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Anxiety in Menopause: A Qualitative Inquiry

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Anxiety in Menopause: A Qualitative Inquiry

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

by

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Table of Contents

List of Figures

Abstract

ANXIETY IN MENOPAUSE: A QUALITATIVE INQUIRY

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

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Background: Anxiety is one of the mood symptoms experienced by menopausal women; however, anxiety symptoms during menopause have received little attention in the literature despite the potential impact on quality of life. Many of the tools used to evaluate and measure anxiety associated with menopause assume that menopausal anxiety shares similar criteria as anxiety disorders and this may not be entirely true. There are very few studies that have assessed anxiety in the context of menopause leaving the concept of menopausal anxiety not well defined and raising the question: Is menopausal anxiety a unique and distinctly different syndrome? The purpose of this study was to explore and gain an in-depth understanding of the experience of anxiety in menopausal women.

Methods: Twenty menopausal women were recruited for this qualitative study to explore the experience of anxiety in menopause. Through the use of a semi-structured interview using open-ended questions, participants were asked to share their experience with anxiety that was new or different with the onset of menopause. Interviews were audio recorded by the researcher and lasted approximately 30 - 60 minutes. Participants described their experience with anxiety and discussed how the anxiety is different in menopause.

Results: Emergent themes revealed that anxiety in menopause is a unique and individual experience. The substantial variation in the onset, timing and severity of the symptoms made it impossible to construct a uniform and consistent definition of the experience. Participants discussed their preferences for management which included non-pharmacologic, lifestyle, relaxation based interventions.

Conclusions: This research supports the existence of a unique and individualized experience of anxiety in menopause. A better understanding of the experience and patient preferences will assist healthcare providers in developing individualized treatment options aimed at improving quality of life.

Key words: *menopause, anxiety, qualitative*

Chapter I

Introduction

Menopause

Menopause is a naturally occurring and inevitable event that will eventually affect all women. With menopause impacting 25 million women worldwide each year, the World Health Organization estimates 1.2 billion women will be postmenopausal by 2030 (Stephenson, Neuenschwander, & Kurdowska, 2013). Menopause is a complex process in which women experience physical and psychological symptoms that may adversely impact quality of life (North American Menopause Society, 2014). As a physiologic event, menopause is characterized by a decline in estrogen and progesterone (Files, Ko, & Pruthi, 2011; Holloway, 2011; North American Menopause Society, 2014; Stephenson et al., 2013). As a psychophysiological event, menopause is experienced by women as a process characterized by a variety of symptoms including anxiety (Files et al., 2011; Holloway, 2011; Stephenson et al., 2013).

Because menopause is associated with a reduction in hormones, menopause is often viewed and treated as a biomedical event. While it is common practice to treat most symptoms associated with menopause with hormone therapy (HT) (Greenblum, Rowe, Neff, & Greenblum, 2013; North American Menopause Society, 2014; Warren, 2007); there is evidence to suggest that HT does not always resolve anxiety symptoms in menopausal women (Demetrio et al., 2011; Greendale et al., 1998; Warren, 2007). If menopausal symptoms were solely biologically based on the decline of hormone levels, it would be reasonable to assume that some sort of a menopausal syndrome would be seen in most women. However the fact that menopausal symptoms are not universal suggests that these symptoms are not entirely biological and that there is some other dynamic that is not well understood (Greenblum et al., 2013). It is possible

that anxiety during menopause is the result of individual variation in an overlapping set of interrelated psychosocial and biologic factors.

Anxiety

The proportion of the global population with anxiety disorders in 2015 was estimated to be 3.6% with more females being affected than males (4.6% compared to 2.6% at the global level) (World Health Organization, 2017). Anxiety disorders cost the U.S. more than $42 billion a year, almost one-third of the country's $148 billion total mental health bill, according to a study commissioned by the Anxiety and Depression Association of America (Greenberg et al., 1999). Aside from economic burdens for both patient and the health care system, anxiety can substantially impact an individual's self-esteem, family life, social interaction, ability to work and quality of life (Greenberg et al., 1999; Siegel & Mathews, 2015).

Anxiety is one of the mood symptoms experienced by menopausal women (Holloway, 2011; North American Menopause Society, 2014; Siegel & Mathews, 2015); and is a problem frequently reported to healthcare providers (Bromberger et al., 2013). The prevalence of anxiety symptoms during midlife in women is reported to be high (Siegel & Mathews, 2015) with studies reporting up to 51% of women aged 40 to 55 experiencing symptoms of nervousness (51.9%) or irritability (51.6%) over the course of a 2 week timeframe (Avis et al., 2001) and as many as 67% of women reporting experiencing feeling tense or nervous daily (Bromberger et al., 2003). The current evidence suggests that anxiety is prevalent and it can have a clinically significant impact on women in menopause (Siegel & Mathews, 2015).

Menopause has been identified as a period of vulnerability for the occurrence of anxiety symptoms and disorders in adult women (Siegel & Mathews, 2015). While many cases may involve chronic anxiety that has developed earlier in life, anxiety can present for the first time in

life during menopause (Siegel & Mathews, 2015). Although anxiety is a prevalent symptom during menopause, there is little research focused on anxiety symptoms despite the association with distress and impaired quality of life (Bromberger et al., 2013; Bryant et al., 2008; Siegel & Mathews, 2015). Studies that focus on anxiety symptoms usually focus on the association with hot flashes (Freeman et al., 2005; Lermer et al., 2011; Soares, 2011) and very few studies have evaluated relationships between stress, psychological distress (e.g., anxiety, depression) and menopause related factors (e.g., menopausal stage) (Bauld & Brown, 2009).

The Concept of Anxiety

Anxiety is a general term that is often used to describe anxiety symptoms and anxiety disorders often not making a clear distinction between the two (Bryant, Judd, & Hickey, 2012). The term anxiety refers to a variety of symptoms that may describe features of different anxiety disorders such as panic disorder (e.g., suddenly feeling fearful for no reason), social phobia (e.g., fear of social or performance situations), or generalized anxiety (e.g., excessive and uncontrollable worry, irritability) (Bromberger et al., 2013). Anxiety symptoms can include physical symptoms such as shortness of breath, racing heart, and sweating (Siegel & Mathews, 2015). More importantly anxiety symptoms may consist of a variety of symptoms that are commonly associated with generalized anxiety disorder (i.e., tension, fatigue, headache, and gastrointestinal upset) and these symptoms may be difficult to distinguish from some of the symptoms associated with menopause or vague symptoms that are commonly associated with the aging process (Siegel & Mathews, 2015).

Evaluation and measurement of menopausal anxiety in terms of a general type of anxiety disorder may misrepresent the anxiety that is experienced in menopause. The fact that the terms anxiety symptoms and anxiety disorders are often used interchangeably makes it difficult to

compare studies and to draw conclusions (Bromberger et al., 2013). There are very few studies that have assessed anxiety in the context of menopause leaving the concept of menopausal anxiety not well defined and raising the question: Is menopausal anxiety a unique and distinctly different syndrome?

To further complicate this issue, anxiety often is studied in menopausal women with other symptoms as a cluster (Bromberger et al., 2013; Cray, Woods, Herting, & Mitchell, 2012; Greenblum et al., 2013) or as it relates to hot flashes (Bryant et al., 2012; Cray et al., 2012; Lermer et al., 2011). Anxiety is frequently included in a group of symptoms labeled mood symptoms (Bromberger et al., 2003) or mood disturbance (Vesco, Haney, Humphrey, Fu, & Nelson, 2007) or menopausal symptoms (Greenblum et al., 2013). The lack of consistency in findings may be a direct result of the use of different definitions and symptoms used to define mood as well as instruments that may tend to measure symptoms such as anxiety and depression as similar (Bryant et al., 2012; Vesco et al., 2007).

Many studies use validated tools designed to measure general scales of anxiety such as the Hospital Anxiety and Depression Scale (HADS-A) (Tangen & Mykletun, 2008), State-Trait Anxiety Inventory (STAI), and the Generalized Anxiety Scale (GAD-7)(Woods et al., 2016); however, interpretation is somewhat limited as these scales have not been designed to assess anxiety specifically related to menopause (Vesco et al., 2007). The use of these tools assumes that menopausal anxiety shares similar criteria as anxiety disorders and this may not be entirely true. Anxiety in menopause may have an intermittent temporal pattern making it difficult to be detected in studies of short duration or cross-sectional designs that are measuring symptoms at one point in time (Vesco et al., 2007). This raises the question: is there a distinct and different type of anxiety associated with menopause and if so, how is it best measured?

Menopausal Status

Researchers frequently evaluate anxiety in women in various stages of menopause (Bromberger et al., 2003; Dennerstein, Dudley, Hopper, Guthrie, & Burger, 2000; Freeman, Sammel, Lin, Gracia, & Kapoor, 2008; Tangen & Mykletun, 2008). Perimenopausal and postmenopausal women have been identified as having a greater risk of developing anxiety symptoms compared to premenopausal women (Bromberger et al., 2003; Siegel & Mathews, 2015); however, studies have reported conflicting results concerning the extent to which the prevalence of anxiety symptoms vary during different stages of the menopausal transition. Some studies have indicated no statistically significant differences by menopausal stage (Dennerstein et al., 2000; Freeman et al., 2008) while others found that early or late perimenopausal women have significantly higher rates of anxiety symptoms compared to premenopausal women (Tangen & Mykletun, 2008).

A longitudinal analysis of data from the multisite Study of Women's Health Across the Nation, reported that women with low anxiety at baseline were more likely to report high anxiety at perimenopause or postmenopause compared to premenopause, suggesting that the menopause transition may be a time of increased risk for the onset or worsening of anxiety symptoms (Bromberger et al., 2013; Bryant et al., 2012). The absence of consistent findings regarding associations between anxiety and menopause status is most likely caused by a combination of the variation in the definition and measurement of anxiety symptoms, different study designs and inconsistent application of criteria used to define menopausal stages (Bromberger et al., 2013).

Potential Variables Affecting Anxiety

Menopause is complex phenomenon and anxiety associated with menopause may be the result of an overlapping set of physiologic, psychologic and situational variables.

Physiologic. While estrogen level decline characterizes the menopause transition, progesterone levels decline even more rapidly (Spark & Willis, 2012; Stephenson et al., 2013). Estrogen levels have been found to decline after progesterone levels around the final menstrual period (FMP) but not to the same extent as progesterone (Spark & Willis, 2012). This low progesterone-to-estrogen ratio can contribute to a variety of mood disorders, including anxiety (Stephenson et al., 2013)

As women age, neuroendocrine hormones become imbalanced as a result of the reproductive hormonal changes associated with menopause (North American Menopause Society, 2014; Woods, Mitchell, & Smith-Dijulio, 2009). The neuroendocrine system is an important regulator of the stress response. This system functions by releasing corticotropin-releasing hormone (CRH), also known as corticotropin-releasing factor (CRF) which stimulates the anterior pituitary resulting in a release of adrenocorticotropic hormone (ACTH) into the blood (Nieto, Patriquin, Nielsen, & Kosten, 2016). Once ACTH is in the bloodstream, it activates the synthesis and release of cortisol from the adrenal glands of the kidneys to shut down the hypothalamic pituitary adrenal (HPA) axis (Nieto et al., 2016). It is hypothesized that the neurochemical process of the HPA axis is altered by the effect of the decrease in the ovarian hormones associated with menopause (Siegel & Mathews, 2015) and the dysregulation of this neurochemical system may contribute to symptoms of anxiety (Nieto et al., 2016).

Psychologic. One of the main variables that affects anxiety disorders is the amount of stress that an individual experiences (Bystritsky & Kronemyer, 2014). It is hypothesized that women may be more sensitive to mood dysregulation following psychosocial stress because of the effects of changing ovarian hormones on the HPA axis which are essential in the function of

the stress response (Newhouse & Albert, 2015). The relationship between stress and anxiety suggests that higher levels of stress may be a risk factor for developing or exacerbating anxiety.

Situational. Recent research on the causes of psychological distress in women in midlife have focused on *current* adversity and hormonal changes associated with menopause and less attention to risk factors over the life span such as adverse childhood experiences (ACE) (Kuh, Hardy, Rodgers, & Wadsworth, 2002). ACE refers to the perception of negative events that occurred during childhood and may include maltreatment and physical and psychological trauma (Burgermeister, 2007). It includes "all types of physical and/or emotional ill-treatment, sexual abuse, neglect, negligence and exploitation, which results in actual or potential harm to the child's health, survival, development or dignity"(World Health Organization, 2016).

ACE have been associated with long-term health risks including anxiety and depression (Pinkerton, Dougherty, & Modesitt, 2008). ACE affect the brain at many levels, ranging from alterations in the HPA axis to changes in neuroanatomy and neurotransmitter levels creating long-term epigenetic changes in the brain that may alter fear and anxiety-related responses later in adulthood (Nieto et al., 2016; Rick & Douglas, 2007).

Current Treatment for Anxiety

While standard treatment for most menopausal symptoms is HT, no studies were found in which the effects of HT on anxiety symptoms were investigated as a primary outcome in menopausal women (Soares, 2011). First line treatment options for anxiety symptoms include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) which have been reported to provide limited symptom relief; however they carry an extensive side effect profile including sexual dysfunction, fatigue and weight gain, all of which may actually exacerbate existing menopausal symptoms (Cascade, Kalali, & Kennedy, 2009).

Efficacy of SSRIs and SNRIs for treating menopausal anxiety has not been well established. In a recent review, Warren (2007) found no placebo-controlled trials specifically assessing the efficacy of SSRIs or SNRIs on mood symptoms associated with menopause as a primary outcome. In studies where mood symptoms were measured as a secondary outcome, results suggested that several SSRIs and SNRIs may improve menopausal mood symptoms, but few studies have demonstrated significant improvement when compared with placebo (Warren, 2007).

Problem Statement

An estimated 6,000 U. S. women reach menopause every day (North American Menopause Society, 2014). For many of these women, anxiety will be a symptom that severely impacts quality of life. To date, studies that are investigating anxiety in menopausal women are using such varied descriptions and measurements of anxiety that it makes it nearly impossible to arrive at consistent conclusions. There is a tremendous need to explore and develop a definition of menopausal anxiety encompassing all of the associated nuances. This detailed understanding of anxiety in menopause will help to better operationalize this concept in research and develop individualized management strategies aimed at improving quality of life.

Qualitative Research Methodology

Qualitative research is the method of choice when exploring a complex phenomenon and when a holistic, rich description of a phenomenon is desired (Merriam & Tisdell, 2016). The overall purpose of qualitative research is to achieve an understanding of how people make sense out of their lives and to describe how people interpret their experiences (Merriam & Tisdell, 2016). The quantitative research paradigm commonly used in clinical research may provide a restricted view since it often incorporates only questions that can be measured and analyzed by

statistical methods (Malterud, 2001). While quantitative research methods use surveys and questionnaires to capture severity of symptoms, those measures do not take into account the complexity of all of the factors that may influence menopause and quality of life (McGinnis et al., 2009). Because all women experience menopause in a unique way it is not possible to predict a consistent uniform symptom experience (Holloway, 2011).

In a qualitative study, McGinnis and colleagues (2009) found that perceptions of quality of life were more involved than the presence or absence of symptoms, concluding that the identification and exploration of physical and psychosocial factors impacting quality of life are necessary in order to achieve a deeper understanding of how a woman's life is affected by the menopause. A descriptive qualitative research design that is focused on understanding anxiety from the perspective of menopausal women will be the first step in understanding how to make a difference in these women's lives.

Purpose of the Study

The purpose of this study was to explore and to gain insight into the concept of anxiety in menopause. A secondary aim of this research was to identify variables that may influence anxiety in the menopausal population which may provide a foundation for future interventional research.

Research Questions

Based on the purpose of the research study, the following research questions were addressed: How do menopausal women describe their anxiety experience? What factors influence the anxiety experience?

Specific Aims

1. Develop a description of anxiety in menopausal women as defined by menopausal women through the use of a descriptive qualitative study.
2. Identify factors and characteristics that may contribute to anxiety in menopausal women.

Definition of Key Terms

Anxiety. Anxiety is defined as emotional feelings such as nervousness, worry, unease, anticipation or mental tension and a fear-based expectation of threat (Bystritsky & Kronemyer, 2014).

Perimenopause. The perimenopause stage is defined as the period from the onset of intermittent menstrual cycle irregularities and/or other menopause-related symptoms, and extends beyond menopause (the final menstrual period) to include the 12 months after menopause (North American Menopause Society, 2014)

Premenopause. The premenopause stage refers to the phase of life that precedes menopause (North American Menopause Society, 2014).

Menopause. Menopause is defined retrospectively as the final menstrual period confirmed by 12 months of amenorrhea (North American Menopause Society, 2014).

Postmenopause. Postmenopause is defined as 12 months after the final menstrual period, which also marks the end of perimenopause (North American Menopause Society, 2014). According to the Stages of Reproductive Aging Workshop (STRAW) tool which provides clinical definitions of the menopause transition, post menopause is divided into two stages.

