HOT FLASHES, BLOOD GLUCOSE AND DIABETIC

POSTMENOPAUSAL WOMEN

JOANN BOORSMA
Bachelor of Nursing, University of Lethbridge 1992

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Dedication page

To my children, Ryan, Brandon, Tobin, Joren, and daughter-in-law Lesley; whom I cherish and am proud of each and every day. To my husband, Dick, you are the love of my life, my friend, and my support.

Abstract

This *ex post facto* correlational study seeks to identify if a relationship between blood glucose values and vasomotor instability intensity exists. The population consisted of a convenience sample of seven type 2 diabetic postmenopausal women experiencing vasomotor instability living in Southern Alberta. This study hypothesizes that a significant negative correlation would be identified between these two variables based on research done by Dormire and Reame (2003).

The correlational results suggest that a small to moderate significant positive relationship exists between blood glucose and vasomotor instability: increased vasomotor instability was associated with increased blood glucose values.

Overall, this study suggests a relationship exists between blood glucose and vasomotor instability but causality or direction of this relationship cannot be determined. Further research studies are recommended to clarify and validate this research. In particular, such a study should include type 1 diabetic postmenopausal women, a larger sample size, and sampling a wider geographical area.

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List of Abbreviations

BMI	Body Mass Index
FSH	Follicle Stimulating Hormone
GLUT1	Glucose Transporter 1
GLUT2	Glucose Transporter 2
GnRh	Gonadotropin-releasing hormone
HbA1c	Glycosylated Hemoglobin
HRT	Hormone Replacement Therapy
LH	Luetinizing Hormone
SISA	Simple Interactive Statistical Analysis
SPSS	Statistical Package for Social sciences
SWAN	Study of Women's Health Across Nations
UCLA	University of California
WHIS	Women's Health Initiative Study

Hot Flashes, Blood Glucose and Diabetic Postmenopausal Women

At the onset of the 20th century, fewer women in western countries experienced menopause and its associated symptoms. This changed by the 21st century as women's lifespans increased by approximately 40 years (Rotem, Kushnir, Levine & Ehrenfeld, 2005), meaning that more women now experience menopause than their female ancestors would have. Today, advances in medical treatment mean that women are living with chronic diseases, such as diabetes, and dealing with multiple symptom manifestations including those of the menopausal transition. One of the symptoms most commonly experienced in perimenopausal, menopausal and postmenopausal women is hot flashes. Why is this issue important? Although most hot flashes cease within five years after onset, this symptom can persist for up to 15 years in 20% of the female population (Notelovitz, 2004). Hot flashes can negatively impact quality of life by causing acute physical discomfort, and by disrupting sleep, causing fatigue and irritability and acute effects on work. To date, the mechanisms and triggers of hot flashes are not well understood. In addition, no specific research exists on how diabetic women experience the menopause and/or postmenopause periods (Dormire, 2003).

The purpose of this thesis is to explore one aspect of postmenopause and its effect on the diabetic woman. Specifically, the goal is to examine the relationship between hot flashes and blood glucose values in diabetic postmenopausal women. This thesis will present the background to this research study, a review of the literature relevant to the menopausal/postmenopausal time frame with an emphasis on hot flashes and the

relationship to blood glucose values in diabetic women, and finally, the research methodology including the research question, hypothesis, ethics, research design and method of data collection, results, discussion and conclusions.

Chapter 1

HOT FLASHES, BLOOD GLUCOSE AND DIABETIC POSTMENOPAUSAL WOMEN

Background

Menopause/postmenopause is a naturally occurring process in a woman's life. Menopause is a physiological event that can be defined as the cessation of menstrual cycles for 12 consecutive months (Lowdermilk, Perry & Bobak, 2000; Xu et al., 2005). Symptoms most commonly associated with this time of life are vasomotor instability, sleep disturbances, urogenital symptoms, breast tenderness and changes in menstrual cycles (Contestabile & Derzko, 2002). Vasomotor instability, often called hot flashes, hot flushes and night sweats (vasomotor instability during sleep), vary in number, frequency, duration and intensity (Dormire, 2003; Neff, Morantz & Torrey, 2004; Seibel, 2003). Hot flashes and/or night sweats are experienced by up to 85% of women in western societies who transition through natural menopause and 90% of those who enter it abruptly via surgical menopause (Contestabile & Derzko, 2002; Kronenberg, 1994; Notelovitz, 2004). Cross-cultural [1]variations reported in the literature have been identified with the most significant incidence of hot flashes following hysterectomy occurring in African American population (Avis et al., 2001; Bachmann, 1999). Vasomotor instability is the symptom for which 40-80% of perimenopausal and postmenopausal women most often seek medical attention (Caiozzi et al., 2004; Whiteman et al., 2003). Pharmaceutical interventions, primarily hormone replacement therapy (HRT), have been the treatment of choice for women whose quality of life is

[1] A number of race/ethnic/cultural factors come into play and researchers often fail to distinguish between race/ethnicity and further tend to include cultural factors within perception of ethnic and racial influences (Kaplan & Bennett, 2003).

disrupted by these symptoms. Use of HRT increased significantly in the 1980s with up to 87% of women considering HRT to be an effective treatment for hot flashes (Caiozzi et al., 2004). Since the media release of the findings from the Women's Health Initiative Study (WHIS) regarding HRT potential risks, there has been a substantial decline in HRT use in the United States. This same decline in HRT use, 32 % in the last quarter of 2002, was seen in Ontario, Canada (Haas, Kaplan, Gerstenberger, & Kerlikowske, 2004; Austin, Mamdani, Tu, & Jankiimainen, (2003) as cited in Huston, Kirking & Shimp 2006).

Decline in HRT use and menopausal hot flashes became a "hot" topic amongst both my professional and social peers. Interest in this area stemmed from my work environment composed of nurses, largely female, primarily in the perimenopausal/menopausal age range of 40-55 years who are experiencing discomforts associated with this time of transition, and from my focus on Women's Health. This topic and demographic workplace description is probably a common scenario in Albertan or Canadian hospitals in general. In 2003, 96.6% of registered nurses (RNs) within Alberta and 94.9% of Canadian RNs were female with 50% of this population being within the perimenopausal age range (Canadian Nurses Association, 2004). As a result of these HRT and hot flash discussions with peers, I delved into the literature and learned that symptoms of perimenopause/menopause are not universal, nor are the mechanism or trigger and variance in occurrence of hot flashes between women well understood (Dormire, 2003). Interestingly, the literature also revealed that research is lacking in menopausal women with chronic disease processes such as diabetes (Dorman et al., 2001; Dormire, 2003).

Women with chronic disease processes such as diabetes may face an even greater challenge. Poirier-Solomon (2001) suggested this time of fluctuating hormones may mimic that of puberty, making blood glucose control difficult and occurrence of hot flashes difficult to differentiate from neuroglucopenic reactions. According to Alberta Health & Wellness in 2003, 100,000 individuals currently live with the diagnosis of diabetes. Of this population, approximately 4% were women between the ages of 40-59 years in 1999 (Alberta Health & Wellness, 2003). A 2005 Canadian Census showed that the number of women over the age of 50 was 5.5 million. This census projected that by 2016 this number will increase to 6.9 million and by 2026 to 7.9 million; approximately 22% of Canadian population will be menopausal (Rowe, Blake, & Belise, 2006). The projected number of people living with diabetes in Alberta will double over the next 15 years, and in those > 65 years of age a three-fold prevalence will be experienced (Alberta Health & Wellness, 2003). The number of women who will be both menopausal and potentially diabetic will be significant in the near future if these statistics follow the projected path. Therefore, more research is needed on menopausal/postmenopausal symptoms in diabetic women.

Research Question

The lack of research on the population of postmenopausal diabetic women and the impact of this transition on diabetes is the impetus for this research study. The research question primarily addressed by this study is "What is the relationship between vasomotor instability and blood glucose values in postmenopausal women with diabetes?" Dormire and Reame (2003) led me to consider correlational relationships between blood glucose values and vasomotor instability.

Hypothesis

Specifically, this research intends to test the hypothesis based on research discussed in the literature review chapter. The hypothesis is as follows: A strong and negative correlational relationship will be found between vasomotor instability and blood glucose values in the postmenopausal diabetic women. The null hypothesis is that correlation will not be different from correlations achieved by chance.

Significance of Study

Approximately one million Canadian women aged 40 or older (15%) and more than 28% of women in the 50 to 64 age group reported using HRT to cope with the symptoms of menopause in the 1996/97 National Population Health Survey (Wilkins, 1999). Since the release of the findings from the Women's Health Initiative Study (WHIS) regarding HRT potential risks, there has been a substantial decline in HRT use in both the United States and Canada (Haas, Kaplan, Gerstenberger, & Kerlikowske, 2004; Austin, Mamdani, Tu, & Jankiimainen, (2003) as cited in Huston, Kirking & Shimp 2006). With the combination of decreasing HRT use (Haas et al., 2004; Huston et al., 2006), an increasing population of menopausal women, and rising incidence of diabetes, the increases in numbers of both diabetic and menopausal women requiring support and/or accessing health professionals may be significant. Without understanding underlying mechanisms of vasomotor instability and potential complications of and effects on diabetic women, health care professionals are left without adequate evidence-based direction and management options for this population of women. Women whose lives have been or are significantly disrupted by symptoms of menopause are, or will be,

faced with difficult decisions regarding alternative therapies and coping strategies such as acupuncture, herbal remedies and self-help groups.

A dearth of research highlights the importance of research on this topic in this population of women. Whether or not this study can establish a correlation between blood sugars and hot flashes, it is hoped that this study will provide impetus for further study of women dealing with menopausal symptoms and a chronic disease processes such as diabetes.

Organization of Thesis

This thesis includes five chapters. The first chapter presents background discussion, the research question, hypotheses and the significance of this study. Chapter 2 consists of a literature review, followed with Chapter 3 in which methodology is presented. Finally, Chapter 4 reports survey and daily journal results, and Chapter 5 provides discussion and interpretation of the findings and concluding remarks.

Chapter 2

Literature Review

This section will review terminology and pathophysiology associated with perimenopause, menopause and postmenopause time periods as well as current hot flash mechanism theories. Diabetes, ethnicity, and lifestyle factors and their relationship to vasomotor instability will also be addressed in this section.

Perimenopause/Menopause/Postmenopause

Menopause is the term most commonly used to encompass the periomenopause, menopause and postmenopause period among the lay and professional communities (Rosenthal, 1999). An important aspect to the study is differentiating between these terms. This section reviews each of these terms as well as outlines and defines this period of transition.

Perimenopause

Perimenopause refers to the time surrounding menopause (Frackiewicz & Cutler, 2000) and is described as the transitioning years from ovulatory menstrual cycles to the cessation of menstrual cycles including the first postmenopausal year (Lowdermilk et al., 2000; Reed & Sutton, 2004; Seibel, 2003; Smith & Contestabile, 2002). Climacteric, a term used more commonly in previous literature, is the time period characterized by the waning ovarian function that is frequently associated with menstrual cycle irregularities and vasomotor symptoms. Menopausal transition is the term that is currently being used to describe decreasing ovarian function and is replacing the terms perimenopause and climacteric (Reed & Sutton, 2004).

The time frame for menopausal transition ranges from 2-8 years with the average range being 5 years, affecting women between the ages of 40-55 years (Lowdermilk et al., 2000; Reed & Sutton, 2004). Physiologically, this time period is characterized by progressively decreasing ovarian response to follicle stimulating hormone (FSH), which leads to decreasing estrogen production by follicular cells. It is during this period of decreased estrogen levels that symptoms of hot flashes or vasomotor instability occur. The pituitary gland responds to this lack of follicular response by increasing FSH levels further. Once follicular development does occur, a surge of estrogen is produced from the follicular cells as a result of significantly elevated FSH levels and symptoms such as breast tenderness, which are associated with premenstrual syndrome, are experienced during menopausal transition (Frackiewicz & Cutler, 2000; Lowdermilk et al., 2000; Seibel, 2003).

Inhibin B, a hormone involved in directing follicular development and suppression of pituitary FSH production, is decreased along with estradiol. Decreases in these hormones stimulates the hypothalamus to increase secretion of gonadotropin-releasing hormone (GnRH), which in turn stimulates the anterior pituitary; the result is an increase in FSH and luetinizing hormone (LH) levels. FSH and LH remain elevated and result in anovulatory cycles where the ovary fails to produce, mature and release eggs. This results initially in a shorter menstrual cycle, followed by lengthening of these cycles during transition, as follicles are depleted and anovulatory cycles increase in frequency. Anovulatory cycles do not support a corpus luteum and therefore produce no progesterone, resulting in increased menstrual flow and clotting due to unopposed estrogen stimulation of the endometrium (Reed & Sutton, 2004). Other symptoms often

experienced during menopausal transition may include vasomotor instability, sleep disturbance, vaginal dryness, painful sexual intercourse and breast tenderness. Missed menstrual cycles continue to increase in frequency until the last menses occurs, signaling the onset of menopause.

Menopause

Natural menopause is a single event that marks the end of ovarian follicular activity, inadequate estrogen production and endometrial stimulation, resulting in the last menstrual period or amenorrhea. This stage is further defined as having occurred when a woman has gone a year without a menstrual flow or spotting not due to pathological/physiological cause. This stage occurs on average at age 51 years, ranging from the late forties to the early fifties (Lowdermilk el al., 2000; Reed & Sutton, 2004; Rowe, Blake & Belisle, 2006; Smith & Contestabile, 2002).

The term induced menopause is often used to indicate the surgical removal of the uterus, a hysterectomy, and/or removal of one or both ovaries or an oophorectomy. Symptoms such as vasomotor instability, associated with induced menopause, are thought to be a result of the dramatic and rapid drop in endogenous estrogen levels (Gallicchio, Whiteman, et al., 2006; Langenberg, Kjerulff & Stolley, 1997). Chung-Park (2006) noted that circulating estrogen and testosterone levels dropped dramatically within 24-48 hour following a hysterectomy with bilateral oophorectomy, resulting in generally more severe menopausal symptoms when compared to natural menopause in women.

Postmenopause

Postmenopause refers to the span of life following menopause. Estradiol, the principal estrogen, drops by 90% in the menopausal period due to follicular atresia.

