

PERSONALITY AS A PREDICTOR OF BIOPSYCHOSOCIAL OUTCOMES IN WOMEN
WITH NON-METASTATIC ENDOMETRIAL CANCER

By

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To the women affected by endometrial cancer

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Abstract of Thesis Presented to the Graduate School
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Personality traits, such as low Neuroticism, high Extraversion, and high Openness to Experience, are characteristic of individuals who can positively adapt in the face of adversity. Among individuals with cancer, these traits are associated with better mood, higher quality of life (QOL), and lower pain. However, few studies have examined personality as a predictor of biopsychosocial outcomes in gynecologic cancers. This study examined relations between personality and (a)perceived stress/mood, (b)pain/cancer-related QOL, and (c)cortisol among women undergoing surgery for endometrial cancer (EC).

Fifty-one women (Age $M=61.25$ yrs, $SD=9.02$ yrs) with EC completed measures of personality, stress/mood, pain/QOL, and collected salivary cortisol samples at pre- and post-operative time points. Data was analyzed using multiple hierarchical regressions.

As expected, greater Neuroticism was associated with negative outcomes such as higher perceived stress (Preop $\beta=.43$, $p<.001$; Postop $r=.51$, $p<.001$), depression (Preop $r=.33$, $p=.021$), anxiety (Preop $r=.30$, $p=.037$), guilt (Preop $r=.48$, $p<.001$; Postop $r=.53$, $p<.001$), anger (Preop $\beta=.52$, $p<.001$; Postop $\beta=.46$, $p<.001$), and pain (Postop $r=.47$, $p=.001$). Greater Openness was associated with higher post-operative affection

($r=.35$, $p=.021$), and less post-operative perceived pain severity ($r=-.27$, $p=.08$) and pain interference ($r=-.34$, $p=.035$), but was also associated with higher anxiety (Preop $r=.33$, $p=.019$; Postop $r=.34$, $p=.02$). Extraversion was not significantly associated with any outcomes examined.

Although based on a small sample, these findings support the hypothesis that personality traits, particularly Neuroticism, may predict some peri-operative biopsychosocial outcomes in women with EC. Future research should examine whether interventions modifying cognitions/behaviors among individuals with high Neuroticism can promote more positive perisurgical outcomes among women with endometrial cancer.

CHAPTER 1 INTRODUCTION

Epidemiology and Treatment of Endometrial Cancer

Endometrial cancer (EC) is a type of uterine cancer that affects the lining of the uterine corpus (endometrium). Although the disease occurs mostly in postmenopausal women (65 years and older), it can occur even earlier, particularly among women with hereditary cancer syndromes that predispose them to endometrial cancer (Ries et al., 2004). Affecting approximately 589,887 women in the US in 2009, endometrial cancer has become the 4th most common cancer among women and is currently the most common gynecologic cancer in the United States (Howlander et al., 2011). The American Cancer Society (2013) estimates that an additional 49,960 new cases will emerge in 2013 with approximately 8,190 deaths from endometrial cancer, ranking endometrial cancer as the 8th leading cause of cancer-related deaths among women and the 2nd deadliest gynecologic malignancy. Despite these statistics, there still remains very little research on endometrial cancer.

Treatment for Stage I (confined to the uterus) endometrial cancer consists mainly of surgical removal of the uterus, ovaries, and fallopian tubes, also known as total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) (NCCN, 2013). However, treatment of endometrial cancers that are more invasive at Stage II (spread to uterus and cervix) and Stage III (spread to outside of the uterus but not beyond the true pelvis area) may involve additional neo-adjuvant treatment such as radiation and/or chemotherapy (NCCN, 2013). By Stage IV (spread to inner surface of the bowel, bladder, abdomen, or other organs), metastasis has already occurred and treatment will usually not involve surgery, but rather solely radiation and/or chemotherapy.

The Biopsychosocial Model of Health and Disease

The biopsychosocial model, originally developed by Dr. George Engel (1977), posits that the combination of biological, psychological, and social factors play a significant role in the context of health and disease. More specifically in cancer, Antoni and colleagues (2006) have adapted this model to describe the mechanisms by which biobehavioral factors may impact tumorigenesis. Specifically, they posit that stress-related changes in mood can influence cancer initiation, progression, and recurrence via dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and neuroendocrine functioning. This dysregulation may then result in poorer quality of life (QOL) and clinical outcomes (i.e. shorter survival) among individuals with cancers, including gynecologic malignancies (Antoni et al., 2003). Therefore, it becomes important to study the combination of biopsychosocial factors that may affect cancer treatment and recovery.

Biobehavioral Factors and Cortisol

Cortisol is a glucocorticoid stress hormone. High perceived stress has been associated with more dysregulated cortisol output in individuals with cancer (Abercrombie, 2004). The cortisol is produced by the adrenal cortex and released by activation of the HPA axis, which is the primary biological pathway through which psychological factors affect the immune system (Haddad, Saade, & Safieh-Garabedian, 2002). Typical diurnal cortisol rhythms in healthy individuals under unstressed conditions are usually characterized by higher levels of cortisol output in the morning and lower levels in the evening. This pattern usually creates a negative slope. During acute stress, cortisol levels can rise and stay high throughout the course of the day, which is illustrated by a more positive slope. Under conditions of chronic stress, the HPA system may become worn out and fatigued, resulting in a blunted or abnormal trough, which is illustrated by a flattened slope. Figure 1-1 illustrates examples of these various diurnal cortisol rhythms.

Flattened diurnal cortisol rhythms are one of the markers of allostatic load, defined as the physiological accumulation of the effects of chronic stress. These abnormal cortisol rhythms have been shown to predict shorter survival, even among individuals already diagnosed with metastatic cancer. In fact, Abercrombie and colleagues (2004) revealed that a deviation from normal diurnal cortisol patterns can predict early mortality in metastatic breast cancer at least seven years later. In their sample, women with metastatic breast cancer had significantly flatter diurnal cortisol slopes when compared to healthy controls. Those with greater disease severity also had higher mean cortisol output and tended to have flatter cortisol rhythms. Therefore, divergence from typical diurnal cortisol patterns can be associated with negative outcomes such as increased tumor growth and early mortality (Sephton, Sapolsky, Kraemer, & Spiegel, 2000; Filipski et al., 2002).

Health-Related Quality of Life (QOL) and Cancer Survival

In addition to the biological factors, such as cortisol, that may relate to survival in cancer, psychosocial factors, such as quality of life, have also been associated with survivorship. Treatment modalities such as surgical and neo-adjuvant techniques have significantly increased the survivorship of patients with gynecologic malignancies. Women with gynecologic cancers are now living longer than they did in the past, making QOL issues even more important in this population (Lai, Tang, & Chung, 2010). In fact, many of the cancer drug approvals made by the US Food and Drug Administration now require clinical trials to showcase more direct evidence of clinical benefit that include improvements in QOL (FDA, 2007).

By definition, health-related quality of life (Hr-QOL) is a person's subjective measure of his/her health status that encompasses the areas of physical, psychological, and social well-being, all of which can be affected by cancer diagnosis and treatment (Robinson, Christensen, Ottesen, & Krasnik, 2012). Physical Well-Being (PWB) is often regarded as

the ability to perform activities of daily living, and includes physical symptoms (e.g. pain) as a result of disease or treatment. Emotional Well-Being (EWB) encompasses distress (e.g. stress, anxiety, depression, etc.), sense of well-being, and cognitive functioning. Social Well-Being (SWB) refers to both the qualitative and quantitative aspects of relationships, interactions, and integrations (Schwartz & Sprangers, 2002).

Although tumor size has often been a predictor of mortality, some studies have shown Hr-QOL to be an independent predictor of survival (Schwartz & Sprangers, 2002). In a sample of 150 women diagnosed with ovarian cancer, Carey and colleagues (2008) found that higher quality of life prior to chemotherapy treatment significantly predicted disease-free survival of up to two years after treatment. Similarly, Sarenmalm and colleagues (2009) found that higher physical well-being prior to treatment significantly decreased the chance for breast cancer reoccurrence after 1 year. These findings suggest that if Hr-QOL can be improved, particularly during the peri-operative treatment period, survivorship may be improved, as well.

Individual Differences in Cancer Outcomes

It is important to note that not all cancer patients will experience a poor Hr-QOL; some may not experience any clinically significant mood changes or perceived pain and may have relatively similar diurnal cortisol rhythms during the course of their treatment. For example, in 1994, Kornblith and colleagues conducted a study involving 151 women with ovarian cancer. Thirty-three percent of their sample experienced moderate to severe levels of anxiety and depression, but 22% reported little to no symptoms. It is plausible that variability in these responses may be at least partially due to individual differences in personality traits. Specifically, it is possible that personality traits may either buffer or exacerbate negative mood states among women undergoing cancer-related stress. Literature exploring this possibility is discussed below.

