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Understanding the relationship between positive affect and cortisol in lung cancer patients.

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UNDERSTANDING THE RELATIONSHIP BETWEEN POSITIVE AFFECT AND CORTISOL IN LUNG CANCER PATIENTS

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DEDICATION

This dissertation is dedicated to

the lung cancer patients and their families

who graciously gave their time and energy to this current research.

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ABSTRACT

UNDERSTANDING THE RELATIONSHIP BETWEEN POSITIVE AFFECT AND CORTISOL IN LUNG CANCER PATIENTS

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Positive psychobiological processes within lung cancer patients are drastically understudied. This dissertation explores the nature of positive affect (PA) and potential associations with diurnal cortisol among lung cancer patients, given the prognostic significance of diurnal cortisol rhythms. Theoretical underpinnings and current literature involving PA, cancer, and diurnal cortisol are first reviewed. An original integrated model of PA and cortisol among cancer patients is then presented, from which the proposed dissertation study and analyses are derived.

Sixty-one non-small cell lung cancer patients provided self-report assessment of mood (PANAS PA and NA subscales, CES-D PA subscale), medical and demographic characteristics, and 10-day salivary cortisol. Aim 1 tested hypotheses that: (1) patients will experience moderate PA, and more PA than NA, (2) PA and NA will emerge as separate factors in factor analyses, and (3) higher PA will correlate with variables reflecting lower disease burden. Aim 1 was assessed through descriptive statistics, correlations, t-tests, and exploratory factor analyses. Aim 2 tested hypotheses that: (1) higher PA will relate to lower cortisol means, (2) higher PA will relate to steeper diurnal

slope, (3) PA will relate more strongly to overall mean cortisol than diurnal slope. Aim 2 was tested through hierarchical linear regressions and path analyses.

Aim 1 results showed that patients generally held positive emotions and endorsed PA items that reflected determination and resilience. They also reported more PA than NA; these two constructs emerged as separate and distinct factors. Race, smoking, and current treatment all significantly related to PA. Aim 2 revealed that PA did not significantly associate with mean cortisol variables or diurnal slope. However, higher NA was associated with flattened slopes, after excluding patients taking corticosteroids. Although the relationship between PA and mean cortisol was consistently stronger than with diurnal slope in path analyses, the associations were non-significant.

Patients reported experiencing positive emotions that may reflect resilience and adaptive coping. Positive affect did not have strong associations with cortisol, which may be due to pre-existing cortisol dysregulation or small sample size. Future studies should continue to explore mind-body associations of positive psychological processes in lung cancer patients.

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INTRODUCTION

The field of psychology is in the midst of a paradigm shift. For decades, the focus of research, clinical work, and policy has been on the identification and treatment of psychopathology. In recent years, however, attention has moved towards the other end of the spectrum—human flourishing. This study of "positive psychology" seeks to understand the benefits of positive emotions on mental and physical health (Seligman & Csikszentmihalyi, 2000). Indeed, evidence of health benefits associated with positive psychological processes is mounting (e.g., Pressman & Cohen, 2005). In healthy samples, positive affect has been shown to independently associate with healthier physiological processes of neuroendocrine, autonomic, and immune systems (Dockray & Steptoe, 2010). What is notably lacking, however, is a particular focus on physiological mechanisms. Given the present evidence, this line of inquiry may have important relevance to processes in medical disorders, yet there is a particular paucity of research in how positive emotions relate to physiological processes in people with serious illness, such as cancer.

The historical context surrounding the topic of positive psychology and cancer outcomes is an emotionally charged one. The associations between positive psychological constructs and cancer progression have typically either been overemphasized or underemphasized, with extremes lending themselves to producing patients' unreal expectations of healing and/or guilt and burden. Given the vast advances

in cancer research, a new and integrative scientific approach to this topic within the field is both timely and necessary. Improvements in cancer treatments and outcomes shift the focus of disease models towards those of survivorship, away from merely increasing *quantity* of life to those of increasing *quality* of life. As such, understanding the link between biology and positive emotional processes in cancer patients helps strengthen the bridge between disease and survivorship models.

Positive Affect

One of the basic areas of research in positive psychology is that of positive affect (PA). Positive affect is the subjective experience of positive moods, like joy and happiness, stemming from pleasurable engagement with one's environment (Clark, Watson, & Leeka, 1989; Pressman & Cohen, 2005). These feelings may be momentary, longer lasting, or even seemingly dispositional (Pressman & Cohen, 2005). Shorter-term PA is referred to as "state PA" (such as joy, happiness, or pleasure) while longer-lasting positive affect is referred to as "trait PA" (Pressman & Cohen, 2005). However, this distinction is not always clear, and trait PA may not necessarily be best represented by an aggregate score of state PA, as seen in some research. Instead, recent research has highlighted the importance of considering affect variability as an indicator of mental health (Houben et al., 2015). For both PA and NA, low variability (within-persons standard deviation from momentary mean affect) and high stability (low change from moment-to-moment) is associated with higher psychological well-being (Houben et al., 2015). This distinction may be particularly important in the cancer context, as moods may shift and reflect varying emotional demands throughout the cancer journey.

Historically, affective valence – the degree to which emotions are considered positive or negative – was considered bipolar, where PA was merely the opposite of negative affect (Wundt, 1897/1998). However, as research progressed, an alternative view of bivalence was put forth. The bivalence hypothesis follows the data supporting that PA and negative affect (NA) are often uncorrelated and thus may be independent constructs (e.g., Watson, Clark, & Tellegen, 1988). This view was furthered by research supporting that PA and NA may be grounded in distinct biological systems (Cacioppo, Gardner, & Bernston, 1999; Diener & Emmons, 1984; Diener, Smith, & Fujita, 1995; Norris et al., 2010). As such, the presence of PA, rather than the absence of NA, deserves unique attention.

Affect may be also described based on the dimension of arousal. The affective circumplex model describes how emotions may be categorized based upon multidimensional circumplex anchored by these two perpendicular scales (valence and arousal; Russell, 1980). For example, a high arousal PA may be "excitement", while low arousal PA may be "relaxed." A nuanced approach to understanding PA in regard to arousal may have particular relevance as it relates to the body's stress response; however, the role of emotional arousal is typically underemphasized in mind-body research.

Researchers commonly note the lack of consensus in defining or referring to PA (e.g., Pressman & Cohen, 2005; Dockray & Steptoe, 2010). From a historical and philosophical perspective, PA has been categorized within two realms: hedonia and eudaimonia. The first concept, hedonia, typically refers to the experience of state and/or trait PA, with the absence of NA (Ryan & Deci, 2001). Hedonia also includes "subjective well-being" (SWB) — the global tendency to experience more positive than negative

affect, as well as judging one's life as satisfactory (Deci & Ryan, 2008; Diener, 2000; Howell, Kern, & Lyubomirsky, 2007). The second concept, eudaimonia, refers to overall psychological well-being (PWB; Ryff, 1989), which includes experiences of PA, but focuses more on living a full life of meaning and growth (Deci & Ryan, 2008; Ryff, 1989). Research supports that hedonia and eudaimonia are separate but related constructs (Davis et al., 2015; Fredrickson et al., 2013; Keyes, Shmotkin, & Ryff, 2002; Ryff et al., 2006; Ryff et al., 2004; Waterman, 1993). In research however, the terms referring to PA and well-being tend to be used interchangeably, contributing to difficulty in understanding how these factors may individually relate to physiology. An important qualitative distinction may be made between the two concepts in how they relate to a flourishing life: hedonia may be considered an endpoint or "result", while eudaimonia may be conceptualized as the "process" or "content" (Seligman, 2004).

Barbara Fredrickson (2001) proposes that PA and broader experiences of psychological well-being are related through a "broaden and build" process. The Broaden and Build Theory suggests that positive emotions are not just markers of well-being, but in fact produce it. In particular, momentary PA encourages thought broadening (such as awareness and creativity) and approach behaviors (like play and exploration). These momentary experiences help people to build physical, social, intellectual, and emotional resources, which together create psychological resources. These psychological resources are similar to the eudaimonic well-being described by Ryff (1989). Experiencing these diverse set of resources feeds back to create more positive emotions.

Cancer

It is difficult to find a person who has not been touched by cancer in some way in the modern age. High incidence and mortality rates, steep costs of treatment, and physical and emotional suffering of both patients and their social networks make cancer an area of prominent scientific, political, and social investment. Cancer refers to a collection of diseases all characterized by the uncontrolled dividing and spreading of cells in the body (National Cancer Institute, n.d.) and is the second leading cause of death in the United States (Centers for Disease Control, 2016). The complex features of tumor cells are characterized into six "hallmark capabilities": sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, and activating invasion and metastasis (Hanahan & Weinberg, 2011). Cancer initiation and progression is the result of multiple factors such as genetics, immune and endocrine function, and lifestyle (Bissell & Hines, 2011). However, the multifaceted nature of cancer extends to psychology, including the role of stress biology, as well as the individual psychological and emotional experience of the cancer journey. Given its implications for public health, science continues to forge forward in efforts to understand both the biology and psychology of cancer.

Lung cancer. Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer related death among men and women worldwide (Centers for Disease Control, 2015). Prognosis among non-small cell lung cancer patients is poor. Five-year survival rates among early stage non-small cell lung cancer patients range from about 53 – 92% (stage I: 68 – 92%, stage II: 53 - 60%; American Cancer Society, 2017); however, many patients are not diagnosed until advanced stages, when the disease has

already spread and become symptomatic (American Cancer Society, 2017). Prognosis among late stage patients is much lower, with 5-year survival rates for stage III ranging from 13-26% and stage IV ranging from 1-10% (American Cancer Society, 2017).

Lung cancer is met with greater distress than most other cancers (Brintzenhofe-Szoc et al., 2009; Linden et al., 2012; Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001). Patients with lung cancer experience a high symptom burden and symptom distress, even among those who are high-functioning (Temel, Pirl, & Lynch, 2006). The most common symptoms reported include fatigue, shortness of breath, lack of energy, and cough. Only a minority of patients respond to treatment, thus many still endure tumor growth throughout their illness (Temel et al., 2006). Furthermore, treatment side effects may outweigh any relief associated with disease improvement, leaving many patients with little clinical or quality of life improvement (Temel et al., 2006).

The emotional burden of a lung cancer diagnosis is unique from other cancers. Given the well-known link between smoking and cancer, the impact of stigma surrounding a diagnosis often brings emotions of guilt and shame and is associated with poorer quality of life and higher psychological distress (Chambers et al., 2012). The compounding physical, emotional, and social burden of lung cancer is associated with patient depression (Graves et al., 2007). As with other cancers, major depressive disorder predicts worse survival among lung cancer patients (Pirl et al., 2012).

The coupling of poor prognosis and painful physical symptoms (e.g., shortness of breath, chest pain, coughing up blood, weakness) make lung cancer particularly disturbing to a patient. These patients face a difficult path of treatment, recovery, and

physical symptoms, all in the context of potentially being at end-of-life in only a few short years or months.

Positive Affect and Cancer

In the face of poor prognosis as well as physical and emotional disease-burden, it may seem that experiences of joy, excitement, contentment, and other positive emotions may be infrequent among lung cancer patients. To date, there is very little research on the experience of positive emotions in this vulnerable population. Some of this literature exists among samples of other cancer types; however, the paucity of research in this area is notable (Louro, Fernández-Castro, & Blasco, 2015). One study found that advanced cancer patients overall experienced more PA than NA on the PANAS; although, the overall levels of PA were slightly lower than in the general population (Voogt et al., 2005). In a recent review, PANAS scores across several cancer types indicated that patients on average experienced low NA and moderate PA (Louro et al., 2015). Positive affect in cancer patients seems to be associated with better general health, better social functioning, benefit finding, low depression and anxiety (Louro et al., 2015). The review also noted that many studies show that changes in PA are greater predictors of quality of life and illness adaption than changes in NA (Louro et al., 2015).

Studies on the role of demographic and medical factors show mixed results, perhaps due to the heterogeneity of cancer types and other sample factors. The role of cancer stage or treatment factors could not be established from the available literature (Louro et al., 2015). However, in a sample of 105 mixed-cancer patients, authors found that older, male, lower income patients for whom surgery was planned experienced less positive feelings than patients of other demographics (Voogt et al., 2005). Advanced

cancer stage has been shown to correlate with lower PA, but not with eudaimonic well-being (Davis et al., 2015). These findings highlight that medical and demographic variables may play a role in the experience of positive emotions; however, more research is needed in this area, and especially within lung cancer patients.

Positive affect in cancer patients may also relate to physical, cognitive, and social factors. Lower PA has been shown to associate with higher fatigue; and lower physical, cognitive, and role functioning (Voogt et al., 2005). In the same study, the researchers found that higher PA was associated with more social support and problem-focused coping. Patients reporting higher PA experienced more meaning, peace, and perceived a role of faith, even after controlling for demographics, coping, and symptoms. The authors suggested that low PA may be driving distress (rather than the presence of high NA as in psychiatric depression and anxiety) as the cancer sample showed lower PA, but similar levels of NA, than the general population (Voogt et al., 2015). Another study drew similar conclusions, after finding a loss of PA from diagnosis to three-month follow-up was associated with greater mood disturbances (Hou, Law, & Fu, 2010).

Among cancer survivors, some research indicates that elements of well-being are similar to that of healthy populations (Bradley, Rose, Lutgendorf, Costanzo, & Anderson, 2006; Helgeson & Tomich, 2005), including psychological and social well-being (Costanzo, Ryff, & Singer, 2009). Although survivors may experience more distress than those who have never been diagnosed with cancer (Rabin et al., 2007), PA may increase with time since diagnosis (Costanzo, Stawski, Ryff, Coe, & Almeida, 2012). One study showed that when survivors experienced daily stress, they demonstrated less pronounced declines in PA than healthy control, which may demonstrate resilience (Costanzo et al.,

2012). Together, the relationship between PA and time since diagnosis may suggest a process of coping and resilience.

Other research suggests that feelings of joy, inner peace, and happiness are associated with increased quality of life in patients, with joy specifically being associated with having a more meaningful life and a good death (Lin & Bauer-Wu, 2003). Other studies suggest that patients with positive affect also experience more meaning, peace, and perceived role of faith (Voogt et al., 2005). Among lung cancer patients, the ability to maintain some level of positive emotion may be a similar sign of resilience and adaptive coping, such as through meaning-making and acceptance.

Cortisol

The role of the stress response and the hypothalamic-pituitary-adrenal (HPA) pathway in tumor progression has become an area of significant focus in the field of psycho-oncology. In the face of stress, the human body responds to a perceived threat via two coordinating systems (Chrousos, 1998; McEwen, 1998). The first response is conducted by the autonomic nervous system: rapid sympathetic nervous system activation modulates responses such as increased heart rate and breathing, and reducing digestion. The slower second system is the HPA axis, which has basal circadian rhythm. The HPA response involves the integration of central nervous system components including cortical and limbic structures, as well as blood borne signals such as hormones and cytokines (Chrousos, 1998). When the body perceives a stressor, the HPA axis activates a cascade of physiological processes, culminating in the release of glucocorticoids including cortisol. Cortisol may be detected in blood, saliva, and urine; however, the levels of detectable hormone differ between these fluids (Hellhammer,

Wüst, & Kudielka, 2009). Cortisol is involved in a host of biological systems and processes including the central nervous system (e.g., learning, memory, and emotion; blood pressure, cardiovascular function), metabolic processes (e.g., glucose utilization), and immune responses (e.g., regulating inflammatory responses; Sapolsky, Romero, & Munck, 2000). Importantly, cortisol also plays a key feedback role in ending the stress response, by acting on receptors in the hippocampus, frontal cortex, hypothalamus, and anterior pituitary gland (Chrousos, 1998; Chrousos & Gold, 1992).

Salivary cortisol provides a relatively simple and reliable measure of human stress responses, particularly in ambulatory studies, and thus is a widely used measure in psychoneuroendocrinology (Kirschbaum & Hellhammer, 1994). In comparison to sympathetic responses such as heart rate or blood pressure, cortisol may easily provide data regarding external and endogenous stress reactivity data as well as longitudinal rhythms. The HPA stress response may be measured by acute cortisol secretion after a stressor or cortisol secretion over the day. Summary measurements may include area under the curve (AUC) for overall secretion over time or a score such as the mean cortisol value measured from several collection points throughout the day.

Diurnal rhythms. Cortisol follows a circadian rhythm. Levels are low in the evening and throughout night, but rise in the morning before waking. As a proxy measure of this rhythm, a diurnal rhythm may be estimated by calculating the slope between the waking and evening levels of cortisol as measured by multiple salivary samples (e.g., Sephton, Sapolsky, Kraemer, & Spiegel, 2000). Diurnal slope is an indicator of strength of HPA rhythmicity (Kraemer et al., 2006).

A second phenomenon of cortisol, known as the cortisol awakening response (CAR), is the spike of cortisol secretion that occurs upon awakening and continues to rise to a peak level about 20-45 minutes later (Chida & Steptoe, 2009; Pruessner et al., 1997). The most common metrics of CAR are the mean difference in waking and peak morning values and the slope of the increase (Chida & Steptoe, 2009). CAR is commonly used in research to provide a unique measure of HPA activity, sparked endogenously by the behavior of awakening, that is partially independent from cortisol secretion over the rest of the day (Chida & Steptoe, 2009). As such, the correlation between CAR and other cortisol values is often low (Edwards, Clow, Evans, & Hucklebridge, 2001).

Healthy cortisol functioning includes the rise and fall with normal daily stressors, as well as general diurnal rhythmicity. Short-term cortisol responses are typically due to acute stressors and are adaptive. Long-term alterations in cortisol responses (such as diurnal cortisol profiles) may be due to more chronic HPA activation. Lower levels of overall cortisol are generally seen as favorable, as they indicate low levels of stress system activation. In diurnal patterns, steeper slopes are generally indicative of better health, while flattened slopes and other patterns of dysregulation usually signify less favorable health (Miller, Chen, & Zhou, 2007). Discerning "healthy" CAR is more complex, as greater morning increases may indicate a heightened HPA response, but findings have been inconsistent as to whether a diminished CAR is associated with better health outcomes (Chida & Steptoe, 2009).

Recent research indicates that mean cortisol levels are more reliable than diurnal slopes in between-subjects analyses, with the minimal reliable measurement collected from at least three days of samples (Segerstrom, Boggero, Smith, & Sephton, 2014). Area

under the curve and diurnal slope require more days of collection to reach reliability (Segerstrom et al., 2014). Further, research suggests differences in overall cortisol levels may be due to genetic influences, sex (with women demonstrating lower levels than men), and nicotine use (Kirschbaum & Hellhammer, 1994). Thus, these factors should be taken into account when interpreting AUC and mean diurnal secretion as indicators of overall health.

Cortisol and Cancer

Animal and human data support the link between cortisol rhythms, cancer incidence, tumor progression, and cancer prognosis (Eismann, Lush, & Sephton, 2010; Sephton & Spiegel, 2003). Disruptions in cortisol and circadian rhythms are linked to vulnerability to tumor incidence, faster tumor progression, and early mortality in cancer patients. Data supports that both biological (e.g., genetic) and behavioral (e.g., sleep disruption, stress) factors contribute to this link, including bidirectional relationships between circadian rhythms, endocrine activation, immune defenses, and psychosocial factors (Eismann et al., 2010). Research shows that 30-70% of cancer patients display disruptions in diurnal cortisol rhythms, including uncoordinated or erratic peaks and nadirs throughout the day, phase shifts, or generally flattened patterns at either abnormally high or low levels (Sephton & Spiegel, 2003). Aberrant patterns are most evident in patients with high tumor burden, poor performance status, and liver metastases (Sephton & Spiegel, 2003). As such, disrupted cortisol rhythms may be an indicator of progressing tumor status or the result of other biological effects of worsening psychosocial functioning (e.g., poor sleep due to pain or anxiety; Eismann et al., 2003; Sephton & Spiegel, 2003). However, the strongest evidence lies in the prognostic

significance of cortisol rhythms in cancer patients. Flattened diurnal rhythms have been shown to predict early mortality in a variety of cancers: breast (Sephton et al., 2000), renal (Cohen et al., 2012), lung (Sephton et al., 2013), and ovarian (Schrepf et al., 2015).

Flattening of the cortisol rhythm is also observed in response to stress. In a study of breast cancer survivors' affective and cortisol responses to daily stressors, survivors showed similar diurnal slopes and CAR as healthy controls, but less total cortisol on days of daily stress (Costanzo et al., 2012). The authors suggest that this may indicate a development of adaptive resilience or a blunted cortisol response to daily stress; although, the clinical significance of this hyporeactivity is unclear (Costanzo et al., 2012). Another study showed lower two-day average waking rise in cortisol in depressed breast cancer patients when compared to non-depressed (Giese-Davis, Wilhelm, et al., 2006). Similar results were observed with breast cancer survivors' responses to upcoming mammograms: survivors had similar rhythms as healthy controls, but blunted overall cortisol on the day before and of their mammogram (Porter et al., 2003). On the other hand, several studies suggest breast cancer patients demonstrate higher cortisol levels than healthy controls (Abercrombie et al., 2004; McGregor & Antoni, 2009).

Positive Affect and Cortisol

Theory. The literature on the relationship between PA and physiology among healthy populations has increased over the past decade. Several reviews have attempted to quantify the effects (Chida & Steptoe, 2008; Dockray & Steptoe, 2010; Howell et al., 2007; Pressman & Cohen, 2005; Steptoe, Dockray, & Wardle, 2009; Vázquez, Hervás, Rahona, & Gómez, 2009). The overall findings indicate that PA and positive well-being are associated with better short-term and long-term objective health outcomes in healthy

samples (Howell et al., 2007). As evidenced in both mood induction and longitudinal studies, for example, PA has related to longer survival and beneficial immune reponses (Chida & Steptoe, 2008; Dockray & Steptoe, 2010; Howell et al., 2007).

PA may relate to positive health outcomes through what is known as the "Undoing Hypothesis" (Fredrickson & Levenson, 1998; Fredrickson, Mancuso, Branigan, & Tugade, 2000). The Undoing Hypothesis states that PA influences biology via encouraging a quick return to physiological baseline in the face of stress. Fredrickson et al. (2000) observed that after a stress-inducing task, participants who watched a film provoking contentment or amusement showed faster cardiovascular recovery (e.g., heart rate, finger pulse amplitude, blood pressure) than those who watched an a neutral or sad film. This data is in line with earlier work finding PA is associated with lower sympathetic activation, reflected in heart rate, skin conductance, body temperature, and muscle tension (Levenson, Ekman, & Friesen, 1990). However, experimental studies of the "undoing" effect of PA and on cortisol specifically are rare. The following sections summarize the state of the current literature on the associations between PA and cortisol, noting that nuances in state/trait PA as well as cortisol outcome measures interfere with the ability to draw firm conclusions on this complex relationship.

Evidence in healthy samples. Despite the growing literature on the role of PA in supporting overall health, the research on PA and cortisol is still evolving (Dockray & Steptoe, 2010; Pressman & Cohen, 2005). The topic has been only briefly reviewed in meta-analyses and reviews (e.g., Pressman & Cohen, 2005). Several caveats exist when examining the current evidence. First, levels of cortisol differ in saliva, blood, and urine; caution must be taken in comparing studies that use different cortisol measurement

methods (Hellhammer, Wüst, & Kudielka, 2009). Second, the number of days of cortisol collection may greatly impact reliability of results. Diurnal slopes should be measured from at least 10 consecutive days if data are to be used for between-subjects analyses, and from at least 5-8 consecutive days if data are to be used for within-subjects analyses (Segerstrom et al., 2014). Third, as diurnal rhythms and CAR are controlled by distinct biological processes, waking samples used for calculating diurnal slope must be anchored at the actual time of waking – e.g., not 30 minutes post-waking (Kraemer et al., 2006). Calculating slopes anchored beyond waking increases the risk of inflating or deflating the true diurnal slope value.

To calculate diurnal cortisol slope, one should therefore first exclude the post-waking cortisol sample from the analyses. Then, all remaining log-transformed cortisol points (waking, bedtime) should be regressed on collection time (numeric, hours). The cortisol points should be from the entirety of the collection period; an average of daily slopes should not be used, as it contributes to data smoothing. The diurnal slope is represented by the unstandardized beta from the regression of all waking and bedtime points onto time (e.g., Turner-Cobb et al., 2000).

State PA and overall cortisol levels. Initial evidence supports that increased state PA is associated with low cortisol secretion; however, reviews note that there are some inconsistencies. Pressman and Cohen (2005) found that when PA was induced in laboratory studies, acute cortisol typically decreased or showed no change; however, a few studies showed that cortisol levels increased. These inconsistencies may be the result of different methods of cortisol measurement, for example via plasma (e.g., Brown et al., 1993; Codispoti et al. 2003) versus saliva (e.g., Hubert et al., 1993; Hubert & Jong-

Meyer, 1991). Sampling times also ranged, such as from just pre-post (Hucklebridge et al., 2000) to every 15 minutes throughout induction (e.g., Hubert & Jong-Meyer, 1991). Sample sizes for theses studies have been typically small ($N < 25$), which may also contribute to inconsistencies.

State PA and diurnal rhythms. The association between diurnal cortisol rhythms and state PA is noteworthy. As previously reviewed, cortisol exhibits a predictable diurnal rhythm in healthy functioning: a peak about 30 minutes upon awakening, followed by a relatively steady decline throughout the day. Interestingly, PA follows a similar temporal pattern to that of the cortisol diurnal rhythm: positive emotions tend to peak early in the day and then substantially decline in the evening (Clark et al., 1989; Simpson et al., 2008; Thayer, 1987, 1989). NA, however, shows no such systematic diurnal rhythm (Simpson et al., 2008; Watson, Wiese, Vaidya, & Tellegen, 1999). This differentiation in diurnal affect patterns echoes the notion that NA and PA have distinct biological systems. Dockray and Steptoe (2010) note that studies do indeed find a coupling of diurnal cortisol patterns and PA. Furthermore, PA shows a similar pattern to other endogenous processes, including body temperature and sleep-wake cycles (Watson et al., 1999).

Trait PA and overall cortisol levels. Among several large-scale studies, higher levels of trait PA tend to be associated with lower total cortisol secretion. One early study of 216 healthy adults showed that higher trait PA (as aggregated over several days) was associated with lower levels of overall cortisol secretion, even after controlling for age, gender, SES, BMI, smoking, and distress (Steptoe, Wardle, & Marmot, 2005). These findings were replicated in a later sample of 2,873 adults (Steptoe, O'Donnell, Badrick,

Kumari, & Marmot, 2008). Reviews mirror this notion, observing that PA is indeed typically linked to lower overall daily cortisol levels (Dockray & Steptoe, 2010; Pressman & Cohen, 2005; Steptoe, Dockray, & Wardle, 2009).

Trait PA and diurnal rhythms. Studies on trait PA and diurnal rhythms show somewhat mixed findings, largely resulting from methodological issues. For example, one study found that trait PA and diurnal rhythms differed by gender: men with low trait PA showed flattened, but high, cortisol levels throughout the day, and women with high trait PA showed flattened patterns of low cortisol (Polk et al., 2005). However, salivary cortisol was sampled only over one 24-hour period, and diurnal slope calculations were anchored with a post-waking sample. Another study found that that eudaimonia, but not hedonia, was associated with the low, flattened patterns of cortisol (Ryff et al., 2004). However, the study again presented methodological issues with cortisol slope calculation by anchoring with a post-waking sample and averaging daily slopes together, thus contributing to data smoothing and minimizing the robustness of the data. Overall, caution is warranted in interpreting such results.

Recent work attempts to elucidate the role of affect variability in the PA/cortisol relationship. Human et al. (2015) conducted two studies, which in aggregate suggested that less favorable cortisol profiles were associated with having either too much or too little PA variability. Flattened slopes and high cortisol means were associated with high within-day PA variability among middle age adults, and with low across-week PA variability among older-adults. The findings highlighted that variability in PA may relate to certain cortisol profiles.

The evidence surrounding the role of arousal in the relationship between affect

and cortisol is another area of growing interest. Item level analyses in the middle aged sample of Human et al. (2015) showed that *alert* was a stronger predictor of cortisol than the affects *good* and *relaxed,* highlighting the potentially important aspect of arousal in the PA/cortisol relationship. Another recent study highlighted a similar pattern of affective arousal on cortisol findings (Hoyt, Craske, Mineka, & Adam, 2015). A large sample of adolescents ($N = 315$) provided salivary cortisol samples and affective state ratings six times a day for three consecutive days. Principle component analysis identified four uncorrelated factors from mood ratings: positive/high-arousal (e.g., alert), positive/low-arousal (e.g., relaxed), negative/high-arousal (e.g., stress), and negative/low-arousal (e.g., sad). Analyses indicated that stronger positive/high-arousal was associated with steeper diurnal slope. Participants with positive/high-arousal had lower bedtime cortisol, but only at higher levels of PA intensity. Positive/low-arousal was not associated with cortisol. As such, a measure such as the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) may serve as a strong scale to capture such associations, given its inclusion of many high-arousal items (e.g., determined, enthusiastic, active).

A recent large-sample study builds evidence that high trait PA is associated with stronger cortisol rhythmicity. Using a sample of 490 healthy adults, Miller et al. (2016) measured personality and trait PA through self and observer rating scales. Participants provided five salivary cortisol samples (waking, +30mins, +4hours, +9hours, bedtime) over four consecutive days. Cortisol values were log-transformed and regressed onto time. Slope calculations were anchored at waking but still included the 30-minute post-waking sample, thus should be interpreted with some caution. Structural equation

modeling assessed the association of positive emotionality (extraversion/PA) with cortisol, and found a positive association with positive emotion with steeper slopes and smaller CAR, but no association with overall cortisol levels.

