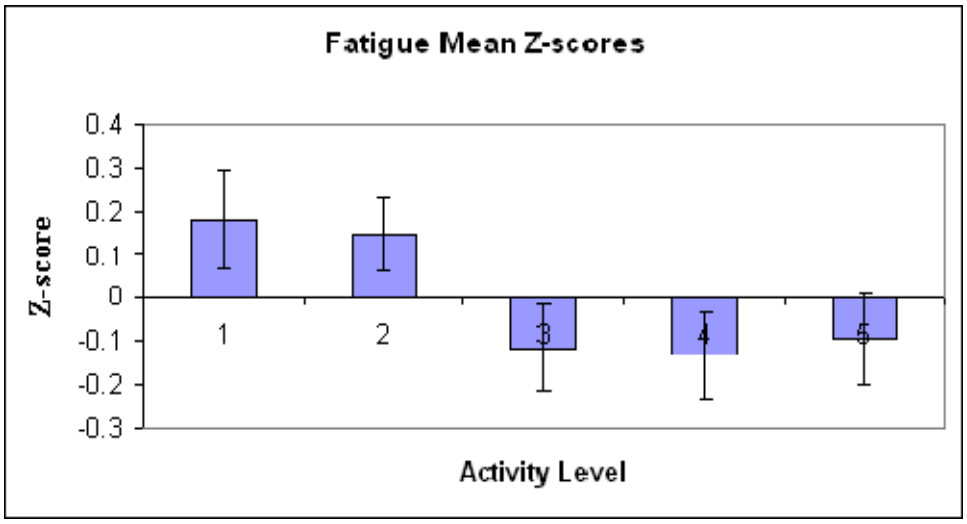


**Figure 3**. Error bars reflect Standard Error

The post-hoc analysis identified that 2 least active groups reported above average fatigue occurrence whereas the 3 most active groups reported below average fatigue occurrence.

There were no significant group differences for insomnia {$F(4,396) = 0.698$, $p$=0.594}, numbness in limbs {$F(4,396) = 0.050$, $p = 0.995$}, psychological symptoms {$F(4,396) = 0.737$, $p = 0.567$}, or urogenital symptoms {$F(4,396) = 0.190$, $p = 0.944$} however hot flashes {$F(4,396) = 2.242$, $p$=0.064}, and headache {$F(4,396) = 2.23$, $p$=0.065} were close to $p \leq 0.05$. The symptom differences across groups are presented in Figures 4-9.

