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**Characteristics of life stress experienced prior to the diagnosis of ovarian cancer: Differential effects on psychosocial functioning and the role of protective resources**

Lauren Zagorski Davis  
*University of Iowa*

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CHARACTERISTICS OF LIFE STRESS EXPERIENCED PRIOR TO THE  
DIAGNOSIS OF OVARIAN CANCER: DIFFERENTIAL EFFECTS ON  
PSYCHOSOCIAL FUNCTIONING AND THE ROLE OF PROTECTIVE  
RESOURCES

by

Lauren Zagorski Davis

A thesis submitted in partial fulfillment  
of the requirements for the Doctor of Philosophy  
degree in Psychology (Clinical Psychology)  
in the Graduate College of  
The University of Iowa

August 2017

Thesis Supervisor: Professor Susan K. Lutgendorf

Graduate College  
The University of Iowa  
Iowa City, Iowa

CERTIFICATE OF APPROVAL

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PH.D. THESIS

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This is to certify that the Ph.D. thesis of

Lauren Zagorski Davis

has been approved by the Examining Committee for  
the thesis requirement for the Doctor of Philosophy degree  
in Psychology (Clinical Psychology) at the  
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## ABSTRACT

Little research has examined the effect of non-cancer life stressors on psychological well-being and recurrence in patients with cancer, and results have been mixed. Furthermore, no studies have examined specific types of stress, including loss, danger, and entrapment in patients with cancer, utilizing data obtained from the Life Events and Difficulties Schedule. Given that specific stressors have been associated with certain psychological responses, this study sought to obtain a more nuanced understanding of the relationship between life stress and psychological well-being. This was examined in a sample of 135 women with ovarian cancer prior to surgery and during the year after diagnosis using latent growth curve analyses. Models of protective psychosocial resources examining social support, mastery, self-acceptance, and purpose in life as potential moderators and mediators of the relationship between life stress and psychosocial outcomes were also evaluated.

Results indicated that cancer-related losses were most closely associated with psychological well-being across several analyses, and non-cancer losses had the greatest impact on psychological outcomes when cancer-related loss was low. Non-cancer losses were significantly related to greater fatigue prior to surgery. Additionally, major non-cancer danger stressors were associated with greater distress prior to surgery. In this sample, no stressors were significantly related to cancer recurrence. Social support was the most consistent moderator of life stress on psychological well-being, and its effects on distress and depression at baseline were mediated through self-acceptance. These findings highlight the importance of both cancer- and non-cancer-related stressors on psychological wellbeing among cancer patients in their first year following surgery and furthers our understanding of the role of protective psychosocial factors.

This study has significant implications for distress screenings in patients with cancer, psychological interventions, and future research.

## **PUBLIC ABSTRACT**

Though cancer is a significant stressors in and of itself, the effects of non-cancer life stress can have an impact on the quality of life in patients with cancer. Few studies have examined the role of recent life stress experienced prior to a diagnosis and their potential effects in combination with the stress of a cancer diagnosis. Furthermore, no studies to date have examined the effects of specific types of stress, including loss, danger, and entrapment in patients with cancer. This study examined the effect of such stressors on psychological well-being, both at surgery and the trajectory over one year post-diagnosis, as well as their effects on cancer recurrence. Cancer-related losses were most related to psychological well-being, and non-cancer losses had impacts on psychological outcomes particularly when cancer-related loss was low. Non-cancer losses were significantly related to greater fatigue prior to surgery. Additionally, major danger stressors not related to cancer were associated with greater distress prior to surgery. No stressors were significantly related to cancer recurrence. Protective psychosocial factors, including social support, mastery, self-acceptance, and purpose in life, were also examined in this study. Social support was the most consistent moderator of life stress, such that the effect of life stress on psychological well-being depended on the level of social support a patient endorses. Additionally, some of these effects were explained by social support's impact on increasing self-acceptance. This study highlights the importance of cancer-related stress, as well as the impact of certain non-cancer related stressors, as well as the protective role of social support. This has significant implications for distress screenings in patients with cancer, psychological interventions, and future research.

## TABLE OF CONTENTS

List of Tables .....	vii
List of Figures .....	viii
Introduction.....	1
Stress and Cancer .....	2
Cancer as a Stressor .....	2
Life Stress in Patients with Cancer .....	6
The Stress Response and Cancer Progression .....	10
Stressful Life Events .....	11
The Concept of Stress .....	11
Measurement of Life Stress .....	14
Life Stress and Psychopathology .....	16
Specificity of Life Stress and Psychological Sequelae .....	17
Protective Psychosocial Resources .....	24
Social Support.....	25
Mastery .....	27
Self-Acceptance .....	29
Meaning .....	31
Summary and Specific Aims .....	32
Methods.....	38
Participants and Procedure.....	38
Measures .....	39
Data Analysis Strategy.....	45
Results.....	49
Preliminary and Descriptive Analyses.....	49
Specific Aim #1 .....	61
Specific Aim #2 .....	78
Specific Aim #3 .....	104
Discussion .....	105
The Impact of Life Events on Psychological Outcomes.....	106
The Role of Protective Resources.....	110
The Impact of Life Events on Recurrence .....	115
Directions for Future Research .....	117
Limitations .....	118
Clinical Implications.....	120
Conclusion .....	122
References.....	124

## LIST OF TABLES

Table 1. Demographic and Clinical Characteristics of Participants .....	50
Table 2. Frequencies of Stressful Life Events and Average Threat Level by Type of Event .....	52
Table 3. Factor Congruencies for 2-Factor Structure of Mood over Time with All Items of CESD and POMS.....	53
Table 4. Item Loadings for 2-Factor Structure of Mood over Time with All Items of CESD and POMS.....	54
Table 5. Factor Congruencies for 2-Factor Structure of Mood over Time after Excluding Items.....	56
Table 6. Item Loadings for 2-Factor Structure of Mood over Time after Excluding Items .....	56
Table 7. Factor Congruencies for Final 2-Factor Structure of Mood over Time.....	58
Table 8. Final Item Loadings for 2-Factor Structure of Mood over Time.....	58
Table 9. Item Loadings for Fatigue Factor over Time.....	59
Table 10. Means and Standard Deviations of Dependent.....	60
Variables over Time.....	60
Table 11. Model Fit Statistics for Unconditional Growth Curve Models.....	62
Table 12. Parameter Estimates from Unconditional Latent Growth Curves .....	63
Table 13. Parameter Estimates for Conditional Latent Growth Curve Predicting Distress.....	65
Table 14. Parameter Estimates for Conditional Latent Growth Curve Predicting Depressed Mood.....	69
Table 15. Parameter Estimates for Conditional Latent Growth Curve Predicting Anger .....	73
Table 16. Parameter Estimates for Conditional Latent Growth Curve Predicting Fatigue .....	77
Table 17. Parameter Estimates from Latent Growth Curves of Independent Effect of Psychosocial Resources .....	79
Table 18. Interaction Effects in Multiple Moderator Models of Psychosocial Resources .....	81
Table 19. Multiple Mediator Models with Social Support as Moderator .....	86
Table 20. Mediated Moderation Model Predicting Distress.....	89
Table 21. Mediated Moderation Model Predicting Depressed Mood.....	90
Table 22. Mediated Moderation Model Predicting Anger.....	91
Table 23. Mediated Moderation Model Predicting Fatigue.....	92
Table 24. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Overall Distress.....	100
Table 25. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Depressed Mood.....	101
Table 26. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Anger.....	102
Table 27. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Fatigue.....	103
Table 28. Effects of Life Stress on Progression.....	105

## LIST OF FIGURES

Figure 1. Independent Effects Model.....	35
Figure 2. Multiple Moderator Model .....	36
Figure 3. Multiple Mediators Model with Social Support as Moderator.....	37
Figure 4. Mediated Moderation Model .....	38
Figure 5. General Model of Conditional Latent Growth Curves .....	64
Figure 6. Effect of Time on Distress at Various Levels of Cancer Loss .....	66
Figure 7. Effect of Major Non-Cancer Danger on Baseline Distress at Varying Levels of Major Cancer Danger.....	68
Figure 8. Effect of Time on Depressed Mood at Different Levels of Cancer Loss .....	70
Figure 9. Effect of Time on Depressed Mood at Low Levels of Cancer Loss Paired With Different Levels of Non-Cancer Loss.....	71
Figure 10. Effect of Non-Cancer Loss on Baseline Anger at Different Levels of Cancer Loss...	75
Figure 11. Effect of Major Cancer Danger on Distress at Baseline at Varying Levels of Social Support.....	82
Figure 12. Effect of Major Cancer Danger on Baseline Depressed Mood at Varying Levels of Social Support.....	83
Figure 13. Effect of Major Cancer Danger on Baseline Anger at Different Levels of Self- Acceptance .....	84
Figure 14. Effect of Time on Distress at Low Levels of Social Support, Paired with Different Levels of Major Non-Cancer Danger.....	87
Figure 15. Effect of Cancer Danger on Baseline Depressed Mood at Different Levels of Social Support.....	93
Figure 16. Effect of Cancer Danger on Baseline Anger at Different Levels of Social Support...	94
Figure 17. Effect of Time on Distress at Low Levels of Social Support, Paired with Different Levels of Cancer Loss .....	95
Figure 18. Effect of Cancer Loss on Self-Acceptance at Differing Levels of Social Support .....	96
Figure 19. Statistical Model of Significant Mediated Moderation Effect Predicting Distress .....	97
Figure 20. Statistical Model of Significant Mediated Moderation Effect Predicting Depressed Mood.....	98

## **Introduction**

The stress associated with a cancer diagnosis is widely recognized both in the scientific literature and popular culture. In addition to the stress from the obvious danger to one's health, many individuals experience an "existential plight" provoked by having cancer. Stress has been widely studied in cancer patients, primarily in the context of adjustment to the stressor of cancer and the physiological effects of stress on cancer progression processes. However, fewer studies have examined the role of recent life stress experienced prior to a diagnosis and their combined effects with the stress of a cancer diagnosis. Further, given the methodological variability, there are mixed results in the extant literature and questions regarding the nature of recent life stress and adjustment to cancer remain. No studies to date have examined the effects of specific types of stress, such as losses, events that place an individual in danger, or the experience of ongoing entrapment in the context of a cancer diagnosis.

The Life Events and Difficulties Schedule (LEDS) provides a unique and thorough account of recent life stress, taking into account the circumstances of the individual's life. With this interview and other measures, the connection between life stress and psychological symptoms has been widely studied. Life stress has been related to onset of depression in a number of studies as well as anxiety disorders. However, not all stressors are created equal. Psychosocial dimensions of stressors categorized in the LEDS, such as loss, danger, and entrapment, have been shown to produce differing psychological sequelae. Namely, loss has been shown to be related to both depression and anxiety, entrapment has most commonly been related to the onset of depression, and danger is related most frequently to anxiety. Importantly, while the psychosocial mechanisms and potential protective factors of stress have been

extensively studied, questions remain regarding the nature of these factors in the context of loss, danger, or entrapment.

To date, no studies have utilized the methodologically rigorous LEADS system to examine life stress in cancer patients and its effects on psychosocial functioning. Further, none have examined the effects of dimensions of life stress on quality of life in patients with cancer, let alone the psychosocial factors that may mediate or moderate these effects. Thus, this study is the first of its kind to examine life stress in patients with cancer, operationalized by its psychosocial effects of either loss, danger, or entrapment. This study examined the implications of such stressors for psychological functioning, both at surgery and the trajectory over one year post-diagnosis. Furthermore, protective psychosocial moderators and mechanisms of these effects were examined to assess potential risk factors and targets for intervention. Given the variability in psychological symptoms and quality of life in patients with cancer, along with their prognostic significance, this is an area of inquiry with noteworthy clinical implications.

## **Stress and Cancer**

### **Cancer as a Stressor**

The diagnosis of cancer represents a significant threat to one's physical and mental well-being. The experience of poor psychological functioning and even psychopathology is common. For example, in a national survey, patients with cancer exhibited worsened depression and anxiety after their diagnosis compared to the change seen over time in a matched control group without cancer (Costanzo, Ryff, & Singer, 2009). Though advances in the treatment of cancer have greatly improved the likelihood of survival, cancer is still synonymous with suffering. Experiencing a sense of danger to one's health and life is an inherent when one receives a

diagnosis of cancer. Additionally, there are many other ways that cancer that can affect psychological adjustment.

With the diagnosis of cancer, individuals come face-to-face with their own mortality, which often leads to self-reflection and assessment of life priorities (Bertero & Wilmoth, 2007). This “existential plight” or search for meaning that is commonly experienced by patients reflects both actual and potential losses engendered by cancer (Weisman & Worden, 1976). The foremost effect that a cancer diagnosis can have involves a challenge to one’s core assumptions about the world. Questions such as “why me?”, “what does this mean for me?”, and “why did this happen?” can represent an incongruence with one’s beliefs in a just world, beliefs about control over one’s life, and security for the future (Janoff-Bulman, 1989; E. J. Taylor, 1995). Thus, loss of these values, beliefs, and cherished ideas can be experienced. Additionally, beliefs about the future – hopes, plans, and the ability to carry these out – can be lost as a result of cancer (Landmark, Strandmark, & Wahl, 2001).

An individual’s sense of identity is another domain which is often impacted by cancer. Within the uncertainty of cancer, the only thing that is certain is that their lives are forever changed – they are now a “cancer patient” (Bertero & Wilmoth, 2007). Further, one’s sense of self can be directly impacted by the symptoms and side effects of cancer and its treatment. Such physical changes can entail loss of functioning, independence, and social roles (Hottensen, 2010). It is clear that these changes brought about by cancer can have profound effects, as values, beliefs, self-identity, and daily functioning are all fundamental aspects of well-being and living a meaningful life.

Cancer can also be associated with emotional isolation and a loss of support from others (Wortman & Dunkel-Schetter, 1979). For example, a review of qualitative studies of breast

cancer patients found that many women reported feeling that their families did not understand what they were going through (Bertero & Wilmoth, 2007). Some patients also feel as though others do not want to discuss their cancer experience with them, which is related to poorer well-being and clinically significant distress (Green, Ferguson, Shum, & Chambers, 2013).

Additionally, physical changes brought about by cancer such as a mastectomy, hair loss, and weight changes can cause changes in feeling of intimacy and impact sexual relationships (Bertero & Wilmoth, 2007). Furthermore, as individuals enter into survivorship, support that was provided throughout treatment may lessen, and leave patients with a sense of loss even after successful treatment (Stanton, 2012).

Understanding the existential concerns of cancer patients is imperative to understanding the emotional experience of cancer and improving quality of life. In fact, measures of existential well-being (characterized by having a meaningful existence and control over one's life, achieving goals, finding life worthwhile, appreciating every day, and positive self-regard) have been highly related to patient's ratings of their overall quality of life (Cohen, Mount, Tomas, & Mount, 1996). Demoralization, caused by loss of purpose and meaning in life, has also been related to depression and anxiety in patients with progressive diseases and cancer (Robinson, Kissane, Brooker, & Burney, 2015). Furthermore, perceived threat of cancer may be more highly related to existential concerns, compared to objective measures of threat (Laubmeier & Zakowski, 2004).

Importantly, psychosocial well-being can have profound effects on an individual's prognosis. For example, depression has been related to greater mortality in cancer patients (Pinquart & Duberstein, 2010). In ovarian cancer patients, quality of life at the time of surgery has been related to survival time (Lakusta et al., 2001). Additionally, while many individuals

report high levels of adjustment after a cancer diagnosis, increased psychological distress around the time of surgery is common, and there remains substantial variability in the trajectories between individuals over time. For example, one study found that while most women with breast cancer reported low and stable levels of anxiety and depression over the year after diagnosis, a portion of individuals experienced chronically high anxiety and depression symptoms (Lam et al., 2013). Other distinct patterns of adjustment have been observed in studies of patients with breast cancer, such as those that improved steadily over time, rapidly improved then remained stable, or steadily declined (Helgeson, Snyder, & Seltman, 2004). These trajectories of adjustment within the first year can have important implications for psychosocial well-being even 6 years later (Lam, Shing, Bonanno, Mancini, & Fielding, 2012).

Much of the research in women with cancer has been done in those with breast cancer. Notably, 61% of breast cancer cases are diagnosed at a localized stage, and this is associated with a 99% 5-year survival rate. This same percentage of patients with ovarian cancer are diagnosed at a distant stage due to the dearth of screening tests, which is associated with a 27% 5-year survival rate (American Cancer Society, 2015). About one-third of patients with ovarian cancer report clinically-significant levels of distress (Kornblith et al., 1995). Additionally, there is a high prevalence of clinical levels of depression and cancer-specific anxiety (e.g., intrusive thoughts, avoidance behaviors) (Bodurka-Bervers et al., 2000; Evans et al., 2005; Norton et al., 2004). Because the nature of ovarian cancer is quite different from breast and other cancers, understanding the psychosocial functioning and longitudinal adjustment of patients, especially in the presence of recent life stress, is of great significance.

## **Life Stress in Patients with Cancer**

Although the diagnosis of cancer represents a significant threat in itself, the negative psychological impact of previously experienced stressful life events remains relevant for determining an individual's experience of allostatic overload (Fava, Guidi, Semprini, Tomba, & Sonino, 2010). Existing allostatic load will undeniably increase vulnerability to experiencing greater distress in response to a future event (e.g., a cancer diagnosis). Thus, it is highly likely that previous life events would impact existential and psychological distress of patients with cancer. Consequently, there is a growing body of evidence examining the effects of life stress in patients with cancer, and several studies have shown that life events do, in fact, influence the psychological well-being of individuals with cancer. However, the extant research varies greatly in methodological approaches and assessment of life events and more research is needed to draw more definitive conclusions.

Around the time of diagnosis, previous stressful life events have been associated with quality of life (Golden-Kreutz et al., 2005), poorer vitality, more depressive symptoms, and greater cancer-specific distress in women with breast cancer (Low, Stanton, Thompson, Kwan, & Ganz, 2006). Approximately 3-4 months after diagnosis, in patients with melanoma and prostate cancer, the number of negative events was associated with worse psychological symptoms, while this relationship was not significant in breast cancer patients (Lehto, Ojanen, Väkevä, Aromaa, & Kellokumpu-Lehtinen, 2008). In this same study, chronic strain predicted worse depressive symptoms in prostate and breast cancer patients.

Several cross-sectional studies examine the effect of life stress at times other than around diagnosis. In a sample of patients with mixed types of cancer, patients with a diagnosis of depression at 1 year post-diagnosis reported having more negative life events occur in the

previous year, though life events were unrelated to the extent of symptoms (Grassi, Malacarne, Maestri, & Ramelli, 1997). Similarly, women who experienced a decline in quality of life throughout 18 months post-diagnosis were more likely to report having one or more non-cancer-related life events at 6 months (Disipio, Hayes, Battistutta, Newman, & Janda, 2011). Further, 6.8 years after initial treatment, the impact of a serious illness, impact of all negative events, and presence of a serious negative event (excluding the loss of a spouse or child) were all related to higher psychological distress in women with breast cancer (Kornblith et al., 2001). However, some studies have found that life stress is unrelated to distress and mood disturbance in breast cancer patients at 9.5 months and 4 years post-diagnosis (Butler, Koopman, Classen, & Spiegel, 1999; Koopman, Hermanson, Diamond, Angell, & Spiegel, 1998).

It may be that the relationship between life events may have differential impact on quality-of-life depending on stage of treatment (Golden-Kreutz et al., 2005; Lutgendorf et al., 2013). For example, in our sample of ovarian cancer patients, number and severity of life stressors (measured by a self-report checklist) were related to poorer QOL at one year, but not around the time of surgery when controlling for depression and anxiety (Lutgendorf et al., 2013). However, life events prior to surgery and their effects on QOL at one year were not examined. Prospective longitudinal studies can shed much more light than cross-sectional or retrospective studies on the long-term effects of life stress in patients with cancer yet there are few conclusive or replicated findings. For example, in patients with melanoma and breast cancer, the number of negative events measured 3-4 months after diagnosis prospectively predicted more psychological symptoms 6 months later but not 15 or 18 months later (Lehto et al., 2008). Similarly, in a sample of patients with head and neck cancer and colorectal cancer, recent life events were related to more depressive symptoms around the time of diagnosis and at 6 and 24 weeks later

(Archer, Hutchison, Dorudi, Stansfeld, & Korszun, 2012). Other studies have found opposite patterns of results, where life stress is related to psychosocial functioning only after at least 6 months have passed. For example, in one study, while chronic strain did not predict psychological symptoms in women with breast cancer 3-4 months after diagnosis, it significantly predicted symptoms 6 and 15 months later (Lehto et al., 2008). Another study found that life events were unrelated to mental health at 4-months post-diagnosis but related to worse mental health at 12-months. (Golden-Kreutz et al., 2005).

The impact of stressors on the trajectory of well-being in patients with cancer has also been studied. In one study of breast cancer patients, life events did not predict vitality or depression at 6 months or 1 year post diagnosis, but had a significant interaction with emotional approach coping strategies (Low et al., 2006). In a prospective longitudinal study of women with breast cancer, women with more life events prior to the diagnosis of cancer had poorer quality of life in a variety of QOL domains (bodily pain, role emotional, social functioning) and vitality throughout 5 years post-diagnosis (Beatty, Lee, & Wade, 2009).

Importantly, these studies vary widely in their measurement of life events and, thus, suffer several methodological issues which are detailed in the following section. Most studies utilize checklist measures assessing specific life events (Archer et al., 2012; Beatty et al., 2009; Butler et al., 1999; Golden-Kreutz et al., 2005; Kornblith et al., 2001). Within these types of measures, the final scores that are used vary highly between studies. For example, some questionnaires weight life events based on the specific event and/or its recency (Butler et al., 1999; Low et al., 2006). Some studies calculate the sum of life events, others assess the impact, and some use a combination of both. Additionally, the number of life events and domains that are probed range from 3 to 64 items. Most studies assess events within the past 12 months

(Beatty et al., 2009; Golden-Kreutz et al., 2005; Kornblith et al., 2001; Low et al., 2006; Lutgendorf et al., 2013). Others set no limit on the range of time (Butler et al., 1999), or assess events within 6 months (Archer et al., 2012). Only one reviewed study utilized a semi-structured interview which assessed 64 possible events that are rated on uncontrollability and undesirability. However, this study only looked at the number of uncontrollable and undesirable events as opposed to threat or objective negative impact (Grassi et al., 1997).

While the current literature supports the hypothesis that stressful life events can negatively impact psychological well-being in patients with various types of cancer, this relationship remains to be further explicated. To the extent that diagnosis and treatment of cancer represents a threat, recent stressful life events may increase vulnerability to perceived distress by contributing to the cumulative effect of stressors. In fact, changes in perceived stress mediate the effects of life stress on QOL (Beatty et al., 2009). Additionally, compared to a matched healthy comparison group, cancer survivors tend to report some daily stressors as more severe and disruptive, and show larger increases in negative affect even with similar numbers and types of events between groups (Costanzo, Stawski, Ryff, Coe, & Almeida, 2012). Furthermore, in patients with chronic lymphocytic leukemia, those with a threat-processing bias to view events as progressing rapidly are more likely to have higher levels of depression and anxiety and worse quality of life (Levin, Riskind, & Li, 2007).

Only one study has examined the threat of events as measured by the LEDS in patients with cancer (Fagundes et al., 2012). However, this study only assessed biomarkers of inflammation and did not include psychosocial measures. No studies have utilized such a rigorous assessment of the cumulative effects of stress and cancer on psychological functioning.

Additionally, none have examined the effect of life stress on psychological symptoms in patients with cancer according to specific psychosocial characteristics of stress, described below.

### **The Stress Response and Cancer Progression**

Much of the work examining stress and cancer has been done on the physiological effects of stress. Stress response systems have been implicated in several pathophysiological processes that are fundamental to cancer progression and growth (Armaiz-Pena, Cole, Lutgendorf, & Sood, 2013; Hanahan & Weinberg, 2011; Reiche, Nunes, & Morimoto, 2004). For example, in ovarian cancer, catecholamines can play a role in facilitating the metastatic pathogenesis of cancer cells (Sood et al., 2006), angiogenesis (Lutgendorf et al., 2003), and resistance to programmed cell death (Sood et al., 2010). They can also stimulate production of pro-inflammatory cytokines, which is important as chronic inflammation has been linked to various steps in the process of tumorigenesis. Pro-inflammatory cytokines such as IL-6, IL-8, and vascular endothelial growth factor (VEGF) can promote growth of the tumor, survival of tumor cells, and angiogenesis. They may also impact tumor progression by inactivating tumor-suppressing genes (Antoni, Lutgendorf, et al., 2006).