Personality and Cancer Resiliency

Resiliency, although defined in many ways, has most commonly been described as a dynamic process of positive adaptation in the face of significant adversity (Luthar, Cichetti, & Becker, 2000). During this process, healthy levels of psychological functioning are maintained despite the emergence of life-threatening events (Bonnano, 2004). Therefore, individuals who are highly resilient are known to have faster recovery and less symptomology after a trauma (Friborg, Barlaug, Martinussen, Rosenvinge, & Hiemdal, 2005). It is important to note that this does not necessarily mean there is an absence of psychopathology; in fact, resilient individuals can experience disturbances in functioning for several weeks, but the key lies in their ability to recover and maintain a stable trajectory while emerging with positive emotions (Hou, Law, Yin, & Fu, 2010).

Interest in the role of resiliency on cancer adjustment has resulted in investigating the trajectory of cancer adaptation. Using Bonnano's model of adjustment (Bonnano, 2004), four distinct patterns emerge in response to a trauma: 1) chronic distress (characterized by persistent high levels of distress and a disruption of normal functioning), 2) recovery (characterized by short-lived disruption of functioning such that a change from initial high levels of distress to normative levels of distress is present), 3) delayed distress (characterized by initial normative distress followed by a rise in high levels of distress), and 4) resilience (characterized by normative psychological functioning falling below the cutoff for clinical distress and with little to no disruption of functioning). In general, the majority of individuals (36-55%) will follow a resilient trajectory and rarely, less than 10% of individuals will follow a delayed distress trajectory (Hou et al., 2010). These general guidelines have been supported in various studies examining the trajectory of breast cancer recovery. In a sample of 285 women diagnosed with breast cancer, 66% reported little to no distress throughout their peri-operative treatment trajectory and appeared to be psychologically

“resilient.” Still, 15% reported chronic psychological distress, 7% were characterized as delay-recovered, and 12% were recovered (Lam et al., 2010). Thus, although the majority of individuals follow a resilient trajectory, there is still a subset of individuals who will experience clinically significant distress at some point during their cancer recovery. If these at-risk individuals could be better identified, it may be possible to minimize risk for poor adjustment and promote a higher overall health related quality of life and well-being.

Emerging research has identified associations between personality and resiliency. Specifically, based on the personality traits from the Big Five model, high resiliency has been associated with low Neuroticism, high Extraversion, high Openness to Experience, and high Conscientiousness among the individuals affected by the 1999 Kosovo crisis (Rioli, Savicki, & Cepani, 2002). In fact, there has been accumulating support for applying the Big Five measure to cluster individuals into well adjusted (resilient) and more vulnerable groups (Aspendorf, Borkenau, Ostendorf, & van Aken, 2001; Rammstedt, Riemann, Angleitner, & Borkenau, 2004). These results provided evidence for building a resilient personality profile characterized by low Neuroticism; and high scores on Extraversion, Openness to Experience, Conscientiousness, and Agreeableness. However, because literature for relations between personality and resilience in the cancer population is sparse, this study examined the three most studied personality traits in the resilience literature: Neuroticism, Extraversion, and Openness to Experience.

Neuroticism (N)

Neuroticism is a factor of particular interest to clinicians. Individuals high in Neuroticism tend to experience more negative affect such as sadness, guilt, and anger compared to those low in Neuroticism. They are also more prone to having irrational ideas, less able to control their impulses, and more poorly cope with stress (Costa & McCrae, 1992). Although individuals scoring high in Neuroticism may be at risk for psychiatric problems such as

depression, it is important to remember that N is a dimension on the NEO-FFI, which measures normal personality. Therefore, it is possible that individuals can score high in Neuroticism and not have a diagnosed disorder.

In a study by Furnham and colleagues (1997), 160 managers completed the NEO-PI (measure of personality) and were rated by psychologists on a number of measures that included resilience. Results revealed that high Neuroticism was strongly correlated with low resilience ($r=-0.71$, $p<.001$). In 2005, Friberg and colleagues created a resilience scale for adults (RSA) and tested its relationship with personality traits from the NEO-PI on a sample of 482 participants. Similar to Furnham and colleagues (1997), they found that high Neuroticism was strongly correlated with low resilience on subscales of the RSA ($r=-.79$ to $-.57$, $p<.001$).

Extraversion (E)

Another defining feature of resiliency is having a positive social orientation toward others. Resilient individuals tend to have good social skills, thrive in social contexts, and leave a positive impression of themselves (Werner, 2001). In other words, these individuals are high in Extraversion (Friberg et al, 2005). Individuals scoring high in Extraversion tend to be very social; prefer to be in large groups; and are assertive, active, and talkative. They are usually upbeat, energetic, and optimistic (Costa & McCrae, 1992). However, not all sub-facets of Extraversion are related to resilience. "Sociability" fits well with the concept of resiliency (Werner, 2001) but not "Competitiveness," as the latter tends to keep others at distance (Friberg, 2005). Still, others argue that "Competitiveness" may not always be viewed as negative either, as high levels of drive and energy found in "Competitiveness" have also been found to increase coping capacity (Cederblad, Dahlin, Hagnelt, & Hansson, 1995).

Openness to Experience (O)

Individuals who are highly Open to Experience are generally creative and unconventional; they are curious about both their inner and outer worlds, and experience both positive and negative emotions more strongly than individuals low in Openness (Costa & McCrae, 1992). Although Openness to Experience as a broad domain has not been associated with resiliency, sub-facets such as “Feelings” ($r=-.26, p<.001$), “Aesthetics” ($r=.21, p<.001$), and “Fantasy” ($r=-.18, p<.01$) have been associated with this construct (Furnham et al., 1996).

Personality and Biopsychosocial Outcomes in Cancer

Using the Lazarus and Folkman (1984) Stress and Coping Model, it has been hypothesized that individual differences can contribute to different health outcomes, especially under stressful conditions. In fact, they proposed that in addition to optimism and coping styles, personality factors may play a part in altering effects of stressful events through appraisal (perception) and stress reduction. For instance, diagnosis of endometrial cancer may meet criteria as a “stressor” that is perceived or “appraised” as challenging and may require the individual to change/adapt in order to survive. This “primary appraisal” can be considered a stressor and may induce stress responses that may accompany the perception, often called a “secondary appraisal” that current coping resources are not available or adequate and hence, result in a perception of a lower Hr-QOL. Using this model, personality traits may operate as either a psychological resource or liability during the stress and coping process (Lai et al., 2010). Thus, it may be important to examine how personality traits affect biopsychosocial outcomes in the cancer population.

Quality of Life

Neuroticism is one personality traits that has been widely studied. In a meta-analysis, Steel and colleagues (2008) found that personality played a much more influential role in determining an individual's QOL than previously thought. In a sample of 184 women diagnosed with gynecologic cancer, Lai and colleagues (2010) discovered that higher Neuroticism at baseline significantly predicted lower QOL in the areas of both PWB and EWB up to one year later. In 2007, van Straten and colleagues examined the relationship between personality traits and Hr-QOL in a sample of 640 medical outpatients with mood and anxiety disorders. They found that individuals scoring high in Openness to Experience surprisingly scored lower in Hr-QOL. However, higher Neuroticism was consistently associated with lower Hr-QOL, while higher Extraversion was associated with higher Hr-QOL. Most importantly, Neuroticism was found to be associated with Hr-QOL even after controlling for a diagnosis of mood and anxiety disorder (van Straten, Cuijpers, van Zuuren, Smits, & Donker, 2007), suggesting that the occurrence of mood/anxiety disorders may not fully account for the relationship between Neuroticism and Hr-QOL.

Perceived Stress

Perceived stress is an individual's subjective interpretation of the negative impact of stressors, such as a chronic illness, death of a family member, or financial stressors. Lillberg and colleagues (2003) found a significant hazard of breast cancer at five years per one-event increase in the total number of major life events experienced among a large Finnish cohort. Consistent with the Antoni model (2006), women with higher chronic stress have a greater expression of neuroendocrine and immune factors that lead to tumor progression in ovarian cancer (Lutgendorf et al., 2008). On the other hand, Nielson and colleagues (2007) found contradicting relationships; in a sample of 6760 Danish women, greater stress was associated with a lower risk for endometrial cancer, particularly among

women undergoing hormonal therapy and having normal weight. However, it is important to note that the biobehavioral factors impacting cancer initiation may be different from those influencing cancer progression (Antoni et al., 2006). Nonetheless, high perceived stress is a common and distressing experience among cancer patients, and as such, is an important factor to assess/treat in the clinical care of cancer. Notably, in its relation to personality, high levels of Neuroticism have been associated higher perceived stress (Horner, 1995), though this has not been tested in the cancer population yet.