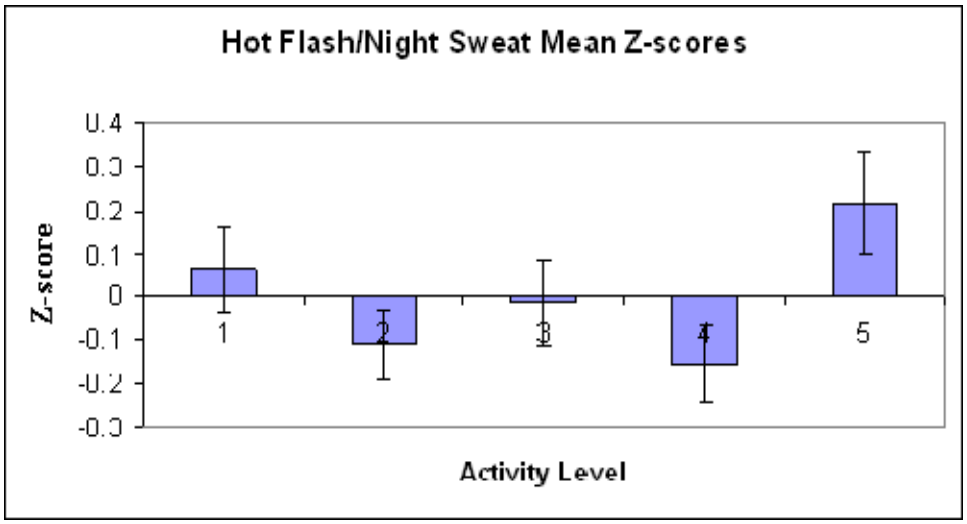


**Figure 4.** Error bars reflect Standard Error

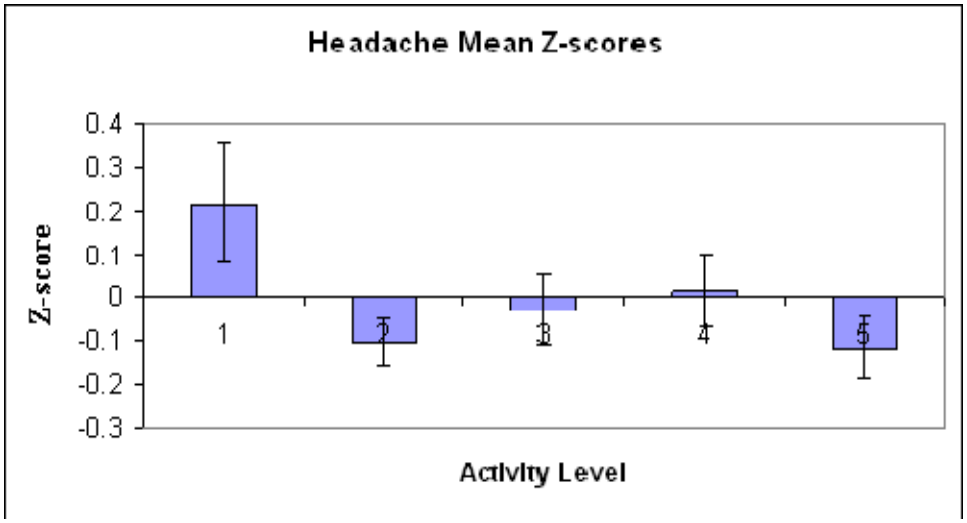


**Figure 5**. Error bars reflect Standard Error

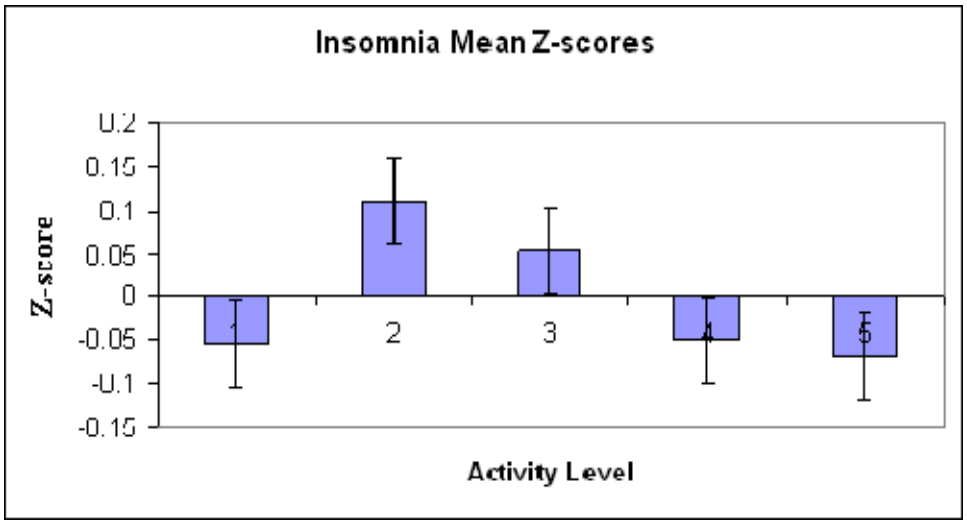


**Figure 6.** Error bars reflect Standard Error

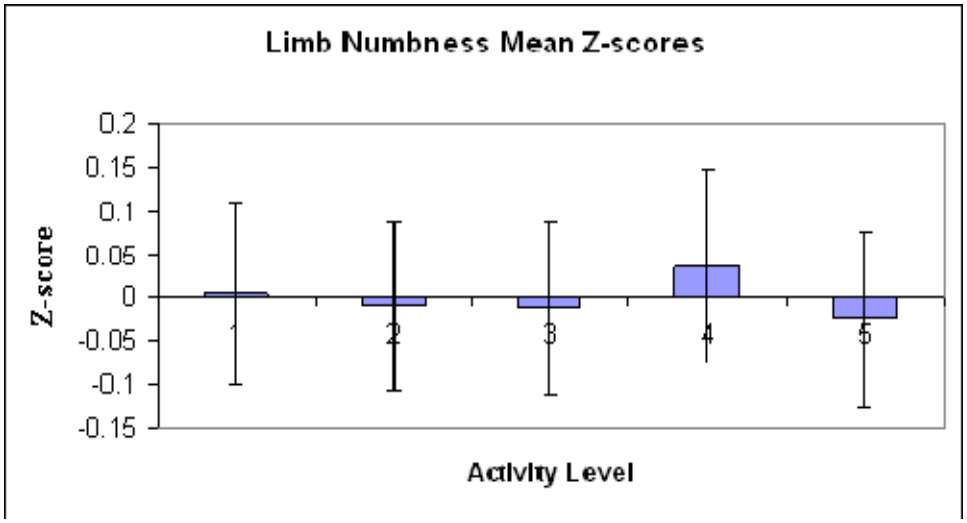


**Figure 7.** Error bars reflect Standard Error

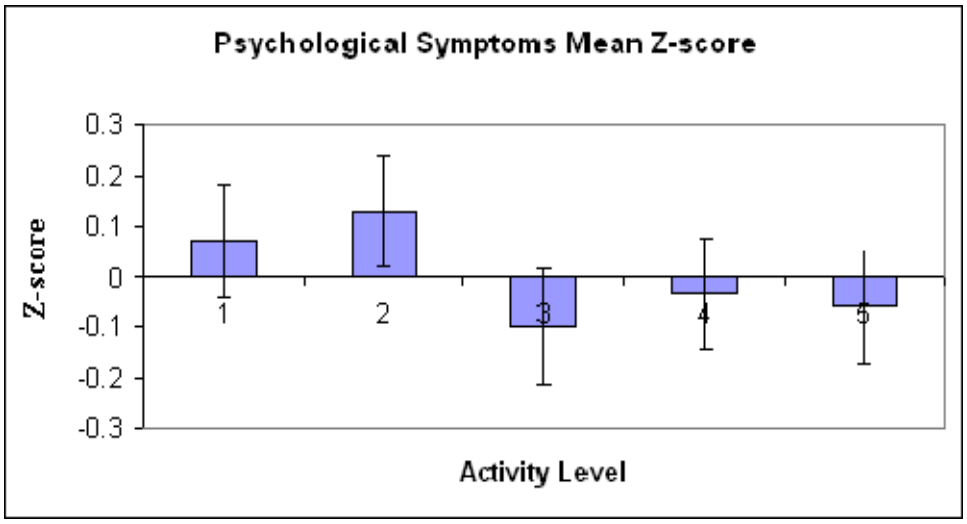


**Figure 8.** Error bars reflect Standard Error

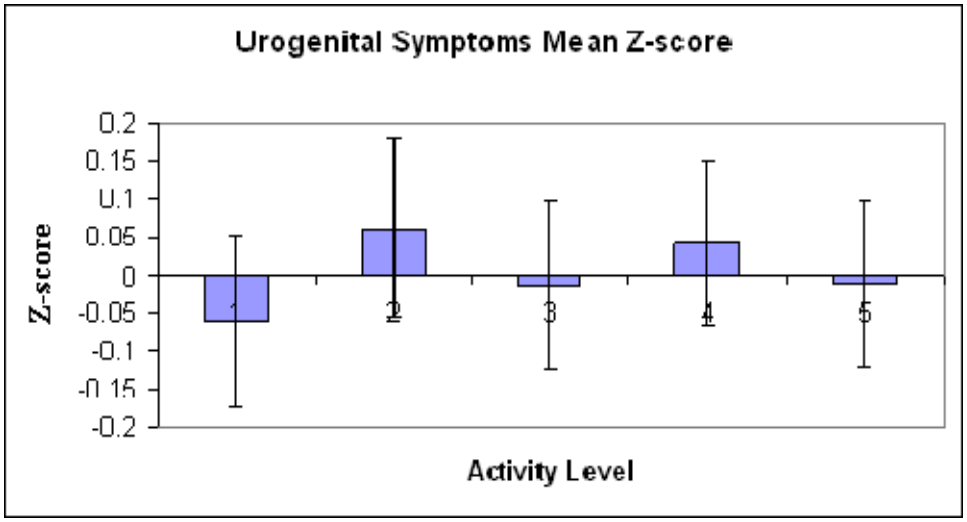


**Figure 9.** Error bars reflect Standard Error

There were no significant group differences for hysterectomy {$F(4,396) = 0.448$, $p=0.774$} or time since menopause {$F(4,396) = 0.941$, $p=0.440$}. However there were significant group differences for percent body fat {$F(4,394) = 5.47$, $p=0$}. Figure 10 shows the differences in mean percent body fat between groups.

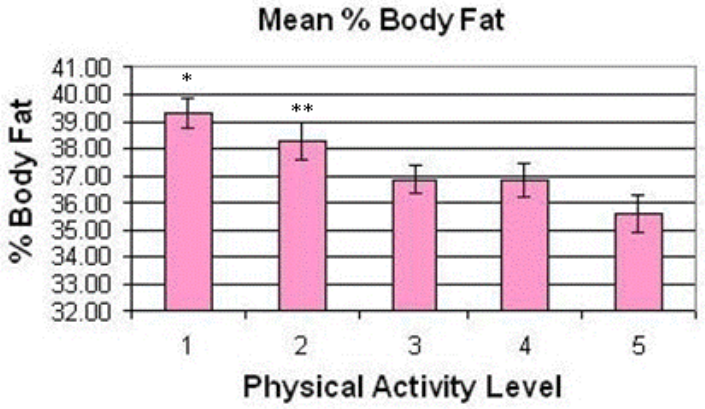


**Figure 10.**

* Group 1 has significantly higher percent body fat than Groups 3, 4 & 5
** Group 2 has significantly higher percent body fat than Group 5.

Since percent body fat was the only covariate that was significantly different among groups it was the only one included in the MANCOVA. This multivariate test was not significant between physical activity groups with percent fat as a covariate {Wilks' Lamda $F(32,1425) = 1.295$, $p = 0.126$}.

# CHAPTER 4 – DISCUSSION

The present study examined the difference of menopausal symptom reporting relative to five activity levels among a sample of non-vigorously active postmenopausal women who were not using hormone replacement therapy. This study was a cross-sectional design and exploratory in nature. When controlling for the group means differences of percent body fat there was no independent effect of physical activity on menopausal symptoms. However when not accounting for effects of percent body fat there were activity level group differences for reporting physical symptoms (only weight gain) and fatigue. In other words, when accounting for group differences of percent fat, physical activity has no independent effect on menopausal symptoms and it can be assumed that any indirect effect of physical activity on menopausal symptoms is through an alteration of body fat.

The results indicate group differences in reported weight gain, which may be explained by the relationship between perceived weight gain and percent body fat. Since the menopausal transition is associated with weight gain and increased obesity (Lovejoy, 2003), exercise may play a role in preventing these body composition changes. Pronk and Wing (1994) found physical activity to be a low-risk method of preventing weight gain and promoting maintenance of weight loss in overweight and obese women. These findings are also in agreement with Irwin et al. (2003) who found that sedentary postmenopausal women who exercised for approximately 3 hours a week for a year lost significant amount of body fat while maintaining their usual diet. Sternfeld et al. (2005) also identified exercise as a beneficial means to maintain optimal body composition.

Increased body fat may increase fatigue through inefficiency in performing everyday activities. Dimeo et al. (1998) found that aerobic training can improve performance by reducing rapid fatigability when carrying out daily activities. These study results identified similar findings to Mirzaiinjmabadi et al. (2006) who found a positive relationship between exercise and reduced tiredness in postmenopausal women.