- Stage +1 (Early) is defined as the first five years after the final menstrual period.
- Stage +2 (late) begins five years after the final menstrual period and ends with death (Harlow et al., 2012).

Assumptions

The following assumptions were made about the participants and procedures prior to conducting the study. For this study examining anxiety in menopausal women, the researcher assumed that there is a distinct, different type of anxiety (*de novo* phenomenon) that is associated with menopause. The researcher assumed that consenting participants would provide honest answers to those questions that they were willing to answer and that the participants would be able to articulate their experience.

Summary

A more nuanced understanding of the concept of menopausal anxiety is the first step in learning how to effectively research and treat it and qualitative exploration is the best choice when a complex, detailed understanding of the issue is needed (Creswell, 2013). Qualitative inquiry in this study aimed to gain a greater understanding of the experience of menopausal anxiety and those variables that may contribute to the symptom of menopausal anxiety. This understanding will aid in the development of personalized health strategies to improve the clinical management of menopausal anxiety.

This research will contribute to the advancement of symptom science research which is one of the high priorities for the National Institute of Nursing Research (NINR). Effective management of anxiety may result in substantial health care cost savings and help to relieve the tremendous economic burden currently associated with anxiety as well as making a significant impact on mortality, morbidity and quality of life for menopausal women.

Chapter II

Review of the Literature

A review of the literature focused on menopause suggests anxiety is a frequently experienced symptom in menopausal women and often adversely affects quality of life. This literature review is organized around anxiety in menopause and variables that may influence the experience of anxiety in menopausal women.

Menopause

Menopause is a normally occurring physiological event which is defined as a woman's final menstrual period (FMP) naturally occurring on average around age 52 (North American Menopause Society, 2014). Natural menopause will eventually affect every woman reaching middle adulthood and it is estimated that more than 2 million women reach menopause every year (North American Menopause Society, 2014, pg. 1). During menopause more than 80% of women report various physical and psychological symptoms that adversely affect quality of life (Freeman, Sammel, Liu, & Martin, 2003; Greenblum et al., 2013). Vasomotor symptoms (VMS) including hot flashes and night sweats, and physical conditions including sleep disturbances, genitourinary symptoms (dryness, pain with sexual intercourse, bladder symptoms and vulvovaginal atrophy) and weight gain are some of the most common symptoms experienced by menopausal women (Lewis, 2009; North American Menopause Society, 2014; Thurston & Joffe, 2011). Psychological symptoms that are frequently associated with menopause include fatigue, irritability, depression and anxiety (Ford, Sowers, Crutchfield, Wilson, & Jannausch, 2005; Lewis, 2009; Soares, 2014).

Although VMS are one of the most commonly reported menopausal symptoms, psychological symptoms including anxiety are also a problem for menopausal women (North

American Menopause Society, 2014). A substantial amount of research has focused on the cause and treatment of VMS (North American Menopause Society, 2015; Thurston & Joffe, 2011) as well as depression and its association with menopause (Freeman, Sammel, Lin, & Nelson, 2006; Soares, 2017; Soares & Frey, 2010); however, there has been little research focused on anxiety symptoms that are new with the onset of menopause (Bryant et al., 2012; Warren, 2007).

A review of the literature addressing the association between anxiety and menopause yielded a small number studies. Much of the literature was focused on the association of anxiety and hot flashes, or interventional studies (pharmacologic and nonpharmacologic) addressing menopausal symptoms, or associations of menopause and concurrent comorbidities and somatic disease. A detailed understanding of anxiety symptoms experienced in menopausal women is needed if healthcare providers are to successfully initiate prevention or self-management strategies to improve quality of life.

Anxiety and Menopause

Measures. Studies addressing anxiety in menopausal women commonly use varied descriptions and measurements of anxiety which is a problem because it results in inconsistent findings and difficulty in making comparisons between studies. In several cross-sectional studies, anxiety was measured through the use of a questionnaire consisting of three questions asking about (1) feeling tense or nervous, (2) feeling irritable or grouchy or (3) experiencing heart pounding within the last two weeks (Avis et al., 2001; Bromberger et al., 2001). Avis et al., (2001) investigated whether a single universal syndrome (cluster of menopausal symptoms) exists and Bromberger and colleagues (2001) investigated prevalence of psychological distress which was defined as the presence of all three symptoms in the previous two weeks. In this study psychologic distress was assessed as either being present or absent with only 24.1% of the

women reporting psychological distress. In a cross sectional study examining the prevalence of menopausal symptoms and the association with aging and lifestyle factors, Moilanen et al. (2010) measured anxiety symptoms through a similar self-administered questionnaire that included 4 questions on anxiety symptoms (nervousness, irritability, trembling and heart palpitations) experienced over the past 4 weeks. Findings indicated that anxiety levels were highest in postmenopausal women.

Although a number of studies evaluating anxiety in menopause did use validated measures, the inconsistency in the instruments being used made it difficult to compare results. Freeman et al. (2005) examined the association of anxiety with menopausal hot flashes in the early transition to menopause using the Zung Anxiety Index (SAS). SAS measures the *current* frequency (over the past few days) of affective and somatic anxiety symptoms which are comprised of the most commonly found characteristics of an anxiety disorder (Zung, 1971). Findings revealed a strong association between anxiety symptoms and hot flashes.

Bansal et al. (2015) conducted a cross-sectional community-based study in rural Punjab, India assessing the level of anxiety and depression in midlife women and possible contributing factors. Anxiety was measured with the SAS and the prevalence of anxiety was found to be 88.9% in the study population. The findings revealed that a significant relationship was observed between age and anxiety levels, rather than menopausal status.

Calvaresi & Bryan (2003) used a cross sectional design to investigate vasomotor, psychological and somatic symptoms that are often attributed to endocrine changes in men and women at midlife and to evaluate their relationship to menopausal status in women. This study used the State Trait Anxiety Inventory-Y which contains two scales each comprising 20 items relating to current anxiety state and to usual trait anxiety (Spielberger, C. D., Gorsuch, R. L.,

Lushene, R., Vagg, P. R., & Jacobs, G. A., 1983). This instrument asks participants to report how they have felt during the last month compared with how they normally feel. Findings supported a significant association between mood and menopausal status.

Muslić & Jokić-Begić (2016) conducted a cross-sectional study using an online survey to examine trait anxiety and anxiety sensitivity as predictors for perimenopausal distress. This study focused on the perimenopausal population which was recruited online from different parts of Croatia. Anxiety was measured with the State Trait Anxiety Inventory (STAI-T) and anxiety sensitivity was measured with the Anxiety Sensitivity Index (ASI), a tool used to measure anxiety sensitivity (the fear of anxiety-related sensations) in adults (Reiss, Peterson, Gursky, & McNally, 1986). The results indicated that trait anxiety and anxiety sensitivity may be important predictors for distress in perimenopausal women with each of the factors having a different significance with age and menstrual symptoms. This study focused on 3 subgroups, age 35-40, 41-45 and 46-52. The study showed that the younger and middle age subgroups who had highest levels of perimenopausal distress demonstrated higher levels of trait anxiety; however, the oldest subgroup experiencing higher levels of perimenopausal distress demonstrated higher levels of anxiety sensitivity.

Bauld & Brown (2009) conducted a cross-sectional study examining relationships between stress, psychological distress, psychosocial factors and menopause symptom severity and physical health in middle aged women. Anxiety was described and measured through the use of the Depression Anxiety Stress Scale (DASS-21) which is designed to assess multiple dimensions of the symptoms of stress, anxiety and depression (Lovibond & Lovibond, 1995). The 21 item scale asks participants to rate their experience of each state over the past week using a 4 point scale. Authors identified that the strength of stress/psychological distress and

menopause symptom associations were likely to have been overestimated due to the overlapping measurement of distress symptoms (e.g. anxiety, depression) in both the distress (i.e. DASS) and menopause symptom scales.

A longitudinal analysis by Bromberger et al. (2013) followed 2,956 women for 10 years to assess the effect of menopausal status and risk for anxiety. This study used the GAD-7 which asks 7 questions about general anxiety symptoms experienced within the past two weeks. Results indicated that women with high anxiety at premenopause may be more often anxious and are not at increased risk for high anxiety at specific stages of the menopausal transition. In contrast, women with low anxiety at premenopause may be more susceptible to high anxiety during and after the menopausal transition than before the menopausal transition.

Tangen & Mykletun (2008) conducted a cross sectional analysis to examine the prevalence of anxious and depressive symptoms and their relation to menopausal status. This study used the HADS which is a self-report questionnaire comprised of 14 questions (7 for depression and 7 for anxiety) that rates symptoms on a four-point Likert scale as experienced over the past week (Zigmond & Snaith, 1983). Findings indicated there was a significantly higher score on depression and anxiety in the perimenopausal and the postmenopausal period compared to the premenopausal period. Comparing the postmenopausal period with the perimenopausal period, the score for depressive symptoms was somewhat higher while the score for anxious symptoms was somewhat lower.

While all of these validated tools are commonly used to evaluate anxiety disorders they may not be entirely suitable for evaluating anxiety symptoms that are associated with menopause because the assumption is being made that menopausal anxiety has features similar to an anxiety disorder. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

defines the criteria used to diagnose generalized anxiety disorder as "excessive anxiety and worry occurring more days than not for at least 6 months; the individual finds it difficult to control the worry; anxiety is associated with three or more of the following six symptoms: (1) restlessness or feeling keyed up or on edge, (2) being easily fatigued, (3) difficulty concentrating or mind going blank, (4) irritability, (5) muscle tension and (6) sleep disturbance" (American Psychiatric Association, 2013). It is further specified that the disturbance is not attributable to the physiologic effects of a substance (e.g., medication) or another medical condition (e.g., hyperthyroidism). The following questions are relevant to explore with regards to anxiety and menopause: How do we know that this is what menopausal women are experiencing? Is this what menopausal women experience? Have we asked menopausal women what they experience? How can we effectively measure the experience of anxiety in menopausal women without more detailed and nuanced understanding of the anxiety experience in menopause?

Descriptions of Anxiety. Anxiety is also frequently studied in a grouping of symptoms that may be labeled as cognitive symptoms or as mood disturbance. This is a problem because mood disturbance is used as a term to describe a cluster of symptoms such as anxiety, depression, depressive mood, irritability, negative mood, feeling blue, mood lability and psychological distress (Bromberger et al., 2001, 2003; Vesco et al., 2007). These individual components of mood are diverse and encompass a wide variety of symptoms that may include anxiety or feelings of panic (Vesco et al., 2007). The use of such a broad description of mood makes it difficult to assess individual symptoms of anxiety and understandably produces conflicting results which may be attributed to the lack of consistency in the definition of mood (Vesco et al., 2007). The use of mood assessment tools such as checklists and surveys may be unreliable in detecting a disturbance in one particular aspect of mood such as anxiety, because

some of these instruments tend to treat symptoms such as anxiety and depression as similar without differentiating between the two (Vesco et al., 2007).

With the wide variation in the description of anxiety and the heterogeneity of anxiety tools used for measurement it is not surprising that there are inconsistent findings in the literature. Studies using a cross sectional design measuring symptoms at one time point may not be capturing the symptoms associated with menopausal anxiety. It is possible that menopausal anxiety differs from a generalized-type of anxiety disorder in that the symptoms are not consistent with the diagnostic criteria for an anxiety disorder or that symptoms may be transient or intermittent with an irregular temporal pattern. Symptoms may be completely missed if they are being measured at the current time or over a one or two week period. Symptom descriptions of feeling 'tense, nervous, irritable, grouchy or heart pounding' are all symptoms that may be associated with an acute stressor and may be confounding, resulting in an inadequate assessment of anxiety that is associated with menopause. Such confusion may leave women wondering how to differentiate their symptoms. "A sudden increase in body temperature, a racing heart, and fear that something else (something bad) might be happening to you or your health, in addition to all other changes (physical and emotional) that are happening at this time in your life; at this point, you might be wondering: Are we talking about anxiety or menopausal symptoms? Or both?" (Soares, 2013, pg. 481).

Populations. Chronologic age may be an unreliable predictor of reproductive age because women vary widely in the onset of the menopause transition (North American Menopause Society, 2014). In an effort to establish consistent menopausal stage terminology, The Stages of Reproductive Workshop (STRAW) developed a standardized classification system

of reproductive aging which is based on menstrual cycle bleeding patterns and endocrine parameters (Harlow et al., 2012).

The STRAW+10 staging system suggests that the menopausal transition involves two phases, the early menopausal transition characterized by changes in menstrual cycle length of 7 days (+/-) or more and the late menopausal transition characterized by the occurrence of amenorrhea for 60 days or longer (Harlow et al., 2012). The early and late stages of the menopausal transition are considered the perimenopause period which ends 12 months after the final menstrual period (FMP) (Harlow et al., 2012). During this transition phase the associated hormone fluctuations may be responsible for mood symptoms such as irritability, fatigue, depressive and anxiety symptoms (North American Menopause Society, 2014). Several studies have suggested that the perimenopausal stage is when most women are vulnerable to mood disturbance; however, without the use of consistent application of reproductive staging it raises questions as to the accuracy and consistency between results (Bromberger et al., 2013; Bryant et al., 2012).

The postmenopause stage begins with the FMP which is defined as 12 consecutive months of amenorrhea and is confirmed retrospectively (North American Menopause Society, 2014). The postmenopause stage is also divided into two stages: early and late menopause (Harlow et al., 2012). Early postmenopause is further divided into 3 substages and the entire stage lasts approximately 5 to 8 years (Harlow et al., 2012). During the early postmenopause period is when vasomotor symptoms (VMS) are most likely to occur and the late postmenopause stage represents the period where reproductive endocrine changes have stabilized and this phase continues through the end of the lifespan (Harlow et al., 2012).

Studies often look to investigate the association of menopausal status and anxiety (Bromberger et al., 2001, 2013; Calvaresi & Bryan, 2003; Li, Yu, Ma, Sun, & Yang, 2008; Tangen & Mykletun, 2008); however, there are inconsistencies in the use of the classification of menopausal stage. In the review of the literature, some studies reported that levels of anxiety symptoms rise during the perimenopausal period and then fall in postmenopause (Avis et al., 2001; Bromberger et al., 2001; Tangen & Mykletun, 2008) while others reported that anxiety was not related to menopausal stage (Li et al., 2008; Moilanen et al., 2010). Li et al. (2008) conducted a study in Beijing, China and found that anxiety symptoms were associated with VMS, stressful work, financial and home environments as opposed to menopausal status; however, there was no mention of the classification used for the menopausal stages (perimenopause, early menopause and late menopause).

Moileanen et al. (2010) had similar results in that there was a strong association with menopausal symptoms and lifestyle factors as opposed to menopausal status. Moilanen et al. (2010) defined menopausal status as women with normal menstrual cycles during the past 12 months as premenopausal; women with an irregular menstrual cycle during the past 12 months as perimenopausal and women whose last menstrual cycle occurred more than 12 months ago were classified as postmenopausal. Calvaresi & Bryan (2003) defined women experiencing no menstrual changes over the past 6 months as premenopausal; those whose periods were irregular and/or who had observed changes in frequency or flow over the past 6 months were defined as perimenopausal; and those who did not experienced a period for 12 months or longer were considered to be postmenopausal. Tangen & Mykletun (2008) defined menopausal status as premenopausal (0-90 days since last menstruation), perimenopausal (91-270 days since last menstruation) and postmenopausal (> 271 days since last menstruation). The inconsistent use of

menopausal staging is a problem because the inconsistencies in results may raise the question as to whether anxiety is in fact associated with menopause and if so, at which stage are women most vulnerable to the onset of anxiety?

It is hypothesized that anxiety symptoms may be associated with hormonal fluctuations that occur with menopause; however, this hypothesis remains controversial due to inconsistent information in the literature (Freeman et al., 2003). If anxiety symptoms during the menopause transition are no different than anxiety in the general population, it would be highly unlikely that anxiety symptoms assessed with a validated measure or clinical interview would be greater during menopause than before or after (Bryant et al., 2012). The wide variation in anxiety descriptions and measurement of menopausal status make it difficult to validate this hypothesis (Bryant et al., 2012).

Potential Variables Associated with Anxiety in Menopause

Age

Midlife (from 45 to 55 years) generally spans the menopause transition making it difficult to tease out whether anxiety may be a result of aging or a result of menopause, or both (Hickey, Bryant, & Judd, 2012). In a review addressing the prevalence of anxiety in older adults, Bryant, et al., (2008) concluded that while anxiety disorders and symptoms of anxiety are relatively common in older adults, the evidence suggests that anxiety symptoms are not necessarily associated with aging (Bryant et al., 2008). Bryant et al. (2008) raised concerns with how anxiety was measured in the studies that were reviewed noting that most studies used checklists or diagnostic criteria not specifically designed for use in older populations and because of the variation in measurement, it is possible that anxiety *symptoms* are highly prevalent in older adults as opposed to anxiety disorders. In a cross-sectional study evaluating associations of

symptoms, aging and menopausal status, Moilanen et al. (2010) had similar results reporting that it is partly unclear which symptoms occurring in middle age are menopause-specific and which are related to aging, health status or lifestyle. These findings raise the question as to whether age is associated with anxiety in menopausal women or whether this is a confounding variable.