Given that stress can elicit such physiological effects, a better understanding of the stressors that may ultimately have effects on recurrence is certainly warranted. However, few studies have examined the effects of life stress on physiological or clinical outcomes. In one study, recent life stress was related to messenger RNA coding for immune markers associated with tumor progression (Fagundes et al., 2012). In another study, women who experienced a breast cancer recurrence were more likely to endorse stressful life events after surgery compared to women without a recurrence (Ramirez et al., 1989). Negative life events over 3 and 4 years post-diagnosis have even been related to survival when measured approximately 11 years later in

patients with melanoma (Lehto, Ojanen, Dyba, Aromaa, & Kellokumpu-Lehtinen, 2012). Additionally, one study found that bereavement after a cancer diagnosis was related to shorter survival (Itzhak et al., 2000). However, several studies have shown no relationship between life stress and recurrence or survival (Fallah, Akbari, Azargashb, & Khayamzadeh, 2016; Graham, Ramirez, Love, Richards, & Burgess, 2002; Lehto, Ojanen, Dyba, Aromaa, & Kellokumpu-Lehtinen, 2006; Maunsell, Brisson, Mondor, Verreault, & Deschênes, 2001; Telepak, Jensen, Dodd, Morgan, & Pereira, 2014). Notably, no studies to the author's knowledge have examined cancer recurrence as an outcome of recent life stress in women with ovarian cancer.

## **Stressful Life Events**

### **The Concept of Stress**

Selye coined the term “stress” as the body’s response to a stimulus (a “stressor”) in the environment that disrupts homeostasis (Selye, 1973). He described a non-specific response to stress, known as General Adaptation Syndrome, consisting of an alarm reaction, resistance phase, and exhaustion (Selye, 1936). In the alarm reaction, endocrine response systems known as the hypothalamic-pituitary-adrenocortical axis (HPA) and the sympathetic-adrenal-medullary system (SAM) signal for various behavioral and physiological responses to maintain homeostasis (e.g., “the fight or flight response”) (Charmandari, Tsigos, & Chrousos, 2005; Chrousos & Gold, 1992). However, while these systems are adaptive, they can also be damaging. Selye himself realized the limits of the body’s natural defense system, as he summarized: “fight for the highest attainable aim, but do not put up resistance in vain” (pg 699, Selye, 1973). Prolonged activation of stress response systems can interfere with the functioning of multiple biological systems (e.g. metabolism, immune function) and can have implications for health (Cohen, Janicki-Deverts, &

Miller, 2007; McEwen & Seeman, 1999). These cumulative effect of stress has been deemed “allostatic load” (McEwen & Seeman, 1999).

**Psychological appraisal processes in the stress response.** At its core, stress is a dynamic concept that involves the interaction of the organism and the environment. Lazarus and Folkman’s Transactional Theory of Stress expanded the concept of stress by including both primary appraisal of the stressor and secondary appraisal of available resources to cope with the stressor (Lazarus & Folkman, 1987). In primary appraisals, stimuli can be deemed as benign, a harm that has already been experienced, a threat involving future harm, or a challenge or benefit with positive potential. This appraisal depends on the extent to which an event is relevant to one’s goals and committed roles (Brown & Harris, 1989; Brown, 2002). Additionally, there are several factors that may influence an individual’s perception of stress, such as one’s general attributional style in making inferences about a stressor.

The Transactional Theory of Stress also expanded the concept of stress as resulting not only from the appraisal of threat, but one that also exceeds the individual’s resources. Thus, stress cannot be defined solely in respect to the environment or the body’s nonspecific arousal response. Coping strategies involve both cognitive and behavioral efforts to help lessen the discomfort of the demands brought about by stress (Folkman & Lazarus, 1988a). This can be accomplished through a variety of functions and used differentially depending on the situational context (i.e., situationally appraised). For example, some strategies are focused on changing the stressful situation (problem-focused) when individuals feel that there is something they can do or they need more information (e.g., planning). The feeling that one must accept a situation or hold back emotional responses is associated with emotion-focused strategies that aim to regulate distress (Carver, Scheier, & Weintraub, 1989; Folkman & Lazarus, 1980, 1988b). Additionally,

individuals may use cognitive strategies to change the meaning of the stressor and reduce its impact (Park & George, 2013; Pearlin & Schooler, 1978). If basic beliefs about the self and the world are violated because of the experience of stressful events, certain coping strategies may be more likely to occur automatically (e.g., denial), or be used more strategically (e.g., self-blame, positive re-interpretations, social comparison) (Janoff-Bulman, 1999). Lastly, seeking instrumental or emotional social support also functions as a separate set of coping strategies (Amirkhan, 1990; Zautra, Sheets, & Sandler, 1996).

Coping may also be assessed in the general sense of an individual's capacity to respond effectively to a stressor (Lazarus & Folkman, 1987). How individuals view themselves can be an internal resource that protects them from stress. For example, self-efficacy or mastery entails a sense that one has control over their environment (Bandura, 1977). Self-esteem maintains positive affect towards the self, which may also enhance efficacy in coping with stress (Pyszczynski, Greenberg, Solomon, Arndt, & Schimel, 2004). Additionally, the extent to which individuals can turn to religious and spiritual beliefs and practices may influence the meaning of stressful events and their response to them (Park, 2005). These beliefs and personal characteristics, in turn, can influence both primary appraisals and specific coping behaviors.

Different types of coping strategies are often used in combination when responding to a stressor. Certain kinds of escapist strategies, such as denial or behavioral disengagement, have been associated with poor mental health with relative consistency in the vast literature on coping (Folkman & Moskowitz, 2004). However, other ways of coping do not exhibit enough consistency to make such broad conclusions. Measurement of the appraisal of resources and engagement in certain coping strategies can be highly correlated with distress and, therefore, outcomes of interest (Stanton, Danoff-Burg, Cameron, & Ellis, 1994). Coping is a complex and

multidimensional process, where the person, the environment, and their interaction all play a role. As such, while individuals may display consistency of coping strategies within a given event or domain, individuals also vary greatly in their coping patterns to different types of stressors (Folkman & Lazarus, 1980). Ultimately, a varied repertoire of coping responses may be most effective at reducing the distress associated with a stressor (Cheng, Bobo Lau, & Chan, 2014).

Clearly, the importance of appraisal and coping processes is crucial in the understanding of stress. Appraisal of a stress that exceeds one's resources not only results in activation of a biological stress response, but also negative affective and psychological changes that can directly or indirectly (e.g., through physiological and behavioral responses) increase vulnerability to physical and mental illness (Cohen, Kessler, & Gordon, 1997; Slavich & Irwin, 2014).

Secondary appraisal of resources is of particular interest clinically, as this is an area that interventions can easily address. In fact, several interventions targeting patients with cancer have explicitly sought to increase psychosocial resources and coping strategies in an attempt to improve psychological and physiological well-being (Andersen et al., 2004; Antoni, Lechner, et al., 2006; Friberg, Sorlie, & Rosenvinge, 2005). Thus, psychosocial resources of interest in the current study are discussed at length in the following section.

### **Measurement of Life Stress**

There are several well-known complexities when assessing stress. Namely, both subjective and objective threat play a role, and these are not always congruent. Researchers often assess the cognitive appraisal of threat by measuring the perception of stress, for example with the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983). This can capture the effect of cumulative life stress but is inherently subjective. The perception of stress can be influenced

by psychopathology, and as such, is highly correlated with measures often used as outcomes (e.g., depression) in life stress research (Monroe & Simons, 1991). In order to make conclusions regarding events themselves without the confounding role of mood, more objective measure of stressful life events are needed.

Typically, studies use checklists of life events, in which participants indicate whether or not they experienced a specific event. However, substantial variability exists in what events people deem as falling into a given stressful event category (Dohrenwend, 2006). For example the event of “starting a new job” may entail many different meanings depending on the individual and their life circumstances: a move to more desirable or less desirable position, a forced or planned change, potential financial difficulty, loss of friendships, etc. Further, these measures that prioritize a “normative” value of stressfulness for specific events fail to take into account the context in which they occur. Life circumstances and coping strategies between people will greatly affect the amount of stress that is experienced.

Measures assessing perceived stress and occurrence of life events with a checklist are considered respondent-based methods. However, these can introduce substantial bias and, rather than reflecting the environmental stressors, these measures of stress might more accurately be reflecting a diathesis-stress interaction (Monroe & Simons, 1991). Thus, the gold standard of life stress measurement is the use of semi-structured and structured interviews. The Life Events and Difficulties Schedule (LEDS) is one commonly used measure in which interviewers gather biographical information about the individual (Brown & Harris, 1978, 1989). In this method of assessing stress, events can be given ratings based on the impact within an individual’s life, regardless of emotional responses to the event. However, this has its disadvantages, as it is significantly more laborious for both researchers and participants.

## **Life Stress and Psychopathology**

The relationship between major life events and the onset of depression has been well-documented (Hammen, 2005; Kessler, 1997; Mazure, 1998; Tennant, 2002). A review of case-control studies found that those diagnosed with depression were about 2.5 times more likely to report having a life event prior to onset than those who did not have depression (Mazure, 1998). This relationship is theorized to be a causal effect, as studies of twins have shown that exposure to life events significantly predicts the onset of depression, even when person-level covariates are similar (Kendler & Gardner, 2010; Kendler, Karkowski, & Prescott, 1999). Additionally, onset of depression after a stressful life event is unrelated to family history of depression (Monroe, Slavich, & Gotlib, 2014). In addition to depression, life events have also been related to the onset of panic disorder (Klauke, Deckert, Reif, Pauli, & Domschke, 2010) and alcohol use disorders (Keyes, Hatzenbuehler, & Hasin, 2011). Additionally, severe events and chronic difficulties can delay recovery of depressive symptoms (Kessler, 1997). An important trend in the work examining life stress and psychopathology is that the effects of stressors diminish over time, and most studies find that acute events predict onset of disorders within the month of occurrence or soon after (Tennant, 2002).

There are numerous models that attempt to explain the relationship between stress and depression, which can include biological, developmental, and psychological factors. The general stress-diathesis model is based on the premise that cognitive, personality, and social factors can contribute to vulnerability that puts individuals at greater risk for distress in response to life events (Brown, Craig, & Harris, 1985; Monroe & Simons, 1991). For example, the kindling hypothesis posits that this relationship lessens in strength in subsequent episodes of depression (Post, 1992; Stroud, Davila, & Moyer, 2008). Additionally, stress sensitization can occur in

individuals who experience early life adversity (Kessler & Magee, 1993). Depression can also increase the likelihood of stress, or stress generation, as individuals may “self-select” certain environments (Liu & Alloy, 2010). There are also several biological mechanisms which are purported to link the effects of stress to depression including the HPA axis, serotonergic neurotransmission, and proinflammatory cytokines (Gutman & Nemeroff, 2010; Hammen, 2005; Schneiderman, Ironson, & Siegel, 2005). However, questions still remain regarding the relationship between life stress and psychological symptoms. For example, stressors may have a cumulative effect even in individuals who were not necessarily exposed to adversity in childhood (Ensel & Lin, 1996). Additionally, the extent to which the content of stressors predicts certain psychological symptoms is an area where further study is needed (Keller, Neale, & Kendler, 2007).

### **Specificity of Life Stress and Psychological Sequelae**

While the comorbidity between depression and anxiety is high, evidence has shown that, unlike the genetic component, the environmental influence on depression and anxiety is specific to the disorder (Eley & Stevenson, 2000; Kendler, Neale, Kessler, Heath, & Eaves, 1992). Along with this, life stress elicits specific emotions depending on the stimulus, and these are subsequently associated with specific physiological, cognitive, and motivational responses (Cramer, Borsboom, Aggen, & Kendler, 2012; Darwin, 1872). In other words, not all stress is created equal. This makes sense when viewed from the lens of evolutionary psychology and our understanding of the behavioral and mental defense strategies in humans (Dixon, 1998).

Mood states are adaptive, as they allow humans to flexibly respond to cues in the environment that are important for our fitness and survival (Price, 1972). For example, the experience of fatigue and anhedonia in depression may serve as a way to conserve energy and

resources in a low-reward environment and to aid in analyzing problems (Andrews & Thomson, 2009; Nettle & Bateson, 2012). Additionally, anxiety serves to protect an individual from the worst possible outcome (Newman, Llera, Erickson, Przeworski, & Castonguay, 2013), and trait anxiety is even related to a reduced risk in mortality (Lee, Wadsworth, & Hotopf, 2006).

Emotions are associated with distinct expressions and behaviors, each of which serves a purpose. An important aspect of emotions and defense strategies is that they are only beneficial to the extent that they are carefully regulated; too much or too little can lead to maladjustment (Marks & Nesse, 1994).

Typically, measures of stressful life events only distinguish between domains of life that the events may affect (e.g., work, relationships, health, etc.). The specific psychosocial characteristics of stress, however, are more likely to influence what an individual's subsequent emotional response is. For example, stressors that include loss may function differently than those that include danger, humiliation, or entrapment. In fact, these dimensions of life stress are differentially rated in the LEDS, yet they have been examined in few studies (Brown, Harris, & Hepworth, 1995; Brown & Harris, 1987; Finlay-Jones & Brown, 1981). Each of these dimensions of life stress represents theoretically and functionally distinct relationships with psychological processes, reviewed below. Because of this, specific dimensions of life stress were considered with respect to their relationship to mental health trajectories in cancer patients in the current study. Because humiliation events happened relatively rarely in our sample, only loss, danger, and entrapment were examined.

**Loss.** It is undeniable that the experience of an interpersonal loss is a distressing event. Attachment behavior is fundamental to human nature for survival, and as such, we are motivated to seek social bonds (Baumeister & Leary, 1995; Bowlby, 1982). When our interpersonal bonds

and resources are disrupted or lost, emotional distress is inevitable and can take many forms (Bowlby, 1977). Expressing sadness through crying communicates to others that help is needed and may strengthen social bonds (Labott, Martin, Eason, & Berkey, 1991; Sadoff, 1966). When this doesn't work, the next best strategy is to withdraw and possibly reassess failing plans (Gilbert, 2006). Bereavement is an excellent example of the difficulty distinguishing between functional versus dysfunctional responses to loss, with a range of reactions including loneliness, guilt, despair, and withdrawal (Stroebe, 2001, 2010). After a loss, grief and hopelessness (specific to the context of the loss) may arise, and in individuals who fail to process their grief or begin to generalize hopelessness to other contexts, these symptoms may cross the dysfunctional boundary to depression (Brown & Harris, 1989). Coping strategies are likely to distinguish which individuals develop clinically significant depression or anxiety after a loss, or complications in the grieving process itself (Stroebe, 2010). Additionally, those with greater interpersonal sensitivity to the disruption of social bonds may be more susceptible to experience depression after a loss (Gilbert, Irons, Olsen, Gilbert, & McEwan, 2006; Hankin, Kassel, & Abela, 2005; Sbarra, 2006).

To the extent that a loss threatens survival resources, anxiety is expected as another normative reaction. For example, events that threaten loss of a mate lead to anxiety and behaviors such as reassurance seeking (Marks & Nesse, 1994). Avoidance of certain actions, such as developing close relationships or engaging in goal oriented behavior, may also serve to protect an individual from future losses (Keller & Nesse, 2005). Importantly, losses aren't always necessarily interpersonal – one may lose important resources such as their health, possessions, skills, and assumptions about the world (Harvey & Miller, 1998). These losses may

signal potential threats to future well-being, therefore increasing vigilance, attention to danger-related cues, and other hallmarks of anxiety.

Several studies have shown that loss may predict the onset of depression (Brown & Harris, 1987; Farmer & McGuffin, 2003; Finlay-Jones & Brown, 1981; Kendler, Hettema, Butera, Gardner, & Prescott, 2003; Paykel, 1994). In one study, death and respondent-initiated separation both resulted in an approximately 10-fold increase in the likelihood of depression during the month of occurrence (Kendler et al., 2003). This is particularly true for loss events that are severe, as high-threat loss events have been found to be the most common type of provoking event before onset of depression (a 32% prevalence in a sample of women who developed depression) (Brown & Harris, 1987). Other lines of research have studied the effects of specific losses. For example, marital disruption has been associated with higher prevalence rates of depression (Bruce & Kim, 1992). Bereaved individuals who would have been excluded from the diagnosis of depression in the DSM-IV but with all other criteria are more severely depressed than other individuals with depression (Corruble, Chouinard, Letierce, Gorwood, & Chouinard, 2009). Additionally, in individuals with bipolar disorder, loss was related to worsening of depressive symptoms but not mania (Hosang, Uher, Maughan, McGuffin, & Farmer, 2012).

There is also some evidence that the experience of loss predicts anxiety symptoms. In one study, compared to other types of events, the risk for anxiety episode was greater for high-threat events of loss (only those categorized as “other key losses” as opposed to death or separation) (Kendler et al., 2003). Interestingly, individuals who displayed mixed cases of depression and anxiety symptoms were more likely to have experienced both loss and danger events (Finlay-

Jones & Brown, 1981). Interpersonal life events involving loss have also been proposed as “candidate stressors” in provoking the onset of panic disorder (Klauke et al., 2010).

**Entrapment.** A stressor that involves entrapment entails the presence of an ongoing difficulty, where there is a sense that it will persist or get worse despite one’s efforts (Brown et al., 1995). The experience of being trapped can be brought about by a perceived lack of control over aversive events or positive events (Gilbert, 2006). In the model of learned helplessness, individuals may learn that outcomes are uncontrollable, and as such, become passive and experience depressed affect (Seligman, 1975; Seligman et al., 1976). In fact, behavioral activation, one of the most efficacious treatments of depression may serve to enhance control over life circumstances in depressed individuals (McEvoy, Law, Bates, Hylton, & Mansell, 2013).

Regardless of the controllability of events, helplessness is influenced by attributional style. This can involve a combination of beliefs about the cause of a stressor being global or specific (e.g., lack of overall intelligence vs. lack of ability in a specific domain), internal or external (e.g., lack of intelligence vs. unfair testing), and stable vs. unstable (e.g., lack of intelligence vs. fatigue from being sick) (Abramson, Seligman, & Teasdale, 1978). These inferences regarding the cause, consequences, and characteristics about the self in the context of a life event can be influenced by many factors besides the situational information, such as dysfunctional attitudes and previous experiences (Abramson & Metalsky, 1989).

One of the most common depression paradigms in animal research is that in which the animal is exposed to an inescapable source of stress (Azzinnari et al., 2014). Additionally, this has been studied in humans with learned helplessness paradigms in the laboratory (Pryce et al., 2011). When exposed to such stress, animals display reduced sensitivity to rewards as evidenced

by reduced intake of palatable foods, reduced preference to previously rewarding environments, and changes in dopamine pathways in response to stimulation (Pizzagalli, 2014). Observable behaviors of depressed patients (e.g., gaze aversion and avoidance, poverty of social signals) are similar to the behaviors of animals in an arrested flight mode, a last resort strategy for escape (Dixon, 1998). This arrested flight, or anhedonia, is a key element of depression, and stress may increase vulnerability through its effects on the mesolimbic dopamine system (Pizzagalli, 2014). Ultimately, when efforts to achieve a desired outcome are not paying off, mental defeat and failure entail, and this disengagement serves a purpose (Keller & Nesse, 2005). An organism would completely exhaust itself if it did not eventually rescind commitment to an impossible goal. This also limits signals that might provoke future attack and make things worse. It makes sense that the subjective experiences of such a state would be aversive so as not to reinforce failure (Klinger, 1975).

Importantly, loss can be a sufficient, but not necessary, condition for experiencing entrapment (e.g., experiencing ongoing financial difficulty or an unwanted pregnancy). Similarly, entrapment is related to humiliation/defeat, except that it involves a total involuntary subordination and an internal, subjective loss of autonomy or sense of identity (Gilbert, 2006; Taylor, Wood, Gooding, Johnson, & Tarrier, 2009). For example, in victims of torture, actions of defeat (e.g., false confessions) may be done without the experience of mental defeat. Those that do experience mental defeat are more likely to have worse PTSD symptom severity (Ehlers, Maercker, & Boos, 2000).

Depressed individuals often report feelings of entrapment, a desire to escape, and perceived obstacles (Gilbert, Gilbert, & Irons, 2004). Two studies using the LEDSA have found that life events involving entrapment, both alone and combined with humiliation, predict the

onset of depression (Broadhead & Abas, 1998; Brown et al., 1995). The prevalence of depression after an entrapment life event in these studies was greater than onset of depression after a loss event. In another study using the LEDDS, entrapment was related to mixed anxiety and depression but only in the month of occurrence (Kendler et al., 2003). In other studies using self-report measures, defeat and entrapment have been moderately to strongly correlated to depression symptoms, increased risk of suicide, and anxiety (Taylor, Gooding, Wood, & Tarrier, 2011).

**Danger.** Survival is central to all of adaptive functions of emotions. No emotion as clearly exemplifies this as fear, which involves readiness to respond to potential punishment. When faced with a threat to one's survival in the environment, fear arises and increases vigilance, attentional bias to danger, and the "fight or flight" stress response (Nettle & Bateson, 2012). Stressful or traumatic events often lead to fear and avoidance of related cues in the future to avoid experiencing the danger again (Marks & Nesse, 1994). Furthermore, when the cost of not responding with an effective defense strategy is near or certain death (as in the case with dangerous events), the likelihood of false positives is greater, a concept termed the "smoke detector principle" (Nesse, 2005). Thus, when a life event signals a fear for the future unpleasantness potential, anxiety is a normative reaction.

Not surprisingly, in the life event literature, those events involving danger have most been associated with anxiety rather than depression (Finlay-Jones & Brown, 1981; Kendler et al., 2003). Other examples of this can be seen from the literature on PTSD after natural and man-made disasters, where the effects of danger on anxiety are mediated by intrusions and avoidance (Spurrell & McFarlane, 1995).

## **Protective Psychosocial Resources**

As detailed above, psychosocial factors can play a critical role in the stress response, as they can promote psychological and physiological resilience in adaptations to adverse events (Frasure-Smith, Lespérance, & Talajic, 1995; Kubzansky, Sparrow, Vokonas, & Kawachi, 2001; McEwen & Seeman, 1999). These factors may be protective in that they prevent distress or poor adjustment after a stressor. There are several important ways in which psychosocial resources can influence the stress response process as outlined by Ensel and Lin (1991). First, they can act as a deterrent to the noxious experience of stress by exerting a main effect on well-being. For example, in the independent model, resources such as social support, self-esteem, and self-efficacy can all have a direct effect on psychological well-being regardless of the presence of a stressor. Second, the stress-suppressing model posits that resources may suppress the experience of both stressors and psychological distress. Third, in the stress-conditioning model, the experience of stressors interacts with pre-existing resources to then influence distress. For example, if one has high levels of self-efficacy, starting a new job may be perceived as a simple task, whereas those with low levels of self-efficacy may find this event very distressing. Fourth, the deterioration model posits that a stressor subsequently reduces resources, and this mediates the effects of stress on psychological well-being. Fifth, the counteractive model, on the other hand, assumes that the effect of stress on resources is positive, and that this serves to offset the deleterious effects of stress on well-being (Ensel & Lin, 1991). Lastly, in the buffering model, resources moderate the effect of stress on well-being, such that distress is high only when resources are low. The deterioration model, the counteractive model, and the stress buffering model all assume resources function as a coping mechanism after the presence of stress (Thoits, 1986).

In research examining protective psychosocial resources, the model that has received the most attention is the buffering model. However, there is evidence that some psychosocial resources can function as mediators of life stress (Chou & Chi, 2001; Pearlin, Menaghan, Lieberman, & Mullan, 1981; Wheaton, 1985). In other words, stress exerts its effects on depression because it reduces resources. Thus, the moderating and mediating effects of protective variables are considered henceforth. Additionally, a multitude of variables have been considered as potential resources. The following review focuses on several resources: social support, mastery, self-acceptance, and meaning. These resources have been studied in the general population, cancer patients, or both, and have relevance for adjustment to cancer in the wake of recent life stress.