Mood/Affect

Primary and secondary appraisals of a diagnosis of cancer, a stressor, may elicit significant distress (Lazarus and Folkman, 1984). One of the most common affective symptoms reported by cancer patients are feelings of depression (van't Spiker, Trijsburg, Duivenvoorden, 1997). Not only have depressive symptoms been associated with lower QOL, they may also lead to poorer treatment compliance (DiMatteo, Lepper, & Croghan, 2000) and increased risk for disease recurrence (Watson, Haviland, Greer 1999). In a sample of 210 women diagnosed with breast cancer, higher levels of Neuroticism were found to significantly correlate with more depressive symptoms (Golden-Kreutz & Anderson, 2004). Similarly, in 2006, Chochinov and colleagues identified a highly significant positive correlation between Neuroticism and level of depression in participants with terminal cancer. At least one study has found that the relationship between Neuroticism and depression in cancer is not moderated by financial difficulty, global stress levels, and cancer-related traumatic stress symptoms (Golden-Kreutz & Anderson, 2004). This suggests that there may be a more direct relationship between Neuroticism and depression in cancer.

Pain

Pain can be an adverse treatment-related side effect in patients with cancer that can significantly impair overall Hr-QOL and PWB. Early intervention/application of pain management skills can be especially useful in cancer patients, primarily before opioids are used (Vissers et al., 2011). In addition to being associated with mood/affect in cancer patients, personality traits may also be related to pain perceptions in cancer. Specifically, high levels of Neuroticism have been significantly correlated with high levels of perceived pain in patients with terminal cancer (Chochinov et al., 2006).

Cortisol

Relatively few studies have examined the relation between cortisol and measures of personality, especially in the cancer population. Vedhara and colleagues (2006) examined cortisol output in a sample of 85 women newly diagnosed with breast cancer. In a series of linear regressions examining the role of psychosocial variables (e.g. anxiety, depression, distress, and personality) in predicting cortisol outcomes, only Neuroticism significantly predicted early morning cortisol output, such that individuals with high Neuroticism had lower early morning cortisol peaks. As mentioned previously, a blunted early morning cortisol peak is typical of a flattened slope that is frequently noted under conditions of chronic, high stress levels. This finding suggests that individuals high in Neuroticism may be at risk for a more dysregulated diurnal cortisol rhythm. To the extent that flattened cortisol rhythms are associated with more advanced disease and earlier mortality in cancer, this also suggests that high Neuroticism may predict compromised clinical outcomes in cancer.

Gaps in the Literature

Much of the current research studied on resiliency has primarily focused on trauma in the context of a war, natural disaster, or personal loss of a beloved family member (Cicchetti et al., 2000; Riolli et al., 2002); relatively little research has been conducted in the context of cancer. These studies have been performed primarily in breast cancer samples (Lam et al., 2010), and virtually none have been conducted in endometrial cancer. In addition, these studies have not conceptualized resilience in terms of its characteristic personality traits. Relationships between personality and resilience have been studied even less; existing research consists of the working population to help employers assess for well-rounded employees (Furnham et al., 1996; Friberg et al., 2005). In addition, the studies examining relationships between personality and biopsychosocial outcomes have mostly been focused on Neuroticism (Golden-Kreutz et al., 2004; Chochinov et al., 2006; Lai et al., 2010), but information describing relationships involving the other Big Five personality traits such as Extraversion and Openness to Experience are rare, especially in the context of cancer.

Current Study

The purpose of this study was to address the aforementioned criticisms and gaps in the literature on cancer resiliency by exploring the relationship between personality and biopsychosocial factors in women diagnosed with endometrial cancer. Specifically, this study examined the relationship between personality traits and biopsychosocial factors, including stress, mood, pain, quality of life, and cortisol rhythm at both pre- and post-operative timepoints. It was hypothesized that individuals with personality traits associated with high resiliency (low Neuroticism, high Extraversion, high Openness to Experience, high Agreeableness, and/or high Conscientiousness) in prior published literature would have better biopsychosocial outcomes across both time points (pre- and post-surgery). However, because most of the published literature on this topic has been conducted using

Neuroticism, Extraversion, and Openness to Experience as predictors, primary analyses focused on the relationships between these three personality traits (N, E, O) and biopsychosocial outcomes. As a result, the following specific aims were explored:

Specific Aim 1: To identify the relationship between personality traits associated with high resiliency and stress/mood at pre- and post-operative timepoints.

Hypothesis: Participants with low Neuroticism, high Extraversion, and/or high Openness to Experience will experience:

1a: less perceived stress at pre- and post-operative timepoints.

1b: less depressive and anxious mood symptoms at pre- and post-operative timepoints.

1c: less guilt, anger, and more affection at pre- and post- operative timepoints.

Specific Aim 2: To identify the relationship between personality traits associated with high resiliency and pain/cancer related quality of life at pre- and post- operative timepoints.

Hypothesis: Participants with low Neuroticism, high Extraversion, and/or high Openness to Experience will experience:

2a: less pain at pre- and post- operative timepoints.

2b: better Hr-QOL at pre- and post- operative timepoints.

Specific Aim 3: To identify the relationship between personality traits associated with high resiliency and diurnal salivary cortisol rhythm at pre- and post- operative timepoints.

Hypothesis: Participants with low Neuroticism, high Extraversion, and/or high Openness to Experience will experience:

3a: more normal diurnal salivary cortisol slopes at pre- and post- operative timepoints.

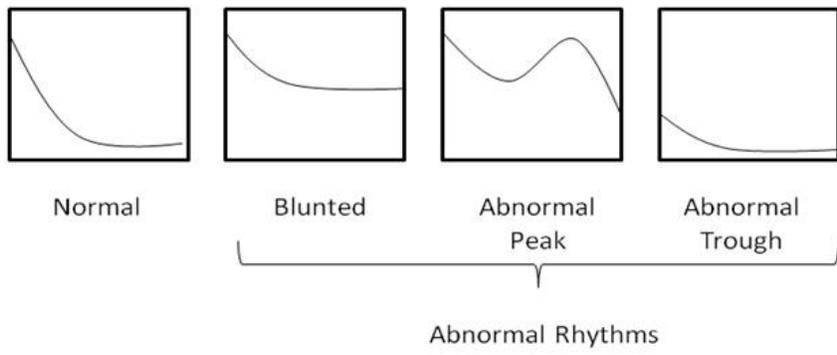


Figure 1- 1. Illustration of various diurnal cortisol rhythms

CHAPTER 2 METHODS

Design

This current study utilized a nonexperimental, longitudinal design. Specifically, participants provided psychosocial data immediately prior to surgery for suspected endometrial cancer, as well as 6-8 weeks after surgery. During these two time points (pre- and post-surgery), participants also collected saliva samples four times a day for three consecutive days.

Participants

Participants for this study included 51 women with complete personality data using the NEO-FFI (Costa & McCrae, 2002). Data were drawn from a larger parent study (N=134) jointly funded by the American Cancer Society and the National Cancer Institute (PI: Deidre Pereira, PhD. RO3 CA 117480) between 2004 and 2009. However, administration of the NEO-FFI was not integrated into the protocol until 2007, and therefore, the sample size for the current study includes the 51 participants enrolled from this point forward.

Inclusion criteria for the parent study were: (a) women with suspected primary non-metastatic endometrial cancer (Stages I-III) at age 18 or older, (b) undergoing surgery for a TAH-BSO, and (c) fluent in English. Exclusion criteria were: (a) diagnosis of metastatic, recurrent, or secondary endometrial cancer, (b) undergoing chemotherapy or radiotherapy prior to surgery, and (c) a current psychotic disorder or suicidal intent. As noted above, women included in this sub-study were selected if they completed the NEO-FFI.

Procedures

Pre-Operative Timepoint (1 week prior to surgery)

Participants for this study were recruited from the Gynecologic Oncology Clinic at the University of Florida. Women who were potentially eligible for participation were identified

during their initial consultation visit with the help of a team of physicians, residents, and nurses. If the patient expressed interest in study participation to the medical staff, she would meet with a trained member of the research team to discuss study procedures and address subsequent questions and concerns. Once the patient confirmed she was interested in participating, the patient read and signed the IRB-approved Informed Consent form. After consent was given, the participant underwent a brief psychiatric screening assessment to rule out the exclusion criteria of a psychotic disorder or suicidal ideation. If no psychosis or suicidality was found, the participant would receive psychosocial questionnaires to complete prior to their pre-surgical appointment, as well as instructions on collecting salivary cortisol samples for the three days prior to their pre-operative appointment.