Overall, the literature on PA and diurnal slopes should be considered cautiously, due to methodological concerns. Although evidence points to a general trend of steeper slopes associated with higher PA, aspects of affect variability and arousal may be confounding results. Methodological rigor is needed in calculating slopes in order to ensure true diurnal rhythms are represented, and not muddied by the anchoring by or inclusion of CAR samples.

Summary. The growing literature on PA and cortisol among healthy samples shows some promise of true association; however, all results must be considered critically in regard to methodology and the role of affect variability and arousal. First, state inductions of PA show evidence that increased PA is associated with lower cortisol levels. Second, diurnal state PA follows a similar temporal pattern as diurnal cortisol. Third, higher trait PA may be associated with lower total cortisol secretion. Fourth, higher trait PA may be associated with steeper cortisol slopes and smaller CAR. Greater methodological rigor is warranted including enduring a minimum of several collection days, anchoring slope at waking, and excluding post-wake samples in slope calculation (Kraemer et al., 2006; Segerstrom et al., 2014).

PA and Cortisol in Cancer Samples

The quality of the relationship between PA and cortisol may differ between cancer and healthy samples in clinically meaningful ways. Receiving a cancer diagnosis results in a range of emotional experiences, more intense and complex than one would

experience under normal, healthy conditions. Thus, the stress of having cancer may significantly alter the quality of emotional experiences. Indeed the majority of research on affect in cancer focuses on negative experiences such as distress and depression. The paucity of research on PA in cancer patients is remarkable, and highlights a gap in the field. Given that relatively little is known about PA in cancer patients in general, the exploration of biological correlates makes for an even more elusive topic (Davis et al., 2015). Another critical point is that neuroendocrine function is altered when the body is fighting tumors (Sephton & Spiegel, 2003). Thus, findings from research of cortisol function in healthy populations may not be fully valid among cancer samples, but may nonetheless be informative.

To my knowledge, only four studies have investigated the association of PA and cortisol in cancer patients (Table 1). The first study compared a sample of breast cancer survivors to healthy controls (Porter et al., 2003). Longitudinal data assessed whether predicted changes in cortisol slope, overall mean levels, and reactivity to a cancer-specific stressor (mammogram). Cortisol and psychosocial data were collected for three days at baseline (one month before mammogram), and for three days at the time of the mammogram (day before, of, after). Baseline slope was calculated via a nested, mixed-linear model. Slopes were not calculated for the one-day stress samples; instead, cortisol reactivity was calculated as the slope from regressing average cortisol level during the stress days onto baseline. The authors found that higher baseline PA was associated with lower cortisol reactivity to mammogram when compared to healthy controls.

The second study was a cross-sectional investigation on whether emotional expression was related to healthier cortisol rhythms among metastatic breast cancer

patients (Giese-Davis, DiMiceli, Sephton, & Spiegel, 2006). Metastatic breast cancer patients were videotaped during the first session of expressive-supportive group therapy and provided salivary cortisol samples (three days, four samples per day). Hierarchical linear regressions assessed the relationship between PA expression and diurnal cortisol slope and average cortisol. Similar to the findings from Porter et al. (2003), the authors found that increased positive emotional expression (affection, humor, joy, etc.) was related to lower mean cortisol levels, even after controlling for negative emotional expression. NA expression, but not PA, was associated with steeper diurnal slope.

The third study was conducted by the same group and explored depression and stress in metastatic breast cancer patients (Giese-Davis, Wilhelm, et al., 2006). The overall findings of that study indicated that depressed cancer patients had less PA and lower waking cortisol levels. However, no direct analyses were conducted between PA and cortisol, thus no conclusions can be drawn about their relationship from that study.

The fourth study was on a sample of breast cancer survivors (Costanzo et al., 2012). Drawing from a large national survey, survivors were age, sex, and education matched to healthy controls. Cortisol was measured via four samples per day, over four days; slopes were anchored at waking. Findings showed that longer time since diagnosis was associated with higher levels of PA and lower levels of total cortisol. However, the relationship between PA and cortisol was not directly measured, thus conclusive associations may not be drawn. Nevertheless, it may be that longer time since diagnosis allows for more space for successful coping, reduced immediate distress about treatments or even reoccurrence, thus improving PA and reducing overall physiological stress.

Indeed some studies have shown that meaning of life scores may increase over time in cancer patients (Hsiao et al., 2013).

Costanzo et al. (2012) also found that on days where daily stressors occurred, cancer survivors showed less pronounced decline in PA and lower overall cortisol levels, but similar patterns of diurnal cortisol slope and CAR in comparison with healthy controls. Again, the direct relationship between PA and cortisol was not specifically assessed. Nevertheless, the results demonstrate an element of emotional resiliency among cancer survivors in that they maintained some PA and low HPA reactivity in the face of stress. The analyses suggest some degree of relationship between experiencing stress, maintaining PA, and minimal disruption of cortisol patterns.

Summary. In light of the minimal amount of published research on PA and cortisol in cancer patients, firm conclusions may not be made. Nevertheless, initial patterns do appear in the work presented and may inform future hypotheses. Specifically, state and trait PA seemed to relate to overall cortisol levels in these samples of cancer patients. In particular, cancer patients who had high PA showed lower overall cortisol levels, even in times of cancer-specific stress. Unlike the findings among the healthy literature, PA did not seem to show a firm relationship with diurnal cortisol rhythms in these samples of cancer patients. As with healthy samples, conclusions on CAR cannot be drawn.

Limitations of Current Literature

A review of the current literature on PA and cortisol sheds light on several limitations in these cancer studies. Several of the limitations are common to those observed in research among healthy samples as well.

Measuring PA. Lack of standard measures and interchangeable terms referring to PA and well-being leads to concerns of reliability and validity. Without consistent application of the term "PA", especially as it relates to broader concepts of subjective well-being and eudaimonia, the nuanced associations of PA with biology will be lost. However, one of the most common measures of PA is the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988), which is used throughout the healthy and cancer literature.

Furthermore, the lack of differentiation between state and trait PA invokes confusion in understanding underlying physiological mechanisms (Pressman & Cohen, 2005). Affective states are closely associated with central nervous system activation, relating directly to both neuroendocrine and cardiovascular functioning (Critchley, 2005), while positive traits such as optimism may affect physiological processes by inducing successful coping strategies (Scheier, Carver, & Bridges, 2001). Measuring self-reported average affect over a brief, set amount of time (e.g., using the PANAS anchored to the past week) may be one method to overcome this issue. Such an approach may be a more valid way of capturing affective experiences by honoring the emotional fluctuations that may occur (for example, week by week with treatment schedules) throughout the cancer journey.

Measuring cortisol. Reliable collection and calculation of cortisol remains an issue across research among both healthy subjects and cancer patients. For example, many studies include post-wake samples in their calculation of cortisol slope or use too few of days to reliably calculate the cortisol variables. Reporting of multiple cortisol metrics is also imperative, given that overall secretion levels, CAR, and diurnal slope

capture different, and somewhat independent, processes (Chida & Steptoe, 2009; Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). For example, mean cortisol levels provide no information as to how steep or flat as slope is.

Sample and design issues. All four of the studies on PA and cortisol in cancer were on breast cancer patients, limiting generalizability to other cancer samples, and in extension, to samples that include males. Gender associations with cortisol may have influenced the findings of the studies, as gender effects are seen in overall cortisol levels (Kirschbaum & Hellhammer, 1994), CAR (Clow, Thorn, Evans, & Hucklebridge, 2004), and slope (Human et al., 2015). Lack of generalizability extends to several of the healthy sample studies as well, with some having strikingly small samples sizes (e.g., 5 experimental participants and 5 controls, all men; Berk et al., 1989), all one gender, or of a certain age range (e.g., Ryff et al., 2004; Steptoe, Gibson, Hamer, & Wardle, 2007). More research is needed with other cancer samples, such as lung cancer, that are inclusive of both genders, wide age range, and have larger sample sizes.

A final and related critique of the current literature is that studies differ on the control variables used in analyses. Costanzo et al. (2012) could not control for certain cancer-specific variables since the data came from a large-scale aging study where these variables were not assessed. The other cancer studies did not use control variables in primary analyses or used analyses that did not allow for them. Most importantly, NA is not consistently controlled for in both healthy and caner studies (Steptoe et al., 2009). Accounting for the effects of NA is essential to understanding the unique contributions of PA in salutary biological effects. Other potential confounding variables that associate

with PA include gender (as previously discussed), age (Mroczek & Kolarz, 1998), socio-economic status (Diener & Biswas-Diener, 2002), and education (Keyes et al., 2002).

A Cancer-Specific Integrated Model

While the literature on physiological processes associated with PA in healthy samples is in its infancy, research among cancer patients can highlight important processes and outcomes. In this light, I present an original integrated model driven by theory and based on the previously reviewed literature (Figure 1). I propose that, in cancer patients, PA and eudaimonia differentially interact with distress effects on the brain and HPA system, and that these effects are different from those seen in healthy samples. Neurobiological mediators are presented, yet an in-depth review of them is beyond the scope of this paper. The model is presented to create a context for more specific future research and to spark foundational research upon which to build.

Pressman and Cohen (2005) suggest that PA may have a direct effect on HPA functioning in healthy samples. However, in cancer patients, PA alone may not be strong enough to have a main effect on biology. The direct effects of PA on the HPA may be masked in cancer due to increased psychological stress, as well as tumor and treatment effects on physiology. Pressman and Cohen (2005) put forth a second model that suggests PA works indirectly on biology through buffering stress and immune responses. However, the model lacked specific theories of mechanisms, did not include the role of neurobiological components, and was not cancer specific. Thus, my proposed model captures these elements to present how PA may relate to cortisol in cancer patients.

Cancer patients experience distress (Zabora et al., 2001; Figure 1, arrow A). Perceived stress affects the HPA system (Chrousos, 1998; arrow B) and other emotion-

related brain structures including the prefrontal cortex (PFC), ventral striatum, amygdala, and hippocampus (Arnsten, 2009; arrow C). These areas of the brain may also interact with HPA function (Chrousos & Gold, 1992; Dedovic et al., 2009; Kern et al., 2008; arrow D). Evidence is building that positive psychological processes may have main effects with these same brain regions (arrows E and F). Positive affect may stem from the activation of "hedonic hotspots" in the limbic system and cortex, thus producing the experience and awareness of state positive emotions (Kringelbach & Berridge, 2009). The chronic experience of state PA (i.e., trait PA) then in turn strengthens these systems (Kringelbach & Berridge, 2009). Increased PA is associated with increased left frontocentral activation (Urry et al., 2004), while eudaimonic processes are associated with the frontal cortex, amygdala, insula, and cingulate cortex (Heller et al., 2013; Lewis et al., 2014; Urry et al., 2004). In relation to the HPA, people with greater ability to maintain activation in brain reward systems (i.e., PFC and striatum) demonstrate higher PA, greater eudaimonic well-being, and lower overall cortisol levels (Heller et al., 2013).

The experience of PA broadens one's cognitive and behavioral repertoire, leading to a building of physical, social, intellectual, and emotional resources ("Broaden and Build"; Fredrickson, 2001). This creation of wide spreading psychological resources mirrors the concept of building eudaimonic well-being (Ryff, 1989). Engaging in these resources then feeds back to creating more positive emotions. This "Broaden and Build" process is evident in cancer patients (arrow G). Feelings of joy, inner peace, and happiness are associated with increased quality of life in patients, with joy specifically being associated with having a more meaningful life and a good death (Lin & Bauer-Wu,

2003). Other studies suggest that patients with higher PA also experience more feelings of meaning and peace (Voogt et al., 2005).

If PA and eudaimonia indeed interact to build each other, their unique effects on cortisol in cancer may be difficult to parse out. Nevertheless, I propose that PA and eudaimonia, although interrelated, produce different cortisol outcomes based on two different, theoretically-driven mechanisms. First, the research suggests that state and trait PA relate to cortisol reactivity (i.e., total cortisol secretion), but perhaps not as strongly to cortisol slopes, in cancer patients. I propose this may be due to Fredrickson's "Undoing Hypothesis" (Fredrickson & Levenson, 1998; Fredrickson et al., 2000; arrow H_1). The Undoing Hypothesis suggests that the experience of PA in the face of stress helps the body return to a physiological baseline faster than neutral or negative emotions do. In this way, state PA (and by extension trait PA) may work to "undo" similar HPA stress responses, by activating parts of the brain such as the PFC and hippocampus that help initiate the stop of cortisol production (Chrousos & Gold, 1992). In other words, once a stressor is faced, patients who also experience PA are better able to discontinue the stress response, thus allowing for a lower accumulation of total cortisol (arrow H_2).

PA in this sense may be conceptualized as a "short term" process, by preventing accumulation of cortisol through "undoing" the negative physiological effects of acute, rather than chronic, stress. Indeed stressors in the cancer studies may be described as short term: daily stressors (Costanzo et al., 2012), current discussion of cancer-related topics (Giese-Davis, DiMiceli, et al., 2006), or a cancer-related stressor happening the next day (Porter et al., 2003). Of note, the women in Costanzo et al. (2012) endorsed experiencing stress, but still maintained high PA, and showed lower overall cortisol

output. Although stress perceptions were not directly measured in the other studies, similar processes may have been at play, as they too observed that patients with high PA showed lower total cortisol levels (Giese-Davis, DiMiceli, et al., 2006) and lower cortisol reactivity (Porter et al., 2003) to their cancer-related stressors. Given that trait PA may be conceptualized as the frequent and consistent experience of state PA, one might consider too that trait PA would also be associated with lower levels of overall cortisol because of this undoing process.

Despite evidence among healthy samples, there is a lack of firm support that PA may relate to longer-term cortisol outcomes such as diurnal rhythms. Since this point is drawn from only four studies of breast cancer patients, more research is certainly needed in this area. However, it may be that eudaimonia, a more enduring process that involves building coping skills and psychological resilience, is a more potent positive psychological process than PA alone in cancer patients. Eudaimonia is therefore more likely *buffer* the effects of stress, through using broad psychosocial resources to adaptively adjust appraisals, coping, and emotional outcomes (arrow I_1; Fredrickson, 2001). This buffering effect is likely to influence biological indicators of chronic (rather than acute) distress, such as disrupted diurnal rhythms (Figure 1, arrow I_2). Although a thorough review of studies was outside the scope of this paper, initial evidence exists that improving experiences of eudaimonia, such as meaning making through psychotherapy, results in steeper cortisol slopes in cancer patients (Hsiao et al., 2012). Extending from this, a recent study on hedonia and eudaimonia in ovarian cancer patients utilized structural equation modeling and found that eudaimonia was associated with lower tumor norepinephrine; however, PA was not (Davis et al., 2015). It may be that although PA

and eudaimonia are related, the more enduring processes involved with building eudaimonia may be more strongly associated with robust biology (e.g., diurnal rhythms) than PA alone.

It also remains unknown if total cortisol output relates to diurnal slopes in a similar way that PA relates to eudaimonia – that they are proxies of each other and work in a feedback process (Fredrickson, 2001). Indeed, the relationships between cortisol output and diurnal slope are yet to be fully understood in cancer patients (Giese-Davis, DiMiceli, et al., 2006). As PA works to produce eudaimonia through Fredrickson's Broaden and Build theory, it may be that the respective effects on cortisol work in a similar way. If a patient is better able to maintain low cortisol reactivity (i.e., low means and quick return to baseline HPA function), the patient may in turn see an overall maintenance of cortisol rhythms and a preservation of steeper slopes. The PA and eudaimonia relationship may work in parallel to the cortisol output and cortisol rhythmicity relationship.

The final stage of the model relates to long-term outcomes. Psychological resilience in the short-term (PA and overall cortisol) coupled with resilience in the long-term (eudaimonia and diurnal rhythms) work jointly to influence other downstream processes, such as inflammation. These psychoneuroimmune and endocrine processes then relate to health outcomes such as disease progression, survival, and quality of life (Lutgendorf & Costanzo, 2003).

THE PROPOSED STUDY

Given the state of the current research, PA seems to relate to biology in meaningful ways. However, the relationship to cortisol may differ between cancer patients and the healthy population. Due to cortisol's particular importance in cancer outcomes, this topic deserves greater attention. While PA seems to be associated with a broad range of cortisol outcomes in healthy samples, data from cancer patients demonstrate more limited associations, implying that certain positive experiences may be related to specific cortisol responses or that mind-body relationship may be masked by disease-related variables. The integrated model highlights recent research on neurobiological pathways as well as theoretically-driven mechanisms. Future research will clarify these processes, leading to improvements in clinical applications and policy.

To help begin filling in the scientific gap concerning the PA/ cortisol relationship in cancer patients, the current study will focus on the proposed direct pathway between PA and cortisol (Figure 1, arrow H_2; Figure 2). The study will use a sample of lung cancer patients, given the relative paucity of literature on psychobiological processes in this vulnerable population. The study will test the association between PA experienced over the past week and subsequent cortisol outcomes over the following ten days.

Research Question and Hypotheses

Aim 1. Understand the frequency and quality of PA among lung cancer patients. Explore what elements of the person (e.g., demographic variables) and his or her cancer

journey (e.g., medical variables) may be associated with experiencing more positive affect. The primary research question is: *What positive emotions, and to what degree, do lung cancer patients experience in a given week? What are the demographic and medical variables that may relate to experiencing more positive affect among these patients?*

Hypothesis 1.1. Positive affect in this sample will be described at an item, subscale, and construct level. Patients will experience moderate PA, and patients will report more PA than NA, as tested by the PANAS.

Hypothesis 1.2. In exploratory analysis, positive and negative affect items will emerge as separate factors.

Hypothesis 1.3. Variables that reflect lower disease burden (e.g., lower stage, no current treatment, longer time since diagnosis) will be associated with higher PA.

Aim 2. Test the relationship between positive affect and cortisol outcomes. The primary research question is: *Does positive affect relate to diurnal cortisol measures in lung cancer patients?*

Hypothesis 2.1. Higher PA will be related to lower mean cortisol levels.

Hypothesis 2.2. Higher PA will be related to steeper diurnal cortisol slope.

Hypothesis 2.3 PA will more strongly relate to mean cortisol than to diurnal slope.

METHOD

Data were collected as part of a larger study investigating the prognostic significance of circadian disruption in lung cancer patients and the utility of a mindfulness-based coping skills intervention (University of Louisville IRB 13.0508).

Recruitment

Study personnel were trained by the University of Louisville to ethically conduct human subjects research. The University of Louisville and the James Graham Brown Cancer Center provided hospital accreditation to recruitment personnel in order for them to have patient contact in the clinic. Lung cancer patients were recruited for the study from thoracic oncology clinic at the James Graham Brown Cancer Center in Louisville, KY. Recruitment personnel reviewed all patients listed on the clinic's outpatient schedule and assessed each patient's eligibility through the use of a standardized screening chart review. The chart review included a summary of inclusion/exclusion criteria as well as other relevant medical and demographic factors. Attending physicians were made aware of which patients met study criteria. Physicians then briefly introduced the study to potential participants after their appointment, at which time the recruitment personnel met with the patient. Patients were given information regarding the purpose and requirements of the study, presented with opportunities to ask questions, and invited to provide consent for participation. If the patient enrolled, the recruitment personnel worked closely with the patient to explain the instructions for data collection and the process of the study in detail.

Participants

Patients were recruited between February 2014 and October 2016. To have met study eligibility criteria, patients must have been between the ages of 18 to 85, have received a diagnosis of non-small cell lung cancer with the previous five years, have no concurrent medical diagnosis likely to influence short-term (i.e., six-month) survival, live within a 120-mile radius of Louisville, KY, have no history of psychiatric hospitalization, no history of drug or alcohol abuse within the previous two months, and no known immune compromising conditions such as hepatitis or HIV/AIDS. Sociodemographic and cancer related history and treatment variables were derived from chart review at the time of eligibility assessment.

Ninety-three patients were invited to participate in the study during the recruitment period. Of those invited, 67 chose to enroll at baseline. Six of these patients withdrew during baseline collection for reasons such as current health issues or current social stressors. The final sample of patients for the current study was therefore 61 patients. Full cortisol data was completed for 57 of these patients.

Data Collection Procedure

Informed consent. All study procedures were conducted in accordance with guidelines set forth by the University of Louisville Human Subjects Protection Program. All study participants provided informed consent and Health Information and Privacy Protection Act (HIPPA) documents prior to enrollment.

All participants were enrolled in a larger study examining the prognostic significance of circadian disruption in lung cancer and the utility of a piloted mindfulness-based coping skills intervention. Data for the current study consisted only of

baseline data collection. After informed consent, participants were provided with a baseline questionnaire packet, a ten-day daily brief questionnaire packet, a salivary cortisol collection kit containing 20 salivary collection tubes ("salivettes"; Walter Sarstedt Inc., Newton, North Carolina), and a wrist-worn actigraphy watch. A trained phlebotomist drew three vials of blood for assessment of immune and metabolic functioning. Participants were compensated with a $100 pre-paid gift card for completing baseline data collection in full. Participants were invited to participate in a mindfulness-based coping skills intervention over the following three months, and a follow-up assessment similar to baseline after completing the intervention.

Demographic and medical variables. Demographic and medical history variables were derived from the medical chart at the time of recruitment. Participants were also instructed to complete a set of demographic items in the beginning of the baseline questionnaire packet.

Psychosocial questionnaires. Participants were asked to complete a set of psychological measures consisting of both risk and resilience factors, which took about an hour and a half to complete. As part of this questionnaire packet, participants completed the Positive and Negative Affect Schedule (Watson et al., 1988) coded to assess affect over the past week. Participants also were given a ten-day daily questionnaire packet, consisting of brief questionnaires on variables that may affect cortisol (e.g., sleep, medications); these questionnaires took about 10 minutes to complete each day.

Salivary cortisol. The daily questionnaire packet provided detailed instructions on salivary cortisol collection, as well as a supplemental document for the participant to

note any deviations from the data collection protocol. Participants were provided with a salivary cortisol collection kit. The kit includes 20 pre-labeled salivettes, each labeled with a sticker for recording the participant's identification code, exact time of saliva sample, and the date. Salivettes were organized by sample time and day of collection in the kit. The kit was provided in a large zip-lock bag and included a sharpie marker to maximize participants' ability to accurately record data on the salivette. Participants were instructed to provide two salivary samples each day for ten consecutive days: one sample immediately upon awakening and one sample at bedtime. To provide a saliva sample, participants removed the cap from the salivette and placed the entire cotton swab in their mouth, keeping the swab there until it was fully saturated (about two minutes). While the swab was in their mouth, participants noted their identifier code, and the exact time and date on the salivette, using their actigraphy watch as a reference point. Participants then spit the saturated swab back in the salivette tube and closed the cap tightly. Participants then placed the fully labeled sample in the zip lock bag and kept all collected samples in the refrigerator. All saliva samples are kept refrigerated until they are returned to the lab for processing.

Recruitment personnel suggested that the cortisol collection kit be kept at the participant's bedside in order to maximize the ease and reliability of collecting the morning sample immediately upon awakening. To ensure accuracy of data collection, study personnel emphasized to the participants that the morning saliva samples must be taken at the moment of awakening. Any delay in this sample will result in an inaccurate waking cortisol value and may instead capture CAR. Participants were reminded of the importance of recording the exact time of all saliva samples on the specified label on the

salivette. They were instructed not to eat, drink, smoke, chew gum, or brush teeth 30 minutes prior to any saliva sample, which minimizes any risk of contaminating the cortisol data. They were advised to note any late sample takings, difficulties they had, or accidental contaminations of any saliva sample on a supplemental document provided with the daily questionnaire. Study personnel called the participant around the third day of the 10-day collection to check in on the status of data collection and clarify any questions or concerns the participant may have had.

Data retrieval. During the data collection, study personnel contacted the participant to schedule a time to meet and collect the baseline data and provide the $100 prepaid gift card. At the scheduled meeting, all study materials were returned. The participant was compensated and was instructed on further study protocol (i.e., intervention and three month follow-up). The study personnel returned to the lab on the University of Louisville Belknap campus to file the questionnaire data and begin processing the biological data.

Cortisol assay. Once salivary cortisol samples were returned to the lab, they remained refrigerated until prepared for assay. All saliva samples were processed within one month of the first sample, but typically within a few days of the last sample. Salivettes were centrifuged for 15 min at 453 g at 25 °C. Any abnormal appearance in the cotton or saliva was recorded. Samples were pipetted into microcentrifuge tubes, placed in freezer boxes, and frozen in a -80 °C freezer until assayed. The cortisol levels were assayed using an enzyme-linked immunoabsorbent assay (ELISA) developed for use in saliva (Salimetrics, Inc., State College, PA). Along with participant assay results, samples of known high and low concentration cortisol were evaluated to obtain reliability

estimates for the assay. Assay sensitivity was 0.007 μg/dL. The average inter-assay and intra-assay coefficients of variation (CV) were under 10% for both the low and high controls.

Measures

Demographic and medical data. In order to explore demographic and cancer-related individual difference factors associated with PA, an array of variables were collected during medical chart review and in the baseline questionnaire packet. Demographic variables included age, gender, race/ethnicity, household income, and years of education. Medical variables of interest included age at diagnosis, cancer stage, smoking history, current or past treatment (radiation, chemotherapy), and current medications. Cancer stage and date of diagnosis were confirmed through chart review. There were no missing data for medical and demographic variables, except smoking. One individual opted not to answer current smoking status. Of patients with a smoking history (n=59, including current smokers), four did not answer how many years they smoked (the distribution remained normal). Smoking history was quantified as pack-years, which is the number of packs of cigarettes per day multiplied by years smoking. Four current smokers indicated a difference between current pack years and historical pack years, all showing a decrease in current smoking; in these cases, historical pack years was used as their total pack years number to account for smoking over the lifetime. Control variables used in Aim 2 analyses were derived through theoretically-based and data-driven verification.

Positive affect. The Positive And Negative Affect Schedule (PANAS) was the primary measure used to assess affect (Watson, et al., 1988). The PANAS is a 20-item

self-report measure, which assesses positive and negative affect scores on a five-point scale ranging from *very slightly or not at all* to *extremely*. The total score from the ten positively valenced items and the ten negatively valenced items comprise the PA and NA subscales, respectively. The PA subscale reflects the extent to which the participant feels positive mood states such as, "inspired", "interested", and "excited". The NA subscale captures aversive mood states such as "irritable", "guilty", and "scared". The PANAS may be coded to either momentary affect, general affect experienced over the past week, or other set timeframes; the PANAS was coded to the past week in this current study. The measure was originally validated and developed in an undergraduate sample. The internal consistency of the measure is excellent, with alpha coefficients for the PA scale ranging from .86 - .90, and for the NA scale ranging from .84 - .87 (Watson et al., 1988). The PANAS has been used in cancer populations, with alpha coefficient of the PA scale at .88 and of the NA scale at .91 (Manne & Schnoll, 2001). The PA-NA inter-correlation ranges from -.12 to -.23, indicating quasi-independence between the subscales (Watson et al., 1988). The test-retest reliability for the PANAS coded to the past week is .47 for both PA and NA (Watson et al., 1988).

The positive affect items of the Center for Epidemiologic Studies Depression scale (CES-D) were used as a secondary measure of PA. The CES-D is a popular, standardized measure used to assess depressive symptoms (Radloff, 1977). It is comprised of a total of 20 items: 16 items measuring depressive symptoms and behaviors, and four items assessing positive affect. Participants are asked to rate the frequency of the feelings or behaviors over the past week. Items are scored on a four-point Likert scale, ranging from *Rarely or None of the Time* to *Most or All of the Time*. Total score is

comprised of the sum of the depressive symptoms items and the reverse score of the positive affect items. The measure has high internal consistency (alpha coefficients ranging from .85 - .90).

The positive affect items of the CES-D include: I felt that I was just as good as other people, I felt hopeful, I was happy, I enjoyed life. These items were originally added to the CES-D in order to break tendencies towards response set and to assess the absence of PA in depressed people (Radloff, 1977). However, in a large sample of both cancer (n = 434) and healthy controls (n = 236), factor analysis found that these PA items consistently loaded onto a separate factor that had relatively low correlation with the depressed affect scale (r = .14), which is consistent with other factor analysis studies (Schroevers et al., 2000). These findings suggest that the PA items of this measure likely represent a construct independent of depression (i.e., positive affect, rather than the absence of depressive symptoms). Cronbach's alpha for PA in that study was 0.75 for the cancer sample and 0.76 for healthy controls (Schroevers et al., 2000). Therefore, in the current study, the total score of PA items (not reverse scored) on the CES-D was used as a secondary measure of PA (CES-D PA). This secondary measure of PA served as both construct validity for PANAS-PA as well as a method to expand the span of arousal that could be captured between the PANAS and CES-D PA items.

In both psychosocial measures (PANAS, CES-D PA), data were reviewed for outliers. Missing data was addressed through imputation. Consistent with the laboratory protocol for missing data, no data were imputed if over half of the data were missing for a subscale. If less than or equal to half of the data were missing, items were replaced with the subscale mean for that individual. Following this criterion, item-level data were

replaced for six individuals for the PANAS. Four patients had missing one or two items replaced. One patient had four missing data points replaced. One patient missed exactly half of the PANAS items (equally split between PA and NA), thus the subscale means were replaced for those ten missing items, and the patient was kept in the dataset. Four individuals had item-level data missing for the CES-D; three patients had one missing item, and one patient had two missing items. Two people did not complete the CES-D, but these individuals were retained in the overall dataset (with no CES-D score) due to small sample size; these individuals did not significantly differ from the overall dataset on demographic or medical features. Missing data were imputed before total or sum scores were calculated.