This study did not find a significant relationship between hot flashes and activity levels. These findings correspond with other studies (Aiello et al., 2004; Nelson et al., 2007; Mirzaiinjmabadi et al., 2006) that also found no association between activity levels and vasomotor symptoms. However many studies have found a positive association between exercise and reduced vasomotor symptoms (Progetto Menopausa Italia Study Group, 2005; Stadberg et al., 2000; Guthrie et al., 2005; Li et al., 2003; Elavsky & McAuley, 2007). Since the most active women (group 5) reported the most hot flashes/night sweats and since they had the lowest percent body fat, it is possible that they had lower levels of circulating estrone, explaining the increased hot flash reports. Some data suggests that heavier women report fewer hot flashes resulting from a fat-related increase in circulating estrone (Longcope, 1979; Erlik et al., 1982; Schwingl et al., 1994). The least active women (group 1) reported the next highest frequency of hot flashes/night sweats. There is a positive association between BMI and vasomotor symptoms (Gold et al., 2000; Gold et al., 2006; Li et al., 2003; Ivarsson et al., 1998) where increased adiposity raises core body temperature and has been said to increase hot flash frequency (Glickman-Weiss, Nelson, Hearon, Prisby,& Caine, 1999); thus one might speculate the possibility that the highest reporting of hot flashes in the least active quintile (group 1) in this study is related to women in this group being more overweight and having the

highest percent body fat (Group 1 mean = 39.3% vs Group 5 mean = 35.6%). Two cross-sectional studies identified that women with BMI over 32 kg/$m^2$ had a higher prevalence of hot flashes/night sweats than women with a BMI less than 19 kg/$m^2$ (Gold et al., 2000) and that a BMI between 25-29.9 was associated with a higher incidence of hot flashes (Li et al., 2003). The current study results did not demonstrate a linear relationship between activity levels and hot flashes or night sweats. One might speculate that the relationship may be parabolic; that is, with low and high levels of physical activity (ie. lower vs higher % body fat) resulting in greater hot flashes/night sweats than moderate levels of physical activity.

This study did not find a significant relationship between physical activity and headache. Past research has stated that regular aerobic exercise decreases headache frequency and severity by as much as 50% (Peterson, 2007). Steiner et al. (2002) found that tension headaches are more commonly reported among sedentary individuals, in which exercise may be a viable preventative treatment. Since exercise has been shown to result in a temporary increase of cortical blood flow and an increase of beta-endorphin release (Oleson, 1971) it may dull or numb headache pain. In this study the least active group reported the highest frequency of headache whereas the most active group reported the least occurrence of headache. Other researchers have found that regular exercise can reduce headache (Progetto Menopausa Italia Study Group, 2005; Mirzaiinjmabadi et al., 2006; Slaven & Lee, 1997).

Longitudinal studies have shown that higher levels of leisure time physical activity are associated with lower risks of depression and depressive symptoms (Dunn et al., 2001). This thesis did not identify a significant association between activity levels and

psychological symptoms in postmenopausal women. It has been suggested that perimenopause is associated with increased reporting of depressive symptoms; however when accounting for confounding variables, depression is not associated with menopausal status (Bosworth et al., 2001). Bosworth et al. (2001) also reported a significant correlation between inactivity and increased depressive symptoms. The findings of this study were contrary to other researchers who have found exercise to reduce psychological symptoms during menopause (Mirzaiinjmabadi et al., 2006; Slaven & Lee, 1997; Nelson et al., 2007; Progetto Menopausa Italia Study Group, 2005). A review by Dunn et al. (2001) identified that both aerobic and resistance exercise can reduce symptoms of depression.

Past research has indicated that exercisers report fewer sleep problems than sedentary individuals (Gold et al., 2000; Progetto Menopausa Italia Study Group, 2005; Slaven & Lee, 1997). Others, however, have also reported no effect of exercise on sleep quality (Elavsky & McAuley, 2007). Elavsky and McAuley (2007) suggested that a four-month moderate-intensity aerobic exercise intervention may be an insufficient stimulus to improve perceived sleep quality in symptomatic menopausal women. The results of this thesis do not demonstrate that those with higher activity levels have fewer sleep problems. Sleep changes in postmenopausal women have been linked to hot flashes/night sweats and to stress (Manber & Armitage, 1999).

This thesis found no significant relationship between activity levels and limb numbness or urogenital symptoms. Of the questions on the Menopausal Index regarding urogenital symptoms (decreased libido, vaginal dryness, uncomfortable intercourse and changes in urinary frequency) often the questions regarding intercourse and libido were

left blank or women reported as not applicable which may have affected the results. Ojanlatva et al. (2006) found that strenuous exercise improved orgasm experience in pre-menopausal women but not in post-menopausal aged women. Although limb numbness is included in the menopausal symptom index, it is not commonly described as being a menopausal symptom in the menopause literature.

Percent body fat was the only covariate that was significantly different among the five activity groups. It was identified that the women in this study who reported performing 4 or fewer sessions of moderate intensity exercise per week lasting a minimum of 15-minutes in duration had significantly higher percent body fat those doing more than 8 sessions per week. This is consistent with findings of Sternfeld et al. (2005) who found that higher levels of physical activity are associated with decreased percent body fat. The fact that there is no significant relationship between higher activity levels and reduced menopausal symptoms when accounting for differences of percent body fat implies that any positive effect of physical activity may be indirectly through a reduction in percent body fat. Although the MANOVA was significant without accounting for percent fat, the effect size was small.

These study results can be generalized to non-vigorously active postmenopausal women who are not using HRT. The majority of the subjects were middle-class Caucasian women.

This study is unique in that it had a homogenous group of women who were considered to be non-vigorously active at the time of recruitment. Perhaps this narrowed the ranges in physical activity too much, making it nearly impossible to distinguish between activity levels and symptom reporting. HRT use was another exclusion criterion

that removed the chance that symptom reduction was occurring as a result of drug therapy. Determination of a minimal effective level of physical activity to reduce menopausal symptoms cannot be addressed based on these results.

### 4.1 Conclusion

In summary, these study results indicate that any effect of physical activity on menopausal symptoms is indirectly through the alteration of body composition. Women with lower percent body fat report less weight gain and fatigue. There was no significant relationship between physical activity levels and reporting of hot flashes/night sweats, insomnia, limb numbness, headache, psychological symptoms or urogenital symptoms.

### 4.2 Limitations

The present study was a cross-sectional design therefore it is not possible to disprove a causal relationship between activity levels and symptom reduction. This design is limited in that it does not verify whether higher levels of physical activity reduce menopausal symptoms or whether women who suffer from menopausal symptoms have a natural propensity to participate in less physical activity. Since this was secondary data analysis there was very little control over the study design and the measurement tools.

Women were included in the study based on self-judgment of whether they were vigorously physically active; they were excluded if they admitted to participating in weight training, running or high impact aerobic activities. Perhaps excluding women in the higher ranges of physical activity may have compromised the ability to identify

effects of physical activity on symptoms. A limitation of the LTEQ questionnaire is that the number of 15-minute exercise sessions at the different intensities may underestimate energy expenditure. Women may have performed 30 to 60 minutes during one exercise session but only accounted for 15 minutes as directed by the questionnaire instructions.

The Menopausal Index by St. Germain et al. (2001) was modified from the Kupperman-Blatt Menopausal index. The Kupperman-Blatt index has been criticized by Zollner, Acquadro & Schaefer (2005) for weighting factors based on intuitive factors, and not on the prevalence and consequence. Zollner et al. (2005) also criticized this questionnaire for its lack of quantitative research on psychometric validation finding it to be less accurate and sound, when compared to other menopausal questionnaires. Freeman et al. (2003) suggested that the Kupperman-Blatt Index was out of date and that it lacked statistical justification for summing or weighting item scores or using factor scales. Utian, Janata and Kingsberg (2002) criticized the Kupperman-Blatt Index for using ill-defined terms, lacking demographic data, having categories with overlapping scores and for scores being summed without being based on independent factors.

Participants were limited from providing additional details that the questionnaire may have failed to capture and questionnaire responses may not accurately portray individual activity levels or symptoms. For example, a woman may experience headache but it may be unrelated to menopause (ie. migraine headaches since childhood) however the questionnaire does not allow for clarification. Both questionnaires were based on a 7-day recall, which may have brought about reporting biases. These results can mainly be generalized to middle-class Caucasian women, who made up the majority of the subjects.

### 4.3 Future Directions

The findings of the present study support exercise not only as a tool to better health and disease prevention, but more specifically to reduce some of the negative symptoms associated with menopause. A randomized controlled trial is currently underway examining the effects of an exercise intervention (ie. weight training 2x/wk and walking 4x/wk or stretching 4x/wk), which will include information on menopausal symptom reporting. Based on the findings of the study in this thesis, it is recommended that future studies match groups based on percent body fat prior to randomization, as reduced percent body fat was identified as an outcome of increased activity levels. It is also recommended that future studies prescribe a greater amount of physical activity than the non-vigorously active women who were recruited for this study. Further research in the area of physical activity and its relationship to menopausal symptoms would provide a clearer description of the minimum amount of physical activity required to reduce menopausal symptoms.