### **Social Support**

One of the most widely studied protective resources is social support. Social support has been shown to be related to a variety of health outcomes and even longer survival (Cohen, 2004; Holt-Lunstad & Smith, 2012). The buffering effect of social support on stress has been widely studied, and evidence suggests support can affect the emotional, physiological, and behavioral responses to a stressor (Cohen & Wills, 1985). Even perceptions of available support can also have this effect (Sarason, Pierce, Shearin, & Sarason, 1991). This “tend and befriend” response to increase affiliative behavior, like the fight or flight response, is rooted in biological signaling and evolutionary theory (Taylor, 2011; Taylor et al., 2000). Thus, social support can affect biological stress response systems as a pathway to health.

Social support may be defined in various ways and, thus, have differential impacts on psychological well-being. There are also numerous pathways in which social support can affect the stress process (Berkman, Glass, Brissette, & Seeman, 2000). The availability of emotional

support as well as the provision of instrumental and emotional support can influence whether a person appraises an event as stressful or benign (Cohen, 1988; Dunkel-Schetter, Folkman, Lazarus, & Dunkel, 1987). Contact with others can also provide soothing, calming, and emotionally supportive input to an individual (Taylor, 2011). Additionally, social networks can influence coping strategies (which can be helpful or unhelpful) and provide tangible support. Importantly, receipt of social support can also have negative effects, as it can engender a sense of indebtedness, thus lowering self-efficacy (Kawachi & Berkman, 2001). In fact, theoretical reviews and conceptualizations of social support have noted that social support may also exert its effects on stress by certain psychological pathways, such as increasing mastery and self-esteem (Berkman et al., 2000; Cohen, 1988). This has been supported by a number of studies in other populations, but has not been examined in patients with cancer (Atienza, Collins, & King, 2001; Symister & Friend, 2003). Further, issues such as imprecise tests of mediation and consideration of one mediator at a time have left the literature of social support devoid of clear psychological mechanisms for its effects (Uchino, Bowen, Carlisle, & Birmingham, 2012).

Social support has been extensively studied in samples of patients with cancer. Generally, emotional support has been linked to better psychological functioning (Helgeson & Cohen, 1996). Additionally, lack of social support has been related to tumor norepinephrine (Lutgendorf et al., 2011), and in conjunction with high depression, an up-regulation of pro-inflammatory transcription factors such as NF-kB/Rel and STAT (Lutgendorf et al., 2009). Social support has even been related to survival in women with ovarian cancer (Lutgendorf et al., 2012).

The effect of social support specifically in the context of life events in patients with cancer has been studied much less frequently. In a study of gynecologic cancer survivors, perceived availability of social support as well as structural support (the breadth of an

individual's social network) moderated the effect of physical symptoms (a potentially cancer-related source of stress) on traumatic stress symptoms (Carpenter, Fowler, Maxwell, & Andersen, 2010). In this study, emotional social support did not interact with stress to predict depressive symptoms, but instead had a direct influence. Furthermore, one study also found that social support did not moderate the effects of life events on depressive symptoms 1 year post-diagnosis (Grassi et al., 1997). Some studies have looked at the effects of unsupportive environments in those with cancer. In one study, patients with stressful life events and aversive emotional support experienced the greatest intrusive and avoidance symptoms (Butler et al., 1999). Similarly, in breast cancer patients, only those with high levels of aversive support and stressful life events experienced the greatest mood disturbance (Koopman et al., 1998).

### **Mastery**

The construct of perceived control in the face of adversity has been extensively discussed in the literature. Further, the extant research is complex due to the many terms used to study this construct, including self-efficacy, self-determination, explanatory style, and mastery (Skinner, 1996). Beliefs that individuals have about their ability to exercise control over their environment can influence their appraisal about an event as well as their future coping behaviors (Bandura, 1977). For example, individuals high in general self-efficacy may be more likely to appraise a potential stressor as a challenge rather than a threat (Luszczynska, Gutiérrez-Doña, & Schwarzer, 2005). Information about control can come from previous experience, observational learning, verbal persuasion, and emotional arousal (Maddux & Stanley, 1986). An important distinction in the literature is that between objective or actual control and perceived control. Early work on learned helplessness clearly demonstrated the importance of perceived control (Abramson et al., 1978). Even exaggerated beliefs about control can be adaptive (Taylor & Brown, 1994; Taylor,

Kemeny, Reed, Bower, & Gruenewald, 2000). In fact, perceived control has generally been related to positive outcomes. For example, general self-efficacy has been positively related to quality of life and higher life satisfaction across several different cultures (Luszczynska et al., 2005).

Perceived control can refer to the belief that an agent (most commonly, oneself) has the effective response in their repertoire or the belief that the agent can produce the desired outcome (Skinner, Chapman, & Baltes, 1988). Additionally, beliefs about the specific causes of desired or undesired outcomes, such as locus of control and explanatory style, can also fall within the umbrella of control. Ultimately, beliefs about control can influence coping processes (Pearlin & Schooler, 1978), and can act as both a mediator and a precursor to social support (Benight & Bandura, 2004). For the purposes of the current study, environmental mastery (or mastery, for short) is used henceforth to reflect general beliefs about one's ability to manage external events and situations (Pearlin & Schooler, 1978; Ryff, 1989).

In the context of a variety of stressors and traumas, mastery has emerged as a key mediator in predicting psychological recovery (Benight & Bandura, 2004). Several studies have also demonstrated the moderating effects of mastery in the relationship between specific stressors and well-being. In one study, a sense of mastery moderated the impact of financial strain on psychological distress (Marum, Clench-Aas, Nes, & Raanaas, 2014). Additionally, in caregivers of patients with Alzheimer's, more stressful life events were associated with elevated was related to higher levels of plasminogen activator inhibitor antigen (a biomarker linked to cardiovascular risk) only in individuals low in mastery (Mausbach et al., 2008). In a study of bereaved women, both mastery and self-esteem were related to initial levels of health and

depression as well as the trajectory of these variables over time (Montpetit, Bergeman, Bisconti, & Rausch, 2006).

In individuals with chronic illnesses, perceived control is typically referred to in terms of patients' perceived control of their illness, and this has been positively related to psychological adjustment (Roesch & Weiner, 2001). However, some studies have found that perception of control has no influence on distress (Carver et al., 2000). No studies to date have examined the relationship between life stress and a general sense of mastery on physical and psychological outcomes in patients with cancer.

### **Self-Acceptance**

Similar to social support and mastery, it has been demonstrated that a positive self-concept can have direct effects on physical and mental health (Mann, Hosman, Schaalma, & De Vries, 2004). When considering stress as a challenge to one's perceived identity (i.e., an incongruence between the perceived self and feedback from the environment), a positive view of the self can be protective (Burke, 1991). Most notably, a positive self-concept can buffer negative emotions in the context of stress (Cast & Burke, 2002; Greenberg et al., 1992).

Until recently, self-esteem was the main construct used when studying positive views of the self. However, given the number of criticisms associated with this construct, the concept of self-compassion, or self-acceptance, has been introduced. Informed by Eastern philosophy and humanistic psychology, self-acceptance involves a non-evaluative and balanced understanding one's strengths and weaknesses and a sense of common humanity (Neff, 2003). This has been distinguished from self-esteem, as they are differently related to several personality traits (Neff & Vonk, 2009). For example, self-esteem is positively related to narcissism while self-

compassion is unrelated. Self-compassion also displays a stronger negative relationship than self-esteem with other self-rumination and anger (Neff & Vonk, 2009).

It is posited that self-acceptance enhances affect regulation by shifting the self-focus to a non-evaluative and adaptive stance and increasing positive affect (Jimenez, Niles, & Park, 2010; Watkins & Teasdale, 2004). This may decrease the likelihood of perceiving a stressor as a threat (Hall, Row, Wuensch, & Godley, 2013). Self-compassion may also have effects on the physiological stress response. For example, after a stressor, individuals high in self-compassion exhibited less stress-induced inflammation than those low in self-compassion (Breines et al., 2014). Self-compassion may also affect coping strategies and, in particular, increase positive cognitive restructuring and decrease avoidance and escape strategies (Allen & Leary, 2010). It may also facilitate self-regulation and motivate behaviors to achieve goals (Breines & Chen, 2012; Terry & Leary, 2011).

Few studies have examined the role of self-compassion in patients with cancer. For example, low self-compassion among breast cancer survivors has been positively related to psychological distress (Przedziecki et al., 2013). Self-compassion has been related to lower symptoms of depression and stress, and higher quality of life in a sample of patients with a variety of cancers (Pinto-Gouveia, Duarte, Matos, & Fráguas, 2014). Notably, mindfulness-based stress reduction, a common intervention in populations with cancer which increases self-acceptance, has been related to improved quality of life and a reduction in biomarkers related to stress (Carlson, Speca, Faris, & Patel, 2007). However, no studies have examined self-acceptance as a moderating or mediating effect of recent life stress in patients with cancer.

## **Meaning**

Stressors can violate an individual's sense of global meaning – their beliefs about themselves and the world, their goals, and their sense of purpose (Janoff-Bulman, 1989). This information surrounding the stressor can be processed by assimilating it into existent worldviews, or through accommodation and changes to core beliefs (Joseph & Linley, 2008). Because cancer entails disruptions to achieving one's goals and challenges to one's beliefs in the context of a threat to one's life, it is particularly likely to lead to accommodation, or a search for meaning and changes in one's worldview (Thompson & Janigian, 1988). A meaning-making framework of coping with stressful events asserts that while global meaning can affect primary appraisal of potential stressors, it can also enhance coping strategies that seek to resolve the distress caused by discrepancies between appraised and global meaning (Park, 2010). Coping with meaning-based processes can include positive reappraisal in terms of values and beliefs, revising goals and engaging in problem-focused coping to maintain a sense of meaning, and turning to spiritual beliefs and experiences to find meaning (Folkman, 1997; Park & Folkman, 1997).

In a review of the literature on the meaning-making model, Park (2010) concluded that there are mixed results regarding the extent to which a search for meaning is associated with adjustment after a stressor. Meaning-making coping strategies have also been studied extensively in cancer patients, primarily by assessing positive reappraisal coping efforts. Similarly, the literature in this domain has displayed mixed results (Kernan & Lepore, 2009; Sears, Stanton, & Danoff-Burg, 2003). Furthermore, cognitive processes focused on the self can be both adaptive and maladaptive, so while a search for meaning may result in improved adjustment, it may also increase rumination and worry (Watkins, 2008).

Most of the work examining meaning focuses on appraised meaning or the search for meaning in regards to a specific event. Less work has assessed the effects of a global sense of meaning on psychological adjustment after a stressor (Lee, Cohen, Edgar, Laizner, & Gagnon, 2004). Having goals, a sense of directedness, and objectives or living reflect having a subjective sense of meaning and well-being (Ryff, 1989). This sense of meaningfulness has been related to greater quality of life and lower distress in several samples of cancer patients (Park, Edmondson, Fenster, & Blank, 2008; Shapiro et al., 2001; Sherman, Simonton, Latif, & Bracy, 2010). However, minimal research has been done in regards to the buffering or mediating effects of having a meaning or purpose in life on particular stressors in patients with cancer. Only one study has looked at this, and found that meaning in life mediated the effects of physical and social functioning impairments on psychological distress (Jim & Andersen, 2007).

### **Summary and Specific Aims**

It is widely recognized that the diagnosis of cancer entails psychological stress, as danger to one's health and potential loss is inherent in this experience. Many individuals also experience an "existential plight" provoked by having cancer that is characterized by a stark challenge to the way individuals view themselves and the world. Stress has been widely studied in cancer patients to the extent that studies have evaluated adjustment to the stressor of cancer. However, few studies have examined the role of recent life stress experienced prior to a diagnosis, and its potential effects in combination (i.e., their interaction) with the stress of a cancer diagnosis. Among those that have, there is substantial methodological variability and mixed results in the extant literature. No studies to date have examined the effects of specific types of stressors, such as losses, events that place an individual in danger, or the experience of ongoing entrapment in patients with cancer.

The Life Events and Difficulties Schedule (LEDS) provides a unique and thorough account of recent life stress, taking into account the circumstances of the individual's life. An extensive body of research has demonstrated the relationship between life stress and psychological symptoms with this interview and other measures. In this research, life stress has been related to onset of depression and anxiety disorders in a number of studies. However, in these studies the effects of life stress diminish over time and most significant results are for the onset of depression or anxiety within the month of occurrence or soon after.

An important conclusion from the research examining life stress is that not all stressors are necessarily created equal. Psychosocial dimensions of stressors categorized in the LEDS, such as loss, danger, and entrapment, have been shown to produce differing psychological sequelae. Namely, loss and entrapment have more commonly been related to the onset of depression, while danger is related more frequently to anxiety. Some research has also shown that loss can also be related to anxiety. Additionally, while the psychosocial mechanisms and potential protective factors of stress have been extensively studied generally, they have not been studied as mediators or moderators of the effects of loss, danger, or entrapment. Further, the consideration of multiple psychosocial variables simultaneously to facilitate comparison has rarely been studied.

To date, no studies have utilized the methodologically rigorous LEDS system to examine life stress in cancer patients and its effects on psychosocial functioning. Further, none have examined the effects of dimensions of life stress on quality of life and progression in patients with cancer, let alone the psychosocial factors that may mediate or moderate these effects. Thus, this study is the first of its kind to examine life stress in patients with cancer, operationalized by its psychosocial effects of loss, danger, or entrapment. This study examined the implications of

such stressors for psychological well-being, both at surgery and the trajectory over one year post-diagnosis, as well as for cancer recurrence. Furthermore, protective psychosocial moderators and mechanisms of these effects were examined to assess potential risk factors and targets for intervention. Ultimately, this study offers a rich understanding of life stress in patients with cancer that has not yet been elucidated. Given the variability in psychosocial well-being and quality of life in patients with cancer, along with their prognostic significance, this is an area of inquiry with noteworthy clinical implications.

**Specific Aim #1:** To examine the effects of prior experiences of loss, danger, and entrapment on psychological functioning both prior to surgery and during the year after diagnosis.

*Hypothesis 1a:* Controlling for potential covariates, the threat of loss experienced in the year prior to surgery will be related to greater depressive symptoms and anxiety in patients prior to surgery as well as less improvement in all psychological outcomes over the year post-diagnosis.

*Hypothesis 1e:* Controlling for potential covariates, the threat of danger experienced in the year prior to surgery will be related to greater anxiety symptoms prior to surgery as well as less improvement in anxiety over the year post-diagnosis.

*Hypothesis 1c:* Controlling for potential covariates, the threat of entrapment experienced in the year prior to surgery will be related to greater depressive symptoms prior to surgery and less improvement in depression over the year post-diagnosis.

*Hypothesis 1d:* Both cancer-related and non-cancer related stressors will be independently related to psychosocial functioning at the time of surgery.

*Hypothesis 1e:* Cancer-related stressors will interact with non-cancer related stressors to predict psychosocial functioning.

**Specific Aim #2:** To evaluate competing models of the functional relationships between protective psychosocial factors (social support, mastery, self-acceptance, purpose in life) and life stress on psychological functioning as women face surgery and throughout the year after.

**Hypothesis 2a:** All four protective variables will have a direct effect on psychological symptoms prior to surgery and throughout one year (independent model, see Figure 1 below).

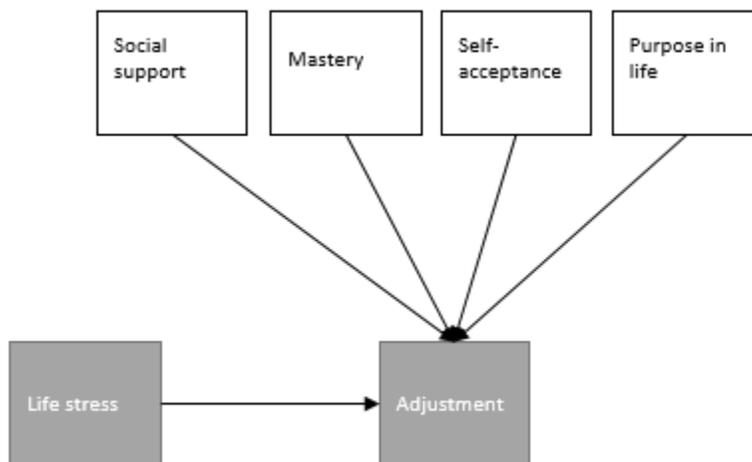


Figure 1. Independent Effects Model

**Hypothesis 2b:** Only social support will moderate the effects of loss, entrapment, and danger on psychological symptoms both prior to surgery and throughout one year (moderator model, see Figure 2 below).

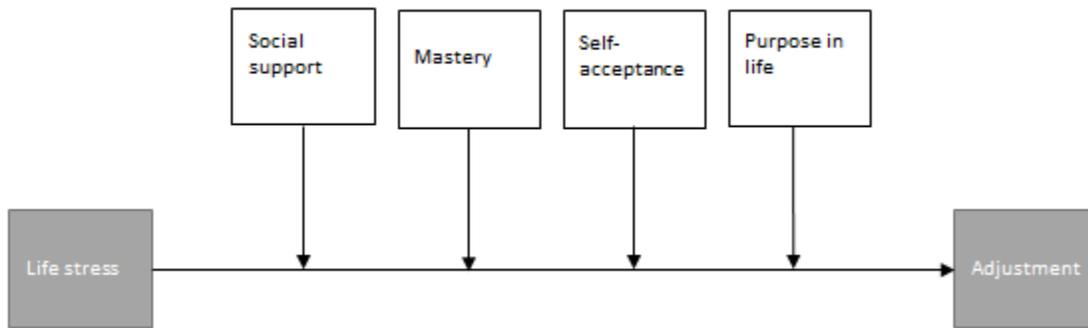


Figure 2. Multiple Moderator Model

**Hypothesis 2c:** Environmental mastery, self-acceptance, and purpose in life will mediate the effects of loss, entrapment, and danger on psychological functioning both prior to surgery and throughout one year, while including the moderating effect of social support in the model (moderator and multiple mediators model, see Figure 3 below.).

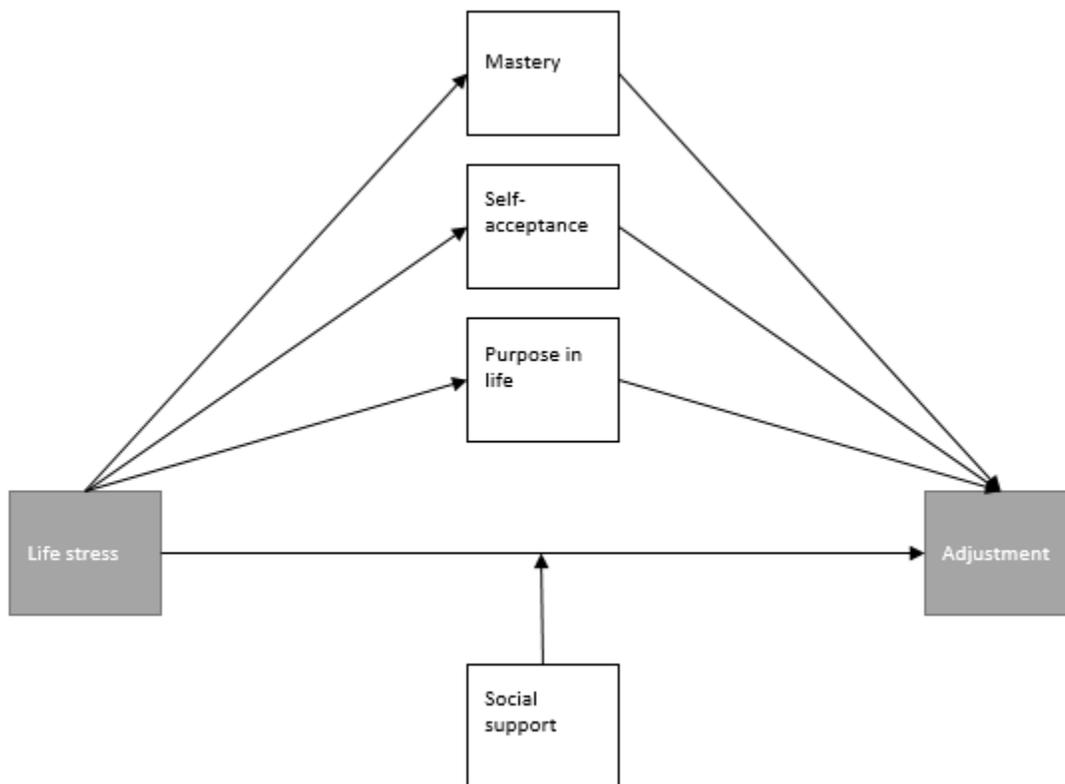


Figure 3. Multiple Mediators Model with Social Support as Moderator

**Hypothesis 2d:** Social support will moderate the relationship between stress and psychological functioning through its effects on mastery, self-acceptance, and purpose in life (mediated moderation, see Figure 4 below).

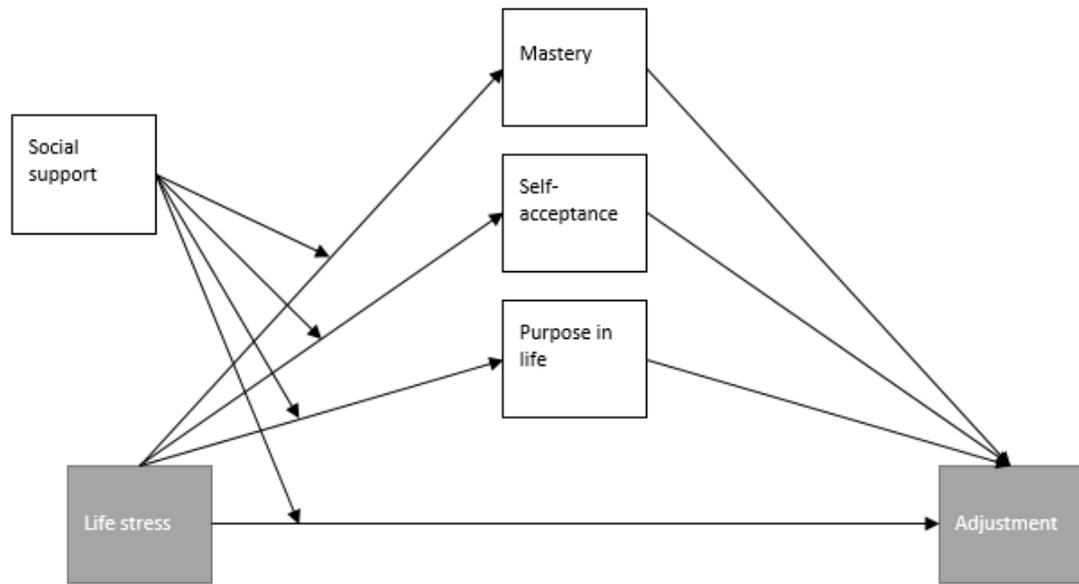


Figure 4. Mediated Moderation Model

**Hypothesis 2e:** All of the hypothesized relationships described above will be significant for both cancer-related and non-cancer related stressors.

**Hypothesis 2f:** The mediated moderation model will have the best fit to the data.

**Specific Aim #3:** To examine the associations between loss, danger, and entrapment on cancer progression.

**Hypothesis 3a:** The experience of loss, danger, and entrapment stressors will be related to faster cancer progression, controlling for relevant demographic and clinical variables.

**Hypothesis 3b:** Both cancer-related and non-cancer related stressors will be independently related to progression.

## Methods

### Participants and Procedure

The current study utilizes data from a larger longitudinal study assessing biobehavioral influences on tumor progression in epithelial ovarian cancer. Women scheduled to have surgery

for a pelvic mass suspected for ovarian cancer were recruited to the study during a clinic visit at the University of Iowa Hospitals and Clinics and Washington University in St. Louis. Patients in this sample were recruited from December 2009 to June 2014. The medical information for new gynecologic oncology referrals was reviewed by a research coordinator, who approached patients that were determined to be eligible by attending physicians. Patients who were interested in participating received more information about the study and consented for participation.