Cortisol. Salivary cortisol data was collected over ten days to maximize the reliability of intended cortisol outcome variables (Segerstrom et al., 2014). The sampling times of waking and bedtime were selected because they will allow calculation of the diurnal cortisol slope (Sephton et al., 2000). Raw cortisol values were log-transformed prior to analysis to account for known skew, and diurnal mean cortisol was calculated using the log-transformed daytime values. Cortisol values were regressed on collection time to yield a diurnal cortisol slope for each individual (Sephton et al., 2000; Sephton et al., 2013). Final cortisol outcome variables consisted of mean log waking value, mean log bedtime value, overall diurnal log mean, and diurnal slope calculations over the ten-day collection period.

Statistical Analyses

Data reduction and scoring. ***Questionnaire data.*** Two research assistants entered questionnaire data into independent databases. The databases were compared to ensure correct entry. Questionnaires were scored after missing data were replaced.

Cortisol. Raw cortisol data consisted of an exact collection time recorded by research subjects on saliva collection tubes and a laboratory-generated cortisol value (μg/dl) from the assay. Collection times were recoded first to military time (i.e., 8:30 PM becomes 20:30) and then transformed to numeric time (i.e., 20:30 becomes 20.5 hr). Bedtime samples collected after midnight (e.g., bedtime sample collected at 12:30 AM) were recoded as occurring beyond 24:00 hours (e.g., 12:30 AM coded as 24.5 hr, 1:15 AM coded as 25.25 hr, etc.). Assay results that were too high to be read by the standard curve were diluted and re-assayed with subsequent results adjusted accordingly. Sample collection times reported by subjects were checked and corrected using wrist-worn actigraphy data, collected for aims of the parent study. Several baseline cortisol samples (7.5%) had collection times that were modified based on one of the following reasons: 1) to ensure records were cohesive in using the military time format, 2) to exclude samples collected more than 15 minutes after actigraphy-based waking as the salivary waking samples, as they instead reflect cortisol awakening response, 3) to correct collection time of bedtime samples such that they were not listed as having been collected after participants were asleep. Prior to calculating cortisol variables of interest, raw cortisol values were transformed using the natural log to account for known positive skew.

Diurnal slope was calculated by regressing the log-transformed cortisol values (waking, bedtime) on time (numeric, hours). A maximum of twenty total cortisol samples

per participant were therefore be entered into the regression. The diurnal slope is represented by the unstandardized beta from the regression. Values for the diurnal cortisol slope are generally negative between 0.9 and -0.9 with higher numbers indicating flattened or aberrant slopes. Mean raw and log-transformed cortisol values were calculated by averaging all cortisol data points collected at waking and bedtime, both together and separately.

Sample characteristics. Characteristics of the sample were determined by calculating frequency, percentage, and mean data on demographic variables.

Descriptive statistics. Descriptive data in the form of means, standard deviations, and percentages were calculated for independent and dependent variables.

Tests of hypotheses. Descriptive analyses were used to determine the fit of the data with regard to all assumptions of analyses. All assumptions were met prior to analysis, and significant outliers were removed if present. Statistical analyses for each Aim are described below.

Aim 1. Hypothesis 1.1 was approached in an exploratory manner. Descriptive statistics (mean, standard deviation, range, frequencies) were used to understand the overall distribution of positive affect (PANAS items, CES-D positive items). A within-subjects two-tailed t-test tested the hypothesis that patients would report more PA than NA (PANAS subscales). To explore PA on the construct level, bivariate correlations between the PA subscale of the PANAS and the PA items of the CES-D and between the PA and NA subscales of the PANAS were conducted.

Hypothesis 1.2 was examined through an exploratory factor analysis, in which it was hypothesized that PA and NA items from the PANAS would fall into two distinct factors in this lung cancer sample.

Hypothesis 1.3 assessed the relationship between PA and demographic/medical features, hypothesizing that variables reflecting lower disease burden (e.g., lower stage, no current treatment, longer time since diagnosis) would be associated with higher PA. Bivariate correlations assessed the strength of the relationship between PANAS scores (subscales, items) and CES-D scores (subscale, items) and demographic/medical factors. Pearson r correlations were used for continuous, linear variables (e.g., age, time since diagnosis); point-biserial procedure of Pearson r correlations was used for dichotomous variables (e.g., gender). Data used in Pearson r correlations met assumptions of linearity and normality prior to analyses. If assumptions were violated, Spearman rank correlations were used. Spearman rank correlations were used for ordinal data (e.g., cancer stage). Data used in Spearman correlations met the assumption of monotonicity. All correlations used two two-tailed tests of significance.

Aim 2. For regression analyses of Aim 2 (Hypotheses 2.1 and 2.2), four regressions were conducted for each of the four cortisol dependent variables. Primary analyses utilized data-driven covariates; ad-hoc analyses utilized both data-driven and theoretically-derived covariates. Across Hypotheses 2.1 and 2.2, the first regression tested PANAS PA and data-driven covariates (Kraemer et al., 2001). The second regression tested PANAS PA included both data-driven and theoretically-driven covariates; theoretical covariates were decided based on previous literature (i.e., NA) and lab conventions (i.e., corticosteroid use), but were limited in number due to small sample

size. The third regression tested PANAS PA and CES-D with data-driven covariates (Kraemer et al., 2001), and the fourth regression tested PANAS PA and CES-D with both data-driven and theoretically-driven covariates.

Hypotheses 2.1 and 2.2 were analyzed using hierarchical linear regressions. Regressions met assumptions of linearity, normality of residuals, and homoscedasticity prior to analysis. In step one, theoretically and/or data-driven control variables (e.g., NA, medical variables) were entered. In step two, the PA subscale was entered. For Hypothesis 2.1, the outcome variables were log mean diurnal cortisol, log mean waking cortisol, and log mean bedtime cortisol, respectively. For Hypothesis 2.2, the outcome variable was diurnal cortisol slope.

Hypothesis 2.3 was explored using path analysis. The primary model included the exogenous variables of PA (PANAS-PA) and endogenous variables of mean diurnal cortisol and diurnal cortisol slope. All statistical assumptions were met prior to analysis. Secondary exploratory models were constructed to assess the contribution of control variables and CES-D PA, similar to the Hypotheses 1 and 2 regressions. The model parameters were reviewed, and model fit was assessed. Adjustments to improve model fit were addressed.

Power analysis. G*Power version 3.1.3 was used to determine the power of the enrollment sample size ($N = 61$) for the study aims. Voogt et al. (2005) found a small to medium effect of age ($r = -.32$) on PA in their sample of 105 mixed cancer patients. There was a medium effect of gender (Cohen's $d = .48$, women had higher PA) and small effect of income (Cohen's $d = .19$, higher income associated with more PA). The authors found a small effect of medical variables: length of disease in months ($r = .06$), planned

surgery (Cohen's d = .87), planned chemotherapy (Cohen's d = .06), planned radiation (Cohen's d = .36). Increased physical functioning was positively associated with PA (r = .26). A small effect size of stage on PA (r = -.04) was found in a sample of 133 lung cancer patients (Hirsch, Floyd, & Duberstein, 2012). Based on the expectation of a small to medium effect size in our sample of 61, our power will range between .33 and .99 for Aim 1.

Previous studies note a small to medium effect size for the relationship between PA and cortisol. Polk et al. (2005) found small effect of .12 for the association of PA and reduced waking cortisol concentration in their sample of 334 healthy adults. They also noted a small effect of PA on diurnal slope (r = -.04 for trait PA, r = .10 for state PA; Polk et al., 2005). Another study of 166 healthy adolescents showed a small but significant effect of PA on steeper diurnal cortisol slope (β = -.04) and a significant medium to large effect size on lower bedtime cortisol (β = -.661; Hoyt et al., 2015). Miller et al. (2016) found a small but significant effect of PA on steeper diurnal cortisol slope (β = -.19) in their sample of 490 healthy adults. In a breast cancer sample (N = 29), Giese-Davis, DiMiceli et al. (2006) found a small to medium effect of .38 for the association of PA expression and reduced mean cortisol. The authors found no effect of PA expression on diurnal cortisol slope (r = -.01) but found a medium effect size on lower 8:00AM cortisol (r = -.33; Giese-Davis, DiMiceli et al., 2006). Based on the expectation of a small to medium effect size on cortisol measures in our sample of 61, our expected power ranged between .19 and .85 for Aim 2.

RESULTS

Patient Characteristics

Patient demographics are presented in Table 2. Medical variables of the patient sample are presented in Table 3 (staging and diagnosis), Table 4 (medications), Table 5 (smoking history), and Table 6 (cancer treatment).

Aim 1

Hypothesis 1.1. Descriptive statistics were used to understand the overall distribution of positive affect. Table 7 presents the descriptive statistics of the items and summary scores for the PANAS and the positive items of the CES-D. Patients reported moderate PA (PANAS: $M = 28.79$, $SD = 8.57$, range = 11 – 47). The distributions of the PANAS PA subscale and the individual PA items appeared normal, with the exceptions of "proud", which was more uniform in distribution, and "inspired", which had a slight positive skew. On the PANAS, the most endorsed positive emotion was "Determined" ($M = 3.31$, $SD = 1.15$), and the least endorsed positive emotion was "Inspired" ($M = 2.59$, $SD = 1.24$). The CES-D PA subscale was negatively skewed, $W(59) = .908$, $p < .001$, with most people reporting moderate to high levels of PA ($M = 8.57$, $SD = 2.98$, range = 1 – 12). The most common positive emotions endorsed on the CES-D were "I enjoyed life" and "I felt just as good as other people" ($M = 2.31$), while the least endorsed item was "I feel hopeful about the future" ($M = 1.81$). The distribution of PANAS PA and NA item means is shown in Figure 3.

A paired samples t-test tested the hypothesis that patients would report more PA than NA. The PANAS NA subscale was positively skewed, $W(61) = .923$, $p = .001$, while the PA subscale was normally distributed, $W(61) = .985$, $p = .661$; however, differences between the scores were computed and checked for normality using the Shapiro-Wilk test. The distribution of the differences between the PA and NA scores was normal, $W(61) = .988$, $df = 61$, $p = .828$, thus no assumptions were violated. The Shapiro-Wilk test of normality was used as it has higher power than the Kolmogorov-Smirnov test (Ghasemi & Zahediasl, 2012). Results indicated that, on average, patients experienced more PA ($M = 28.79$, $SD = 8.57$) than NA ($M = 19.46$, $SD = 8.26$), as measured by the PANAS. This difference, 9.33, 95% CI [6.52, 12.14], was significant $t(60) = 6.633$, $p < .001$, and represented a large effect, $d = 1.12$.

Bivariate correlations explored whether the PA subscale of the PANAS related to the CES-D PA subscale. The PANAS PA subscale was positively correlated with positive emotion (CES-D positive items, $r_s = .528$, $p < .001$), which reflected a large effect size (Cohen, 1992). Although PANAS PA and CES-D were significantly correlated (thus risking multicollinearity), the CES-D was included in subsequent regression analyses (Aim 2) given that the correlation was less than .80 (Fields, 2013, p. 325).[1] The PANAS PA and NA subscales were not significantly correlated ($r = .138$, $p > .05$).

Summary of hypothesis 1.1 results. Hypothesis 1.1 was supported. Patients reported experiencing moderate levels of PA over the previous week. On average, they endorsed experiencing significantly more PA than NA. The PA subscales of the PANAS

[1] CES-D was included in regression analyses also at the request of a committee reviewer at the time of the proposal review.

and CES-D were significantly correlated, providing construct validity. Last, the PA and NA subscales of the PANAS were not correlated, in line with previous literature.

Hypothesis 1.2. Given the small sample size, the results of the EFA must be interpreted with caution. Some data suggests that 10-15 participants per variable is most reliable (Fields, 2012, p. 683); although, other research suggests a 3:1 participant-to-variable ratio may be adequate enough to detect underlying factors (Anderson & Rubin, 1956). Thus, with 61 participants and 20 variables (each of the 20 PANAS items), the available data meets a minimum requirement for an EFA. Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) for this sample suggested an adequate and acceptable sample size (KMO = .734). Furthermore, communalities prior to extraction ranged from .556 - .856, again suggesting data were adequate to explore underlying factor structure.

An initial check of correlations between items was conducted to examine data for extreme levels of multicollinearity ($r > .8$) and singularity ($r = 1$). No correlation exceeded $r = .8$. The highest item correlations were between active and determined ($r = .742$, $p < .001$) and scared and afraid ($r = .757$, $p < .001$). Bartlett's test confirmed that the correlation matrix contained acceptable levels of correlations between variables ($\chi^2 (190) = 761.605$, $p < .001$). All 20 PANAS items were therefore used in the EFA. Output was sorted by loading size, and factor loadings were not suppressed by loading size.

EFA was conducted using Principal Axis Factoring. The first extraction was based on Kaiser's rule and eigenvalues greater than 1. Since missing data had already been imputed and given the small sample size, pairwise case exclusion was selected to minimize any loss of data. Although theoretical and objective data from this sample suggest that PA and NA are independent and distinct dimensions, an oblique rotation

using promax criterion was conducted due to the exploratory nature of this analysis (Costello & Osborne, 2005). Oblique rotation allows for the potential for underlying factors to be correlated *or* uncorrelated, whatever best fits the data. Thus, if the underlying factors were indeed uncorrelated in this sample, a largely orthogonal solution would nevertheless emerge, despite using an oblique rotation method.

Using the eigenvalue greater than 1 criterion, the EFA extracted five factors. Of variance accounted for by these factors, factors 1 and 2 explained the most (29.8% and 23.1%, respectively), while factors 3 through 5 explained much less (8.0%, 5.9%, 5.6%, respectively). The scree plot (Figure 4) demonstrated points of inflexion at the third, fourth, and sixth factors, suggesting a two, three, or five factor solution may be most appropriate for the data. These three solutions were therefore explored more thoroughly by re-running the analyses with forced cut-off criteria of two, three, and five factor solutions.

Two-factor solution. In the two-factor solution, all 20 PANAS items fell into the same PA and NA subscales as identified on the standardized measure. The pattern matrix (Table 8) revealed PA items strongly loaded onto factor 2 (coefficients ranged from .441 - .816) and not factor 1 (coefficients ranged from -.230 - .152), while NA items strongly loaded onto factor 1 (coefficients ranged from .326 - .827) and not factor 2 (coefficients ranged from -.184 - .148). Consistent with previous bivariate correlations, the intercorrelation matrix indicated that these PA and NA factors were mildly positively correlated (r = .12). The factor plot demonstrates that all PA and NA items strongly load onto two factors representing the respective PA and NA subscales of the PANAS (Figure 5).

Three-factor solution. In the three-factor solution, all 10 PA items remained a cohesive factor, with coefficients ranging from .422 to .802. The PA items with the highest coefficients (>.7) were strong, proud, inspired, determined, attentive, and active. The pattern matrix (Table 9) showed that the NA items fell into two factors, with shame and guilt emotions emerging as a separate factor from the other items (factor 3; coefficients of .873 and .694). These two factors were moderately positively correlated (*r* = .336). The PA factor remained mildly correlated with the NA factor (*r* = .113) and the shame/guilt factor (r = .135). The three-dimensional factor plot provides a visual representation of the three-factor solution (Figure 6).

Five-factor solution. In the five-factor solution, the pattern matrix (Table 10) showed that items most strongly loaded onto the first four factors, suggesting the five factor solution is least parsimonious. In this solution, PA items fell into two factors, with excited and enthusiastic emerging as a separate factor (factor 4; coefficients of .682 and .583). The other PA items remained loaded together (factor 2; coefficients ranged from .358 - .866). The PA items with the highest coefficients (>.7) were determined, attentive, active, and strong. The NA items remained divided into two factors of general NA (factor 1; coefficients ranged from .606 to .882) and shame/guilt (factor 3; coefficients of .647 and .927). The PA factors were moderately correlated to each other (*r* = .502), but were uncorrelated to the other factors (all *r*'s < .10).

Summary of hypothesis 1.2 factor analysis. Overall, the factor analysis remained consistent with previous literature that indicates that PA and NA are separate and distinct constructs. Using oblique rotation, the PA items consistently grouped together and remained uncorrelated to NA items. The two-factor solution explained the large majority

of the variance of the model and aligned exactly with the previously validated PA and NA subscales of the PANAS measure. The three-factor solution suggested that feelings of shame and guilt may be uniquely experienced in a lung cancer sample, separate from other negative emotions. Similarly, based on the five-factor solution, feelings of excitement and enthusiasm may be experienced differently than other positive emotions among lung cancer patients.

Hypothesis 1.3. ***Associations with the PANAS.*** Associations with higher positive affect were explored through correlations with demographic, diagnosis and staging, smoking history, and treatment variables. Positive affect was significantly correlated with race (r_s = -.265, p = .039), such that African American patients endorsed higher positive affect than White patients. Positive affect was not correlated with gender, years of education, or income.

PA was not correlated with diagnosis and staging variables (age at diagnosis, time since diagnosis, stage, whether they had a comorbid medical condition). Positive affect was not correlated to current medications. Of the smoking history variables, PA was negatively correlated to years smoking (the longer the patient smoked, the less PA; r = -.296, p = .028).

Of the cancer treatment variables, PA was correlated with current chemotherapy treatment, such that patients endorsed less PA if they were currently in treatment (r_s = -.374, p = .004). Similarly, having received chemotherapy in the past two months was correlated with lower PA, but at a trend level (r_s = -.246, p = .068). Positive affect was not correlated to overall endorsement of ever receiving chemotherapy or with any radiation therapy variables.

Overall, some support for hypothesis 1.3 was found with the PANAS. Some variables indicating higher disease burden (longer smoking history, current or recent chemotherapy) were related to lower PA. Patients who endorsed significantly lower PA were White patients, those with a long history of smoking, and those who were currently receiving chemotherapy. African American patients, those who had smoked for fewer years, and those who were not currently in chemotherapy endorsed higher PA.

Post-hoc analyses explored which PA items were potential drivers of the significant correlations observed with the PA subscale as a whole. Six PA items were significantly related to race: strong (r_s = -.423, p = .001), attentive (r_s = -.395, p = .002), determined (r_s = -.368, p = .004), active (r_s = -.356, p = .005), inspired (r_s = -.315, p = .013), and interested (r_s = -.238, p = .037). Three PA items were significantly related to number of years smoking: active (r = -.377, p = .005), alert (r = -.303, p = .024), and determined (r = -.293, p = .030). Six PA items were significantly related to current chemotherapy status: enthusiastic (r_s = -.351, p = .006), inspired (r_s = -.346, p = .007), strong (r_s = -.334, p = .010), determined (r_s = -.320, p = .013), interested (r_s = -.313, p = .016), and active (r_s = -.307, p = .018).

Associations with CES-D PA. The CES-D PA subscale showed a mostly similar pattern, with a few key differences. Again, race was associated with PA, with African Americans endorsing higher PA (r_s = -.227, p = .033). Post-hoc item level analysis showed that race was significantly correlated (in the same direction) with two items: feeling just as good as other people (r_s = -.295, p = .023) and enjoying life (r_s = -.358, p = .005). Gender, education, and income were not associated with CES-D PA.

Again, CES-D PA was not correlated with diagnosis and staging variables (age at diagnosis, time since diagnosis, stage, whether they had a comorbid medical condition). However, while no medications were associated with PANAS PA, use of benzodiazepines (r_s = -.282, p = .030) and use of estrogen medications (r_s = -.256, p = .050) were associated with lower CES-D PA. Post-hoc item level analysis revealed that benzodiazepine use was negatively related to three of the four items: feeling hopeful about the future (r_s = -.284, p = .029), feeling happy (r_s = -.333, p = .010), and enjoying life (r_s = -.320, p = .013).

Correlations between PA and smoking variables differed between the PANAS-PA and CES-D PA. Of the smoking history variables, CES-D PA was negatively correlated with current number of packs/week (r = -.604, p = .029) and cigarettes/day (r = -.606, p = .022), but not with number of years the patient smoked as with the PANAS-PA. Post-hoc item level analysis revealed that items of 'feeling happy' and 'enjoying life' were related to currently smoking fewer packs per week (happy: r = -.637, p = .019; enjoying life: r = -.817, p = .001) and fewer cigarettes per day (happy: r = -.585, p = .028; enjoying life: r = -.750, p = .002). Lower number of current cigarettes per day was also correlated with "feeling just as good as other people" (r = -.563, p = .035). Other smoking variables were not significantly correlated to PA.

Similar to the PANAS PA, patients who were currently in chemotherapy (r_s = -.412, p = .001) or had chemotherapy in the past two months (r_s = -.386, p = .004) had less PA on the CES-D. Post-hoc item level analysis revealed that patients who were currently in chemotherapy or had chemotherapy in the past two months reported less hopefulness about the future (current: r_s = -.343, p = .008; past two months: r_s = -.307, p = .023) and

enjoying life less (current: r_s = -.497, p < .001; past two months: r_s = -.358, p = .007). CES-D PA was not correlated to overall endorsement of ever receiving chemotherapy or with any radiation therapy variables.

Overall, some support for hypothesis 1.3 was again found with the CES-D. Higher PA was experienced among African American patients and those not currently or recently in chemotherapy treatment. In particular, current or recent chemotherapy treatment was correlated with less hopefulness and less enjoyment of life. Positive affect was also associated with smoking variables, but captured different aspects than the PANAS. Current smoking behaviors, not years of overall smoking, were related to PA. Patients smoking less (packs/week, cigarettes/day) reported higher PA, and in particular endorsed being happier and enjoying life more. The CES-D PA also appeared to relate to medication use, while the PANAS PA did not. Patients not taking benzodiazepines or estrogen medication reported higher PA on the CES-D.

Summary of hypothesis 1.3 results. Associations with the PANAS and CES-D both showed that African American race and not currently being treated with chemotherapy predicted higher PA. Nuances in the relationship between PA and medications and smoking history emerged between the two measures. Use of benzodiazepine and estrogen were associated with lower CES-D PA, but were not related to PANAS PA. Patients who smoked less (historically, as captured by PANAS PA, or currently, as captured by CES-D) endorsed higher PA. Taken together, higher PA seems to be associated with African American race, no current chemotherapy treatment, and smoking less.

Aim 2

Data-driven covariates of cortisol outcomes. A description of cortisol variables is presented in Table 11. Correlation analyses tested significance of potential covariates of cortisol variables to be selected for use in analyses of Aim 2 hypotheses. Potential covariates included gender, race, age of diagnosis, stage, years of education, income, time since diagnosis, total pack years, current corticosteroid use, and current chemotherapy. Raw mean waking cortisol had no significant correlates. Raw mean bedtime cortisol was correlated at a trend level with whether the patient was currently receiving chemotherapy treatment (r_s = .248, p = .068). Log mean waking cortisol did not significantly correlate with any variables. Log mean bedtime cortisol significantly correlated with age at diagnosis (r = .322, p = .014) and number of years smoking (r = .299, p = .033). Log mean diurnal cortisol correlated at the trend level with stage (r_s = .241, p = .071). Cortisol slope was not significantly correlated with any covariates. Only the significant correlates for each cortisol outcome were used as control variables (covariates) in data-driven models for hypotheses 2.1 and 2.2. Thus no data-driven covariates were used for regressions with log mean diurnal cortisol, log mean waking cortisol, or cortisol slope. Data-driven covariates were only used for log mean bedtime cortisol regressions (i.e., age at diagnosis and number of years smoking) (Kraemer et al., 2001).

All independent variables were centered prior to regression analysis (Kraemer & Blasey, 2004). Continuous variables were centered to their median. Dichotomous independent variables were coded as −1/2 and +1/2. Ordinal variables were coded as deviations around their median values, and categorical variables with m response options were dummy coded into $-1/m$ and $1-1/m$ (e.g., −0.25 and 0.75) instead of 0 and 1.

For each regression conducted, the data were first explored for violations of assumptions of linearity, homoscedasticity, normal distribution of residuals, and absence of collinearity. Among all variables, no significant outliers were noted or removed, and relationships were deemed to be linear. Assumptions of linearity and normal distribution of residuals were met for all regressions. In all regressions, missing cases were removed pairwise to maintain power.

Hypothesis 2.1. ***Mean Diurnal Cortisol.*** Hierarchical linear regressions tested the association between PA and mean diurnal cortisol. The first regression analysis did not necessitate any data-driven covariates and revealed that PANAS-PA was not associated with mean diurnal cortisol ($p > .05$; Table 12).

A second regression analysis included theoretically-driven covariates (Step 1; PANAS-NA and corticosteroid use) and PANAS-PA (Step 2; Table 13). Corticosteroid use was significantly associated with mean diurnal cortisol ($p = .043$); PANAS-NA and PANAS-PA were non-significant ($p > .05$).

A third regression analysis tested the association of both PANAS-PA and CES-D PA (no covariates) with mean diurnal cortisol also revealed no significant associations ($p > .05$; Table 14).

A final regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use) and PA independent variables (Step 2; PANAS-PA, CES-D PA; Table 15). Corticosteroid use was associated with mean diurnal cortisol at a trend level ($p = .062$); no other covariates or independent variables were significantly associated with mean diurnal cortisol ($p > .05$).

Waking Cortisol. Hierarchical linear regressions tested the association between PA and mean waking cortisol. The first regression analysis did not necessitate any data-driven covariates and revealed that PANAS-PA was not associated with mean waking cortisol ($p > .05$; Table 16).

A second regression analysis included theoretically-driven covariates (Step 1; PANAS-NA and corticosteroid use) and PANAS-PA (Step 2; Table 17). Corticosteroid was significantly associated with waking cortisol ($p = .020$); PANAS-NA and PANAS-PA were non-significant ($p > .05$).

A third regression analysis tested the association of both PANAS-PA and CES-D PA (no covariates) with mean waking cortisol. The analysis revealed that higher CES-D PA was associated with lower mean waking cortisol at a trend level ($\beta = -.292$, $p = .053$), while PANAS-PA was not associated with waking cortisol ($p > .05$; Table 18).).

A final regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use) and PA independent variables (Step 2; PANAS-PA, CES-D PA; Table 19). Corticosteroid use was associated with mean waking cortisol ($\beta = -.295$, $p = .030$), and CES-D PA significance fell to a trend-level ($\beta = -.269$, $p = .080$). No other covariates or independent variables were significantly associated with mean waking cortisol.

Bedtime Cortisol. Hierarchical linear regressions tested the association between PA and mean bedtime cortisol. The first regression analysis included data-driven covariates (Step 1; age at diagnosis, years smoking) and PANAS-PA (Step 2) and revealed that no variables were significantly associated with mean bedtime cortisol (p's > .05; Table 20).

A second regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use), data-driven covariates (Step 1; age at diagnosis, years smoking) and the PANAS-PA (Step 2; Table 21). Corticosteroid was significantly associated with mean bedtime cortisol ($p = .020$); PANAS-NA and PANAS-PA were non-significant ($p > .05$).

A third regression analysis testing the association of data-driven covariates (Step 1; age of diagnosis, years smoking) and both PANAS-PA and CES-D PA (Step 2) with mean bedtime cortisol again revealed that no variables were significantly associated with mean bedtime cortisol ($p > .05$; Table 22).

A final regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use), data-driven covariates (Step 1; age at diagnosis, years smoking), and PA independent variables (Step 2; PANAS-PA, CES-D PA; Table 23). Again, no variables were significantly associated with mean bedtime cortisol and no models were significant overall (p's $> .05$).

Hypothesis 2.2. ***Diurnal Cortisol Slope.*** Hierarchical linear regressions tested the association between PA and diurnal slope. The first regression analysis did not necessitate any data-driven covariates and revealed that PA was not significantly associated with diurnal slope ($p > .05$; Table 24).

A second regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use) and the PANAS-PA (Step 2; Table 25). All variables were non-significant ($p > .05$).

A third regression analysis testing the association of both PANAS-PA and CES-D PA (Step 1) with diurnal slope again revealed that no variables were significantly associated with slope ($p > .05$; Table 26).

A final regression analysis included theoretically-driven covariates (Step 1; PANAS-NA, corticosteroid use) and PA independent variables (Step 2; PANAS-PA, CES-D PA; Table 27). Again, no variables were significantly associated with cortisol slope and no models were significant overall (p's > .05).

Post-hoc analyses: Exclusion of patients on corticosteroids. To check that inclusion of patients on corticosteroids did not bias regression outcomes, patients currently on corticosteroid regimen ($n = 20$) were excluded from the dataset. Correlations of demographic and medical variables with cortisol outcomes were repeated to assess for potential covariates again; no significant covariates of cortisol outcomes were identified. Thus, regressions were conducted first with no covariates. A second regression adjusted for NA. A third regression included CES-D PA with no covariates. A final regression included NA, as well as CES-D PA.