Depression

In the general population anxiety and depression are increasing worldwide with the World Health Organization (2016) reporting that between 1990 and 2013, the number of people suffering from depression and/or anxiety increased by nearly 50%, from 416 million to 615 million. According to the World Health Organization (2015) depression is the leading cause of disability worldwide, with an estimated 350 million people affected. Depression is the result of a complex interaction of various social, psychological and biological factors (World Health Organization, 2015). It is well known that more women are affected by depression than men (World Health Organization, 2015) and depression is commonly reported by menopausal women (Bromberger et al., 2001, 2003).

Menopause related depression has been scientifically debated for years (Soares, 2014). Much of the controversy may be attributed to the wide variety of study designs, inconsistencies in population groups (menopausal staging) and wide variation in measurement tools which includes validated and nonvalidated measures (Soares, 2014). It is hypothesized that symptoms of depression in menopausal women are related to the shift in the hormone milieu, largely the fluctuation in estradiol (Freeman et al., 2006; Soares, 2017). As estrogen levels begin to decline at the onset of menopause biochemical changes begin to occur including a decrease in serotonin levels which has been linked to depression (Brashers, 2006; Soares & Frey, 2010). Anxiety symptoms are common in women with depression (Hickey et al., 2012) and anxiety is often

associated with other adverse symptoms such as stress, depressive symptoms and sleep disturbance (Hickey et al., 2012; Holloway, 2011; Joffe et al., 2009; Soares, 2014; Stephenson et al., 2013). The difficulty in evaluating anxiety symptoms at menopause is confounded by the similarity and overlap between some symptoms of anxiety and depression, such as fatigue, concentration and subjective memory problems, sleep disturbance, sexual dysfunction, and palpitations which are also common symptoms of menopause (Hickey et al., 2012; Soares, 2014, 2017). Because of considerable overlap in anxiety, depressive and menopausal symptoms, clinically the challenge lies in determining which symptoms are attributable to menopause or which are related to a psychological condition (Bryant et al., 2012; Judd, Hickey, & Bryant, 2012; Soares, 2014).

Stress

Stress has been defined as "a process related to an environmental demand that exceeds the adaptive capacity of a living being resulting in biological and/or psychological changes that increase the risk of negative health outcomes" (Cuadros et al., 2012, pg. 367). The terms stress and anxiety have become somewhat confusing because the scientific community and the lay public use the terms interchangeably to describe both a threat (stress) and the response to it (anxiety) (Bystritsky & Kronemyer, 2014). Anxiety is described as a fear-based *response* to an environmental stimulus which is perceived as a threat and anxiety is a *reaction* to stress that may include a variety of feelings such as nervousness, worry and anticipation of fear (Bystritsky & Kronemyer, 2014). Stress and anxiety are part of a synergistic process in which stress has the potential to produce anxiety and anxiety can in turn create stress and the extent of stress that is being applied can have a direct effect on the amount of anxiety being experienced (Bystritsky & Kronemyer, 2014).

It is well known that stress plays a significant role in the development of numerous health problems and may have a substantial impact on mood and menopausal symptoms (Alexander et al., 2007). Common sources of stress experienced by midlife women include health status, demanding jobs, family responsibilities, partner relationships, relationships with other family members, caring for sick or elderly relatives and the lack of time for oneself (Alexander et al., 2007; Woods, Mitchell, Percival, & Smith-DiJulio, 2009). It is hypothesized that the decrease in estradiol associated with the menopause transition may have a direct effect on the neuroendocrine system that is responsible for regulating emotional processes (Newhouse & Albert, 2015; Woods, Mitchell, & Smith-Dijulio, 2009). The domino effect of reproductive hormone decline coupled with effects on the neuroendocrine system may adversely affect women's response to stress (Alexander et al., 2007; Newhouse & Albert, 2015). It is further hypothesized that this dysregulation of the neuroendocrine system may contribute to symptoms of anxiety, with postmenopausal women responding more intensely than premenopausal women (Alexander et al., 2007; Nieto et al., 2016). This hypothesis is supported by the fact that the late stage of menopause is when the reproductive hormone decline has stabilized and the lower levels of ovarian hormones and the accompanying effects on the neuroendocrine system may very well set the stage for the new-onset anxiety experience in menopausal women.

Sleep Disturbance

Anxiety is often associated with other adverse symptoms including sleep disturbance (Files et al., 2011; Holloway, 2011; Soares, 2014; Stephenson et al., 2013). Sleep disturbance during menopause is a common complaint reported by many women (Soares, 2014; Woods & Mitchell, 2010) and the prevalence of sleep disturbance has been reported as high as 35% to 60% during postmenopause (Kravitz et al., 2008). Sleep disturbance has been associated with age, a

decline in estrogen, depression and anxiety; however, the influence of each factor remains unclear (Ameratunga, Goldin, & Hickey, 2012; Moreno-Frías, Figueroa-Vega, & Malacara, 2014).

Sleep disturbance is defined as a subjective self-reported measure which may include the assessment of sleep duration, difficulty in falling asleep, difficulty in staying asleep and overall quality of sleep (Ameratunga et al., 2012). Anxiety, depression and sleep disturbance are also affected by the variable of psychological stress (Bystritsky & Kronemyer, 2014). In a recent cross-sectional study of women age 40 - 60, perceived stress and insomnia were correlated suggesting that a bidirectional, mutually enhancing relationship exists between stress and sleep disturbance (Cuadros et al., 2012). Woods & Mitchell (2010) conducted a longitudinal analysis on data from the Seattle Midlife Women's Health Study, in which they assessed sleep disturbance across the menopausal transition. Results indicated that the severity of falling asleep and nighttime awakening were associated with multiple factors which included anxiety and perceived stress, suggesting that management strategies need to address multiple symptoms rather than placing an individual focus on the menopause transition.

Adverse Childhood Experiences (ACE)

Childhood adversity has received national attention because of findings from the National Comorbidity Survey (NCS) (Burgermeister, 2007). The study was conducted in the United States from 1990-1992 and found that 35% of adults (N=8,090) between ages of 15 and 54 years reported at least three types of adverse experiences during childhood (Burgermeister, 2007). Childhood adversity refers to the perception of negative events occurring in childhood including maltreatment, trauma and stress (Burgermeister, 2007) and includes " all types of physical and/or emotional ill-treatment, sexual abuse, neglect, negligence and commercial or other exploitation,

which results in actual or potential harm to the child's health, survival, development or dignity in the context of a relationship of responsibility, trust or power" (World Health Organization, 2014). It has been well documented that the exposure to early childhood trauma is a risk factor for altered psychological functioning in adulthood (Merrick et al., 2017).

Adult survivors of ACEs commonly have psychological and behavioral difficulties (Arias, 2004; Rick & Douglas, 2007). Much of what we know about the long-term consequences of ACEs comes from studies focusing on women (Arias, 2004). Alexander et al., (2007) reviewed current evidence for the potential interactions between acute stress, chronic stress, childhood stress and the development of depression and/or anxiety in the context of association with a symptomatic menopausal transition. Evidence for associations between mood disorders and stressful life events, suggest that an adult's stress response may be directly related to ACEs. Merrick et al. (2017) concluded that childhood emotional abuse is a key risk factor for the development of psychological symptoms in adulthood. There is an emergent body of literature examining the effect of adverse events in childhood and functional polymorphisms in the serotonin transporter (5-HTT) gene and brain-derived neurotrophic factor (BDNF) gene suggesting that these genetic alterations may contribute to an increased risk in the development of anxiety or depression as a result of the experience of adverse events in childhood (Alexander et al., 2007).

This review of literature has identified many issues associated with the study of anxiety in menopause. First is the paucity of studies that focus on the concept of anxiety in menopausal women. In studies that have examined anxiety in menopause, the wide variety in descriptions and measurement of anxiety make comparison and conclusion extremely difficult. Studies measuring anxiety with validated measures are making the assumption that menopausal anxiety

symptoms may share features of anxiety disorders, which may not be entirely true. Further, the grouping of anxiety with other symptoms of mood disturbance further serves to cloud specifics that are crucial to understanding the nuances of the anxiety experience in menopause. Inconsistent use of menopausal staging further confounds the issue making it difficult to link anxiety with specific menopausal stages.

There are several variables that are associated with anxiety including age, depression, stress, sleep disturbance and adverse child experiences. Several of these variables overlap with menopausal symptoms and the exact impact of these variables on anxiety in menopause remains unclear. There are no known studies that have qualitatively explored the concept of anxiety in menopausal women. A qualitative descriptive research design will provide a detailed, in-depth, rich description of anxiety by the women who are experiencing it which will inform future research as to the most appropriate measurement of anxiety in menopause as well as variables that may influence the anxiety experience.

Current Treatments

Prescription Hormone Therapy

The standard treatment for symptoms associated with menopause is hormone therapy (HT) that consists of estrogen (for women who have had a hysterectomy) and an estrogen/progestogen combination (for those women with an intact uterus) (North American Menopause Society, 2014). To date, there have been no studies that have thoroughly examined the effects of HT on anxiety as a primary outcome in menopausal women (Soares, 2014). The Postmenopausal Estrogen/Progestin Interventions Trial (PEPI) was a randomized, double-masked, placebo-controlled trial conducted with 875 postmenopausal women, examining the effects of estrogen alone or in combination with three progestin regimens on 52 possible

symptoms including anxiety (Greendale et al., 1998). Women were required to be between 45 and 64 years of age; at least 1 year, but not greater than 10 years postmenopausal; not taking estrogen or progestin for at least 2 months before screening; if treated with thyroid replacement, to have been on a stable dose for at least 3 months before screening; and to be free of major medical contraindications to hormone use (Greendale et al., 1998). Women assigned to the treatment groups showed vasomotor symptom relief resulting from treatment with estrogen and each of three estrogen-progestin treatment regimens versus placebo; however, postmenopausal hormone therapy *did not* affect self-reported anxiety symptoms (Greendale et al., 1998). Of note, one of the most commonly cited studies about hormone therapy, the Women's Health Initiative which evaluated the impact of HT in more than 160,000 women, did not directly evaluate the effects of HT on anxiety (Department of Health and Human Services, 2010).

In a double-blind, randomized, placebo-controlled study investigating the efficacy of estrogen therapy for improving mood and anxiety in non-depressive postmenopausal women, Demetrio et al. (2011), analyzed two treatment groups: one receiving conjugated equine estrogen (CEE) at 0.625 mg/day and the other placebo (both administered orally and for six cycles of 28 days each. Study results concluded that estrogen therapy *was not* associated with improvements in mood or anxiety symptoms in postmenopausal women. Girdler, et al. (1999) investigated the effect of estrogen with or without a progesterone on mood and physical symptoms in postmenopausal women and concluded that the estrogen/progestogen therapy was associated with a mild *increase* in anxiety symptoms. These results suggest that the experience of anxiety in menopausal women is more complicated than mere hormone deficiency, which requires further in-depth exploration.

The primary use of progestogen therapy in menopausal women is to reduce the risk of endometrial cancer associated with the use of unopposed estrogen (North American Menopause Society, 2014) however, progesterone has been identified as playing an important role in alleviating anxiety symptoms through its action at GABA-A receptors (Wirth, 2011). Of the few studies that have examined the effects of progesterone on anxiety in menopausal women, the type of progesterone (bioidentical or synthetic) was varied and the progesterone may have been used in combination with other hormone therapy (Bjorn, Backstrom, Lalos, & Sundstrom-Poromaa, 2006; Cagnacci et al., 2004; Girdler, O'Briant, Steege, Grewen, & Light, 1999; Greendale et al., 1998; Heikkinen, Vaheri, & Timonen, 2006). Of those studies where bioidentical progesterone was used as the intervention, it was often used in combination with bioidentical estrogen and/or other hormones including DHEA and testosterone and these studies used varying dosages and delivery routes (oral, topical, vaginal) making comparisons impossible (de Lignieres & Vincens, 1982; Ruiz & Daniels, 2014; Ruiz, Daniels, Barner, Carson, & Frei, 2011; Spark & Willis, 2012; Stephenson et al., 2013). The use of progesterone as monotherapy to treat menopausal symptoms such as VMS and sleep disturbance have only been investigated in a few small trials (Spark & Willis, 2012). Currently, there is an NIH funded study in progress (NCT01464697) that is testing the effect of micronized progesterone as an intervention for sleep disturbances and anxiety as a secondary outcome. This study will provide important insights into this possible intervention for women experiencing menopausal anxiety.

Prescription Pharmacologic Therapy

Treatment of anxiety disorders usually involves psychotherapy, medication or a combination of therapies (North American Menopause Society, 2014; Siegel & Mathews, 2015). Selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors

(SNRIs) and anxiolytics are the first line medications used in treatment of anxiety disorders (North American Menopause Society, 2014; Siegel & Mathews, 2015). Although pharmacologic treatment for mood disturbances in menopausal women is common (North American Menopause Society, 2014), Warren (2007) found no placebo-controlled clinical trials specifically assessing the efficacy of SSRIs or SNRIs for treatment of mood symptoms associated with menopause as primary outcomes. In studies examining the efficacy of SSRIs and SNRIs for mood disturbance as a secondary outcome, Warren (2007) found that many studies were lacking placebo groups and the results from pilot studies of several SSRIs and SNRIs suggested that they may improve menopausal mood symptoms, but few studies have demonstrated significant improvement compared with placebo.

Information on patient-reported side effects from a cross-section of real-world patients taking a SSRI found that 38% of approximately 700 patients surveyed experienced a side effect as a results of taking a SSRI (Cascade et al., 2009)**.** The most common side effects reported by patients included sexual dysfunction, sleepiness and weight gain (Cascade et al., 2009). The most frequent reasons reported for SSRI discontinuation were sexual dysfunction and weight gain (Cascade et al., 2009). The side effect profile of these medications are the reason that many women either discontinue or do not initiate therapy for menopausal symptoms (Lewis, 2009). Currently there is no comprehensive therapy to treat different menopause symptoms; therefore, women who are seeking treatment must often take multiple medications for different symptoms and the inconvenience and safety issues associated with long-term use often lead to treatment discontinuation (Lewis, 2009).

Psychotherapy and Behavioral Therapies

Cognitive-behavioral therapy, (CBT), mindfulness-based therapy (MBT) and other types of supportive psychotherapy have demonstrated efficacy in treating several menopausal symptoms including anxiety (Green, Haber, McCabe, & Soares, 2013; Khoury et al., 2013; North American Menopause Society, 2014; Siegel & Mathews, 2015). In a recent meta-analysis, Khoury et al., (2013), found that MBTs demonstrated clinically significant effects in treating anxiety and depression. It is well established that stress reduction is beneficial in managing mood symptoms associated with the menopause transition (Alexander et al., 2007) and relaxation and stress reduction therapies have been identified as therapeutic options for treating psychological symptoms associated with menopause including anxiety (Hickey et al., 2012; North American Menopause Society, 2014).

Preliminary Observations and Interviews

Internet resources such as support groups and blogs have become a popular source of health communication for both patients and healthcare providers (Thielst, 2007). Blogs are online websites that allow the user the opportunity to view or share stories via text, pictures and video clips (Keim-Malpass et al., 2013). Blogs provide an opportunity for online communication presenting a unique opportunity for people to use social media tools not only for emotional support, but for practical tips in treatment decision making (Keim-Malpass et al., 2013; Thielst, 2007).

Preliminary observations of women's comments on anxiety in menopause were retrieved from four online forums including:

(1) I Am Going through Menopause (www.experienceproject.com),

(2) Menopause Support Group.com,

(3) Menopause Forum – eHealth Forum (*ehealthforum.com/health/menopause.html)* and

(4) http://www.dailystrength.org/c/Menopause/forum

to gain an initial perspective on how menopausal women describe anxiety. The following posts reflect textural descriptions as self-reported by menopausal women.

"I am really struggling with menopause. It's affecting my health, my relationships with my children and my marriage."

"Anxiety is worse – antidepressants haven't helped much – bad side effects. Taking Xanax."

"Anxiety and perimenopause – "crushing chest, palpitations and fear. 100% complete relief during the week of my period."

"I have become so irrational. I feel so indifferent; I feel so lonely but want to be alone."

"My anxiety gets so bad I can't even get out of the house."

"I get anxiety attacks so bad that I miss work 3 and 4 days at a time."

"My anxiety is so severe I can't breathe. I pray for women who are suffering with this."

"Initially I was bothered by insomnia that made me feel like I could plow a field at 3 a.m. and now it feels like panic has ushered in. I get a racing heart beat that puts my mind in an anxious state and I find myself obsessing about any potentially stressful topic." "I have panic attacks and a lot of crying at night."

"When I'm overwhelmed with anxiety I see everything negative in my life and these thoughts are worsening the anxiety. On days when I feel good, I see my life as o.k., I mean, who has a perfect life with no needs to improve or change something? So I believe that the hormones are changing my view in a negative way. But when I feel totally anxious again, I can't believe that this is hormones, I think there must be something completely wrong with me and my life and

I will never feel "normal" again. Do you know what I mean? That's why I would like to see if there are also ladies who are happy with their lives, but they are experiencing anxiety and depressive moods since the menopause started."