At the pre-operative appointment, trained members from the research team met with the patient and collected the completed questionnaires and salivary cortisol samples. A psychosocial interview was also given in one of the private clinic rooms. Upon completion of the interview and collection of the questionnaires, participants were provided \$20 as compensation for parking and transportation expenses. All study procedures were conducted in accordance with the rules and regulations of the University of Florida IRB.

Post-Operative Timepoint (6 to 8 weeks after surgery)

Two weeks prior to their post-operative appointment, participants were mailed a salivary cortisol collection kit. This kit was identical to the one that was provided at their pre-operative appointment and instructions remained the same. Members from the research team met with the participant at their post-operative appointment to collect the saliva samples, which were then transported to the College of Nursing's laboratory and placed in the freezer storage for analyses. A medical chart review was also conducted to gather diagnosis and biobehavioral control variable data such as age, medication

use, and post-operative complications. In addition, participants completed psychosocial measures that were identical to the ones given at the pre-operative appointment (interview and self-report questionnaires). Upon completion of their visit, participants were provided \$20 as compensation for parking and transportation expenses.

Screening Assessment

Suicidality

Presence and severity of suicidal ideation was assessed using the Beck Scale for Suicide Ideation (BSS; Beck, Steer, & Ranieri, 1988). This self-report measure consisted of a 21 items that have been with well-established validity and sensibility. Coefficient alphas range from .87-.90 and concurrent validity of the BSS demonstrated moderate to high correlations with other measures of suicidal constructs (Beck et al., 1988; Cunha, 2001). Although it has been used extensively among inpatient and outpatient psychiatric populations, recent studies have also used the BSS as a screening tool among cancer populations (Madeira, Albuquerque, Santos, Mendes, & Roque, 2011).

Psychoticism

Symptoms of psychosis were measured using the Psychotic Screening Module of the Structured Clinical Interview for DSM-IV for non-clinical populations (SCID-IV-NP; First, Spitzer, Gibbon, & Williams, 1996). This measure is a semi-structured interview for making DSM-IV diagnoses in non-psychiatric populations. It has been used widely as a brief screening measure of psychotic disorders among patients with medical illness, such as HIV (Penedo et al., 2003).

Demographic characteristics

Race (Caucasian, African-American, Asian, or other) and ethnicity (Hispanic or non-Hispanic) were assessed using the MacArthur Sociodemographic Questionnaire (MSQ; Adler, Epel, Castellazzo, & Ickovics, 2000). Although the MSQ also assesses socioeconomic status, for purposes of this study, only race and ethnicity were analyzed as variables potentially associated with mood and pain level.

Medical Chart Review

A medical chart review was completed to gather information about age and medical diagnosis (tumor stage and type). In addition, body mass index (BMI), length of hospital stay after surgery, presence of acute post-operative complications (yes/no), presence of wound healing complications following discharge from surgery (yes/no), and prescription of opioid pain medications upon hospital discharge (yes/no) were collected and examined as potential control variables that could affect mood and level of pain.

Substance Use

Use of prescribed and/or illicit psychoactive substances during salivary cortisol collected was gathered using the Recent Health Behaviors (RHB) questionnaire. This self-report instrument assesses the use of cannabis, cocaine/amphetamines, hallucinogens, opioids, sedatives/hypnotics/anxiolytics, and inhalants during the three days of saliva collection. This information was gathered because psychoactive substance use may affect levels of cortisol output (Nakajima, al'Absi, Kumar, Wittmers, & Scott, 2013). However, examination of the data revealed that no participants reported any use the above substances on the RHB. Therefore, substance was not examined as a control variable.

Psychosocial Assessment

Personality

Personality traits were assessed using the NEO Five Factor Inventory Form (NEO-FFI, Form S-Adult; Costa & McCrae, 1992). This is self-report measure is based on the five-factor model of trait personality and assesses Neuroticism, Extraversion, Openness to Experience, Agreeableness and Conscientiousness (McCrae & Costa, 2002). The NEO-FFI is comprised of 60 items. Individuals rate the degree to which they believe each statement describes them using a five-point Likert scale ranging from “strongly agree” to “strongly disagree.” NEO-FFI items were derived by Costa & McCrae from a factor analysis of the 1986 administration of the NEO-Personality Inventory (NEO PI-R; Costa & McCrae, 1992) and are considered to be useful in research populations when time availability for testing is limited, and global information on personality is sufficient (Klee & Machin, 1992; Costa & McCrae, 2002). Correlations between the NEO PI-R and NEO-FFI ranged from .75 to .89.

Each of the five personality domains are comprised of 12 items. Each of these 12 items are summed and transformed into T-scores, which allow categorization of personality traits from “very low” (T-scores ≤ 44) to “very high” (T-scores ≥ 56). Examples of NEO-FFI items include: “When I’m under a great deal of stress, sometimes I feel like I’m going to pieces”(Neuroticism), “I like to have a lot of people around me”(Extraversion), “I often enjoy playing with theories or abstract ideas”(Openness to experience), “I try to be courteous to everyone I meet”(Agreeableness), and “I have a clear set of goals and work toward them in an orderly fashion”(Conscientiousness). Internal consistency of the 12 items for each of these domains has been demonstrated (Cronbach’s alpha = .73-.86) and considerable empirical support has also been shown across cultures (Costa & McCrae, 1992; McCrae & Costa,

2002). Missing values were given a response score of 3 (“neutral”), as recommended in the NEO-FFI manual.

Perceived Stress

Perceived stress was assessed using the Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983), a 14-item self-report scale used to measure an individual's appraisal (perceptions) of situations as stressful during the week prior to surgical evaluation and the week prior to their post-operative appointment. Participants rated the frequency of these feelings, cognitions, and situations on a 5-point scale (0 = never; 4 = very often). Examples of these items include: “In the last week, how often have you felt nervous and stressed?” and “In the last week, how often have you felt that you were unable to control the important things in your life?” Several items were reverse scored so that higher ratings corresponded to greater perceived stress. Ratings were summed to yield a total perceived stress score, with higher scores indicating greater perceptions of stress. Items demonstrated good internal validity in the present study (Cronbach's alpha = 0.78-0.87).

Depressive and Anxious Symptomatology

Depression and anxiety were assessed using the Structured Interview Guide for the Hamilton Anxiety/Depression Scales (SIGH-AD) (Williams, 1988), which assessed symptoms of depression and anxiety over the past week. This measure is a semi-structured interview based on the Hamilton Anxiety Scale and the Hamilton Depression Scale and has been used in the past with medical populations (Cruess et al., 2000). The present study used an abbreviated version that consisted of a 15 item depression subscale and a 9 item anxiety subscale that excluded items plausibly associated with endometrial cancer symptomatology. Examples of these items include: “Have you been

feeling down or depressed? Sad or hopeless?” (Depression subscale), “How much have you been worrying about the worst that can happen, or been afraid of what’s going to happen?” (Anxiety subscale). This abbreviated version of the SIGH-AD demonstrated good concurrent validity with the Affects Balance Scale (ABS; Derogatis, 1975) such that SIGH-AD anxiety scores were significantly correlated with anxiety on the ABS at both pre-operative and post-operative time-points, $r(40) = .62, p < .001$ and $r(41) = .31, p = .043$, respectively. Likewise, SIGH-AD depression scores were significantly correlated with depression on the Affect Balance Scale at pre-operative and post-operative time-points, $r(40) = .48, p = .001$ and $r(41) = .31, p = .043$, respectively. Scores were calculated by summing all anxious symptomology items and then all depressive symptomology items excluding items with scores potentially attributable to biological factors (non-organic depression). Scores for the anxiety subscale ranged from 0 (no anxious symptoms) to 29 (severe anxious symptoms); scores on the non-organic depression subscale ranged from 0 (no depressive symptoms) to 48 (severe depressive symptoms). Adequate internal consistency was identified for both domains (anxiety subscale Cronbach’s alpha = .77-.82; depression subscale Cronbach’s alpha = .80-.84).