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**Appendix A**

**INCLUSION AND EXCLUSION CHECKLIST**

## Inclusion Criteria

- **Postmenopausal women (no menstrual period in past 12 months)** Yes☐ No☐
  **If the answer to this question is NO, the subject is NOT eligible.**

## Exclusion Criteria

- **Previous fragility fractures** Yes☐ No☐
- **Have Taken bisphosphonates (Didronel, Didronel, Actonel, Fosamax), hormone** Yes☐ No☐
  **replacement therapy, selective estrogen receptor modulators (Raloxifene), parathyroid hormone, or calcitonin within the past 12 months**
- **Currently taking corticosteroids or thiazide diuretics** Yes☐ No☐
- **Crohn's Disease** Yes☐ No☐
- **Cushing's Disease** Yes☐ No☐
- **Kidney Disease** Yes☐ No☐
- **Allergy to Soy** Yes☐ No☐
- **Severe osteoarthritis** Yes☐ No☐
- **Currently involved in vigorous exercise training** Yes☐ No☐
- **Planning to travel outside of Saskatoon for an extended period (greater than 2 weeks)** Yes☐ No☐
  **during the study**
- **Previously diagnosed Osteoporosis** Yes☐ No☐
- **Current or previous breast cancer** Yes☐ No☐
- **Current or previous endometrial cancer** Yes☐ No☐

**Form completed by:** _____ **Date:** _____

**Signature of PI:** _____ **Date:** _____

## Appendix B

## Consent Form

**Title of the study**: Effect of combined exercise therapy and isoflavone supplementation on prevention of osteoporosis

**Researchers:** Philip D. Chilibeck, Ph.D., Associate Professor, College of Kinesiology, University of Saskatchewan (966-1072), role: principal researcher; H. Jay Biem, M.D., Department of Medicine, Royal University Hospital, University of Saskatchewan (966-7951), role: clinical trials consultant, Allison Case, M.D., Department of Obstetrics, Gynecology and Reproductive Sciences, Royal University Hospital, University of Saskatchewan (966-1953), role: medical supervision, uterine ultrasound assessment, Olufemi Olantunbosun, M.D., Department of Obstetrics, Gynecology and Reproductive Sciences, Royal University Hospital, University of Saskatchewan (966-8033), role: medical supervision, uterine ultrasound assessment; Roger Pierson, Ph.D. Department of Obstetrics, Gynecology and Reproductive Sciences, Royal University Hospital, University of Saskatchewan (966-4458), role: clinical trials consultant, Susan Whiting, Ph.D., Professor, College of Pharmacy and Nutrition, University of Saskatchewan (966-5837), role: nutritional analyses, Punam Pahwa, Assistant Professor, Department of Community Health and Epidemiology, University of Saskatchewan (966-7941), role: statistical consultant.

**Purpose of the study**: Exercise training and dietary intake of soy protein increase bone mineral density and favorably affect blood cholesterol levels and therefore have the potential for preventing osteoporosis and heart disease. The compound in soy protein that has a beneficial effect is called a “phytoestrogen”. Phytoestrogens have beneficial effects on bone, but unlike estrogen, does not affect breast or endometrial tissue. The purpose of this study is to determine the effect of exercise training, phytoestrogen supplementation, and combined exercise training and phytoestrogen supplementation on bone mineral density, bone quality, body composition, serum lipids, and menopausal symptoms in post-menopausal women.

**Possible benefits of the study**: Possible benefits include an increase in bone mineral density, an improvement in bone quality, a loss of body fat, an increase in muscle mass, an increase in flexibility, a reduction in cholesterol levels and an improvement in menopausal symptoms (i.e. reduction of hot flashes). These benefits are not guaranteed.

**Procedures to be followed**: You will be randomized to one of four groups: 1) Exercise training by weight lifting and brisk walking and phytoestrogen placebo (i.e. you will receive a compound that looks like phytoestrogen, but is really an inactive substance); 2) Exercise training by flexibility training and phytoestrogen supplementation (90 mg per day); 3) Exercise training by weight lifting and brisk walking and phytoestrogen supplementation; or 4) Exercise training by flexibility training and phytoestrogen placebo. You will have an equal chance of being placed into one of the four groups. The study will be double blind, that is, neither you nor the researchers will be aware of

whether you are taking phytoestrogen or placebo until the end of the study. You will receive 1000 mg of calcium supplement and 20 μg of vitamin D per day throughout the study (24 months). If in the weight lifting and brisk walking exercise group, you will be required to perform strength training twice per week (45 minutes to an hour each session) and brisk walking four times per week (about 30 minutes each time) for 24 months. If in the flexibility training exercise group, you will be required to perform flexibility exercises (20-30 minutes per day) four days per week. Your bone mineral density and body composition will be measured at entry into the study, at 12 months and again at 24 months by dual-energy x-ray absorptiometry. The bone in your lower leg and wrist will be measured by ultrasound (to measure bone quality) at baseline, 12, and 24 months. Blood will be collected at baseline, 12 months and at 24 months for assessment of serum lipids. Blood and urine will also be collected at baseline for standard laboratory tests. Approximately of 11 mL of blood will be collected at each time point. At baseline and after 2 years, a mammogram will be performed for screening of breast cancer and an ultrasound will be performed for screening of endometrial cancer. You will be required to fill out questionnaires to assess your food intake every 6 months and menopausal symptoms every 3 months during the study. You will be required to keep records of your physical activity daily. Exercise testing will be performed at baseline, at 12 months and at 24 months. This will involve determining the maximal amount of weight you can lift on several exercises, a walking test over 80 meters, a flexibility test, and a test of balance. You will be phoned periodically for two years after the study for assessment of cancers, coronary heart disease, lung disease, and stroke. This is to assess whether the phytoestrogen is associated with the same risks as regular estrogen.

With your permission, your family physician will be informed of your enrolment and of your test results.

**Foreseeable risks, side effects and discomfort**: There is some radiation exposure with the dual energy x-ray absorptiometry and the mammogram. Because these measurements are being performed at yearly intervals (dual energy x-ray absorptiometry) or 2 years apart (mammogram), the annual exposure is not considered to be a hazardous level.

There is a risk of injury during exercise testing or training. This will be minimized by proper warm-up procedures and supervision by qualified exercise trainers.

There will be some discomfort when blood is drawn for testing serum lipids. Bruising or infection at the sight of the blood draw is a possibility, but care will be taken to minimize these risks.
The side effects of phytoestrogens are unknown.

There may be unforeseen risks during the study or after the study is completed.

You will be asked to keep a diary card on which you will record any side effects or discomfort you may experience from the exercise program or phytoestrogen supplementation.

You are free to withdraw from the study at any time and this withdrawal will not affect access to health care or other services.

Precautions will be taken to protect your anonymity. The data may be published in a graduate student thesis or journal article, but you will not be identified and only aggregate data will be reported. All data will be stored in a locked office in the College of Kinesiology.

There will be no cost to you for participation in this study. You will not be charged for the phytoestrogens / placebo, calcium, vitamin D, or any research procedures. In the event that you become ill or injured as a result of participation in this study, necessary medical treatment will be made available at no additional cost to you. By signing this document you do not waive any of your legal rights.

If you have any questions with regard to the research project, you can call Philip Chilibeck (966-1072 or 343-6577), Jay Biem (966-7951), Allison Case (966-1953), Olufemi Olantunbosun (966-8033), Roger Pierson (966-4458) or Susan Whiting (966-5037).

If you have any questions about your rights as a research subject, or concerns about your participation in this study, you should contact the Chair of the Biomedical Research Ethics Board, c/o the Office of Research Services, University of Saskatchewan at (306) 966-4053.

We will advise you of any new information that will have a bearing on your decision to continue in the study.

**Alternative treatments:** You do not have to participate in this study to increase your bone mineral density. Other treatments, including bisphosphonates and standard hormone replacement therapy are available for increasing bone mineral density. Blood cholesterol levels can be improved by modifying dietary intake of saturated fats.

By signing below, I acknowledge that the study and contents of the consent have been explained and that I understand the contents, and that I have received a copy of the consent form for my own records.

You will be informed of your results at the completion of the study. Because subjects are being staggered into the study and we want to maintain blinding of the study throughout its duration, you may not be informed of your results until a couple of years after you complete the study.