Estradiol production during the postmenopausal period occurs in the adrenal glands, adipose, brain, muscle, liver and, minimally, the ovarian tissues, as a result of the conversion of estrone, now the dominant but less potent estrogen, (Reed & Sutton, 2004; Smith & Contestabile, 2002). Often the symptoms of menopausal transition, such as vasomotor instability, continue 1-2 years into the postmenopausal period, although some women can experience these symptoms for as long as l0-20 years. The prevalence of vasomotor instability in women during this time period is estimated to be 30-80% (Lowdermilk et al., 2000; NIH State-of-the-Science Panel, 2005).

External influences and hot flashes

The yet to be defined mechanism(s) and trigger(s) of hot flashes have led researchers to examine not only internal but also external influences in women who experience hot flashes. Several studies in the literature have examined factors such as ethnicity (which as indicated on page 3 is often a term used interchangeable with culture and race), smoking, body mass index (BMI), alcohol consumption, exercise, food consumption and stress to identify potential relationships to hot flash occurrence. The following sections will address these factors and their relationships to hot flashes.

Ethnicity

Ethnicity (beliefs, behaviors and socio-cultural traditions) has been identified as a factor that may be associated with and potentially increase the incidence and frequency of hot flash occurrences (Canadian Race Relations Foundation, 2005). Since ethnicity is often not conceptually distinct from concepts of race, authors such as Gold, Colvin, et al. (2006) and Gold, Sternfeld, et al. (2000) use the term “race/ethnicity” in their research. The following discussion reflects the tendency of researchers to assign research subjects

arbitrarily to categories of race and ethnicity without providing clear definitions and methods for such assignments (Kaplan & Bennett, 2003; Malley-Morrison & Hines, 2007). From this point forward race/ethnicity will be used to be consistent with researchers' usage.

Hot flashes occur in 70-80% of women in Europe and the western world with variances in number, frequency, duration and intensity (Dormire, 2003; Neff, 2004; Seibel, 2003). A lower incidence of hot flash occurrence is reported in Asian populations, which are cited as 10-22% in Hong Kong, 17% in Japan, and 23% in Thai women (Caiozzi et al., 2004). Reasons for this lower incidence have not been identified, but studies have suggested genetic factors, BMI, dietary intake of phytoestrogens and cultural meanings attached to menopausal transition (Ho et al., 1999). Shea (2006) studied hot flash occurrence and other menopausal symptoms in women in Beijing and found a 13.5% hot flash occurrence in Chinese women compared to 12.5% in Japanese women. This author identified a rise in menopausal symptom reporting and suggested this may be related to changes in cultural and governmental sources, which previously discouraged older women in China and Japan to publicly identify and attend to these types of symptoms. Shea (2006) also suggests that a higher rate in reporting hot flashes may be related to increasing westernization of diet and lifestyle, stress from sociocultural and economic changes, and medicalization of midlife and menopause. This trend identified by Shea may more accurately reflect reality, as The Study of Women's Health Across Nations (SWAN) identifies a Japanese American hot flash reporting rate of 34.3% that is more than double that identified by Shea (2006).

Researchers have revealed that the risk for hot flash occurrence in African American groups is one and a half times higher compared to Caucasian women (Rice, 2005). Several studies suggest that this finding may be related to a higher body mass index (BMI), a history of premenstrual syndrome, and passive smoke exposure in African American women (Miller et al., 2006: Rice, 2005).

SWAN, a large, longitudinal, racially and ethnically diverse study, followed 2784 women through premenopause, perimenopause to the postmenopausal time period. The participants of this study were from seven sites across the United States, ensuring ethnic minority and community-based populations were represented. Various lifestyle factors and menopausal symptoms were assessed over a period of 5 years, 1997-2002. Data from the SWAN supports the conclusions of a previous study indicating African American women had the highest rate of hot flash reporting. This study reported that the African American group was followed by Hispanic, Caucasian and lastly Asian women, who had the lowest reporting frequency of hot flashes across the menopausal transition (Gold, Colvin, et al., 2006). Gold, Colvin, et al. (2006) believed that increased hot flash reporting in African Americans may be related to their lower tolerance and perceptions (rating temperature as more unpleasant than Caucasian women) of cold and heat as shown in several experimental studies. These authors also found that menopausal status was most strongly related to hot flashes, and that reporting frequency was comparable in the postmenopausal period to the late perimenopausal period across ethnic/racial groups; this differed from Japanese and Hispanic groups, which saw decreased hot flash frequency in the postmenopausal to late perimenopausal period.

One limitation of many of the studies on race/ethnicity and hot flash occurrence may be that the studies have been carried out largely in western cultures (Avis et al., 2001). This is identified in Shea's (2006) study, which cites the difference in hot flash occurrence in Japanese women related to their geographical location. Interestingly, Sievert and Flannagan (2005) explored geographical distributions of hot flash frequency in studies done on menopausal women around the world and found that the narrowing of the thermoneutral zone does not change to the same degree among menopausal women living in warmer climates or those exposed to less seasonal climate changes. It may be that racial/ethnic differences in hot flash occurrence may be related to multiple lifestyle factors including geographical climate and seasonal changes.

Cigarette smoke

Both body mass index (BMI) and smoking have been identified in some cohorts of menopausal women as increasing the frequency and severity of hot flashes. Researchers have shown that smokers will have an earlier onset of menopause transition, report increased severity of hot flashes and are at risk for increased occurrence of hot flashes with the amount smoked (Cramer, Harlow, Xu, Fraer & Barbieri, 1995; Whiteman et al., 2003). The mechanism between smoking and hot flashes is unknown, but is thought to work via several mechanisms that interfere with, cause fluctuation in or reduce estrogen levels. One mechanism by which estrogen levels may be lowered is through drug metabolism in the liver, which is enhanced in cigarette smokers, and estrogen metabolism may, therefore, occur more quickly in smokers (Greendale & Gold, 2005). This theory is just one of several put forth by researchers as a mechanism by which smoking induces earlier menopause and increased risk of vasomotor instability.

The SWAN, as cited in Greendale and Gold (2005), reported that exposure to passive rather than active smoke was significantly associated with vasomotor symptoms. It was also found in the SWAN (Greendale & Gold, 2005) and a study by Gallicchio, Miller, et. al. (2006) that endogenous estrogen levels in smokers (active or passive) was not associated with hot flashes as previously thought. Gallicchio, Miller, et al. (2006) suggested a couple of possible mechanisms for the association between smoking and hot flashes. One mechanism may be that elevated androgen levels have been identified in smokers and may be responsible or alternatively that the cigarette smoke constituents, whether active or passive, interfere with the thermoregulatory pathways associated with hot flashes.

Many studies have identified an association between cigarette smoke and hot flash occurrence. Elucidation of the causal mechanisms may further our understanding of hot flash mechanism(s) and trigger(s) in general.

BMI

Studies examining BMI as a risk factor for vasomotor instability have yielded mixed results. Gallicchio, Visvanathan, et al. (2005) concluded that there is an increased risk of the incidence and severe of hot flashes in perimenopausal women with BMI > 35 kg/m^2, and that there is an elevated risk, although not statistically significant, in perimenopausal women with a BMI > 30 kg/m^2. Several studies support a correlation of higher BMIs with hot flash occurrence at various phases of menopausal transition and age. Researchers have identified that in perimenopausal women in the 40-50 year age group with a BMI > 30 kg/m^2 there is an increased tendency for vasomotor instability. This tendency was not found in a group of postmenopausal women aged 51-60 years with

the same BMI (den Tonkelaar, Seidell, & van Noord, 1996; Riley, Inui, Kleinman, & Connelly, 2004; Whiteman et al., 2003). Greendale and Gold (2005) recount current postulations that women with higher BMIs are predisposed to hot flash occurrence due to altered ovarian function and the adipose layer may promote insulative action that contributes to narrowing the hypothalamic thermoneutral zone.

Despite mixed conclusions concerning BMI and its association with hot flash occurrence, there were consistent reports in most studies that there is no association between hot flashes and BMI in postmenopausal women, only in the perimenopausal group (den Tonkelaar et al, 1996; Gold, Sternfeld, et al., 2000; Riley et al., 2004; Whiteman et al., 2003)

Alcohol Consumption

Moderate amounts of alcohol consumption, that is less than one drink daily, appears to have no impact or minimal influence on vasomotor instability. In fact, Riley et al. (2004) found in their analysis that perimenopausal women who reported having 1-5 drinks per week reported lower hot flash occurrence than women who did not drink, and that alcohol use was not significantly associated with hot flashes in postmenopausal women. A few studies reviewed by Riley et al. (2004) indicated consumption of considerably larger amounts of alcohol appears to have more of an impact, and that this appears to be due to similar pathways as outlined with cigarette exposure. The SWAN found no effect of alcohol on hot flash reporting (Gold, Colvin, et al., 2006). Sievert, Obermeyer & Price (2006) suggest any associations between women who consumed alcohol daily and hot flash occurrence may be explained in part by the increased tendency to smoke, which may account for hot flash occurrence in this population of women.

Exercise

Physical exercise has been postulated as both protective against and as a trigger for hot flashes. Physical activity in perimenopausal and postmenopausal woman has been studied with varied results. Greendale and Gold (2005) and the SWAN (Gold, Colvin, et al., 2006) perceived physical activity to have little to no effect on hot flashes. Greendale and Gold's (2005) review of the literature states that few of the studies demonstrated no effect as the population under study had a lower incidence of hot flashes at the outset than those with no exercise. Milan (2005) also reviewed many of these same studies noting limitations and problems with sample size, methodology etc., and suggested that the data is inadequate to show whether exercise is beneficial, has no effect or increases hot flash occurrence in postmenopausal women. He noted one Swedish randomized study that was able to demonstrate a hot flash reduction in a group of previously sedentary postmenopausal women who undertook a 12-week exercise program. Fifty percent of this group noted a 28% reduction in hot flashes at 12 weeks, and further decreases in both hot flash frequency and severity of 75% at 24 weeks and 72% at 36 weeks. Milan (2005) further suggested that the intensity of the exercise, i.e., vigorous, may be needed to elevate endorphin levels to affect hypothalamic thermoregulation.

Dormire (2003) also identified that exercise has a positive effect in decreasing hot flash occurrence and frequency. She noted the increased levels of endorphins with regular exercise may be important when linked to the potential endorphin involvement in hot flash physiology. Of note, Hammar, Hammar-Henriksson, Frisk, Rickenlun and Wyon (2000) noted a similarity between postmenopausal women and oligo-amenorrheic

(infrequent menstrual period intervals of 40 days or longer) and amenorrheic (the cessation of menses for 6 month after a period of menstruation) athletes. (For a discussion of the terminology see Lowdermilk et al., 2000). Hammar et al. (2000) examined hormonal levels in oligo-amenorrheic and amenorrheic women and found comparable estradiol levels to postmenopausal women but the athletes did not suffer from hot flashes. The authors noted that the ß-endorphin levels were significantly elevated in the athletic women as compared to the low ß-endorphin activity in postmenopausal women. The theory postulated in this study is that the high ß-endorphin levels in the athletes stabilized thermoregulation that is otherwise unstable in the postmenopausal women with low ß-endorphin activity and hot flashes.

Food Consumption

Another lifestyle factors frequently associated with hot flash occurrence are dietary. Caffeine, hot fluids, and spicy foods are thought to increase core temperature because decreasing the use of these dietary substances has been shown to decrease hot flashes (Neff, 2004). Thurston, Blumenthal, Babyak & Sherwood (2005) found that objective occurrences of hot flashes were noted during or within 20 minutes of caffeine consumption. Of note, several studies have examined methylxanthine derivatives of caffeine impact on the counter-regulatory response to hypoglycemia in diabetics and have found it to magnify the response as well as the recovery from and perception of hypoglycemia (White, 2007). This may contribute to the plausible involvement of norepinephrine, a hormone released in counter-regulatory response, in hot flash mechanism and thermoregulation. A more detailed discussion of the counter-regulatory response follows in the Diabetes discussion section. Results regarding the ingestion of

the above dietary items have been mixed and may require additional examination of their involvement in hot flash mechanism (Gold, Colvin, et al., 2006).

Soy products have received specific attention and been tagged as a predominant and consistent feature in Asian cultures diet that may have impact on low incidence of hot flashes in this ethnic population. The phytoestrogens in soy products have similar properties to estradiol but have a weaker estrogenic effect. Findings in these studies have had inconsistent results, suggesting more research is needed to clarify dietary impact of soy products (Dormire, 2003; Gold, Colvin, et al., 2006).

Stress

The role of stress as a contributor to hot flash physiology is infrequently addressed in studies on hot flash mechanism. Thurston et al. (2005) reported that several studies that have assessed stressors or negative emotions as triggers of hot flashes have been very small, uncontrolled or self-reported. Carmody, Crawford, & Chruchill, (2006) conducted a pilot study looking at stress reduction via meditation and its impact on hot flash frequency in a group of 15 women. The authors found after 8 weeks of stress reduction there was a decrease in hot flash severity by 40 % and frequency by 39 %. Interestingly, Thurston et al. (2005) study found results contrary to this. The authors identified that objectively measured hot flashes were more likely to occur when a group of perimenopausal and postmenopausal women were in a happy, relaxed, and feeling-in-control state, and less likely to occur when they were feeling stressed, frustrated or sad. Subjectively reported hot flashes, that were false-positive flashes, were more likely to be reported after increased frustration and decreased when feeling in control. These contradictory results have led Thurston et al. (2005) to caution and suggest that studies

should include both an objective and subjective measure of hot flashes to ensure valid interpretation of study results.

Summary

Greendale and Gold (2005) and Riley et al. (2004) reviewed and summarized the literature on modifiable lifestyle factors specifically: alcohol use, cigarette exposure and physical exercise to identify their relationship to hot flashes in menopausal transition and in postmenopausal women. Li et al. (2003) suggested that severe intensity of hot flashes is linked to part-time employment, oophorectomy, heavy smoking, high alcohol consumption, a BMI of 25.1-29.9 $kg/m^{2,}$ weight gain, or a history of cancer, and that lower intensity was associated with age, high education or vigorous exercise. In addition, Riley et al. (2004) suggest that impact of the various lifestyle factors may vary with menopausal phase.