Women were excluded if they had a history of cancer, a non-ovarian primary tumor site, a non-epithelial tumor, a tumor of low malignant potential, or a comorbidity known to influence the immune system. Additional exclusion criteria include age less than 18 years, systemic corticosteroid medication use in the previous month, and current pregnancy. Patients receiving either adjuvant or neoadjuvant chemotherapy (or no chemotherapy - e.g. IA) were eligible for inclusion. Eligibility was confirmed following histological diagnosis. Psychosocial measurements were completed at 1-2 weeks prior to diagnostic surgery or beginning of neoadjuvant chemotherapy (baseline), and at 6 month and 1 year follow-up visits. At initial assessment, the sample consisted of 137 patients. However, two participants later withdrew from the study, for a total sample of 135. Follow-up data were available for 114 of these patients at 6 months and 100 patients at 1 year. All research procedures were approved by the institutional review boards at The University of Iowa and Washington University in St. Louis.

## **Measures**

**Demographic and clinical characteristics.** Sociodemographic information was collected by self-report in the initial study questionnaire. This information includes age, race, ethnicity, marital status, employment status, level of education, and yearly income. Clinical information including tumor stage according to the International Federation of Gynecologists

and Obstetricians (FIGO) guidelines (stages I-IV), tumor grade assessed by pathology (low vs. high), tumor histology, tumor debulking status (optimal debulking with less than 1cm residual tumor, or suboptimal bulking with greater than 1cm residual tumor), receipt of chemotherapy, medication use, and comorbid diagnoses. The diagnoses considered include previous cardiovascular events (atrial fibrillation, myocardial infarction, arrhythmia, tachycardia), peripheral vascular disease, diabetes, renal disease, liver diseases (cirrhosis and hepatitis), and previous cerebrovascular events such as strokes.

To assess cancer progression, date of recurrence was determined from patient records. In the current study, this is assessed at regular intervals, the last measurement being December 2016. A categorical yes/no variable is created to indicate patients who have experienced cancer progression. Additionally, a censored variable was created to reflect number of days between date of surgery and date of recurrence.

**Life stress.** The Life Events and Difficulties Schedule (LEDS), a semi-structured interview, was used to assess recent life stress (Brown & Harris, 1978, 1989). This was administered after confirmation of a diagnosis of ovarian cancer. Interviewers received approximately 16 hours of training, with supervision throughout the remainder of the study. Interviews were conducted either in the hospital following surgery or during chemotherapy, or by phone. Interviews were completed an average of 61 days following surgery or neoadjuvant chemotherapy. At the beginning of each interview, biographical information was collected to assess the context of events within an individual's life. Interviewers then determined if an individual experienced stressors in 10 life domains, such as housing, education, work, health, and relationships. In this study, the time frame of interest for experiencing these stressors was 1 year prior to diagnosis. Interview summaries were sent to a panel of extensively trained LEDS raters

at the University of California, Los Angeles. Ratings were completed independently by 2-3 raters utilizing the 520-page manual (Brown & Harris, 1989), followed by a consensus meeting in which raters agree upon final scores taking the patients' life circumstances into consideration. Inter-rater reliability was examined by calculating the Kappa coefficient corrected for differences in the number of raters per stressor (Uebersax, 1982). Inter-rater agreement for the stressor severity ratings ranged from  $k = .85$  to  $k = .89$  (mean  $k = .87$ ), indicating good reliability. Ratings included the following categories:

*Stressful events.* Stressful life events are events that occurred to the patient or to a patient's close ties. Examples of stressful events from the current sample include ending a relationship, losing a job, or having a CT scan for abdominal pain. The degree of unpleasantness and negative impact on the patient's life that is associated with the event is scored in terms of both short-term threat (distress on the day of or immediately following the event) and long-term threat (distress 10-14 days after the event). Threat was rated on a 4-point scale: 4) marked, 3) moderate, 2) some, 1) little or no threat. Severe life events are those that are defined as events rated as 3 or 4 on long-term threat. Common severe events include

*Difficulties.* Ongoing problematic conditions were classified as difficulties if they lasted a minimum of 4 weeks. This includes the chronic stress associated with a provoking event that would not be captured by only assessing threat for the following 2 weeks. Examples of difficulties include working at a job with unmanageable responsibilities, having frequent marital conflict, and experiencing ongoing financial difficulties. Threat associated with difficulties was rated on a 6-point scale ranging from high-marked threat to low or some threat. Difficulties that are rated 1-3 are categorized as major difficulties.

*Stressor focus and relevance to cancer.* Stressors were rated on the subject's involvement and were categorized as pertaining only to the subject, a joint focus involving the subject and another individual, or a stressor primarily involving another person in the subject's network. Only stressors that are subject- or joint-focused were included in the current study. Additionally, for stressors related to health, raters determined whether they involved non-cancer health symptoms, treatment, or procedures or if they were related to the patient's cancer. Cancer-related and non-cancer-related stressors were examined separately.

*Stressor characteristics.* Stressful events and difficulties were categorized according to the primary psychosocial characteristic of the stressor, which may include loss, humiliation, entrapment, and danger. The frequency of humiliation events in this sample was quite small, so these events were not be considered due to lack of power. Loss includes several types of events. Individuals may experience loss due to death, separation, or physical functioning. Additionally, if a patient reported loss of employment, material possessions, or a cherished idea (e.g., violating the expectation that someone is trustworthy, faithful by learning of infidelity), these stressors were categorized as loss. Examples of cancer-related losses include having test results confirmed or being told surgery is needed. Stressors categorized as danger include events involving physical, interpersonal (e.g., disapproval from family), and financial danger as well as those that entail a danger to one's employment or health. Cancer-related danger events include events such as having a CT scan for a suspicious lump, or being told that one may have cancer. Entrapment stressors are those that entail a sense of hopelessness and lack of ability to escape (e.g., ongoing difficulties with job, living situation, relationships, etc.). Some examples of entrapment stressors in the current sample include financial difficulties, ongoing fights and problems in relationships, and caretaking responsibilities.

These analyses utilized summed threat scores to assess cumulative stress. For events, the short-term and long-term threat rating were summed to obtain an overall threat score. These scores include all recent life stress within each characteristic that an individual has experienced (e.g., one may experience multiple kinds of losses), thereby measuring the total cumulative threat. Additionally, to examine if even relatively milder stressors can impact psychological functioning in the presence of a cancer diagnosis, scores were created for both *all* stressors within a given category as well as only *severe or major* stressors. Events and difficulties were also combined within a given stress category (though entrapment stressors are inherently only categorized as difficulties).

**Psychosocial outcomes.** Exploratory Factor Analyses (EFAs) were used in this study to determine psychosocial outcomes for the current analyses (described further in Data Analysis Strategy). Items from the Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item self-report scale (Radloff, 1977) were used as potential indicators of psychosocial outcomes. In this measure, participants are asked to rate the frequency of certain experiences over the past week, e.g., “I was bothered by things that usually don’t bother me.” The subscales of this questionnaire include vegetative, positive, negative, and interpersonal symptoms (Radloff, 1977). Items from the short-form of the Profile of Mood States (POMS-SF) were also used as potential indicators of psychosocial outcomes. The POMS-SF is a measure of psychological distress with subscales for fatigue, vigor, tension/anxiety, depression/dejection, confusion, and anger/hostility (Shacham, 1983). Respondents rate items based on their mood over the past week, with higher scores representing greater mood symptoms.

Though fatigue and vegetative symptoms of mood may be related to physical symptoms associated with cancer and its treatment, previous research has shown that these measures, even

while including the physical components of mood, are reliable in samples of cancer patients (Baker, Denniston, Zabora, Polland, & Dudley, 2002; Curran, Andrykowski, & Studts, 1995; Hann, Winter, & Jacobsen, 1999). In fact, all subscales of the POMS-SF, as well as the total scale score (referred to as total mood disturbance), are significantly related to the CES-D as well as other measures of positive affect, negative affect, and physical functioning (Baker et al., 2002). Furthermore, one study examining the CES-D found a reliable 2-factor structure of depressed and positive affect in cancer patients, with the items from the vegetative subscale loading highly onto depressed affect (Schroevers, Sanderman, van Sonderen, & Ranchor, 2000). Thus, all items from these scales, including the vegetative items from the CES-D and the fatigue and vigor items from the POMS-SF were used as potential indicators of psychosocial outcomes.

**Mastery, self-acceptance, and purpose in life.** Subscales from the Psychological Well-Being Scale (PWBS) were used as measures of psychological resources (Ryff, 1989). The self-acceptance scale was used in analyses as a measure of positive self-regard. Additionally, the environmental mastery scale was used as a measure of mastery and perceived control over one's environment. The purpose in life scale served as a measure of patients' global sense of meaning. Each scale has 7-items that assess the extent to which respondents agree or disagree with statements reflecting general beliefs. Higher scores indicate greater well-being.

**Social support.** Social support was measured using the emotional attachment subscale of the Social Provisions Scale (SPS; Cutrona, 1984). This scale assesses the extent to which respondents perceive that certain relational provisions are being met in their social relationships, including emotional attachment, social integration, reassurance of worth, reliable alliance, guidance, and opportunity for nurturance (Weiss, 1974). Because emotional attachment has been shown to be most correlated to health outcomes in our previous work (e.g., Lutgendorf et al.,

2012), only this subscale was used. This scale consists of 4 items assessing the presence or absence of a relational provision (e.g. “I feel a strong emotional bond with at least one other person”).

### **Data Analysis Strategy**

**Preliminary and descriptive analyses.** Preliminary and cross-sectional analyses were conducted using the Statistical Package for the Social Sciences v. 21 (SPSS, Armonk, NY). Distributions of all variables were examined for normality and outliers were deleted. To assess potential differences in demographic and clinical variables between participants who completed interviews and those who did not, chi-square tests (for categorical variables) and one way ANOVAs (for continuous variables) were used. Means and standard deviations of outcome variables were examined to describe the average psychosocial functioning of the sample as a whole. *A priori* covariates included age and cancer stage (stage I/II vs. III/IV). Additional control variables were determined by examining bivariate correlations between psychosocial outcomes and clinical variables.

To determine accurate measurement of psychological outcomes in this sample, replicability across measurements over time was examined. This entailed an iterative process in which EFAs were conducted at baseline, 6 months, and 1 year using items from multiple mood measures, followed by evaluation of factor structure similarity across these measurements via examination of Tucker’s Congruence Coefficients (TCC) (Lorenzo-Seva & ten Berge, 2006; Tucker, 1951). EFAs were conducted using Mplus (Version 6.12, Los Angeles, CA) with a weighted least squares means and variance–adjusted estimator and Geomin rotation. Congruence coefficients were calculated using the psych package in R (Revelle, 2016).

For the first EFAs, all items from the CESD and POMS (a total of 57 items) were included as potential indicators of mood. All items ask patients to describe their mood over the past week. Factor structures were determined for 1-15 factors. Next, the factor structure with closest similarity (highest TCCs) across all 3 time points was then examined further. Items without a factor loading  $>.4$  on any factor within any one measurement were excluded. Next, another factor analysis with the new set of items was conducted. This process was repeated until all congruence coefficients across measurements for a given factor structure were  $>.95$ , which indicates that the factors can be considered to be equal (Lorenzo-Seva & ten Berge, 2006). Finally, after consistent factors across time were determined, these items were summed to create factor scores to be used in all further analyses.

**Analysis of Specific Aim #1.** Latent growth curve (LGC) analysis was used to examine changes in psychological outcomes over one year after surgery (measurements at pre-surgery, 6 months post-surgery and 1 year post-surgery) (Duncan, Duncan, & Stryker, 2006). Analyses were conducted in Mplus (Version 6.12, Los Angeles, CA) using maximum likelihood estimation, which allows for the presence of data that are missing at random. Given that sample sizes approaching 100 are preferred and the current sample size is 135, this method offers a powerful way to examine longitudinal data (Curran, Obeidat, & Losardo, 2010). Like multilevel models, LGC models can evaluate individual differences in trajectories over time, and these two methods yield similar results. However, an advantage of LGC modeling is the estimation of goodness-of-fit parameters (C.-P. Chou, Bentler, & Pentz, 1998). In this study, overall model fit was evaluated by examining the comparative fit index (CFI; Bentler, 1990), the Tucker-Lewis Index (TLI) (Tucker & Lewis, 1973), the root mean square error of approximation (RMSEA)(Steiger, 1990), and the standardized root-mean-squared residual (SRMR).

Recommended cut-off points of  $\geq .95$  for CFI and TLI,  $\leq .06$  for RMSEA, and  $\leq .08$  for SRMR were used to evaluate model fit (Hu & Bentler, 1999). Non-nested models were compared by evaluating the difference between the Bayesian Information Criterion (BIC) for each model, which does not have a recommended cut-off point, but allows for relative comparison of models (Schwarz, 1978).

In the first step (level 1), a simple unconditional growth curve calculating intra-individual change was examined (Willet & Sayer, 1994). In this model, time was the only predictor and both the intercept and slope were calculated, allowing for variability between individuals. The slope parameter was examined to assess the overall rate of change in the sample. Additionally, the variance of the slope parameter was examined for significance, to determine whether the trajectory varies significantly between individuals.

Next, a conditional model was used to assess inter-individual predictors in growth parameters (level 2). The effects of time-invariant measures, including covariates and predictors of interest, were examined. The main effects of stress variables and the interactions between cancer and non-cancer stressors were included as predictors of intercept and slope. All variables were centered prior to creating interaction terms, along with all additional covariates in the model, to obtain an accurate measure of average intercept and slope. Unstandardized interaction terms were evaluated for significance, as this is a more reliable method than using standardized coefficients (Friedrich, 1982). Interactions were probed with online utilities created by Preacher, Curran, & Bauer (Preacher, Curran, & Bauer, 2006), and plotted using R (R Core Team, 2015).

**Analysis of Specific Aim #2.** Figures 1-4 depict the four models tested in these analyses. In the initial model, control variables, the main effect of life stress, and the main effect of each psychosocial protective factor were included (an independent effects model; see Figure 1). A

multiple moderator model was then examined, with social support, mastery, purpose in life, and self-acceptance as moderators of stressor variables (Figure 2). Next, a model including social support as a moderator and mastery, self-acceptance, and purpose in life as mediators operating in parallel was analyzed (Figure 3). Finally, a model examining mediated moderation was assessed. In this model, social support acts as a moderator of life stress that is mediated through its effects on mastery, self-acceptance, and purpose in life (Figure 4).

All models utilized latent growth curve modeling, with latent intercept and slope regressed on the predictor variables and covariates. The overall significance of the models was examined as well as beta coefficients for main effects, interaction terms, and indirect effects. Model fit indices were examined as described above to compare the four models. To reduce bias, confidence intervals for indirect effects were computed using 1000 bootstrap samples and maximum likelihood estimation (Lau & Cheung, 2012; von Soest & Hagtvet, 2011). If the 95% confidence intervals do not contain 0, this indicated significant indirect effects. For significant moderators, conditional effects of life stress at different values of the moderator (the mean, 1 SD above, and 1 SD below) were calculated and plotted. Again, all variables were centered prior to creating interaction terms and unstandardized interaction terms were evaluated for significance (Friedrich, 1982).

**Analysis of Specific Aim #3.** The effects of loss, danger, and entrapment as predictors of cancer progression were analyzed using Cox proportional hazards regression models, where a  $p$  value  $<0.05$  was considered statistically significant (Cox, 1972). Similar to the above analyses, *a priori* covariates included age and cancer stage. Demographic and clinical variables that were significantly correlated with the censored variable of days to progression were included as additional covariates. Unadjusted hazard ratios from these models were examined, and

significance was evaluated with the Wald  $\chi^2$  statistic. To illustrate significant effects, Kaplan-Meier plots were used to compare differences in time to progression by life stress group variables (Kaplan & Meier, 1958). For Kaplan Meier plots, life stress threat variables were dichotomized by using a median split to create categories of high versus low threat in a given stress category.

## **Results**

### **Preliminary and Descriptive Analyses**

**Patient characteristics.** The sample at baseline consists of 135 women who completed LEDS interviews. Demographics for this sample are shown in Table 1. The patients in this sample were primarily Caucasian and non-Hispanic (94.8%). Participants were an average of 59.14 years of age. A majority of the women in this sample (73.3%) were diagnosed with late-stage disease (stage III or IV), with high-grade tumors (88.9%) and serous histology (68.1%). Additionally, a majority of the women in this sample had postsecondary education (64.5%) and were married or living with a partner (67.4%). Most women had not had a recurrence at the 1 year measurement (65.9%).

Table 1. Demographic and Clinical Characteristics of Participants

<i>Characteristic</i>	<i>Mean (SD)</i>
Age (years)	59.14 (10.9)
	<i>N (%)</i>
Race (N=132)	
Asian	1 (0.7)
Black/African American	4 (3)
White	128 (94.8)
Ethnicity (N=129)	
Non-Hispanic	128 (94.8)
Hispanic	1 (0.7)
Education (N=133)	
Less than high school graduate	4 (3)
High school graduate	42 (31.1)
Trade school/some college	37 (27.4)
College graduate	34 (25.2)
Postgraduate degree	16 (11.9)
Relationship status	
Married, living with partner	91 (67.4)
Single, separated, widowed, divorced	44 (32.6)
Cancer stage	
I	25 (18.5)
II	10 (7.4)
III	87 (64.4)
IV	12 (8.9)
Grade	
Low	15 (11.1)
High	120 (88.9)
Histology	
Serous	92 (68.1)
Endometrioid	5 (3.7)
Mucinous	4 (3)
Clear cell	13 (9.6)
Other/unknown/missing	21 (15.5)
Recurrence at 1 year (N=134)	
No	89 (65.9)
Yes	45 (33.3)

Note: N=135.

One-way ANOVAs were used to compare demographic information between the 135 participants who completed the LEDS interviews and the 210 women in the larger study recruited during the same time period who did not complete interviews. There were no significant differences between those who completed LEDS interviews and those who did not in regards to race ( $\chi^2=0.24$ ,  $df=1$ ,  $p=0.63$ ), education ( $\chi^2=1.14$ ,  $df=4$ ,  $p=0.89$ ), employment ( $\chi^2=0.21$ ,  $p=0.65$ ), income ( $\chi^2=3.51$ ,  $df=8$ ,  $p=0.90$ ), presence of comorbidities ( $\chi^2=0.03$ ,  $df=1$ ,  $p=0.86$ ), history of psychiatric treatment ( $\chi^2=0.20$ ,  $df=1$ ,  $p=0.66$ ), or current use of pain medications ( $\chi^2=0.63$ ,  $df=1$ ,  $p=0.43$ ), antidepressant medications, ( $\chi^2=0.33$ ,  $df=1$ ,  $p=0.56$ ), or anxiety medications ( $\chi^2=0.03$ ,  $df=1$ ,  $p=0.87$ ). Those who completed the interviews also did not differ from those who did not in terms of age ( $F_{1,340}=0.01$ ,  $p=0.95$ ), stage ( $\chi^2=0.42$ ,  $df=3$ ,  $p=0.94$ ), grade ( $\chi^2=0.59$ ,  $df=1$ ,  $p=0.44$ ), or histology (comparing serous versus non-serous:  $\chi^2=0.10$ ,  $df=1$ ,  $p=0.75$ ).

**Descriptive analyses of life events.** Descriptive statistics for the various life events examined in this study are displayed in Table 2. At least 74.1% of all women endorsed some type of cancer-related stressor (including losses and danger stressors), and a significant portion experienced at least one major stressor related to their cancer (69.6%). Similarly, non-cancer losses were reported quite frequently in this sample. A majority of the women in this sample (71.9%) experienced a loss unrelated to their cancer and 47.4% experienced more than one non-cancer-related loss. Over half of the women in this sample endorsed at least one non-cancer related danger (57.8%). Fewer women reported major losses (37.7%) and major danger stressors (27.4%) unrelated to cancer. About half of the sample experienced an entrapment stressors (47.4%). There was some variability in average levels of cumulative threat associated with each

stressor with average cumulative threat ranging from 4.11-10.17, and total threat across stressors ranging from 1-33.

Table 2. Frequencies of Stressful Life Events and Average Threat Level by Type of Event

Type of life stress	0		1		>1		Average total threat	
	N	%	N	%	N	%	M	SD
<b>Loss (not cancer-related)</b>								
All stressors	38	28.1	33	24.4	64	47.4	9.19	6.71
Only major stressors	84	62.2	37	27.4	14	10.3	7.49	3.67
<b>Cancer Loss</b>								
All stressors	22	16.3	92	68.1	21	15.6	7.73	2.57
Only major stressors	30	22.2	95	70.4	10	7.4	7.58	2.28
<b>Danger (not cancer-related)</b>								
All stressors	57	42.2	45	33.3	33	24.4	8.47	5.88
Only major stressors	98	72.6	28	20.7	9	6.6	8.05	3.57
<b>Cancer Danger</b>								
All stressors	35	25.9	45	33.3	55	40.7	10.17	4.18
Only major stressors	41	30.4	61	45.2	33	24.5	9.12	3.77
<b>Entrapment</b>								
All stressors	71	52.6	46	34.1	18	13.3	4.11	3.70
Only major stressors	116	85.9	14	10.4	5	3.6	6.68	4.06

**Measurement model of psychological outcomes.** After conducting EFAs using all 57 items of the CESD and POMS, congruence coefficients were examined across factor structures and measurements (baseline, 6 months, and 1 year). A 2-factor structure resulted in the highest congruence coefficients across measurements, with TCCs ranging from .91 to .97 (Table 3). Examination of item loadings for the 2-factor structure at each measurement revealed one factor representing fatigue symptoms and a general mood factor (Table 4). The fatigue factor consisted of several items from the vigor and fatigue subscales from the POMS as well as 2 items from the CESD (“I felt everything I did took effort” and “I could not ‘get going’”). Two items from the

POMS (“cheerful” and “forgetful”) and 5 items from the CESD (“I did not feel like eating,” “I felt as good as other people,” “I talked less than usual,” “I felt that people disliked me,” and “People were unfriendly”) met criteria for exclusion.

Table 3. Factor Congruencies for 2-Factor Structure of Mood over Time with All Items of CESD and POMS

	M6 Factor 1	M6 Factor 2	Y1 Factor 1	Y1 Factor 2
BL Factor 1	.99	.23	.98	.17
BL Factor 2	.13	.97	.22	.93
M6 Factor 1			.97	.14
M6 Factor 2			.28	.91

Note: BL=baseline; M6=6 months; Y1=1 year. Pattern with greatest congruence coefficients is highlighted.