Date: _____

Participant Signature: _____

Researcher:_____

## Certificate of Approval

University of Saskatchewan
Biomedical Research Ethics Board (Bio-REB)

08-Mar-2005

# Certificate of Approval

PRINCIPAL INVESTIGATOR
Philip D. Chilibeck

DEPARTMENT
Kinesiology

BMC #
03-1077

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

College of Kinesiology
105 Gymnasium Place
Saskatoon SK S7N 5C2

SPONSORING AGENCIES

CANADIAN INSTITUTES FOR HEALTH RESEARCH (CIHR)

TITLE:

Protocol Effect of Combined Exercise Therapy and Isoflavone Supplementation on Prevention of Osteoporosis

ORIGINAL APPROVAL DATE
01-Aug-2003

CURRENT EXPIRY DATE
01-Aug-2005

CERTIFICATION UPDATE
Letter to Physicians, Chiropractors, and Physiotherapists (rec'd 01 Mar 2005)

APPROVED ON
08-Mar-2005

**CERTIFICATION**

The University of Saskatchewan Biomedical Research Ethics Board (Bio- REB) has reviewed the above-named research project including the protocol and consent form, where applicable. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility of ensuring that the authorized research is carried out according to governing law. This Approval is valid for the above time period provided there is no change in experimental protocol or in the consent process.

**ONGOING REVIEW REQUIREMENT(S) / REB ATTESTATION**

In order to receive annual renewal, a status report must be submitted to the Chair for Committee consideration within one month of the current expiry date each year the study remains open, and upon study completion. Please refer to the following website for further instructions: http://www.usask.ca/research/ethics.shtml. In respect to clinical trials, the University of Saskatchewan Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. This approval and the views of this REB have been documented in writing.

APPROVED

Barry D. McLennan, Ph.D., Chair
University of Saskatchewan
Biomedical Research Ethics Board (Bio-REB)

Please send all correspondence to:

Ethics Office
University of Saskatchewan
Room 305, Kirk Hall, 117 Science Place
Saskatoon, SK S7N 5C8
Phone: (306) 966-4053 Fax: (306) 966-2069

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB)
Ethics Office (VP Research), University of Saskatchewan
Room 305 Kirk Hall, 117 Science Place
Saskatoon, SK S7N 5C8

JUL 1 0 2007

# STATUS REPORT FORM

**This form is submitted for the following purpose**

___X__ Annual status report and re-approval request. When was the ethics approval for this study due to expire? Date:____August 1, 2007_____

_____ Notice of study closure.

Report Prepared by: _____Phillip Chilibeck_____ Date: _____July 4, 2007_____

**ONGOING REVIEW REQUIREMENTS:** This approval is valid for up to one year. The REB will require the submission of an annual status report at least one month prior to the expiration date indicated below. Please note if the Status Report Form is not submitted by the one-year expiry date, the ethics certificate will automatically expire.

1. **PRINCIPAL INVESTIGATOR**
   **Philip Chilibeck**

   NOTE: An investigator who does not maintain a physical presence at the trial site in proportion to the inherent level of risk that subjects will be exposed to cannot continue to be identified as the principal investigator. The responsibility must be transferred to a new principal investigator.

2. **DEPARTMENT/DIVISION**
   **College of Kinesiology**

3. **REB FILE #**
   **#03- 1077**

4. **STUDY SITE(S)** **College of Kinesiology and Royal University Hospital**

5. **TITLE OF PROTOCOL AND PROTOCOL # (where applicable)**
   Effect of Combined Exercise therapy and isoflavone supplementation on the prevention of osteoporosis

6. **SPONSOR (where applicable)**
   **Canadian Institutes of Health Research**

7. **BRIEF SUMMARY OF PROGRESS OF STUDY** (projected completion date for recruitment and data collection, number of subjects admitted to date, target enrollment, anticipated end-date). Are subjects currently receiving study treatment or interventions, or is the study only active for follow-up to endpoints?

**Completion date for recruitment = January 31, 2006**
**Projected completion date for data collection = May 2008**
**Final number of subjects admitted = 351**
**Target enrollment had been = 360**
**Anticipated end date = May 2008**

**All subjects are postmenopausal women and have been randomized to 4 groups: 1) soy isoflavone (90mg aglycone eq. per day) + walking/weight training; 2) isoflavone placebo + walking/weight training; 3) soy isoflavone + flexibility (stretching) exercises; 4) isoflavone placebo + flexibility exercises. Subjects are receiving the interventions for 2 years.**

**207 Subjects are currently receiving interventions. 75 subjects have completed the 2 year intervention. 69 subjects have dropped-out or have been withdrawn from the study.**

**ARE THERE ANY ASPECTS OF THIS STUDY WHICH SHOULD BE BROUGHT TO THE ATTENTION OF THE REB** (i.e., any new information or knowledge bearing on the anticipated risks or anticipated benefits, and therefore possibly affecting subjects' ongoing decision to participate in this study. Clinical trialists should reflect upon adverse events associated with their protocol).

**There have been 719 adverse events reported to date with 24 of these being serious adverse events (SAE). All adverse events have been reviewed by an external Data Safety Monitoring Board (DSMB); in addition, all SAE have been reported to the chair of the Bio-REB.**

**Over half of the adverse events were unlikely (163) or were not related (237) to the study protocol (i.e. data collection, isoflavone supplementation or exercise training).**

**All non-serious adverse events that were definitely related (20) ranged from mild to moderate intensity (9 to the supplement; 8 to the exercise; and 3 to other protocol). Those that were probably related (37) ranged from mild to moderate intensity (23 supplement; 12 exercise; and 2 other). Adverse events that were possibly related (264) ranged from mild to severe intensity (162 supplement; 101 exercise; and 2other). Non-serious adverse events classified as possibly related, probably related, or definitely related include: joint pain, arthritis, muscle spasms (exercise training), abdominal bloating, nausea, constipation, diarrhea, headache, heart burn, hot flashes, indigestion, menstrual bleeding, and blood chemistries (blood counts, or liver enzymes) that were outside the normal ranges (isoflavone or calcium/vitamin D supplement).**

**Of the 24 SAE, only 1 SAE (hysterectomy) was ranked as being possibly related to the protocol with moderate intensity. There were 8 SAE unlikely related with intensities of mild to severe and 15 SAE not related with intensities ranging from mild to life threatening.**

**SAEs included:**

1) **An appendectomy**
2) **A broken wrist from a fall on the ice (occurred before the subject was randomized)**
3) **A ganglion cyst on a wrist that was removed**
4) **Bleeding from a cancerous tumor on the kidney (tumor was removed), pathology report was examined by the DSMB.**
5) **Laparoscopic gall bladder surgery**
6) **Melanoma removed from right forearm and right breast biopsy. Pathology report showed no malignancy in right forearm and no pathology for breast tissue**
7) **Tumor discovered by endometrial ultrasound before subject had been randomized - she has been excluded**
8) **Tumor on bladder initially reported as a bladder infection (tumor has been removed and subject has deceased).Subject had never been randomized to the study**
9) **Lesion on the lung (previous lesion on lung had been removed in 1997) - CT scan on Jan 26/06 showed lesion has decreased in size, no biopsy was required.**
10) **Abnormal Heart Rhythm -pacemaker implanted**
11) **Surgery to realign broken left femur resulting from falling down stairs**
12) **Moles removed from face and leg which showed to have basal cell carcinoma.**
13) **Surgery to remove hemorrhoids**
14) **Subject hospitalized to stabilize elevated heart rate due to hyperthyroid condition.**
15) **Broken olecranon from a fall at work**
16) **Broken arm from a fall on ice**
17) **Tubes placed in ear to correct vertigo**
18) **Hysterectomy**
19) **Lumpectomy to remove benign breast cyst**
20) **Dizziness and numbness in arms and leg – subject hospitalized and released**
21) **Trans-ischemic attack**
22) **Knee replacement surgery**
23) **Surgery for colon cancer**
24) **Tear duct surgery**

9. **WHAT ARE YOUR CURRENT SAFETY REVIEW PROCEDURES FOR THIS RESEARCH PROJECT** (i.e., drug safety monitoring board (DSMB), clinical end-point committee (CEC), hotline, periodic reporting to the ethics board)?

**All Serious adverse events are reported to a Data Safety Monitoring Board (DSMB) and the ethics committee. Our DSMB meets every six months to review all adverse events. During the past year, the DSMB met in September 2006 and April 2007. The minutes of the most recent meeting is attached. The next planned DSMB meeting is October 2007 (exact date is still to be arranged with the DSMB).**

10. **PRINCIPAL INVESTIGATOR**

Signature _____ Date: July 9 2007

For Administrative Use Only:

Approved On: July 12 2007 Expiry Date: 31-Jul-2008

Signature of Chair or designate: _____

**Please note that this form, once signed by the chair or designate, serves as your official re-approval certificate.**

January 2006

**Appendix C**

## LEISURE-TIME EXERCISE QUESTIONNAIRE

(Godin, Canadian Journal of Applied Sport Sciences 10: 141-146, 1985).