These studies have underlined the importance of more rigorous and sound studies, which are needed to delineate the impact of various lifestyle factors on hot flash occurrence and triggers.

Hot flash mechanisms

Hot flashes are not reported globally as a symptom of concern, but it is the symptom for which 40-80% of menopausal/ postmenopausal women most often seek medical attention (Caiozzi et al., 2004; Whiteman et al., 2003). The peak prevalence for hot flashes has been identified as occurring in the late menopausal transition and early postmenopausal time periods (Woods & Mitchell, 2005).

Vasomotor instability or hot flash is associated with, but not causally related to, fluctuating estrogen levels and the trigger(s) and variance in occurrence between women

are not well understood. Hot flashes and night sweats (vasomotor instability during sleep) are characterized by fluctuating vasodilation resulting in flushing skin and perspiration, warmth in the chest, neck and head, and are often accompanied by palpitations, anxiety, and/or insomnia. Throughout the remainder of this thesis, hot flash will refer to vasomotor instability occurring during nocturnal (night sweats) as well as daytime hours.

Hot flashes are thought to be due to a combination of hormonal, metabolic and psychogenic factors resulting in a thermoregulatory center disturbance in the hypothalamus (Bachmann, 1999; Contestabile & Derzko, 2002; Lowdermilk et al., 2000; Weir, 2004). Freedman (2001) identified multiple studies which found that urinary, vaginal, and plasma levels of estrogen do not correlate with hot flash occurrence. In addition, he showed that estrogen levels between symptomatic and asymptomatic women do not differ. It is thought that it is the estrogen withdrawal rather than the low serum estrogen level that may explain the differences in occurrences of hot flashes between women (AACE Menopause Guidelines Revision Task Force, 2006; Berendsen, 2000; Shanafelt, Barton, Adjei, & Loprinzi, 2002). Shanafelt et al. (2002) explained that women who have low levels of estrogen, as in gonadal dysgenesis, do not experience hot flashes until they are exposed to a course of estrogen therapy over several months followed by an abrupt discontinuation. They also identified an abrupt occurrence of hot flashes in women who experience estrogen withdrawal following an oophorectomy.

Several studies have suggested that hot flashes result from a change in the central thermoregulatory center. Freedman's (2005) studies have illustrated that a narrowing of the thermal neutral zone exists in women with hot flashes. The thermoneutral zone can

be explained as the temperature zone between sweating and shivering. In symptomatic women, sweating and peripheral vasodilation or hot flash occurs when the core temperature reaches the upper threshold then declines when the lower threshold is crossed, resulting in shivering. Freedman determined that interthreshold temperatures for asymptomatic women are 0.4°C and for symptomatic women 0.0°C. Freedman (2001) identified that hot flash occurrence lagged the circadian thermoregulatory variations by approximately three hours, peaking around 0000 to 0400 hours, 1500 hours and 2200 hours. Shanafelt et al. (2002) suggested that the preoptic area of the hypothalamus and several sites in the complex neuroendocrine pathways that regulate thermoregulation may explain core temperature changes and associated involvement in hot flash mechanism.

Since not all women experience hot flashes, estrogen deficiency cannot solely explain hot flash mechanisms or occurrences. In addition, several studies have also noted that perimenopausal women experience hot flashes with normal estrogen hormonal values (Notelovitz, 2004). Notelovitz (2004) suggests a multifactorial approach to delineate the underlying mechanisms involved. The next sections will explore the relationship between serotonin, norephinephrine, glucose and their hot flash involvement.

Hot flashes and serotonin

Serotonin, a neurotransmitter in the brain, plays a role in modulation of the core temperature. Studies show that estrogen enhances serotonin synthesis and increases its transport into neurons. Withdrawal or deficiency of estrogen, as in menopause, decreases serotonin and destabilizes the thermoregulatory set-point by changing the ratio of hyperthermic to hypothermic serotonin receptors in the brain (Notelovitz, 2004). This action triggers an autonomic response to cool the body and, thus, the sensation of a hot

flash. Notelovitz (2004) suggested that the interaction and balance between the hyperthermic and hypothermic serotonin receptors and estrogen is essential in thermoregulation. Berendsen (2000) also identified this imbalance but theorized that in addition to higher levels of hyperthermic serotonin receptors, external stimuli such as mild stressors (e.g., anxiety, alcohol, ambient temperature changes, caffeine, etc.) are thought to contribute to triggering of hot flashes. Berendsen further suggested that dreams could be considered a mild stressor and act as triggers for nocturnal hot flashes referred to as night sweats.

Hot flashes and norepinephrine

Norepinephrine and LH pulses are the two more common mediators identified as possible hot flashes triggers. LH pulses released from the anterior pituitary in response to dropping estrogen levels in the luteal phase of the menstrual cycle, have been explored as a hot flash trigger mechanism. To date, LH pulses are considered co-events but are not supported as the sole mechanism underlying hot flashes, as women with no pituitary report the occurrence of hot flashes (Dormire, 2003; Freedman, 2001; Shanafelt, et al., 2002).

Norepinephrine is thought to be the primary neurotransmitter involved and has been implicated in the thermoregulation disruption of hot flashes. Norepinephrine brain levels during hot flashes have been studied by measuring the presence of its metabolite in the blood. The research demonstrated that elevation of plasma basal levels of this brain metabolite, but not the peripheral metabolite, occurs with both induced and spontaneous hot flashes, which suggests norepinephrine involvement in hot flash physiology (Dormire, 2003; Freedman, 2001; Lipov et al., 2007). In Freedman's study (2005),

measurement of norepinephrine metabolites were found unchanged when exogenous estrogen was administered and hot flashes were alleviated. Despite this result, Freedman believes that elevated norepinephrine levels are involved in narrowing the thermoregulation zone and serve as part of the hot flash triggering mechanism.

Other studies seem to support Freedman's theory. Dormire (2003) and Lipov et al. (2007) have examined the use of a drug called Clonidine, a norepinephrine agonist that reduces brain norepinephrine. Clonidine has been used successfully to treat hot flashes in both postmenopausal women and breast-cancer therapy patients. These studies suggest that hot flashes are due to increased sympathetic nervous system activity accompanied by norepinephrine release, but as yet, it is not understood why norepinephrine is released as estrogen declines. A connection between norepinephrine regulation, decreased endorphin levels, and a metabolic by-product of estrogen metabolism has been identified. It is thought that the decreasing estrogen levels result in decreased endorphin levels, which are important in norepinephrine modulation. These decreased endorphin levels leads to an increase in both norepinephrine and serotonin levels resulting in destabilization of the thermoregulatory set point and consequently a hot flash occurs with any subtle increase in core temperature (Ivarsson, Spetz, Hammar, 1998; Shanafelt et al., 2002).

Hot flashes and decreased glucose availability

Recently neuroglucopenia, a decrease in glucose availability in the brain as regulated by estrogen, has been suggested as a hot flash trigger. It is thought that declining estrogen levels affect the transport of glucose and its availability and/or use in the brain (Dormire, 2003). Simpkins and Katovich (1989), studied a group of three

postmenopausal women, monitoring ambient, skin and vaginal temperatures every 2 minutes and blood glucose values every 15 minutes over a 5-7 hour period for 2 days, following the ingestion of identical breakfasts. They found that hot flashes did not occur until blood glucose values dropped below 6.8 mmol/L. This study suggests that the triggering of the hot flash may be a result of hypothalamic counter-regulatory activation resulting in a sympathetic response and heat dissipation through peripheral vasodilation or hot flash.

Dormire and Reame (2003) repeated this experiment with 10 postmenopausal women. In this study, participants were monitored for 30 hours over 3 days. The study participants were given either intravenous glucose or saline randomly for 3.5 hours for 2 days, interspersed with an observational phase between the 2 days. Blood glucose was monitored every 5 minutes during the titration period (30 minutes) then every 15 minutes thereafter, to maintain blood glucose level $\geq$ 7.2 mmol/L for 3 hours during glucose administration as well as during a "sham" saline administration. Participants noted perceived hot flashes using an event marker, and continuous monitoring of skin conductance provided objectively measured hot flashes. Dormire and Reame found that significantly more objectively measured hot flashes occurred when blood glucose values were <5.2 mmol/L. Twenty-three hot flashes were noted when blood glucose fell to <5.2 mmol/L and three hot flashes occurred when blood glucose values were in the 7.2-7.7 mmol/L range.

The impaired glucose delivery model put forth by Dormire and Reame (2003) suggests that low estrogen levels in the postmenopausal woman decreases the number and efficiency of glucose transporter 1 (GLUT 1) at the blood brain barrier. GLUT 1 is a

specific glucose transport protein, which transports glucose from the cerebral circulation across the blood brain barrier (Thomas, Sherwin, Murphy, & Kerr, 1997). This effect on the GLUT 1 decreases the amount of glucose transported to the brain and with decreased glucose available for transport during fasting states, the hypothalamic glucose sensing cells trigger a release of norephinephrine. This process is part of the counter-regulatory mechanism to mobilize adequate glucose for the brain, resulting in vasomotor response or hot flashes.

Moreover, Simpkins and Katovich (1989) recognized this mechanism also as a possible hot flash trigger model by noting similar symptomatic responses in diabetic patients undergoing intensive insulin therapy and experiencing episodes of hypoglycemia. They suggested that the counter-regulatory mechanism involved in glucose regulation in diabetics parallels and may be the same mechanism responsible for hot flash symptoms in postmenopausal women as well. This counter-regulatory mechanism will be discussed further in the next section on diabetes and the postmenopausal woman.

Diabetes

In Canada, 1.2 million people currently live with diabetes and more than 60,000 new cases are diagnosed each year (Alberta Health & Wellness, 2003). Alberta Health & Wellness projects that the number of Albertans living with diabetes will double over the next 15 years. This projection means that the number of women who are both diabetic and menopausal/postmenopausal will increase significantly. Dorman et al. (2003) and Dormire (2003) pointed out the lack of research on this cohort of women is evident and an in depth review of the literature supported this claim. Studies done with diabetic

women reveal that they tend to enter into the menopausal transition/postmenopausal stages almost 10 years earlier, 37-50 years (Dorman et al., 2001), than the general population of healthy females. Poirier-Solomon (2001) suggests that the labile hormones of menopausal transition mimic those of puberty, making blood glucose control difficult to attain and maintain and menopausal symptoms unpredictable. During puberty transition, insulin resistance has been observed (Amiel, Sherwin, Simonson, Lauritano & Tamborlane, 1986). Rosenthal (2005) states that this insulin resistance, demonstrated during the pubertal transition, persists and occurs for 3-5 days during menstrual cycle. In this review of diabetic women, Rosenthal indicated that during menopausal transition, as in puberty, the diabetic woman is faced with periods of insulin resistance interspersed with increased insulin sensitivity. Kalish, Barrett-Connor, Laughlin and Gulanski (2003) found insulin resistance was significantly associated with higher total and bioavailable estradiol levels in postmenopausal women, but neither the mechanism nor the direction of the association is understood.

In diabetic postmenopausal women, as in their non-diabetic counterparts, estrogen and progestin levels drop significantly, increasing insulin sensitivity and dropping insulin requirements by as much as 20%, making these women more vulnerable to low blood sugars (Rosenthal, 2005). This response can occur in both type 1 (a result of decrease in or a complete absence of insulin production) and type 2 (a result of increased resistance to the action of insulin in body tissues and/or an insulin secretory defect) diabetics (Ekoe, Zimmet, & Williams, 2001). Low blood glucose values, or hypoglycemia, can result in inadequate supply of glucose to the brain. Moreover, the counter-regulatory mechanism mentioned in studies reviewed earlier in this thesis regarding hot flash mechanism is also

the first defense in a diabetic against hypoglycemia, and constitutes an attempt to protect the brain from glucopenia.

The counter-regulatory mechanism involves the release of epinephrine, norepinephrine, glucagon, and adrenocorticotropic hormones (Davidson, 2000). This mechanism is thought to be initiated simultaneously in the hypothalamus, the autonomic centers and the hypothalamic-pituitary system (Frier, Fisher, Gray & Beastall, 1988). This mechanism produces autonomic symptoms such as sweating, palpitation, tremor, or hunger due to both sympathetic and parasympathetic stimulation. It also produces neuroglucopenic symptoms such as warmth, weakness, difficulty thinking, confusion, tiredness and drowsiness due to direct effect on cerebral function (Bhalla & Singh, 2002; McAulay, Deary, & Frier, 2001). As diabetics age, this counter-regulatory mechanism may not function as effectively, since pancreatic cell secretion of glucagon may be inappropriate and may release less epinephrine because of autonomic neuropathy (Frier et al., 1988). Fier et al. (1988) also noted subnormal responses of beta-endorphins to hypoglycemia in the diabetic participants, suggesting an underlying hypothalamic dysfunction. White (2007) identified a reduced intensity in the counter-regulatory response to hypoglycemia in aging non-diabetic women. In the general diabetic population, he noted that frequent hypoglycemic episodes reduce the counter-regulatory response by $\geq 50\%$ (White, 2007). This may suggest that blunting of the counter-regulatory responses may be more significant in aging, female, diabetic women experiencing frequent hypoglycemic episodes.

Interestingly, endorphins, which regulate norepinephrine, are decreased in both postmenopausal women and in the diabetic population suggesting that the blunted

hypoglycemia response and hot flash occurrence may have the same origin of dysfunction. In addition, Frier et al. (1988) further suggest that the hypothalamic dysfunction might be related to glucose receptor insensitivity or a problem with glucose transport across the blood brain barrier, which was identified by Dormire and Reame (2003) as the possible mechanism involved in hot flash etiology. With the combination of altered counter-regulatory mechanism, frequent hypoglycemia and decreasing estrogen and progestin levels, the etiology of the autonomic and neuroglucopenic symptoms may be a challenge in the postmenopausal diabetic woman. In fact, this cohort of women may inappropriately recognize and respond to hot flashes as low blood glucose values. They may employ treatments that elevate blood glucose or they may miss a significantly low blood glucose value believing it to be a hot flash and not treat initially at all.