"I feel so much anxiety. I go to therapy every two weeks, and I have tried a few antidepressants, but I am really sensitive and don't seem to have consistent results. Anxiety is so heavy that it consumes most of my days."

"I'm thinking all the time what should I change in my life, what could be the reason for my anxiety? I already thought it's my marriage (we are 20 years together), but my husband loves me, I love him, we don't have any bigger problems. The anxiety is hindering me from more active social and career life (I'm a freelancer artist), so I feel frustrated about my not enough exciting life, but I don't have enough courage to be more outgoing and active since I have this anxiety. I feel safer at home, but also more imprisoned. It's a vicious cycle."

These women are identifying anxiety as fear, negative thinking, paralyzing (can't leave the house), anxious, panic, shakes and an "out of control feeling." These posts reveal that for most women the anxiety is new-onset in menopause and for those who do have a previous history of anxiety/depression they report that when it resurfaces in menopause it is much worse. Most women acknowledged that life is stressful and that they can cope with regular life stressors; however, the anxiety associated with the menopausal transition, which seems to come from nowhere, can be debilitating.

In preliminary interviews with two women, one woman reported that she was three years into menopause before anxiety symptoms began. She reported that she started thinking "what's wrong with me" "…something's happening to me". She described the anxiety experience as feeling "like crawling out of my skin", "my heart racing" and "feeling scared". This woman

confirmed that at 5 years into menopause she felt that the anxiety episodes were increasing in frequency. She reported that the episodes were mostly before she went to bed at night and she was unsure what triggers it.

The second participant reported that after being in menopause for approximately 1 year, she began having the anxiety experience several times a day (maybe 6 – 10 times a day). She reported that the feeling came on suddenly, and described it as "like maybe how a dog acts before a thunderstorm", "just a crazy feeling."

These experiences cannot be captured through the use of a survey tool. Keim-Malpass et al., (2013) suggests that the use of naturalistic inquiry and analysis of online internet blogs represents an innovative methodology and these preliminary observations may be a useful first step in beginning to understand the experiences of these women. This preliminary work supports that next steps should include a more in depth qualitative inquiry to obtain a detailed nuanced description of the anxiety experience in menopausal women.

Summary Statement

This comprehensive review of the literature of anxiety in menopausal women has identified various physiologic, psychologic and situational variables that may be associated with anxiety. Most clinical trials addressing symptoms during the menopausal transition and early postmenopause focus on the management of hot flashes (Cray et al., 2012). Many studies have explored interventions (exercise, yoga, acupuncture, hormone therapy) for various menopausal symptoms and there is a large body of literature that focuses on hot flashes and the relationship with anxiety (Freeman et al., 2005; Freeman & Sammel, 2016; Lermer et al., 2011; Parry, 2016; Soares, 2011; Woods et al., 2016). After an extensive review of the literature, there are few

studies that explored the concept of anxiety in menopause and there were no studies found that explored the phenomenon of anxiety in menopause using a qualitative approach.

Current literature is characterized by inconsistent measurement of anxiety, through the lack of differentiation and definitions of anxiety symptoms, anxiety disorder, mood disturbance, psychologic disturbance, dysphoric mood, cognitive or mood symptoms. The use of multiple validated and non-validated tools and inconsistent measurement of menopausal status makes comparisons nearly impossible. Anxiety has been measured in the menopausal population with validated tools such as the Hospital Anxiety and Depression Scale (HADS-A) (Tangen & Mykletun, 2008), the State-Trait Anxiety Inventory (STAI), and the Generalized Anxiety Disorder Questionnaire (GAD-7) (Caan et al., 2015; Woods et al., 2016). The use of these survey-type tools may capture the severity of symptoms; however, due to the complexity of factors influencing menopause, these tools may be missing the important nuances that comprise menopausal anxiety.

This review exposes a gap in the literature which is the need to establish a more nuanced understanding of the anxiety experience as defined by the women who are experiencing it. Understanding a phenomenon is the first step in learning how to research it. There are many physiologic, psychologic and situational hypotheses for causes of anxiety in menopausal women, including age, decline of ovarian hormones and neurobiological changes that may occur in individuals with a history of childhood adversity. Variables of age, stress, depression and sleep disturbance, which are associated with menopause, may be confounders as they have also been identified as being closely linked with anxiety.

It is easy to understand how this entanglement of physical, psychological and behavioral symptoms makes it difficult to fully comprehend the concept of anxiety in menopausal women.

Because all women experience menopause in a unique way, a qualitative research methodology will be especially useful in the exploration of anxiety in menopausal women in that it will provide a more detailed description that may be of special significance to healthcare practitioners (North American Menopause Society, 2014; Sandelowski, 2000). This qualitative study aims to gain a deeper understanding of the particulars associated with women's experience of anxiety in menopause.

Chapter III

Methods

To date, quantitative studies have demonstrated inconsistencies in the measurement of anxiety and the lack of differentiation between anxiety symptoms and anxiety disorders make comparisons nearly impossible. It is easy to understand how difficult it is to measure the concept of anxiety in menopausal women without a clear understanding of the experience. There is tremendous overlap of physical, psychological and behavioral symptoms that may influence the anxiety experience and qualitative exploration is needed to detangle and elucidate the nuances of the anxiety experience in menopause. After an extensive review of the literature, there were no published studies found describing the phenomenon of anxiety in menopausal women through the use of qualitative research, therefore, this qualitative study was designed to explore and develop a description of the anxiety experience in the context of menopause.

In the study of anxiety in menopausal women, the use of a naturalistic descriptive qualitative methodology provided a means of obtaining a rich description of anxiety experienced by women within the context of menopause. The naturalistic paradigm refers to research that is carried out in the natural setting because the context in which the phenomenon occurs is considered essential in order to gain the fullest understanding of the phenomenon under study (Lincoln & Guba, 1985). Within a naturalistic study design, there is no pre-selection of variables to study, no manipulation of variables and no *apriori* commitment to any one theoretical view allowing the phenomenon to unfold as if it were not being studied (Sandelowski, 2000).

Qualitative methodology is particularly advantageous when research focuses on human and social experiences and is an appropriate choice when a complex, detailed understanding of phenomenon is needed (Creswell, 2013; Malterud, 2001). The detail is achieved by speaking

directly with people who are experiencing the phenomenon and allowing them to tell their stories free of what a researcher may expect to find (Creswell, 2013). Throughout the entire qualitative research process, the researcher keeps a focus on learning the experience of the participants from the perspective of the participants *not* the meaning that the researcher brings to the research from the literature (Creswell, 2013). Through the analysis of themes and patterns that materialize in the narrative data, descriptive qualitative research ultimately provides a comprehensive, rich description of the phenomenon being studied (Merriam & Tisdell, 2016).

Qualitative inquiry encompasses many distinct methods including phenomenology, grounded theory, ethnography, narrative analysis and naturalistic inquiry. While each of the types of qualitative research has some characteristics in common, they each have a different focus. This results in variations in how the research question may be asked, decision making on sample selection, and in how data is collected and analyzed (Merriam & Tisdell, 2016). Naturalistic inquiry is one of the most common qualitative research designs and is described by the focus on understanding how people make sense of their lives and their experiences (Lincoln & Guba, 1985; Merriam & Tisdell, 2016).

While all qualitative research seeks to uncover participants' understandings of their experiences, other types of qualitative studies have additional dimensions (Merriam & Tisdell, 2016). Phenomenology aims to describe and understand the essence or the basic structure of a phenomenon (Creswell, 2013; Merriam & Tisdell, 2016). Ethnography strives to describe and interpret the shared patterns and interaction of individuals within the culture of the society in which they live (Creswell, 2013; Merriam & Tisdell, 2016). Grounded theory aims to both understand and build a substantive theory about a phenomenon of interest (Merriam & Tisdell, 2016). Grounded theory is used to study a process, an action or interaction which involves many

individuals and has the ultimate goal of generating a theory which is grounded in the data that is collected (Creswell, 2013). Narrative analysis most often is used to explore the life of an individual or a small number of individuals through the use of stories that people tell to help understand the meaning of their experiences (Creswell, 2013; Merriam & Tisdell, 2016). Various types of narratives include biographical study, autoethnography and life histories (Creswell, 2013).

In summary, all qualitative research is focused on the experience as described by the individuals actually living that experience and how they make sense of their lives. All of the other types of qualitative research share the same characteristics of naturalistic inquiry but have a specific methodologic focus (Merriam & Tisdell, 2016; Sandelowski, 2000). Naturalistic inquiry was selected for this study because the aim of this method is consistent with the goal of this study which is to achieve a detailed understanding of the experience of anxiety in menopausal women.

Research Design and Setting

This qualitative descriptive study exploring anxiety in menopausal women took place with participants from Richmond and the surrounding area. Richmond is the capital city of the Commonwealth of Virginia and is surrounded by rural/semi-rural areas. Richmond is home to many major institutions of higher education, including Virginia Commonwealth University, a public research university. As of 2016, the population was estimated to be 223,170 (U. S. Department of Commerce, n.d.). As of 2015 the age distribution was approximately 25% under the age of 18, approximately 64% between 18-64 years old and approximately 11% of the population over 65 years old (U. S. Department of Commerce, n.d.). The racial distribution as of

2015 was approximately 45% white, 49% black and 0.6% American Indian, 2.5% Asian, 0.2 Native Hawaiian and 6.5% Hispanic (U. S. Department of Commerce, n.d.)

Criteria for Sample Selection

Participants selected for this study were women who have experienced natural menopause (defined as no menstrual period for 12 months) with self-reported anxiety symptoms that were new onset in menopause. The objective of this study was to understand the experience of anxiety within the context of menopause and to identify any factors that may influence the anxiety experience. This objective was achieved through the recruitment of women who had experienced natural menopause because it afforded the opportunity to explore the anxiety experience through assessment of the natural onset, duration, intensity and any temporal associated patterns which may not be experienced by women with surgically induced menopause. Inclusion criteria also included the ability to speak and understand English. Exclusion criteria included women who had surgically induced menopause. Surgically induced menopause was excluded because it represents a different type of a menopause experience which is sudden, unlike the typical transition of a natural menopause (North American Menopause Society, 2014). The abrupt loss of ovarian hormones usually causes a more drastic symptom experience than those seen with natural menopause (North American Menopause Society, 2014).

Subject Recruitment

Purposive sampling was used to recruit a group of menopausal women experiencing anxiety. Purposive sampling involves the selection of participants who have experience with and can provide insight on the phenomenon of interest thus informing the research (Creswell, 2013; Merriam & Tisdell, 2016). Study participants were recruited through an email advertisement (Appendix A) within the Virginia Commonwealth University (VCU) community and through

flyer advertisements (Appendix B) and letters sent to healthcare providers (Appendix C) in the community. Snowball sampling was utilized, where existing study subjects referred other interested participants to the researcher. No participant was required to participate in snowball sampling, however, all participants were offered a participant study information sheet (Appendix D) should they wish to refer others.

The researcher provided her email address and telephone number as contact information for those individuals who were interested in participating. As potential participants contacted the researcher, they completed a screening interview (Appendix E) at which time the researcher explained the research study and verified that the individuals met study criteria. If the individuals met study criteria they were invited to participate in the study. An appointment was scheduled at which time the consent process was completed and those interested in participating signed the consent form (Appendix F) and participated in the interview. Participants were instructed that they would receive a $10 gift card to a local business for participation in the study after interview completion. A sequential subject number was assigned to each participant and all data was coded with the participant number.

Recruiting continued until convergence was reached, meaning that the data and analysis was comprehensive and yielded a coherent and comprehensive answer to the research question (B. L. Rodgers, personal communication, March 20, 2017). It was estimated that 18-25 subjects would be sufficient to reach convergence. After 20 women were interviewed, it was determined that there was sufficient redundancy and convergence was reached.

Human Subjects Protections

Prior to beginning the study, the researcher applied and obtained approval from the Institutional Review Board (IRB) of Virginia Commonwealth University in Richmond, Virginia.

Participants were given two copies of the IRB Approval and Informed Consent Form (Appendix F) and the researcher provided a verbal explanation of all components to ensure the potential participant understood her rights as a participant in this study. The researcher asked the participant to read the consent and sign one copy for the researcher's records. The second copy was given to the participant for her own personal record. Each participant was advised that her participation was voluntary and that if she chose to participate, she may stop at any time without any penalty. Participants were also informed that they may choose not to answer particular questions that may be asked in the course of the interview. Participants were informed that they may stop the interview at any time. The researcher offered to answer any questions that the participant may have about the study. Participants were asked if they would be willing to be contacted by the researcher at a future date if additional interviews were necessary for clarification.

Data Collection

Qualitative Interview

Interviews are a primary source of data in qualitative research (Merriam & Tisdell, 2016). Effective interviewing utilizes a skill set defined by Gorden (1998) as three distinct phases: planning, doing and analyzing. The planning phase is important in constructing questions that are relevant to the objectives of the interview, structuring the questions so that they will be motivating enough to encourage participants to fully answer the questions and to help create a comfortable and communicative atmosphere (Gorden, 1998). The objective of the interview was to capture the experience of anxiety in menopausal women. This objective was achieved through the use of a semi-structured interview guide with relevant and open ended questions developed to help the researcher obtain specific points of information that may be needed. Broad questions are

most useful in the exploratory phase of an interview and these questions were carefully phrased so as not be too specific or unintentionally leading (Gorden, 1998). Probing, which consists of asking more specific questions was used to clarify or elicit more detail from the broad questions being asked.

The doing phase of the interview process involves establishment of a communicative atmosphere with a focus on the researcher's nonverbal behavior and listening techniques and evaluation of the participant's responses. The interview was a one-time face-to-face meeting conducted at a location that was mutually agreeable and in a physical setting conducive to the interview process. The interview environment was assessed for comfort (physical temperature, quiet, privacy) and chairs were arranged to help the participant feel at ease. Chairs were positioned facing each other with three or four feet of distance which is conducive to a private conversation. The researcher explained the interview process to the participant and answered any questions. The researcher informed the participant that the recording device was on and that the interview was beginning. The interview was conducted using a semi-structured guide (Appendix G) consisting of open ended questions and prompts to serve as a general guide to explore the participant's experience with anxiety in menopause.

The interview began with a statement asking the participant to tell a little bit about herself (age, age of onset of menopause, relationship status) and then the interview proceeded with additional questions such as "Tell me about your experience with anxiety in menopause." Additional probing questions were asked to help clarify the onset, duration, severity, temporal pattern and associated symptoms. During the interview, note taking was minimal and discrete so as not to be disruptive or distracting. The audio recorder was placed in an inconspicuous place out of the line of sight of both researcher and participant so as not to be a distraction.

In asking questions, the researcher stayed mindful of body position with a focus on "leaning in" towards the participant which is a way to subtly indicate interest. Eye contact is another way to let the participant know she has the undivided attention of the interviewer (Gorden, 1998). Care was taken not to have too much or too little eye contact so as not to be intimidating or appear disinterested. Attention was given to the pacing of the interview and making sure that there was no time constraint allowing the participant to feel unrushed and to feel that there was ample time to tell her story. Throughout the interview, the researcher was mindful of the use of *silence*. Often times silence can make for an uncomfortable pause; however, it can be a powerful tool in the interview (Gorden, 1998). By waiting a few extra seconds and not jumping immediately to another question, the participant may continue to elaborate on her response revealing valuable information.

As questions were asked, the researcher was listening and observing the participant trying to understand what the words meant to the participant as well has how the meaning related to the objectives of the interview (Gorden, 1998). This was achieved by watching for nonverbal cues such as respondent's tone of voice, silence, and pacing which can provide a context that can help to augment the interpretation of the verbal information obtained in the interview (Gorden, 1998).

Evaluating responses entails assessment of the relevance of the response, probing to elicit details to gain a deeper understanding of the questions being asked and the adequate recording of the response (Gorden, 1998). The face-to-face interviews were recorded and transcribed verbatim by a trained transcriptionist under confidentiality agreement to ensure completeness of information. The interviews lasted anywhere from 30 to 60 minutes and were conducted by the primary researcher, a Ph.D. student who is a registered nurse with over 20 years of experience and a certified family nurse practitioner with 5 years of clinical experience.

During the data collection process, the researcher kept field notes in a journal with observational comments to assist with later analysis about what was seen and what was heard in the interviews. Field notes are recorded observations that may include the physical setting, descriptions of the participants, activities and interactions, subtle factors (i.e., nonverbal communication) as well as the researcher's thoughts (Merriam & Tisdell, 2016). Notes were written on the computer as soon as possible after the interviews to capture important details about the participant and the interview. The entries were dated and coded with the participants' identification number. The observations were later used to augment data obtained in the interview which helped to provide a more holistic view of the participant and provide a more complete detailed picture of the phenomenon.