1. Considering a **7-day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your **free-time**? (Write the appropriate number in each box)

**TIMES PER WEEK**

**a) STRENUOUS EXERCISE (Heart beats rapidly)**
(i.e. running, jogging, hockey, football, soccer, squash, basketball, cross-country skiing, judo, roller skating, vigorous swimming, vigorous long-distance bicycling). ☐

**b) MODERATE EXERCISE (Not exhausting)**
(i.e. fast walking, baseball, tennis, easy bicycling, volley ball, badminton, easy swimming, alpine skiing, popular and folk dancing). ☐

**c) MILD EXERCISE (Minimal effort)**
(i.e. yoga, archery, bowling, horseshoes, golf, snow-mobiling, easy walking) ☐

**Appendix D**

## MENOPAUSAL SYMPTOMS QUESTIONNAIRE

**Menopausal Index (7-day recall) (St. Germain et al., Menopause 8: 17-26, 2001).**

**Hot flushes/Night sweats**

1. How frequently do you have hot flushes and/or night sweats? _____ (# per week)
2. How long do they last? _____ (minutes)
3. Rate Severity:
   **___ 0 = no symptoms**
   **___ 1 = mild** (uncomfortable – fanning to alleviate symptoms)
   **___ 2 = moderate** (warrants removal or changing of clothing **or** cooling ambient temperature)
   **___ 3 = severe** (warrant removal/changing of clothing **and** cooling ambient temperature)

**Insomnia**

1. How often do you have insomnia? _____ (# per week)
2. How long does it last each night? _____ (minutes)
3. Rate Severity:
   **___ 0 = no symptoms**
   **___ 1 = mild** (tossing and turning in bed)
   **___ 2 = moderate** (alert enough to get up and have a drink or go to the bathroom)
   **___ 3 = severe** (Alert enough to read or work)
4. Answer **Yes** or **No** to each of the following:
   a. Do you have difficulty going to sleep? _____
   b. Do you have difficulty staying asleep? _____
   c. Do you wake up too early in the morning? _____

**Numbness (pins and needles) in limbs**

1. How frequently do you have numbness in your limbs? _____ (# per week)
2. How long does it last? _____ (minutes)
3. Rate Severity:
   **___ 0 = no symptoms**
   **___ 1 = mild** (slight tingling in extremities)
   **___ 2 = moderate** (partial numbness with ability to move extremities)
   **___ 3 = severe** (complete numbness, similar to having foot fall asleep)

**(turn page over)**

**Fatigue**

1. Frequency _____ (# per week)
2. Duration _____ (minutes)
3. Rate Severity
   - ___ **0 = no symptoms**
   - ___ **1 = mild** (slight feeling of fatigue during the day)
   - ___ **2 = moderate** (trouble staying awake, i.e. nodding off during the day)
   - ___ **3 = severe** (need to go to bed during the day or early evening)

**Headaches**

1. How frequent do you get headaches? _____ (# per week)
2. How long do your headaches last? _____ (minutes)
3. Rate Severity:
   - ___**0 = no symptoms**
   - ___**1 = mild** (minor annoyance/inconvenience)
   - ___**2 = moderate** (warrants taking pain medication)
   - ___**3 = severe** (extreme enough to take pain medication and go to bed)

Please answer **Yes** or **No** to the following symptoms:

1. Mood changes _____
2. Depression _____
3. Irritability _____
4. Anxiety _____
5. Decreased concentration _____
6. Decreased sexual desire (libido) _____
7. Vaginal dryness _____
8. Uncomfortable intercourse _____
9. Changes in urinary frequency _____
10. Aches and pains (backache, muscle, joint) _____
11. Breast tenderness _____
12. Weight gain _____
13. Changes in bleeding pattern _____
(intensity, duration, etc.) during past 6 weeks

**Appendix E**

# Subject Information Sheet

(Use black ink only)

| For office use only |
| --- |
| Subject's Initials |
| |
| Recruitment # |
| |

Name:_____

(first) (middle initial) (Last)

Birth Date_____
(day/month/year)

HSP # _____ Email:_____

Address:_____

_____

_____

Phone: (h) _____ (w)_____ Other:_____

Family Physician: _____ Phone Number: _____

Approximate Date of Last Menstrual Period:_____

Hysterectomy: ☐ Yes No ☐

**Appendix F: SPSS Output**

## One way ANOVA – Confirming possible confounding variables

**ANOVA**

MonthsMenopausal

| | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 19411.280 | 4 | 4852.820 | .941 | .440 |
| Within Groups | 2042687 | 396 | 5158.301 | | |
| Total | 2062098 | 400 | | | |

**ANOVA**

Hysterectomy

| | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | .248 | 4 | .062 | .448 | .774 |
| Within Groups | 54.889 | 396 | .139 | | |
| Total | 55.137 | 400 | | | |

**ANOVA**

PercentFat

| | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 651.714 | 4 | 162.929 | 5.470 | .000 |
| Within Groups | 11736.233 | 394 | 29.787 | | |
| Total | 12387.948 | 398 | | | |

# MANCOVA (% fat) OUTPUT

**Between-Subjects Factors**

| | | N |
|---|---|---|
| PALevel5 | 1.00 | 81 |
| | 2.00 | 80 |
| | 3.00 | 82 |
| | 4.00 | 80 |
| | 5.00 | 76 |

**Multivariate Tests[c]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Intercept | Pillai's Trace | .097 | 5.189[a] | 8.000 | 386.000 | .000 |
| | Wilks' Lambda | .903 | 5.189[a] | 8.000 | 386.000 | .000 |
| | Hotelling's Trace | .108 | 5.189[a] | 8.000 | 386.000 | .000 |
| | Roy's Largest Root | .108 | 5.189[a] | 8.000 | 386.000 | .000 |
| PercentFat | Pillai's Trace | .099 | 5.294[a] | 8.000 | 386.000 | .000 |
| | Wilks' Lambda | .901 | 5.294[a] | 8.000 | 386.000 | .000 |
| | Hotelling's Trace | .110 | 5.294[a] | 8.000 | 386.000 | .000 |
| | Roy's Largest Root | .110 | 5.294[a] | 8.000 | 386.000 | .000 |
| PALevel5 | Pillai's Trace | .104 | 1.298 | 32.000 | 1556.000 | .124 |
| | Wilks' Lambda | .900 | 1.295 | 32.000 | 1425.093 | .126 |
| | Hotelling's Trace | .107 | 1.292 | 32.000 | 1538.000 | .128 |
| | Roy's Largest Root | .043 | 2.068[b] | 8.000 | 389.000 | .038 |

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c. Design: Intercept+PercentFat+PALevel5

# MANOVA OUTPUT

**Between-Subjects Factors**

| | | N |
|---|---|---|
| PALevel5 | 1.00 | 82 |
| | 2.00 | 80 |
| | 3.00 | 82 |
| | 4.00 | 80 |
| | 5.00 | 77 |

**Multivariate Tests[c]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Intercept | Pillai's Trace | .000 | .002[a] | 8.000 | 389.000 | 1.000 |
| | Wilks' Lambda | 1.000 | .002[a] | 8.000 | 389.000 | 1.000 |
| | Hotelling's Trace | .000 | .002[a] | 8.000 | 389.000 | 1.000 |
| | Roy's Largest Root | .000 | .002[a] | 8.000 | 389.000 | 1.000 |
| PALevel5 | Pillai's Trace | .119 | 1.509 | 32.000 | 1568.000 | .034 |
| | Wilks' Lambda | .885 | 1.510 | 32.000 | 1436.156 | .034 |
| | Hotelling's Trace | .125 | 1.510 | 32.000 | 1550.000 | .034 |
| | Roy's Largest Root | .061 | 2.991[b] | 8.000 | 392.000 | .003 |

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c. Design: Intercept+PALevel5