In line with findings from the full dataset, PA (PANAS or CES-D) was not significantly associated with overall diurnal cortisol, mean log waking cortisol, mean log bedtime cortisol, or diurnal slope in any model (all p's > 0.5). PANAS-NA was also not significantly associated with overall diurnal cortisol, mean log waking cortisol, or mean log bedtime cortisol (all p's > .05). One difference did emerge however: PANAS-NA was associated with diurnal slope at a trend level the model that included PANAS-PA (Table 28), and this association became statistically significant in the model with both PANAS-PA and CES-D PA (Table 29). In these models, having more NA was associated with

having a flatter (i.e., more disrupted) diurnal slope (Figure 14); however, the overall model remained non-significant.

Hypothesis 2.3. Data were prepared in order to meet all statistical assumptions prior to path analysis. Centered data were used for exogenous (predictor) variables in order to remain consistent with the multiple regressions previously conducted. First, patients who did not have cortisol outcome data were excluded from the analysis ($n = 4$) in order to meet the criterion of having no missing data. Second, two participants had not completed the CES-D PA, thus their total scores were missing; however, they were not missing any other data points. Therefore, the overall mean CES-D PA value from the sample (then centered to the median) was imputed for these two data points.

Path analyses were performed using Amos version 25. An initial path analysis was used to evaluate the hypothesized model that PA would more strongly relate to overall diurnal mean than to diurnal cortisol slope. The purpose of this model was to compare the path coefficients (beta weights) between PA and mean diurnal cortisol as well as PA and diurnal cortisol slope in one simultaneous model. The primary hypothesis was that the relationship between positive affect and mean diurnal cortisol would be greater (higher absolute value of path coefficient) than the relationship between positive affect and diurnal cortisol slope. Standardized regression weights (β) are reported. In line with previous regression model hypotheses, it was expected that positive affect would be negatively associated with mean diurnal cortisol and positively associated with diurnal slope.

Model 1. Model 1 is a path diagram of the predicted interrelationships between the basic variables of the hypothesized model (Model 1; Figure 7): the exogenous

variable was PANAS PA; the endogenous variables were mean diurnal cortisol and diurnal cortisol slope. Error terms were derived from the endogenous variables. Path analysis demonstrated that PA was not significantly associated with cortisol variables (mean diurnal cortisol: $\beta = -.088$, $p = .507$), diurnal cortisol slope: $\beta = .080$, $p = .549$). The error terms of the cortisol variables were not significantly correlated ($r = -.19$, $p = .163$).

Fit indices of Model 1 were reviewed to assess the match between the model and the data. When the error terms of the cortisol variables were free to correlate, the Chi Square statistic had zero degrees of freedom ($\chi^2 = .000$, $df = 0$), thus the probability level could not be computed and model fit could not be assessed. However, when the error terms were fixed as uncorrelated, the Chi Square statistic showed a non-significant difference between the predicted covariance matrix and the actual covariance matrix (CMIN = 2.049, $df = 1$, CMIN/$df = 2.049$, $p = .152$). Yet, the model demonstrated overall poor fit to the data (CFI = .000; IFI = .432; RMSEA = .137; NFI = .280). No modification indices were suggested in order to improve model fit.

This first model's poor fit to the data and the non-significant p-values of the paths do not lend full support for the hypothesis. However, the hypothesis may be partially supported in that the absolute value of the beta weight for the association between PA and mean diurnal cortisol was indeed greater than that of the cortisol slope. Further, the beta weight was in the hypothesized direction for overall mean cortisol.. Therefore, although the paths did not reach significance, the findings may suggest that this model is underpowered.

Model 2. An exploratory second model with more observed variables was constructed, based on the previous multiple regression analyses (Model 2; Figure 8). Secondary predictive variables (control variables) were included in the model given the theory-driven relationships previously established: corticosteroid use and PANAS negative affect. It was hypothesized that corticosteroid use will be associated with both cortisol variables. It was hypothesized that negative affect will be associated with higher mean cortisol and disrupted (i.e., flattened, lower) slope values. Overall model fit and hypothesized associations within Model 2 were reviewed.

Model 2 exogenous variables included positive affect (PANAS), negative affect, and corticosteroid use; endogenous variables were mean diurnal cortisol and diurnal cortisol slope. Error terms were derived from the endogenous variables. Path analysis demonstrated that PA was not significantly associated with cortisol variables (mean diurnal cortisol: $\beta = -0.141$, $p = .268$; diurnal cortisol slope: $\beta = 0.081$, $p = .533$). Negative affect was also not significantly associated with cortisol variables (mean diurnal cortisol: $\beta = 0.071$, $p = .576$; diurnal cortisol slope: $\beta = 0.150$, $p = .247$). Corticosteroid use was associated with lower overall cortisol mean ($\beta = -0.274$, $p = .030$), but not with diurnal slope ($\beta = 0.165$, $p = .203$).

Fit indices of Model 2 were reviewed to assess the match between the model and data; the model demonstrated good fit to the data. The Chi Square statistic showed a non-significant difference between the predicted covariance matrix and the actual covariance matrix (CMIN = 3.042, $df = 3$, CMIN/$df = 1.014$, $p = .385$). Other indicators also supported good model fit (CFI = .986; IFI = .996; RMSEA = .016), while one index

suggested less of a fit (NFI = .764). No modification indices were suggested in order to improve model fit.

The absolute value of the beta weight for the association between PA and mean diurnal cortisol was again indeed greater than that of the cortisol slope in this model. Several associations were in the predicted directions: higher PA and lower NA were related to a pattern of lower mean cortisol. All other variables seemed to be associated with flattened slopes; although, NA and corticosteroid use seemed to be more strongly suggestive of flatter slopes than PA. The non-significance coupled with the near-zero beta weights prevents us from drawing any firm conclusions regarding PA's relative associations to the cortisol variables. Thus, the hypothesis could not be firmly supported. However, the model did demonstrate better fit to the data than Model 1 and the beta weight from PA to mean cortisol increased strength from Model 1.

Model 3. An exploratory third model was created to consider the relationship between CES-D PA and cortisol outcomes (Model 3; Figure 9). In line with previous regressions, this model included PANAS PA and NA, CES-D PA, and corticosteroid use as the exogenous variables, while mean diurnal cortisol and diurnal cortisol slope remained the endogenous variables. Overall model fit and hypothesized associations within Model 3 were reviewed.

Path estimates were similar to those of Model 2. Path analysis demonstrated that PANAS PA was not significantly associated with cortisol variables (mean diurnal cortisol: $\beta = -0.046$, $p = .718$; diurnal cortisol slope: $\beta = -0.013$, $p = .916$). CES-D PA was also not significantly associated with cortisol variables (mean diurnal cortisol: $\beta = -0.192$, $p = .128$; diurnal cortisol slope: $\beta = 0.187$, $p = .142$). Negative affect was also not

significantly associated with cortisol variables (mean diurnal cortisol: β = 0.030, *p* = .812; diurnal cortisol slope: β = 0.190, *p* = .136). Corticosteroid use was associated with lower overall cortisol mean (β = -0.252, *p* = .046), but not with diurnal slope (β = 0.139, *p* = .275).

Fit indices of Model 3 were reviewed to assess the match between the model and data; the model demonstrated poor fit to the data. The Chi Square statistic showed significant difference between the predicted covariance matrix and the actual covariance matrix (CMIN = 19.866, *df* = 6, CMIN/*df* = 3.311, *p* = .003). Other indicators also suggested poor model fit (CFI = .210; IFI = .478; NFI = .390; RMSEA = .203). Modification indices suggested correlating PANAS PA and CES-D PA (MI = 11.205, Par Change = 10.672) as a way to improve model fit.

When this modification was completed, the model demonstrated better fit to the data. The PANAS PA and CES-D PA were moderately, but significantly correlated (*r* = .447, *p* = .002). The Chi Square statistic showed a non-significant difference between the predicted covariance matrix and the actual covariance matrix (CMIN = 7.363, *df* = 5, CMIN/df = 1.473, *p* = .195). Other indicators also suggested improved model fit (CFI = .865; IFI = .914; NFI = .774; RMSEA = .092). No modification indices were suggested in order to improve model fit.

In again partial support of the hypothesis, the absolute value of the beta weight for the association between PANAS-PA and mean diurnal cortisol was indeed greater than that of the cortisol slope. Higher PA (CES-D and PANAS-PA) and lower NA seemed to be related to lower mean diurnal cortisol. All other variables seemed to be associated with flattened slopes. As previously noted however, the non-significance of the beta

weights prevents us from drawing any significant conclusions regarding PA's relative associations to the cortisol variables. The model including CES-D PA did not demonstrate as good of a fit as the Model 2. As expected, correlating PANAS-PA and CES-D PA, improved model fit however.

Summary. Hypotheses and overall findings (whether each hypothesis was supported) are presented in Table 30. PA seemed to have a stronger relationship to mean diurnal cortisol than to diurnal slope. Further, higher PA and lower NA seemed to be related to lower mean cortisol. Most variables seemed to be associated with flattened slopes, likely due to pre-existed cortisol dysregulation. Findings must be interpreted cautiously, given the overall lack of statistical significance.

DISCUSSION

This dissertation explored the experience of positive affect, and its biological correlates, in a sample of non-small cell lung cancer patients. The importance of understanding the emotional experiences of these patients cannot be underestimated. Indeed, cancer diagnosis and treatment may be met with sadness, grief, and anxiety. However, experiences of positive emotions and their underlying psychological processes must be better understood to capture the full authentic emotional experiences of lung cancer patients. This topic is drastically understudied in the current literature. Thus, the results of this study highlight the nature of positive emotions as well as the potential relationships to physiological pathways associated with a known prognostic feature among lung cancer patients – cortisol dysregulation.

Capturing a snapshot of lung cancer patients served among the greater Louisville area, the patients of the current study were mostly female, White, in their late 50s to early 60s, and had a high school education. Most patients (57.5%) had a household income of under $40K per year. The majority of these patients had an initial diagnosis of stage III or stage IV lung cancer and had been diagnosed about two years previously. Patients diagnosed with this stage and type of cancer typically have had poor prognosis; patients with stage III have a 5-year survival rate of 13-36%, while patients with IV have a 5-year survival rate of <1-10% (American Cancer Society, 2017). As a somber representative of this poor prognosis, several patients passed away during the duration of this study. As

such, the patients in this current study were undergoing unique set of psychological and physiological stressors as they faced a potentially terminal illness. However, as highlighted in this work, the majority of these reported positive mood states, even more so than negative mood. In honoring the complexity of emotional experiences when facing lung cancer, this dissertation deeply explores the quality and correlates of these positive emotions, while delving into the science behind the mind-body interaction of positive affect and psychophysiology.

Aim 1 Discussion: Experiencing Positive Affect

Hypothesis 1.1. Aim 1 of the current study sought to understand the frequency and quality of PA among lung cancer patients. By exploring elements of the person (e.g., demographic variables) and his or her cancer journey (e.g., medical variables), this aim helped to capture the patient experience of PA on an item, subscale, and construct level. Hypothesis 1.1 proposed that patients would experience moderate PA and would report more PA than NA, as tested by the PANAS. **Hypothesis 1.1 was supported.**

Patients experienced moderate levels (scoring around 3 on a scale of 1-5) of PA. This finding highlights that patients did, in fact, experience PA while facing their cancer. As will be explored later, not only did the patients endorse actually experiencing positive mood, they reported having more positive than negative emotions over the past week in general. This endorsement of PA aligns with previous literature noting that, on average, most people endorse feeling neutral to positive emotions, rather than negative emotions (Diener & Diener, 1996). The experience of PA among cancer patients is also not uncommon (Louro et al., 2015) and is the reason why it deserved scientific attention.

The consistency of this pattern among this sample highlights a potential normative experience of emotions overall, even in the face of cancer.

A closer look at the most highly endorsed individual positive emotions revealed an interesting representation of the positive emotional states of these lung cancer patients, and captured a theme of overall resilience. On the PANAS, the most endorsed positive emotion was *determined.* In lung cancer patients, this may reflect psychological resilience and active approaches to coping and overcoming their cancer diagnosis. In other words, *determined* may reveal a "fighting spirit" coping strategy of these cancer patients, which reflects a tendency to actively confront and face cancer (Watson et al., 1994). In a study of 102 cancer patients, path analysis demonstrated that a fighting spirit was significantly associated with positive affect and was a partial mediator between optimism and positive emotions (Hodges & Winstanley, 2012). *Determination* in this sample may be revealed in the medical context as the patient being motivated to adhere to treatment, attend scheduled appointments, and even participate in this current research. (The latter of which may also reflect a potential sample bias.) In a psychological context, these patients' determination may reflect a desire to live a full and meaningful life given the diagnosis of a potentially terminal illness. *Determination* may be a product or proxy of underlying resilient processes such as emotional flexibility, benefit finding, and post-traumatic growth. More research is needed to elucidate the underlying processes contributing to this most commonly endorsed positive emotion in this sample. As such, further analyses using the fighting spirit subscale of the Mini-MAC (Mini Mental Adjustment to Cancer Scale; Watson et al., 1994) may elucidate the presence and extent

of fighting spirit and its association with other positive psychological processes in this sample.

The other most highly endorsed PA items were *alert* and *interested* (Figure 3). Together, these three top PA items (*determined, alert, interested*) paint the picture of an engaged and resilient cancer patient. Again, in the medical context, someone with these features may be determined to fight his or her cancer by being alert and interested in the recommendations and treatment planning of his or her oncology team. Outside the medical setting, these three emotions may reflect a person who is present and engaged in their current life, by showing interest and alertness to meaningful activities and a determination to live life in a meaningful way in the face of a terminal illness.

On the CES-D, the highest rated positive items were "I enjoyed life" and "I felt just as good as other people." These again seem to reflect a sense of resilience: that these patients are still enjoying life and have maintained a sense of esteem despite lung cancer. This finding of feeling "just as good as other people" is interesting given the common experience of shame and self-blame associated with smoking among lung cancer patients (Else-Quest et al., 2009; LoConte et al., 2008). This is especially interesting as the current sample was made up of almost entirely patients who had a history of smoking or currently smoke. Of course, it is difficult to know how these patients understood and interpreted the term "good". It may be that these patients engaged in cognitive flexibility about how to enjoy life despite their physical and emotional symptoms, which in turn led them to feel just as good as others without medical conditions. Conversely, given the high frequency of smoking in Kentucky, perhaps patients were comparing themselves to their

peers or family members, who also smoke, thus removing much of the stigma and allowing them to find commonality among other people.

The least endorsed positive emotion on the PANAS was *inspired.* Inspiration denotes creating something new or having the urge to do or feel something. After a diagnosis of lung cancer, these patients may not be feeling inspired to make large changes in life (start new projects, etc.), but rather to enjoy what they have already. Consistent with this, the least endorsed positive emotion on the CES-D was *feeling hopeful about the future*. Again, these patients are facing a sobering reality of the poor prognosis of lung cancer. Therefore the lack of inspiration and hope may not necessarily be pessimism, but rather, realism.

PA vs. NA. Patients reported experiencing more overall PA than NA, and there was a large effect size. This finding is similar to other previous research indicating that cancer patients do indeed tend to report more PA than NA (Louro et al., 2015). Among lung cancer patients, this finding may be surprising given that these patients also tend to endorse more distress than other cancer samples (Brintzenhofe-Szoc et al., 2009; Linden et al., 2012; Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001). However, it appears that the current set of patients is also experiencing normative, and high, levels of positive emotions, as seen in other cancer samples (Louro et al., 2015).

On the other hand, one may also consider that this finding could reflect the tendency for people to avoid experiencing negative emotions – either by actively pushing them away or denying their presence in general – or to judge themselves for feeling negative emotions (David, 2017; Hayes, Strosahl, & Wilson, 2012). The endorsement of PA and relative lack of NA in the sample may be a reflection of either false positivity,

false non-negativity, or perhaps both. While we cannot say for certain whether the patients are engaging in active denial of negative emotions and/or falsely inflating their perception of their own positive mood states, it remains important to take this human tendency into consideration while interpreting the results of the study.

As expected, the PA measures (PANAS-PA and CES-D PA) were positively correlated, which also reflected a strong effect size. Their strong correlation offers convergent construct validity for positive affect in this sample. Similarly, as seen in other samples, the PA and NA subscales of the PANAS were not correlated, offering discriminant validity to the measure. As suggested by previous studies, the current data again suggests that PA and NA are two distinct constructs (e.g., Watson, Clark, & Tellegen, 1988). With both convergent and discriminant validity of the PANAS PA, it can be assumed that this measure is indeed capturing what we hoped to explore in the current study – the experience of positive emotions.

Hypothesis 1.2. The second hypothesis of Aim 1 proposed that positive and negative affect items will emerge as separate factors in an exploratory factor analysis. **Hypothesis 1.2 was supported.** The factor analysis most strongly suggested a two-factor solution (Figure 4); although, three and five factor solutions also warrant attention. In the two-factor solution, the PA and NA factors emerged separately in the factor analysis, again indicting that they are separate and unique constructs. The two-factor solution demonstrated that the items fell into the respective PA and NA subscales of the standardized measure, offering support that the measure is valid among a sample of lung cancer patients.

Interestingly, in the three-factor solution, shame and guilt separated out from the NA subscale, suggesting that these two negative emotions may be experienced differently in the lung cancer sample. Among lung cancer patients, the experience of shame and guilt often relates to smoking history and the stigma associated with lung cancer (Else-Quest et al., 2009; LoConte et al., 2008). The finding that these two emotions emerged separately in this sample seems to highlight the uniqueness of these emotions among lung cancer patients. Given that all but two patients in the sample were either past or current smokers, it is likely that smoking history may relate to the separation of shame/guilt from other negative emotions in this sample. Future analyses may explore the unique contribution of these negative emotions in psychophysiological pathways.

In the five-factor solution, *excitement* and *enthusiasm* separated out from the other positive emotions. Compared to the other positive affect items on the PANAS, these two emotions reflect a more active valence, which may not well suited to the diagnosis (i.e., functional ability). The other positive items (i.e., strong, determined, attentive, interested, etc.) seem to fit better with a mindset of facing cancer as they may reflect a slightly less active valence.

Overall, the factor analysis validated that PA and NA exist as separate constructs in this sample. Further, a lack of negative emotion does not necessarily indicate a presence of positive emotion, and vice versa. Instead, these emotions may exist together in a dialectical relationship within the patient; distress and positive emotions can exist together (Folkman & Moskowitz, 2000). That is, the patient may be scared and nervous, but also feels strength and determination. As such, controlling for the effects of NA in the

subsequent regression analyses remained an appropriate method for elucidating the relative contributions of these separate emotional experiences.

Hypothesis 1.3. The third hypothesis of Aim 1 explored what demographics would be associated with higher PA and specifically proposed that lower disease burden (e.g., lower stage, no current treatment, longer time since diagnosis) would be associated with higher PA. **Hypothesis 1.3 was partially supported**.

In considering demographic variables, African Americans endorsed more PA than White patients. Among seminal happiness studies, research shows that African Americans and European Americans typically endorse nearly the same levels of overall happiness and life satisfaction (Myers & Diener, 1995). Thus in this sample, a unique set of resilience factors may have contributed to this difference between races. Interestingly, a closer look at the PA items revealed that "strong" was most significantly correlated with race (i.e., African Americans endorsing "strong" more so than White patients). Research suggests that African Americans endorse more meaning/peace and faith when facing a chronic illness (including cancer), when compared to White or Latino counterparts (Peterman et al., 2002). African American breast cancer patients also report utilizing religious coping more so than non-Hispanic White patients (Culver et al., 2002). Other unique coping strategies of African American cancer patients include developing a positive attitude and avoiding negative people, having a will to live, and receiving a variety of social support (Henderson et al., 2003). Therefore, there are unique cultural factors to be further explored about the meaning of "strength" and its multidimensional qualities in the context of cancer. In this sample, strength may be differentially

interpreted as physical, emotional, spiritual, or social strength, depending on unique coping strategies associated with ethnicity.

Among medical variables, the first finding was that a higher number of years smoking was negatively correlated to PA, especially items of "active", "alert", "determined". The first two terms may reflect behaviors associated with smoking, such as sedentary behavior (Strine et al., 2005). A person who has smoked for fewer years may more highly endorse feeling determined, which may reflect quitting earlier or being determined to reduce smoking. The CES-D PA (i.e., feeling happy, enjoying life) was negatively associated with current number of packs per week and cigarettes per day, but was not correlated with historical factors of smoking. Taken together, current smoking habits seem to relate to emotional experiences related to engaging in life and feeling happy, while history of smoking (i.e., years smoked) seem to relate to emotional experiences that may more strongly reflect health-behavior type PA items (active, alert, determined).

Second, current chemotherapy was negatively associated with PA, especially items of "enthusiastic", "inspired", "strong", "determined", "interested", and "active". Patients currently undergoing chemo are typically much more physically ill because of side effects, so these findings are not surprising. On the CES-D, chemotherapy (current and in the past two months) was negatively associated with enjoying life and feeling hopeful about the future. Of course, chemotherapy requires frequent and lengthy appointments at cancer treatment sessions for infusions, thus the large amount of time spent in the hospital coupled with the difficult side effects would naturally make it very difficult to enjoy life on a daily basis. However, because these items also correlated with

chemotherapy status two months prior, these findings seem to capture some of the longer-term associations with treatment on mood and quality of life. Undergoing chemotherapy serves as a stark reminder of the gravity of cancer, which may decrease patients' hopefulness about the future in the immediate timing around that treatment as well as several months after.

Other medical factors were not associated with PA, including cancer stage. Similar to national averages, the majority (66%) of the patients in this sample were stage III (n = 26) or IV (n = 14), with 23% of the sample being metastatic, thus limiting the variance based on stage. This limited variance may have masked any differences in mood based on stage.

In this sample, age at diagnosis may not have related to PA since the majority of patients were older in age when they were diagnosed. There is a known preservation and even increase of positive emotions with advancing age (Mroczek & Kolarz, 1998), partially explained by improved emotion regulation over the lifespan (Carstensen, 1991; Carstensen, 1995). Therefore, this known effect of age and positive emotion may override any effects of age at diagnosis related to PA, given that age at study enrollment and age at diagnosis were relatively similar and both later in life (61 vs. 59 years old). Further, time since diagnosis may not have related to PA given that many of the patients have not been recently diagnosed (i.e., within the past several months), thus any acute effects on mood may have dissipated over time. Sixty percent of patients were diagnosed in the past two years, with only seven patients being diagnosed in the past three months. The lack of correlation between time since diagnosis and PA reflects the work of Duh, Diener, and Fuhita (1996), who discovered that life events (good or bad) only affected

happiness if they occurred in the previous two months. Thus the overall lack of correlation between certain medical/demographic characteristics may reflect emotional rebound that occurs after major life events (Diener, Lucas, Scollon, 2006).

Aim 2 Discussion: Positive Affect and Cortisol

Aim 2 focused on understanding the relationship between PA and diurnal cortisol among the sample. In order to better understand the diurnal patterns of the current sample and aid in discussion, several descriptive graphs were made post-hoc. Figure 10 shows the raw mean waking and bedtime cortisol values to create a graphic representation of the overall diurnal slope. Graphically, the diurnal slope indeed shows a descending pattern, indicating some maintenance of HPA rhythm. However, slope change of raw cortisol scores of less than approximately 0.2 μg/dL is conventionally considered flattened or aberrant (Sephton et al., 2000; Sephton et al., 2013). The overall raw slope change observed in this sample (0.17 μg/dL) and demonstrated in Figure 10 is nearly identical to the flattened pattern observed in a previous study of cortisol and early mortality in lung cancer (Sephton et al., 2013). As such, Figure 10 suggests an overall flattening of diurnal slope in this sample, despite a general decline from morning to evening raw values.

Figure 11 qualitatively demonstrates the average "steep" vs. "flattened" diurnal slope of the sample. In this figure, diurnal cortisol slope was split at the median slope value and log mean waking and bedtime values were again graphed. The variability among the waking the bedtime values among the steep and flattened slopes again suggests an overall disruption of the HPA in this sample.

To elucidate typical patterns observed in this sample, a third figure was created. Figure 12 demonstrates three representative patterns of diurnal slope from three patients in the sample: steep, flattened, and ascending. For descriptive purposes, relatively steep slopes were qualitatively and conservatively categorized as a decline of 0.20 μg/dL from raw waking to bedtime values; ascending were categorized as any increase from waking and bedtime. About 36% of patients showed steep slopes, 52% showed flattened slopes, and 13% had ascending slopes. These qualitative categorizations are similar to other cancer samples with disrupted rhythms (Sephton et al., 2000). Further, when compared to other cancer samples, patients in the current study seemed to have overall lower levels of diurnal cortisol and overall flatter slopes (Table 31; Abercrombie et al., 2004; Cash et al., 2015; Sephton et al., 2013).

Last, Figure 13 presents the raw mean waking and bedtime cortisol values for patients who were taking corticosteroids versus those who were not. The graph demonstrates that patients taking corticosteroids had lower raw waking values, thus potentially contributing to an overall flattening of the diurnal slope. Such an effect is consistent with research showing that corticosteroid use suppresses HPA activity (Chourous, Pavlaki, & Magiakou, 2011).

The descriptive characterization of cortisol among the sample highlights the high level of disruption of HPA rhythms evident at baseline. Research shows that 30-70% of cancer patients display disruptions in diurnal cortisol rhythms, including uncoordinated or erratic peaks and nadirs throughout the day, phase shifts, or generally flattened patterns at either abnormally high or low levels (Sephton & Spiegel, 2003). Such patterns are most evident in patients with high tumor burden, poor performance status, and liver

metastases (Sephton & Spiegel, 2003). As such, disrupted cortisol rhythms may be an indicator of progressing tumor status or the result of other biological effects of worsening psychosocial functioning (e.g., poor sleep due to pain or anxiety; Eismann et al., 2003; Sephton & Spiegel, 2003). Further, use of systemic corticosteroids can disrupt cortisol levels through HPA suppression (Chourous, Pavlaki, & Magiakou, 2011). Thus, associations among positive affect and cortisol may have been masked by the overall disruption of the HPA at baseline, contributing disease-related variance that may have led to the overall lack of findings for Aim 2 in this study.

Hypothesis 2.1. Aim 2 tested the relationships between positive affect and cortisol variables, and hypothesis 2.1 stated that higher PA would be related to lower mean cortisol levels. **Hypothesis 2.1 was not supported.**

Higher CES-D PA was associated with lower waking cortisol at a trend level. No other significant findings or trends were observed with CES-D PA or PANAS PA and mean cortisol levels. The CES-D PA finding remains interesting despite the other non-significant findings. Perhaps the CES-D PA items serve to capture PA in a contextual sense. That is, CES-D may capture a sense of trait or even "lifestyle" positive affect – enjoying life, feeling as good as others, feeling happy, being hopeful about the future; while the PANAS-PA items don't have as much of a sense of being placed in the context of life (e.g., hopeful about the future vs. just hopeful).

Overall, higher PA was not related to overall mean diurnal cortisol, bedtime cortisol, or waking cortisol. Similarly, negative affect also did not show strong associations with cortisol means. Again, the lack of findings (for both PA and NA) may be a result of the overall cortisol dysregulation already in place, masking any associations

with psychosocial variables. Instead, other factors may have played a larger role (behavior, tumor biology, medications) in cortisol levels.

As expected, higher log mean bedtime cortisol significantly correlated with older age of diagnosis and more years of smoking. Also, raw mean bedtime cortisol was observed to be higher at a trend level when a patient was currently receiving chemotherapy treatment. Research shows that elevated bedtime cortisol is observed among people with sleep disturbance and insomnia (Buckley and Schatzberg, 2005). Research affirms that about 30-50% of newly diagnosed or recently treated oncology patients report sleep disturbance and that this number is significantly higher than healthy controls (Savard & Morin, 2001). Among lung cancer samples, clinical insomnia may be present in about 30% of patients (Ginsburg et al., 1995; Sarna, 1993). Therefore, these trend-level findings may hint towards a mechanism of cancer-related insomnia.

Hypothesis 2.2. The second hypothesis of Aim 2 stated that higher PA will be related to steeper diurnal cortisol slope. **Hypothesis 2.2 was not supported.** In all regressions, PA was not associated with diurnal slope.

However, when patients on corticosteroids were excluded from the sample, higher NA was associated with flatter cortisol slopes (Figure 14). This finding mirrors research demonstrating that depression is associated with flattened diurnal rhythms and disruption of the HPA (Spiegel & Giese-Davis, 2003). As presence of NA (and lack of PA) is a core feature of depression, it may be that NA (as a proxy of depressive symptoms) potentially masks the effects of PA on slope in this subsample. Or, it may be that the patients with higher NA were not experiencing sufficient levels of PA to combat depressive symptoms (Folkman & Moskowitz, 2000), thus leading to an association with biology.

Overall, the null findings regarding PA and slope in this sample may be a function of other (stronger) influences on cortisol, such as medications (corticosteroids), sleep, treatment effects, or tumor biology variables. Further, NA seemed to have a stronger relationship to slope, suggesting the known strong biological effects of depressive symptoms may mask contributions of PA on HPA function. As suggested in the integrated model (Figure 1), eudaimonia and the experience of psychological well-being may be more effective than PA on cortisol outcomes due to synergy among multiple psychological resilience factors. The psychological resources of eudaimonia create emotional resilience that interacts with appraisal, coping, and/or emotional responses. This model is consistent with other stress-and-coping models of positive psychological resilience factors, such as mindfulness (Salmon, Sephton, & Dreeben, 2011). Cancer patients who demonstrate self-acceptance and have made meaning of their diagnosis may appraise stressors as less threatening and cope more efficiently, thus avoiding the biological disruption of chronic stress. Last, the null findings with cortisol slope may also relate to variability in PA (Human et al., 2015), as coping with cancer likely is met with a wide range of both positive and negative emotional experiences that may vary from day to day.