A reflexive journal is an introspective journal that documents the investigator's thought processes, philosophical position and the basis of decision making throughout the research process (Lincoln & Guba, 1985). The concept of reflexivity reflects the researcher's awareness of the biases, values and experiences that she brings to a qualitative research study (Creswell, 2013). Prior to beginning the study, the researcher documented her past experiences with the phenomenon and discussed how those experiences may shape her interpretation of the phenomenon. The researcher maintained a very detailed, comprehensive reflexive journal reflecting thoughts and feelings as the research progresses. These notes were used to identify specific bias and the potential impact it may have on the data collection and analysis.

Data Analysis Methods

Demographic Data

Demographic data collected in the interview were analyzed by descriptive statistics using JMP 13 software (SAS Institute, Inc., Cary, NC).

Interview Data

In qualitative research, data collection and data analysis are usually a simultaneous and ongoing process (Merriam & Tisdell, 2016; Sandelowski, 2000). The data analysis process used was an inductive and comparative analysis strategy which is a primary form of analysis used in most qualitative studies (Merriam & Tisdell, 2016). The process of data analysis consisted of consolidating and reducing the data and interpreting what was seen in the interview and what was read in the transcripts (Merriam & Tisdell, 2016).

Following each interview, the recording was transcribed verbatim by a professional, trained transcriptionist under confidentiality agreement. The researcher verified the accuracy of each transcript by listening to the recording while reviewing the transcript. Transcripts were read several times to become familiar with and gain insight into the data. Transcripts were formatted with a wide right margin to allow space to make notes and enable the researcher to do manual coding. The first few transcripts and field notes were reviewed and significant phrases or sentences pertaining to the anxiety experience were identified and written in the right margin. The field notes (observations and researcher's thoughts) were available to augment the interview data allowing the researcher to make descriptive notations about participants that may be useful as the data was interpreted. The researcher's comments further helped to expand ideas by reminding the researcher of thoughts that were occurring during the interview. Observations included relevant notes regarding appearance, nonverbal behavior such as making eye contact or emotional states such as crying, laughing or appearing nervous, all of which were useful in supporting thoughts and ideas the researcher was having during analysis. At this stage of data analysis, the process is referred to as open coding meaning that the researcher was open to all possibilities (Merriam & Tisdell, 2016). The coding included a verbatim repeating of words from

the participant or a concept that was identified by the researcher as potentially relevant in answering the research question (Merriam & Tisdell, 2016).

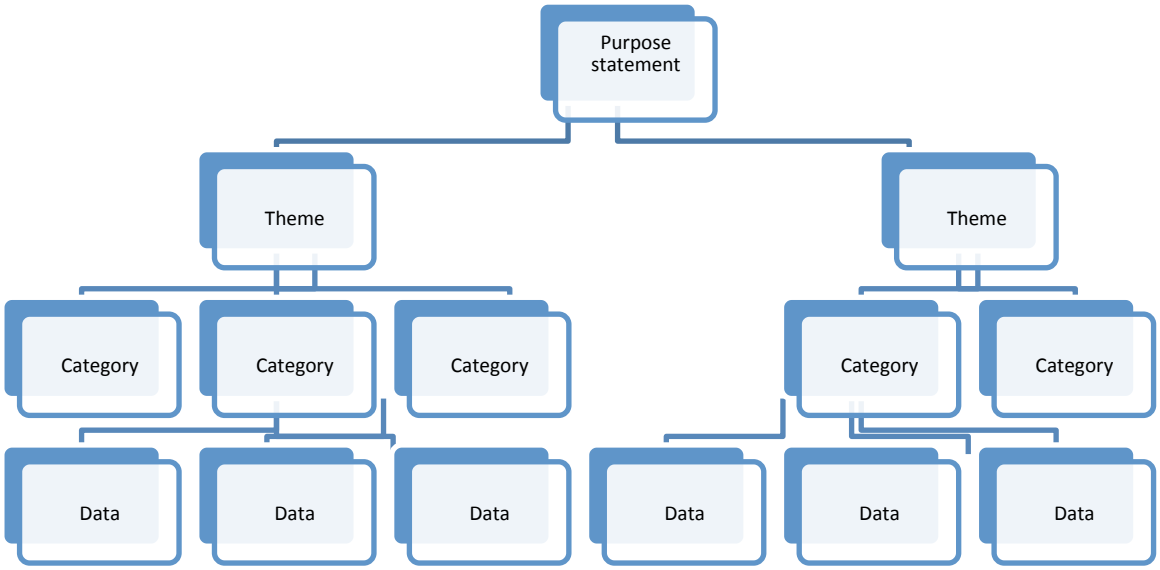
After open coding was completed on the first few transcripts, the coding was reviewed by a committee member who has extensive experience in qualitative research to ensure that the coding was in fact open and accurately reflected the content of the interview transcript. The next step after the review of the open coding was for the researcher to go back over the codes in the transcripts and begin to group codes that are similar into categories or themes. Categories should be comprehensive so that all significant data fit into a category; there should be enough categories to incorporate all of the data and the categories should be relevant to answering the research question (Merriam & Tisdell, 2016).

After several transcripts had been analyzed in the same way, the groupings identified in the transcripts were reviewed for agreement and the researcher began forming a master list of categories for subsequent data to be sorted. The researcher continued to add categories which were continuously compared for overlap and possible relationships, combining or subdividing the categories as needed (Lincoln & Guba, 1985). This process was repeated until all of the transcripts had been reviewed, coded and the data were categorized.

After a tentative set of coding categories had been established, the work was reviewed again by several of the dissertation committee members who are experienced qualitative researchers. Once there was agreement on the categories, the categories were grouped into themes and then reviewed to look for emerging relationships among the themes (Braun & Clarke, 2006). The process of grouping the data into categories and themes was achieved by utilizing a visual conceptual map (Figure 1) which allowed the researcher to look at the basic structure of the data and begin to systematically construct categories and themes and analyze the

relationships between the themes to effectively address the purpose of the study and answer the research question (Merriam & Tisdell, 2016).

Figure 1: Example of a Conceptual Map



The analysis continued on the data from all of the interviews until convergence was reached, meaning that the themes and relationships that were identified sufficiently described the phenomenon and answered the research question with no outstanding gaps. Prior to writing, an outline was created arranging the significant themes in a cohesive order to effectively explain and support the purpose and findings of the study (Merriam & Tisdell, 2016). The topics included key themes and categories, pertinent observations and direct quotes from the interviews. The themes and relationships between the themes helped to describe what the participants had experienced and their textural descriptions included observations recorded in the field notes and verbatim quotes from the participants (Creswell, 2013).

The narrative description was then prepared as a written report focused first on defining the concept of anxiety in menopause which was the purpose of the study. The report also included categories or themes identifying any potentially influencing variables that may have

surfaced. The researcher also looked to identify similar symptomology, temporal patterns and individual descriptions of anxiety. The researcher then arranged and combined the narrative and observational data into an in-depth textural description of the experience by summarizing the themes and concepts that had been developed from the data (Braun & Clarke, 2006; Creswell, 2013; Sandelowski, 2000).

Methodological Rigor

Lincoln & Guba (1985) developed standards for the trustworthiness of qualitative research that serve the same purpose as the standards of reliability and validity that are used in quantitative research. The emphasis, overall, is on documenting the quality and rigor of the investigation. In qualitative research the terms credibility, transferability, dependability and confirmability are the criteria used for assessing rigor (Merriam & Tisdell, 2016). Credibility refers to the confidence in the truth of the data and the interpretation of them (Lincoln & Guba, 1985). Truth value in conventional quantitative research represents the extent to which findings of an inquiry display a one-to-one relationship with that reality (Lincoln & Guba, 1985). Within the naturalistic paradigm, this determination is impossible because the underlying assumption is that there are multiple constructed realities; therefore, there is no single benchmark to make comparisons (Lincoln & Guba, 1985). In order to demonstrate truth value, the researcher must demonstrate that she has adequately represented the multiple reality constructions accurately and with neutrality (Lincoln & Guba, 1985). Major techniques that increase the likelihood of producing credible findings and interpretations include prolonged engagement and peer debriefing (Lincoln & Guba, 1985). The purpose of prolonged engagement is to "afford the inquirer sufficient time to establish trust and rapport with the participant and to gain a deeper understanding of the phenomenon by appreciating the multiple influences (mutual shapers and

contextual factors) that impact the phenomenon being studied" (Lincoln & Guba, 1985, pg. 304; Petty, Thomson, & Stew, 2012). For purposes of this study, prolonged engagement was achieved by spending as much time as was needed to gather data, sufficient immersion in the data and the data analysis process so as to obtain a complete description of the participants' experiences.

Peer debriefing is the process of working with a colleague who maintains an impartial view of the study (Lincoln & Guba, 1985). The impartial peer examines the researcher's transcripts, field notes, and reflexive journal and reviews the general procedures used for analysis of the data. The peer debriefing serves the purpose of "exploring aspects of the inquiry including identification of underemphasized points or vague descriptions that might otherwise remain only within the researcher's mind as well as biases or assumptions made by the researcher" (Lincoln & Guba, 1985, pg. 308). This process helps to keep the researcher honest by exposing her to probing questions by a peer who is playing the devil's advocate to clarify meanings and interpretations (Lincoln & Guba, 1985). Debriefing also provides an opportunity to discuss insights and ideas that may be developing in the researcher's mind (Lincoln & Guba, 1985, Petty et al., 2012). In this study, peer debriefing occurred with an experienced member of the dissertation committee who reviewed the data, provided opposing views, verified relationships that were identified by the researcher and ensured that the researcher was fully aware of her biases and the role that they played in the process (Lincoln & Guba, 1985).

Transferability refers to the extent to which findings from the data can be transferred to other settings or groups (Lincoln & Guba, 1985). The concept of transferability in naturalistic inquiry is very different from the concept of external validity in conventional research (Lincoln & Guba, 1985). In a study using naturalistic inquiry, the researcher cannot specify the external validity of an inquiry; he or she can only provide the rich description of the phenomenon being

studied and the conclusion as to whether transferability is feasible remains the responsibility of the individual who is considering the possibility (Lincoln & Guba, 1985). The assumption made in qualitative research is that the findings are context specific and therefore the research does not aim to generalize the findings (Petty et al., 2012). To the extent that the women under study are typical of other women, the researcher may enhance the transferability of study through the use of a purposive sample of menopausal women which allows the researcher to obtain specific information in the specific context of menopause in which anxiety is being studied. The selective sample contained participants who possessed the characteristics that can best inform the objective of the research study. To achieve the rich description of data, a semi-structured interview guide was used to ask broad questions and probes were used to help elicit the specific details necessary to achieve a better understanding of the participants and their experience.

Dependability and confirmability can be simultaneously assessed through the use of an inquiry audit (Lincoln & Guba, 1985). The external audit process involves the use of a researcher who is not directly involved in the research examining the process and the product of the research study, examining the records from the point of view of their accuracy and evaluating whether the findings, interpretations and conclusions are supported by the data (Lincoln & Guba, 1985). In qualitative research what is being investigated are participant's constructions of reality and how they have experienced a particular phenomenon (Merriam & Tisdell, 2016). There is no objective truth or reality to which the study can be compared (Merriam & Tisdell, 2016). For this study, a qualitative research audit trail was used as a means of a formal review of the processes and procedures used for decision-making and interpretation of the data throughout the research process (Petty et al., 2012; Rodgers & Cowles, 1993).

An audit in qualitative studies entails reviewing documentation that describes in detail how data were collected, how categories were determined and how decisions were made throughout the research process (Merriam & Tisdell, 2016). Rodgers and Cowles (1993) proposed four basic types of documentation needed to construct the audit trail: contextual documentation, methodologic documentation, analytic documentation and personal response documentation. Contextual documentation refers to the field notes which contain observations that are made during the process of data collection including descriptions of setting, participants, any interruptions or distractions that occur and nonverbal behavior of participants (Rodgers & Cowles, 1993). These documented observations provided important insights to augment participants' descriptions during the interview process (Rodgers & Cowles, 1993). In qualitative research where interviews are the primary source of data, field notes provide the contextual data which will be used during data analysis, augmenting the interview data to provide the thick description desired with a qualitative methodology (Rodgers & Cowles, 1993).

Methodological documentation refers to all of the documentation that it used to make methodological decisions throughout the study such as field notes, interview transcripts and the reflexive journal (Rodgers & Cowles, 1993). As qualitative research usually involves a design that is evolving (Lincoln & Guba, 1985), it is essential that the researcher maintains comprehensive methodological documentation in which the rationale for decision making is clearly documented. For this study, an experienced qualitative researcher on the dissertation committee reviewed the research proposal, the transcribed interviews, the researcher's journals (field notes and reflexive) to assess for accuracy and to evaluate how the information was used in decision making. This assessment included rationale for interview questions, how new questions

or probes had emerged over the course of the study and what role the researcher's past experience played in the inquiry and the interpretation of the data.

Analysis of qualitative data is largely dependent on the researcher's thought process which makes it essential that the researcher maintain consistent and clear documentation regarding all phases of the analysis including the sorting, categorizing and comparing of data and the conceptualizing of themes that emerge as the data are studied and coded (Rodgers & Cowles, 1993). Analytic notes make it possible for the auditor to retrace the researcher's steps in the data analysis process and to examine the researcher's thought processes and the rationale used for coding, sorting and developing themes (Rodgers & Cowles, 1993). Within this study, the researcher kept very detailed notes during all phases of analysis and recorded pertinent thoughts and questions at the time that they occurred or as soon as possible thereafter. Notes were dated to provide a chronological timeline and the notes included researcher insights associated with specific interviews and were documented by interview number and specific page and line of the interview.

In most qualitative research, the researcher plays a key role in data collection and the researcher's background and biases may influence the analysis of the data and final outcome of the study (Lincoln & Guba, 1985; Rodgers & Cowles, 1993). In this study the use of personal response documentation including the researcher's ongoing self-awareness documented in a reflexive journal provided both the researcher and auditor a means of evaluating the rational for decisions, as well as any personal biases that may have been relevant to the study (Lincoln & Guba, 1985).

Summary

This chapter provided a description of the methods that were used in this study and the rationale for the use of a naturalistic descriptive qualitative design to explore anxiety in menopausal women. Effective interviewing skills were reviewed and the rationale and incorporation into the study design were explained. The issue of methodological rigor was discussed in the context of the naturalistic research paradigm addressing the concepts of credibility, transferability, dependability and confirmability of the research study. The outcome of this study aimed primarily to answer the research question by providing a detailed description of the experience of anxiety in menopause and secondarily to identify variables that may influence the anxiety experience. The identification of the nuances associated with the anxiety experience in menopause will help to effectively operationalize this concept in future research and identification of variables that may influence anxiety in menopause will provide tremendous insight for future interventional research to improve quality of life for menopausal women. The following chapters will present the findings of this research as well as a discussion of the findings and the relevance to the current body of literature as well as implications for future research.

Chapters 4 and 5: Final Manuscript Results and Discussion

Anxiety in Menopause: A Qualitative Inquiry

Abstract

Objective: Although anxiety is a common mood symptom experienced by menopausal women, it has received little attention in the literature despite the potential impact on quality of life. There are very few studies that have assessed anxiety in the context of menopause leaving the concept of menopausal anxiety not well defined raising the question: Is menopausal anxiety a unique and distinctly different syndrome? The aim of this study was to explore and gain an in-depth understanding of the experience of new-onset anxiety in menopausal women.

Methods: Twenty menopausal women were recruited for this qualitative study to explore the experience of anxiety in menopause. Through the use of a semi-structured interview using open-ended questions, participants were asked to share their experience with anxiety that was new or different with the onset of menopause. Interviews were audio recorded by the researcher and lasted approximately 30 - 60 minutes.

Results: Emergent themes revealed that anxiety in menopause is a unique and individual experience. The substantial variation in the onset, timing and severity of the symptoms makes it impossible to construct a uniform and consistent definition of the experience. Participants discussed their preferences for management which included non-pharmacologic, educational and relaxation-based interventions.

Conclusions: This research supports the existence of a unique and individualized experience of anxiety in menopause. A better understanding of the experience and patient preferences will facilitate individualized treatment options aimed at improving quality of life.

Key words: *menopause, anxiety, qualitative*

Introduction

Menopause is a normally occurring physiological event defined as a woman's final menstrual period (FMP) naturally occurring on average around age 52 (North American Menopause Society, 2014). Natural menopause will eventually affect all women reaching middle adulthood and it is estimated that 6,000 U. S. women reach menopause every day (North American Menopause Society, 2014). As a physiologic event, menopause is characterized by a decline in estrogen and progesterone (Files et al., 2011; Holloway, 2011; North American Menopause Society, 2014; Stephenson et al., 2013). As a psychophysiological event, menopause is experienced by women as a process characterized by a variety of symptoms including anxiety (Files et al., 2011; Holloway, 2011; Stephenson et al., 2013).