Affect

The Derogatis Affects Balance Scale Revised (ABS; Derogatis, 1975) was used to measure affect experienced in the prior week and has demonstrated clinical utility and validity with medical populations, including in research among HIV infected women with cervical precancer (Jensen et al., 2005). This self-report measure consists of 40 affect terms. Subjects rated the frequency of each type of affect experienced over the prior week on a scale from 1 (“never”) to 5 (“always”). Domains included both negative and positive affect across 8 dimensions: Anxiety, Depression, Guilt, Anger, Joy,

Contentment, Vigor, and Affection. However, for the purposes of this analysis, only non-anxiety/depressive negative affect (Guilt and Anger) and Affection were examined, the latter of which was chosen to represent positive affect guided by prior research (Jensen et al., 2005). Items were averaged within each domain. The ABS demonstrated high internal consistency for the positive affect scales (Cronbach's alphas=.87-.90) and acceptable internal consistency for most of the negative affect scales (Cronbach's alphas=.62-.77).

Pain

Perceived pain was measured using the Brief Pain Inventory (BPI; Cleeland, 1991), which has been primarily used to assess patients with cancer-related pain and has demonstrated considerable validity and reliability, $r=.83-.93$, Cleeland et al., 1996. Patients rated their current pain intensity as well as their pain in the last 24 hours at its worst, least, and average using a numerical rating of 0 ("no pain) to 10 ("pain as bad as you can imagine"). Using the same scale from 0 to 10, patients also rated the extent to which their pain interfered with their quality of-life in the areas of general activity, walking, mood, sleep, work, relations with other persons, and enjoyment of life. These scales ranged from 0 ("does not interfere") to 10 ("interferes completely"). Thus, pain was measured in two domains: pain severity and pain interference. Items across each domain were averaged. High internal consistency was demonstrated for both the pain severity (Cronbach's alpha=.93-.94) and pain interference (Cronbach's alpha=.96).

Quality of Life

Quality of life was assessed using the Functional Assessment of Cancer Therapy for Endometrial Cancer (FACT-En). The FACT was developed specifically for use in cancer populations, particularly to assess Hr-QOL among patients receiving treatment (Cella et al.,

1993). The FACT-En is a 43-item questionnaire that assessed different domains of well-being, including physical, social, emotional, and functional well-being over the past week. Additionally, there is a subscale of items assessing physical concerns specific to endometrial cancer. Participants were asked to rate the extent to which each statement applied to them. Response choices are on a scale ranging from 0 (“not at all”) to 4 (“very much”). The minimum and maximum of possible scores range from 0 to 172 for global quality of life; the total raw sum score was used. For this analysis, only global quality of life was examined. Internal consistency was demonstrated at the pre-operative timepoint (Cronbach’s $\alpha=.72$), but was not optimal at the post-operative administration (Cronbach’s $\alpha = .48$).

Physiological Assessment

Saliva Collection and Storage

Saliva samples were collected at four time points (8 AM, 12 PM, 5 PM, and 9 PM) for 3 consecutive days prior to the participants’ pre-operative visit in the Gynecologic Oncology Clinic, which is standard for saliva collection (Sephton et al., 2000). Participants were instructed to collect saliva samples using a Salivette (Starstedt, Inc., Newton, N.C.), a cylindrical plastic tube containing a cotton roll. Participants were asked to place this cotton roll in their mouth and let it saturate with saliva for approximately 1-2 minutes. Additionally, for the 30 minutes prior to collection, participants were asked not to smoke, eat, drink, or brush their teeth, as this could interfere with the cortisol analysis. Participants were also asked to write the exact time of collection (if different from the given time points) and their stress ratings (0 – 10) on the Salivette tube.

To maximize adherence to the salivary cortisol collection procedures, participants were asked to wear a WatchMinder device (WatchMinder[®], Irvine, CA, www.WatchMinder.org) during the three days of salivary cortisol collection. This WatchMinder device is a digital, watch-like training and reminder system that can be worn on the wrist. The device was preprogrammed to vibrate at the appropriate collection times to remind the participant to collect samples. At each collection time, the device would vibrate and a code word appeared on the face of the device. Participants were asked to use the cryovial marker that was included in the saliva kit and label the tube with the code that appeared on the WatchMinder. If the code word was missing or incorrect, cortisol values for that specific time frame were excluded, as it could signal an adherence problem that would affect the validity of the results.

For each sample that was collected, participants were instructed to refrigerate them in the provided cooler bag and return them to our research team at the Gynecologic Oncology Clinic during their pre-operative visit. Once the samples were returned to the researchers, they were stored in a freezer maintained at -70 degrees Celsius. Batches of samples were then shipped to Salimetrics, Inc. (State College, PA), where they were assayed.

Quantitation of Salivary Cortisol

Salivary cortisol concentrations were assayed using an Enzyme-Linked Immunosorbent Assay (ELISA) kit (Salimetrics, Inc., State College, PA). This method is commonly used in laboratory settings and involves combining an antigen with an antibody linked to a highly sensitive enzyme for binding to take place. Finally, a substance is added to aid the enzyme's conversion, resulting in the formation of various complexes that are seen via the magnitude of emitted fluorescence. This magnitude is

read by a standard plate reader, which detects the optical density and determines cortisol levels based on the intensity of the color following the binding with the substrate tetramethylbenzidine. Assays were tested for sensitivity, each using 25 μ l of saliva, which resulted in a lower limit sensitivity of 0.003 μ g/dl and a standard curve range of 0.012 μ g/dL to 3.0 μ g/dL. Reliability was high, with an average intra-assay coefficient of variation of 3.5% and an average inter-assay coefficient of variation of 5.1%.

Operationalization of Cortisol

Cortisol slopes were generated by regressing cortisol concentrations at each collection time on the prescribed times of collection (8am, 12pm, 5pm, 9pm) or, as noted by the participant, on the actual time of collection. Slopes were represented by the unstandardized beta weights generated by these regression analyses and equaled the average change in cortisol per unit time. As per standard convention in the psychoneuroendocrinology literature, a steeper, negative cortisol slope (i.e., greater decrease in cortisol per unit time) indicated a more normal rhythm, whereas a flattened (i.e., smaller decrease per unit time) or positive slope (i.e., increase in cortisol per unit time) indicated more abnormal rhythms (Sephton et al., 2000).

Statistical Analyses

An a priori power analysis was conducted using PASS 11 statistical software (Hintze, 2011). Correlations between personality and biopsychosocial outcomes were drawn from published literature (e.g., Vedhara et al., 2006; Chochinov 2006; Horner 1996; Golden-Kreutz & Anderson, 2004) to estimate effect sizes. These effect sizes were used to determine the number of participants needed to obtain adequate statistical power (.80) with a two-tailed $\alpha = .05$.

The power analysis determined that when evaluating relationships between Neuroticism (evaluated using the Eysenck Personality tests) and perceived stress using an effect size $r=.55$ (Horner, 1996), a total of 23 participants would be needed. To evaluate relationships between Neuroticism and depression using an effect size $r=.44$ (Golden-Kreutz & Anderson, 2004), a total of 38 participants would be needed. Using the effect size $r=.44$ (Chochinov et al., 2006) found for relationships between Neuroticism and perceived pain (evaluated using the McGill Pain Inventory) in terminal cancer patients, it was determined that a total of 38 participants would be needed. Using the effect size $r=-.39$ (Lai et al., 2010) for relationships found between Neuroticism (measured using the Eysenck Personality Inventory) and Emotional-Well being (an aspect of QOL that was measured using the FACT-G; Functional Adjustment of Cancer Therapy - General) in gynecological cancer survivors, it was determined that a total of 49 participants would be needed. Using the effect size $r=-.25$ in the same study by Lai and colleagues (2010), for relationships found between Neuroticism and overall QOL, it was determined that 123 participants would be needed. Using the effect size $r=.38$ (Vedhara et al., 2006) for relationships found between Neuroticism and early morning salivary cortisol peak in breast cancer patients, it was determined that a total of 52 participants would be needed. Using the effect size $r=-.12$ (Vedhara et al., 2006) for relationships found between Extraversion and early morning salivary cortisol peak in breast cancer patients, it was determined that 571 participants would be needed. Effect sizes for the relation between personality and affect could not be located in the literature.

Given that 51 participants from the parent study had complete data on the NEO-FFI, it was determined that the study was adequately powered to detect significant relationships between Neuroticism and perceived stress, depression, anxiety, perceived pain, quality of life, and cortisol were adequately powered. It was determined that the study was not

adequately powered to detect significant relationships between Neuroticism and overall QOL. However, because this current study's measure of overall QOL was specific to endometrial cancer (FACT-En), rather than overall QOL as in the study by Lai and colleagues (2010), these analyses commenced with the caveat that they could be underpowered. In addition, power analyses revealed that the study was not adequately powered to detect relations between Extraversion and cortisol, but because the majority of effect sizes could not be located for the relationship between Extraversion/Openness to Experience and biopsychosocial outcomes in cancer, these analyses were pursued in the present study with the caveat that they could be underpowered.