Hypothesis 2.3. The third hypothesis of Aim 2 used path analysis to test whether PA would more strongly relate to mean diurnal cortisol than to diurnal cortisol slope. **Hypothesis 2.3 was partially supported**. In all three path analysis models, the beta weight between PANAS PA and mean diurnal cortisol was consistently stronger than that between PANAS PA and diurnal slope. Second, the beta weights were consistently in the negative direction, suggesting an underlying pattern that higher PA (PANAS and CES-D)

is associated with lower mean diurnal cortisol. These two points are in support of the hypotheses. However, the path estimations were not statistically significant, thus firm support of the hypotheses cannot be assumed. However, the findings support of the proposed integrated model that PA may work to have an undoing effect on mean diurnal cortisol, yet may need to be in conjunction with other resilience factors to more strongly associate with robust cortisol slopes. The consistency of the direction and strength of the beta weights among the models suggest that further investigation may be fruitful. The lack of statistical significance but consistency in hypothesized direction of the path estimates may suggest that the study is underpowered and that these pathways may reach significance in a larger sample. Further, the fact that all of the predictor variable seemed to be associated with flattened slopes again highlights that pre-existed cortisol dysregulation may be present in the sample.

The models from the path analysis reflected the findings from the individual regression analysis (beta weights remained consistent between analyses). However, the benefit of these models is that they allow us to consider the effect of mood on both cortisol variables at the same time. Model 1 presented the most simple path analysis, using only the primary variables of interest. The model demonstrated poor fit, likely due to the fact that PA did not relate strongly to either of the cortisol variables and explained only a small portion of the variance in mean cortisol and cortisol slope. Fit improved however when other variables were added to the path diagram, suggesting that these elements help explain the cortisol variables.

Model 2 demonstrated the best overall fit of all of the models. All but one index suggested good fit, with the exception of NFI. However, NFI tends to underestimate fit in

small sample sizes, such as in this current study, which likely explains why it differed from the other more robust fit indicators (Iacobucci, 2010). This again builds the case that this current study may be underpowered for these analyses.

In Model 3, the CES-D PA variable demonstrated a stronger relationship (i.e., higher absolute value of beta weights) to the cortisol variables than the PANAS-PA. This is consistent with the regression analyses of Aim 2. Although again these paths did not reach statistical significance, it seems worthy to consider how the CES-D PA items may be capturing positive psychological processes that are different, albeit correlated, to those reflected in the PANAS-PA. Or, perhaps, the CES-D PA items mask the effects of the PANAS-PA because they are highly correlated. That is, the CES-D items may capture a superordinate positive psychological process that may mask the effects of the positive affective states of the PANAS-PA. For example, a recent study on hedonia and eudaimonia in ovarian cancer patients utilized structural equation modeling and found that eudaimonia was associated with lower tumor norepinephrine, while PA was not, despite the high correlation between eudaimonic well-being and PA (Davis et al., 2015).

Models 2 and 3 included PANAS NA. In both of these models, association between NA and diurnal slope was stronger than between NA and mean diurnal cortisol and between PA and diurnal slope. Although these paths were not statistically significant, it may be possible that NA accounts for more variance in diurnal slope, thus masking any effect of PANAS PA.

STUDY LIMITATIONS

There are several limitations to the current study to be considered. As previously mentioned, the study may have been underpowered to capture the nuanced relationships between positive affect and biology. The relatively small sample size keeps us from drawing large conclusions based on the findings. Further, the study did not include a comparison group of healthy controls upon which to compare the nature of PA as well as the potential relationships with the HPA.

Second, the study captured a sample that was mostly female, non-Hispanic White patients, of lower socio-economic status. While this cohort of patients deserves attention, the sample demographics limit the generalizability of the finding to more diverse patient groups, in regard to gender, race, and income. Importantly however, since much research is conducted among breast cancer patients/survivors, this current sample had relative strength in including both male and female patients.

The current study had an enrollment criterion of having a diagnosis within the past five years. However, five years time offers a wide range of psychological experiences for patients. Newly diagnosed patients may have a radically different emotional experience than those who are several years since diagnosis or early treatment. Given this wide range of time and potentially different stages of coping among the patients, associations among psychosocial and physiological factors may have been masked by disease-related variance.

Last, this study relied on self-report for all psychological measures. As with any self-reported variable, one runs the risk of hindsight bias, variations in mood, and overall difficulty in capturing true representation of an emotional experience. Further, the study was limited to the positive affect measures that were included at the outset of the study, which limited the range of PA measures to the PANAS and CES-D PA subscale.

FUTURE DIRECTIONS

Many researchers note that the field would greatly advance from more research on PA and neuroendocrine function, particularly among unhealthy samples (e.g., Chida & Steptoe, 2008; Davis et al., 2015; Howell et al., 2007). Several avenues of future research may improve the quality of research and address several points derived from this current work. First, studies should seek to include broad measures of PA – both hedonic and eudaimonic – to be able to deeply explore the quality and outcomes of these complex emotional experiences among cancer patients. Studies should seek to use similar and standardized measures of PA and consistent terminology. Clarification of whether PA measured is state or trait will also help to untangle short-term versus long-term associations with biology, and will help parse out potential overlap with confounding variables. Positive affect measurements and study designs should also seek to elucidate the role of arousal and PA variability (Hoyt et al., 2015; Human et al., 2015). Underlying mechanisms of positive mood, such as the fighting spirit, adaptive coping, and social support, may render fruitful avenues for broadening the understanding of positive psychological processes in mind-body medicine.

Similarly, close attention to subtypes of positive mood may seem to play a particularly important role in physical well-being. In particular, a recent large-scale study (N = 5,554) found that low PANAS PA was significantly associated with mortality, and this finding was equally as strong among cancer-related and cardiovascular-related deaths (Petrie et al., 2018). Importantly, the PANAS PA item "active" largely explained this finding (Petrie et al., 2018). Given that "active" was significantly associated with smoking and chemotherapy status in this sample, future research may explore the role of

sedentary behavior and its physical and mental effects among lung cancer patients. Overall, the relationship between specific positive emotions and modifiable health behaviors in the context of cancer prevention and control warrants greater attention.

Second, future studies should employ reliable cortisol calculation and collection methods and report on multiple cortisol outcomes. Such rigor may highlight differential pathways and mechanisms, and clarify the relationships between overall secretion, slope, and CAR, and related clinical outcomes. The use of standardized collection times and measures will help to reduce variation between study designs, and will facilitate more reliable cross-study comparisons.

Third, future studies should seek to enroll larger, diverse samples, with a comparison group of healthy controls. Such studies may wish to focus on a certain time point since diagnosis (e.g., within months as opposed to years) to capture more specific associations between mood and biology. Future studies may also benefit from using ecological momentary assessment to capture a more accurate picture of the patients' positive mood states, as well as their variability within-person.

Fourth, more studies should also be conducted within the lung cancer population. The vast majority of cancer research, and all of the current PA and cortisol research among cancer samples, is among breast cancer patients. Given the implications for coping, meaning-making, and resilience factors, the field would benefit from research in highly distressed cancer populations, such as lung cancer. Building this body of research lends practical utility in psychological and medical care domains, and highlights the importance of granting cancer patients greater access to psychologists. Future psychosocial interventions for cancer patients may seek to promote authentic and realistic

experiences of PA, while simultaneously building psychological resources to create eudaimonic well-being. Research on mindfulness-based therapies shows that this may be a promising avenue for linking PA, eudaimonia, and cortisol (Jimenez, Niles, & Park, 2010; Tang et al., 2007).

Fifth, in considering the roles of NA and PA, special attention must be paid to confounding effects of syndromal and subsyndromal depression. Such symptoms commonly co-occur in cancer patients (Spiegel & Giese-Davis, 2003). Importantly, depression has prognostic significance among lung cancer patient (Pirl et al., 2012), and even subclinical levels can be associated with early mortality in cancer (Zimmaro et al., 2017). Depression is characterized not only by presence of NA, but lack of PA (Folkman & Moskowitz, 2000; Radloff, 1977). Depression also has known associations with HPA dysregulation (Currier & Nemeroff, 2014). Therefore, future studies should carefully ensure analyses control for the effects NA when testing the associations of PA with cortisol in cancer patients. Further, special attention should be made to the experiences of shame and guilt in this population, given that these experiences may be qualitatively different among different cancer types. Future studies may also wish to utilize the ratio of positive to negative affect (Critical Positivity Ratio; Fredrickson & Losada, 2005) as deeper exploration of the relationship between positive and negative emotions within this population.

Last, future research should continue to explore the proposed pathways of the integrated model outlined at the outset (Figure 1). Direct effects should first be examined. Moderators of the model should also be tested, with particular attention to individual difference factors and cancer-related variables. Mediational analyses might examine the

neurobiological pathways of hedonia and eudaimonia in cancer patients, especially pathways that involve the HPA. Controlled experiments could explore the undoing and buffering hypotheses as outlined in the model. Last, the clinical significance of cortisol total secretion as it relates to survival, prognosis, or other tumor-relevant factors deserves greater attention.

FINAL CONCLUSIONS

The blossoming research on positive psychology is making its way into policy on a national and global scale, and indeed this progress is moving into the healthcare field. In 2015, the World Health Organization launched a series of Sustainable Development Goals, aimed to increasing health and well-being on a global scale (World Health Organization, 2016). However, specific efforts within the cancer field have yet to be established, allowing for large-scale opportunities of growth in this area.

This current research highlighted that while typically lung cancer patients are considered some of the most distressed cancer patients, they are also experiencing positive and resilient emotions. While the biological associations of these emotions may have been masked by tumor-relevant physiological disruption, the everyday experience of positive states may have considerably increased a patient's quality of life. In the face of a terminal illness, it may not be the quantity of life that matters the most, but rather, the quality of the days left.

Tables

Table 1

Studies with Cancer Samples, PA, and Cortisol

Authors, Year	**Cancer Sample**	**PA Measure**	**PA Conceptual Framework**	**Cortisol Measure/Methods**	**Association Between PA and Cortisol**	**Other Notable Findings**
Porter et al., 2003	Breast cancer survivors (n=33) vs. healthy controls (n=21)	Four PA adjectives, rated 0-6 Likert scale. Measured 3x/day (midmorning, midafternoon, evening) on each day of data collection. Items were summed over the three days.	Hedonic, trait (baseline, before mammogram), state (stressor days of mammogram)	Salivary; 6 samples/day, at two timepoints:1) three consecutive days one month prior to mammogram, 2) day before, day of, and day after procedure. Measures were average cortisol level, diurnal slope, and cortisol reactivity (slope change score from time 1 to time 2)	Higher baseline PA was associated with lower cortisol reactivity to mammogram	Breast cancer survivors had higher baseline cortisol, but no differences in slope or CAR
Giese-Davis, DiMiceli, Sephton, & Spiegel, 2006	Metastatic breast cancer patients (N=29)	Coded video-recorded PA expression during therapy session; PA expression included affection (verbal and touch), interest, validation, accurate	Hedonic, state (may also be trait if expression is thought of as personality trait)	Salivary; 4 samples per day (8:00, 12:00, 17:00, 21:00h), for 3 consecutive days. Diurnal cortisol slope and mean cortisol level were used in analyses.	PA expression associated with lower mean cortisol levels, even when NA expression was controlled for.	

		emotions, genuine humor, excitement/joy/delight			but not PA, related to cortisol slope.	
Giese-Davis, Wilhelm et al., 2006	Metastatic breast cancer patients (N=90): 45 depressed, 45 non-depressed	PANAS, measured as state during Trier Social Stress Test (TSST)	Hedonic, state	Salivary; 5 samples per day (waking, +30mins, 12:00h, 17:00h, 21:00h) for 2 consecutive days, 1 week prior to TSST and day after TSST. 10 salivary samples throughout TSST. Diurnal slope, waking levels, CAR, and recovery levels of evening, next day waking and CAR (baseline levels minus levels after TSST)	Relationship not directly measured	Depressed patients had lower waking cortisol levels and lower PA at TSST.
Costanzo et al., 2012	Breast cancer survivors (n=111), healthy controls (n=111)	Daily telephone interview for 8 consecutive days; rated frequency (5point scale) of 13 PA items experienced that day. Ratings were averaged to obtain overall PA measure.	Hedonic, trait (average of 8 days)	Salivary; 4 samples per day (waking, waking+30mins, before lunch, before bed), for 4 consecutive days. Measures were diurnal slope, total output (AUC), and CAR slope	Relationship not directly measured	Patients rated daily stressors as more disruptive. More time since diagnosis was associated with more PA, and less total cortisol. On stressor days,

					cancer survivors declined less PA, had less overall cortisol output, but similar patterns of slope and CAR as healthy controls.

Table 2

Sample Demographics

Variable	Levels	Frequency (n)	Percent of Sample (%)	Mean (SD)
Age				60.8 (
Gender	Male	20	32.8	
	Female	41	67.2	
Race	Black or African American	13	21.3	
	White	48	78.7	
Education Completed	Middle School (7-8 years)	4	6.6	
	High School (12 years)	34	55.7	
	AA/Technical (14 years)	16	26.2	
	BA/BS (16 years)	4	6.6	
	MA/MS (18 years)	3	4.9	
Income	<$15,000	17	27.9	
	%15,001-$19,999	5	8.2	
	$20,000 - $29,999	9	14.8	
	$30,000 -$39,999	4	6.6	
	$40,000 - $49,000	7	11.5	
	$50,000 - $59,999	1	1.6	
	$60,000 - $69,999	6	9.8	
	$70,000 - $79,999	1	1.6	
	$80,000 - $89,000	2	3.3	
	$90,000 - $99,999	1	1.6	
	$100,000 - $149,999	4	6.6	
	$150,000 - $249,999	1	1.6	

Table 3

Cancer Staging and Diagnosis Variables

Variable	Levels	Frequency (n)	Percent of Sample (%)	Mean (SD)
Age at diagnosis				58.97 (8.76)
Time since diagnosis (months)				22.28 (17.32)
Summary stage	I	14	23	
	II	7	11.5	
	III	26	42.6	
	IV	14	23	
Diagnosed with other medical condition	No	18	29.5	
	Yes	43	70.5	

Table 4

Patients' Current Medications

Medication Type	Frequency (n)	Percent of Sample (%)
Adrenals	0	0
Anti-convulsants	7	11.5
Anti-depressants	15	24.6
Anxiolytics	0	0
Benzodiazepine	10	16.4
Systemic Contraceptives	0	0
Corticosteroids	20	32.8
Estrogens	3	4.9
Opiate Agonists	17	27.9
Tranquilizers	0	0
Sedatives/Tranquilizers	0	0
Sleep aids	5	8.2

Table 5

Smoking History

Smoking Variable	Mean (SD)	Levels	Frequency (n)	Percent of Sample (%)
History of Smoking (including current)		No	2	3.3
		Yes	59	96.7
Currently smoke cigarettes		No	44	72.1
		Yes	16	26.2
	Current Smokers (n=16)			
Current packs per week	3.12 (3.17)			
Current cigarettes per day	11.28 (8.91)			
How many years have you been smoking	39.54 (15.24)			
	Patients with a Smoking History (Including Current Smokers; n=59)			
History of smoking cigarettes		No	2	3.3
		Yes	59	96.7
How many years did you smoke?	36.11 (12.12)			
Years since quitting smoking	8.08 (9.14)			
How many packs/week did you smoke?	7.76 (4.93)			
How many cigarettes/day did you smoke?	22.66 (12.94)			
Pack Years (Current) (packs/day x years smoking)	20.00 (14.35)			
Pack Years (History)	42.07 (29.47)			
Total Pack Years	41.43 (30.05)			

Table 6

Cancer Treatment Variables

Variable	Level	Frequency (n)	Percent of Sample (%)
Have you ever received chemo?	No	12	19.7
	Yes	48	78.7
Are you currently receiving chemo?	No	38	62.3
	Yes	21	34.4
Have you received chemo in the past 2 months?	No	34	55.7
	Yes	22	36.1
Have you ever received radiation?	No	22	36.1
	Yes	38	62.3
Are you currently receiving radiation?	No	57	93.4
	Yes	3	4.9
Have you received radiation in the past two months?	No	50	82.0
	Yes	7	11.5

Table 7

Positive and Negative Affect Descriptives

Scale	Mean (SD)	Score Range
PANAS – Positive Affect Items		
Interested	3.16 (1.05)	1-5
Excited	2.64 (1.08)	1-5
Strong	2.85 (1.11)	1-5
Enthusiastic	2.64 (1.17)	1-5
Proud	2.87 (1.43)	1-5
Alert	3.26 (1.14)	1-5
Inspired	2.59 (1.24)	1-5
Determined	3.31 (1.15)	1-5
Attentive	2.97 (1.13)	1-5
Active	2.93 (1.06)	1-5
PA Subscale Mean	***2.92 (0.83)***	*1.10-4.70*
PA Total Score	***29.24 (8.30)***	*11-47*
PANAS – Negative Affect Items		
Distressed	2.13 (1.06)	1-5
Upset	2.15 (1.18)	1-5
Guilty	1.46 (0.91)	1-5
Scared	2.10 (1.31)	1-5
Hostile	1.43 (0.83)	1-5
Irritable	2.38 (1.21)	1-5
Ashamed	1.40 (0.86)	1-5
Nervous	2.45 (1.35)	1-5
Jittery	2.11 (1.27)	1-5
Afraid	2.10 (1.43)	1-5
NA Subscale Mean	***1.97 (0.82)***	*1-4*
NA Total Score	***19.71 (8.21)***	*10-40*
CES-D – Positive Items		
Felt I was just as good as other people	2.31 (0.92)	0-3
Felt hopeful about the future	1.81 (1.04)	0-3
I was happy	2.14 (0.82)	0-3
I enjoyed life	2.31 (0.90)	0-3
CES-D Positive Items Mean	***2.14 (0.74)***	*0.25–3.00*
CES-D PA Total Score	***8.57 (2.98)***	*1-12*

Note. PA = positive affect; NA = negative affect

Table 8

Two-Factor Pattern Matrix

	Factor	
PANAS Items	1	2
PA Items		
interested	.152	**.535**
excited	.214	**.441**
strong	-.133	**.748**
enthusiastic	.011	**.667**
proud	-.141	**.686**
alert	.159	**.623**
inspired	-.230	**.816**
determined	.060	**.725**
attentive	.016	**.770**
active	.094	**.758**
NA Items		
distressed	**.755**	-.086
upset	**.827**	.058
guilty	**.326**	.131
scared	**.694**	-.025
hostile	**.605**	-.054
irritable	**.742**	-.184
ashamed	**.370**	.005
nervous	**.748**	.148
jittery	**.702**	.087
afraid	**.826**	.050

Note. Extraction Method: Principal Axis Factoring. Rotation Method: Promax with Kaiser Normalization. Item loadings are bolded for each appropriate factor.

Table 9

Three-Factor Pattern Matrix

	Factor		
PANAS Items	1	2	3
PA Items			
interested	**.542**	.168	-.039
excited	**.422**	.112	.225
strong	**.744**	-.139	.007
enthusiastic	**.673**	.032	-.053
proud	**.715**	-.047	-.221
alert	**.613**	.107	.113
inspired	**.802**	-.292	.128
determined	**.729**	.074	-.036
attentive	**.791**	.081	-.149
active	**.742**	.017	.167
NA Items			
distressed	-.057	**.862**	-.195
upset	.075	**.857**	-.050
guilty	.066	.040	**.694**
scared	-.020	**.676**	.044
hostile	-.053	**.576**	.067
irritable	-.184	**.701**	.099
ashamed	-.091	.027	**.873**
nervous	.163	**.769**	-.037
jittery	.085	**.658**	.101
afraid	.051	**.784**	.093

Note. Extraction Method: Principal Axis Factoring. Rotation Method: Promax with Kaiser Normalization. Item loadings are bolded for each appropriate factor.

Table 10

Five-Factor Pattern Matrix

PANAS Items	Factor 1	2	3	4	5
PA items					
interested	.118	**.358**	-.073	.251	.326
excited	.051	-.012	.178	**.682**	.206
strong	-.182	**.703**	.008	.062	.311
enthusiastic	.051	.299	-.115	**.583**	-.048
proud	.002	**.480**	-.245	.350	-.156
alert	.151	**.533**	.126	.185	-.179
inspired	-.277	**.579**	.104	.348	-.001
determined	.087	**.859**	.011	-.153	.065
attentive	.107	**.866**	-.120	-.094	.038
active	.033	**.844**	.224	-.071	-.025
NA Items					
distressed	**.882**	.133	-.166	-.278	.024
upset	**.871**	.026	-.051	.103	-.051
guilty	.019	.045	**.647**	.146	.064
scared	**.606**	-.109	.003	.103	.483
hostile	**.596**	-.105	.072	.121	-.135
irritable	**.765**	-.093	.132	-.071	-.278
ashamed	.007	.028	**.927**	-.006	-.112
nervous	**.718**	.116	-.042	.067	.271
jittery	**.626**	.202	.128	-.139	.181
afraid	**.734**	-.157	.046	.313	.281

Note. Extraction Method: Principal Axis Factoring. Rotation Method: Promax with Kaiser Normalization. Item loadings are bolded for the appropriate factor.

Table 11

Cortisol Variable Descriptives

Cortisol Variable	Mean (*SD*)	Range
Raw Waking Cortisol (μg/dL)	0.289 (.133)	0.013 – 0.745
Log Waking Cortisol, log(μg/dL)	-1.553 (.756)	-5.097 – -0.342
Raw Bedtime Cortisol (μg/dL)	0.119 (.093)	0.011 – 0.447
Log Bedtime Cortisol, log(μg/dL)	-2.840 (.946)	-5.841 – -1.190
Log Diurnal Mean, log(μg/dL)	-2.189 (.666)	-4.738 – -1.168
Diurnal Slope, log(μg/dL)/Hr	-0.049 (.107)	-0.257 – 0.305
Raw Slope (μg/dL)	0.170 (.151)	-0.18 – 0.63

Note. Raw slope is the change score between raw bedtime and raw waking cortisol values. Positive values indicate a descending slope.

Table 12

PANAS-PA and Data-Driven Controls Regressed onto Mean Diurnal Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.008	.008			.433	.513
PANAS-PA	-.088	-.658	.513	-.088						

Note. sr = semipartial correlation

Table 13

PANAS-PA and Theoretically-Driven Controls Regressed onto Mean Diurnal Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.256	.064	.065	.161	1.889	.161
PANAS-NA	.044	.336	.738	.044						
Steroid	-.253	-1.925	.060	-.253						
Step 2					.290	.084	.019	.301	1.626	.194
PANAS-NA	.064	.485	.630	.064						
Steroid	-.276	-2.071	.043*	-.272						
PANAS-PA	-.141	-1.045	.301	-.137						

Note. sr = semipartial correlation

Table 14

PANAS-PA, CES-D PA and Data-Driven Controls Regressed onto Mean Diurnal Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	$p\ (\Delta R^2)$	*F*	*p*
Step 1					.234	.055			1.506	.231
PANAS-PA	.019	.126	.901	.017						
CES-D-PA	-.242	-1.607	.114	-.217						

Note. sr = semipartial correlation

Table 15

PANAS-PA, CES-D PA and Theoretically-Driven Controls Regressed onto Mean Diurnal Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.256	.065			1.819	.172
PANAS-NA	.044	.330	.743	.044						
Steroid	-.253	-1.889	.065	-.253						
Step 2					.345	.119	.054	.229	1.688	.167
PANAS-NA	.012	.089	.929	.012						
Steroid	-.258	-1.908	.062	-.253						
PANAS-PA	-.035	-.223	.825	-.030						
CES-D PA	-.216	-1.404	.167	-.186						

Note. sr = semipartial correlation

Table 16

PANAS-PA and Data-Driven Controls Regressed onto Waking Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.057	.003			.178	.675
PANAS-PA	-.057	-.422	.675	-.057						

Note. sr = semipartial correlation

Table 17

PANAS-PA and Theoretically-Driven Controls Regressed onto Waking Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.300	.090			2.672	.078
PANAS-NA	.028	.214	.831	.029						
Steroid	-.300	-2.308	.025*	-.300						
Step 2					.320	.102	.012	.401	2.011	.124
PANAS-NA	.044	.334	.739	.044						
Steroid	-.318	-2.409	.020*	-.314						
PANAS-PA	-.113	-.847	.401	-.116						

Note. sr = semipartial correlation

Table 18

PANAS-PA, CES-D PA and Data-Driven Controls Regressed onto Waking Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	$p\ (\Delta R^2)$	*F*	*p*
Step 1					.265	.070			1.960	.151
PANAS-PA	.071	.477	.635	.064						
CES-D-PA	-.292	-1.934	.053	-.259						

Note. sr = semipartial correlation

Table 19

PANAS-PA, CES-D PA and Theoretically-Driven Controls Regressed onto Waking Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.300	.090			2.573	.086
PANAS-NA	.028	.210	.834	.028						
Steroid	-.300	-2.264	.028*	-.300						
Step 2					.395	.156	.066	.152	2.311	.070
PANAS-NA	.021	-.153	.879	-.020						
Steroid	-.295	-2.232	.030*	-.290						
PANAS-PA	.019	-.127	.900	.016						
CES-D PA	-.269	-1.786	.080	-.232						

Note. sr = semipartial correlation

Table 20

PANAS-PA and Data-Driven Controls Regressed onto Bedtime Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.359	.129			3.545	.037*
Age at Diagnosis	.230	1.472	.148	.198						
Years Smoking	.182	1.167	.249	.157						
Step 2					.359	.129	.000	.973	2.315	.088
Age at Diagnosis	.229	1.432	.159	.195						
Years Smoking	.184	1.100	.277	.150						
PANAS-PA	.005	.035	.973	.005						

Note. sr = semipartial correlation

Table 21

PANAS-PA and Theoretically-Driven Controls Regressed onto Bedtime Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.397	.158			2.154	.089
Age at Diagnosis	.028	1.608	.115	.218						
Years Smoking	.015	1.202	.236	.163						
PANAS-NA	.012	.745	.460	.101						
Steroid	-.285	-1.050	.299	-.142						
Step 2					.398	.159	.001	.814	1.699	.154
Age at Diagnosis	.029	1.607	.115	.220						
Years Smoking	.014	1.041	.303	.142						
PANAS-NA	.012	.766	.448	.105						
Steroid	-.295	-1.063	.293	-.145						
PANAS-PA	-.004	-.237	.814	-.035						

Note. sr = semipartial correlation

Table 22

PANAS-PA, CES-D PA and Data-Driven Controls Regressed onto Bedtime Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.359	.129			3.545	.037*
Age at Diagnosis	.230	1.472	.148	.198						
Years Smoking	.182	1.167	.249	.157						
Step 2					.373	.139	.010	.760	1.857	.134
Age at Diagnosis	.223	1.384	.173	.189						
Years Smoking	.197	1.163	.251	.159						
PANAS-PA	.059	.364	.717	.050						
CES-D PA	-.114	-.743	.461	-.102						

Note. sr = semipartial correlation

Table 23

PANAS-PA, CES-D PA and Theoretically-Driven Controls Regressed onto Bedtime Cortisol

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.397	.158			2.154	.089
Age at Diagnosis	.257	1.608	.115	.218						
Years Smoking	.189	1.202	.236	.163						
PANAS-NA	.103	.745	.460	.101						
Steroid	-.143	-1.050	.299	-.142						
Step 2					.404	.163	.005	.873	1.427	.226
Age at Diagnosis	.255	1.527	.124	.211						
Years Smoking	.186	1.082	.285	.149						
PANAS-NA	.089	.596	.554	.082						
Steroid	-.141	-1.001	.322	-.138						
PANAS-PA	.005	.028	.978	.004						
CES-D PA	-.075	-.466	.643	-.070						

Note. sr = semipartial correlation

Table 24

PANAS-PA and Data-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.080	.006			.353	.555
PANAS-PA	.08	.594	.555	.080						

Note. sr = semipartial correlation

Table 25

PANAS-PA and Theoretically-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	$p\ (\Delta R^2)$	*F*	*p*
Step 1					.230	.053			1.509	.230
PANAS-NA	.116	1.250	.217	.166						
Steroid	.154	1.164	.250	.154						
Step 2					.245	.060	.007	.536	1.24	.348
PANAS-NA	.153	1.139	.260	.152						
Steroid	.168	1.244	.219	.166						
PANAS-PA	.085	.623	.536	.083						

Note. sr = semipartial correlation

Table 26

PANAS-PA, CES-D PA and Data-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	$p\ (\Delta R^2)$	*F*	*p*
Step 1					.163	.027			.709	.497
PANAS-PA	.010	.062	.950	.009						
CES-D-PA	.158	1.038	.304	.142						

Note. sr = semipartial correlation

Table 27

PANAS-PA, CES-D PA and Theoretically-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.230	.053			1.453	.243
PANAS-NA	.166	1.227	.225	.166						
Steroid	.154	1.142	.259	.154						
Step 2					.301	.091	.038	.361	1.247	.303
PANAS-NA	.203	1.432	.158	.193						
Steroid	.151	1.099	.277	.148						
PANAS-PA	-.015	-.095	.925	-.013						
CES-D PA	.204	1.303	.199	.181						

Note. sr = semipartial correlation

Table 28

Exclusion of Patients on Corticosteroids: PANAS-PA and Theoretically-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.302	.091			3.613	.065
PANAS-NA	.302	1.901	.065	.302						
Step 2					.304	.093	.001	.818	1.786	.183
PANAS-NA	.295	1.805	.080	.292						
PANAS-PA	.038	.232	.818	.037						

Note. sr = semipartial correlation

Table 29

Exclusion of Patients on Corticosteroids: PANAS-PA, CES-D PA and Theoretically-Driven Controls Regressed onto Diurnal Cortisol Slope

Variable	β	*t*	*p*	sr	*R*	R^2	ΔR^2	*p* (ΔR^2)	*F*	*p*
Step 1					.302	.091			3.512	.069
PANAS-NA	.302	1.874	.069	.302						
Step 2					.377	.064	.051	.387	1.822	.162
PANAS-NA	.379	2.170	.037*	.350						
PANAS-PA	-.085	-.457	.651	-.074						
CES-D PA	.261	1.380	.177	.222						

Note. sr = semipartial correlation

Table 30

Hypotheses and Findings Summary

Hypothesis		Finding
Aim 1	*Understand the frequency and quality of PA among lung cancer patients*	
1.1	Patients will experience moderate PA and will report more PA than NA.	Supported
1.2	Positive and negative affect items will emerge as separate factors.	Supported
1.3	Variables that reflect lower disease burden will be associated with higher PA.	Partially Supported
Aim 2	*Test the relationship between positive affect and cortisol variables*	
2.1	Higher PA will be related to lower mean cortisol levels.	Not Supported[1]
2.2	Higher PA will be related to steeper diurnal cortisol slope.	Not Supported[2]
2.3	PA will more strongly relate to mean cortisol than to diurnal slope.	Partially Supported[3]

Note. Superscript indicates significant or trend findings for relevant hypothesis. [1] Higher CES-D PA was associated with lower waking cortisol at a trend level. [2] Higher NA was associated with flatter slopes when not including patients on corticosteroids. [3] Absolute values and direction of beta weights were in hypothesized directions, but did not reach statistical significance.