Because menopause is associated with a reduction in hormones, menopause is often viewed and treated as a biomedical event. While it is common practice to treat most symptoms associated with menopause with hormone therapy (HT) (Greenblum et al., 2013; North American Menopause Society, 2014; Warren, 2007); there is evidence to suggest that HT does not always resolve the issue of anxiety in menopausal women (Demetrio et al., 2011; Greendale et al., 1998; Warren, 2007). If menopausal symptoms were solely based on the biologic decline of hormone levels, it would be reasonable to assume that some sort of a menopausal syndrome would be seen in most women and HT would reverse symptoms when they occur. However, the fact that menopausal symptoms are not universal suggests that these symptoms are not entirely biological and that there is some other dynamic that is not well understood (Greenblum et al., 2013). It is possible that anxiety during menopause is the result of an overlapping set of interrelated psychosocial and biologic factors.

Anxiety is a mood symptom commonly experienced by menopausal women (Holloway, 2011; North American Menopause Society, 2014; Siegel & Mathews, 2015); however, to anxiety symptoms during menopause have received less attention in the literature despite the potential impact on quality of life (Greenblum et al., 2013; Siegel & Mathews, 2015). Anxiety is a general term that is often used to describe anxiety symptoms and anxiety disorders, often not making a clear distinction between the two (Bryant et al., 2012). The term anxiety refers to a variety of symptoms that may describe features of different anxiety disorders such as panic disorder (e.g., suddenly feeling fearful for no reason), social phobia (e.g., fear of social or performance situations), or generalized anxiety (e.g., excessive and uncontrollable worry, irritability) (Bromberger et al., 2013). Anxiety symptoms can include physical symptoms such as shortness of breath, racing heart, and sweating (Siegel & Mathews, 2015). More importantly anxiety symptoms may consist of a variety of symptoms that are commonly associated with generalized anxiety disorder (i.e., tension, fatigue, headache, and gastrointestinal upset) and these symptoms may be difficult to distinguish from some of the symptoms associated with menopause or vague symptoms that are commonly associated with the aging process (Siegel & Mathews, 2015). The fact that the terms anxiety symptoms and anxiety disorders are often used interchangeably makes it difficult to compare studies and to draw conclusions (Bromberger et al., 2013).

Many studies use validated tools designed to measure general anxiety such as the Hospital Anxiety and Depression Scale (HADS-A) (Tangen & Mykletun, 2008), State-Trait Anxiety Inventory (STAI) and the Generalized Anxiety Scale (GAD-7)(Woods et al., 2016). Because these scales have not been designed to assess anxiety specifically related to menopause interpretation may be somewhat limited (Vesco et al., 2007). Evaluation and measurement of menopausal anxiety in terms of a general type of anxiety disorder assumes that menopausal

anxiety shares similar criteria as anxiety disorders and this may not be true. Anxiety in menopause may have a more insidious or intermittent temporal pattern, making it difficult to detect in studies of short duration or cross-sectional designs that are measuring symptoms at one point in time (Vesco et al., 2007).

To further complicate this issue, anxiety often is studied in menopausal women with other symptoms as a cluster (Bromberger et al., 2013; Cray et al., 2012; Greenblum et al., 2013) or as it relates to hot flashes (Bryant et al., 2012; Cray et al., 2012; Lermer et al., 2011). Anxiety is frequently included in a group of symptoms labeled 'mood symptoms' (Bromberger et al., 2003) or 'mood disturbance' (Vesco et al., 2007) or 'menopausal symptoms' (Greenblum et al., 2013). In a systematic review, Bryant et al., (2012) examined nine articles assessing the relationship between menopause and anxiety and anxiety and hot flashes. The findings were inconsistent which the authors attributed to the use of different definitions and symptoms used to define mood, poor measurement of both menopausal status and anxiety symptoms as well as the use of nonvalidated measures of anxiety symptoms (Bryant et al., 2012). In addition, no two studies used the same measure, making direct comparison impossible.

Because there are very few studies that have assessed anxiety in the context of menopause, the concept of menopausal anxiety is not well defined. Consequently, the question remains: Is menopausal anxiety a unique and distinctly different syndrome? A recent study evaluating depressive symptoms in perimenopausal women, suggests that there is a unique presentation of perimenopausal depression compared to depressive symptoms experienced in child-bearing years (Gibbs, Lee, & Kulkarni, 2015). Worsley et al. (2012) reported that women describe perimenopausal depressive symptoms as an "on–off" phenomenon where they experience episodes of sadness or irritability for minutes to hours which spontaneously resolve,

similar to the lability seen with premenstrual syndrome. “It is tempting to think of new onset perimenopausal depression as a distinct entity, a menopausal equivalent of premenstrual syndrome” (Worsley et al., 2012, pg. 129). This study aims to explore a similar hypothesis that there is a unique and different anxiety experience in menopausal women.

There are many physiologic, psychologic and situational hypotheses for causes of anxiety in menopausal women. Research has suggested there may be a role for age (Bryant et al., 2008; Moilanen et al., 2010), stress (Alexander et al., 2007; Newhouse & Albert, 2015; Woods, Mitchell, & Smith-Dijulio, 2009), depressive symptoms (Freeman et al., 2006; Soares, 2017) and sleep disturbance(Files et al., 2011; Holloway, 2011; Soares, 2014). Several of these variables overlap with menopausal symptoms and the exact impact of these variables on anxiety in menopause remains unclear. It is easy to understand how the entanglement of physical, psychological and behavioral symptoms makes it difficult to fully comprehend the concept of anxiety in menopausal women.

No studies were found that have qualitatively explored the concept of anxiety in menopausal women. A qualitative research approach can help to illuminate these nuances and provide a more detailed understanding of the anxiety experience in menopause. Qualitative research is the method of choice for exploring a complex phenomenon and allows women to tell their stories in order to achieve a better understanding of their experiences (Merriam & Tisdell, 2016). The quantitative research paradigm commonly used to research clinical issues can provide a limited view of clinical knowledge by incorporating questions and phenomena that can only be measured and analyzed by statistical methods (Malterud, 2001). While quantitative research methods use surveys and questionnaires to capture severity of symptoms, those measures do not take into account the complexity of all of the factors that may influence menopause and quality

of life (McGinnis et al., 2009). Because all women experience menopause in a unique way it is not possible to predict a consistent uniform symptom experience (Holloway, 2011), hence, in this study, a qualitative approach is warranted.

Methods

Research Design

A naturalistic descriptive methodology was selected for this study in order to achieve a detailed, greater understanding of the experience of new-onset anxiety in menopausal women. This qualitative descriptive study exploring anxiety in menopausal women was conducted in Richmond, Virginia and the surrounding area.

Participants

Purposive sampling was used to recruit a group of menopausal women who reported experiencing anxiety. Participants were recruited through email advertisement within the Virginia Commonwealth University (VCU) community and through flyer advertisements and letters sent to healthcare providers in the community. The sample consisted of women who have experienced natural menopause (defined as no menstrual period for 12 months) with self-reported anxiety symptoms that were new or different with the onset of menopause. Inclusion criteria also included the ability to speak and understand English. Exclusion criteria included women who have had surgically induced menopause. Surgically induced menopause was excluded because it represents a different type of a menopause experience which is sudden, unlike the typical transition of a natural menopause (North American Menopause Society, 2014). Participants were recruited by a member of the research team. A total of 27 participants were screened for eligibility. Of these women, 20 were eligible to participate in the study. Of those participants who were not eligible, 3 were still menstruating, 3 had surgical menopause and 1

reported the onset of anxiety symptoms much earlier in her life, years before the onset of menopause.

Data Collection

Qualitative data was obtained through face-to-face interviews through the use of a semi-structured interview using open-ended questions such as "tell me about your anxiety experience in menopause" and "how has anxiety affected your life". Participants were asked to share their experiences with anxiety that was new or different with the onset of menopause.

Procedure

Prior to beginning the study, the researcher obtained approval from the Institutional Review Board (IRB) of Virginia Commonwealth University in Richmond, Virginia. Written informed consent was obtained from participants prior to their enrollment in the study. Eligible women who consented and agreed to participate were scheduled for an interview. The interview location was mutually agreed upon in a physical setting conducive to the interview process. The researcher explained the interview process to the participant and answered any questions. Interviews were audio recorded by the researcher and lasted approximately 30 - 60 minutes. The researcher informed the participant that the recording device was on and that the interview was beginning. The interview followed a semi-structured guide consisting of open ended questions and prompts to serve as a general guide to explore the participant's experience with anxiety in menopause. During the interview, notetaking was done to record observations that may be useful in the data analysis. Following the interviews, any additional observations were recorded by the researcher. These observations were used to augment data obtained in the interview to provide a more holistic view of the participant and a more detailed picture of the

phenomenon. After completion of the interview, participants were given a $10 gift card to a local business for participation in the study.

Rigor of the study was enhanced by verifying accuracy of each transcript which was achieved by listening to the recording while the transcript was initially reviewed. The data were independently coded and sorted into categories by 3 investigators. A detailed audit trail (Rodgers & Cowles, 1993) was maintained and periodically reviewed by an experienced qualitative researcher. The audit entailed a review of documentation specifically describing how data were collected, how categories were determined, and how decisions were made throughout the research process (Merriam & Tisdell, 2016). The audit trail included a very detailed, comprehensive reflexive journal documenting the investigator's thought processes, philosophical position and the basis of decision making (Lincoln & Guba, 1985). These notes were used to help identify specific bias and the potential impact it may have on the data collection and analysis. Peer debriefing is the process of having an impartial peer examine the researcher's transcripts, field notes, reflexive journal and general procedures used for analysis of the data. This process was performed by an experienced qualitative researcher and was done at multiple points throughout the data analysis to discuss insights and ideas as well as provide opposing views to clarify meanings and interpretations of the data.

Data Analysis

Following each interview, the recording was transcribed verbatim by a professional transcribing company with IRB and HIPAA compliance, into a de-identified word document. Demographic data collected in the interview were analyzed by descriptive statistics using JMP 13 software (SAS Institute, Inc., Cary, NC). The qualitative data were analyzed using an inductive and comparative analysis strategy which consists of consolidating and reducing the

data and interpreting what was seen in the interview and what was read in the transcripts (Merriam & Tisdell, 2016). Transcripts were read several times to become familiar with and gain insight into the data. Participants' collective responses were analyzed line by line and a conceptual map was developed to organize the data into categories. Similar categories were then combined and grouped into key themes, at which point we analyzed the relationships between the themes and created an in-depth textural description which described the anxiety experience and variables that may contribute to anxiety thus achieving the aim of the study.

Results

Demographics

The participants' ages ranged from 48 to 71 years with a mean of 56.8 years (5.4) and the age of onset of menopause ranged from 45 to 56 years with a mean of 50.9 (3.5). The majority of the participants (n =13) have been in menopause for 1 – 4 years and the remainder (n =7) have been in menopause for 7 – 20 years. The majority of the participants were not married (65%) and all participants with the exception of one were working either full or part-time. The participant who was not working is retired and does volunteer work weekly. All of the participants had children with the exception of one. The number of children ranged from 1 – 4 with a mean of 2 (1.1) children.

Emergent Themes

In the interviews, participants described their experience with anxiety providing detailed descriptions of the onset of anxiety, duration and severity of episodes, timing, triggers and associated symptoms. Participants further articulated how anxiety symptoms are different in menopause and how the anxiety in menopause has affected their lives. Participants discussed interventions they have tried for managing the anxiety, discussed their preferences for

management, as well as what they would like from their relationships with health care providers. Four key themes emerged from the comments obtained in the interviews (Figure 2).

Figure 2: Emergent Themes and Subthemes

Themes	**Subthemes**
Anxiety in Menopause is a Unique and Individual Experience	Description Triggers (worry about family, insomnia, hot flashes, night sweats, stress)
I Am Different Now	Insignificant things become major stressors Inability to focus Decreased tolerance for stress Worry is increased Irrational thoughts Isolation Depression Change of self
Help Me Help Myself	Preferred Treatment Options What I want from my health care provider Support system
The Power of Knowing	If I only knew You're not crazy

Theme 1: Anxiety in Menopause is a Unique and Individual Experience

The majority of participants reported that the onset of anxiety symptoms began in menopause; however, several participants noticed symptoms beginning in the perimenopause period but worsening in menopause. Varied descriptions included a stress-related type of anxiety response with anxiety symptoms lasting minutes to hours resolving simultaneously with resolution of the stressful situation. Some participants reported nighttime-related anxiety lasting minutes to hours and some of the participants identified anxiety as a constant, ongoing low level, mild background type of anxiety that is present all the time but is exacerbated by stressful situations. One woman said, "…it's so hard to describe … I've talked to other women about it, and they say, 'oh, gosh, I know exactly…how you feel'."

The severity of symptoms varied considerably with participants rating it anywhere from 10/10 as an overwhelming, debilitating, paralyzing experience when it occurred, while others reported it as mild, more annoying but manageable. There was substantial variation in the timing. All participants reported that anxiety could happen either provoked (mainly by stressful situations) or unprovoked (random, intermittently and for no reason). While most participants reported having intermittent anxiety episodes triggered by stressful situations, many of the women reported having anxiety episodes mainly at night. Several participants said they experienced anxiety when everything was quiet or when waking up in the middle of the night while others reported that the anxiety is worse in the mornings. One woman described it as:

> "…you know the first awareness would be…not that I'm awake…it would be something's wrong and…feeling a little short of breath, having my heart beat too fast, being all sweaty and then becoming aware of what I was thinking…then that would cycle into stupid things, like…did I pick the right color to paint the living room…but that would seem like a life-threatening issue at 3:00 in the morning."

Other women gave similar descriptions describing the anxiety typically starting by waking up between 2:00 and 3:00 am, with racing thoughts and worries that including a feeling of a sense of loss of control and an overwhelming sense of dread or uneasiness. One woman described it as a sudden "creepy feeling…a distinct feeling that comes on suddenly like going from 0 to 60, feeling like something horrible has happened". When the anxiety occurs many participants reported that they can't identify the cause and that overall, anxiety was very unpredictable which contributed to the feeling of being out of control. One woman stated "…it's a very debilitating feeling. It's like you lose control…" Another woman said "You can't really put your finger on when, why, where, how or who… none of that…it just happens." For many of the participants anxiety was reported as not constant, but more dependent on situations and would increase with high stress. One participant reported having a period of several months

where anxiety symptoms had completely resolved but a subsequent stressful situation triggered the return of symptoms.

Many participants reported worrying about their children as a major trigger for anxiety. Most of the participants described the anxiety experience as an exaggerated more intense response to stress; almost like an overreaction – blowing things out of proportion, and some of the women reported conjuring unrealistic fears. One of the mothers confided:

> "…things were definitely different. I got very reactionary …when it…came…to my kids…I started thinking about worst-case scenarios…and end up getting all worked up over nothing…it's kind of like…a shock just going through my body that starts with this burning, tense, tightening sensation that starts in…my gut. I just kind of know something's wrong…you can feel the adrenaline just going right up into my head and by the time it got to my head, I'm like, 'something horrible has happened.' When it was done, it was all of a sudden, everything…it was like putting the genie back in the bottle."

Most participants reported associated symptoms that can occur with or trigger the anxiety included insomnia, hot flashes, night sweats and stress. Insomnia was a major trigger for all of the women either by waking up in the night with an anxiety experience or not being able to sleep which caused anxiety over losing sleep. One participant described it as "…right as I'm about to fall asleep, it's like I am struck with this…panicky…overwhelming dread." Another woman described the experience as:

> "…I find myself just getting ready to crash out, but I know I can't go to sleep…I would be tired and go to sleep…I might drift off and go to sleep and then…night sweats will hit and I'll wake right up and then I have to try to fall back to sleep again...it's just a vicious cycle and then by the time I feel as though I'm really getting ready to sleep it's time to get up."

The majority of women who reported hot flashes identified them as a major disruptor of sleep and for many of the women the hot flashes were a trigger for anxiety. One woman explained that the majority of the time she wakes up with a hot flash, but other times something wakes her up and she finds that she is feeling anxiety from it:

> "Most times I still have insomnia and I'm wondering when is it gonna stop…will I ever be able to sleep all night…I would go to sleep…and then in the middle of the night…I wake up and I'm like agitated and it's just hot…it felt like I was losing control and…it's like you wanna pull your hair out almost because you get so wet. I mean I was soak and wet, my gown…all around my neck…I had a towel I used to have over my bed just to wipe myself down…and it drove me crazy…I was like 'oh, I can't stand this'…what can I do and how long is it gonna last?"

Many women reported waking up frequently and once awake becoming aware of mind racing and experiencing an "unnerving feeling" unable to put a finger on the cause. One woman said, "it's like your mind just won't turn off and then it's like oh wait…what if and what if and what if…." Only a few of the participants reported noticing anxiety episodes increased during the winter or on dark rainy days; however, the majority did not notice seasonal variability.

Theme 2: I am Different Now

The majority of participants reported that anxiety feels different in menopause. Most reported experiencing a normal anxiety type of response in stressful situations prior to menopause but noticed a big change after menopause. Almost all of the participants said when stressful situations arise they feel magnified or more monumental than they would have been before menopause. Several participants acknowledged prior to menopause their lives were much more stressful than they are currently and they never experienced this type of anxiety until they started in menopause. Most participants agreed that the anxiety response feels more magnified and frequent in stressful situations; although one participant reported "…even being on vacation and being out of a situation and removing myself and having a positive experience I would still get it [anxiety]". One woman confided that prior to menopause, anxiety would largely be triggered by something specific but she said now anxiety seems to be on a schedule, occurring every night and nothing obvious has triggered it.