Summary

For diabetic menopausal/postmenopausal women, the addition of fluctuating estrogen levels may increase the likelihood of increased vasomotor response as the body attempts to mobilize glucose for the brain, presenting the additional challenge of differentiating the symptoms of hypoglycemia from those of hot flashes. Some women have reported that low blood glucose symptoms are stronger and more frequent, especially during the night, increasing the difficulty in determining whether it is a hypoglycemic reaction or hot flash occurrence (Poirier & Coburn, 2000). The literature review demonstrates a gap in research, specifically the lack of thorough investigations of the relationships between blood glucose values and postmenopausal symptoms in diabetic women.

Chapter 3

Methodology

Presented in this chapter are the research design, operational definitions, sample selection, size and recruitment, a review of the study sheets and ethics. This chapter ends with a description of the procedure including initial contact, consent, collection of data and statistical analysis.

Research Design

A quantitative framework was employed in this research study. This design reflects a deterministic philosophy in that it reflects the idea that every event has an antecedent cause and the cause probably determines the effect and/or outcome. This design, then, is based on careful observations that exist "out there," taking place in the real world. It is reductionistic in that it reduces the research to small discrete ideas to be tested. Overall, a quantitative framework is employed to collect data that can be used to develop theories or laws that govern our world. Such theories are dynamic because, in the real world, we often cannot be absolutely positive about our claims when studying human behaviors and actions and, thus, these claims or theories require testing, verification and/or revision (Black, 2003; Creswell, 2000). My research, while insufficient to generate theory or law, is grounded in these principles.

The knowledge claim or theory that is currently espoused as a mechanism for vasomotor instability is that it is related to decreasing estrogen levels. This theory has been supported in the literature as the mechanism or trigger for vasomotor instability occurrence until recently and, as such, requires revision and/or verification. This study explores an alternate theory as described in studies by Dormire and Reame (2003) and

Simpkins and Katovich (1989), which suggests the existence of a possible relationship between blood glucose values and vasomotor instability, with the hope of providing support for potentially more extensive studies in postmenopausal diabetic women.

An *ex post facto*/correlation design was chosen to explore the connection/association among postmenopausal women with diabetes. This study explored a potential relationship, without inferring cause, between blood glucose values and vasomotor instability occurrence in this group of women. Limitations identified with this design are lack of direct control over the independent variable, in this case, blood glucose values and inability to control for intervening or extraneous variables. Further limiting this type of study is time; other events and/or biological and/or psychological changes are allowed to intervene.

A daily journal was supplied to the study population to record data about the variables of interest as well as other activities. The rationale for including these activities was two-fold. First, they are potential hot flash triggers and are used to provide a personal profile for participants. Second, by having participants record these activities I hoped to 'blind' and thus limit bias in their responses. Data resulting from recording these other activities were not intended for analysis. To lessen the impact of time events and maturation on the study population, participants were given instruction to collect the multiple data entries successively within the shortest time period possible.

Operational Definitions

The variable, vasomotor instability, is defined as being characterized by a combination of the following: sudden onset of flushing skin, perspiration, warmth in the

chest, neck and head (Contestabile & Derzko, 2002; Lowdermilk et al., 2000; Weir, 2004). Further, the participants classified vasomotor instability occurrence as:

- **Mild** - producing a sensation of heat without sweating
- **Moderate** - producing a sensation of heat with sweating, able to continue activity
- **Severe** - producing a sensation of heat with sweating that disrupts their usual activity (Carpenter, 2005; Gallicchio et al., 2005).

This variable is considered an ordinal level variable in this study with four levels including:

0 – No Hot Flash

1 – Mild Hot Flash

2 – Moderate Hot Flash

3 – Severe Hot Flash.

The blood glucose value variable is defined as the blood glucose value reported in mmol/L as measured by the participants' blood glucose meter. This variable is considered an interval level variable in this study.

Sample Selection and Size

A stratified random sample of women was desired. However, as discussed below this was not possible and a convenience sample of women with characteristics as identified in the inclusion/exclusion criteria was obtained utilizing strategies initially employed to obtain a quota sample (Loiselle, Profetto-McGrath, Polit, & Beck, 2007). A number of difficulties limited the scope of this study; the inclusion/exclusion criteria led to a small sample. The inclusion criteria for this study population included women between the ages of 37-65 years, who are either type 1 or type 2 diabetics and who

monitor blood glucose values daily. In addition, these women experienced either a natural or surgically induced menopause, are currently postmenopausal, and experience some vasomotor instability. The exclusion criteria for the study population were women who are non diabetic, diabetic women who have a physiological process that is known to affect blood glucose values or who do not monitor their blood glucose values. Any women who were not postmenopausal were excluded from the study. This exclusion barred several women who had expressed interest in participating.

Recruitment methods were mixed. On the one hand, strategies were used to create the greatest possibility of randomness; on the other self-selection in response to recruitment posters added an element of convenience. Initially, stratification was utilized in this study as a method to determine on a proportional basis the subpopulation with specific traits (Gillis & Jackson, 2002; Knapp, 1998). The stratums as described in the inclusion criteria and researched in this study are postmenopausal women who are diabetic and who experience hot flashes. The diabetic stratum represents both type 1 and type 2 diabetic women. Within the diabetic population, the normal split is 5-10% type 1 and 90-95% type 2 (Alberta Health & Wellness, 2003). Based on this split the expected numbers within this stratum would be a 9:1 ratio of type 2 to type 1 diabetes. This stratum split was not achieved resulting in a self-selected sample of type 2 diabetic postmenopausal women.

The second stratum within this study is postmenopausal women experiencing hot flashes. As described earlier in the literature review, prevalence of vasomotor instability in women during this time period is estimated to be 30-80% (Lowdermilk et al., 2000; NIH State-of-the-Science Panel, 2005). Utilizing the percentages for diabetes and

postmenopausal women experiencing hot flashes, along with population statistics from the City of Lethbridge 2005 Census Results and the Alberta Diabetes Strategy 2003, the sample size was determined (Table 3.1).

Sample size determination for quantitative research has been suggested at ten percent of the population or alternatively as the largest sample possible to reduce sampling error and ensure representation of population (Gillis & Jackson, 2002; Loiselle et al., 2007). Another general suggestion for sample size determination, as outlined in Knapp (1998), is to have at least 10 times as many subjects as variables. Other considerations in determining sample size are time and/or economics constraints, so that the sample as represented by N is whatever is feasible for the researcher (Knapp, 1998).

Considering these various methods, the calculation of a sample size using the available data determined an N for this study as outlined in Table 3.1.

Table 3.1.

Sample Size Determination Calculations

Parameters	Calculation	Total
Females Aged 40-59 in Lethbridge, 2005*	10,114	10,114
Percent of Diabetic Women aged 40-59 = 3.6% †	10,114 x 3.6%	364
Percent of Diabetic, Postmenopausal Women with Hot Flashes = 30-80%	364 x 30% 364 x 80%	109 291
Percent of Type 1 to Type 2 Diabetics, Postmenopausal Women with Hot Flashes		
Type 1 = 10%	109 x 10% 291 x 10%	11 29
Type 2 = 90%	109 x 90% 291 x 90%	98 262
Sample Size required = N		
10 times the number of variables to subjects = 2 (Hot Flashes & Blood Glucose)	2 x 10	N = 20
10 % of Population	109 x 10% 291 x 10%	N = 11-29

*City of Lethbridge 2005 Census, n.d.. †Alberta Health & Wellness, 2003; Health Canada, 2002.

As shown in Table 3.1 it is estimated that population of diabetic (both type 1 and type 2) women experiencing postmenopausal hot flashes in the Lethbridge area is estimated to be 109-291 women. Using the 10% as well as the 10 times the subjects to the number of variable calculations for sample size determination, N is suggested to be 11-29 and 20 women respectively (Table 3.1). The sample size was also confirmed using

the online UCLA power calculator which produced an N of 25 at a power of 80% and significance level of $p<0.05$ (UCLA Department of Statistics, n.d.). Based on these various calculations, it was decided to pursue a sample size of 25 for this study, with the intention to have the split of participants with type 1 and type 2 diabetes (10% vs. 90%) being two and 23 respectively.

The sample of postmenopausal diabetic women are the observational units which further provided the basic units of analysis which are the 40 samples of blood glucose values with hot flash ratings. Usually human subjects are the units of analysis, but Babbie (1983) and Loiselle et al. (2007) states that the population under study is the aggregate of entities of research interest, as in this study. This also appears to be the case in both key research studies by Dormire and Reame (2003) and Simpkins and Katovich (1998), which have been presented previously. Both of these studies had small participant numbers, 10 and 3 women respectively, with the authors basing their study samples on the multiple blood sampling per person attained over 2-3 days.

The forty data entry points (units of analysis) per participant sought for the correlation analysis was confirmed by utilizing the Simple Interactive Statistical Analysis (SISA) sample size calculator for a correlation analysis available online (Uitenbroek, 1997). The selected correlations, (r), $r = 0.35$ and 0.5 (in this case two correlations were selected to reflect a moderate/ large correlation), at significance $p<0.05$ and power 80%, one-tailed, when entered in the SISA calculator suggested 49 and 23 cases respectively would be needed (Cohen, 1988 as discussed in Hopkins, 2003). These numbers fit what had been suggested earlier as a reasonable number of blood sugar tests and therefore each participant would be instructed to collect and document 40 blood sugar data entries.

Sample Recruitment

Subjects were recruited by study poster invitation (Appendix A). Study posters provided background information on the study: why it was being undertaken, the requirements of the study, and provision of free blood glucose test strips for each participant. In keeping with ethics principles the poster also informed potential participants of my role as a graduate student. Recruitment took place over a 12-month period initially in the City of Lethbridge and ended with recruitment strategies extended Canada wide. During these 12 months, quota sampling proved ineffective and convenience sampling was implemented.

The initial recruitment phase involved distribution of the study posters to potential participants by staff (physicians and nurse practitioner) in a physician clinic. High numbers of diabetic clients in this particular clinic, as identified by the Chinook Health Diabetes and Lipid Education Center, and agreement to distribute study posters by the physicians and nurse practitioner aided in the decision to choose this clinic. A letter outlining the study was sent to both the key contact physician and the nurse practitioner at the clinic (Appendix B).

After six weeks of poster distribution, a follow-up phone call revealed that few posters had been distributed due to physician holidays, no clients meeting participant inclusion criteria and to the lack of a computer program that could identify potential study participants. The inability to recruit participants through the clinic prompted a broader distribution of the study posters to include multiple physician clinics within the City of Lethbridge. These clinics posted the invitation posters in appropriate, highly

visible areas, in lieu of personal distribution to each potential participant. Most of the physician clinics required the approval of clinic managers prior to posting of the poster. In addition, several key physicians were sent a letter with study information and posters (Appendix C). Follow-up four weeks later revealed that several physician clinics had not posted the poster due to summer vacations within the clinics. The majority of physician clinics agreed to post the study poster in waiting areas and exam rooms, after permission had been obtained. Summer vacations continued to make recruitment difficult.

In September 2006, the recruitment strategy was altered to include, but was not limited to, posting posters in areas such as pharmacies, senior centers, internet web site (targeting diabetic and women's sites), etc., and recruitment efforts were extended to December 31, 2006. Posters were then distributed within the City of Lethbridge in pharmacies, grocery stores, women's gyms, dental offices, physiotherapy offices, Diabetes and Lipid Education center, senior centers and at senior presentations on diabetes, church bulletins and several internet web sites. Posters were also sent to a Public Health Nurse staffing a health unit office on one of the regional native reserves and were posted in the Native Women's Transition Center as well. Four webmasters were asked to post the study poster. Fifty percent of the webmasters agreed after review and some modification to the poster. Surprisingly, local offices for Canadian Diabetes declined to post the study participant invitation, citing that local newsletters did not support this type of information. The Canadian Diabetes webmasters did not respond to the request at all. Several professional nursing magazines also declined placing information about the study within their publications.

A television interview for the study aired as a public service announcement on Global Television "Seen & Heard" following the noon hour and 11:00 p.m. news for the week of Oct 30, 2006. The Lethbridge Herald ran a newspaper article highlighting the study the week of December 18, 2006.

As a result of changes to recruitment efforts, two potential participants identified themselves following the television airing, but when screened, did not meet the inclusion criteria. An additional four participants responded to the study posters and met inclusion criteria. Of the four, two participants withdrew, one no longer met inclusion criteria of postmenopause as menstruation had recommenced, and one asked to begin data collection in January 2007, which was amenable.

Since previous strategies failed to recruit the targeted number of participants, strategies for recruitment were reviewed and modified again in January 2007. The inclusion criteria, which excluded women who had undergone surgical menopause, was reviewed and revised to include these women and the study area was broadened to include women Canada wide. At this point, the sample size was discussed with the thesis committee and it was agreed to include all participants who met criteria regardless of geographic location. The study poster was also reviewed and modified to outline the study more briefly and highlighted the free participant profile and blood glucose test strips (Appendix D). These new posters were redistributed again to areas as outlined previously. Eleven additional internet websites were contacted to post the study invitation poster and seven agreed to post information for the study in a text format only. It was decided to complete the recruitment phase by the end of May 2007 and to move forward due to time restraints. Finally, the study commenced with eight postmenopausal

diabetic women participating. These women came from three Southern Alberta communities: Crowsnest Pass, Lethbridge, and Taber. Efforts to recruit beyond the region failed. One participant withdrew early in the study when her menses recommenced resulting in a final number of seven.

Study Sheets

The study sheets for participants included letter of consent, cover letter, survey and a daily journal.

Letter of Consent and Cover Letter

The letter of consent (Appendix E) and the cover letter (Appendix F) outlined the following:

- Purpose and procedure
- Benefits to population under study
- Participation is voluntary and confidential
- Participants are free to ask questions and withdraw without prejudice with any data collected being destroyed
- Data retention and storage
- Key contacts for more information.

Survey

As indicated earlier, participants recorded information on health issues and activities that are known to influence hot flashes. This information was included to blind the participants and to provide to them information of personal interest. Demographics and health information were also included in order to provide the reader with a fuller understanding of the participants. Recognizing that preliminary non-experimental studies

do not provide analyses of causal relationships, rather preliminary information only, it is important to provide this information to assist future researchers. Demographics and health information is captured in the survey (Appendix G). Information collected in the demographic section of the survey included age, ethnicity, surgery and other health concerns. Following the literature, which identified potential extraneous variables on hot flash occurrence, activities with potential effects on vasomotor instability are included. These were exercise and smoking habits, medications, height and weight (to calculate BMI), and caffeine and alcohol consumption information.