Table 31

Comparison of Cortisol Variables to Other Research Samples

Cortisol Variable	Cortisol Mean (SD) in Comparative Samples				
	Current Sample	Lung Cancer	Breast Cancer	Metastatic Breast Cancer	Healthy Sample
Mean Waking Value, log(μg/dL)	-1.553 (0.76)	NR	-1.330 (0.54)	NR	NR
Mean Bedtime Value, log(μg/dL)	-2.840 (0.95)	NR	-2.791 (0.99)	NR	NR
Diurnal Cortisol Mean, log(μg/dL)	-2.189 (0.67)	NR	-1.213 (0.39)	-1.22 (0.39)	-1.27 (0.46)
Diurnal Slope, log(μg/dL)/Hr	-0.049 (0.11)	-0.114 (0.06)	-.071 (0.09)	-0.092 (0.03)	-0.113 (0.03)

Note. NR = not reported. Lung cancer sample statistics are from Sephton et al., 2013. Breast cancer sample statistics are from Cash et al., 2015. Metastatic breast cancer sample and healthy sample statistics are from Abercrombie et al., 2004.

Figures

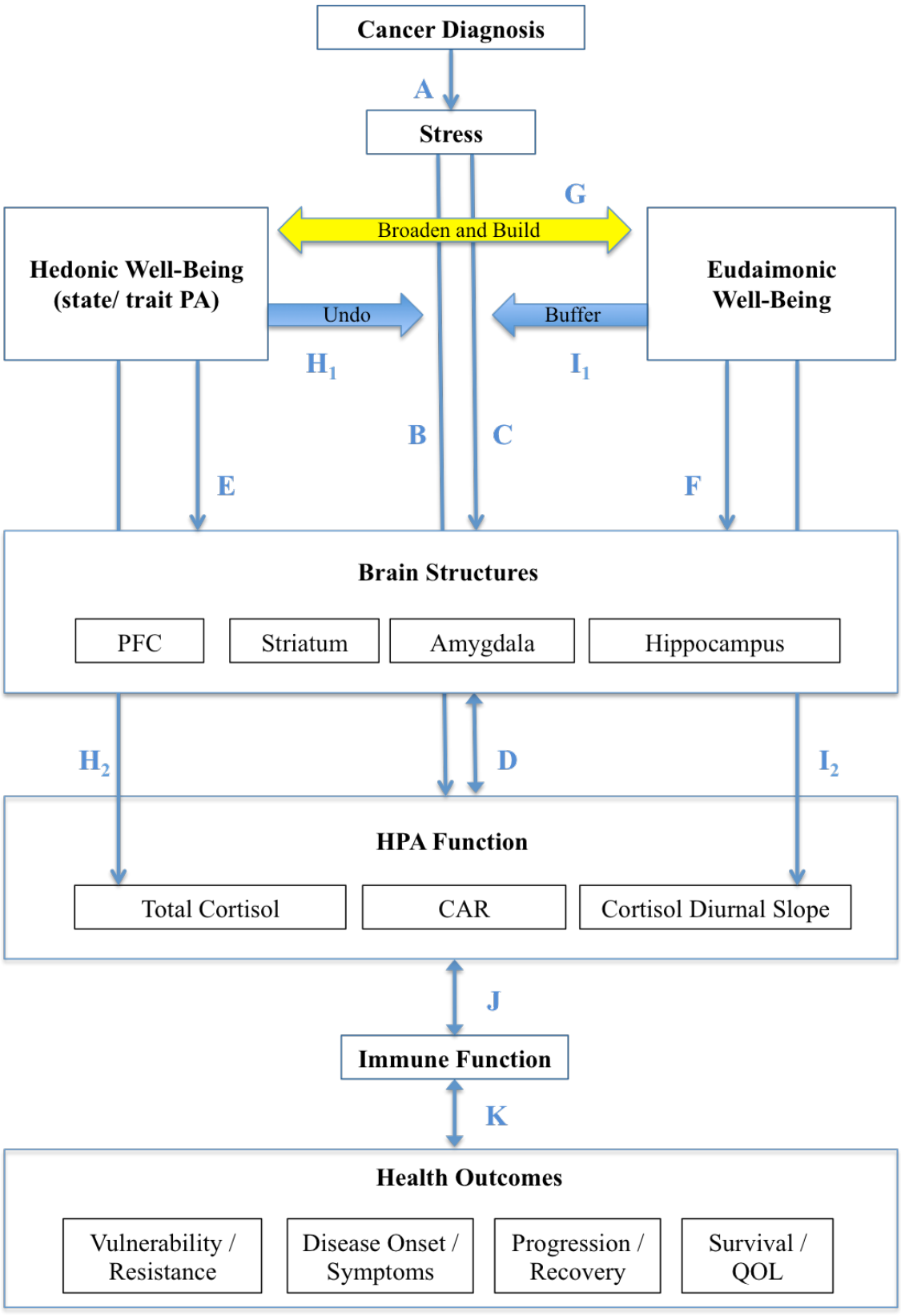
Cancer Diagnosis
A
Stress
G
Broaden and Build
Hedonic Well-Being (state/ trait PA)
Undo
Buffer
Eudaimonic Well-Being
H1
I1
B
C
E
F
Brain Structures
PFC
Striatum
Amygdala
Hippocampus
H2
D
I2
HPA Function
Total Cortisol
CAR
Cortisol Diurnal Slope
J
Immune Function
K
Health Outcomes
Vulnerability / Resistance
Disease Onset / Symptoms
Progression / Recovery
Survival / QOL

Figure 1. An integrated model of PA and cortisol in cancer patients. Lettered arrows indicate processes and relationships. Arrow A: Cancer is associated with psychological distress (stress). Arrows B and C: Stress influences the areas of the cortex, limbic system, and HPA, which interact to result in the release of cortisol (total cortisol level, diurnal slopes, CAR; Arrow D). Arrows E and F: Neuroimaging literature indicates that PA and eudaimonia influence brain structures involved in regulating HPA system. Arrow G: PA encourages eudaimonia in cancer through the Broaden and Build Theory. Arrow H: Based on the Undoing Hypothesis, patients' PA undoes effects of *acute* stress on the HPA (H_1), leading to a lower total cortisol levels and reactivity (H_2). Arrow I: Based on the Buffering Hypothesis, eudaimonia buffers effects of *chronic* stress through building psychological resources (I_1), influencing more robust cortisol outcomes like diurnal slopes. Arrows J and K: Neuroendocrine and immune processes interact to influence health outcomes.

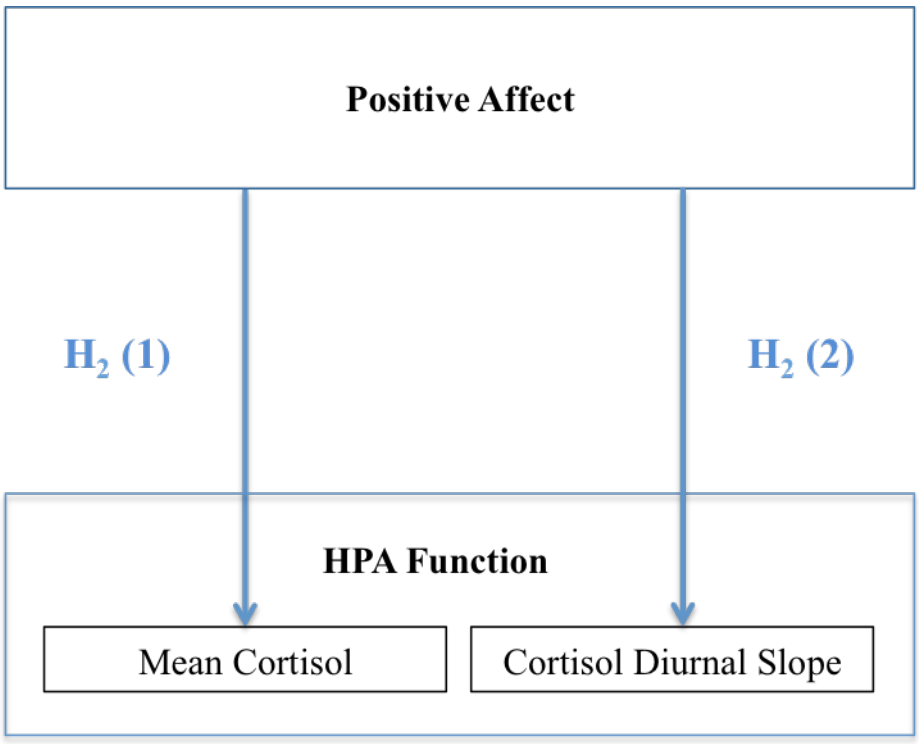

Figure 2. Hypothesized relationships for current study. Figure demonstrated proposed pathways to be tested in a sample of lung cancer patients. Pathway to be tested is adapted from arrow H_2 from Figure 1. Hypothesis 1 states that positive affect will be associated with lower mean cortisol variables. Hypothesis 2 states that positive affect will be associated with steeper diurnal slope.

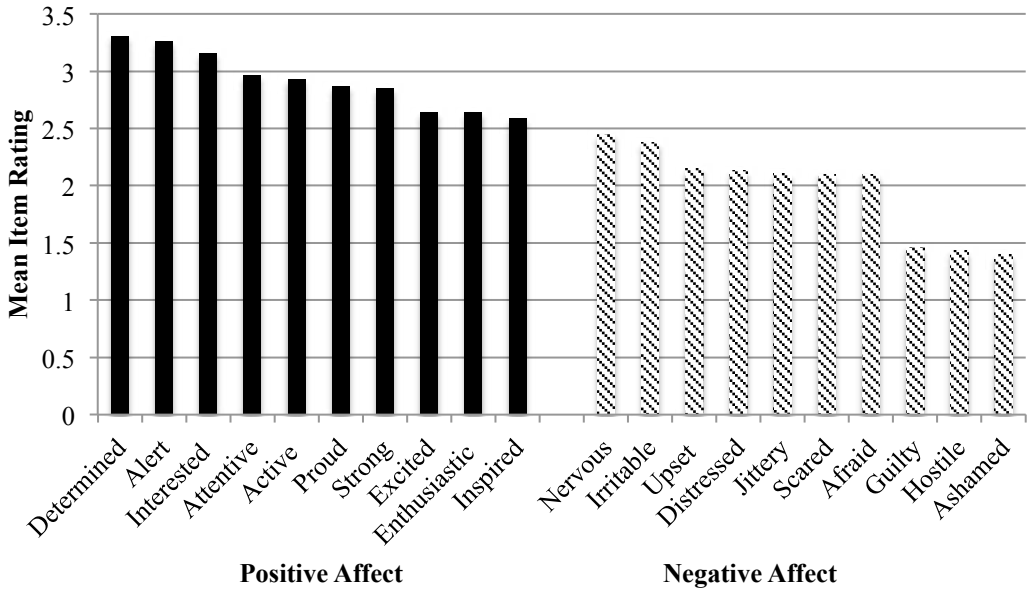

Figure 3. Mean score for each positive and negative affect item on the PANAS. Scores reflect the extent to which patients felt each of the emotions over the past week. Each item was endorsed on a 1-5 Likert scale *of very slightly or not at all* to *extremely*. Item means are presented in descending order. Solid bars represent the positive affect items; striped bars represent the negative affect items.

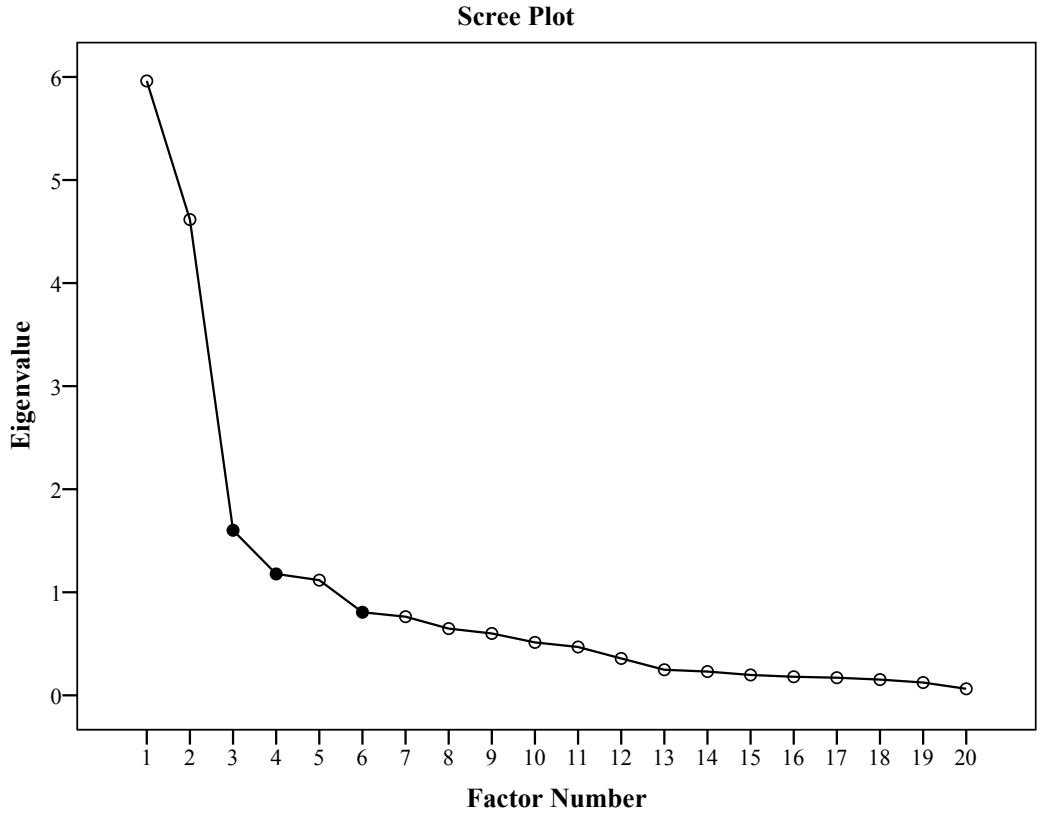

Figure 4. Scree plot from factor analysis of PANAS items. Scree plot demonstrates points of inflexion (bolded dots) at the third, fourth, and sixth factor numbers, suggesting a two, three, or five factor solution may be most appropriate for the data.

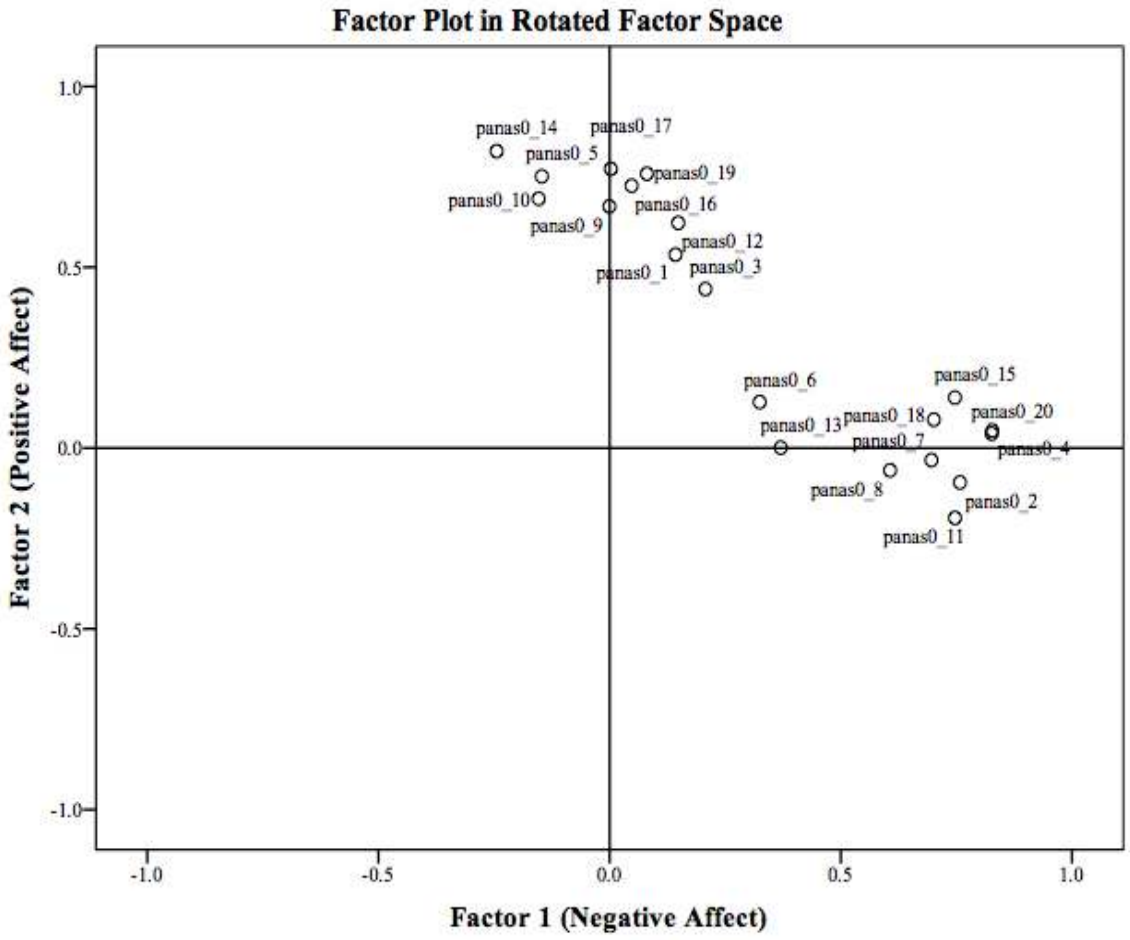

Figure 5. Factor plot in rotated factor space showing two-factor solution. PANAS PA and NA items strongly loaded onto the respective PA and NA subscales identified on the standardized measure.

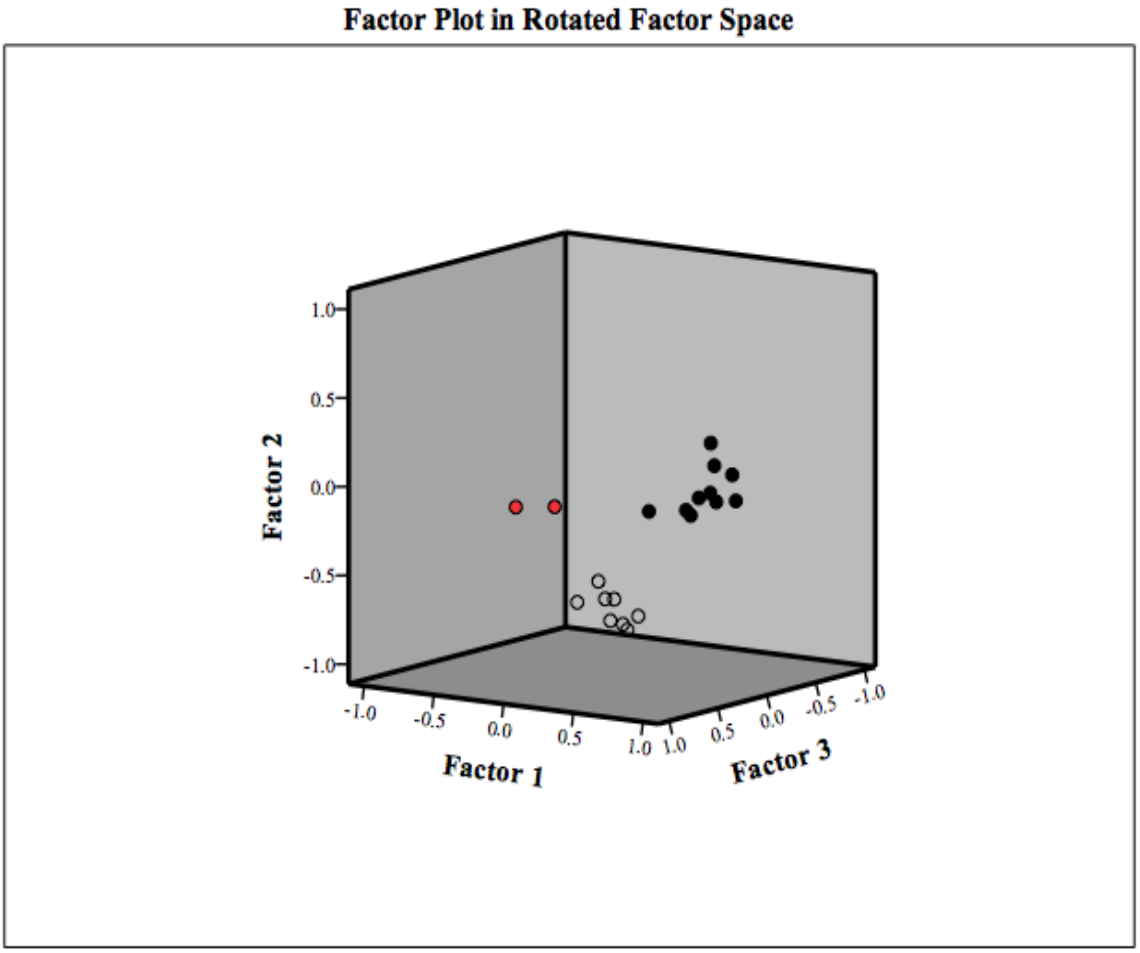

Figure 6. Factor plot in rotated factor space showing three-factor solution. PANAS PA items remained as their own factor (open circles). NA items fell into two factors, with NA items of "ashamed" and "guilty" loading independently onto a separate factor (red circles) from the rest of the NA items (closed black circles).

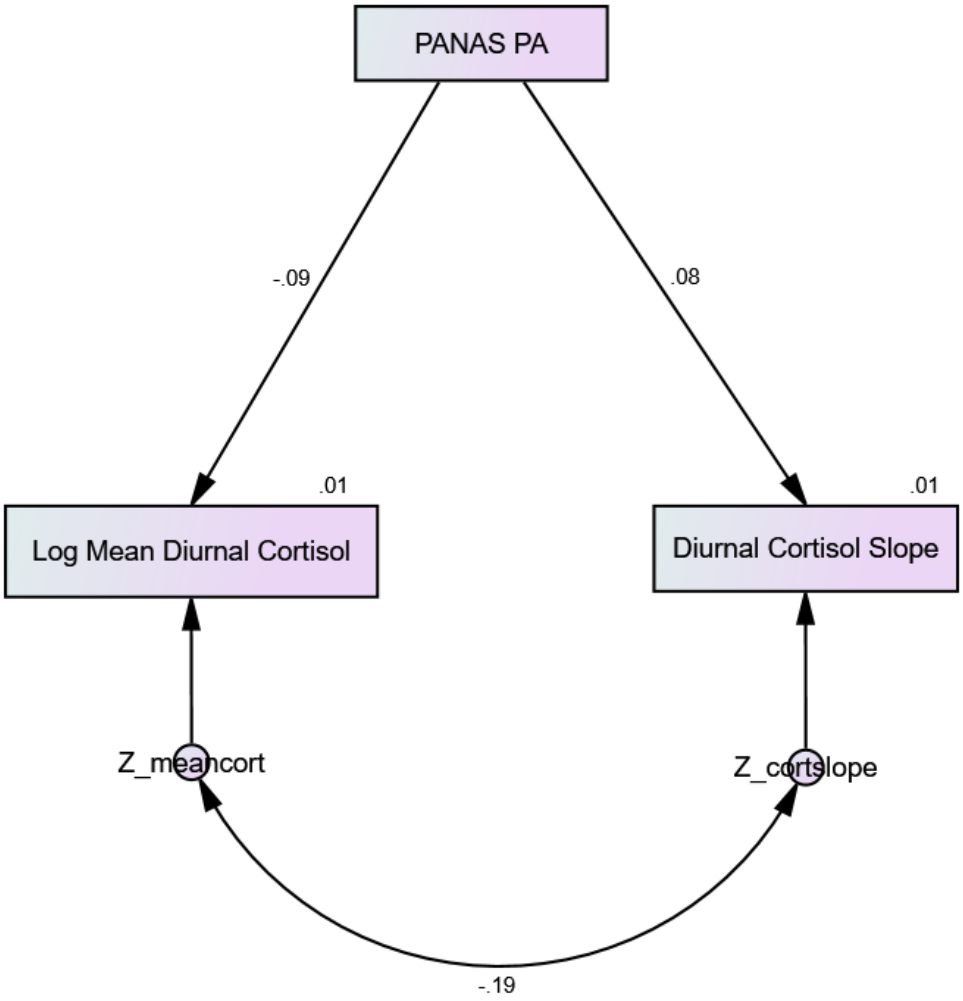

Figure 7. Model 1 path analysis. Standardized regression weights are displayed on arrows from PANAS PA to cortisol variables. Squared multiple correlations are displayed above the endogenous variables. The correlation between the error terms is displayed on the double arrow. No relationships were statistically significant.

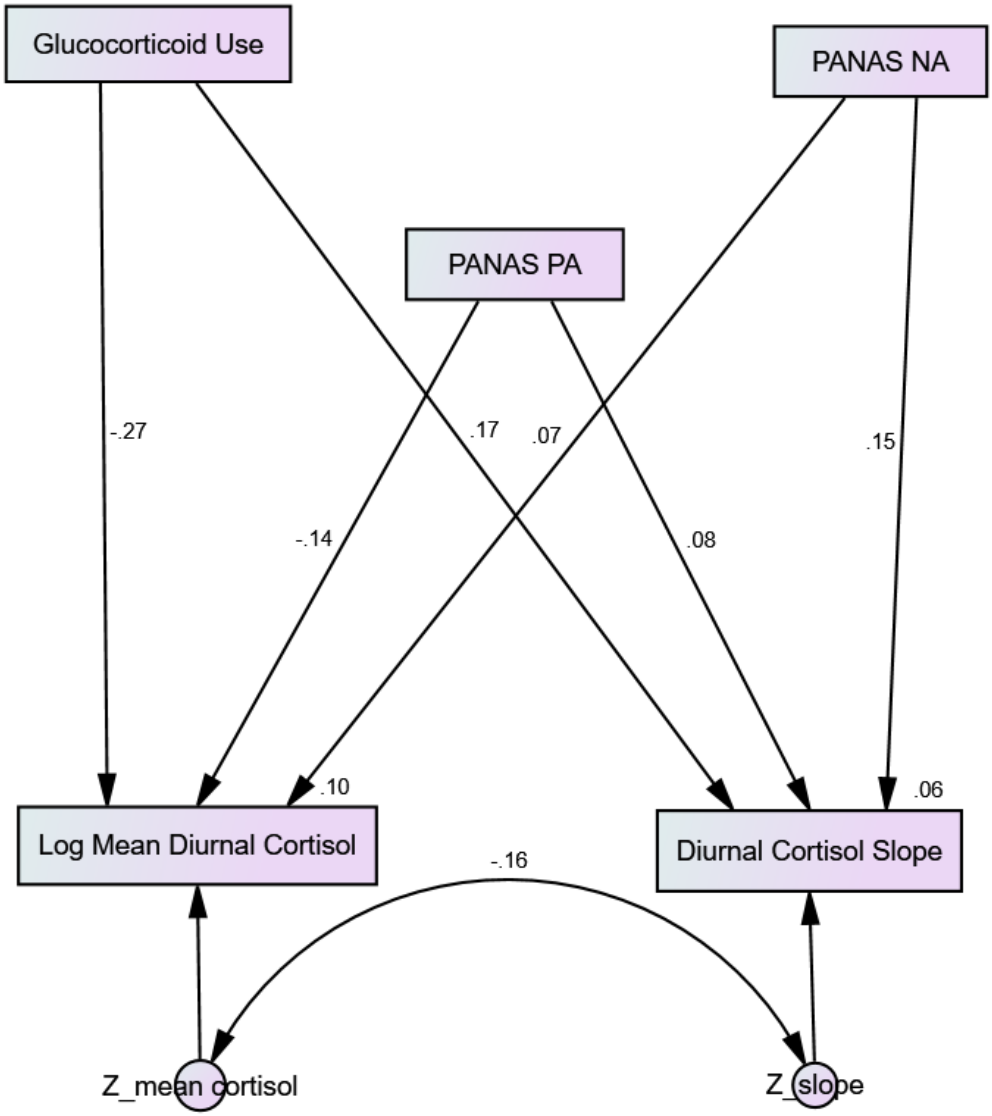

Figure 8. Model 2 path analysis. Standardized regression weights are displayed on arrows from control variables (glucocorticoid use, PANAS NA) and PANAS PA to cortisol variables. Squared multiple correlations are displayed above the endogenous variables. The correlation between the error terms is displayed on the double arrow. Glucocorticoid use was negatively associated with mean diurnal cortisol ($p = .030$); no other relationships were statistically significant.