**Tests of Between-Subjects Effects**

| Source | Dependent Variable | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Corrected Model | FlushFSMeanZ | 6.825[a] | 4 | 1.706 | 2.242 | .064 |
| | InsFSMEANZ | 1.995[b] | 4 | .499 | .698 | .594 |
| | NumbFSMEANZ | .169[c] | 4 | .042 | .050 | .995 |
| | FatigueFSMEANZ | 7.634[d] | 4 | 1.909 | 2.341 | .054 |
| | HeadFSMEANZ | 5.900[a] | 4 | 1.475 | 2.230 | .065 |
| | PsychMeanZscore | 2.942[b] | 4 | .735 | .737 | .567 |
| | SexMeanZscore | .771[e] | 4 | .193 | .190 | .944 |
| | PhysicalMeanZscore | 14.797[f] | 4 | 3.699 | 3.844 | .004 |
| Intercept | FlushFSMeanZ | .001 | 1 | .001 | .001 | .975 |
| | InsFSMEANZ | .000 | 1 | .000 | .001 | .981 |
| | NumbFSMEANZ | .002 | 1 | .002 | .003 | .958 |
| | FatigueFSMEANZ | .000 | 1 | .000 | .000 | .985 |
| | HeadFSMEANZ | .002 | 1 | .002 | .003 | .956 |
| | PsychMeanZscore | .000 | 1 | .000 | .000 | .986 |
| | SexMeanZscore | .003 | 1 | .003 | .003 | .960 |
| | PhysicalMeanZscore | .003 | 1 | .003 | .003 | .957 |
| PALevel5 | FlushFSMeanZ | 6.825 | 4 | 1.706 | 2.242 | .064 |
| | InsFSMEANZ | 1.995 | 4 | .499 | .698 | .594 |
| | NumbFSMEANZ | .169 | 4 | .042 | .050 | .995 |
| | FatigueFSMEANZ | 7.634 | 4 | 1.909 | 2.341 | .054 |
| | HeadFSMEANZ | 5.900 | 4 | 1.475 | 2.230 | .065 |
| | PsychMeanZscore | 2.942 | 4 | .735 | .737 | .567 |
| | SexMeanZscore | .771 | 4 | .193 | .190 | .944 |
| | PhysicalMeanZscore | 14.797 | 4 | 3.699 | 3.844 | .004 |
| Error | FlushFSMeanZ | 301.397 | 396 | .761 | | |
| | InsFSMEANZ | 282.891 | 396 | .714 | | |
| | NumbFSMEANZ | 337.756 | 396 | .853 | | |
| | FatigueFSMEANZ | 322.836 | 396 | .815 | | |
| | HeadFSMEANZ | 261.871 | 396 | .661 | | |
| | PsychMeanZscore | 395.372 | 396 | .998 | | |
| | SexMeanZscore | 401.729 | 396 | 1.014 | | |
| | PhysicalMeanZscore | 381.053 | 396 | .962 | | |
| Total | FlushFSMeanZ | 308.222 | 401 | | | |
| | InsFSMEANZ | 284.887 | 401 | | | |
| | NumbFSMEANZ | 337.927 | 401 | | | |
| | FatigueFSMEANZ | 330.471 | 401 | | | |
| | HeadFSMEANZ | 267.771 | 401 | | | |
| | PsychMeanZscore | 398.314 | 401 | | | |
| | SexMeanZscore | 402.502 | 401 | | | |
| | PhysicalMeanZscore | 395.850 | 401 | | | |
| Corrected Total | FlushFSMeanZ | 308.222 | 400 | | | |
| | InsFSMEANZ | 284.887 | 400 | | | |
| | NumbFSMEANZ | 337.925 | 400 | | | |
| | FatigueFSMEANZ | 330.471 | 400 | | | |
| | HeadFSMEANZ | 267.771 | 400 | | | |
| | PsychMeanZscore | 398.314 | 400 | | | |
| | SexMeanZscore | 402.500 | 400 | | | |
| | PhysicalMeanZscore | 395.850 | 400 | | | |

a. R Squared = .022 (Adjusted R Squared = .012)

b. R Squared = .007 (Adjusted R Squared = -.003)

c. R Squared = .001 (Adjusted R Squared = -.010)

d. R Squared = .023 (Adjusted R Squared = .013)

e. R Squared = .002 (Adjusted R Squared = -.008)

f. R Squared = .037 (Adjusted R Squared = .028)

# Post Hoc Tests

**Multiple Comparisons**

Bonferroni

| Dependent Variable | (I) PALevel5 | (J) PALevel5 | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower Bound | Upper Bound |
| FatigueFSMEANZ | 1.00 | 2.00 | .0300 | .14189 | 1.000 | -.3705 | .4306 |
| | | 3.00 | .2948 | .14101 | .372 | -.1032 | .6929 |
| | | 4.00 | .3126 | .14189 | .282 | -.0879 | .7131 |
| | | 5.00 | .2747 | .14328 | .559 | -.1298 | .6792 |
| | 2.00 | 1.00 | -.0300 | .14189 | 1.000 | -.4306 | .3705 |
| | | 3.00 | .2648 | .14189 | .627 | -.1357 | .6653 |
| | | 4.00 | .2826 | .14276 | .485 | -.1204 | .6856 |
| | | 5.00 | .2447 | .14415 | .904 | -.1622 | .6516 |
| | 3.00 | 1.00 | -.2948 | .14101 | .372 | -.6929 | .1032 |
| | | 2.00 | -.2648 | .14189 | .627 | -.6653 | .1357 |
| | | 4.00 | .0178 | .14189 | 1.000 | -.3828 | .4183 |
| | | 5.00 | -.0201 | .14328 | 1.000 | -.4246 | .3843 |
| | 4.00 | 1.00 | -.3126 | .14189 | .282 | -.7131 | .0879 |
| | | 2.00 | -.2826 | .14276 | .485 | -.6856 | .1204 |
| | | 3.00 | -.0178 | .14189 | 1.000 | -.4183 | .3828 |
| | | 5.00 | -.0379 | .14415 | 1.000 | -.4448 | .3690 |
| | 5.00 | 1.00 | -.2747 | .14328 | .559 | -.6792 | .1298 |
| | | 2.00 | -.2447 | .14415 | .904 | -.6516 | .1622 |
| | | 3.00 | .0201 | .14328 | 1.000 | -.3843 | .4246 |
| | | 4.00 | .0379 | .14415 | 1.000 | -.3690 | .4448 |
| PhysicalMeanZscore | 1.00 | 2.00 | -.1053 | .15415 | 1.000 | -.5404 | .3299 |
| | | 3.00 | .2904 | .15320 | .588 | -.1421 | .7228 |
| | | 4.00 | .3709 | .15415 | .166 | -.0642 | .8061 |
| | | 5.00 | .3296 | .15567 | .349 | -.1098 | .7690 |
| | 2.00 | 1.00 | .1053 | .15415 | 1.000 | -.3299 | .5404 |
| | | 3.00 | .3956 | .15415 | .106 | -.0395 | .8308 |
| | | 4.00 | .4762* | .15510 | .023 | .0384 | .9140 |
| | | 5.00 | .4348 | .15660 | .058 | -.0072 | .8769 |
| | 3.00 | 1.00 | -.2904 | .15320 | .588 | -.7228 | .1421 |
| | | 2.00 | -.3956 | .15415 | .106 | -.8308 | .0395 |
| | | 4.00 | .0806 | .15415 | 1.000 | -.3546 | .5157 |
| | | 5.00 | .0392 | .15567 | 1.000 | -.4002 | .4786 |
| | 4.00 | 1.00 | -.3709 | .15415 | .166 | -.8061 | .0642 |
| | | 2.00 | -.4762* | .15510 | .023 | -.9140 | -.0384 |
| | | 3.00 | -.0806 | .15415 | 1.000 | -.5157 | .3546 |
| | | 5.00 | -.0414 | .15660 | 1.000 | -.4834 | .4007 |
| | 5.00 | 1.00 | -.3296 | .15567 | .349 | -.7690 | .1098 |
| | | 2.00 | -.4348 | .15660 | .058 | -.8769 | .0072 |
| | | 3.00 | -.0392 | .15567 | 1.000 | -.4786 | .4002 |
| | | 4.00 | .0414 | .15660 | 1.000 | -.4007 | .4834 |

Based on observed means.

*. The mean difference is significant at the .05 level.