Health information collected concerned the participants' diabetes, menopausal status, and hot flash information. Specifically, diabetes information included the diabetes type and management, HbA1c in last 3-6 months and meter used in order to purchase blood glucose strips for participants. The glycosylated hemoglobin (HbA1c) value provides an evaluation of the average blood glucose control over the previous 2-3 months (Canadian Diabetes Association, n.d.).

The menopausal information identified the type of menopause the participant experienced and the years since menopause occurred. Presence of hot flashes and night sweats was further evaluated. This information provided another method of screening participants for inclusion criteria following the initial telephone contact and screening. In this study, hot flash refers to both hot flashes and night sweats, which were defined previously as hot flashes that occur at night. The separate category of night sweats was retained to allow women to participate who experienced night sweats only and who might not recognize the inclusive terminology of hot flashes. The frequency, severity and length provided additional descriptive information of the participant population. It also

provided some parameters as to number of days or weeks that each participant might need to take to complete the study.

The last page of the survey includes a detachable page to thank participants for participation and extends an invitation to have a personalized profile of their results mailed to them. This page has the name and address of the participant and is coded to match their data for later reference.

Daily Journal

The daily journal (Appendix H) is designed to collect data about hot flash occurrence, intensity rating, blood sugar values, date, time and activity at the time the hot flash occurs. The activities include sleeping, sitting, eating, and the category labeled other to capture activities not listed. Based on the literature review, several variables are identified as having potential influence on hot flash occurrence. The influences most commonly linked to hot flash occurrence are alcohol, hot fluids, exercise, BMI, smoking, and stress. So that the study participants would not focus on the blood sugar values and the occurrence of hot flashes only, these activities were inserted into the daily journal between blood sugar readings and hot flash rating in essence blinding participants to the focus of the study.

A minimum of 40 blood tests were required from each participant. These were recorded in their daily journal. Each page of the daily journal (Appendix H) has four sections for separate date entries that allow up to four blood sugar tests with or without hot flashes to be recorded per section. This allows a maximum of 16 entries per sheet and each booklet contains four sheets. Instructions printed on the daily journal direct the participant to collect 20 blood sugar tests in the presence of a hot flash and 20 blood

sugar tests in the absence of a hot flash. Definitions distinguishing mild, moderate, and severe hot flashes are also included.

Ethics

Upon completion of study sheets and determination of sample size needed, a University of Lethbridge Application for Ethical Review of Human Subject Research was completed and submitted. Included in the application was the acknowledgement of funding provided for this study by the Centre of Management Research, University of Lethbridge. Funding covered the costs of the 50 free test strips provided to participants to alleviate the cost of extra blood glucose testing.

The Committee Chair made suggestions and comments regarding wording and follow up with participants. The cover letter, letter of consent, survey, and the daily journal were amended to reflect these changes and resubmitted to the committee. These changes were accepted and a Certificate of Human Subject Research was issued (Appendix I).

Changes made to the study poster, the inclusion criteria and extension on participant recruitment, further to initial acceptance, were submitted to the ethics committee and approved prior to implementation.

Procedure

The procedure will outline initial contact, attaining informed consent, collection of data and closes with statistical analysis review.

Initial Contact

The participants initiated telephone or email contact with the researcher. When the initial contact occurred, the research study was outlined for the potential participant

and questions were asked to ensure that inclusion criteria were met. Arrangements were made to meet at a destination determined by the participant to review study participation, consent, and participant study sheets.

Consent

The letter of consent was reviewed with the participant. Consent followed the principle of self-determination as outlined in Loiselle et al. (2007), in that each participant had the right to participate voluntarily without risk of adverse outcomes, to ask questions, to decline sharing information as they saw fit and to withdraw at any time without prejudice, followed by the destruction of their data. Data collection was reviewed with each participant, including the amount that was expected to be collected. Anonymity was discussed in that results would be reported in general terms and that participants sheets were to be coded and presented in the thesis in such a way to prevent identification of individuals.

Participants were informed that randomly selected numbers would be assigned to their study sheets and the number would be recorded on a sheet with their name. In keeping with standards of ethic practices, they were also told that data sheets are stored in locked files and referred to only when data are tabulated and results are ready to be sent to participants. Participants were also ensured that identification numbers would be entered into the computer database rather than names or other identifying information to prevent accidental breach of confidentiality. Participants completed the consent with date, printed and written name, and detached the bottom portion for retention by the researcher.

Pariticipants did not question the information provided to them. None withdrew after learning of the ethics procedures and the practices described to the participants were followed. Data received from one participant who withdrew very early in the study was destroyed.

Collection of Data

The cover letter remained in the booklet for participant referral along with the daily journal. The instruction for completion of both the survey and the daily journal was reviewed verbally and participants were encouraged to refer to the cover letter or contact the researcher via telephone or email if they had concerns or questions surrounding completion of the sheets. Five out of the seven participants completed the survey and consent during the initial meeting with the researcher present. The two remaining participants posted the survey and consent in a postage paid envelope supplied by the researcher. One of the seven participants required help; she cited an inability to spell medications and surgical procedures and difficulty with writing and requested the researcher to act as a scribe for the survey. Participants were instructed to complete the daily journal in a timely manner, taking into consideration the frequency of hot flash occurrence.

Participants used their own blood glucose meters to collect data. Common practice within the region of Chinook Health is to validate client meters through lab to meter tests prior to use. Given this practice it was not necessary to conduct further tests for the purposes of this study. Using their meters, participants were instructed to document 20 blood sugar tests in the absence of hot flashes, recording the date, time, and activity and circling no hot flash present at the time of the tests. Blood sugar tests that

were being done routinely by the participants in the absence of hot flashes were encouraged to be used to avoid unnecessary additional punctures. Additional punctures were required for the 20 blood sugar tests with hot flashes. These additional tests were to be spread out over 10-20 days therefore requiring only one to two extra tests per day, reasonable and bearable number for the participants to manage. For each of these 20 additional tests date, time, activity, and intensity of the hot flash were recorded. Varied timing of collection of blood sugar tests was encouraged including during night sweats in participants who experience them. The definition of the hot flash intensity was reviewed verbally and participants were then referred to the definition at the bottom of each page of the daily journal. Participants were invited to ask questions and/or seek clarification. Contact with the participants throughout data collection was discussed and arrangements were established individually as most participants were unavailable for weekly contact and some participants preferred email correspondence to being telephoned. In addition to the established times for contact participants were told they were free to contact me at any time. Upon completion of the daily journal, participants were instructed to remit the booklet in a prepaid postage researcher addressed envelope or to contact the researcher for pick up.

Not all participants were able to collect the 40 samples requested. Two participants collected fewer than the 40 data entry points because vasomotor instability either ceased completely or became very infrequent. One participant cited that when monitoring her activity and the occurrence of vasomotor instability, she noted that she was consuming very high sugar foods, and when the participant discontinued this activity and started an exercise program, the vasomotor instability ceased. Another two

participants found that following surgery with an anesthetic the vasomotor instability activity diminished significantly. One participant had collected most of the data prior to the surgery and was able to obtain 41 data entry points, whereas the other participant collected 29 data entry points, as vasomotor instability was very infrequent. In consequence, the sample sizes used in individual analysis were varied.

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences SPSS for Windows 15.0 software (University of Lethbridge). Descriptive data are presented as frequency, percentages, range, mean, median and standard deviation for participant demographic and health information data, as well as for vasomotor instability and blood glucose values from the daily journal. Kendall's tau-b correlation was utilized to identify the relationship between vasomotor instability and blood glucose values. The Pearson's *r*, being a more familiar statistical test, is presented along with the Kendall's tau-b to allow for comparable interpretation of the results. The correlational analysis was run on individual and aggregated data from each of the seven participants. All data statistical significance was set at $p<0.05$.

Summary

Survey collection and daily journaling are the focus of this quantitative study. The chapter to follow will provide a presentation of the results of the statistical analyses described.

Chapter 4

Results

All data were entered into the SPSS 15.0 version database at the University of Lethbridge for statistical analysis. The chapter begins with presentation of the results of the survey, which are reported separately as demographic and health information portions. The correlational analysis run on data from the daily journal will complete the results chapter.

Survey findings

Demographic data

The participant sample comprised six Caucasians and one Hispanic participant (see Table 4.1). Age distribution of the sample ranged from 47-65 with the average age of 57 (SD=6.1) (see Table 4.2). Tables 4.1 and 4.2 reflect the data presented in this section.

Height and weight were self-reported by the women (not measured) and were used to calculate the BMI's, using Canadian Guidelines for Body Weight Classification in Adults (Health Canada, 2003). BMI range from 28.7-40.7 kg/m^2, the average being 33.9 kg/m^2 (SD =4.4).

Data on smoking status, caffeine and alcohol consumption were collected. None of the participants in the sample was a current smoker, but two had smoked in the past; one for 47 years and another for 15 years. Caffeine consumption, which included coffee, tea and cola, was reported as 28.6% for no consumption, 42.9% for two cups/day, and 28.6% for four or more cups per day. More than half of the participants reported no

alcohol consumption (57.1%) at all and 42.9% indicated they drank less than one drink per day.

Exercise habits were also collected from the participants, specifically the activities they engaged in and the number of times per week they did so. Exercise for the participants included walking (57%), cardio and weight training (29%), yoga and employed in janitorial work (14%). Participants reported engaging in these activities less than once per week (14.3%), 1-3 times per week (14.3%), and more than 3 times per week (71.4%).

Table 4.1

Demographic Data Characteristics Frequency and Percentage.

General Characteristics Of Sample Population*		Frequency	Percentage
Ethnicity/Race	Caucasian	6	85.7
	Hispanic	1	14.3
Caffeine Intake	None	2	28.6
	2 cups/day	3	42.9
	≥4 cups/day	2	28.6
Smoker	Current	0	0
	Never	5	71.4
	Past	2	28.6
Alcohol consumption	None	4	57.1
	<1 drink /day	3	42.9
Amount Exercises	<1 time/week	1	14.3
	1-3 times/week	1	14.3
	>3 times/week	5	71.4

*Based on 7 Participants' Survey Data.

Table 4.2

Demographic Data Characteristics Mean, Median, Standard Deviation and Range.

General Characteristics Of Sample Population*	Mean	Median	Standard Deviation	Range
Age: years	57	56	6.1	47-65
Height: inches	62.7	63	2.5	59-66
Weight: lbs	189	180	23.4	158-230
BMI: kg/m^2	33.4	31.9	4.4	28.7-40.7

*Based on 7 Participants' Survey Data.

Other data collected listed medications currently used, including over the counter, herbal or prescription. Use of these medications is not described for each participant as these data could inadvertently reveal identity. Surgical and other health concerns are similarly treated for the same reason. Table 4.3 provides comprehensive lists of medications, surgical procedures and the participants' health concerns. Medication was examined to establish any side effects that might be mistaken for hot flashes. Only Nitroglycerin produces a symptom of flushing, which may be mistaken for a hot flash if the physician or pharmacist had not made the participant aware of this side effect. All medications were reviewed for their effect on blood glucose. Several medications, specifically Acebutolol, Celexa and Metoprolol, described a low incidence of inducing hypoglycemia. Paxil was identified as having a very low incidence of producing either

hypoglycemic or a hyperglycemic effect. Hyperglycemia was a potential side effect of Combivent (only if maximum dose was surpassed) and Salmon Oil preparations (the extent of the effect or dosage needed to produce symptoms was not discussed) (Wilson, Shannon, Shields & Stang, 2007). Upon review of the participants' data, no significant hypoglycemic or hyperglycemic events were noted specific to these individuals. These data provided an understanding of the participants' personal circumstances but were not further analyzed, as to do so would be beyond the scope of this study.

Table 4.3

Medications, Surgical Procedures, and Health Concerns.

Medications, Surgical Procedures, and Health Concerns.*		
Medication – Over the Counter	• Vitamin C & D • Calcium	• Baby Aspirin • Magnesium
Medication – Herbal	• Salmon oil • Vinegar Pill	
Medication - Prescription	• Combivent, Advair, Singular • Metoclopromide • Pantoloc • Novolin NPH • Novolin Rapid • Gliclazide • Premarin • Medroxy • Arthrotec • Acebutolol • Ramipril • Avalide • Amaryl • Avandia	• Tylenol #3 • Loperamide • Cotazym • Dicetel • Metformin • Gluconorm • Celexa • Altace • Fluconazole • Metoprolol • Nitroglycerin • Crestor • Thiazide • Paxil • Amitriptyline
Surgical Procedures	• Tonsilectomy • Appendectomy • Tubaligation • Carpal Tunnel repair • Varicose Vein Stripping • Oophorectomy • Eye Surgery	• Cholecystectomy • Ceasarean Section • Hysterectomy • Laparotomy • Breast surgeries • Hernia repair • Knee surgery
Health Concerns	• Angina • Depression • Degenerative disc disease	• Asthma • Arthritis • Hypertension • Diverticulitis

*Based on 7 Participants' Survey Data.

Health Information Data

All of the participants in this sample had type 2 diabetes, which they managed with oral medication (57.1%), oral medication and diet (28.6%), or a combination of insulin, oral medication and diet (14.3%) (see Table 4.4). The participants had been type 2 diabetics for between 1-59 years (M=14.4, SD=20.7) at the time of this study. The average hemoglobin A1c recorded in the last six months for five of the participants is 9.4% (Mdn=8.9, SD=3.2, 2 missing values), ranging from 7-14.9% (see Table 4.5). Hemoglobin A1c reflects blood glucose control over 3-4 months. In the five participants that reported their HbA1c values, blood glucose control could be considered suboptimal with the average HbA1c value being 9.4% reflecting an average blood glucose of 11.7 mmol/L. The suggested target for HbA1c is <7%, equivalent to a blood glucose value of <8.3 mmol/L (Canadian Diabetes Association Clinical Practice Guideline Expert Committee, 2003; Strock, 2001). Literature has suggested that glycemic thresholds for counter-regulatory response shifts to higher levels in individuals with suboptimally controlled diabetes (Childs, Cypress, & Spollett, 2005). The collection of the HbA1c data was obtained as information on participant glucose control.