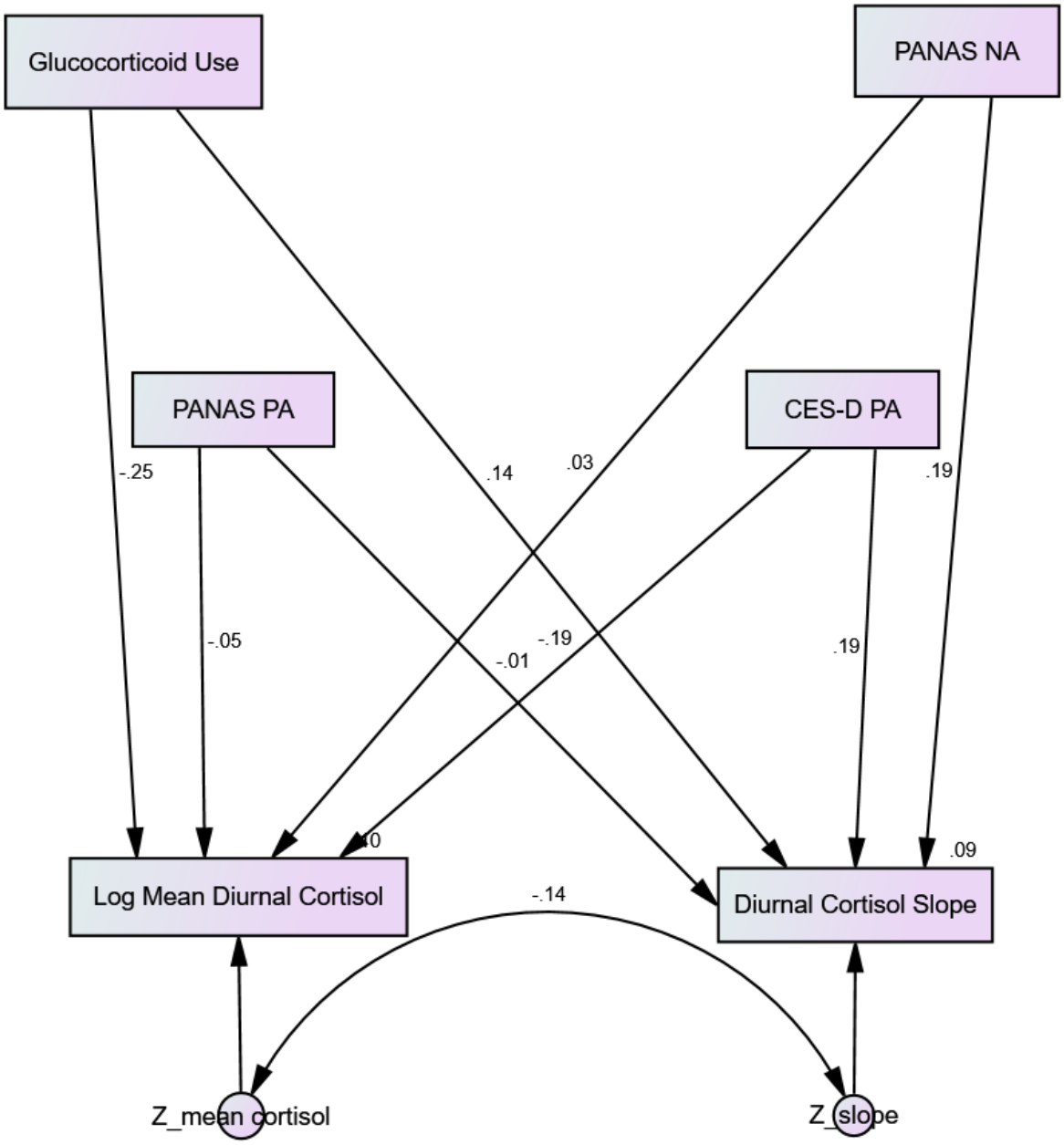

Figure 9. Model 3 path analysis. Standardized regression weights are displayed on arrows from control variables (glucocorticoid use, PANAS NA) and PANAS PA to cortisol variables. Squared multiple correlations are displayed above the endogenous variables. The correlation between the error terms is displayed on the double arrow. Glucocorticoid use was negatively associated with mean diurnal cortisol ($p = .046$); no other relationships were statistically significant.

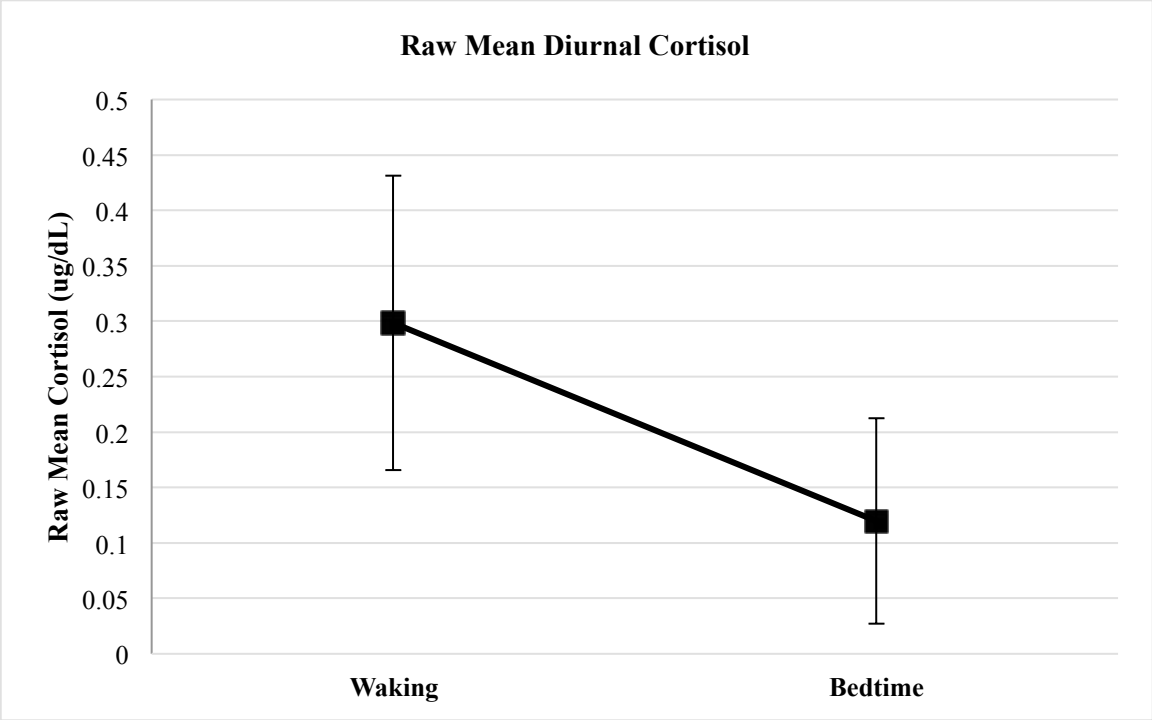

Figure 10. Raw mean (error bars show standard deviation) diurnal salivary cortisol levels (µg/dl) at waking and bedtime for overall sample. Mean diurnal slope for the sample equaled -0.049 log(µg/dl)/Hr.

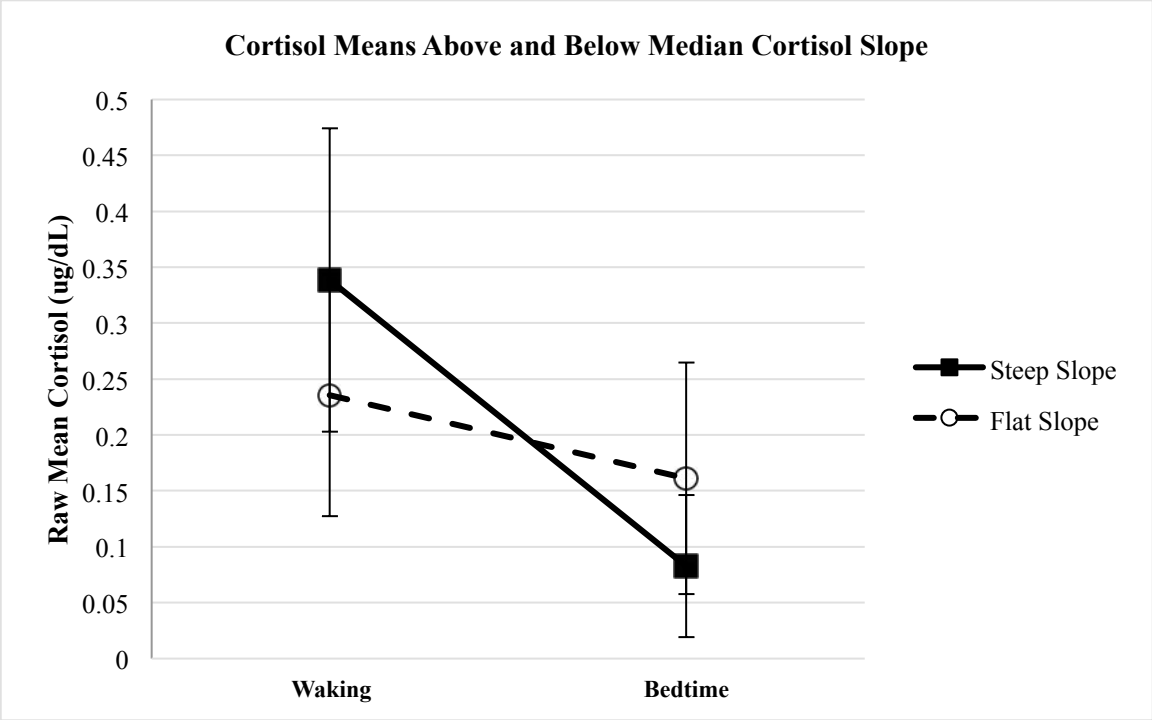

Figure 11. Raw mean (error bars show standard deviation) diurnal salivary cortisol levels at waking and bedtime for two groups of patients split at the median diurnal slope (-0.05 log (µg/dl)/Hr). Mean slope for flat slope group (n=28) was 0.028 log(µg/dl)/Hr and for the steep slope group (n=29) it was -0.123 log(µg/dl)/Hr.

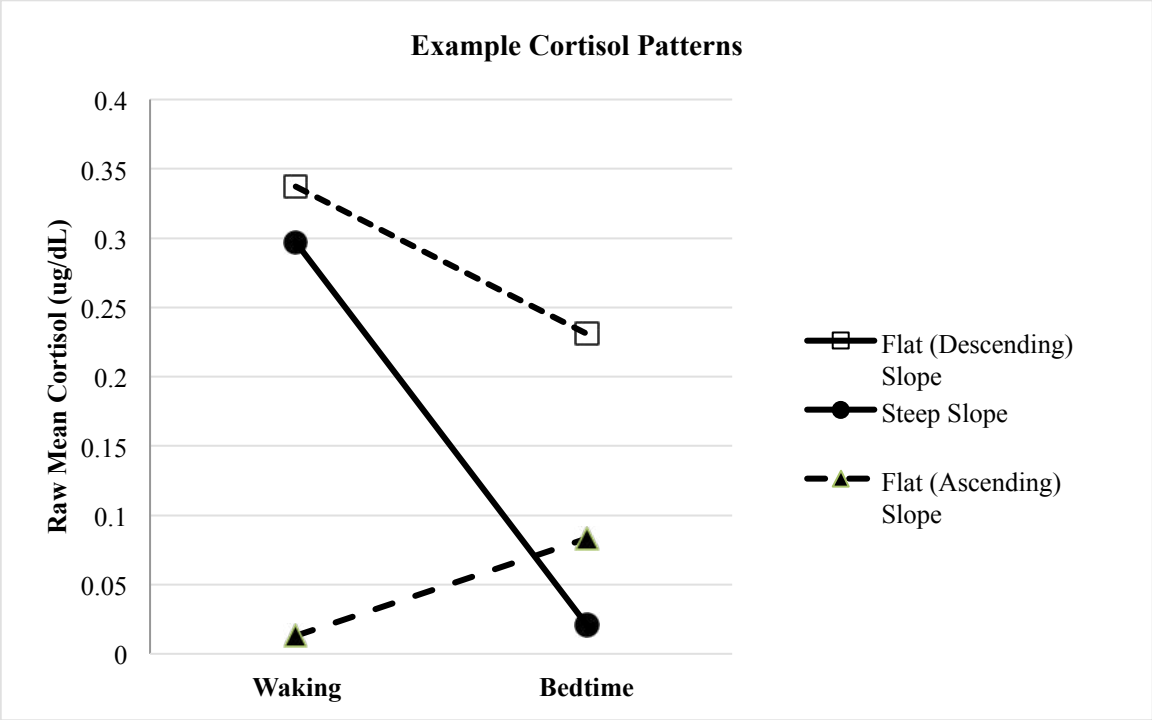

Figure 12. Raw mean diurnal salivary cortisol levels at waking and bedtime for three study participants with representative cortisol profiles observed: flattened descending slope (open square), steep slope, flattened ascending (closed triangle).

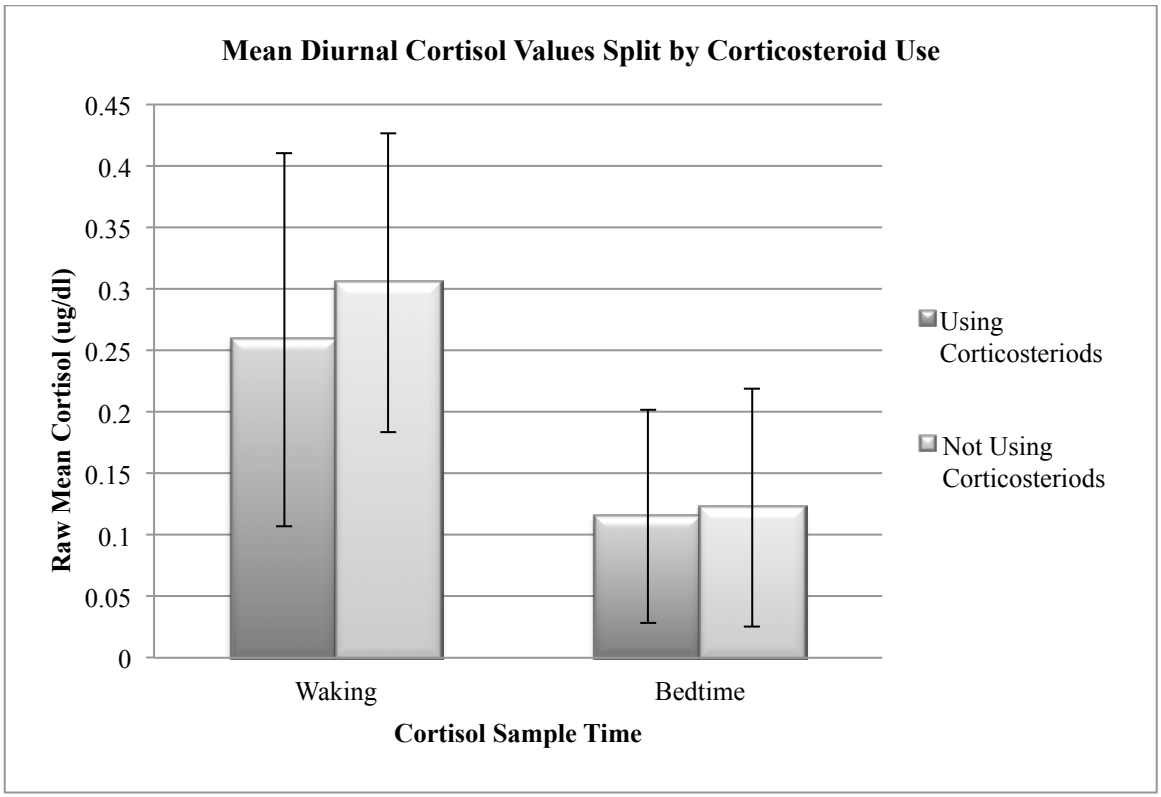

Figure 13. Raw mean salivary cortisol levels at waking and bedtime, split by patients who were taking corticosteroids versus those who were not. Patients on corticosteroids appear to have lower mean morning values; although, cautious interpretation is warranted, given the large standard deviations.

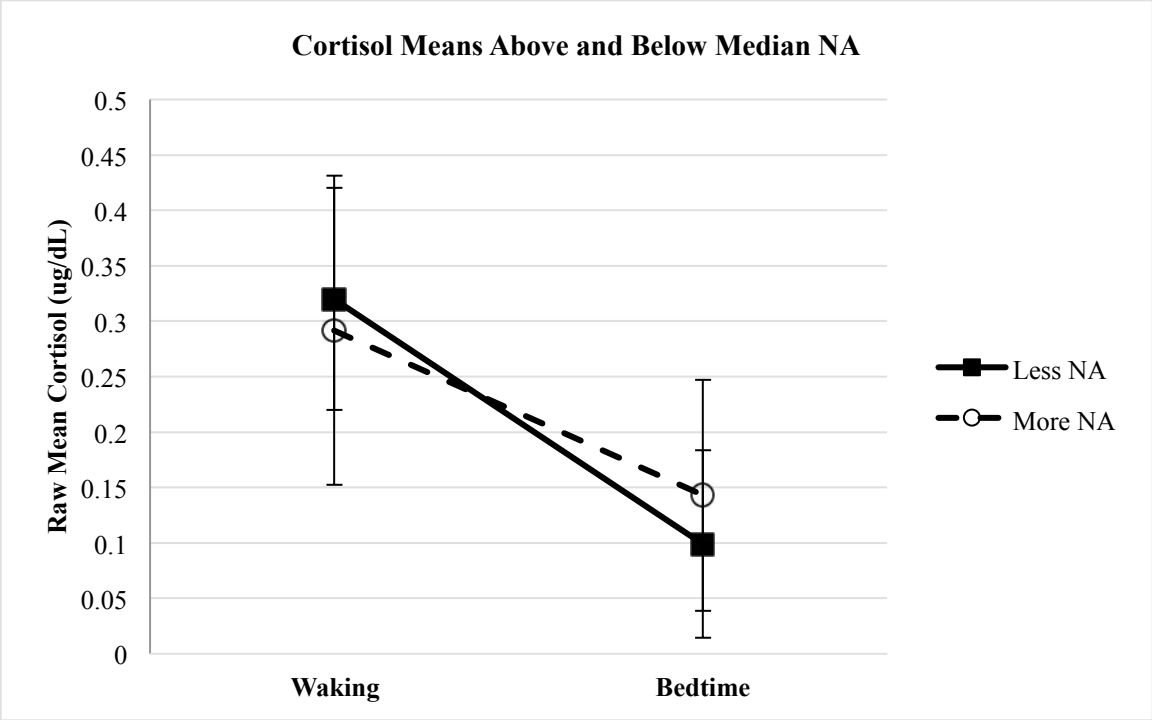

Figure 14. Raw mean (error bars show standard deviation) diurnal salivary cortisol levels at waking and bedtime for two groups of patients split at the median NA score (NA = 18). Patients in this figure are not taking corticosteroids (*n* = 41*)*. The group with less NA (*n* = 20, *M* = 12.15) had steeper slopes (-0.094 log(μg/dl)/Hr) than the group with more NA (*n* = 21, *M* = 26.05; slope = -0.031 log(μg/dl)/Hr).

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CURRICULUM VITAE

Lauren A. Zimmaro, M.A.

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Durham, NC 27701

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EDUCATION

2017 – Present **Duke University Medical Center**
Durham, NC
Clinical Psychology Internship, Medical Psychology Track

2015 – Present **University of Louisville**
Louisville, KY
Doctor of Philosophy in Clinical Psychology (Expected May 2018)
GPA: 4.0
Dissertation: The Relationship Between Positive Affect and Cortisol in Lung Cancer Patients

2013 – 2015 **University of Louisville**
Louisville, KY
Master of Arts in Clinical Psychology
Cumulative GPA: 4.0

2006 – 2010 **Wake Forest University**
Winston-Salem, NC
Bachelor of Arts in Psychology, minor in Biology
Cumulative GPA: 3.8, Psychology GPA: 4.0
Magna Cum Laude

2008 **University of Sydney**
Sydney, NSW, Australia
Study Abroad Student

DISSERTATION

Title: The Relationship Between Positive Affect and Cortisol in Lung Cancer Patients

Topic: Lung cancer patients experience more distress than other cancer types, yet little is known about positive psychological processes in the population. Dissertation examines associations of positive affect and diurnal cortisol rhythms, which have prognostic significance in cancer.

Funding: Kentucky Lung Cancer Research Grant
Dissertation Chair: Sandra Sephton, PhD
Committee Members: Paul Salmon, PhD; Ben Mast, PhD; Janet Woodruff-Borden, PhD; Tamara Newton, PhD; Elizabeth Cash, PhD

CLINICAL EXPERIENCE

July 2017 – July 2018

Duke University Medical Center, *Durham, NC*
Duke Cancer Institute
Role: Medical Psychology Intern
Supervisors: Tamara Somers, PhD; Rebecca Shelby, PhD; Licensed Clinical Psychologists

Clinical psychology intern on year-long rotation, with 50% of weekly time spent at the Duke Cancer Institute. Provide individual, couples, and group psychological services for diverse cancer patients, families, and caregivers. Services include inpatient and outpatient CBT and mindfulness-based psychotherapy, manualized behavioral interventions for symptom management, and health behavior interventions. Conduct psychological evaluations and cognitive assessments, and provide written reports and feedback sessions. Receive weekly supervision and didactics.

July 2017 – July 2018

Duke University Medical Center, *Durham, NC*
Department of Obstetrics and Gynecology: Duke Fertility Center
Role: Medical Psychology Intern
Supervisor: Julia Woodward, PhD; Licensed Clinical Psychologist

Clinical psychology intern on year-long rotation, with 30% of time spent at the Duke Fertility Center. Provide individual, couples, and group psychological services for patients of diverse backgrounds working to achieve parenthood. Psychotherapeutic services include CBT, ACT, and crisis management for patients facing fertility treatment, recurrent pregnancy loss, perinatal mood disorders, or fertility preservation. Independently and co-lead consultation groups for future parents who need an egg donor, sperm donor, or gestational carrier. Conduct psychological evaluation and assessment for egg donors and gestational carriers. Lead weekly meditation for Duke Fertility Center staff. Receive weekly supervision and didactics.

July 2017 – July 2018

Duke University Medical Center, *Durham, NC*
Behavioral Sleep Medicine Clinic
Role: Medical Psychology Intern

Supervisors: Meg Danforth, PhD; Licensed Clinical Psychologist

Clinical psychology intern on year-long rotation, with 20% of time spent at the Behavioral Sleep Medicine Clinic. Conduct psychological assessments sleep disorders and co-morbid psychological conditions. Provide individual CBT-I for patients experiencing insomnia, circadian rhythm disorders, other sleep disorders, and/or sleep apnea treatment adherence. Receive weekly supervision and didactics.

April 2016 – June 2017 **University of Louisville Physicians Outpatient Center,** *Louisville, KY*

Role: Practicum Student in Diagnostic Interviewing and Assessment

Supervisor: Elizabeth Cash, PhD, Licensed Clinical Psychologist

Clinical practicum at outpatient medical center for geriatric patients with cognitive disorders. Performed diagnostic interviewing, neuropsychological assessment and scoring. Conducted collateral interviews and patient feedback. Prepared integrative reports including history, key symptoms, assessment results and interpretation, diagnosis, and clinical recommendations. Received weekly supervision.

May 2015 – June 2017 **Gilda's Club,** *Louisville, KY*
Moment of Mindfulness Program

Role: Mindfulness Meditation Group Facilitator

Supervisor: Paul Salmon, PhD, Licensed Clinical Psychologist

Clinical practicum co-facilitating guided mindfulness meditation classes for a group of cancer patients and their relatives. Led mindfulness meditations; facilitated group discussions on the applications of mindfulness for stress and cancer-related topics. Group met twice/month, averaging 8 attendees per session. Received weekly supervision.

Feb. 2013 – June 2017 **University of Louisville,** *Louisville, KY*
Noble H. Kelley Psychological Services Center

Role: Practicum student: Therapist

Supervisors: Paul Salmon, PhD; Janet Woodruff-Borden, PhD; Licensed Clinical Psychologists

Clinical practicum at an outpatient clinic at the University of

Louisville. Provided cognitive-behavioral, mindfulness and acceptance-based therapy to adult clients each week. Participated in weekly team and individual supervision, peer consultation, individual supervision of other peers, case conceptualizations, audio/digital recording review and live observations, chart reviews, clinical report writing, and administrative duties.

Aug. 2014 – June 2017 **University of Louisville,** *Louisville, KY*
Nobel H. Kelley Psychological Services Center
Role: Practicum Student in Diagnostic Interviewing and Assessment
Supervisors: David Winsch, PhD, Licensed Clinical Psychologist

Clinical practicum at an outpatient clinic at the University of Louisville. Independently administered semi-structured interviewing for diagnostic and intake assessments of adults. Independently conducted psychological and neuropsychological assessment batteries and scoring for diagnostic and assessment purposes. Prepared integrative client reports including history, key symptoms, assessment results and interpretation, diagnosis, and clinical recommendations. Conducted feedback sessions with clients. Received weekly individual supervision. Clients include diverse community-based (urban/rural) individuals referred to clinic by self, doctors, or mental health professionals for assessment in psychological, neurodevelopmental, intellectual functioning.

Aug. 2014 – June 2017 **University of Louisville,** *Louisville, KY*
Nobel H. Kelley Psychological Services Center
Role: Practicum Student in Diagnostic Interviewing and Assessment
Supervisors: Bernadette Walter, PhD, Licensed Clinical Psychologist

Clinical practicum at an outpatient clinic at the University of Louisville. Independently conducted advanced placement and intellectual assessments for children, and semi-structured interviewing of parents/legal guardians. Prepared integrative reports including history, symptoms, assessment results and interpretation, diagnosis, and clinical recommendations. Conducted feedback sessions with parents/guardians and child. Received weekly individual supervision.

May 2015 – Dec. 2015 **The Office of David Winsch, PhD***, Louisville, KY*

Role: Practicum Student in Diagnostic Interviewing and Assessment
Supervisor: David Winsch, PhD, Licensed Clinical Psychologist

Clinical practicum at local private practice. Independently conducted psychodiagnostic interviews and assessments on children and adults seeking disability. Clients include children with medical, behavioral, developmental or learning disabilities, and adults with various medical, cognitive, behavioral, and/or mental health issues. Received weekly supervision.

May 2015 – Dec. 2015 **University of Louisville, Humana Gym,** *Louisville, KY*
Get Healthy Now Program
Role: Mindfulness Meditation Group Facilitator
Supervisor: Paul Salmon, PhD, Licensed Clinical Psychologist

Co-facilitated guided mindfulness meditation sessions for University of Louisville employees at local wellness center. Class met weekly, averaging 5 attendees/week.

June 2012 – June 2013 **Children's National Medical Center,** *Washington, DC*
Department of Neuropsychology
Role: Research Assistant
Supervisor: Madison Berl, PhD, Licensed Clinical Neuropsychologist

Independently administered and scored batteries of pediatric neuropsychological assessments on children with epilepsy and typically developing children. Aided in report writing of neuropsychological evaluations.