Table 4. Item Loadings for 2-Factor Structure of Mood over Time with All Items of CESD and POMS

Item label	BL factor 1	BL factor 2	M6 factor 1	M6 factor 2	Y1 factor 1	Y1 factor 2	Item
POMS1	0.822	-0.041	0.591	0.09	0.656	0.105	Tense
POMS2	0.813	-0.221	0.787	-0.057	0.951	-0.139	Angry
POMS4	0.802	0.146	0.902	-0.022	0.836	0.07	Unhappy
POMS6	0.681	0.001	0.782	0.139	0.674	0.125	Confused
POMS7	0.738	-0.118	0.801	-0.062	0.865	-0.153	Peeved
POMS8	0.891	-0.027	0.927	-0.073	0.939	0.045	Sad
POMS10	0.802	-0.076	0.84	-0.044	0.768	0.124	On edge
POMS11	0.562	0.058	0.697	0.005	0.61	0.251	Grouchy
POMS12	0.883	0.033	0.829	0.101	0.919	0.098	Blue
POMS14	0.793	0.133	0.829	0.224	0.821	0.064	Hopeless
POMS15	0.753	-0.009	0.769	-0.004	0.95	-0.234	Uneasy
POMS16	0.71	0.031	0.623	-0.013	0.653	0.212	Restless
POMS17	0.652	0.184	0.489	0.391	0.449	0.386	Unable to concentrate
POMS19	0.665	-0.081	0.79	-0.109	0.79	-0.017	Annoyed
POMS20	0.785	0.038	0.839	0.122	0.762	0.224	Discouraged
POMS21	0.878	-0.205	0.886	-0.146	0.945	-0.162	Resentful
POMS22	0.859	-0.116	0.667	-0.071	0.867	-0.148	Nervous
POMS23	0.517	0.472	0.673	0.28	0.704	0.338	Miserable
POMS25	0.9	-0.123	0.918	-0.184	0.883	-0.001	Bitter
POMS27	0.781	-0.082	0.706	0.012	0.88	-0.1	Anxious
POMS28	0.684	0.309	0.793	0.182	0.874	-0.059	Helpless
POMS30	0.804	-0.003	0.815	0.097	0.82	0.064	Bewildered
POMS31	0.909	-0.249	0.911	-0.072	0.986	-0.251	Furious
POMS33	0.701	0.249	0.694	0.288	0.751	0.158	Worthless
POMS36	0.709	-0.108	0.756	-0.111	0.679	0.157	Uncertain about things
CESD1	0.466	0.168	0.615	0.267	0.68	0.048	I was bothered by things that usually don't bother me.
CESD3	0.748	0.157	0.554	0.238	0.885	0.049	I felt I could not shake off the blues.
CESD5	0.511	0.202	0.51	0.229	0.404	0.379	I had trouble keeping my mind on what I was doing.
CESD6	0.794	0.057	0.782	0.136	0.962	-0.066	I felt depressed.
CESD8	-0.512	-0.184	-0.587	-0.094	-0.597	-0.091	I felt hopeful about future.
CESD9	0.748	0.096	0.812	0.075	0.749	-0.097	I thought my life was a failure.
CESD10	0.644	-0.037	0.696	-0.187	0.813	-0.204	I felt fearful.

Table 4 – Continued

CESD11	0.513	0.094	0.481	0.304	0.463	0.246	My sleep was restless.
CESD12	-0.485	-0.281	-0.615	-0.319	-0.836	-0.073	I was happy.
CESD14	0.629	0.181	0.716	0.146	0.698	0.103	I felt lonely.
CESD16	-0.456	-0.257	-0.545	-0.423	-0.651	-0.243	I enjoyed life.
CESD17	0.71	0.021	0.646	0.119	0.735	0.094	I had crying spells.
CESD18	0.851	0.004	0.884	0.008	0.862	-0.022	I felt sad.
POMS3	0.235	0.793	0.076	0.813	0.324	0.687	Worn out
POMS5	-0.001	-0.759	-0.116	-0.71	-0.102	-0.769	Lively
POMS9	0.102	-0.899	-0.045	-0.765	0.033	-0.841	Active
POMS13	0.126	-0.975	0.037	-0.931	-0.005	-0.917	Energetic
POMS18	0.152	0.803	-0.142	0.914	0.189	0.74	Fatigued
POMS26	0.195	0.815	-0.038	0.885	0.251	0.763	Exhausted
POMS29	0.435	0.484	0.329	0.588	0.532	0.48	Weary
POMS32	0.036	-0.86	0.091	-0.904	-0.003	-0.851	Full of pep
POMS35	0.093	-0.868	0.17	-0.854	0.201	-0.897	Vigorous
POMS37	0.26	0.707	0.05	0.856	0.221	0.733	Bushed
CESD7	0.34	0.611	0.261	0.599	0.455	0.452	I felt everything I did was an effort.
CESD20	0.279	0.632	0.315	0.583	0.525	0.434	I could not get "going."
POMS24	-0.361	-0.357	-0.376	-0.594	-0.446	-0.38	Cheerful
POMS34	0.492	0.085	0.433	0.103	0.351	0.218	Forgetful
CESD2	0.323	0.373	0.243	0.538	0.683	-0.141	I did not feel like eating, my appetite was poor.
CESD4	-0.139	-0.446	-0.375	-0.454	-0.393	-0.339	I felt as good as other people.
CESD13	0.365	0.362	0.313	0.474	0.482	0.287	I talked less than usual.
CESD19	0.31	-0.032	1.014	-0.229	0.386	0.232	I felt that people disliked me.
CESD15	0.348	-0.027	0.84	-0.083	0.424	-0.062	People were unfriendly.

Note: BL=baseline; M6=6 months; Y1=1 year. Factor loadings >.4 and consistent over time are highlighted.

To assess for the presence of sub-factors of mood, the remaining 38 items that loaded onto the general mood factor were used in the next round of analyses. Evaluation of factor congruence across measurements supported the presence of a general mood factor (TCCs of .98, .99, and .99). The 2 factor structure produced fair congruence across measurements (TCCs ranging from .65-.86, see Table 5), which was explored further. Evaluation of item loadings

across the measurements for the 2-factor structure revealed that 14 items consistently loaded onto the 2 factors over time (see Table 6 for item loadings).

Table 5. Factor Congruencies for 2-Factor Structure of Mood over Time after Excluding Items

	M6 Factor 1	M6 Factor 2	Y1 Factor 1	Y1 Factor 2
BL Factor 1	.66	.55	.84	.28
BL Factor 2	.67	.65	.52	.86
M6 Factor 1			.77	.55
M6 Factor 2			.59	.66

Note: BL=baseline; M6=6 months; Y1=1 year. Pattern with greatest congruence coefficients is highlighted.

Table 6. Item Loadings for 2-Factor Structure of Mood over Time after Excluding Items

Item label	BL factor 1	BL factor 2	M6 factor 1	M6 factor 2	Y1 factor 1	Y1 factor 2	Item
POMS2	0.854	0	0.851	-0.057	0.894	0.007	Angry
POMS7	0.816	-0.024	0.815	-0.007	1.154	-0.389	Peeved
POMS11	0.574	0.097	0.825	-0.122	0.799	-0.017	Grouchy
POMS19	0.747	0.002	1.104	-0.364	0.925	-0.127	Annoyed
POMS20	0.482	0.43	0.542	0.429	0.454	0.512	Discouraged
POMS21	0.918	-0.017	0.54	0.386	0.752	0.143	Resentful
POMS25	0.798	0.169	0.535	0.393	0.566	0.371	Bitter
POMS31	0.989	-0.09	0.744	0.224	0.857	0.014	Furious
POMS14	0.46	0.497	0.381	0.624	0.254	0.68	Hopeless
POMS17	0.224	0.547	0.196	0.503	-0.278	1.034	Unable to concentrate
CESD5	-0.08	0.667	0.12	0.549	-0.152	0.858	I had trouble keeping my mind on what I was doing.
CESD10	-0.216	0.847	0.111	0.602	0.16	0.596	I felt fearful.
CESD17	0.078	0.701	0.005	0.771	-0.006	0.859	I had crying spells.
CESD18	0.013	0.886	0.282	0.695	0.18	0.754	I felt sad.
POMS1	-0.117	0.924	0.865	-0.209	0.42	0.348	Tense
POMS4	0.305	0.641	0.601	0.386	0.841	0.078	Unhappy
POMS6	0.386	0.382	0.591	0.309	0.172	0.636	Confused
POMS8	0.28	0.699	0.546	0.449	0.702	0.324	Sad
POMS10	0.115	0.726	0.837	0.033	0.576	0.315	On edge

Table 6 – Continued

POMS12	0.373	0.633	0.565	0.385	0.674	0.369	Blue
POMS15	-0.009	0.793	0.743	0.079	0.322	0.561	Uneasy
POMS16	0.039	0.732	0.585	0.091	0.268	0.577	Restless
POMS22	-0.141	0.96	0.597	0.103	0.372	0.475	Nervous
POMS23	0.411	0.352	0.286	0.579	0.784	0.159	Miserable
POMS27	-0.116	0.869	0.566	0.212	0.207	0.679	Anxious
POMS28	0.51	0.388	0.64	0.297	0.39	0.513	Helpless
POMS30	0.419	0.489	0.799	0.11	0.264	0.665	Bewildered
POMS33	0.844	0.032	0.127	0.736	0.421	0.47	Worthless
POMS36	0.182	0.57	0.49	0.298	0.077	0.77	Uncertain about things
CESD1	0.099	0.47	0.317	0.474	0.54	0.216	I was bothered by things that usually don't bother me.
CESD3	0.078	0.779	0.26	0.448	0.642	0.331	I felt I could not shake off the blues.
CESD6	0.172	0.717	0.241	0.67	0.598	0.391	I felt depressed.
CESD8	-0.51	-0.168	0.137	-0.816	-0.448	-0.245	I felt hopeful about future.
CESD9	0.54	0.315	-0.017	0.853	0.836	-0.151	I thought my life was a failure.
CESD11	-0.076	0.646	0.346	0.306	0.049	0.62	My sleep was restless.
CESD12	-0.42	-0.269	0.127	-0.922	-0.918	0.008	I was happy.
CESD14	0.479	0.296	0.247	0.592	0.666	0.142	I felt lonely.
CESD16	-0.595	-0.05	0.001	-0.749	-0.727	-0.09	I enjoyed life.

Note: BL=baseline; M6=6 months; Y1=1 year. Factor loadings >.4 and consistent over time are highlighted.

These 14 items were then used for the next round of analyses, which resulted in congruence coefficients for the 2 factors ranging from .94-.99 (Table 7), and consistent item loadings across time (Table 8). Evaluation of items revealed that the first factor contained primarily items from the POMS anger subscale, with one additional item from the depression subscale (“discouraged”). The second factor contained 4 items from the CESD, with items from the interpersonal, depressed mood, and vegetative subscale. Additionally, 2 items from the POMS (“hopeless,” “unable to concentrate”) loaded onto the second factor. Thus, the first factor

is called “anger” while the second one is referred to as “depressed mood.” Of note, this reflects symptoms of depressed mood, rather than a diagnosis of Major Depression.

Table 7. Factor Congruencies for Final 2-Factor Structure of Mood over Time

	M6 Factor 1	M6 Factor 2	Y1 Factor 1	Y1 Factor 2
BL Factor 1	.96	.22	.97	.23
BL Factor 2	.23	.94	.18	.95
M6 Factor 1			.98	.28
M6 Factor 2			.22	.95

Note: BL=baseline; M6=6 months; Y1=1 year. Pattern with greatest congruence coefficients is highlighted.

Table 8. Final Item Loadings for 2-Factor Structure of Mood over Time

Item label	BL factor 1	BL factor 2	M6 factor 1	M6 factor 2	Y1 factor 1	Y1 factor 2	Item
POMS2	0.846	0.086	0.825	0.001	0.808	0.141	Angry
POMS7	0.784	0.068	0.849	0.011	1.061	-0.231	Peeved
POMS11	0.744	-0.098	0.901	-0.154	0.653	0.195	Grouchy
POMS19	0.861	-0.109	1.011	-0.273	0.911	-0.024	Annoyed
POMS20	0.499	0.444	0.51	0.509	0.542	0.483	Discouraged
POMS21	0.917	0.004	0.659	0.384	0.752	0.194	Resentful
POMS25	0.825	0.156	0.726	0.285	0.679	0.333	Bitter
POMS31	0.941	-0.022	0.86	0.186	0.91	0.004	Furious
POMS14	0.327	0.638	0.392	0.616	0.333	0.633	Hopeless
POMS17	0.142	0.637	-0.002	0.723	-0.022	0.832	Unable to concentrate
CESD5	-0.081	0.674	-0.151	0.877	-0.126	0.885	I had trouble keeping my mind on what I was doing.
CESD10	-0.041	0.685	0.234	0.527	0.32	0.443	I felt fearful.
CESD17	0.093	0.757	0.109	0.732	0.033	0.894	I had crying spells.
CESD18	-0.001	0.935	0.393	0.613	0.141	0.836	I felt sad.

Note: BL=baseline; M6=6 months; Y1=1 year. Factor loadings >.4 and consistent over time are highlighted.

Lastly, the fatigue/vegetative items were examined separately to confirm this as a stable factor over time, which resulted in TCCs of 1 across measurements. Factor loadings for the fatigue factor over time are displayed in Table 9. For all further analyses, the anger, depressed mood, and fatigue items were summed, respectively, to create scores to be used as outcomes. Items were not weighted, and the CESD items were re-scaled to have range of 0-4 to ensure equal weight with the POMS items. Additionally, a general mood factor was also created utilizing items loading onto the mood factor in the second round of analyses in order to compare the predictive validity of the 1-factor and 2-factor structures of mood in this sample. This mood factor is henceforth called “distress,” as higher scores indicate worse mood. Means, standard deviations, and reliability coefficients for these measures are displayed in Table 10.

Table 9. Item Loadings for Fatigue Factor over Time

Item label	Baseline	6 Months	1 Year	Item
POMS3	0.895	0.829	0.909	Worn out
POMS5	-0.731	-0.714	-0.807	Lively
POMS9	-0.861	-0.793	-0.813	Active
POMS13	-0.938	-0.926	-0.914	Energetic
POMS18	0.868	0.882	0.874	Fatigued
POMS26	0.911	0.892	0.939	Exhausted
POMS32	-0.847	-0.879	-0.83	Full of pep
POMS35	-0.839	-0.814	-0.756	Vigorous
POMS37	0.799	0.862	0.875	Bushed
CESD7	0.726	0.695	0.73	I felt everything I did was an effort.
CESD20	0.731	0.676	0.771	I could not get "going."

Table 10. Means and Standard Deviations of Dependent Variables over Time

<b>DISTRESS</b>			
	Baseline	M6	Y1
M	37.58	23.40	23.94
SD	26.09	22.36	25.10
N	126	104	98
$\alpha$	0.96	0.96	0.97
<b>FATIGUE</b>			
	Baseline	M6	Y1
M	22.71	20.67	18.14
SD	9.90	9.78	10.07
N	128	105	98
$\alpha$	0.93	0.92	0.94
<b>ANGER</b>			
	Baseline	M6	Y1
M	4.85	3.75	4.22
SD	5.33	4.72	5.36
N	128	104	98
$\alpha$	0.91	0.90	0.92
<b>DEPRESSED MOOD</b>			
	Baseline	M6	Y1
M	6.85	3.94	3.76
SD	5.19	4.22	4.25
N	131	114	100
$\alpha$	0.82	0.84	0.84

*A priori* covariates included age and cancer stage (stage I/II vs. III/IV). Correlations between potential covariates and outcomes were examined for additional control variables. Additional control variables include use of pain medications ( $r=0.31$ ,  $p<0.001$ ) and cancer grade ( $r=0.33$ ,  $p<0.001$ ) for fatigue, history of psychiatric treatment for anger ( $r=0.21$ ,  $p=0.02$ ) and distress ( $r=0.17$ ,  $p=0.05$ ), and presence of comorbidities for anger ( $r=0.18$ ,  $p=0.04$ ). No significant additional control variables emerged for depressed mood.

**Specific Aim #1: To examine the effects of prior experiences of loss, danger, and entrapment on psychological functioning both prior to surgery and during the year after diagnosis.**

**Unconditional Models.** First, unconditional growth curve models were used to examine the change in outcomes over time. In the first unconditional growth model for each outcome, slope factor loadings were specified as BL=0, M6=1, and Y1=2, so that the slope factor represents linear growth from baseline to 1 year. Additionally, this centers the intercept factor at baseline. These models were examined and then re-specified as needed to improve model fit. For distress, depressed mood, and fatigue outcomes, the variance in slope was fixed at 0, as the initial model indicated a negative variance for this factor. Similarly, the variance in slope for anger was not significant and was fixed at 0 as well. This resulted in increased model fit for all outcomes (See Table 11). The finding that variance in slope was not significant for any outcome indicates little variability between individuals in the rate of change in these models.

Next, because the greatest changes in distress, depressed mood, and anger occurred between baseline and 6 months, the slope factor loading for the 6 month measurement was freely estimated, while baseline remained specified at 0 and 1 year measurement was specified at 1. This model continues to represent growth from baseline to 1 year, without the restriction of linearity. This resulted in substantial improvement to model fit for all 3 outcomes (Table 11). However, examination of parameter estimates revealed a nonsignificant mean for the slope factor for anger ( $M=-.28$ ,  $p=.31$ ), indicating no change over time between baseline and 1 year. Thus, the slope loadings were re-specified to BL=0, m6=1 and y1=\* (\* indicating that this loading was freely estimated) to examine change from baseline to 6 months, which resulted in the same model fit. Parameter estimates for final unconditional latent growth models are displayed in

Table 12. On average, each outcome decreased over time, as evidenced by significant negative slopes.

Table 11. Model Fit Statistics for Unconditional Growth Curve Models

<b>Outcome Variable</b>	<b>Model</b>	<b>Chi-square</b>	<b>RMSEA</b>	<b>CFI</b>	<b>TLI</b>	<b>SRMR</b>	<b>BIC</b>
<b>Distress</b>	Basic unconditional growth curve, BL=0, M6=1, and Y1=2	13.65 (df=1), p<.0002	.31	.78	.33	.09	2974.30
	Slope variance fixed to 0	12.92 (df=3), p=.005	.16	.83	.83	.12	2969.91
	Slope variance fixed to 0, BL=0, M6=*, and Y1=1	2.40 (df=2), p=.30	.04	.99	.99	.08	2953.68
<b>Depressed Mood</b>	Basic unconditional growth curve, BL=0, M6=1, and Y1=2	9.21 (df=1), p=.002	.25	.81	.42	.09	2005.25
	Slope variance fixed to 0	10.81 (df=3), p=.01	.14	.82	.82	.10	1998.06
	Slope variance fixed to 0, BL=0, M6=*, and Y1=1	1.05 (df=2), p=.59	0	1	1.03	.04	1986.77
<b>Anger</b>	Basic unconditional growth curve, BL=0, M6=1, and Y1=2	3.68 (df=1), p=.06	.14	.90	.71	.04	1981.71
	Slope variance fixed to 0	2.27 (df=3), p=.52	0	1	1.03	.07	1974.34
	Slope variance fixed to 0, BL=0, M6=*, and Y1=1	.72 (df=2), p=.70	0	1	1.07	.05	1975.45
<b>Fatigue</b>	Basic unconditional growth curve, BL=0, M6=1, and Y1=2	.23 (df=1), p=.63	0	1	1.07	.01	2443.26
	Slope variance fixed to 0	2.52 (df=3), p=.47	0	1	1.01	.06	2435.97

Table 12. Parameter Estimates from Unconditional Latent Growth Curves

	<b>Distress</b>	<b>Depressed Mood</b>	<b>Anger*</b>	<b>Fatigue</b>
<b>Intercept Mean</b>	37.86 (2.33)	6.90 (.45)	4.83 (.47)	22.91 (.80)
<b>Intercept Variance</b>	387.25 (78.25)	10.43 (2.20)	13.87 (3.59)	41.45 (6.94)
<b>Slope Mean</b>	-13.34 (2.42)	-3.12 (.47)	-1.04 (.49)	-2.41 (.51)

Note: Standard errors are in parentheses. All values are significant at  $p < .05$ . Slope variance was fixed at 0 for all models. \*Slope for anger represents change from baseline to 6 months.

**Conditional models.** Next, conditional models were used to evaluate the impact of life events on both the intercept and slope, while controlling for the covariates described above. All cumulative life event threat variables (non-cancer loss, cancer loss, non-cancer danger, cancer danger, and entrapment) were entered as predictors. Slope variance was set to 0 as indicated by the unconditional models. However, covariates were still included as potential predictors of the slope growth factor, since the average slope in unconditional models was significant. This offers more power to detect variability in average slope as a function of inter-individual differences. Hence, residual variance of slope was fixed to 0, and significant predictors of slope, in models where average slope was significant, were examined.

Additionally, interaction terms for loss and danger (cancer-related events \* non-cancer-related events) were created and entered into the model as predictors to test whether the effect of cancer-related stress is impacted by the presence of non-cancer stress, given the importance of the cumulative effects of stress. Variables were mean-centered prior to creating interaction terms. Figure 5 displays a general depiction of these conditional models.

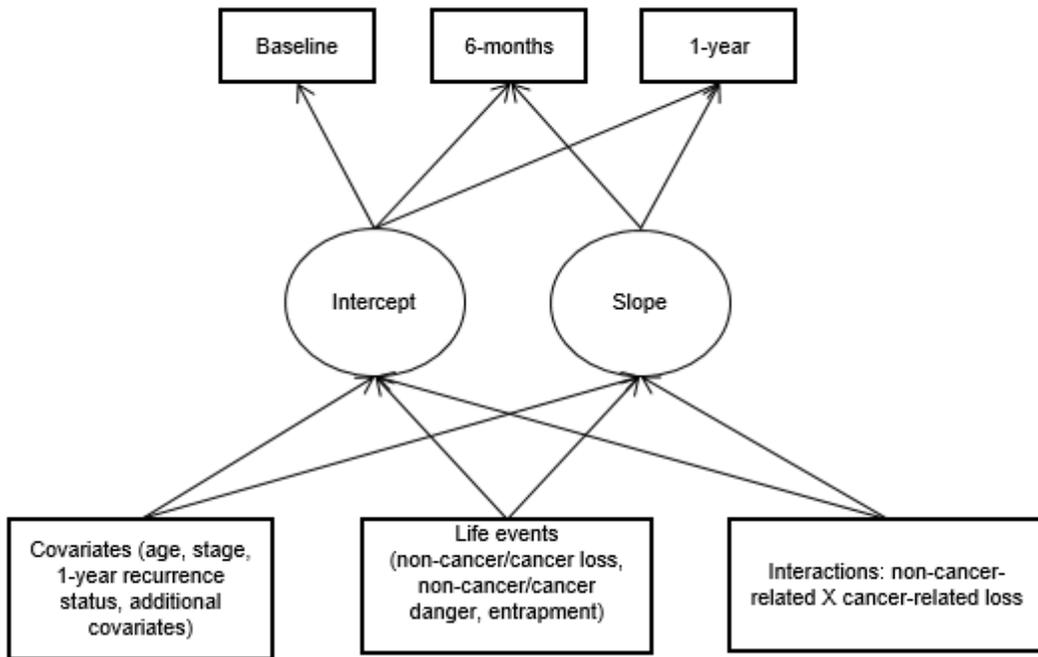


Figure 5. General Model of Conditional Latent Growth Curves

*Distress.* The conditional model for distress using all stressors as predictors had good fit to the data ( $\chi^2=12.59$ ,  $p=.56$ ; RMSEA=0; CFI=1; TLI=1.03; SRMR=.02; BIC=2960.03).

Parameter estimates are displayed in Table 13. Surprisingly, the only significant predictor that emerged was cancer loss ( $\beta=0.71$ ,  $p=.03$ ) predicting the slope of distress over time.

Table 13. Parameter Estimates for Conditional Latent Growth Curve Predicting Distress

Outcome Variable	Predictor Variables	All stressors		Major stressors	
		$\beta$	p-value	$\beta$	p-value
Intercept	Age	-0.10	0.39	-0.15	0.15
	Stage	0.12	0.30	0.15	0.20
	History of psychiatric treatment	0.20	0.11	0.24	0.05
	Loss (non-cancer)	0.05	0.73	0.08	0.42
	Cancer loss	-0.17	0.26	-0.10	0.47
	Danger (non-cancer)	0.07	0.63	0.23	0.05
	Cancer danger	-0.07	0.61	0.07	0.60
	Entrapment	0.13	0.52	-0.08	0.52
	Loss interaction (cancer x non-cancer)	-0.09	0.32	-0.12	0.23
	Danger interaction (cancer x non-cancer)	-0.05	0.42	-0.22	0.04
	Slope	Age	0.25	0.38	0.16
Stage		-0.30	0.32	-0.21	0.56
History of psychiatric treatment		0.04	0.89	-0.003	0.99
1 year recurrence status		-0.04	0.83	-0.12	0.64
Loss (non-cancer)		0.16	0.68	0.37	0.14
Cancer loss		0.71	0.03	0.62	0.06
Danger (non-cancer)		0.11	0.67	0.02	0.95
Cancer danger		0.10	0.75	0.03	0.92
Entrapment		0.42	0.09	0.55	0.10
Loss interaction (cancer x non-cancer)		-0.15	0.20	-0.13	0.38
Danger interaction (cancer x non-cancer)		-0.06	0.22	-0.05	0.62
Growth parameters	Intercept Mean	30.06	<0.001	28.44	<0.001
	Slope Mean	-11.32	0.02	-10.99	0.02

Note. Models examining all stressors included both minor and major stressors. Unstandardized coefficients for interaction terms are shown.