The onset of menopause was reported as occurring naturally in 23.8% of the participants, with the remaining five participants experiencing a surgical menopause either with the ovaries intact (42.9%) or with ovaries removed (28.3%) (see Table 4.4). The number of years in postmenopause ranged from 2-25 years, with the average being 11.8 years (Mdn=11.5, SD=8) (Table 4.5).

Hot flash data was also collected to identify most frequent occurrence, length, rating or strength, and duration. All of the women in this group reported having night

sweats (hot flashes occurring during the night) and only 1 woman reported not having hot flashes occurring during daytime hours. Participants were asked to report the most commonly experienced intensity of hot flashes (including night sweats), as outlined by the three categories, mild, moderate or severe. Moderate and severe hot flashes were reported equally accounting for 85.7% of the hot flashes experienced by this group of women, with only 14.3% experiencing mild hot flashes. On average, the frequency of occurrence is 6.8 hot flashes per week (SD=4.7, Range=2-14), lasting between 30 seconds and three minutes for 71.5% of the group (see Table 4.4 for detailed analysis).

Table 4.4

Health Information Data Characteristics Frequency and Percentage.

General Characteristics *		Frequency	Percentage
Diabetes	Type 1	0	0
	Type 2	7	100
Diabetes Management	Oral Medication	4	57.1
	Oral Medication & Diet	2	28.6
	Insulin, Oral Medication & Diet	1	14.3
Menopause	Natural	2	28.3
	Surgical – Ovaries intact	3	42.9
	Surgical – Ovaries Removed	2	28.3
Hot Flashes	Yes	6	14.3
	No	1	85.7
Night Sweats	Yes	7	100
	No	0	0
Hot Flash/Night Sweat Severity *Most commonly experienced*	Mild	1	14.3
	Moderate	3	42.9
	Severe	3	42.9
Hot Flash/Night Sweat Length	<30 seconds	1	14.3
	30-60 seconds	3	42.9
	1-3 minutes	2	28.6
	3-5 minutes	1	14.3

*Based on 7 Participants' Survey Data.

Table 4.5

Health Information Data Characteristics Mean, Median, Standard Deviation, and Range.

General Characteristics	Mean	Median	Standard Deviation	Range
Diabetic Years	14.4	9	20.7	1-59
HbA1c*	9.4	8.9	3.2	7-14.9
Post Menopause Years	11.8	11.5	8	2-25
Hot Flash Frequency – Number/week	6.8	7	4.7	2-14

*Reported by 5 Participants only.

Data Analyses

A Kendall's tau-b correlation was run to test the hypothesis that a strong and negative correlational relationship will be found between vasomotor instability and blood glucose values in postmenopausal diabetic women. This correlation test was run on both the individuals' data (7 participants) and on the aggregated data (all participants data combined) and reported accordingly. This provided an N per participant ranging from 19-73 and an aggregated sample with an N of 297. The Pearson's *r*, being a more familiar statistical test, is presented in Table 4.6 along with the Kendall's tau-b to allow for comparable interpretation of the results. Table 4.9 presents the individual results for all seven participants as well as the aggregated sample results.

In Table 4.6 (and tables that follow which report individual data), each participant was recoded with letters "A, B, C, etc.", replacing numeric coding previously assigned to booklets and utilized in data entry, to provide and ensure confidentiality. There were no missing data in any of the seven participants' dependent and independent variable data

sets. Descriptive data for blood glucose values and vasomotor instability is presented next, followed by correlational analyses results.

Descriptive Data

The mean blood glucose value was 7.9 mmol/L, with a range of 3.4-20.1 mmol/L, in the aggregate sample. Individual participants' blood glucose values mean, standard deviation and range are reported in Table 4.6.

The frequency of severe and moderate occurrences of vasomotor instability in the aggregate sample was found in this study to be 43.2% and 30.9% respectively, with the fewest reported vasomotor instability occurrences categorized as mild (25.9%) (see Table 4.7). Vasomotor instability frequency for the individual participants is recorded in Table 4.8. This individual frequency distribution of vasomotor instability intensity, as self-reported by participants, is reported in Table 4.4 and reflects the analyzed frequency of vasomotor instability occurrences found in the aggregate sample.

Activity and frequency of hot flash occurrence, expressed as a percentage, is presented in Table 4.9. Each activity is exclusive of the other activity categories in the reported frequency of occurrence with vasomotor instability. No further analyses is presented on this data, as these activities were inserted into the daily journal between blood sugar readings and hot flash rating in essence to blind participants from the focus of the study and was provided to participants as part of their profile.

Table 4.6

Statistics: Blood Glucose - Daily Journal

Blood Glucose mmol/L	Mean	Standard Deviation	Range
Aggregate Sample N = 297	7.9	2.9	3.4-20.1
Participant:			
A N = 40	8.0	2.8	4-13.4
B N = 41	6.0	0.8	4.8-8.5
C N = 54	7.3	5.9	3.4-12.9
D N = 41	6.1	1.5	4.1-11.2
E N = 29	11.6	3.2	8.2-20.1
F N = 73	8.7	3.3	4.4-19.5
G N = 19	8.4	2.0	5.8-12.9

Table 4.7.

*Frequency Table: Vasomotor Instability - Daily Journal**

Vasomotor instability*	Frequency	Percent
Mild	36	25.9
Moderate	43	30.9
Severe	60	43.2

*Based on Aggregate Sample Data, N=297.

Table 4.8.

Frequency Table: Individual Vasomotor Instability Data - Daily Journal.

Participant	N	Vasomotor Instability - Frequency/Percent			
		None	Mild	Moderate	Severe
A	40	16 (40%)	2 (5%)	1 (2.5%)	21 (52.5%)
B	41	21 (51.2%)	0	14 (34.1%)	6 (14.6%)
C	54	37 (68.5%)	7 (13%)	3 (5.6%)	7 (13%)
D	41	23 (56.1%)	12 (29.3%)	6 (14.6%)	0
E	29	24 (82.8%)	4 (13.8%)	1 (3.4%)	0
F	73	31 (42.5%)	5 (6.8%)	15 (20.5%)	22 (30.1%)
G	19	5 (26.3%)	6 (31.6%)	4 (21.1%)	4 (21.1%)

Table 4.9

Activity and Hot Flash Occurrence.*

Activity	Hot Flash - Percent Occurring with Activity	
	Yes	No
Medication	3%	93%
Exercise	11%	81%
Sleep	22%	78%
Sitting	16%	84%
Eating	32%	68%
Hot Fluid Consumption	3%	97%
Alcohol Consumption	0%	100%
Smoking (In room with smokers)	4%	96%
Stress	0%	100%
Other	9%	91%

*Aggregate Sample Data, N=125 hot flashes recorded with activity.

Correlation - Aggregate and Individual Participant Sample Results

The number of units in the aggregate sample analyzed was 297. A significant positive correlation was obtained, $\tau = .12$, $p = .008$ (2-tailed), indicating that as the intensity of the vasomotor instability increased, higher blood glucose values were observed.

The analysis for participants B through G yielded significant positive correlations, $\tau = .50$, $p = .000$, $\tau = .45$, $p = .000$, $\tau = .44$, $p = .001$, $\tau = .39$, $p = .015$, $\tau = .19$, $p = .038$, $\tau = .33$, $p = .037$ (2-tailed), respectively. These individual correlations (see Table 4.10)

indicate that intensity of the vasomotor instability occurrences increased along with increasing blood glucose values. Participant A provided the only significant negative correlation obtained, $\tau = -.34$, $p = .008$ (2-tailed), indicating that as the intensity of the vasomotor instability increased, lower blood glucose values were observed.

According to Cohen (1988) (Hopkins, 2003; Munro, 2001), *r* correlations may be interpreted as small $r = 0.1$, moderate $r = 0.3$, and large $r = 0.5$. Loiselle et al. (2007) reviewed and confirmed Cohen's correlational interpretations but suggested that it is difficult to assign an interpretive value of strong or weak to a correlational relationship without considering the nature of the variable. These authors suggest that the nature of a variable influences the results and clarified this by explaining that variables producing a correlation such as $r = 0.7$ may be considered low in one situation, such as body temperature when measured at two different sites, but would be considered as a high value in a variable such as stress (a psychosocial variable).

To interpret the Kendall's tau-b results obtained in this study, it was decided to use a conversion table taking into consideration the value interpretation as suggested by Cohen (1988) as well as the nature of the variables being examined. Kendall's tau-b cannot be considered an equivalent statistic to Pearson's *r*, and in order to interpret results using Cohen's rating for *r*, a conversion of Kendall's tau-b to Pearson's *r* is needed (Gilpin,1983). Gilpin (1983) presents a table to facilitate the conversion of Kendall's tau-b into several other correlations including Pearson's *r*. The Pearson's *r* equivalent values, based on the table of conversion presented by Gilpin (1983), are reported in Table 4.10.

The correlational result obtained for the aggregate sample suggests that a small to moderate (r = .19) significant positive relationship was discovered indicating that when vasomotor instability increased or became more severe, blood glucose values also increased. When the results were examined on an individual basis, the analysis demonstrated a significant positive relationship in six samples, in that blood glucose values increased with increasing vasomotor instability intensity. Five of the six participants demonstrated a large significant positive relationship (r = .50-.71) and one showed a moderate significant positive relationship (r = .29) which supports the aggregate sample results (Table 4.10). An inverse relationship in one of the seven participants' samples was obtained. Participant A's result revealed that the blood glucose values decreased with increasing vasomotor instability intensity, τ = -.34, p = .008 (2-tailed), suggesting a significantly large negative relationship (r = -.51).

Table 4.10

Kendall's Tau-b Correlations.

Participant	Kendall's Tau b Blood Sugar	Significance (2-tailed)	†Pearson's r As function of Kendall' s Tau b	N
Aggregate 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.12(**)	.008	.19	297
Participant A 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	-.34(**)	.008	-.51	40
Participant B 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.50(**)	.000	.71	41
Participant C 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.45(**)	.000	.65	54
Participant D 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.44(**)	.001	.64	41
Participant E 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.39(*)	.012	.58	29
Participant F 0=No Hot flash, 1=Mild 2=Moderate, 3=Severe	.19(*)	.038	.29	73
Participant G 0=No Hot flash, 1=Mild, 2=Moderate, 3=Severe	.33(*)	.037	.50	19

†Gilpin, 1993. *p<.05. **p<.01.

Summary

This study used an *ex post facto*/correlation design to answer the research question regarding a relationship between vasomotor stability and blood glucose values. Specifically, a Kendall's tau-b with a significance of >95% (2-tailed), examined this relationship and found a statistically significant positive correlation between blood sugar and vasomotor instability. The implications of these results are discussed in the next chapter.

Chapter 5

Discussion and Conclusions

The purpose of this study was to examine vasomotor instability and blood glucose values to identify a potential relationship. This was examined through an *ex post facto*/correlational design. The data analysis results provided in Chapter 4 of this thesis will be discussed here as they apply to this relationship. Recruitment challenges, limitations and recommendations, and implications for postmenopausal diabetic women will round out the discussion, which ends with study conclusions.

Study Results Discussion

The research question "What is the relationship between vasomotor instability and blood glucose values in postmenopausal women with diabetes?" was answered in that a statistically significant and positive correlation was found between blood glucose values and vasomotor instability for both aggregate and individual samples. Overall, a significant positive correlation was identified, indicating that as blood glucose values increased vasomotor instability intensity also increased, $\tau = .12$, $p = .008$ (2-tailed). What does this result tell us about this relationship?

Overall, this study suggests that a relationship exists between blood glucose and vasomotor instability but causality or direction of this relationship cannot be determined (Black, 2003). That is to say that one cannot conclude that blood glucose elevation caused the hot flash to occur or conversely that the hot flash caused the blood glucose value to increase. Although a relationship exists, the significant positive relationship found does not support the hypotheses that an inverse relationship would be found, specifically that a strong and negative correlational relationship would be found between

vasomotor instability and blood glucose values in postmenopausal diabetic women. Research by Dormire and Reame (2003) and Simpkins and Katovich (1989) provided the basis for the hypotheses statement in this study. The different outcome may be accounted for by the study population; while both Dormire and Reame (2003), and Simpkins and Katovich (1989) used samples of postmenopausal women who were not diabetic, this exploratory study was limited to postmenopausal diabetic women. A number of factors specifically related to the disease process of diabetes may explain the different outcome arrived at in this study. These factors may be: participants' ability to differentiate hypoglycemic reaction from hot flashes, the counter-regulatory response in concert with defective insulin usage and/or secretion and the hormonal changes of postmenopause, and lastly, the variation in the counter-regulatory response to peripheral and central blood glucose levels in both hypoglycemia and vasomotor instability.

The results of this study, although exploratory in nature, may suggest that postmenopausal diabetic women may be able to differentiate between autonomic related sweating episodes due to hypoglycemia, and those associated with postmenopause, since an inverse relationship was not identified in the aggregate sample. As Simpkins and Katovich (1989) identified, the similarity in response symptoms to both hot flashes and hypoglycemia may be traced back to the same counter-regulatory response resulting in hypothalamic and autonomic activation. Women in this study may be able to differentiate these events based on the extent to which hypothalamic and/or autonomic activation occurs in response to either the hot flash or hypoglycemic event. Further, the addition of other symptoms that can often accompany hypoglycemic reactions may provide enough additional information to allow these women to distinguish between these two events.

Alternatively, the impaired glucose delivery model put forth by Dormire and Reame (2003) may apply to this population of women but needs to be explored further in light of these results. The counter-regulatory response in concert with defective insulin usage and/or secretion and the hormonal changes of postmenopause may provide a theoretical basis for the difference in study outcomes. Dormire and Reame suggest that low estrogen levels in postmenopausal women decreases the number and efficiency of glucose transporter 1 at the blood brain barrier. With this decreased glucose delivery to the brain, especially during fasting states, norepinephrine mobilizes glucose for the brain resulting in vasomotor instability or hot flash. The difference in this study from the studies that the hypothesis was based on is the unique population characteristic of diabetes. The study population most probably has the same decrease in the number and efficiency of glucose transporter 1 but with the addition of increased insulin resistance in body tissues and/or an insulin secretory defect that is characteristic of type 2 diabetes. As well, in type 2 diabetics the activation of the counter-regulatory response to a perceived glucose deficit by the glucose-sensitive neurons in the brain may leave their systems unable to handle adequately the flood of additional glucose that may have been mobilized. Defective insulin usage and/or production in concert with no additional medication to handle this surge may hypothetically result in and explain the elevated peripheral blood glucose levels seen during hot flash blood glucose testing in the study.