Many women complained of mental changes that included slower thinking, a decrease in ability to focus and the inability to respond as quickly as they did before menopause which they feel contributes to anxiety and has affecting daily functioning. One woman told me "…my mind just didn't feel as sharp or as clear…I didn't feel like myself. I didn't feel like I could count on my mind to work like it had always worked before…and that made the anxiety worse." Many participants also reported feeling less able to handle stressful situations comfortably, feeling more unsure about things that were previously taken for granted and seemingly insignificant things that wouldn't have been concerning before menopause now cause anxiety. One woman said "…being anxious all the time…has created a sense of doubt…am I going to be able to cope with that…what if it doesn't go well…doubts I never had before." Other women shared similar thoughts about feeling weaker and not being able to cope and manage as well they did before menopause.

Several participants reported that anxiety has largely affected their relationships with their children. One of the mothers said that anxiety caused her to be more abrupt with her children and that the children interpreted the anxiety as anger or a lack of trust. Another mother told me that when it came to issues regarding her children she would go through such an irrational thought process worrying about her children she would get to the point of feeling physically ill. She described how her worry led her to feel like a different person:

> "…my daughter started driving on her own…I'll track her on my phone. I sit in my living room and I watch where she's going and you know I just worry…she's…gonna get in to an accident, or someone's gonna run in to her…my mind just goes, wanders, makes up this whole story of what's going to happen…it's sort of made me a different person."

Other participants confirmed similar experiences including conjuring irrational thoughts and worst case scenarios about things that could happen to their children.

Many of the participants identified as being very social prior to their menopause experience; however, now they reported isolating themselves socially because of the fear of having anxiety or hot flashes in public. Several women stated if they knew that a situation may be potentially anxiety producing for them they would choose not to engage in the situation. Many reported not going out in an effort to minimize the environmental stimuli because they didn't feel like they could tolerate it as well in menopause. One woman told me "…I get invited out and I'm like 'no, I don't wanna go' coz sometimes being around people does make me anxious. I don't understand that. That's something new for me. What is wrong?"

Depression seemed to be a central component of the anxiety for several of the participants. A few of the women had a feeling that everyday life felt so overwhelming and activities that used to seem matter of fact would take extra energy and become chore-like. One participant said that the low grade background anxiety was exhausting and on days off, she didn't get dressed or leave the house because that was how she could reset. Although several participants felt their anxiety impacted their family life, none of the participants felt that anxiety adversely affected their ability to do their job. One participant commented that usual coping tactics didn't seem to work as well and she wondered if her anxiety stemmed from not being able to cope as well.

The majority of the women stated they were not anxious prior to menopause. Many of the women experienced a change of self with the anxiety experience in menopause wondering "is this the new normal?" For some of the women, being anxious has created a sense of doubt that they had not experienced before. For example, one woman confided that she feels weaker and less confident than she did before menopause. Another participant confided:

> "…I don't know what to do with it [anxiety] once it comes on…I don't want to be like this…This is not who I am and I don't want this to be how people see me."

This sense of self-doubt and frustration with the experience of anxiety is reflected in another participant's statement:

> "It doesn't feel like me to be anxious... I'm not a worrier – so when I find myself worrying I start thinking 'that's not me', 'that's not how I handle stuff'… I don't want to become an anxious person."

Theme 3: Help Me Help Myself

The majority of women said they did not want to take medication for the anxiety. Overwhelmingly, the preferred management of symptoms was self-help with nonpharmacologic interventions. Of those who used HT (2 women), it was reported that it helped with menopausal symptoms (i.e., hot flashes, irritability) but they still experienced anxiety. One participant tried estrogen and said it made the anxiety worse. Of those who tried or are currently using anti-depressants (2 women), they reported that it helped overall with mood symptoms but did not relieve the menopausal-type of anxiety that they are experiencing (e.g., nighttime anxiety episodes). Only a few of the participants had tried over the counter supplements which included Estroven, black cohosh and melatonin. One participant said the Estroven helped to decrease hot flashes so she is not waking up and having anxiety as much; the other participant reported that the Estroven worsened hot flashes and anxiety.

Most of the participants reported using a combination of various nonpharmacologic interventions for anxiety including breathing (*n*=5), walking (*n*=7), yoga (*n*=3), listening to music (*n*=3), running a fan at night/white noise (*n*=5) , self/talk/ self-reassurance (*n*=4), meditation (*n*=7), grounding (*n*=2), watching their diet (*n*=4) and drinking more water (*n*=2). All of the women reported these interventions helped substantially. One participant said, "…if I can be outside exercising, doing like a vigorous kind of exercise…when I go to sleep I have… more sense of calm." Other participants shared similar comments confirming exercise helps them sleep

better at night and anxiety tends to be less frequent. Most of the participants reported that they had not tried psychotherapy for the anxiety in menopause. When anxiety started in menopause, one woman reported she started seeing a therapist because she thought she was having mental health issues:

> "Counseling helped me understand there wasn't anything clinically wrong with me. What I was feeling was normal. It's my body's reaction to this hormonal shift. She helped me learn how to be more present. Validating that this is not who you are – it's just a symptom of something you have to go through – that was empowering and made this doable."

The majority of the participants reported they had not discussed anxiety in menopause with their women's health provider largely because they had no idea that the anxiety could be associated with menopause. One woman said, "I actually would have never thought to talk to my GYN about it – it would've never crossed my mind…I just wouldn't have associated it [anxiety and menopause] together". Other reasons included lack of desire for medication. One participant said, "If I say something to my doctor she'll want to prescribe something and I don't want medication." Only a few of the participants said that their health care providers had initiated a conversation about menopausal symptoms and offered medication for symptom management or verbal encouragement.

Women wanted healthcare providers to know first and foremost, that "anxiety is real" and "it's not just in my head". They want healthcare providers to initiate conversations about menopausal symptoms, provide education, ask detailed questions about anxiety and provide ways to manage it. Women want individualized treatment and they want healthcare providers to focus on the whole self and not just symptoms such as hot flashes or decreased libido. The majority of women said they would like to see healthcare providers educate women on what's coming and to learn what they can do *prior* to experiencing the symptoms. Most of the women

agreed that they don't want medication to be the first intervention. They prefer that healthcare providers just acknowledge it [anxiety] and let women know there is a correlation between menopause and anxiety and that it can be normal, just like postpartum depression.

The majority of participants reported having good social support systems and said that support systems help tremendously; for example, one participant stated:

> "Talking with a friend with similar symptoms helped remove isolation by finding out that others were feeling the same way. We could turn to each other and say 'I feel crazy'. I started working with a support group to try to figure out how to tame irrational thoughts."

Theme 4: The Power of Knowing

The majority of the women said they wished someone would have told them prior to menopause so that they might have been better prepared to deal with it. One woman told me, "…I always thought that menopause was just hot flashes…I'm in the middle of this mind thing…but I would have never associated that with menopause." Many participants agreed that simply not knowing the cause of the anxiety contributed to an increase in the anxiety and many, if not most, told me that once they knew that the anxiety could be related to menopause it was empowering and made it more tolerable and easier to manage the symptoms. One woman said: "We should be told…this is going to happen…I think I would have handled it a lot better coz I thought I was gonna lose my mind in the beginning two years ago." Another woman said "just knowing…has reduced my anxiety."

Overwhelmingly, the message that most of the participants wanted to give to other women is for them to know: "you're not crazy, anxiety in menopause is real, and no one understands it unless you've experienced it." Many of the women told me that they had no idea what was happening to them and that created even more anxiety. One woman said "I thought there was something wrong with me. I went to therapy and my therapist said 'welcome to

menopause'. I started talking with friends and found out others were feeling the same way." Another participant pointed out "we do a great job of preparing young women for what's going to happen beginning with your menstrual period or with pregnancy but we don't do such a great job with woman as they age." All of the women felt that education was critical and they all agreed that "knowledge is power".

Discussion

The purpose of this study was to explore and gain insight into the concept of anxiety in menopause. A secondary aim of this research was to identify variables that may influence anxiety in the menopausal population which may provide a foundation for future interventional research. The findings support the contention that anxiety in menopause presents with a unique symptom profile and is a unique and individual experience. Anxiety in menopause was generally described by participants as anxiety symptoms that may occur completely unprovoked or in response to a stressful situation. Symptoms were reported as being intermittent in nature – lasting a few minutes to hours with spontaneous resolution or as a mild, ongoing, background sensation of feeling unsettled or uneasy. Symptoms with a nighttime onset were described as occurring either prior to going to sleep or waking from sleep with associated mind racing and a sensation of dread and anxiety. Anxiety symptoms occurred with or without hot flashes and anxiety was described as producing a heightened, more exaggerated response to stressful situations. The unpredictability of the onset of symptoms contributed to a sense of loss of control. It was also noted that depression may be a common element of the anxiety experience.

The menopausal anxiety experience reported by the participants in this study is qualitatively different from generalized anxiety disorder criteria. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines the criteria used to diagnose

generalized anxiety disorder as “excessive anxiety and worry occurring more days than not for at least 6 months; the individual finds it difficult to control the worry; anxiety is associated with three or more of the following six symptoms: (1) restlessness or feeling keyed up or on edge, (2) being easily fatigued, (3) difficulty concentrating or mind going blank, (4) irritability, (5) muscle tension and (6) sleep disturbance” (American Psychiatric Association, 2013).

The majority of participants did not report excessive anxiety or worry that was persistent or difficult to control occurring more days than not. Many of the participants reported only a nighttime anxiety lasting minutes to hours and then there was complete resolution of symptoms. For those participants who experienced an ongoing, mild, background type of anxiety, it was not reported as excessive or difficult to control. To further confound the issue, some of the anxiety symptoms that women experienced (e.g., tension, fatigue, inability to concentrate, sleep disturbance) overlap with other menopausal symptoms or some of the vague symptoms that are commonly associated with the aging process which includes sleep disturbance (Siegel & Mathews, 2015). The majority of the anxiety experiences described by the participants do not fall within the diagnostic criteria for generalized anxiety disorder.

All of the participants reported having a heightened, more intense response to stressful situations which is supported in the current literature. The domino effect of the decline in reproductive hormones coupled with the effects on the neuroendocrine system as a biological event may adversely affect women’s response to stress (Alexander et al., 2007; Newhouse & Albert, 2015). This dysregulation of the neuroendocrine system may contribute to symptoms of anxiety in postmenopausal women (Alexander et al., 2007; Nieto et al., 2016). With the late stage of menopause being characterized with the stabilization of the reproductive hormone decline, the lower levels of ovarian hormones and the accompanying effects on the

neuroendocrine system may very well set the stage for this new-onset anxiety experience in menopausal women.

Sleep disturbance during menopause is a common complaint reported by many women (Soares, 2014; Woods & Mitchell, 2010). All of the women in this study reported some type of sleep disturbance and identified a cyclic association with disturbed sleep triggering anxiety or anxiety in turn disrupting sleep. The mechanisms of sleep disturbance remain poorly understood and sleep disturbance has been associated with many factors including age, a decline in estrogen, and anxiety; however, the influence of each factor remains unclear (Ameratunga et al., 2012; Moreno-Frías et al., 2014).

Several of the participants reported that depressive symptoms were a component of the anxiety experience. Menopause related depression has been scientifically debated for years (Soares, 2014). It is hypothesized that symptoms of depression in menopausal women are related to the shift in the hormone milieu, largely the fluctuation in estradiol (Freeman et al., 2006; Soares, 2017). As estrogen levels begin to decline at the onset of menopause biochemical changes begin to occur including a decrease in serotonin levels which has been linked to depression (Brashers, 2006; Soares & Frey, 2010). There is considerably difficulty in evaluating anxiety symptoms in menopause because there is significant overlap between some symptoms of anxiety and depression, such as fatigue, concentration and subjective memory problems and sleep disturbance (Hickey et al., 2012; Holloway, 2011; Joffe et al., 2009; Soares, 2014).

Most of the women did not want medications prescribed to treat the anxiety. Two participants were using or had tried HT and reported that while they had improvement in menopausal symptoms; the anxiety symptoms were still present. This experience is supported in the literature; for example, the Postmenopausal Estrogen/Progestin Interventions Trial (PEPI), a

randomized, double-masked, placebo-controlled trial conducted with 875 postmenopausal women, examined the effects of estrogen alone or in combination with three progestin regimens on 52 possible symptoms including anxiety (Greendale et al., 1998). Women assigned to the treatment groups showed vasomotor symptom relief resulting from treatment with estrogen and each of three estrogen-progestin treatment regimens versus placebo; however, postmenopausal hormone therapy *did not* affect self-reported anxiety symptoms (Greendale et al., 1998). Demetrio et al., (2011) investigated the efficacy of estrogen therapy for improving mood and anxiety in postmenopausal women and found that estrogen therapy was not associated with improvements in mood or anxiety symptoms.

Treatment of anxiety disorders usually involves psychotherapy, medication or a combination of therapies (North American Menopause Society, 2014; Siegel & Mathews, 2015). First line treatment options for anxiety symptoms include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) which have been reported to provide limited symptom relief; however they carry an extensive side effect profile including sexual dysfunction, fatigue and weight gain, which may actually exacerbate existing menopausal symptoms (Cascade et al., 2009; North American Menopause Society, 2014; Siegel & Mathews, 2015). Although pharmacologic treatment for mood disturbances in menopausal women is common (North American Menopause Society, 2014), Warren (2007) found no placebo-controlled clinical trials specifically assessing the efficacy of SSRIs or SNRIs for treatment of mood symptoms associated with menopause as primary outcomes. In studies examining the efficacy of SSRIs and SNRIs for mood disturbance as a secondary outcome, Warren (2007) found that many studies were lacking placebo groups and the results from pilot studies of several SSRIs and SNRIs suggest that they may improve menopausal mood symptoms, but few studies

have demonstrated significant improvement compared with placebo. Of the two women who reported currently using antidepressant medications, one reported that the medication was effective in treating her generalized anxiety symptoms but was not effective on the nighttime menopausal anxiety; the other participant reported she thought it helped her mood and that it may help with anxiety.

All participants reported wanting a relationship with their healthcare providers that would focus on holistic care, education and shared decision making. In a qualitative study assessing healing relationships, Scott et al., (2008) found that relationships between clinician and patient can foster healing and improve quality of life. One patient said "He gets you feeling better even without the medication. You just have that feeling that you're going to feel better after you see him." (Scott et al., 2008, pg. 320). Empowering patients by providing education and letting them know they are being heard will facilitate the knowledge needed for self-care (Scott et al., 2008). Participants in this study consistently discussed the feeling of a loss of control; hence a sense of empowerment would be an important aspect in addressing this component of the symptom experience.

Strengths of this study include the qualitative design allowing for a level of detail that could not have been achieved through a quantitative design. The subtleties and nuances that were obtained through interview would not have easily been achieved with quantitative surveys and measures. Limitations of the study include the small sample size of 20 women however, after 20 interviews sufficient redundancy was achieved and the data and analysis yielded a comprehensive description of the anxiety experience in menopause. Another limitation with qualitative research is that the analysis of the data is subject to researcher interpretation;

however, the data were reviewed and analyzed by several researchers who ultimately agreed on results.

Potential Clinical Value

This study has revealed important information that is relevant for research and clinical practice. While many validated tools are used to measure and diagnose anxiety it is important for healthcare providers to be aware that the experience of anxiety in menopause may not share the same criteria as generalized anxiety and a more individualized approach may be necessary to diagnose and treat the type of anxiety being experienced. The difficulty in evaluating anxiety symptoms at menopause is confounded by the similarity and overlap between some symptoms of anxiety and depression, such as fatigue, concentration and subjective memory problems, sleep disturbance, sexual dysfunction, and palpitations which are also common symptoms of menopause (Hickey et al., 2012; Soares, 2014, 2017). Because of considerable overlap in anxiety, depressive and menopausal symptoms, the clinical challenge lies in determining which symptoms are attributable to menopause or which are related to a psychological condition (Bryant et al., 2012; Judd et al., 2012; Soares, 2014).

Women experiencing menopausal anxiety may benefit from a different approach to management. Education and anticipatory guidance were identified as key issues and may be considered as prevention/intervention tools by alerting women to the possibility of anxiety as a symptom of menopause and exploring individualized management options. Addressing psychosocial issues and patient preference is important when considering treatment. The majority of women reported a preference for nonpharmacologic management of anxiety symptoms. Cognitive-behavioral therapy, (CBT), mindfulness-based therapy (MBT) and other types of supportive psychotherapy have demonstrated efficacy in treating several menopausal

symptoms including anxiety (Green et al., 2013; Khoury et al., 2013; North American Menopause Society, 2014; Siegel & Mathews, 2015). In a recent meta-analysis, Khoury et al., (2013), found that MBTs demonstrated clinically significant effects in treating anxiety and depression. It is well established that stress reduction is beneficial in managing mood symptoms associated with menopause (Alexander et al., 2007) and relaxation and stress reduction therapies have been identified as therapeutic options for treating psychological symptoms associated with menopause including anxiety (Hickey et al., 2012; North American Menopause Society, 2014).