**ANOVA**

WeightGain

| | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 3.689 | 4 | .922 | 3.902 | .004 |
| Within Groups | 93.593 | 396 | .236 | | |
| Total | 97.282 | 400 | | | |

**Multiple Comparisons**

Dependent Variable: WeightGain

Bonferroni

| (I) PALevel5 | (J) PALevel5 | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| 1.00 | 2.00 | -.054 | .076 | 1.000 | -.27 | .16 |
| | 3.00 | .061 | .076 | 1.000 | -.15 | .28 |
| | 4.00 | .209 | .076 | .066 | -.01 | .42 |
| | 5.00 | .152 | .077 | .494 | -.07 | .37 |
| 2.00 | 1.00 | .054 | .076 | 1.000 | -.16 | .27 |
| | 3.00 | .115 | .076 | 1.000 | -.10 | .33 |
| | 4.00 | .263* | .077 | .007 | .05 | .48 |
| | 5.00 | .206 | .078 | .083 | -.01 | .43 |
| 3.00 | 1.00 | -.061 | .076 | 1.000 | -.28 | .15 |
| | 2.00 | -.115 | .076 | 1.000 | -.33 | .10 |
| | 4.00 | .148 | .076 | .541 | -.07 | .36 |
| | 5.00 | .091 | .077 | 1.000 | -.13 | .31 |
| 4.00 | 1.00 | -.209 | .076 | .066 | -.42 | .01 |
| | 2.00 | -.263* | .077 | .007 | -.48 | -.05 |
| | 3.00 | -.148 | .076 | .541 | -.36 | .07 |
| | 5.00 | -.056 | .078 | 1.000 | -.28 | .16 |
| 5.00 | 1.00 | -.152 | .077 | .494 | -.37 | .07 |
| | 2.00 | -.206 | .078 | .083 | -.43 | .01 |
| | 3.00 | -.091 | .077 | 1.000 | -.31 | .13 |
| | 4.00 | .056 | .078 | 1.000 | -.16 | .28 |

*. The mean difference is significant at the .05 level.

## Appendix G:

## Literature Review Grid

| Authors/Year | Objective | Design | Population | Major Findings |
|---|---|---|---|---|
| Nelson, Sammel, Freeman, Lin, Gracia, & Schmitz, 2007 | - determine whether PA decreases risk of menopausal symptoms among African American and Caucasian women | 9-yr non-randomized prospective observational study | N=380<br>Ages: 35-47 | - walking 4.0 mph for 1.5 h, five times a week, associated with lower levels of stress<br>- No relationship between PA and vasomotor symptoms<br>- Suggest that maintaining or increasing PA during the menopausal transitional period and postmenopause may assist in reducing a variety of psychological symptoms, including anxiety, stress, and depression. |
| Elavsky & McAuley, 2007 | - evaluate effects of 4-month moderate-intensity walking and low-intensity yoga interventions on self-reported sleep quality | Randomized control trial | N= 164<br>Ages: 42-58<br>Mean age: 49.9 | - walking and low-intensity yoga programs were ineffective in yielding statistically significant improvements in sleep quality |
| Elavsky & McAuley, 2007 | Effects of 4-mo walking and yoga intervention on mental health and QOL | Randomized control trial | N= 164<br>Ages: 42-58<br>Mean age: 49.9 | - PA enhances mood and menopause-related QOL<br>- Cardio fitness may reduce symptoms |
| Mirzaiinjmabadi, Anderson, & Barnes, 2006 | Examine relationship between exercise and BMI on menopausal symptoms | Cross-sectional | N= 886<br>Ages: 45-60 yrs<br>Australian women | - relationship exists between somatic symptoms, psychological symptoms, depression and anxiety<br>- No relationship between exercise and vasomotor symptoms & sexual function<br>- Exercise effective in relieving somatic and psychological symptoms, including depression and anxiety.<br>- relationship between exercise and feeling tired, psychological symptoms, headache, limb numbness<br>- no relationship between BMI and menopausal symptoms |
| Progetto Menopausa Italia Study Group, 2005 | identify correlates of climacteric symptoms in women around menopause attending menopause clinics in Italy | Cross-sectional | N= 66,501<br>Mean age: 54.4 yrs | - Lower PA associated with depression, difficulties to sleep, forgetfulness, irritability<br>- hot flashes/night sweats more common in women with higher BMI and reporting lower levels of PA<br>- Women, who performed regular exercise, experienced less frequent depression, headache, urinary leakage, irritability, hot flashes/night sweats, forgetfulness and difficulty to sleep.<br>- Minimal physical activity associated with higher BMI than women who performed regular physical activity. |
| Guthrie, Dennerstein, Taffe, Lehert, & Burger, 2005 | investigate factors associated with the presence, severity, and frequency of hot flushes | 9-yr non-randomized prospective observational study | N= 381<br>- Australian women<br>- Ages: 45-55 yrs | - Menopause status, FSH and estradiol levels, age, exercise level, and smoking status all contributed to the experience of bothersome hot flushes. |
| Villaverde-Gutierrez,Araujo, Cruz, Roa, Barbosa, & Ruiz-Villaverde, 2006 | Examine effects of physical exercise on QOL in menopausal women | Quasi-experimental study with random assignment | N = 48<br>Ages: 55-72 yrs | - women meno symptoms and HRQOL worsened |
| Aiello, Yasui, Tworoger, Ulrich, Irwin, Bowen, et al., 2004 | evaluate the effect of moderate-intensity exercise on the occurrence and severity of menopause symptoms | Randomized control trial | N= 173<br>Mean Age: 60.7yrs<br>Overweight, postmenopausal | - Exercise does not seem to decrease the risk of having menopause symptoms in overweight, postmenopausal women not taking hormone therapy |

| | | | | |
|---|---|---|---|---|
| Li, Samsioe, Borgfeldt, Lidfeldt, Agardh, & Nerbrand, 2003 | analyze influence of sociodemographic characteristics and environmental factors on self-reported menopause-related symptoms among middle-aged women | Population based survey | N=6917<br>Swedish women<br>Mean age: 56<br>Age range = 50-64 | - higher incidence of flashes for women who report weight gain (BMI b/w 25-30)<br>- vigorous PA associated with less vaginal dryness, lower intensity flashes<br>- weight gain major risk factor for aggravation of menopausal symptoms<br>- weight gain increased the risk of hot flushes by 30% - 38%,<br>- Menopausal symptoms may commence earlier and be of longer duration in obese women. |
| Li & Holm; 2003 | to examine the influence of PA alone and in combination with HRT on vasomotor symptoms at menopause<br>to identify factors that are predictive of vasomotor symptoms | Cross-sectional | N= 239<br>Mean Age: 54.7 yrs | - inactive women without HRT experienced MORE vasomotor symptoms than women with HRT, regardless of PA levels.<br>- PA may be synergistic to HRT<br>- active women tended to report fewer vasomotor symptoms than inactive women |
| Gold, Sternfeld, Kelsey, Brown, Mouton, Neame, Salamone, & Stellato, 2000 | to investigate relations of a limited number of risk factors and health outcomes | Cross sectional study community based survey | N = 12,425<br>Ages: 40-45 yrs<br>Mostly pre/peri menopause | - Japanese and Chinese women report least symptoms<br>- African American women complain more of vasomotor symptoms and vaginal dryness, but less complaints of urine leakage and difficulty sleeping than Caucasian women<br>- High BMI associated with increased hot flash/night sweats, urine leakage and stiff/soreness |
| Stadberg, Mattsson & Milsom, 2000 | investigate factors associated<br>with climacteric symptoms and the use of HRT | - Cross sectional | N= 4504<br>Ages: 46-62 yrs<br>Swedish women | - Women with a higher education and regular exercise = more often symptom-free.<br>- 69% of 54 yr olds report flashes<br>- 50% of 62 yr olds still report vasomotor symptoms<br>- 52% reported sleeping problems<br>- 37% reported decreased libido |
| Ivarsson, Spetz, & Hammar, 1998 | Assess whether physically active women have fewer vasomotor symptoms than sedentary women | Cross sectional | N = 793<br>Ages 55-56<br>Swedish women | - Exercise promotes Beta-endophine release which stabilizes thermoregulation<br>- Women who exercise have fewer vasomotor symptoms<br>- No difference between hot flash frequency for high and low BMI |
| Slaven & Lee, 1997 | Study 1: Examine effects of exercise on menopausal symptom reporting | Cross sectional survey | N= 220 | - Exercisers report fewer symptoms than non-exercisers<br>- Exercising menopausal women experience less menopausal distress |
| Slaven & Lee, 1997 | Study 2: Examine mood and symptom reporting on regular exercisers before and after exercise sessions | Completed questionnaire before and after fitness class | N= 47 | - Enhancements in mood and reduction in reported somatic and vasomotor symptoms immediately following aerobic class |