The findings of this study may be further discussed in light of other research that identifies variation in the counter-regulatory response to blood glucose levels peripherally and centrally. McCall (2005) identified that hypothalamic glucopenia is more important than systemic glucose levels in the counter-regulatory response. He reviewed a study in

which hypoglycemia was induced in the brain in the presence of systemic euglycemia (normal blood glucose levels), which resulted in a counter-regulatory response and a systemic hyperglycemic state. The same study also examined hyperglycemic state in the brain in the presence of systemic hypoglycemia, and found that the counter-regulatory response was blocked. Further, Burcelin and Thorens (2001) note that the activation of the hypothalamus in response to glycemic levels are not completely understood. Burcelin and Thorens discuss their animal research that suggests an additional glucose transporter, namely GLUT2, is also required for maintaining appropriate responses to various glycemic states. They hypothesize that in the graded counter-regulatory response separate glucose sensors that rely on different glucose transporters in the brain are activated at different hypoglycemic levels. These researchers found that in the absence of GLUT2 an increase in autonomic nervous system activity occurred in response to both low and high glucose levels resulting in increased glucagon secretion. Additionally, insulin resistance may impair brain function as insulin promotes glucose uptake in specific areas of the brain, affects levels of neurotransmitters such as serotonin, modulates membrane potential, receptors and neuronal firing rates (Bloomgarden, 2006; Rasgon and Jarvik, 2004).

Consideration of all of these studies together may offer a possible explanation for hyperglycemia in the presence of vasomotor instability. The demonstration of neuronal glucose levels dominating the counter-regulatory response, with the consideration of an additional glucose transporter adding dysfunction, which is further complicated by the presence of insulin resistance compromising brain glucose availability, may provide a plausible explanation for the results of this study. These results may follow that of

Dormire and Reame (2003) but the difference lies in the addition of diabetic dysfunction as presented by these other researchers and is indicated as a possibility in this present study.

Of note, one participant's correlational result indicated a significantly large negative relationship, indicating that the blood glucose values decreased with increasing vasomotor instability intensity as in the population examined by Dormire and Reame (2003). Closer examination of this participant's survey information revealed the addition of exogenous insulin for blood glucose control and estrogen replacement therapy. If this exogenous insulin lowered the blood glucose to normal ranges, as it is intended to do, followed by any potential surge of glucose in response to norepinephrine, additional endogenously produced insulin may have been able to respond accordingly. With the addition of conjugated estrogen therapy to increase blood glucose transport across the blood brain barrier, this participant's blood glucose response may more closely resemble that of the non-diabetic population used in research by Dormire and Reame (2003).

An interesting consequence was found following surgical procedures in two participants regarding decreased hot flash occurrence and frequency. Lipov et al. (2007) identified that an anesthetic agent, namely Marcaine, used for a sympathetic block was effective in relieving hot flashes in postmenopausal women. In an earlier study by Lipov, Lipov, and Stark (2005), repeated anesthetic blocks provided total hot flash relief in six postmenopausal women for 2-5 week period, followed by a period of attenuated hot flashes. With repeated anesthetic blocks, the length of hot flash relief increased (4-18 weeks) with one participant who received a third anesthetic block experiencing relief for a 48-week period. Lipov et al. (2007) suggest that the sympathetic block may provide

relief by interrupting the sympathetic nervous system and allowing the temperature regulating mechanism to reset. The identification of an anesthetic sympathetic block involvement in hot flash mechanism may provide a theoretical explanation for the two women in this study who were asymptomatic or experienced attenuated hot flashes following surgical procedures with anesthetic. The type of anesthetic, that is, a general, spinal or epidural anesthetic, received by these participants was not investigated further as it was beyond the scope of the current study undertaken. Further research studies of postmenopausal women following anesthetic procedures may have significant bearing in clarifying hot flash physiology.

In conclusion, when these studies are considered all together, it appears likely that multiple aspects of dysfunction may be involved in the underlying physiology of the diabetic postmenopausal woman, and all of them need to be addressed. It may be that this study does support the studies done by Dormire and Reame (2003), Simpkins and Katovich (1989) but the results must be considered in the specific context of type 2 diabetic postmenopausal women, with diabetes being the factor that altered findings. In addition to the hot flash mechanism put forth by Dormire and Reame (2003), consideration of one or more additional glucose transporters, potentially some degree of insulin resistance, and dysfunctional counter-regulatory response in postmenopausal without diabetes could be considered in further vasomotor instability research. My findings do not indicate a causal relationship in that increased intensity in vasomotor instability causes elevated blood glucose values or vise versa, but does suggest a relationship and may provide some insight into the affects of menopause on postmenopausal diabetic women, specifically those with type 2 diabetes.

Implications of recruitment barriers

The process of conducting this study raises questions about how to understand the barriers to recruitment and how to develop recruitment strategies to overcome them. Implications of failed recruitment strategies calls into question how, where and with whom we do our research. Beyond the scope of this study lies an investigation into the particular social, cultural and economic factors shaping women's responses to calls for research participants. However, given the challenges faced in conducting this study, and limited literature that addresses research challenges in Southern Alberta, it is important to discuss recruitment issues and to offer recommendations for research practice.

Specific challenges in recruitment in this study extended the recruitment and data collection period approximately six months beyond initial expectations for completion of this phase of the study. Some of the more significant challenges included timing, inadequate research databases which may have identified potential participants, refusal of organizations and professional magazines, recruitment ads, and a culture in which remuneration for activities takes precedence over volunteerism.

Summer may not be the best time for recruitment. In order to recruit through clinics, staff and physicians would have to take on extra work. Summer vacations often leads to lower staffing levels and increased workload stress on remaining clinic staff, a situation also experienced during winter holiday season. This raises the question: Is there a preferred time for seeking assistance from medical clinics? Pinto, et al. (2004) reviewed recruitment strategies and identified workload as an issue in physician clinics, as physicians often have limited resources or time to dedicate to recruitment. However, they did not address the effect seasonal workload cycles have on recruitment strategies.

Involvement in the clinic and access to client records may have resulted in more effective recruitment strategy by increasing visibility of the researcher to clinic physicians and staff and improved client access. The initial clinic contacted cited an inability to effectively access clinic records due to lack of time and inefficient computer system used at the clinic. Southern Alberta is divided into three health regions and physicians' offices do not necessarily have access to all potentially pertinent databases. While inadequate databases and limited access to them may have been a factor limiting recruitment, research shows personal contact is a more effective method of recruiting and has been identified as yielding more respondents (Pinto, et al., 2004; Riedel-Heller, Busse, & Angermeyer, 2000). This is of particular importance to graduate student research since time is limited and personal contact requires time.

Research with groups of participants sharing specific health conditions leads researchers to voluntary and professional organizations. Assistance in recruitment might be expected from these organizations. However, as social concerns arise regarding privacy, increased emphasis is placed on organizations to be financially independent and voluntary and paid staff carries increased workloads, and therefore these organizations may not be in a better position than medical clinics to assist researchers (Metzler, et al., 2003). Internet recruitment, including voluntary and professional organization websites was used in this study as well, recognizing the ability to quickly and effectively reach a larger number of potential participants. An additional four participants, resulting from websites posting the study, had initially shown interest in participating in the study but eventually declined. Two of these potential participants requested cash reimbursement

for participation in the study but declined when only test strips for their time and participation were offered. This method yielded few inquiries and no participants.

Potential participants requested monetary reimbursement for participation and declined to participate in the study when only free test strips were offered. Herman, et al. (1997) examined the volunteer's perspective and reasons for volunteering in studies and found that financial compensation was likely the prime motive, especially in younger participants, and free medical checkups for the older participants. These researchers also identified that often those motivated by monetary incentives would frequently provide inaccurate information as it might otherwise exclude them from enrolment and the monetary incentive. Toneatto (2005) identified a trend for potential participants to refuse to participate in studies if they deem compensation inadequate, which was experienced in this study.

A number of issues may be affecting participant recruitment in Southern Alberta. One such issue is that low levels of literacy prevail in the region of Chinook Health, with 24-40% of its population (seniors and minorities included) with less than a high school education (Chinook Health Region, 2003). Also a number of faith communities and minority populations in Southern Alberta for whom certain cultural taboos and upper levels of education are not significant, particularly for girls and women, may contribute to reluctance to participate (Hall & Kulig, 2004; Rootman & Ronson, 2005). This suggests that studies investigating research participation in such groups will help us understand and overcome barriers to successful recruitment.

In summary, the recruitment challenges experienced in this study may be less of an isolated problem, as Riedel-Heller, Busse, & Angermeyer (2000) identify that a

general trend over the past decade in the ease of contacting and willingness to participate in research studies has declined substantially, especially in urban areas. They feel this may be attributed to fear of crime, a reluctance to share personal information, and annoyance at telemarketing intrusion. Passive recruitment through posters in clinics, libraries, internet, community bulletin boards in senior centers, pharmacies, churches etc., and television and newspaper advertising was the primary method of recruitment used in this study. Passive recruitment has been addressed by other researchers as potentially being costly, especially television and newspaper advertising, with relatively low yield of potential participants (Pinto, et al., 2004; Riedel-Heller, Busse, & Angermeyer, 2000; Scholle, et al., 2000). Several studies suggest that the more personal the contact the more likely that recruitment will be successful, but have emphasized the need to not exclude other methods, such as passive recruitment (Pinto, et al., 2004; Riedel-Heller, Busse, & Angermeyer, 2000).

Limitation and Recommendations

Limitations

This study explored a potential relationship without inferring cause between blood glucose values and vasomotor instability occurrence in the study population. A quantitative framework was employed in this research study specifically, an *ex post facto*/correlation design. Limitations identified with this design are: a) lack of direct control over the independent variable, in this case blood glucose values, b) inability to control for intervening or extraneous variables, and c) time, allowing other events to intervene, or biological and/or psychological changes within the study population (Black, 2003). Extraneous variables identified as having potential influence on hot flash

occurrence were discussed in the literature review and are identified as having potential influence on the relationship identified in this study, but were not directly examined as part of the research question. These variables are alcohol, hot fluids, exercise, BMI, smoking, and stress. Identification and control of these variables in further research in this population of women is recommended to delineate their impact and/or involvement in hot flash mechanism(s).

Additionally, recruitment challenges resulting in a small sample size, may limit the power of the results obtained. The sample population also lacked type 1 diabetics, which limits generalizibility of the study to this group of women. The convenience sample obtained limits interpretation of the results. The study sample may be atypical of the postmenopausal diabetic population and thus generalizability is not possible, resulting from a lack of control over sampling bias or representativeness. The geographic area sampled, Southern Alberta, also limits generalizibility beyond this area as variances in social, cultural and economic factors influence population lifestyles.

This study relied solely on subjective reporting of vasomotor instability occurrence and rating without verification using objective temperature measurement. In studies conducted on vasomotor instability by other authors, it was identified that subjective measures of hot flashes were not always supported by objective data collected (Dormire & Reame, 2003; Freedman, 2001, 2005; Simpkins & Katovich, 1989). Without using a more rigorous measure, it is difficult to determine if all self-reported hot flashes resulted in actual vasomotor responses and therefore may skew data results and analyses.

Lastly, the participants were allowed to choose which blood glucose values and vasomotor instability occurrences they reported. This may limit the correlational

interpretation since data that either may have influenced the results, positively or negatively, are not captured in the analyses.

In summary, there were several limitations identified that can be linked to the study design chosen. This study design may lack the rigor of an experimental design, but was chosen and incorporated as a preexperimental study to determine if a relationship could be identified to warrant more extensive research. This particular research design is strong in real world experience as opposed to artificial laboratory experiments even when considering its limitations (Black, 2003; Knapp, 1998). Taking into consideration the limitations presented in this section, recommendations for further study on this group of women are presented next.

Recommendations

Postmenopausal diabetic women represent an understudied population. This study identified a positive relationship between blood glucose values and vasomotor instability in this group of women. In consideration of this result, further study is recommended as outlined in the following suggestions.

1. Use of an experimental design for any further research conducted on vasomotor instability in postmenopausal diabetic women.
2. Measuring and controlling extraneous variables and inclusion of data collection on both objectively and subjectively measured vasomotor instability for valid interpretation of study results.
3. Clear definition of concepts such as race/ethnicity including use and assignment within research study outlined.

4. Conduct research to explore cultural attitudes concerning research participation within both the medical and the public communities in Southern Alberta.
5. Collection of all blood glucose values and vasomotor instability occurrences over a continuous time frame, rather than allowing study participants to choose which blood glucose values and vasomotor instability occurrences to report. This may avoid omission of potentially valuable data that could affect results obtained.
6. Consider implications of diabetes complications and management in sample population selected and impact on research results.
7. Utilize random sampling methods and seek a larger sample size to increase power of the study. Consider employing methods such as face-to-face recruitment, identifying busy time periods if clinics are used for recruitment, and offering incentives for both participants and clinic staff if employing their help.
8. Consider researchers' time constraints and funding availability in all aspects of study especially if face-to-face recruitment utilized.
9. Finally, include both type 1 and type 2 diabetic postmenopausal women sampled in several geographic areas to increase generalizability of the study results.

In summary, consideration of these recommendations to conduct a more rigorous study of this group of women will hopefully identify and provide direction for diabetic women navigating the postmenopause years.

Implications for Health Care Professionals

Menopausal symptoms were first noted in medical literature in 1837, highlighting the disagreement around treatment and understanding of this female "disease" (Pinkerton and Zion, 2006). Today, efforts continue to increase understanding of menopausal

symptoms, including vasomotor instability. For health care professionals the challenges to understand research, which are riddled with inconsistent definitions of menopausal symptoms, difficulty in determining the mechanism underlying vasomotor instability and appropriate treatment for severe cases, can be enormous. Surveys have indicated that health care professionals spend a great deal of time counseling menopausal women on treatment approaches and that health care professionals substantially underestimate women's level of concern about their symptoms (Pinkerton & Zion, 2006). Additionally, research often excludes women who suffer from chronic diseases such as diabetes, exaggerating the challenge for health care professionals to use research to treat these particular groups of women.