The interaction between cancer loss and time was probed for simple slopes at various levels of cancer loss (the mean and  $\pm 1$  SDs above/below the mean), which are shown in Figure 6. For those with high cancer loss, the effect of time on distress is not significant ( $b=-5.77$ ,  $p=0.29$ ). In other words, distress stays the same over time if one experiences high levels of cancer loss. For average levels of cancer loss ( $b=-11.32$ ,  $p=0.01$ ) and low levels of cancer loss ( $b=-16.87$ ,  $p=0.003$ ), the effect of time on distress is significantly negative, indicating that distress decreases over time. This relationship is strongest when cancer loss is below average. In other words, only in those with low or average levels of cancer-related loss does distress improve over the year post-diagnosis.

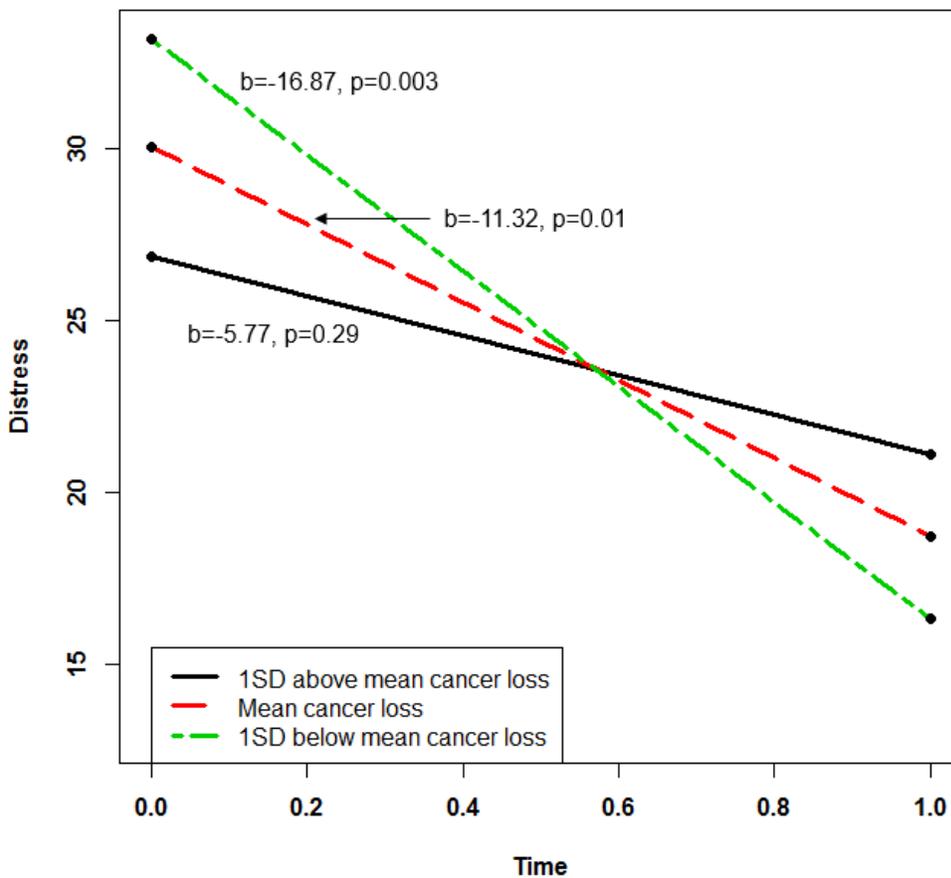


Figure 6. Effect of Time on Distress at Various Levels of Cancer Loss

The model examining only major stressors also had good fit to the data ( $\chi^2=11.19$ ,  $p=.67$ ; RMSEA=0; CFI=1; TLI=1.06; SRMR=0.02; BIC=2960.48). Again, parameter estimates are shown in Table 13. In this model, major cancer loss was only marginally related to slope ( $\beta=0.62$ ,  $p=0.06$ ). Additionally, history of psychiatric treatment, non-cancer-related danger stressors, and the danger stressor interaction (non-cancer-related \* cancer-related) significantly predicted baseline levels of distress. History of psychiatric treatment (coded 1 for yes) was related to higher overall distress ( $\beta=0.24$ ,  $p=.05$ ). Greater threat associated with major non-cancer-related danger was associated with higher overall distress at baseline ( $\beta=0.23$ ,  $p=0.05$ ).

The interaction between major cancer-related danger and major non-cancer related danger was negative ( $b=-0.22$ ,  $p=0.04$ ), indicating that, as cancer-related danger increases, the effect of non-cancer danger on baseline levels of distress decreases. Simple slopes of the relationship between major non-cancer danger and distress at differing levels of major cancer-related danger (the mean and  $\pm 1$  SDs above/below the mean) are displayed in Figure 7. At high levels of major cancer-related danger ( $b=-0.32$ ,  $p=0.68$ ) and average levels of major cancer-related danger ( $b=1.08$ ,  $p=0.06$ ), the effect of major non-cancer danger on distress was not significant. In other words, at average and high levels of major danger related to cancer, additional major non-cancer danger has no impact on overall distress at baseline. However, at low levels of major cancer-related danger, the effect of major non-cancer danger is significant ( $b=2.45$ ,  $p=0.005$ ), such that higher levels of threat experienced due to major non-cancer danger stressors is associated with higher distress at baseline.

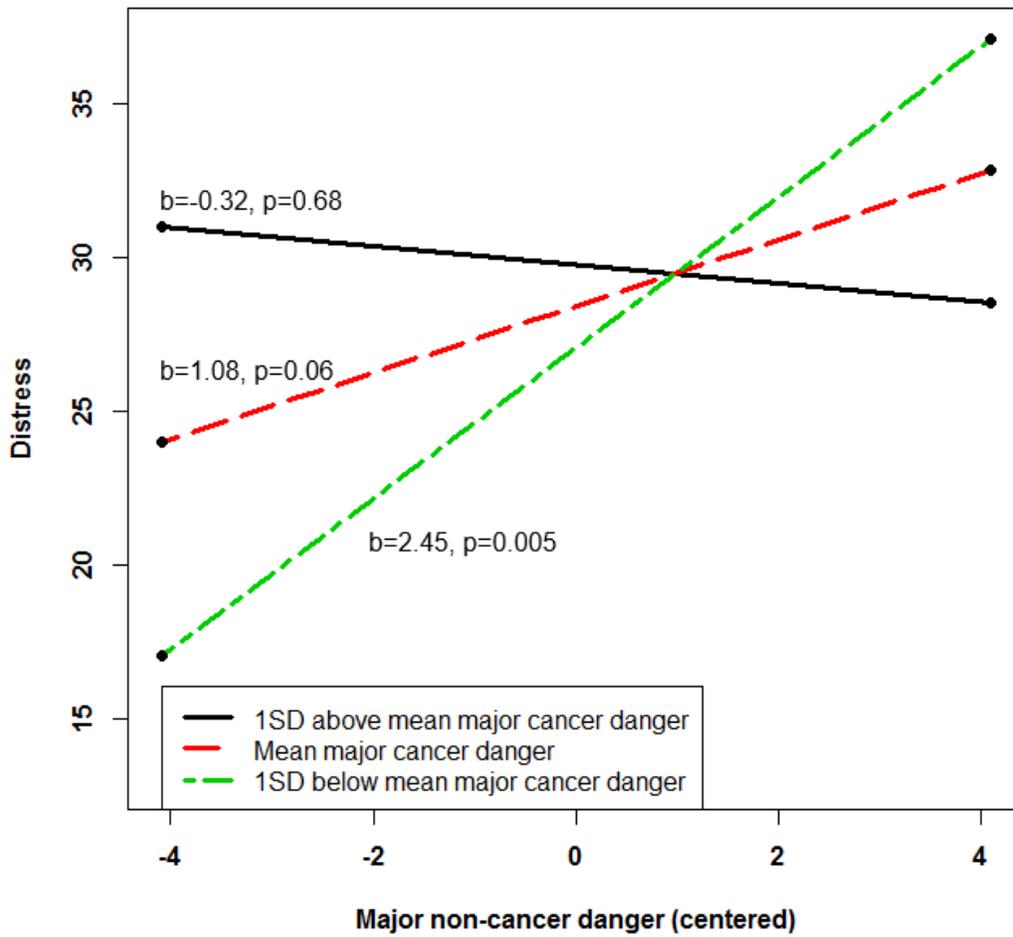


Figure 7. Effect of Major Non-Cancer Danger on Baseline Distress at Varying Levels of Major Cancer Danger

**Depressed mood.** The conditional model for depressed mood using all stressors as predictors had good fit to the data ( $\chi^2=8.86$ ,  $p=0.78$ ; RMSEA=0; CFI=1; TLI=1.14; SRMR=.02; BIC=1019.12). No variables emerged as significant predictors of baseline depressed mood (See Table 14).

Table 14. Parameter Estimates for Conditional Latent Growth Curve Predicting Depressed Mood

Outcome Variable	Predictor Variables	All stressors		Major stressors	
		$\beta$	p-value	$\beta$	p-value
<b>Intercept</b>	Age	-0.20	0.08	-0.26	0.02
	Stage	0.18	0.21	0.21	0.13
	Loss (non-cancer)	-0.07	0.70	0.04	0.76
	Cancer loss	-0.30	0.09	-0.29	0.06
	Danger (non-cancer)	0.09	0.61	0.20	0.22
	Cancer danger	-0.19	0.25	-0.09	0.55
	Entrapment	0.09	0.50	-0.08	0.51
	Loss interaction (cancer x non-cancer)	-0.001	0.95	-0.01	0.92
	Danger interaction (cancer x non-cancer)	-0.009	0.60	-0.24	0.13
	<b>Slope</b>	Age	0.29	0.12	0.30
Stage		-0.29	0.18	-0.25	0.27
1 year recurrence status		-0.13	0.40	-0.13	0.42
Loss (non-cancer)		0.34	0.26	0.38	0.03
Cancer loss		0.73	0.004	0.76	<0.001
Danger (non-cancer)		-0.22	0.39	-0.15	0.56
Cancer danger		0.16	0.57	0.22	0.31
Entrapment		0.16	0.40	0.27	0.16
Loss interaction (cancer x non-cancer)		-0.04	0.05	-0.40	0.02
Danger interaction (cancer x non-cancer)		-0.01	0.36	-0.08	0.74
<b>Growth parameters</b>	Intercept Mean	5.76	<0.001	5.52	<0.001
	Slope Mean	-2.19	0.02	-2.13	0.02

Note. Models examining all stressors included both minor and major stressors. Unstandardized coefficients for interaction terms are shown.

Cancer loss ( $\beta=0.73$ ,  $p=0.004$ ) was significantly related to slope of depressed mood over time, such that greater loss resulted in less of a decrease in depressed mood over time. Simple

slopes for the effect of time on depressed mood at different levels of cancer loss are displayed in Figure 8. Similar to the relationship between cancer loss and overall distress, the effect of time at high levels of cancer loss is not significant ( $b=-0.71$ ,  $p=0.51$ ). However, at average levels of cancer loss ( $b=-2.19$ ,  $p=0.02$ ) and low levels of cancer loss ( $b=-3.66$ ,  $p<0.001$ ), depressed mood significantly decreases over time. In other words, only those with low or average levels of cancer loss exhibit an improvement in depressed mood throughout the year post-diagnosis, while those with high levels of cancer loss show increased depressed mood over time. Of note, this effect controls for the effect of cancer loss on depressed mood at baseline, which was not statistically significant ( $\beta=-0.30$ ,  $p=0.09$ ).

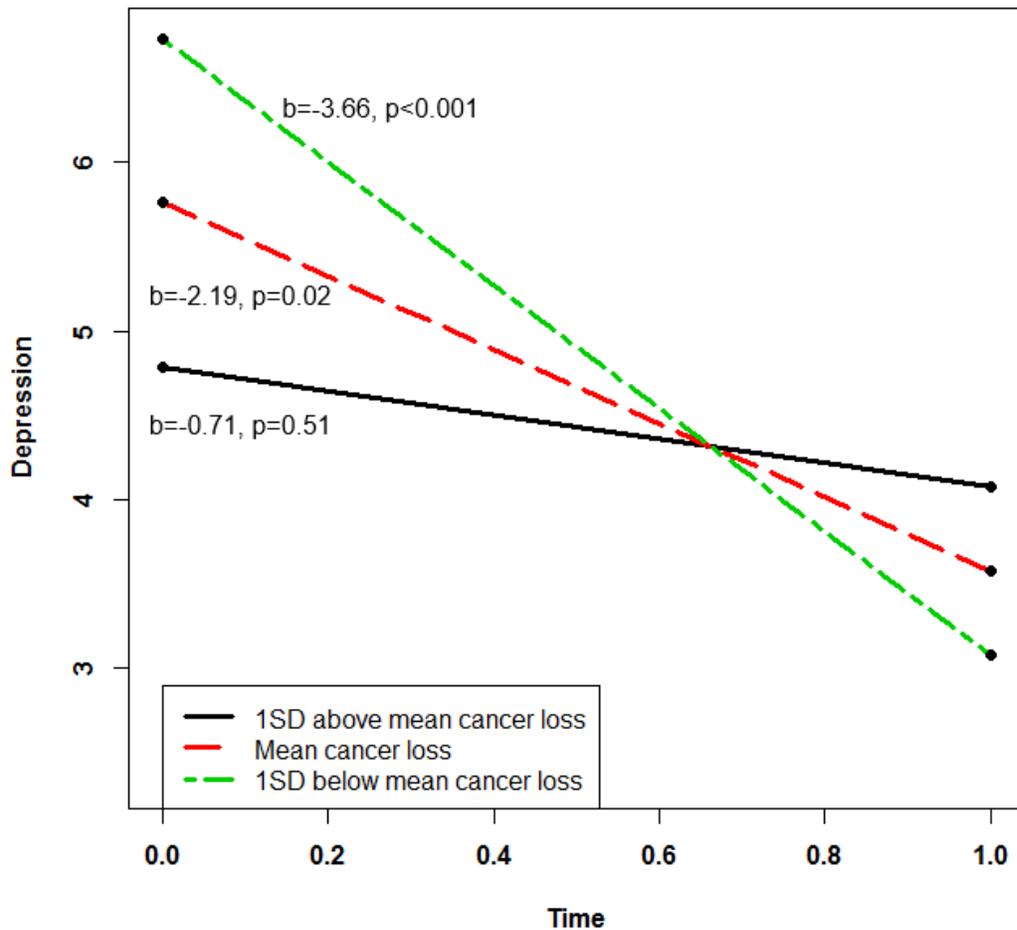


Figure 8. Effect of Time on Depressed Mood at Different Levels of Cancer Loss

Furthermore, the interaction between cancer loss and non-cancer loss in predicting depressed mood over time was significant ( $b=-0.04$ ,  $p=0.05$ ) and was probed further. Simple slopes revealed that only when cancer loss and non-cancer loss is low (both at 1SD below the mean) does depressed mood decrease significantly over time ( $b=-5.49$ ,  $p<0.001$ ). When threat experienced to either type of loss or to both types of losses is high (1SD above the mean), the effect of time on depressed mood is not significant ( $b$ 's ranging from  $-1.84$  to  $-0.25$ , all  $p$  values  $>0.14$ ). In other words, only those with both low levels of non-cancer loss and cancer loss showed improvement in depressed mood symptoms throughout the year post-diagnosis. Simple slopes for the effect of time at different levels of non-cancer loss and at 1SD below the mean of cancer loss are displayed in Figure 9.

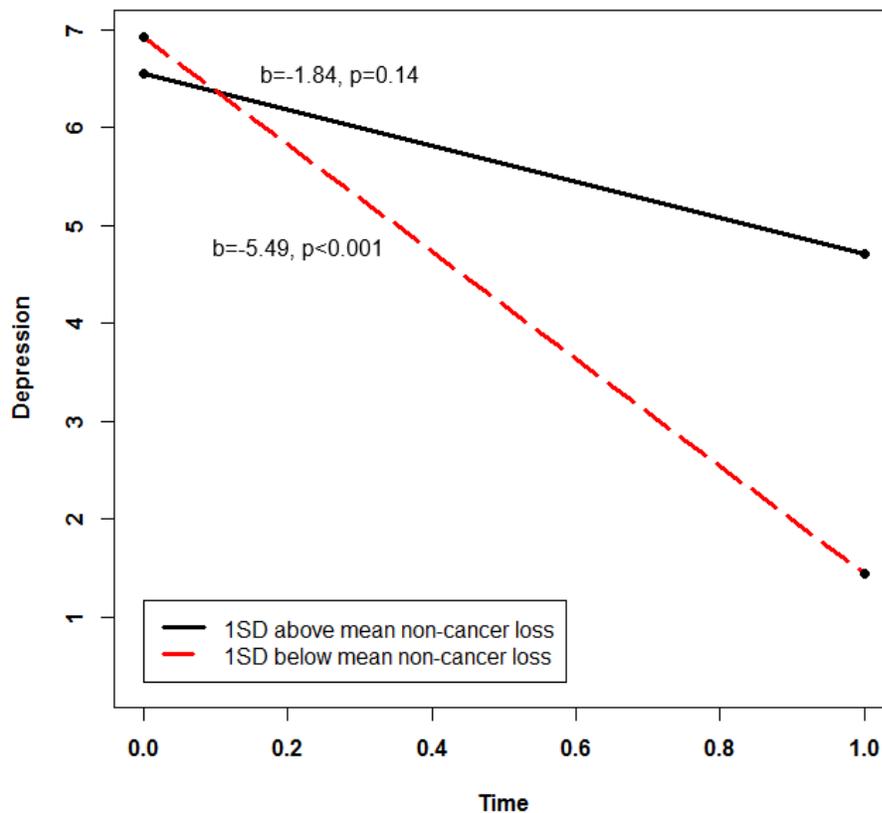


Figure 9. Effect of Time on Depressed Mood at Low Levels of Cancer Loss Paired With Different Levels of Non-Cancer Loss

The model including only major stressors predicting depressed mood had good fit to the data as well ( $\chi^2=7.53$ ,  $p=0.87$ ; RMSEA=0; CFI=1; TLI=1.17; SRMR=0.02; BIC=2018.33), and indicated a significant change in depressed mood over time ( $M=-2.13$ ,  $p=0.02$ ). Age was a significant predictor of depressed mood at baseline, such that higher age was associated with lower depressed mood ( $\beta=-0.26$ ,  $p=0.02$ ). Again, no major stressor variables significantly predicted depressed mood at baseline. However, major non-cancer loss ( $\beta=0.38$ ,  $p=0.03$ ) and major cancer loss ( $\beta=0.76$ ,  $p<0.001$ ), both predicted slope of depressed mood over time, such that greater levels of threat associated with each type of stressor was related to a flatter slope. The patterns in simple slopes were similar to the findings for all cancer losses and depressed mood, as the effect of time on depressed mood was not significant at high levels of major cancer-related loss ( $b=-0.56$ ,  $p=0.58$ ) and major non-cancer loss ( $b=-1.40$ ,  $p=0.14$ ). In other words, high levels of major loss (both non-cancer related and cancer-related) prevents improvement in depressed mood throughout the year after diagnosis. The interaction between major cancer losses and major non-cancer losses was similar to the interaction effect when including all losses ( $b=-0.20$ ,  $p=0.02$ ), as only at low levels of both types of losses did depressed mood decrease over time ( $b=-5.36$ ,  $p<0.001$ ). Having high levels of either major cancer loss, major non-cancer loss, or both, predicted consistent depressed mood over time.

**Anger.** The conditional model for anger using all stressors as predictors had good fit to the data ( $\chi^2=7.77$ ,  $p=0.93$ ; RMSEA=0; CFI=1; TLI=1.24; SRMR=0.02; BIC=1982.87), and parameter estimates are displayed in Table 15. Interestingly, though no life stress variables significantly predicted anger at baseline or over time directly, the interaction between cancer-related loss and non-cancer loss significantly predicted baseline anger ( $b=-0.38$ ,  $p=0.04$ ). This interaction was not significant when including only major stressors ( $b=-0.19$ ,  $p=.21$ ), a model

which also fit the data well ( $\chi^2=11.12$ ,  $p=0.74$ ; RMSEA=0; CFI=1; TLI=1.12; SRMR=0.02; BIC=1984.38). In the model including only major stressors, history of psychiatric treatment was related to greater anger at baseline ( $\beta=0.26$ ,  $p=0.03$ ). In both the models with all stressors and only major stressors, the slope of anger over time was not significant, so variables that emerged as significant predictors of slope were not examined.

Table 15. Parameter Estimates for Conditional Latent Growth Curve Predicting Anger

Outcome Variable	Predictor Variables	All stressors		Major stressors	
		$\beta$	p-value	$\beta$	p-value
Intercept	Age	-0.12	0.33	-0.15	0.25
	Stage	0.12	0.24	0.15	0.16
	History of psychiatric treatment	0.21	0.09	0.26	0.03
	Presence of comorbidities	0.22	0.11	0.24	0.08
	Loss (non-cancer)	0.08	0.54	0.12	0.28
	Cancer loss	-0.06	0.69	-.01	0.95
	Danger (non-cancer)	-0.09	0.50	-0.05	0.68
	Cancer danger	0.05	0.74	0.11	0.48
	Entrapment	0.03	0.76	-0.03	0.85
	Loss interaction (cancer x non-cancer)	-0.38	0.04	-0.05	0.23
	Danger interaction (cancer x non-cancer)	-0.001	0.93	-0.001	0.97
Slope	Age	0.05	0.88	-0.11	0.76
	Stage	-0.38	0.16	-0.18	0.45
	History of psychiatric treatment	0.08	0.77	0.03	0.92
	Presence of comorbidities	-0.19	0.52	-0.11	0.72
	1 year recurrence status	-0.12	0.51	-0.15	0.43
	Loss (non-cancer)	0.13	0.62	0.18	0.50
	Cancer loss	0.50	0.09	0.29	0.30
	Danger (non-cancer)	0.53	0.01	0.60	0.001
	Cancer danger	0.10	0.77	0.02	0.95
	Entrapment	0.50	0.04	0.21	0.47
	Loss interaction (cancer x non-cancer)	-0.001	0.97	-0.02	0.56
Danger interaction (cancer x non-cancer)	-0.02	0.08	-0.04	0.01	

Table 15 – Continued

<b>Growth parameters</b>	Intercept Mean	2.78	0.002	2.42	<0.001
	Slope Mean	0.24	0.80	-.01	0.99

Note. Models examining all stressors included both minor and major stressors. Unstandardized coefficients for interaction terms are shown.

The interaction between cancer and non-cancer losses in predicting baseline anger was probed further. Simple slopes of the relationship between non-cancer loss and anger at differing levels of cancer-related loss (the mean and  $\pm$ SD above/below the mean) are displayed in Figure 10. At average levels of cancer-related loss ( $b=0.04$ ,  $p=0.53$ ) and high levels of cancer loss ( $b=-1.10$ ,  $p=0.13$ ), the threat experienced due to non-cancer loss was unrelated to anger at baseline. At low levels of threat due to cancer losses, the effect of non-cancer loss on anger is positive ( $b=0.18$ ,  $p=0.001$ ), such that greater threat is associated with greater anger. In other words, only when cancer-related loss is low does non-cancer loss predicted more anger at baseline.