Chi-square and t-test statistics were performed to determine whether the 51 participants with complete NEO-FFI data and the remaining participants without NEO-FFI data differed on key demographic and medical variables, including age, ethnicity, race, BMI, and tumor stage.

Then, descriptive statistics were calculated on all variables of interest. The distributions of the biopsychosocial variables were examined for normality and were transformed, as needed, in order to allow for the use of parametric statistics.

Bivariate, zero-order Pearson correlations between personality variables and outcomes were then conducted. Following this, potential control variables associated with the outcome variables were examined. These potential control variables included age, tumor stage, body mass index (BMI), length of hospital stay after surgery, post-surgical discharge with opioid pain medication prescription (yes/no), presence of acute post-op complications (yes/no), presence of wound healing complications following hospital discharge (yes/no), and use of prescribed or illicit psychoactive substances during saliva collection (yes/no). Control variables associated with outcome variables at $p < .10$ were partialled out of the relationship between the predictor and outcome via hierarchical

regression analyses, in which Block 1 contained the relevant control variables and Block 2 contained the personality traits of interest. If no significant relationships were found between the selected control and outcome variables, then the initial bivariate, zero-order Pearson correlations were reported.

CHAPTER 3 RESULTS

Preliminary Analyses

Sample Characteristics

A total of 134 women met the eligibility requirements for participation and were enrolled in the parent study. A subset of 51 women had complete NEO-FFI data and thus, was selected for participation in the present study. Age ranged from 36-84 years old ($M=61.25$ years, $SD=9.02$ years) and BMI ranged from 19.21 to 72.62 kg/m^2 ($M=35.33$ kg/m^2 , $SD=10.78$ kg/m^2). T-tests of continuous variables indicated that there were no statistically significant differences between the group without NEO-FFI data ($N = 27$) and the group with NEO-FFI ($N = 51$) across age [$t(63)=-.74$, $p=.46$, $d=-.25$] and BMI [$t(61)=-.13$, $p=.90$, $d=-.04$] (Table 3-1). Table 3-2 shows that the majority of the included participants reported they were Caucasian ($N=48$, 94%) and non-Hispanic ($N=35$, 70%). Chi-Square analyses revealed no statistically significant differences between the group without NEO-FFI data and the group with NEO-FFI data on ethnicity [$\chi^2(1)=.86$, $p=.36$, Cramer's $\phi=.13$] (Table 3-2). However, group differences were significant on race [$\chi^2(1)=12.34$, $p<.001$, Cramer's $\phi=-.40$], such that there were significantly more Non-Caucasians in the group without NEO-FFI data (Table 3-2).

The majority of included participants were diagnosed with Stage I endometrial cancer ($N=32$, 63%). Two (4%) participants were classified as having benign disease following surgery and two (4%) participants were classified as having complex endometrial hyperplasia with atypia, a pre-cancerous stage with a high risk of transformation into cancer if not promptly treated. The two participants with complex hyperplasia with atypia were coded as having Stage 0 cancer (entered as "0" on tumor stage) and retained in all analyses. In addition, the two patients with benign, non-precancerous disease were also

retained in all analyses, as their exclusion from analyses did not alter the significance of any results obtained. These participants were also coded “0” on “tumor stage.”

Normality Assumptions

Table 3-3 and Table 3-4 shows the descriptive statistics for personality and outcome variables in the sample. On average, personality domains fell within the Average range (T-scores= 45-55), though it can be seen that that the range included both extremes of the scale (Low to High). In addition, values for outcome variables at the pre-operative and post-operative timepoints are noted in Table 3-4.

Pre-operative cortisol slope, affection, and overall quality of life were determined to be non-normally distributed due to skewness and kurtosis greater than ± 1 . As a result, Blom transformation (Blom, 1958) was used to normalize the data so that parametric statistics could be used. In addition, outcome variables of pre-operative anger, pre- and post-operative perceived pain, pre- and post-operative depression, and pre- and post-operative guilt, as well as control variables such as BMI and length of hospital stay had kurtosis and skewness values greater than ± 1 . Use of square root transformation was sufficient to normalize these values within the ± 1 range of accepted skewness and kurtosis.

Associations between Control Variables and Biopsychosocial Outcome Variables

Table 3-5 reveals that higher pre-operative perceived stress was significantly associated with higher BMI, $r(43)=.33$, $p=.025$, and marginally significant with younger age at diagnosis, $r(44)=-.25$, $p=.092$; post-operative perceived stress was not significantly associated with any control variables. Likewise, pre-operative depression was not significantly associated with any control variables, but higher levels of post-operative

depression was marginally associated with younger age, $r(46)=-.26$, $p=.075$. Higher levels of pre-operative anxiety were significantly associated with younger age at diagnosis, $r(48)=-.38$, $p=.006$, and more advanced tumor stage, $r(48)=.34$, $p=.016$; higher levels of post-operative anxiety were marginally associated with more advanced tumor stage, $r(46)=.27$, $p=.08$, and absence of opioid pain medications prescribed at post-op, $r(44)=-.27$, $p=.081$.

Table 3-6 shows the correlations between the control variable and pain/Hr-QOL outcome variables. Higher pre-operative perceived pain severity was significantly associated with more number of hospital days after surgery, $r(38)=.35$, $p=.025$; post-operative perceived pain severity was not significantly associated with any outcome variables examined. Likewise, pre- and post-operative perceived pain interference was not associated with any outcome variables examined. Higher pre-operative Hr-QOL was significantly associated with less advanced tumor stage, $r(38)=-.35$, $p=.025$, and lower BMI, $r(38)=.46$, $p=.003$; higher post-operative Hr-QOL was marginally associated with older age, $r(42)=.27$, $p=.078$, and use of pain medications after surgery, $r(37)=.28$, $p=.089$.

Lastly, pre-operative salivary cortisol slope was not associated with any potential control variables examined; however, a more positive (more abnormal) post-operative salivary cortisol slope was marginally associated with greater length of hospital stay after surgery, $r(40)=.28$, $p=.072$ (Table 3-6).

Relationships between Personality (N,E,O) and Stress/Mood

Analyses revealed that, as expected, higher levels of Neuroticism were significantly associated with higher levels of pre-operative perceived stress ($\beta=.43$, $p<.001$, Cohen's $f^2=.54$) after controlling for Age and BMI (Table 3-10). In addition, higher levels of Neuroticism were also significantly associated with higher levels of post-operative perceived stress, $r(42)=.51$, $p<.001$ (Table 3-7). In terms of mood, higher

levels of Neuroticism were significantly associated with higher levels of pre-operative depression, $r(48)=.33$, $p=.021$, and marginally associated with post-operative depression, $r(46)=.27$, $p=.063$ (Table 3-7). Higher levels of Neuroticism were significantly associated with higher levels of pre-operative anxiety, $r(48)=.30$, $p=.037$, but not with post-operative anxiety. In addition, higher levels of Neuroticism were significantly associated with more pre-operative guilt, $r(40)=.48$, $p<.001$, and post-operative guilt, $r(42)=.53$, $p<.001$ (Table 3-7). Higher levels of Neuroticism were also associated with more pre-operative anger, $\beta=.52$, $p<.001$, Cohen's $f^2=.52$, and post-operative anger, $\beta=.46$, $p<.001$, Cohen's $f^2=.37$, (Table 3-11 and Table 3-12). Neuroticism was not significantly associated with affection.

Table 3-7 shows the relations between Openness to experience and perceived stress/mood. Contrary to hypotheses, higher levels of Openness to experience were associated with higher pre-operative anxiety, $r(48)=.33$, $p=.019$, and post-operative anxiety, $r(43)=.34$, $p=.02$. In addition, higher levels of Openness to experience were marginally associated with higher levels of depression, $r(48)=.24$, $p=.089$. Consistent with hypotheses, higher levels of Openness to experience was associated with higher post-operative affection, $r(42)=.35$, $p=.021$, though no significant relationship was found with pre-operative affection. Extraversion was not significantly associated with any perceived stress or mood/affect variables examined.

Relationships between Personality (N,E,O) and Pain/Quality of life

Table 3-8 shows the relations between personality traits (N,E,O) and pain/Hr-QOL. Analyses revealed that, as expected, higher levels of Neuroticism were associated with more perceived post-operative pain severity, $r(42)=.47$, $p=.001$; however, Neuroticism was unrelated to perceived pre-operative pain severity. Similarly,

higher levels of Neuroticism were marginally associated with lower post-operative Hr-QOL, $r(42)=-.27$, $p=.073$; however, they were not associated with pre-operative Hr-QOL.