Conclusion

This study has provided new insights and confirmed that anxiety has a unique and different presentation in menopause. Anxiety in menopause has been described as an individualized experience that may occur provoked or unprovoked, be intermittent in nature, and may occur largely at night. Common triggers for anxiety included stress, insomnia, hot flashes/night sweats. Menopausal women reported that anxiety is different in menopause in terms of how stressful situations now elicit a dysfunctional response to stress and the degree of worry that they now experienced has increased and associated thoughts may be more irrational than they were prior to menopause.

Menopausal women reported preferences for management with the most common strategies consisting of nonpharmacologic interventions such as walking, breathing, meditation and relaxation. Menopausal women want healthcare providers to focus on holistic care, shared decision making and education including anticipatory guidance on anxiety symptoms and their association with menopause. Each woman will have a unique symptom experience in menopause and will need to manage symptoms differently. This nuanced symptom profile may help the healthcare provider in identifying and diagnosing anxiety for the individual and to develop

individualized treatment plans which will make a significant contribution to improving the quality of life for menopausal women.

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Appendix A

Text for On-Line Advertising

Are you a woman in menopause experiencing anxiety? Would you like to talk about your experiences? Researchers at the VCU School of Nursing are interested in learning more about women's health in menopause. Participation in this qualitative study would involve a face to face interview (approximately 1 hour) to discuss your personal experience with anxiety in menopause. The interview will be audio recorded and will take place at a location convenient to you. You will receive a gift card to a local business for participation in the study. For more information, please contact Ellie Bremer, MSN, RN, FNP-C, at Virginia Commonwealth University School of Nursing, bremeres@vcu.edu. VCU IRB APPROVAL NO: HM20010855.

Appendix B

Women's Health

Are you a woman in menopause? Would you like to talk about your experience with anxiety?

Researchers at the
Virginia Commonwealth University School of Nursing
are interested in learning more about women's health in menopause.

Who is Eligible?

- Menopausal women which is defined as no menstrual period for 12 months
- Self-reported anxiety symptoms which are **new onset in menopause**

What will you be asked to do?

- Complete an interview (approximately 1 hour) to discuss your personal experience with anxiety in menopause. The interview will be audio recorded and take place at a location convenient to you.

Compensation Available

- Participants will receive a gift card to a local merchant for participation in this study.

For more information or if you would like to participate please contact:
Ellie Bremer, PhDc, VCU School of Nursing, email: bremeres@vcu.edu

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Appendix C

DATE

Dear Colleague:

I am writing to let you know about a study that will examine anxiety in menopausal women. Researchers Ms. Ellie Bremer and Dr. Nancy Jallo from Virginia Commonwealth University School of Nursing are studying the experience of anxiety in menopausal women. Ms. Bremer is a family nurse practitioner and a PhD Student at VCU and Dr. Jallo is a women's health nurse practitioner and faculty at VCU. This study has been approved by the VCU Institutional Review Board (IRB APPROVAL #HM20010855).

Menopause impacts 25 million women worldwide each year and the World Health Organization estimates 1.2 billion women will be postmenopausal by 2030. While the association between depression and menopause has been established, the association between anxiety and menopause remains largely unexplored. Compared with depression, anxiety symptoms have generated far less attention in studies of midlife women despite the prevalence of anxiety and their association with distress, impaired quality of life and morbidity (see for example: Bromberger et al., 2013; Bryant, Jackson, & Ames, 2008).

A greater understanding of the unique influence of menopause on the occurrence of anxiety symptoms is important because not only are anxiety symptoms prevalent in community populations, ranging from 15% to 52.3%, but anxiety is also a problem frequently reported to healthcare providers by midlife women.

We are interested in exploring anxiety that is new onset in menopause and we hope this knowledge will help to find ways of developing individualized treatments to improve the quality of life for menopausal women. We would appreciate it if you could share this information with any of your patients who may be interested or eligible to participate in this study. The enclosed information sheet is for your reference and may be shared with your patients.

Thank you for your consideration.

Ellie Bremer, MSN, RN, NP-C
Virginia Commonwealth University
School of Nursing

Encl: Study information sheet

Appendix D

VCU IRB Approval# HM20010855

Participant Study Information Sheet

The purpose of this study is to explore the experience of anxiety in menopausal women.
Here is what would happen if you decide to participate in this study:

- You'll be asked to complete a face to face interview with Ms. Bremer which may take approximately 60 minutes to complete.
- The interview will consist of questions asking about your experience with anxiety in menopause. Sample questions may include, "Tell me about your experience with anxiety in menopause. How has the anxiety affected your quality of life? What things make the anxiety better or worse?"
- After this interview, Ms. Bremer may ask to speak with you a second time to clarify information.
- Participants will be compensated for their participation in the study with a gift card to a local business.

If you think you might be willing to be in this study, you can:

- Contact Ms. Bremer and set up a time for the two of you to talk. Ms. Bremer will need to ask you some questions to see if you are eligible for the study.

All interested participants are being offered resources that will provide additional information and support addressing symptoms affecting menopausal women.

Student Researcher:
Eleanor S. Bremer, MSN, RN, NP-C
Virginia Commonwealth University School of Nursing
P. O. Box 98057
Richmond, VA 23298
P: 804-356-8914
E: bremeres@vcu.edu

Principal Investigator:
Nancy Jallo, Ph.D., RNC, FNP-BC, WHNP-BC, CNS
Associate Professor
Department of Family and Community Health Nursing
Virginia Commonwealth University School of Nursing
PO Box 980567
Richmond, VA 23298
P: 804-828-3365
E: njallo@vcu.edu

Appendix E

IRB Script of Screening Phone Call

VCU IRB Approval#HM20010855

"Hello, this is [investigator name] returning a call from [potential participant]. Is she available?"

Confirm identity before proceeding.

"Thank you for your interest in our study. The purpose of this study is to explore the experience of anxiety in menopausal women. Before we can invite you to participate I need to ask you a few questions about your health – is it OK to do that now?"

Confirm it is ok to talk or reschedule for a convenient time.

Have you had no menstrual period for at least 12 months?

Are your anxiety symptoms NEW with the onset of menopause?

If the inclusion criteria are met:

"Thank you; it looks like you are eligible to take part in the study. Before we schedule a time to meet I want you to know that participation is completely voluntary and you may withdraw from the study at any time, for any reason, without penalty.

Do you have any questions for me?"

(Answer any questions).

Great – let's schedule a time and place to meet. I look forward to working with you.

(If the inclusion criteria are NOT met):

"Unfortunately based on your answers to the questions, you are not eligible to participate in the study. I certainly appreciate your interest and willingness to be considered for this study. We do have a list of resources that may be useful to you as you go through menopause – would you like to hear that information?"

Provide information as requested.

"Thank you so much for your time."

Appendix F

IRB Approval Letter

Office of Research and Innovation
Office of Research Subjects Protection
BioTechnology Research Park
800 East Leigh Street, Suite 3000
Box 980568
Richmond, Virginia 23298-0568

(804) 828-0868
Fax: (804) 827-1448

TO: Nancy Jallo, PhD
Eleanor Bremer
CC: Amy Heineman

FROM: VCU IRB Panel A
RE: IRB HM20010855 Anxiety in Menopause: A Qualitative Inquiry

On 8/22/2017, the referenced research study was ***approved*** by expedited review according to 45 CFR 46.110, categories 6 and 7, by VCU IRB Panel A.

- The information found in the electronic version of this study's smart form and uploaded documents now represents the currently approved study, documents, informed consent process, and HIPAA pathway (if applicable). You may access this information by clicking the Study Number above.

This approval expires on 7/31/2018. Federal Regulations/VCU Policy and Procedures require continuing review prior to continuation of approval past that date. Continuing Review notices will be sent to you prior to the scheduled review.

If you have any questions, please contact the Office of Research Subjects Protection (ORSP) or the IRB reviewer(s) assigned to this study.

The reviewer(s) assigned to your study will be listed in the History tab and on the study workspace. Click on their name to see their contact information.

Attachment – Conditions of Approval

Conditions of Approval:

In order to comply with federal regulations, industry standards, and the terms of this approval, the investigator must (as applicable):

1. Conduct the research as described in and required by the Protocol.
2. Obtain informed consent from all subjects without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate (unless Waiver of Consent is specifically approved or research is exempt).
3. Document informed consent using only the most recently dated consent form bearing the VCU IRB "APPROVED" stamp (unless Waiver of Consent is specifically approved).
4. Provide non-English speaking patients with a translation of the approved Consent Form in the research participant's first language. The Panel must approve the translated version.
5. Obtain prior approval from VCU IRB before implementing any changes whatsoever in the approved protocol or consent form, unless such changes are necessary to protect the safety of human research participants (e.g., permanent/temporary change of PI, addition of performance/collaborative sites, request to include newly incarcerated participants or participants that are wards of the state, addition/deletion of participant groups, etc.). Any departure from these approved documents must be reported to the VCU IRB immediately as an Unanticipated Problem (see #7).
6. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.
7. Report Unanticipated Problems (UPs), including protocol deviations, following the VCU IRB requirements and timelines detailed in VCU IRB WPP VII-6:
8. Obtain prior approval from the VCU IRB before use of any advertisement or other material for recruitment of research participants.
9. Promptly report and/or respond to all inquiries by the VCU IRB concerning the conduct of the approved research when so requested.
10. All protocols that administer acute medical treatment to human research participants must have an emergency preparedness plan. Please refer to VCU guidance on http://www.research.vcu.edu/human_research/guidance.htm.
11. The VCU IRBs operate under the regulatory authorities as described within:
    a. U.S. Department of Health and Human Services Title 45 CFR 46, Subparts A, B, C, and D (for all research, regardless of source of funding) and related guidance documents.
    b. U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.
    c. Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

Appendix G

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Anxiety in Menopausal Women

VCU IRB NO.: HM20010855

INVESTIGATOR: Dr. Nancy Jallo

If any information contained in this consent form is not clear, please ask the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY

The purpose of this study is to explore the experience of anxiety in menopausal women. You are being asked to participate in this study because you have described yourself as a menopausal woman who is experiencing anxiety.

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT

If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered and understand what will happen to you.

- In this study you will be asked to participate in a face to face interview where you will discuss your experience with anxiety in menopause with a member of the study staff. The interview will follow a semi-structured guide consisting of open ended questions to help identify your anxiety experience in menopause. Questions may include things like, "Tell me about your experience with anxiety in menopause? How has anxiety affected your quality of life?" Interviews will last approximately 60 minutes, will be recorded using secured audio equipment and be professionally transcribed under confidentiality agreement. After the initial interview, the study staff may ask to speak with you a second time to clarify information. If you agree to a second interview, that interview may last for 30 to 60 minutes.

RISKS AND DISCOMFORTS

Sometimes talking about anxiety may cause people to become upset. You do not have to talk about any subjects that you do not want to talk about, and you may stop the interview at any time. All interested participants will be given a list of supportive referral services should they wish to access services after the interview. Breach of confidentiality is a potential risk; however, a de-identification/coding process will be used as a safeguard to minimize this risk.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authority to Request Protected Health Information

The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Research Collaborators
- Others as Required by Law
- Institutional Review Boards

Authority to Release Protected Health Information

The VCU Medical Center (VCUMC) may release the information identified in this authorization from my medical records and provide this information to:

- Others as Required by Law
- Research Collaborators
- Principal Investigator and Research Staff
- Institutional Review Boards

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released

The following types of information may be used for the conduct of this research:

☐ Complete health record ☐ Diagnosis & treatment codes ☐ Discharge summary

☐ History and physical exam ☐ Consultation reports ☐ Progress notes

☐ Laboratory test results ☐ X-ray reports ☐ X-ray films / images

☐ Photographs, videotapes ☐ Complete billing record ☐ Itemized bill

☐ Information about drug or alcohol abuse ☐ Information about Hepatitis B or C tests

☐ Information about psychiatric care ☐ Information about sexually transmitted diseases

X Other (specify): self-reported anxiety symptoms

Expiration of This Authorization

☒ This authorization will expire when the research study is closed, or there is no need to review, analyze and consider the data generated by the research project, whichever is later.

Right to Revoke Authorization and Re-disclosure

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator named above or in the Informed Consent document.

BENEFITS TO YOU AND OTHERS
You may not get any direct benefit from this study, but, the information we gain from people in this study will help to inform future studies so that we can develop interventions to help improve the lives of menopausal women.

COSTS
There are no costs for participating in this study other than the time you will spend in the interview and your transportation.

PAYMENT FOR PARTICIPATION
You will receive a $10 gift card to a local business after completion of the interview.

CONFIDENTIALITY
Potentially identifiable information about you will consist of an audio recording of the interview. Email and/or a phone number may be collected for contact purposes only and will be kept separate from the data using a code key. The code key will be destroyed after completion of the study or at the time required by VCU to maintain data has elapsed, whichever is longer.
Your data will be identified by ID numbers, not names, and stored separately from research data in a locked research area. All personal identifying information will be kept in password protected files and these files will be deleted after the study is complete or at the time required by VCU to maintain data, whichever is longer. Access to all data will be limited to study personnel.
The interview will be audio recorded. The recordings and the investigator's notes will be stored in a locked cabinet. The recordings will be stored until completion of the study or until the time required by VCU to maintain data has elapsed, whichever is longer. The recordings will be erased at that time.

Information from the study and the consent form signed by you may be looked at or copied for research or legal purposes Virginia Commonwealth University. Personal information about you might be shared with or copied by authorized officials of the Department of Health and Human Services or other federal regulatory bodies.

If something we learn through this research indicates that you may intend to harm yourself or others, we are obligated to report that to the appropriate authorities.

What we find from this study may be presented at meetings or published in papers, but your name will not ever be used in these presentations or papers.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
You do not have to participate in this study. Refusal to participate will involve no penalty or loss of benefits. If you choose to participate, you may stop at any time without any penalty or loss of benefits to which you are otherwise entitled. You may also choose not to answer particular questions that are asked in the study.

Your participation in this study may be stopped at any time by the study staff without your consent. The reasons might include:

- the study staff thinks it necessary for your health or safety;
- you have not followed study instructions; or
- administrative reasons require your withdrawal

QUESTIONS
If you have any questions, complaints, or concerns about your participation in this research, contact:

Eleanor S. Bremer, MSN, RN, NP-C
Virginia Commonwealth University School of Nursing
P. O. Box 980567
Richmond, VA 23298
P: 804-356-8914
E: bremeres@vcu.edu

Nancy Jallo, Ph.D., RNC, FNP-BC, WHNP-BC, CNS
Associate Professor
Department of Family and Community Health Nursing
Virginia Commonwealth University School of Nursing
PO Box 980567
Richmond, VA 23298
P: 804-828-3365
E: njallo@vcu.edu

The researcher/study staff named above is the best person(s) to contact for questions about your participation in this study.

If you have any general questions about your rights as a participant in this or any other research, you may contact:

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
P.O. Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk with someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

CONSENT

I have been given the chance to read this consent form. I understand the information about this study. Questions that I wanted to ask about the study have been answered. My signature says that I am willing to participate in this study. I will receive a copy of the consent form once I have agreed to participate.

Participant name (Printed)	Participant signature	Date

Name of Person Conducting Informed Consent Discussion/Witness (Printed)

Signature of Person Conducting Informed Consent Discussion/Witness	Date

Principal Investigator Signature (if different from above)	Date

Appendix H

VCU IRB Approval# HM20010855

INTERVIEW GUIDE

I'm interested in anxiety in menopausal women

1. Tell me a little bit about yourself.
    - Age
    - Age of onset of menopause
    - Relationship status
    - Family
    - Employment (full-time/part-time)
    - Type of Work
    - Health Insurance Status

2. Tell me about your anxiety experience in menopause.

    - associated symptoms
    - onset
    - duration
    - severity
    - timing
    - seasonal variability
    - triggers

3. How has the anxiety affected your life?

    - Relationships
    - Socializing
    - Job
    - Daily functioning
    - Sleep

4. What have you tried to manage it?

    - Medications
    - Discussion with health care provider
    - Lifestyle change
    - Supplements – over the counter
    - Psychotherapy

5. Is there anything else you think I should know?

6. What would you like others to know about anxiety in menopause?

    - Health care providers
    - Women
    - Society in general

Vita

Eleanor Susan Bremer was born on January 22, 1958, in Pittsburgh, Pennsylvania and is an American citizen. She graduated from Lakeview High School, Battle Creek, Michigan in 1975. She earned an Associate in Applied Science in Nursing from J. Sargeant Reynolds Community College, in 1994. She worked as a registered nurse in community hospitals focusing on the care of women and children. She went on to receive a Bachelor of Science in Nursing from Virginia Commonwealth University in 2001 and continued work as a registered nurse in the community. In 2012, Eleanor graduated from the University of Virginia with a master's degree in nursing and became certified as a family nurse practitioner through the American Academy of Nurse Practitioners and has worked in various primary care settings for the last five years.