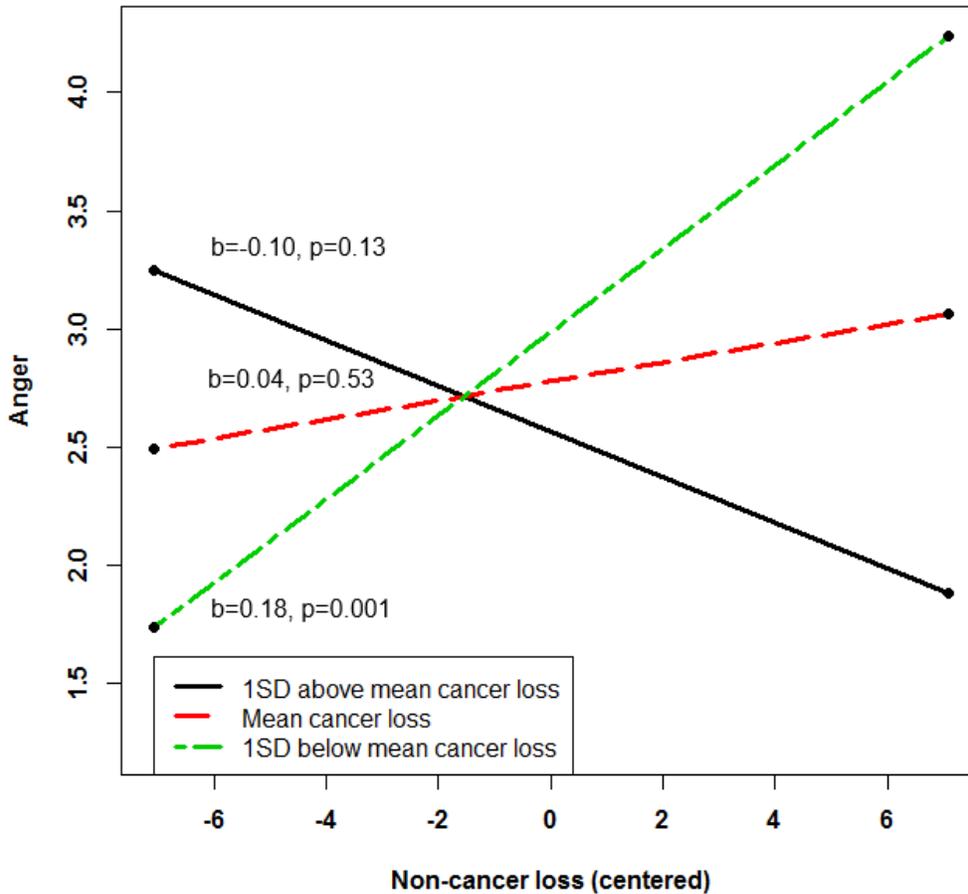


Figure 10. Effect of Non-Cancer Loss on Baseline Anger at Different Levels of Cancer Loss

**Fatigue.** The conditional model for fatigue including all stressors had good fit to the data ( $\chi^2=19.69$ ,  $p=0.23$ ; RMSEA=0.04; CFI=0.95; TLI=0.87; SRMR=0.04; BIC=2302.49), along with the model including only major stressors ( $\chi^2=15.49$ ,  $p=0.49$ ; RMSEA=0; CFI=1; TLI=1.02; SRMR=0.03; BIC=2315.21). In both models, the slope of fatigue over time was not significant, indicating that fatigue did not change over time (for parameter estimates, see Table 16). Thus, only predictors of baseline fatigue were examined. In both models, high cancer grade, and the use of pain medications were significantly related to greater fatigue at baseline ( $\beta$ s ranging from 0.30-0.46, all  $p$ 's<0.02). The only stressor that predicted fatigue at baseline was non-cancer loss,

such that total threat of all non-cancer losses ( $\beta=0.43$ ,  $p=0.003$ ), as well as total threat of only major non-cancer losses ( $\beta=0.26$ ,  $p=0.03$ ) were related to greater fatigue at baseline.

Table 16. Parameter Estimates for Conditional Latent Growth Curve Predicting Fatigue

Outcome Variable	Predictor Variables	All stressors		Major stressors	
		$\beta$	p-value	$\beta$	p-value
<b>Intercept</b>	Age	-0.03	0.72	-0.07	0.44
	Stage	-0.13	0.35	-0.11	0.41
	Cancer grade	0.40	<0.001	0.46	<0.001
	Use of pain medications	0.30	0.007	0.30	0.01
	Loss (non-cancer)	0.43	0.003	0.26	0.03
	Cancer loss	0.01	0.94	-0.01	0.95
	Danger (non-cancer)	-0.14	0.15	0.04	0.72
	Cancer danger	-0.07	0.61	0.02	0.88
	Entrapment	0.01	0.96	0.03	0.71
	Loss interaction (cancer x non-cancer)	0.02	0.49	-0.001	0.93
	Danger interaction (cancer x non-cancer)	-0.01	0.56	-0.04	0.15
	<b>Slope</b>	Age	0.15	0.41	0.16
Stage		0.05	0.82	0.21	0.54
Cancer grade		-0.56	0.002	-0.68	0.01
Use of pain medications		-0.49	0.02	-0.60	0.03
1 year recurrence status		0.07	0.74	0.09	0.77
Loss (non-cancer)		-0.09	0.78	0.15	0.59
Cancer loss		0.57	0.04	0.44	0.20
Danger (non-cancer)		0.12	0.55	0.01	0.97
Cancer danger		0.41	0.18	0.32	0.32
Entrapment		0.02	0.94	-0.07	0.86
Loss interaction (cancer x non-cancer)		-0.05	0.04	-0.03	0.46
Danger interaction (cancer x non-cancer)		-0.01	0.46	0.002	0.92
<b>Growth parameters</b>	Intercept Mean	15.11	<0.001	13.71	<0.001
	Slope Mean	1.25	0.35	0.68	0.67

Note. Models examining all stressors included both minor and major stressors. Unstandardized coefficients for interaction terms are shown.

**Specific Aim #2: To evaluate competing models of the functional relationships between protective psychosocial factors (social support, mastery, self-acceptance, purpose in life) and life stress on psychological functioning as women face surgery and throughout the year after.**

**Independent effects.** The first set of models examining the impact of psychosocial resources on psychological functioning included direct effects for social support, mastery, self-acceptance, and purpose in life. Again, each model was run twice – once with all stressor variables included and another with only major stressor variables included. Each model included control variables from the previously described analyses. Each model of independent effects fit the data well. Parameter estimates for the main effects of protective psychosocial resources on all outcomes are shown in Table 17. Surprisingly, social support was positively related to fatigue at baseline in both models (all stressors:  $\beta=0.39$ ,  $p=0.006$ ; major stressors:  $\beta=0.27$ ,  $p=0.04$ ). Self-acceptance was related to lower fatigue at baseline, but only in the model including all stressors ( $\beta=-0.33$ ,  $p=0.05$ ). Independent effects of mastery and self-acceptance were approaching significance for predicting baseline depressed mood in the model with all stressors as control variables ( $p$  values of .07 and .08, respectively). Mastery was related to lower distress ( $\beta=-0.39$ ,  $p=0.05$ ) and depressed mood ( $\beta=-0.47$ ,  $p=0.02$ ) in the models including major stressors. No protective resources had direct effects on anger.

No psychosocial resources were directly related to the slope of distress or depressed mood. Furthermore, in these models, the average slope of anger and fatigue over time was not significant so effects of psychosocial resources on slope were not examined. Thus, clearly the hypothesis that each protective resource would be independently related to psychological functioning was rejected.

Table 17. Parameter Estimates from Latent Growth Curves of Independent Effect of Psychosocial Resources

<b>Outcome</b>	<b>Social Support</b>	<b>Mastery</b>	<b>Purpose in Life</b>	<b>Self-acceptance</b>
	<b>β</b>	<b>β</b>	<b>β</b>	<b>β</b>
<b>Distress Intercept</b>				
All stressors	-0.16	-0.34	-0.02	-0.35
Major stressors	-0.22	-0.39*	-0.01	-0.30
<b>Distress Slope</b>				
All stressors	0.48	-0.13	0.55	-0.45
Major stressors	0.55	-0.11	0.50	-0.40
<b>Depressed Mood Intercept</b>				
All stressors	0.12	-0.41	-0.05	-0.47
Major stressors	0.05	-0.47*	0.09	-0.44
<b>Depressed Mood Slope</b>				
All stressors	-0.34	0.04	0.31	0.10
Major stressors	-0.13	0.09	0.19	0.04
<b>Anger Intercept</b>				
All stressors	-0.21	-0.22	-0.11	-0.25
Major stressors	-0.21	-0.24	-0.11	-0.26
<b>Fatigue Intercept</b>				
All stressors	0.39*	-0.21	-0.12	-0.33*
Major stressors	0.27*	-0.31	-0.06	-0.30

Note: Models examining all stressors included both minor and major stressors. \* $p < .05$ . Anger and fatigue did not exhibit significant change over time, so effects on slope of these variables were not examined.

**Multiple moderators.** The next set of models examined each protective resource as a moderator of life events. Models including all stressors did not fit the data well compared to models including only major stressors, as evidenced by higher and significant  $\chi^2$  values, RMSEAs, lower CFIs and TLIs, and significantly higher BIC scores (see Tables). Furthermore, the model examining fatigue over time including only major stressors did not fit the data well, with a significant  $\chi^2$  value, RMSEA >0.04, and CFI and TLI <0.95. Thus, only significant effects from models including major stressors, and predicting distress, depressed mood, and anger were examined. Parameter estimates for the interaction effects from these models are displayed in Table 18.

Table 18. Interaction Effects in Multiple Moderator Models of Psychosocial Resources

Outcome	Stressor	Psychosocial Resource	b, Distress	b, Depressed Mood	b, Anger
<b>Intercept</b>	Interactions with major loss (non-cancer)	Social support	-0.08	0.04	-0.02
		Mastery	-0.04	-0.02	-0.02
		Purpose in life	-0.05	-0.02	0.02
		Self-acceptance	0.01	0.004	-0.02
	Interactions with major cancer loss	Social support	-0.06	0.01	0.10
		Mastery	0.03	0.02	-0.03
		Purpose in life	-0.06	-0.02	0.00
		Self-acceptance	0.35	0.06	0.05
	Interactions with major danger (non-cancer)	Social support	-0.01	0.02	-0.08
		Mastery	-0.13	0.00	-0.03
		Purpose in life	-0.07	-0.01	-0.01
		Self-acceptance	0.15	-0.01	0.06*
	Interactions with major cancer danger	Social support	-0.57*	-0.13*	-0.09
		Mastery	-0.12	-0.02	-0.01
		Purpose in life	-0.02	-0.01	0.00
		Self-acceptance	0.16	0.02	0.01
	Interactions with major entrapment	Social support	-0.39	-0.04	-0.08
		Mastery	0.24	0.04	0.07*
		Purpose in life	0.03	-0.01	0.01
		Self-acceptance	-0.10	-0.02	-0.03
<b>Slope</b>	Interactions with major loss (non-cancer)	Social support	0.31	0.03	0.06
		Mastery	0.06	0.01	0.03
		Purpose in life	-0.03	0.01	-0.03
		Self-acceptance	-0.03	-0.01	0.01
	Interactions with major cancer loss	Social support	-0.25	-0.03	-0.15
		Mastery	-0.08	-0.01	0.00
		Purpose in life	0.06	0.05	-0.02
		Self-acceptance	-0.35	-0.10 <sup>a</sup>	-0.03
	Interactions with major danger (non-cancer)	Social support	-1.40 <sup>a</sup>	-0.26 <sup>a</sup>	-0.28
		Mastery	0.14	0.03	0.01
		Purpose in life	0.13	0.01	0.03
		Self-acceptance	-0.19	-0.02	-0.04
	Interactions with major cancer danger	Social support	0.24	0.04	0.10
		Mastery	0.21 <sup>a</sup>	0.04	0.03
		Purpose in life	-0.09	-0.02	-0.02
		Self-acceptance	-0.19	-0.03	-0.04
	Interactions with major entrapment	Social support	0.41	0.06	-0.10
		Mastery	-0.11	0.00	-0.03
		Purpose in life	-0.24	-0.03	-0.01
		Self-acceptance	0.23	0.02	0.04

Note. Models examining all stressors included both minor and major stressors. \* $p \leq 0.05$ . <sup>a</sup> $p \leq 0.05$ , but average slope is not significant. Models included all main effects as well as control variables from previous models.

Social support emerged as a significant moderator of major cancer danger on distress ( $b=-0.57$ ,  $p=0.04$ ) and depressed mood ( $b=-0.13$ ,  $p=0.02$ ), such that the positive relationship between major cancer stressors and worse psychological functioning at baseline decreased as social support increased. Simple slopes for the effect of major cancer danger on distress at varying levels of social support (the mean and  $\pm 1SD$  above/below the mean) are displayed in Figure 11. At average levels of social support ( $b=0.81$ ,  $p=0.05$ ) and low levels of social support ( $b=1.94$ ,  $p<0.001$ ), the effect of major cancer danger on distress is significantly positive, such that higher threat associated with major cancer danger stressors results in higher distress at baseline. At high levels of social support, this effect is non-significant ( $b=-0.32$ ,  $p=0.69$ ). In other words, major cancer danger results in greater distress at baseline only when social support is average or below average.

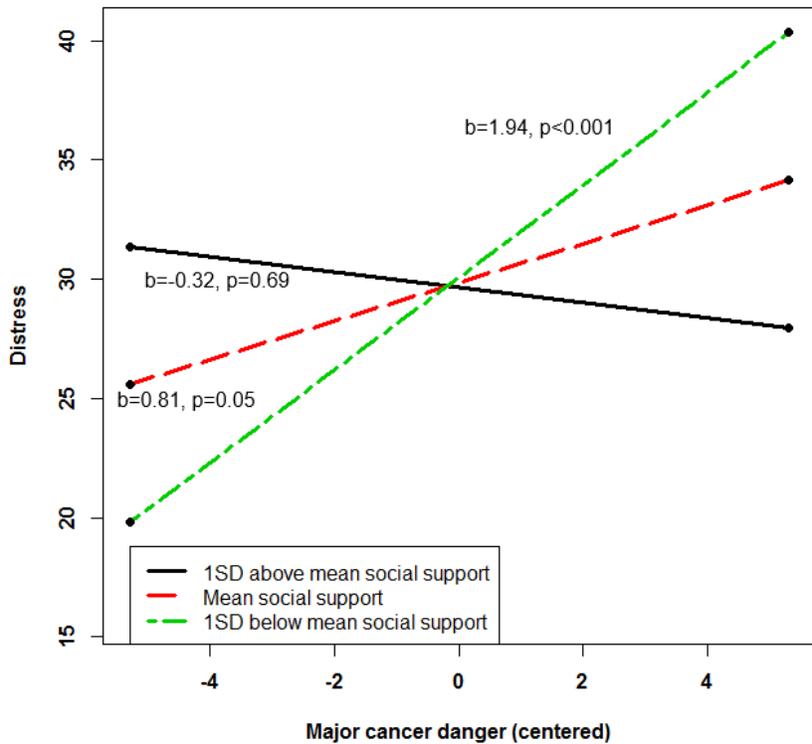


Figure 11. Effect of Major Cancer Danger on Distress at Baseline at Varying Levels of Social Support

Alternatively, the relationship between major cancer danger and depressed mood becomes significant only when social support is high ( $b=-0.34$ ,  $p=0.03$ ), such that high levels of threat due to major cancer danger paired with high levels of social support results in less depressed mood at baseline (Figure 12). The effect of major cancer danger on depressed mood at baseline was not significant at average ( $b=-0.09$ ,  $p=0.31$ ) and low levels of social support ( $b=0.17$ ,  $p=0.16$ ).

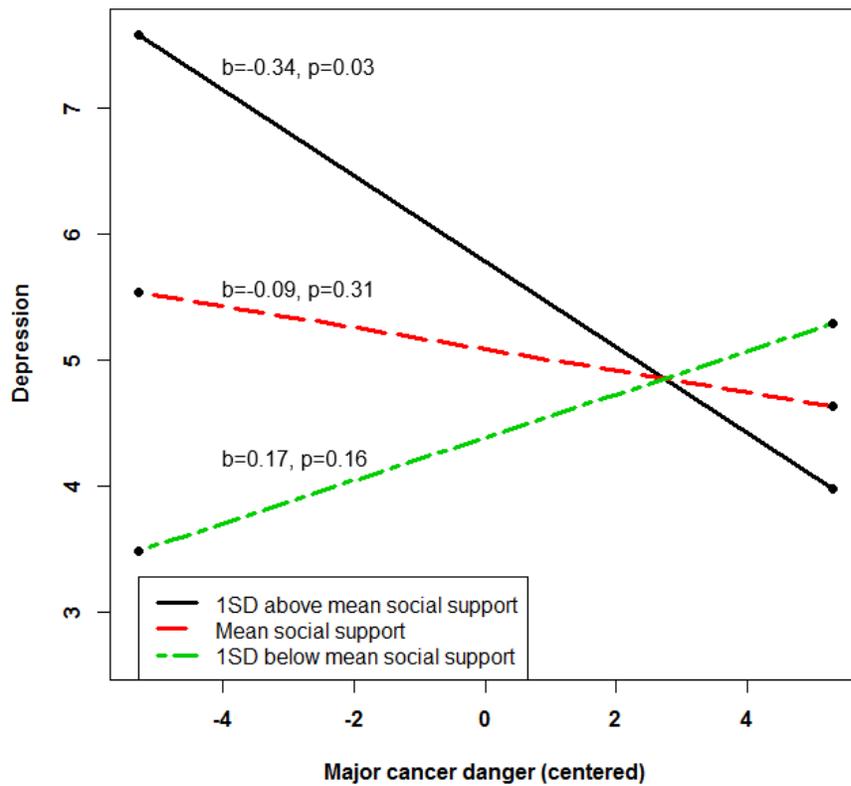


Figure 12. Effect of Major Cancer Danger on Baseline Depressed Mood at Varying Levels of Social Support

Interestingly, self-acceptance significantly moderated the effects of major non-cancer danger on anger, but in a different direction than the previous relationships ( $b=0.06$ ,  $p=0.03$ ). Simple slopes at the mean  $\pm$  1SD above/below the mean of self-acceptance (shown in Figure 13) revealed that, only at low levels of self-acceptance was the relationship between major cancer danger and anger significant, such that greater threat was related to less anger ( $b=-0.49$ ,  $p=0.02$ ). At average levels of self-acceptance ( $b=-0.01$ ,  $p=0.94$ ), and high levels of self-acceptance ( $b=0.46$ ,  $p=0.15$ ), threat due to major cancer danger was unrelated to anger. Similarly, mastery moderated the effects of major entrapment on anger ( $b=0.07$ ,  $p=0.04$ ), with a significant negative relationship between entrapment and anger only at low levels of mastery ( $b=-0.57$ ,  $p=0.02$ ).

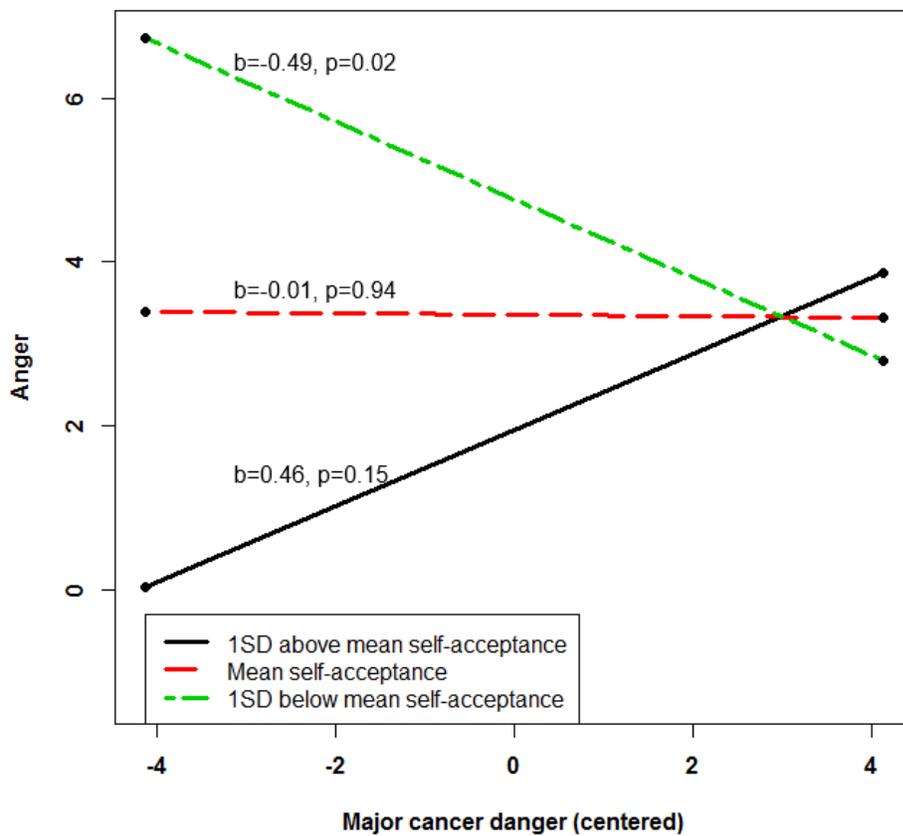


Figure 13. Effect of Major Cancer Danger on Baseline Anger at Different Levels of Self-Acceptance

**Multiple mediators and social support as moderator.** The first model that was run with multiple mediators of purpose in life, mastery, and self-acceptance with social support as a moderator (distress as the outcome), had very poor model fit ( $\chi^2=280.69$ ,  $p<0.001$ ; RMSEA=0.20; CFI=0.45; TLI=-0.08; SRMR=0.12; BIC=4970.48). Upon examination of modification indices, correlations between psychosocial resources were included in the model. This resulted in substantial fit improvement, ( $\chi^2=95.99$ ,  $p=0.004$ ; RMSEA=0.07; CFI=0.92; TLI=0.86; SRMR=0.09; BIC=5255.30), and thus, all following models included these correlations.

Across all outcomes, these models fit significantly worse than the independent effects models, as evidenced by higher  $\chi^2$  values, higher RMSEAs, lower CFIs and TLIs, and significantly higher BIC scores. The models predicting distress, depressed mood, and anger and including only major stressors fit the data relatively well compared to models examining all stressors. Because the models predicting distress and depressed mood with only major stressors had good fit according to multiple, but not all criteria (RMSEA $\leq$ 0.06, CFI $\geq$ 0.95, SRMR $\leq$ 0.08), the model parameters were examined further. Parameter estimates, including bootstrapped confidence intervals for indirect effects, for these models are displayed in Table 19.

Table 19. Multiple Mediator Models with Social Support as Moderator

Outcome	Stressor	Psychosocial Resource	$\beta$ , Distress (95% CI)	$\beta$ , Depressed Mood (95% CI)	
<b>Intercept</b>	Interactions with social support <sup>a</sup>	Major loss (non-cancer)	-0.26	0.03	
		Major cancer loss	0.64	0.12	
		Major danger (non-cancer)	-0.27	-0.11	
		Major cancer danger	-0.42	-0.10	
		Major entrapment	0.16	0.01	
	Indirect effects: major loss (non-cancer)	Mastery	0.05 (-0.03, 0.12)	0.05 (-0.02, 0.12)	
		Purpose in life	0 (-0.03, 0.03)	-0.01 (-0.04, 0.03)	
		Self-acceptance	0.03 (-0.03, 0.09)	0.04 (-0.03, 0.12)	
	Indirect effects: major cancer loss	Mastery	-0.01 (-0.07, 0.05)	-0.01 (-0.08, 0.06)	
		Purpose in life	0.001 (-0.04, 0.038)	0.01 (-0.03, 0.06)	
		Self-acceptance	-0.01 (-0.07, 0.05)	-0.01 (-0.08, 0.05)	
	Indirect effects: major danger (non-cancer)	Mastery	0.01 (-0.05, 0.07)	0.01 (-0.05, 0.07)	
		Purpose in life	0 (-0.02, 0.02)	-0.003 (-0.03, 0.03)	
		Self-acceptance	0.04 (-0.04, 0.11)	0.06 (-0.03, 0.14)	
	Indirect effects: major cancer danger	Mastery	0.002 (-0.06, 0.06)	0.002 (-0.06, 0.07)	
		Purpose in life	0 (-0.02, 0.02)	-0.002 (-0.03, 0.03)	
		Self-acceptance	-0.04 (-0.12, 0.04)	-0.06 (-0.15, 0.02)	
	Indirect effects: major entrapment	Mastery	0.05 (-0.06, 0.16)	0.05 (-0.06, 0.17)	
		Purpose in life	0.001 (-0.02, 0.03)	0.01 (-0.02, 0.04)	
		Self-acceptance	-0.04 (-0.16, 0.07)	-0.07 (-0.20, 0.06)	
	<b>Slope</b>	Interactions with social support <sup>a</sup>	Major loss (non-cancer)	0.49	0.04
			Major cancer loss	-1.20	-0.19
			Major danger (non-cancer)	-1.15*	-0.09
			Major cancer danger	0.10	0.03
Major entrapment			0.27	-0.02	
Indirect effects: major loss (non-cancer)		Mastery	0.001 (-0.06, 0.06)	-0.01 (-0.07, 0.05)	
		Purpose in life	-0.01 (-0.06, 0.04)	-0.01 (-0.05, 0.04)	
		Self-acceptance	0.01 (-0.04, 0.06)	-0.01 (-0.06, 0.04)	
Indirect effects: major cancer loss		Mastery	0 (-0.03, 0.03)	0.002 (-0.04, 0.04)	
		Purpose in life	0.03 (-0.02, 0.09)	0.02 (-0.04, 0.07)	
		Self-acceptance	-0.004 (-0.04, 0.03)	0.004 (-0.04, 0.04)	
Indirect effects: major danger (non-cancer)		Mastery	0 (-0.03, 0.03)	-0.002 (-0.04, 0.03)	
		Purpose in life	-0.01 (-0.05, 0.03)	-0.004 (-0.04, 0.03)	
		Self-acceptance	0.02 (-0.05, 0.08)	-0.02 (-0.09, 0.05)	
Indirect effects: major cancer danger		Mastery	0 (-0.03, 0.03)	0 (-0.04, 0.04)	
		Purpose in life	-0.01 (-0.05, 0.04)	-0.003 (-0.04, 0.03)	
		Self-acceptance	-0.02 (-0.08, 0.05)	0.02 (-0.05, 0.09)	
Indirect effects: major entrapment		Mastery	0.001 (-0.07, 0.08)	-0.01 (-0.09, 0.07)	
		Purpose in life	0.02 (-0.02, 0.06)	0.01 (-0.03, 0.05)	
		Self-acceptance	-0.02 (-0.10, 0.06)	0.02 (-0.07, 0.11)	

Note. Models examining all stressors included both minor and major stressors. Models included all main effects as well as control variables of age, stage, history of psychiatric treatment on intercept and slope. 1 year recurrence status was an additional predictor of slope.