DIVERSITY TRAININGS & OTHER CERTIFICATIONS

August 2017 Cognitive Processing Therapy for PTSD 3-Day Training (6-month certification completion expected March 2018)
Durham Veterans Affairs Medical Center, Durham NC

June 2017 Mindful Yoga for Cancer Training (50-hour Certification)
Duke Integrative Medicine, Durham, NC

Nov. 2016 – May 2017 Yoga Teacher Training (200-hr Registered Yoga Teacher Certification)
502-Power Yoga, Louisville, KY

March 2016 Suicide Prevention

University of Louisville

Feb. 2016 Intimate Partner Violence
Center for Women and Families, Louisville, KY

Oct. 2015 Safe Zone Ally Training for LGBTQ
University of Louisville

Sept. 2015 Microagressions, Racial Stress, and Trauma
University of Louisville

Jan. – May 2015 Completed course in "Cultural Neuroscience"
University of Louisville

May 2014 Cultural competency training session for treating obsessive compulsive disorder
University of Louisville

Sept. 2010 Trauma-Informed Outreach Yoga Training
Street Yoga and *Yoga Activist, Washington, DC*

RESEARCH EXPERIENCE

July 2013 – July 2017 **University of Louisville,** *Louisville, KY*
Department of Psychological and Brain Sciences
Mindfulness and Biobehavioral Health Research Lab
Roles: Research Coordinator, Graduate Student Research Fellow
Primary Mentor: Sandra Sephton, PhD

Project coordinator for study entitled "Understanding the Prognostic Significance of Circadian Disruption in Lung Cancer and Piloting an Intervention" under principle investigator Sandra Sephton, PhD. Collaborate with multidisciplinary medical team to perform and manage recruitment of cancer patients from Thoracic Oncology Clinic at the James Graham Brown Cancer Center of the University of Louisville Hospital. Work closely with collaborators at University of Louisville Hospital and University of Kentucky. Collect, prepare, and analyze psychosocial and psychoneuroimmune/endocrine data through laboratory techniques. Manage all data. Direct an average of four undergraduate research assistants each semester and delegate tasks. Oversee contributions and roles of all other graduate student laboratory members. Manage IRB duties. Assist in grant writing and submissions. Contribute to conceptualization, writing, and submission of original research manuscripts and conference abstracts/presentations.

June 2012 – June 2013 **Children's National Medical Center**, *Washington, DC*

Department of Neuropsychology
Role: Research Assistant
Supervisor: Madison Berl, PhD

Analyzed functional MRIs on executive functioning networks within pediatric epilepsy patients and typically developing volunteers. Independently administered and scored neuropsychological testing batteries for NIH-funded working memory study. Performed primary and secondary fMRI data analysis in MatLab with Statistical Parametric Mapping (SPM versions 2-8): 3D automated reconstruction, threshold determination and region of interest analysis on activation extent and magnitude, connectivity analyses, and DTI analysis through TORTOISE. Maintained clinical neuropsychology research database through REDCap. Trained and oversaw research projects of two undergraduate students. Trained summer students in neuroimaging techniques. Contributed in conceptualization, writing, and submission of original research manuscripts and conference abstracts/presentations.

June 2010 – June 2012

National Institutes of Health, *Bethesda, MD*
National Institute of Neurological Disorders and Stroke (NINDS)
Children's National Medical Center, *Washington, DC*
Center for Neuroscience Research
Role: Research Assistant
Supervisor: William D. Gaillard, MD

Independently performed and analyzed functional MRIs on language and memory networks for presurgical pediatric and adult epilepsy patients and for typically developing volunteers. Performed primary and secondary fMRI data analysis in MatLab with Statistical Parametric Mapping (SPM versions 2-8): 3D automated reconstruction, threshold determination and region of interest analysis on activation extent and magnitude, connectivity analyses, and DTI analysis through TORTOISE. Trained and helped oversee research projects of five medical students, one doctorate student, and one undergraduate student. Trained summer students in neuroimaging techniques. Contributed in conceptualization, writing, and submission of original research manuscripts and conference abstracts/presentations.

June 2009 – May 2010

Wake Forest University Medical School, *Winston-Salem, NC*
Department of Psychiatry and Behavioral Medicine
Role: Research Assistant
Supervisor: Barbara Lasater, B.A.

Assisted in clinical research trials concerning numerous psychological disorders such as schizophrenia, major depressive

disorder, and traumatic brain injury. Recruited and prescreened study participants, performed computer based data entry. Helped develop IRB and managed clinical data.

Jan 2009 – May 2010 **Wake Forest University,** *Winston-Salem, NC*
Department of Biology
Roles: Undergraduate Research Fellow, Undergraduate Research Assistant
Supervisor: Robert Browne, PhD

Awarded the Wake Forest University Research Fellowship in May 2009 to work independently on biology research project in conjunction with the Environmental Program Director. Collected and analyzed beetle species biodiversity of the southern Appalachian Mountains both independently and as part of graduate research team.

PUBLICATIONS

Original articles: Peer-Reviewed Journals

1. Berl, M.M., **Zimmaro, L.A**., Khan, O. I., Dustin, I., Ritzl, E., Duke, E.S., Sepeta, L.N., Sato, S., Theodore, W.H., & Gaillard, W.D. (2014). Characterization of atypical language activation patterns in focal epilepsy. *Annals of Neurology*, *75*(1), 33–42. doi: 10.1002/ana.24015
2. Croft, L., Baldeweg, T., Sepeta, L.S., **Zimmaro, L.A.**, Berl, M. M., Gaillard, W.D. (2014). Vulnerability of the ventral language network in children with focal epilepsy. *Brain, 137*(8), 2245-2257.
3. Sepeta, L.S., Croft, L., **Zimmaro, L.A.**, Duke, E.S., Yerys, B.E., Vaidya, C.J., Gaillard, W.D., Berl, M.M. Reduced Language Connectivity in Pediatric Epilepsy. (2015). *Epilepsia*, *56*(2), 273-282.
4. Cash, E., Salmon, P., Weissbecker, I., Rebholz, W., Bayley, R., **Zimmaro, L**., Floyd, A., Dedert, E., Sephton, S.E. (2015). Mindfulness meditation alleviates fibromyalgia symptoms in women: Results of a randomized trial. *Annals of Behavioral Medicine, 49*(3), 319-330.
5. Cash, E., Sephton, S.E., Chagpar, A.B., Spiegel, D., Rebholz, W.N., **Zimmaro, L.A.**, Tillie, J.M., Dhabhar, F.S. (2015). Circadian disruption and biomarkers of tumor progression in breast cancer patients awaiting surgery. *Brain, Behavior, and Immunity*, *48,* 102-114.
6. **Zimmaro, L.A**., Phillips, K., Salmon, P., Giese-Davis, J., Patel, H., Rowe, J., Rebholz, W. N., Bayley-Veloso, R., Altman, J. K., Cash, E., Siwik, C., Hicks, A., Sephton, S. E. (2015). Association of Dispositional Mindfulness with Stress, Cortisol, and Well-being Among University Undergraduate Students. *Mindfulness, 7(*4), 874-885.
7. Rebholz, W. N., Cash, E., **Zimmaro, L.A.,** Baley-Veloso, R., Phillips, K., Chagpar, A. B., Dhabhar, F. S., Spiegel, D., Bell, B. S., Sephton, S. E. (2016). Distress and QOL in an ethnically diverse sample awaiting breast cancer surgery. *Journal of Health Psychology*. DOI: 1359105316659916.

8. Altman, J.K., Zimmaro, L.A, & Woodruff-Borden, J. (2017). Targeting body compassion in the treatment of body dissatisfaction: A case study. *Clinical Case Studies, 16*(6), 431-445.
9. Zimmaro, L. A., Sephton, S. E., Siwik, C. J., Phillips, K. M., Rebholz, W. N., Kraemer, H. C., ... & Cash, E. D. (2018). Depressive symptoms predict head and neck cancer survival: Examining plausible behavioral and biological pathways. *Cancer*, *124*(5), 1053-1060.
10. Siwik, C., Hicks, A., Phillips, K., Rebholz, W. N., Zimmaro, L. A., Weissbecker, I., ... & Sephton, S. E. (2017). Impact of coping strategies on perceived stress, depression, and cortisol profiles among gynecologic cancer patients. *Journal of health psychology*, 1359105317740737.

Manuscripts Under Review

1. Hicks, A., Salmon, P., Siwik, C., Phillips, K., **Zimmaro, L.A**., Burke, N., Albert, C., Fields, O., Dorsel, D., Sephton, S.E. (2016). Brief Report: Dispositional Mindfulness is Associated Lower Basal Sympathetic Arousal and Less Psychological Stress. Under Review, *Journal of Health Psychology.*

Manuscripts in Progress

1. **Zimmaro, L.A.,** Burke, N., Sephton, S.E., Salmon, P. Review of Yoga Interventions and Cortisol Outcomes in Cancer Patients. *Submitting to Health Psychology.*
2. **Zimmaro, L.A.,** Dhabhar, F.S., Barve, S.S, Sephton, S.E. Optimism moderates psychoneuroimmune pathways in lung cancer patients. *Submitting to Journal of Clinical Oncology.*
3. **Zimmaro, L.A.,** Sephton, S.E. Optimism moderates age and psychological distress in lung cancer patients. *Submitting to Psycho-Oncology.*
4. Rebholz, W.N., Cash, E., Weissbecker, I., Bayley-Veloso, R., **Zimmaro, L.A**., Phillips, K., Siwik, C.J., Sephton, S.E.. Diurnal cortisol rhythms and systemic norepinephrine in gynecologic cancer survival. *Submitting to Brain, Behavior, Immunity.*
5. **Zimmaro, L.A.,** Carson, J.W., Olsen, M. K., Sanders, L., Keefe, F. J., Porter, L.S. Greater Mindfulness Associated with Lower Pain, Fatigue, and Psychological Distress in Women with Metastatic Breast Cancer.

Published Abstracts (* Platform or paper presentation)

1. Sepeta, L.S., **Zimmaro, L.A.**, Duke, E.S., Berl, M.M., Yerys, B.E., VanMeter, J., Vaidya, C.J., Gaillard, W.D. (2011, August). *Functional Connectivity of Language Activation in Childhood Focal Epilepsy.* Poster presented at the meeting of International League Against Epilepsy, Rome, Italy.
2. **Zimmaro, L.A.**, Duke, E.S., Berl, M.M., Khan, O.I., Sato, S., Theodore, W.H., Gaillard, W.D. (2011, October). *Atypical Language Patterns in Childhood Onset Epilepsy*. Poster presented at the annual meeting of Child Neurology Society, Atlanta, GA.
3. **Zimmaro, L.A.**, Berl, M.M., Sepeta, L.N., Yerys, B.E., Duke, E.S., Khan, O.I., Ritzl, E.K., Sato, S., Theodore, W.H., Gaillard, W.D. (2011, December). *Atypical Language Localization Patterns in the Epilepsy Population*. Poster presented at the annual meeting of American Epilepsy Society, Baltimore, MD.
4. Duke, E.S., Berl, M.M., **Zimmaro, L.A.**, Khan, O.I., Martinez, A.R., Sato, S., Theodore, W.H., Gaillard, W.D. (2011, December). *Functional Topography of Cerebellar Activation during a Language Task in Patients with Localization-Related*

Epilepsy. Poster presented at the annual meeting of American Epilepsy Society, Baltimore, MD.

5. ***** Sepeta, L.S., Xu, B., **Zimmaro, L.A.**, Berl, M., Gaillard, W.D. (2011, December). *Hippocampal Activation during Preoperative Functional MRI in Children with Epilepsy.* Platform presentation for Pediatric Highlights at the annual meeting of American Epilepsy Society, Baltimore, MD.
6. Stokum, J.A., Berl, M.M., Yerys, B., Dustin, I., Khan, O.I., **Zimmaro, L.A.**, Duke, E.S., Martinez, A.R., Sato, S., Theodore, W.H., Gaillard, W.D. (2011, December). *Functional Network Connectivity in Patients with Left Temporal Lobe Epilepsy.* Poster presentation at the annual meeting of the Left Temporal Lobe Epilepsy.December).sy SMiller, K.L., Berl, M.M., **Zimmaro, L.A.**, Gaillard, W.D. (2012, December). *How are two language fMRI paradigms affected by clinical factors in patients with left hemispheric epilepsy?* Poster presentation at the annual meeting of the American Epilepsy Society, San Diego, CA.
8. **Zimmaro, L.A.,** D'Alfonso, A., Berl, M.M., Sepeta, L.N., Dustin, I., Yaun, A.L., Heiss, J.D., Sato, S., Theodore, W.H., Gaillard, W.D. (2012, December). *Pre and Post Operative Laterality of Language Regions Assessed by fMRI in Temporal Lobe Epilepsy*. Poster presentation at the annual meeting of the American Epilepsy Society, San Diego, CA.
9. Berl, M.M., Fisher, E.L., Sepeta, L.N., **Zimmaro, L.A.**, Tsuchida, T. (2012, December). *Home-based computerized intervention for working memory in pediatric epilepsy.* Poster presentation at the annual meeting of the American Epilepsy Society, San Diego, CA.
10. Sepeta, L.N., Xu, B., Berl, M.M., **Zimmaro, L.A.**, D'Alfonso, A., Theodore, W.H., Gaillard, W.D. (2012, December). *Hippocampal functioning in children and adults with epilepsy.* Poster presentation at the annual meeting of the American Epilepsy Society, San Diego, CA.
11. ***** Rebholz, W.N., Weissbecker, I., Cash, E., Bayley R., **Zimmaro, L**., Sephton, S.E. (2014, March). *Distress and support: links with circadian disruption and quality of life in gynecologic cancer.* Paper presentation at the American Psychosomatic Society 72nd Annual Scientific Conference, San Francisco, CA.
12. Bayley, R.C., Dedert, E., Rebholz, W.N., Cash, E., **Zimmaro, L.A.**, Salmon, P., Sephton, S.E. (2014, March). *Recent traumatic events may complicate adjustment to gynecologic cancer.* Poster presentation at the American Psychosomatic Society 72nd Annual Scientific Conference, San Francisco, CA.
13. **Zimmaro, L.A.**, Cash, E., Dedert, E., Rebholz, W.N., Bayley, R.C., Salmon, P., Sephton, S.E. (2014, March). *Distress, coping, and support in lung cancer: Gender differences and associations with psychopathology*. Poster presentation at the American Psychosomatic Society 72nd Annual Scientific Conference, San Francisco, CA.
14. ***** Sephton, S.E., Cash, E., Chagpar, A., Spiegel, D., Rebholz, W.N., Bayley, R.C., **Zimmaro, L.A.**, and Dhabhar, F.S. (2014, March). *Biological correlates of marital status in recently diagnosed breast cancer patients.* Paper presentation at the American Psychosomatic Society 72nd Annual Scientific Conference, San Francisco, CA.
15. Croft, L.J., Baldeweg, T., Sepeta, L., **Zimmaro, L.A.**, Berl, M.M., Gaillard, W.D. (2014, June). *Vulnerability of the ventral language network in children with focal epilepsy.* Poster presentation at the 11th European Congress on Epileptology, Stockholm, Sweden.
16. Rebholz, W.N., Weissbecker, I., Cash, E., Bayley-Veloso, R., **Zimmaro, L.A.,** Phillips, K., Sephton, S.E. (2015, March). *Diurnal cortisol rhythms and systemic*

norepinephrine predict gynecologic cancer survival. Poster presentation at the American Psychosomatic Society 73rd Annual Scientific Conference, Savannah, GA.

17. Bayley-Veloso, R., Weissbecker, I., Rebholz, W.N., Cash, E., **Zimmaro, L.A**., Phillips, K., Salmon, P., Sephton, S.E. (2015, March). *Do traumatic events build resilience and promote survival through social support in gynecologic cancer?* Poster presentation at the American Psychosomatic Society 73rd Annual Scientific Conference, Savannah, GA.
18. **Zimmaro, L.A.,** Rebholz, W.N., Cash, E., Bayley-Veloso, R., Phillips, K., Salmon, P., Sephton, S.E. (2015, March). *Optimism as a moderator of psychoneuroimmune pathways in lung cancer patients.* Poster presentation at the American Psychosomatic Society 73rd Annual Scientific Conference, Savannah, GA.
19. ***** Cash, E., Chilton, P., Rebholz, W.N., Bayley-Veloso, R., **Zimmaro, L.A.,** Chagpar, A.B., Spiegel, D., Dhabhar, F.S., Sephton, S.E. (2015, March). *HPA and rest/activity rhythms independently associate with different aspects of inflammatory response in patients awaiting treatment for breast cancer.* Paper presentation at the American Psychosomatic Society 73rd Annual Scientific Conference, Savannah, GA.
20. Phillips, K., Salmon, P., Patel, H., Rowe, J., Rebholz, W.N., **Zimmaro, L.A.,** Bayley-Veloso, R., Cash, E., Giese-Davis, J., Sonnier, H., Sephton, S.E. (2015, March). *The role of mindfulness in stress and health outcomes in university undergraduate students.* Poster presentation at the American Psychosomatic Society 73rd Annual Scientific Conference, Savannah, GA.
21. **Zimmaro, L.A.,** Sephton, S.E. (2015, July). *Psychophysiological pathways of fatigue in lung cancer patients.* Poster presentation at the World Congress on Psycho-Oncology (International Psycho-Oncology Society & American Psychosocial Oncology Society), Washington, DC.
22. Hicks, A.M., Salmon, P., Phillips, K., **Zimmaro, L.A**., Siwik, C., Bayley-Veloso, R., Cash, E., Sephton, S.E. (2016, March*). The Role of Mindfulness in Stress and Depression of Undergraduate Students.* Poster presentation at the American Psychosomatic Society 74th Annual Scientific Conference, Denver, CO.
23. Siwik, C.J., Phillips, K., **Zimmaro, L.A.,** Bayley-Veloso, R., Hicks, A.M., Cash, E., Salmon, P., Sephton, S.E. (2016, March). *Psychological and Physiological Effects of Problem-focused and Emotional Approach to Coping Styles in Gynecological Cancer Patients.* Poster presentation at the American Psychosomatic Society 74th Annual Scientific Conference, Denver, CO.
24. Phillips, K., Bayley-Veloso, R., **Zimmaro, L.A.**, Siwik, C., Hicks, A.M., Cash, E., Salmon, P., & Sephton, S.E. (2016, March*). Living situation and quality of life among cancer patients.* Poster presentation at the American Psychosomatic Society 74th Annual Scientific Conference, Denver, CO.
25. **Zimmaro, L.A.,** Segerstrom, S., Cash, E., Siwik, C., Phillips, K., Rebholz, W., & Sephton, S. E. *Moderating role of mindfulness on daily affect and cortisol in lung cancer patients.* (2017, March). Poster presentation at the American Psychosomatic Society 75th Annual Scientific Conference, Sevilla, Spain.
26. Rebholz, W.N., Cash, E., Siwik, C., Phillips, K., Albert, C., **Zimmaro, L.A.**, Dhabhar, F.S., Barve, S., Sephton, S.E. (2017, June*). Pro-inflammatory, Chemotactic, and Anti-Inflammatory Cytokine Responses Associate with HPA, but not SNS, Function in Lung Cancer Patients*. Poster presentation at Psychoneuroimmunology Research Society 24th Annual Meeting, Galveston, TX.
27. Siwik, C., Rebholz, W., Phillips, K., Cash, E., Dhabhar, F.S., Barve, S., **Zimmaro, L.A.**, Sephton, S.E. (2017, June). *Sense of Coherence in Lung Cancer Patients: Association with Coping, Immune Function, and Fatigue.* Poster Presentation at Psychoneuroimmunology Research Society 24th Annual Meeting, Galveston, TX.

28. Cash, E., Rebholz, W., Albert, C., Fields, O., **Zimmaro, L.A.,** Siwik, C., Phillips, K., Sephton, S.E. (2017, June). *Associations between the Prognostics Indicators Rest/Activity Rhythm and Diurnal Cortisol Profiles in Patients with Lung Cancer.* Poster presentation at Psychoneuroimmunology Research Society 24th Annual Meeting, Galveston, TX.
29. Sephton, S.E., Cash, E., **Zimmaro, L.A.,** Rebholz, W.N., Albert, C., Fields, O., Siwik, C., Phillips, K. *An iPod-based adaptation of MBSR for lung cancer: Associations of usage with depressive symptoms and behavioral and endocrine circadian markers.* (2017, June). Poster presentation at Psychoneuroimmunology Research Society 24th Annual Meeting, Galveston, TX.
30. * Carson, J.W., Olsen, M.K., Sanders, L., Keefe, F., **Zimmaro, L.A.,** Porter, L.S. *Greater mindfulness associated with lower pain, fatigue, and psychological distress in women with metastatic breast cancer.* (2018, March). Paper Presentation at Society for Behavioral Medicine 39th Annual Meeting, New Orleans, LA.
31. Sephton, S.E., Hicks, A., Phillips, K., Siwik, C., Albert, C., **Zimmaro, L.A.,** van der Gryp, K.A., and Salmon, P. A brief iPod-based mindfulness intervention for undergraduates: Effects on psychological and physiological outcomes. Abstract submitted for consideration for presentation at the 75th annual meeting of the American Psychosomatic Society in Louisville, KY, March 7-10, 2018.
32. Siwik, C., Segerstrom, S., Phillips, K., Cash, E., Rebholz, W., Zimmaro, L.A., Hicks, A., van
der Gryp., K., & Sephton, S. E. Associations of Actigraphically Measured Daytime Sedentariness and Nighttime Restfulness with Waking and Bedtime Salivary Cortisol Levels. Abstract submitted to the American Psychosomatic Society 76th Annual Meeting, Louisville, KY.
33. Van der Gryp., K., Siwik, C., **Zimmaro, L. A.,** Phillips, K., Rebholz, W., Cash, E., Hicks, A,., & Sephton, S. E. Lung cancer-related distress is associated with elevated mean diurnal cortisol levels. Abstract submitted to the American Psychosomatic Society 76th Annual Meeting, Louisville, KY.
34. Phillips, K., Siwik, C., Segerstrom, S., **Zimmaro, L. A.**, Rebholz, W., Cash, E., Hicks, A., van der Gryp, K., Sephton, S.E. Associations between daily affect, intrusive thoughts, and cortisol levels among lung cancer patients. Abstract submitted to the American Psychosomatic Society 76th Annual Meeting, Louisville, KY.
35. Hicks, A., Salmon, P., Rebholz, W., Phillips, K., Siwik, C., **Zimmaro, L.A.,** Cash, E., van der Gryp., K., & Sephton, S. E. The Role of Self-Compassion in a Stress-Health Pathway. Abstract Submitted to the American Psychosomatic Society 76thAnnual Meeting, Louisville, KY.

Other Abstracts and Presentations

1. Cheerharan, M., Blackstone, K., **Zimmaro, L.A.**, Gaillard, W.D., & Berl, M.M. (2011, August). *DTI of Working Memory in Pediatric Epilepsy Patients vs. Controls.* Poster presentation at the George Washington University Medical School Research Day, Washington, DC.
2. Fisher, E.L., Blackstone, K., Cayless, S., **Zimmaro, L.A.**, Gaillard, W.D., Berl, M.M. (2011, April). *Executive Functioning in Pediatric Epilepsy Population.* Poster presentation at the ChildrenEpilepsy Population. Medr Research Day, Washington, DC.
3. Packer, T., **Zimmaro, L.A.**, Cash, E., Sephton, S.E. (2014, September). *Circadian disruption: Distress and sleep quality in breast cancer patients*. Poster presentation at the annual Research!Louisville conference, Louisville, KY.

4. Fields, O., Cash, E., **Zimmaro, L.A.,** Hicks, A., Albert, C., Sephton, S.E. (2016, July). *Rest-activity rhythms and quality of life in lung cancer patients.* Poster presentation at the National Cancer Institute/ R25 Cancer Research Program Presentation Day, Louisville, KY.

LABORATORY AND DATA ANALYTIC SKILLS

fMRI
Experience in independently operating GE 3T fMRI scanner. Experience utilizing Linux OS, and fMRI preprocessing and individual and group analysis through SPM2-8, FSL, and TORTOISE.

Endocrinology
Experience in collecting, preparing, processing, and preserving human saliva samples. Proficient in cortisol data cleaning and reduction.

Immunology
Experience processing and preserving serum and plasma human blood samples. Experience preparing under sterile technique and preserving human whole blood samples for stimulated immunomodulator analysis.

Circadian Rhythms
Experience in initializing and downloading MicroMini Motionlogger Actiwatches.

Data Analysis
Experience in conducting univariate and multivariate analyses, structural equation modeling, survival analyses. Experience using the following statistical software: SPSS, AMOS. Experience in REDCap data capture system.

HONORS, AWARDS, & SCHOLARSHIPS

Oct. 2016 Yoga Teacher Training Scholarship Recipient
Kentucky Yoga Initiative, Louisville, KY

July 2015 "Best Student Poster" Award
World Congress on Psycho-Oncology, Washington, DC

May 2015 Excellence in Research Award
University of Louisville, Department of Psychological and Brain Sciences

March 2015 Research Presentation Selected for Press Release (Zimmaro et al., 2015)
American Psychosomatic Society, Savannah, GA

March 2014 Student Spotlight Award
University of Louisville, School of Interdisciplinary and Graduate Studies

July 2013 UofL SIGS Doctoral Research Fellowship Recipient
University of Louisville, School of Interdisciplinary and Graduate Studies

April 2011 First Place winner, Clinical Research Abstract: Trainee category. (Zimmaro et al., 2011)
Children's National Medical Center Research Day, Washington, DC

April 2011 First Place winner, Clinical Research Abstract: Post-Doc category. (Sepeta, Zimmaro, et al., 2011)
Children's National Medical Center Research Day, Washington, DC

May 2010 Magna Cum Laude
Wake Forest University

April 2010 Psi Chi Psychology Honor Society
Wake Forest University

March 2010 Phi Beta Kappa Honor Society
Wake Forest University

May 2009 Undergraduate Research Fellowship Recipient
Wake Forest University, Department of Biology

2009, 2014 Golden Key International Honour Society
Wake Forest University (2009); University of Louisville (2014)

2006 - 2010 Dean's List
Wake Forest University, College of Arts and Sciences

PROFESSIONAL EXPERIENCE AND MEMBERSHIPS

2016 Ad-Hoc Peer Reviewer (Journal of Health Psychology, Mindfulness)

May 2015 – Present Student Member: International Positive Psychology Association, Health Division

July 2014 – Present Student Member: American Psychosomatic Society

ACADEMIC TEACHING EXPERIENCE

Nov. 2014 **University of Louisville**
College of the Arts and Sciences
Role: Contributing Member for Workshop

Salmon, P.G., Altman, J., Bayley-Veloso, R., Cash, E., Ellsworth, M., Phillips, K., Rebholz, W., Sephton, S., **Zimmaro, L.A.** (November 1, 2014) *A Day of Mindfulness*, Workshop for

the University of Louisville Alumni Association, College of Arts and Sciences.

Sept. 2014 **University of Louisville**
College of the Arts and Sciences, School of Social Work
Role: Guest Co-Lecturer with Paul Salmon, PhD

Salmon, P., **Zimmaro L.A.** (September 9, 2014). *Mindfulness and Cancer*, Guest Lecture for Course Entitled 'Psychosocial Oncology'

VOLUNTEER ACTIVITIES

April 2016 – June 2017 **Kentucky Yoga Initiative,** *Louisville, KY*
Role: Volunteer Yoga Instructor

Independently lead weekly yoga classes for non-English-speaking elderly refugees in Louisville area. Create sequence of chair and standing yoga positions. Classes are in collaboration with Kentucky Refugees Ministries. Class attendance ranges from 12-20 refugees per class. Other involvement includes questionnaire development for outcome research of all yoga classes provided around the city.

May 2015 – Nov. 2016 **502 Power Yoga,** *Louisville, KY*
Role: Energy Exchange Team Member

Volunteer 3 hours each week to aid in administrative functions of local yoga studio.

Sept. 2014 **Zion Baptist Church Health Fair***, Louisville, KY*
Role: University of Louisville Psychological Services Center Representative

Volunteered as a University of Louisville Psychological Services Center representative from the mindfulness clinical team. Discussed brief mindfulness-based techniques to reduce stress with community members.

May 2012 – June 2013 **Yoga District Studios**, *Washington, DC*
Role: Volunteer Intern

Participated in launching programs and events promoting

accessibility to mindfulness and fitness techniques through yoga. Volunteered aiding in administrative functions of the yoga studio once a week.

March 2011 – June 2013 **Yoga Activist**, *Washington, DC*
Role: Volunteer Understudy Yoga Instructor

Co-led yoga classes to groups of homeless men and women from shelters and recovery programs around the Washington, DC area. Create sequence of chair and standing yoga positions. Classes were in collaboration with "Back On My Feet" program and various local homeless shelters.

LEADERSHIP ACTIVITIES

July 2009 – May 2010 **Embassy of Australia,** *Washington, DC*
Australian Education International
Role: Student Ambassador

Selected to serve by Embassy of Australia, University of Sydney, and Wake Forest University. Planned, marketed, and implemented four events at Wake Forest University to promote studying in Australia for study abroad and exchange, undergraduate and graduate education. Communicated frequently with Embassy of Australia, University of Sydney, and Wake Forest University's Study Abroad office.

Jan. 2009 – May 2010 **Arcadia University Study Abroad Program,** *Glenside, PA*
Role: Student Advisor

Advised potential study abroad students and helped prepare students for education abroad.

Aug. 2009 – Jan. 2010 **Wake Forest University, Delta Delta Delta Sorority**
Role: Panhellenic Recruitment Counselor

Advised and counseled potential new Greek organization members who were participating in recruitment.

Jan. 2008 – May 2008 **Wake Forest University Student Government**
Role: *Co-chair*, Campus Life Committee

Co-led team of 10 student government members on issues of campus interest. Delegated tasks to members, facilitated weekly meetings, and collaborated with multiple campus activity groups.

Aug. 2007 – May 2008 **Wake Forest University Student Government**
Role: *Chair*, Springfest Carnival Committee

Created and allocated $24,000 budget; negotiated services, pricing, and approved contracts with food and entertainment vendors. Planned and implemented annual campus-wide event, oversaw committee activities, and delegated duties for 10.

Aug. 2007 – May 2008 **Wake Forest University Student Government**
Role: Co-chair, Executive Advisory Committee on Sustainability

Co-coordinated forum of 50 to discuss campus-wide environmental issues. Collaborated with other environmental awareness groups on campus.