Higher levels of Openness to experience were significantly associated with less perceived post-operative pain interference, $r(42)=-.34$, $p=.035$, and marginally associated with less post-operative pain severity, $r(42)=-.27$, $p=.08$. No relations were found between Openness to experience and pre-operative pain. In addition, no significant relationships were found between Openness to experience and Hr-QOL. Extraversion was also not significantly associated with any perceived pain or Hr-QOL variables examined.

Relationships between Personality (N,E,O) and Cortisol Slope

Higher levels of Extraversion were not significantly associated with pre-operative salivary cortisol slope; however, they were marginally associated with a more positive (more abnormal) post-operative cortisol slope, $\beta=.30$, $p=.074$, Cohen's $f^2=.19$, which was not in the expected direction (Table 3-13). Neither Neuroticism nor Openness to experience was significantly associated with salivary cortisol slope.

Table 3-1. Comparison of continuous demographics and biological variables between study sample with NEO-FFI data and study sample without NEO-FFI data

Variable Name	Included Participants (N=51)		Excluded Participants (N=27)		<i>df</i>	<i>t</i>	<i>p</i>	Cohen's <i>d</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>				
Age (yrs)	61.25	9.02	63.14	6.01	63	-0.74	0.46	-0.25
BMI (kg/m ²)	35.33	10.78	35.78	13.1	61	-0.13	0.90	-0.04

Table 3-2. Comparison of categorical demographic and biological variables between study sample with NEO-FFI data and study sample without NEO-FFI data

Variable Name	Included Participants (N=51)		Excluded Participants (N=27)		$\chi^2 (1)$	<i>p</i>	Cramer's Phi
	<i>N</i>	%	<i>N</i>	%			
Race					12.34	<.001	-0.40
Caucasian	48	94	17	63			
Other	3	6	10	37			
Ethnicity					0.86	0.36	0.13
Hispanic	5	10	3	23			
Non-Hispanic	35	70	10	77			

Table 3-3. Descriptive statistics of personality traits (N=51)

Personality Trait	<i>M</i>	<i>SD</i>	Median	Range
Neuroticism	44.37	9.32	43.00	26-66
Extraversion	50.10	9.85	50.00	31-75
Openness to experience	50.33	10.26	50.00	31-75
Agreeableness	50.90	11.61	53.00	25-72
Conscientiousness	48.24	10.85	48.00	20-72

Table 3-4. Descriptive statistics of outcome variables

Variable Name		<i>M</i>	<i>SD</i>	Median	Range	N
Perceived Stress	Pre-Op	22.11	7.94	23.00	3-42	46
	Post-Op	19.98	8.22	19.50	1-39	44
Depression	Pre-Op	6.64	5.03	6.00	0-22	50
	Post-Op	5.27	4.36	4.00	0-20	48
Anxiety	Pre-Op	5.04	3.82	4.00	0-15	50
	Post-Op	3.73	2.89	3.50	0-14	48
Guilt	Pre-Op	1.59	0.68	1.25	1-3.6	47
	Post-Op	1.48	0.57	1.20	1-3.0	44
Anger	Pre-Op	1.78	0.71	1.60	1-4.2	47
	Post-Op	1.77	0.60	1.60	1-3.5	44
Affection	Pre-Op	3.55	0.76	3.60	1-5	49
	Post-Op	3.55	0.58	3.60	2-4.8	44
Pain Severity	Pre-Op	2.27	2.48	1.25	0-8.75	41
	Post-Op	1.96	2.01	1.50	0-9.25	44
Pain Interference	Pre-Op	1.78	1.97	1.28	0-8	37
	Post-Op	2.18	2.51	1.21	0-8.43	40
Overall QOL	Pre-Op	132.71	21.68	133.07	68.47-164	41
	Post-Op	131.61	18.61	133.17	81-168	44
Cortisol ($\mu\text{g/dL}$)	Pre-Op	-0.10	-0.10	0.05	-0.25 – 0.03	43
	Post-Op	-0.08	0.06	-0.07	-0.21 – 0.05	42

Table 3-5. Correlations between potential biobehavioral control variables and stress, mood, and affect outcome variables

	Perceived Stress		Depression		Anxiety		Guilt		Anger		Affection	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Age	-.25†	-0.18	-0.23	-.26†	-.38**	-0.19	-0.11	-0.13	†-0.26	-0.25	0.04	0.10
Tumor Stage	0.24	0.12	0.24	0.15	.40**	.27†	-0.06	-0.12	-0.01	-0.19	0.04	0.21
BMI	.33*	-0.15	0.14	-0.08	0.17	-0.04	-0.04	0.16	0.22	0.23	-0.27†	-0.19
Length of hospital stay	0.04	0.13	0.21	0.04	0.16	0.01	0.11	0.13	0.10	0.16	-0.09	0.02
Use of opioid pain medications	n/a	-0.18	n/a	-0.16	n/a	-.27†	n/a	-0.15	n/a	-0.14	0.17	0.13
Presence of acute post-op complications	n/a	0.04	n/a	0.15	n/a	0.03	n/a	0.13	n/a	0.05	0.03	0.18
Presence of wound healing complications post-discharge	n/a	0.1	n/a	-0.18	n/a	-0.15	n/a	0.04	n/a	0.12	-0.05	-0.18

*p ≤ .05, **p ≤ .01, ***p ≤ .001, †p ≤ .10

Note: N/A = potential control variables only relevant for post-op timepoint

Table 3-6. Correlations between potential biobehavioral control variables and pain, QOL, and cortisol slope outcome variables

	Pain Severity		Pain Interference		QOL		Cortisol Slope	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Age	0.18	-0.10	0.06	-0.14	0.15	.27†	0.05	-0.22
Tumor Stage	-0.04	-0.22	-0.07	-0.18	-0.37*	-0.16	0.04	0.11
BMI	-0.02	-0.06	0.03	0.03	-0.46**	-0.07	0.07	0.07
Length of hospital stay	0.35*	0.17	0.21	0.01	-0.02	-0.01	0.12	0.28†
Use of opioid pain medications	0.22	-0.19	0.25	-0.16	-0.05	.28†	0.15	-0.23
Presence of acute post-op complications	0.26	0.09	0.08	0.02	0.15	0.02	-0.09	0.12
Presence of wound healing complications post-discharge	0.09	0.08	0.06	-0.02	0.01	-0.18	-0.05	0.16

*p≤ .05, **p≤ .01, ***p≤ .001, †p≤ .10

Note: N/A = potential control variables only relevant for post-op timepoint

Table 3-7. Correlations between personality and perceived stress, mood, and affect

	Perceived Stress		Depression		Anxiety		Guilt		Anger		Affection	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Neuroticism	0.46***	0.51***	0.33*	.27†	0.30*	0.17	0.48***	0.53***	0.53***	0.49***	-0.01	-0.12
Extraversion	-0.04	-0.18	-0.18	-0.23	-0.04	-0.004	-0.13	-0.18	-0.08	-0.07	0.19	0.18
Openness	0.22	-0.14	0.24 †	0.11	0.33*	0.34*	-0.11	0.06	-0.16	-0.07	0.12	0.35*

*p≤ .05, **p≤ .01, ***p≤ .001, †p≤ .10

Table 3-8. Correlations between personality and perceived pain/Hr-QOL

	Pain Severity		Pain Interference		QOL	
	Pre	Post	Pre	Post	Pre	Post
Neuroticism	-0.01	.47***	-0.17	0.17	-0.09	-0.27†
Extraversion	-0.02	-0.15	0.07	-0.23	-0.23	-0.11
Openness	-0.17	-0.27†	-0.05	-.34*	-0.16	0.10

* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$, † $p \leq .10$

Table 3-9. Correlations between personality and cortisol slope

	Cortisol slope	
	Pre	Post
Neuroticism	-0.02	0.12
Extraversion	0.10	.32*
Openness	-0.14	0.16

* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$, † $p \leq .10$

Table 3-10. Predicting perceived stress at pre-op from Neuroticism

Step Number	Predictor Variable	B	95% CI		R ²	ΔR ²	F of ΔR ²	Cohen's f ²
			Lower	Upper				
1					0.17	0.17	4.21*	0.20
	Age	-0.24	-0.5	0.05				
	BMI	0.31*	0.19	5.34				
2					0.35	0.19	11.72***	0.54
	Age	-0.2	-0.44	0.05				
	BMI	0.31*	0.5	5.09				
	Neuroticism	.43***	0.16	0.61				