What additional implications does this study add to these already existing challenges for health care professionals? This study highlights the need for more research in symptomatic postmenopausal diabetic women by the academic and medical community. It is also recommended that increased education by health care professionals outlining potential impact of both menopausal symptoms and diabetes on quality of life and the possible need for increased surveillance of blood glucose be discussed.

Implications for Postmenopausal Diabetic Women

The postmenopausal years are a period in which diabetic women are trying to manage an already difficult chronic disease face additional challenges. This study does suggest that a relationship exists between hot flashes and blood glucose, but the direction of that relationship is not clear. Lack of studies specific to this group of women is evident when trying to establish how the symptoms of postmenopause, including vasomotor instability, affect blood glucose control and whether poorly controlled blood

glucose has significant impact, if any, on postmenopausal symptoms. What has been presented in the research is the challenges diabetic women face in their life due to the affects of the insulin resistance, which as discussed in this study, may shed light on the relationship this study found. Finally, the importance for diabetic women to be more vigilant in blood glucose monitoring when dealing with physiological changes of postmenopause, including vasomotor instability symptoms, is recommended and emphasized to enable them to clearly identify physical impact and/or need for changes in diabetic management.

Conclusion

With an increasing population of menopausal women, and rising incidence of diabetes, the numbers of both diabetic and menopausal women in the coming years requiring support and/or accessing health professionals may be significant. Without understanding underlying mechanisms of vasomotor instability and potential complications of and effects on diabetic women, health care professionals are left without adequate evidence-based direction and management options for this population of women. Menopausal diabetic women whose lives have been or are significantly disrupted by symptoms of menopause are, or will be, faced with difficult decisions regarding alternative therapies or coping strategies.

This quantitative *ex post facto*/correlational study did establish that a relationship exists between blood glucose and vasomotor instability. The women who participated in this study provided a glimpse of the impact of managing both vasomotor instability and diabetes during the postmenopausal years. The scarcity of research highlights the importance of research on this topic in this population of women. It is hoped that this

study will provide impetus for further study of women dealing with menopausal symptoms and chronic disease processes such as diabetes.

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Appendix A

Hot Flashes, Diabetes and Post Menopause

After menopause women can suffer from hot flashes. We know very little about diabetic women and menopause. Hot flashes can be affected by what we eat, drink and what we do. The reason why hot flashes occur in some women and not others is unknown.

I am a master's student, studying at the University of Lethbridge, doing my thesis research study on hot flashes and their occurrence in diabetic post menopausal women. Your response on this survey and your record of activity will help us to understand hot flashes in post menopausal women with diabetes.

Who can participate?

- You are diabetic and testing your blood glucose daily AND
- You are post menopausal and have gone one (1) complete year without a period and this menopause occurred naturally AND
- You have hot flashes/night sweats or both.

What would I have to do? Is there a cost?

- Complete a survey and keep a record of activity when hot flashes occur and activities at the time including blood glucose value.
- 40 blood glucose meter tests over 3 weeks, Twenty (20) when hot flashes occur and 20 when there are no hot flashes will be needed.
- There is no cost. A **free** package of 50 test strips for blood glucose testing will be included.

How do I participate in this study?

- To participate, please call Joann Boorsma, RN, BN, Masters Student, University of Lethbridge, at [redacted].

Appendix B

July 20, 2006

Dr.
Medical Clinic
Lethbridge, Alberta

Dear Dr. :

Please find enclosed the information concerning my research study and the inclusion criteria for participants. After meeting with Nurse Clinician and reviewing in detail the study outline, Nurse Clinician recommended sending this information to you as well. The sheets behind the inclusion criteria are the sheets that I will be handing out to participants when I meet with them. I have supplied Nurse Clinician with 25 posters to distribute to potential participants and additional posters can be provided if needed. All participants will be given 50 test strips for their meter testing for this study, free of charge. If you require any further information please feel free to contact me at any time. Thank you for your part in this study.

Joann Boorsma, RN, BN, Masters Student,
University of Lethbridge
XX Street South
Lethbridge, Alberta
Postal Code
Phone: 403-XXX-XXXX
Email: email@XXX.XX.XX

Appendix B

July 20, 2006

Dr.
Medical Clinic
Lethbridge, Alberta

Dear Nurse Clinician:

Please find enclosed the 25 posters to distribute to potential participants. Additional posters can be provided if needed. All participants will be given 50 test strips for their meter testing for this study, free of charge. If you require any further information please feel free to contact me at any time.

Thank you for your part in this study.

Joann Boorsma, RN, BN, Masters Student,
University of Lethbridge
XX Street South
Lethbridge, Alberta
Postal Code
Phone: 403-XXX-XXXX
Email: email@XXX.XX.XX

Appendix C

July 20, 2006

Dr.
Ave. South
Lethbridge, Alberta

Dear Dr.:

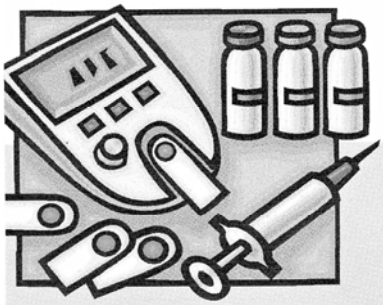
Please find enclosed the information concerning my research study and the inclusion criteria for participants. We had discussed my research study briefly at the presentation that you had given at the end of May. The Ethics and Research committee at the University of Lethbridge have recently approved the study. I have included the inclusion criteria for participants and a poster (on patterned paper). The poster can be handed out individually as well as posted in rooms as you see appropriate. The sheets behind this are the sheets that I will be handing out to participants when I meet with them and I just wanted to include them for your information. All participants will be given 50 test strips for their meter testing for this study, free of charge.

Please contact me if you require additional information and to let me know if you would be willing to distribute and post this information for clients in your office.

Thank you for your time and hope to hear from you soon,

Joann Boorsma, RN, BN, Masters Student,
University of Lethbridge
XX Street South
Lethbridge, Alberta
Postal Code
Phone: 403-XXX-XXXX
Email: email@XXX.XX

Appendix D



Free Personalized Profile

Free Blood Glucose Meter Strips!!

Are your Hot Flashes affected by your Diabetes?

- Little is known about Diabetic Women with Hot Flashes
- You can help us to understand hot flashes in diabetic postmenopausal women by participating in a study on Hot Flashes & Diabetes in Postmenopause
- You can join this study if you are diabetic, in menopause, having hot flashes/night sweats or both
- Receive *FREE Package of 50 Test Strips and your own Personalized profile*

For More information, Call Joann Boorsma, University of Lethbridge Masters Student at [ ] **or email** [ ]

Appendix E
Letter of Consent

_____
Date

Dear

I am inviting you to participate in a study relating post menopausal hot flashes to a variety of life activities. These activities include exposure to cigarette smoke, hot fluids, alcohol, food consumption, sleeping, sitting, exercising, stress, blood glucose values and any other significant activity during hot flash occurrence. I will provide you with a daily journal to record 20 hot flash occurrence activities and 20 random recordings of these activities in the absence of hot flashes. You will be asked to complete a brief survey prior to collecting this data. Blood glucose meter strips will be provided to cover the 20 extra strips required in this study. Your participation in the study will be completed once 40 data entries on the log have been collected. You will not benefit directly from this study but the data collected will be used to help identify possible relationships between hot flashes and life activities as well as effects in diabetic women.

The information from this study will be reported in general terms, without reference to your individual results. Both the daily journal and survey will be coded to maintain anonymity. Data will be stored in a locked filing cabinet for a period of 5 years, and then destroyed in an appropriate manner. Only I will have access to this data. The complete results of the study will be available in about six months. If you wish to obtain study results you may do so by completing the page at the end of the survey.

I hope you will participate in this study, but if for any reason at any time you decide to withdraw, you are free to do so without prejudice and your data will be destroyed.

If you have any questions about the study, please call me at 403-XXX-XXXX. I will call you once a week to answer any questions you have and to see how things are progressing. Questions regarding your rights as a participant in this research may be addressed to the Office of Research Services, University of Lethbridge (Phone: 403-XXX-XXXX). You may also contact my theses research supervisor, Jo-Anne Fiske, Coordinator Women's Studies University of Lethbridge (Phone: 403-XXX-XXXX) with any questions or concerns.

Joann Boorsma, RN, BN, Masters Student
School of Health Sciences
University of Lethbridge

----------✂ Detach and Return Signed----------

I consent to participate in the study entitled; "Hot Flashes, Diabetes, and Post menopause" as described in the letter dated 200 /0 / .

_____ _____
Printed Name and Signature Date

Personalized profile of your results can be sent to you along with the results of the study. If you would like to receive these, please fill in the sheet attached to the end of the survey.

Appendix F
Hot Flashes Diabetes and Post Menopause

After menopause women can suffer from hot flashes. We know very little about diabetic women and menopause. Hot flashes can be affected by what we eat, drink and what we do. The reason why hot flashes occur in some women and not others is unknown.

Your response on this survey and your record of activity will help us to understand hot flashes in post menopausal women with diabetes. This survey is designed to provide health information on a group of post menopausal diabetic women.

Please take a few minutes to read the following information before you begin answering questions.

When

- Once the consent is read, understood and signed, complete the survey.

How

- Place the survey in the attached envelope with consent and return.

Privacy of Responses

- The privacy of your individual responses will be maintained. No person will be identified in any way. Your answers and data will be grouped with other peoples' responses when presented and reported, so you cannot be identified.

The Survey and Data Log

- The survey is printed on both sides of the page. Please respond to all questions.
- The daily journal is printed on both sides of the page. Please complete all 40 data entries as described on the data log.

Questions or Concerns

- If you have any questions, concerns, or need help completing the survey or data log, please call Joann Boorsma at XXX-XXXX.

Results

- If you would like a copy of the results of the study mailed to you, please fill out the attached page at the end of the survey.

Appendix G

Hot Flashes, Diabetes, and Post Menopause Survey

Demographics

Birth Date _____/_____/_____
Day Month Year

Ethnicity: ____ Caucasian ____ Aboriginal ____ Asian

Other (please list) _____

Height: _____ Weight: _____

Medication(s):

Over the Counter: _____

Prescription: _____

Herbal: _____

Caffeine Intake (includes coffee, tea): _____ # cups/day

Smoker: ____ Yes ____ No # of years smoked ____

# of Cigarettes/day____

Alcohol: ____ N/A

# of Drinks: ____ <1/Day ____ 1-3/day ____ >3/day

Exercise Habits: Exercise type (list all): _____

< Once/week ____ 1-3 times/week ____ > 3 times/week ____

Surgery _____

_____

Other Health Concerns (such as arthritis, high blood pressure etc.) _____

Appendix G

Health Information - Diabetes

Type 1 ____ Type 2 ___ # of Years as a Diabetic ____

Management of your diabetes:

Insulin ____ Oral Medication ____ Diet only ____

Combination (please specify) _____

HgbA1C: _____ **(collected in last 3-6 months)** Date done:

_____/_____/_____

Meter used (please specify type/model) _____

Health Information - Menopause

Menopause is defined as 12 consecutive months without a menstrual period.

Onset: ___ Natural ___ Surgical (hysterectomy) ___ Ovaries Removed

Years since Menopause: _____

Hot flash: ____ Yes ____ No Night Sweats: ____ Yes ____ No

Hot flash/Night sweat (check all that apply):

Frequency (please specify number):

____ #/Week ____ #/Day ____ #/Month

Severity **(most commonly experienced)**:

Mild (sensation of heat without sweating) _____

Moderate (sensation of heat with sweating) _____

Severe (sensation of heat with sweating that disrupts your usual activity) ____

Length **(most commonly experienced):** <30 sec. ____ 30-60 sec. ____

1-3 min. ____ 3-5 min. ____ > 5 min. ____

Appendix G

Thank you for taking the time to complete this survey and for your involvement in this research. If you would like a copy of the results please indicate below and include your name and address for mailing purposes. ***A personalized profile, including your average blood glucose value, hot flash intensity and most frequent life activity in the presence of hot flashes, can be provided to you by checking YES beside Personalized profile below.*** *Please complete this page and mail it in with the completed consent and survey.*

Name: _____

Address: _____

_____

_____

Personalized profile: Yes ☐ No ☐

Appendix H

Daily Journal

*Please record **Twenty** (20) blood sugar readings in the presence of a hot flash and intersperse an additional **Twenty** (20) blood sugar readings in the absence of hot flashes.*

Time Please circle a.m. or p.m.		**Blood Sugar Value**	**Activity**										**Hot Flash Rating** 0-No flash 1-Mild 2-Moderate 3-Severe
			Meds	Exercise	Sleeping	Sitting	Eating	Hot Fluid	Alcohol	Smoking	Stress	Other	
Date													
	a.m. p.m.												0 1 2 3
	a.m. p.m.												0 1 2 3
	a.m. p.m.												0 1 2 3
	a.m. p.m.												0 1 2 3
Date													
	a.m. p.m.												0 1 2 3
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	a.m. p.m.												0 1 2 3
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	a.m. p.m.												0 1 2 3
	a.m. p.m.												0 1 2 3

Hot Flash Rating:

1. **Mild**: Sensation of heating without sweating
2. **Moderate**: Sensation of heat with sweating
3. **Severe**: Sensation of heat with sweating that disrupts your usual activity

Appendix I

CERTIFICATE OF HUMAN SUBJECT RESEARCH
University of Lethbridge
Human Subject Research Committee

PRINCIPAL INVESTIGATOR:	Joann Boorsma
ADDRESS:	School of Health Sciences University of Lethbridge 4401 University Drive Lethbridge, AB T1K 3M4
PROJECT TITLE:	Hot Flashes, Diabetes and Post Menopause (Protocol #646)
FUNDING SOURCE:	Centre of Health Management Research

The Human Subject Research Committee, having reviewed the above-named proposal on matters relating to the ethics of human subject research, approves the procedures proposed and certifies that the treatment of human subjects will be in accordance with the Tri-Council Policy Statement, and University policy.

Human Subject Research Committee — Date: July 2006