N=45. Significance of Model, $F(3, 41) = 7.43$, $p \leq .001$

* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$, † $p \leq .10$

Table 3-11. Predicting anger at pre-op from Neuroticism

Step Number	Predictor Variable	B	95% CI Lower	Upper	R ²	ΔR ²	F of ΔR ²	Cohen's f ²
1					0.07	0.07	2.93†	0.08
	Age	-0.26†	-0.02	0.001				
2					0.34	0.27	15.72***	0.52
	Age	-0.25†	-0.01	0.001				
	Neuroticism	0.52***	0.006	0.02				

N=42. Significance of Model, $F(2,39)=9.87, p<.001$

* $p\leq .05$, ** $p\leq .01$, *** $p\leq .001$, † $p\leq .10$

Table 3-12. Predicting anger at post-op from Neuroticism

Step Number	Predictor Variable	B	95% CI Lower	Upper	R ²	ΔR ²	F of ΔR ²	Cohen's f ²
1					0.06	0.06	2.71	0.06
	Age	-0.02	-0.04	0.01				
2					0.27	0.21	11.58***	0.37
	Age	-0.18	-0.03	0.006				
	Neuroticism	0.46***	0.01	0.05				

N=44. Significance of Model, $F(2,41)=7.49, p=.001$

* $p\leq .05$, ** $p\leq .01$, *** $p\leq .001$, † $p\leq .10$

Table 3-13. Predicting cortisol slope at post-op from Extraversion

Step Number	Predictor Variable	B	95% CI Lower	Upper	R ²	ΔR ²	F of ΔR ²	Cohen's f ²
1					0.08	0.08	3.41†	0.09
	Length of hospital stay	0.28†	-0.23	-0.07				
2					0.16	0.08	3.57†	0.19
	Length of hospital stay	0.18	-0.02	0.06				
	Extraversion	0.30†	0.00	0.004				

N=41. Significance of Model, $F(3,38)=3.60, p=.037$

* $p\leq .05$, ** $p\leq .01$, *** $p\leq .001$, † $p\leq .10$

CHAPTER 4 DISCUSSION

Personality traits, such as low Neuroticism, high Extraversion, and high Openness to Experience, are characteristic of individuals who can positively adapt in the face of adversity. Among individuals with cancer, these traits are associated with better mood, higher quality of life (QOL), and lower pain. However, few studies have examined personality as a predictor of biopsychosocial outcomes in gynecologic cancers. This study examined relations between personality and (a) perceived stress/mood, (b) pain/cancer-related QOL, and (c) cortisol among women undergoing surgery for endometrial cancer, the most common gynecologic cancer in the United States.

Overall, Neuroticism was one of the strongest predictors of biopsychosocial outcomes, while Extraversion appeared to be the weakest. As expected, individuals with low Neuroticism experienced significantly more positive peri-operative outcomes such as lower perceived stress, and less guilt and anger, even after controlling for age and BMI. Significantly less pre-operative depressive and anxious symptoms and lower post-operative pain severity were also found in individuals with lower Neuroticism. However, contrary to hypotheses, no relations were found between Neuroticism and Hr-QOL or diurnal cortisol slope, though this may have been attributed to small sample size since initial power analyses indicated that the study was not adequately powered to detect relations between Neuroticism and QOL.

These findings are mostly consistent with previous research on personality and biopsychosocial outcomes in the cancer population. Individuals with low Neuroticism were found to have less perceived stress (Horner, 1995), depression (Golden-Kreutz &

Anderson, 2005), and pain (Chochinov et al., 2006) compared to individuals with higher Neuroticism. Although relationships between Neuroticism and Hr-QOL were not found as in the study by Lai and colleagues (2010), Hr-QOL in this study measured overall Hr-QOL while Lai and colleagues (2010) examined only a few subscales of QOL. Thus, future studies should explore whether Neuroticism is indeed associated with global Hr-QOL, or if this relationship is due to a strong relationship between Neuroticism and only one or two facets of Hr-QOL. The lack of relationship between Neuroticism and cortisol slope, although contrary to hypotheses, may not be wholly unexpected, as prior research has found a relationship between Neuroticism and blunted early morning cortisol peak (e.g., Vedhara et al., 2006) rather than slope. Future research should examine the extent to which Neuroticism may be associated with cortisol awakening response (CAR) in this sample in order to replicate the results of Vedhara and colleagues (2006).

Relationships between Openness to Experience and biopsychosocial outcomes from this study were more variable than those with Neuroticism. As expected, individuals with higher levels of Openness to Experience experienced significantly more post-operative affection and less post-operative pain interference. Although previous studies have not examined relationships between Openness to Experience and biopsychosocial outcomes in the cancer population, these findings are consistent with the literature suggesting that Openness to Experience is a key facet of resiliency (Furnham et al., 1996).

Contrary to hypotheses, this study also found that higher levels of Openness to Experience were associated with more peri-operative anxious symptoms. This

unexpected finding may be understood in several ways. There has been some research suggesting that high Openness to Experience may be associated with clinically significant anxiety disorders (e.g., Obsessive-Compulsive Disorder), and that both may share an “openness to fantasy”(Samuels et al, 2000). Individuals scoring high on “openness to fantasy” tend to entertain more novel ideas and are more likely to imagine scenarios or worst-case situations. In the current study, it is possible that participants high in “openness to fantasy” may vividly imagine all possible outcomes, including negative outcomes, of surgery and cancer. This may have evoked elevated anxiety. In addition, individuals scoring high on facets of “openness to feelings” tend to experience emotions more intensely than others, and this may have been reflected by elevated anxiety scores on self-report instruments among individuals high on Openness to Experience. Of note, this rationale may also explain why van Straten and colleagues (2007) found negative relationships between Openness to Experience and QOL. Thus, facets of Openness to Experience should be explored to better understand these findings.

Extraversion, another personality trait associated with resiliency (Friborg et al., 2005), was not found to be significantly correlated with any biopsychosocial outcome variables examined. This finding may have been attributed to the sample size. Initial power analysis revealed that relations between Extraversion and cortisol were not adequately powered. Although initially significant when correlated with post-operative diurnal cortisol slope, after controlling for length of hospital stay, higher Extraversion was marginally associated with a flatter (more abnormal) diurnal cortisol slope, albeit with a moderate effect size. This finding is inconsistent with the literature suggesting

that (a) resiliency factors are associated with a more normal cortisol slope, and (b) steeper (more normal) diurnal cortisol slopes may confer resistance to pathophysiological disease processes, an indication of potential psychological and physiological resiliency (Gunnar & Vazquez, 2001; Young, Haskett, Pande, Weinberg, & Watson, 1994). Future studies should seek to replicate these findings in a larger sample.

When examining the relationships between personality and biopsychosocial outcomes occurring during the peri-operative period, Neuroticism was associated with the majority of psychosocial outcomes (i.e. perceived stress, mood, and affect) at both the pre- and post-operative time-points; however, it was associated with physical/biological outcomes (i.e. perceived pain, Hr-QOL) at only the post-operative time-point. Given that Neuroticism predicts distress at both pre- and post-surgery, individuals high in Neuroticism and distress at pre-surgery may benefit from peri-surgical assessment/intervention in order to buffer/reduce distress at post-surgery.

Study Limitations

This current study includes some limitations that would warrant caution when making interpretations. First, since this study focuses on non-metastatic endometrial cancer, results would not be generalizable to women diagnosed with Stage IV endometrial cancer. Additionally, the majority of the women in this sample were Non-Hispanic Caucasians, so results may differ for other ethnicities and racial groups.

In addition, although this study was mostly adequately powered, the sample size was still modest. Internal consistency was not optimal at the post-operative administration of the FACT-En (Cronbach's alpha = .48), which may have been attributed to the small sample size at the post-operative time-point. A larger sample

would allow for categorization of participants on each personality dimension according to NEO-FFI clinical cut-offs and then comparison among these groups on outcome variables.

Most importantly, the current study did not assess resiliency using a well-established, valid measure. The current study relied upon a secondary dataset, and a measure of resiliency was not administered within the parent study. Future studies should consider incorporating a resiliency measure in order to assess its relationship with both personality and biopsychosocial outcomes. These limitations serve as important considerations for future research assessing personality and biopsychosocial outcome correlates.

Future Directions and Clinical Impact

This study is among the first to examine relationships between personality traits and biopsychosocial outcomes in the context of patients with endometrial cancer. Although based on a small sample, these results support the hypotheses that personality traits characteristic of resiliency are significantly associated with some biopsychosocial outcomes in endometrial cancer. The most stable findings emerged between high Neuroticism and poorer outcomes. Future studies should explore whether peri-surgical psychological interventions can modify discrete cognitions and behaviors common among individuals high in Neuroticism, improve resilience, and promote more positive peri-operative biopsychosocial outcomes in women with endometrial cancer.

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BIOGRAPHICAL SKETCH

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