<sup>a</sup>Unstandardized betas.

The only significant effect that emerged in these models was the interaction between social support and major non-cancer danger in predicting distress over time. Simple slopes were examined at  $\pm 1$  SD above/below the mean for both major non-cancer danger and social support. The effect of time on distress in those with low social support, and at varying levels of major non-cancer danger, is displayed in Figure 14.

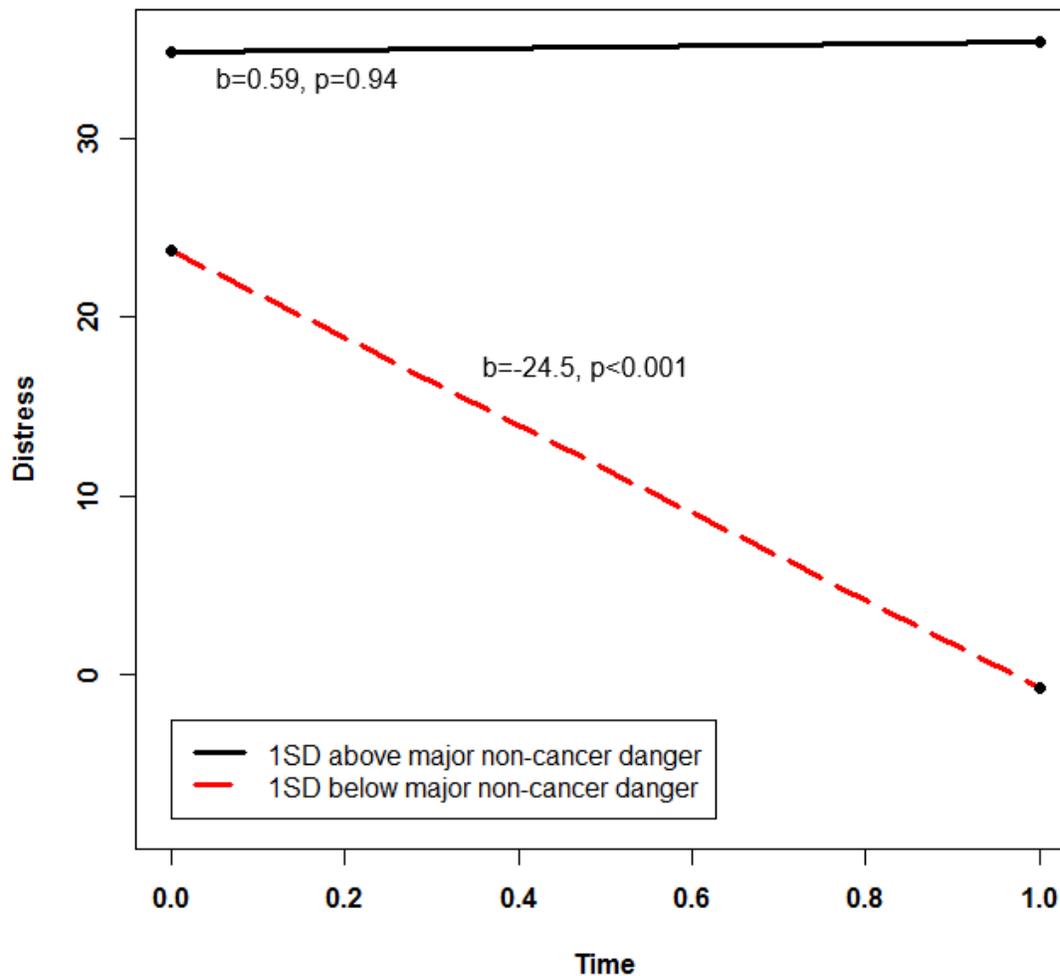


Figure 14. Effect of Time on Distress at Low Levels of Social Support, Paired with Different Levels of Major Non-Cancer Danger

When both major non-cancer danger and social support is low, distress decreases over time ( $b=-24.5$ ,  $p<0.001$ ). However, in those with low social support and high levels of threat associated with non-cancer danger stressors, distress does not decrease over time ( $b=0.59$ ,  $p=0.94$ ). Interestingly, in those with high levels of both social support and major non-cancer danger, distress also decreases over time, but to a lesser extent ( $b=-17.05$ ,  $p=0.01$ ). The effect of time on distress was non-significant at high levels of social support paired with low levels of major non-cancer danger ( $b=-5.16$ ,  $p=0.44$ ). In other words, those with low levels of both social support and major non-cancer danger as well as those with both high levels of social support and major non-cancer danger exhibited an improvement in distress over time. In individuals with high levels of threat due to major non-cancer danger paired with low levels of social support, distress stays consistent over time. Additionally, individuals with low levels of threat due to major non-cancer danger paired with high levels of social support also displayed consistent levels of distress throughout the year post-diagnosis.

**Mediated moderation.** The models examining mediated moderation all fit the data well. For all outcomes besides fatigue, the mediated moderation model was the only model of protective resources to have significant effects when including all stressors. Effects for these models are displayed in Tables 20-23.

Table 20. Mediated Moderation Model Predicting Distress

			<b>b, all stressors</b> (95% CI)	<b>b, major stressors</b> (95% CI)
<b>Intercept</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	-0.04	-0.25
		Cancer loss	0.55	0.64
		Danger (non-cancer)	-0.33	-0.27
		Cancer danger	-0.53	-0.42
		Entrapment	0.02	0.14
	Mediated moderation: loss (non-cancer)	Mastery	-0.05 (-0.30, 0.02)	-0.03 (-0.23, 0.11)
		Purpose in life	0.002 (-0.05, 0.07)	-0.002 (-0.09, 0.08)
		Self-acceptance	-0.07 (-0.41, 0.01)	-0.04 (-0.32, 0.05)
	Mediated moderation: Cancer loss	Mastery	-0.08 (-0.56, 0.08)	-0.06 (-0.10, 0.14)
		Purpose in life	-0.002 (-0.18, 0.10)	0 (-0.12, 0.11)
		Self-acceptance	-0.32* (-0.98, -0.01)	-0.12 (-0.57, 0.03)
	Mediated moderation: danger (non-cancer)	Mastery	-0.01 (-0.20, 0.12)	-0.12 (-0.52, 0.06)
		Purpose in life	-0.002 (-0.12, 0.06)	0.004 (-0.10, 0.10)
		Self-acceptance	-0.13 (-0.54, 0.03)	-0.12 (-0.67, 0.04)
	Mediated moderation: Cancer danger	Mastery	0.01 (-0.11, 0.17)	-0.05 (-0.34, 0.04)
		Purpose in life	0.001 (-0.06, 0.08)	0 (-0.05, 0.09)
		Self-acceptance	-0.06 (-0.40, 0.02)	-0.02 (-0.31, 0.05)
	Mediated moderation: entrapment	Mastery	0.11 (-0.12, 0.57)	0.09 (-0.12, 0.48)
		Purpose in life	-0.001 (-0.15, 0.07)	-0.001 (-0.17, 0.08)
		Self-acceptance	0.10 (-0.09, 0.64)	0.08 (-0.15, 0.62)
<b>Slope</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.29	0.48
		Cancer loss	-1.45*	-1.21
		Danger (non-cancer)	-0.40	-1.15
		Cancer danger	0.10	0.09
		Entrapment	0.12	0.21
	Mediated moderation: loss (non-cancer)	Mastery	-0.03 (-0.24, 0.02)	0 (-0.09, 0.09)
		Purpose in life	-0.03 (-0.19, 0.06)	-0.03 (-0.2, 0.03)
		Self-acceptance	-0.01 (-0.17, 0.06)	-0.01 (-0.24, 0.04)
	Mediated moderation: Cancer loss	Mastery	-0.04 (-0.50, 0.03)	0 (-0.16, 0.13)
		Purpose in life	0.03 (-0.23, 0.34)	0.003 (-0.12, 0.17)
		Self-acceptance	-0.03 (-0.50, 0.24)	-0.03 (-0.32, 0.04)
	Mediated moderation: danger (non-cancer)	Mastery	-0.01 (-0.19, 0.07)	0 (-0.19, 0.17)
		Purpose in life	0.03 (-0.10, 0.24)	0.05 (-0.03, 0.47)
		Self-acceptance	-0.01 (-0.27, 0.14)	-0.03 (-0.41, 0.06)
	Mediated moderation: Cancer danger	Mastery	0.003 (-0.07, 0.13)	0 (-0.10, 0.07)
		Purpose in life	-0.02 (-0.24, 0.08)	0.01 (-0.05, 0.20)
		Self-acceptance	-0.01 (-0.17, 0.06)	-0.01 (-0.18, 0.03)
	Mediated moderation: entrapment	Mastery	0.06 (-0.09, 0.46)	0 (-0.20, 0.29)
		Purpose in life	0.02 (-0.08, 0.33)	-0.02 (-0.16, 0.09)
		Self-acceptance	0.01 (-0.17, 0.32)	0.02 (-0.11, 0.36)

Note. Models examining all stressors included both minor and major stressors. Models included all main effects as well as control variables of age, stage, history of psychiatric treatment on intercept and slope. 1 year recurrence status was an additional predictor of slope.

<sup>a</sup>Unstandardized betas.

Table 21. Mediated Moderation Model Predicting Depressed Mood

			<b>b, all stressors (95% CI)</b>	<b>b, major stressors (95% CI)</b>	
<b>Intercept</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.03	0.03	
		Cancer loss	0.06	0.12	
		Danger (non-cancer)	-0.09	-0.11	
		Cancer danger	-0.13*	-0.10	
		Entrapment	-0.08	-0.01	
	Mediated moderation: loss (non-cancer)	Mastery	-0.01 (-0.05, 0.003)	-0.01 (-0.04, 0.02)	
		Purpose in life	0.001 (-0.01, 0.02)	-0.003 (-0.03, 0.01)	
		Self-acceptance	-0.02 (-0.07, 0.002)	-0.01 (-0.07, 0.01)	
	Mediated moderation: Cancer loss	Mastery	-0.014 (-0.11, 0.02)	-0.01 (-0.09, 0.03)	
		Purpose in life	-0.001 (-0.04, 0.02)	0 (-0.02, 0.04)	
		Self-acceptance	-0.08* (-0.21, -0.02)	-0.03 (-0.12, 0.003)	
	Mediated moderation: danger (non-cancer)	Mastery	-0.001 (-0.03, 0.03)	-0.02 (-0.11, 0.01)	
		Purpose in life	-0.001 (-0.02, 0.01)	0.01 (-0.01, 0.08)	
		Self-acceptance	-0.03 (-0.11, 0)	-0.03 (-0.14, 0.01)	
	Mediated moderation: Cancer danger	Mastery	0.001 (-0.02, 0.03)	-0.01 (-0.07, 0.01)	
		Purpose in life	0 (-0.01, 0.02)	0.001 (-0.01, 0.03)	
		Self-acceptance	-0.01 (-0.08, 0.01)	-0.01 (-0.06, 0.02)	
	Mediated moderation: entrapment	Mastery	0.02 (-0.02, 0.10)	0.02 (-0.03, 0.09)	
		Purpose in life	0 (-0.03, 0.01)	-0.002 (-0.04, 0.02)	
		Self-acceptance	0.03 (-0.02, 0.14)	0.02 (-0.03, 0.13)	
	<b>Slope</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.07	0.04
			Cancer loss	0.11	-0.19
			Danger (non-cancer)	0.01	-0.09
			Cancer danger	-0.01	0.03
Entrapment			-0.17	-0.03	
Mediated moderation: loss (non-cancer)		Mastery	-0.01 (-0.05, 0.002)	0.001 (-0.01, 0.02)	
		Purpose in life	-0.004 (-0.04, 0.01)	-0.002 (-0.03, 0.01)	
		Self-acceptance	0.01 (-0.003, 0.04)	0.002 (-0.01, 0.04)	
Mediated moderation: Cancer loss		Mastery	-0.01 (-0.10, 0.01)	0.002 (-0.02, 0.04)	
		Purpose in life	0.004 (-0.03, 0.07)	0 (-0.03, 0.03)	
		Self-acceptance	0.03 (-0.01, 0.14)	0.01 (-0.01, 0.07)	
Mediated moderation: danger (non-cancer)		Mastery	-0.001 (-0.03, 0.01)	0.003 (-0.02, 0.05)	
		Purpose in life	0.004 (-0.01, 0.05)	0.01 (-0.01, 0.07)	
		Self-acceptance	0.01 (-0.01, 0.07)	0.01 (-0.01, 0.06)	
Mediated moderation: Cancer danger		Mastery	0.001 (-0.01, 0.03)	0.001 (-0.01, 0.03)	
		Purpose in life	-0.003 (-0.05, 0.01)	0.001 (-0.01, 0.03)	
		Self-acceptance	0.01 (-0.004, 0.06)	0.001 (-0.01, 0.03)	
Mediated moderation: entrapment		Mastery	0.01 (-0.01, 0.11)	-0.002 (-0.06, 0.04)	
		Purpose in life	0.003 (-0.01, 0.05)	-0.001 (-0.03, 0.02)	
		Self-acceptance	-0.01 (-0.10, 0.02)	-0.004 (-0.06, 0.02)	

Note. Models examining all stressors included both minor and major stressors. Models included all main effects as well as control variables of age, stage, history of psychiatric treatment on intercept and slope. 1 year recurrence status was an additional predictor of slope.

<sup>a</sup>Unstandardized betas.

Table 22. Mediated Moderation Model Predicting Anger

			<b>b, all stressors (95% CI)</b>	<b>b, major stressors (95% CI)</b>	
<b>Intercept</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	-0.04	-0.15	
		Cancer loss	0.17	0.16	
		Danger (non-cancer)	-0.06	0.02	
		Cancer danger	-0.13*	-0.09	
		Entrapment	0.07	0.05	
	Mediated moderation: loss (non-cancer)	Mastery	-0.01 (-0.07, 0.01)	-0.004 (-0.05, 0.02)	
		Purpose in life	0 (-0.02, 0.01)	0 (-0.02, 0.02)	
		Self-acceptance	-0.01 (-0.07, 0.01)	-0.004 (-0.06, 0.02)	
	Mediated moderation: Cancer loss	Mastery	-0.01 (-0.14, 0.02)	-0.01 (-0.09, 0.03)	
		Purpose in life	0 (-0.03, 0.04)	0 (-0.03, 0.03)	
		Self-acceptance	-0.04 (-0.17, 0.03)	-0.01 (-0.09, 0.02)	
	Mediated moderation: danger (non-cancer)	Mastery	-0.002 (-0.04, 0.03)	-0.02 (-0.12, 0.01)	
		Purpose in life	0 (-0.02, 0.02)	-0.001 (-0.04, 0.02)	
		Self-acceptance	-0.02 (-0.11, 0.02)	-0.01 (-0.12, 0.02)	
	Mediated moderation: Cancer danger	Mastery	-0.001 (-0.04, 0.02)	-0.01 (-0.07, 0.01)	
		Purpose in life	0 (-0.02, 0.01)	0 (-0.01, 0.02)	
		Self-acceptance	-0.01 (-0.07, 0.01)	-0.002 (-0.05, 0.01)	
	Mediated moderation: entrapment	Mastery	0.03 (-0.04, 0.12)	0.02 (-0.03, 0.12)	
		Purpose in life	0 (-0.02, 0.02)	0 (-0.03, 0.03)	
		Self-acceptance	0.01 (-0.03, 0.15)	0.01 (-0.04, 0.10)	
	<b>Slope</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.09	0.12
			Cancer loss	-0.23 <sup>a</sup>	-0.23 <sup>a</sup>
			Danger (non-cancer)	-0.08	-0.28 <sup>a</sup>
			Cancer danger	0.06	0.03
Entrapment			-0.04	-0.01	
Mediated moderation: loss (non-cancer)		Mastery	-0.01 (-0.10, 0.001)	-0.001 (-0.04, 0.01)	
		Purpose in life	-0.01 (-0.06, 0.01)	-0.01 (-0.07, 0.01)	
		Self-acceptance	-0.01 (-0.05, 0.002)	-0.004 (-0.05, 0.01)	
Mediated moderation: Cancer loss		Mastery	-0.01 (-0.15, 0.01)	-0.003 (-0.05, 0.01)	
		Purpose in life	0.01 (-0.03, 0.13)	0.001 (-0.04, 0.05)	
		Self-acceptance	-0.03 (-0.14, 0.01)	-0.01 (-0.07, 0.001)	
Mediated moderation: danger (non-cancer)		Mastery	-0.002 (-0.06, 0.01)	-0.01 (-0.09, 0.01)	
		Purpose in life	0.01 (-0.01, 0.08)	0.01 (-0.01, 0.14)	
		Self-acceptance	-0.01 (-0.09, 0.01)	-0.01 (-0.13, 0.001)	
Mediated moderation: Cancer danger		Mastery	0 (-0.03, 0.01)	-0.003 (-0.05, 0.004)	
		Purpose in life	-0.01 (-0.08, 0.01)	0.001 (-0.02, 0.06)	
		Self-acceptance	-0.01 (-0.06, 0.002)	-0.002 (-0.04, 0.003)	
Mediated moderation: entrapment		Mastery	0.02 (-0.02, 0.19)	0.004 (-0.03, 0.10)	
		Purpose in life	0.01 (-0.01, 0.1)	-0.01 (-0.05, 0.02)	
		Self-acceptance	0.01 (-0.01, 0.11)	0.01 (-0.01, 0.14)	

Note. Models examining all stressors included both minor and major stressors. Models included all main effects as well as control variables of age, stage, history of psychiatric treatment on intercept and slope. 1 year recurrence status was an additional predictor of slope. <sup>a</sup>p≤0.05, but average slope not significant. <sup>a</sup>Unstandardized betas.

Table 23. Mediated Moderation Model Predicting Fatigue

			<b>b, all stressors (95% CI)</b>	<b>b, major stressors (95% CI)</b>	
<b>Intercept</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.09	0.18	
		Cancer loss	0.04	0.05	
		Danger (non-cancer)	-0.09	-0.24	
		Cancer danger	-0.08	-0.04	
		Entrapment	-0.11	-0.05	
	Mediated moderation: loss (non-cancer)	Mastery	-0.01 (-0.11, 0.01)	0.003 (-0.03, 0.10)	
		Purpose in life	0.01 (-0.01, 0.06)	0.01 (-0.02, 0.08)	
		Self-acceptance	-0.02 (-0.10, 0.01)	-0.003 (-0.07, 0.04)	
	Mediated moderation: Cancer loss	Mastery	-0.01 (-0.20, 0.02)	-0.01 (-0.14, 0.03)	
		Purpose in life	0.001 (-0.07, 0.1)	0.001 (-0.04, 0.04)	
		Self-acceptance	-0.08 (-0.27, 0)	-0.04 (-0.17, 0.01)	
	Mediated moderation: danger (non-cancer)	Mastery	-0.001 (-0.05, 0.04)	-0.03 (-0.16, 0.02)	
		Purpose in life	-0.004 (-0.07, 0.02)	-0.01 (-0.12, 0.02)	
		Self-acceptance	-0.03 (-0.13, 0.01)	-0.05 (-0.18, 0.01)	
	Mediated moderation: Cancer danger	Mastery	0.004 (-0.02, 0.07)	-0.01 (-0.10, 0.01)	
		Purpose in life	0.01 (-0.01, 0.07)	0.001 (-0.02, 0.03)	
		Self-acceptance	-0.01 (-0.10, 0.02)	-0.01 (-0.08, 0.02)	
	Mediated moderation: entrapment	Mastery	0.02 (-0.03, 0.19)	0.02 (-0.04, 0.21)	
		Purpose in life	-0.01 (-0.12, 0.02)	0.001 (-0.03, 0.06)	
		Self-acceptance	0.03 (-0.03, 0.16)	0.02 (-0.08, 0.16)	
	<b>Slope</b>	Interactions with social support <sup>a</sup>	Loss (non-cancer)	0.04	0.11
			Cancer loss	-0.13	-0.05
			Danger (non-cancer)	-0.06	-0.21
			Cancer danger	-0.06	-0.09
Entrapment			-0.05	-0.03	
Mediated moderation: loss (non-cancer)		Mastery	-0.01 (-0.08, 0.004)	0.001 (-0.02, 0.04)	
		Purpose in life	-0.01 (-0.05, 0.01)	-0.004 (-0.05, 0.01)	
		Self-acceptance	0.001 (-0.02, 0.04)	0 (-0.03, 0.03)	
Mediated moderation: Cancer loss		Mastery	-0.01 (-0.17, 0.02)	-0.004 (-0.08, 0.02)	
		Purpose in life	-0.001 (-0.07, 0.04)	-0.001 (-0.05, 0.03)	
		Self-acceptance	0.003 (-0.07, 0.09)	-0.001 (-0.05, 0.04)	
Mediated moderation: danger (non-cancer)		Mastery	-0.001 (-0.05, 0.02)	-0.01 (-0.10, 0.02)	
		Purpose in life	0.003 (-0.02, 0.06)	0.004 (-0.02, 0.08)	
		Self-acceptance	0.001 (-0.04, 0.06)	-0.001 (-0.08, 0.05)	
Mediated moderation: Cancer danger		Mastery	0.004 (-0.01, 0.06)	-0.003 (-0.06, 0.01)	
		Purpose in life	-0.01 (-0.05, 0.01)	0 (-0.03, 0.02)	
		Self-acceptance	0 (-0.02, 0.03)	0 (-0.02, 0.02)	
Mediated moderation: entrapment		Mastery	0.02 (-0.02, 0.15)	0.01 (-0.03, 0.15)	
		Purpose in life	0.01 (-0.01, 0.08)	-0.001 (-0.05, 0.03)	
		Self-acceptance	-0.001 (-0.08, 0.05)	0 (-0.05, 0.06)	

Note. Models examining all stressors included both minor and major stressors. Models included all main effects as well as control variables of age, stage, history of psychiatric treatment on intercept and slope. 1 year recurrence status was an additional predictor of slope.

<sup>a</sup>Unstandardized betas.

The significant interaction between social support and major non-cancer danger that was found in the previous set of models was not significant ( $b=-1.15, p=0.06$ ). In these models, social support was a significant moderator of cancer-related danger on depressed mood and anger at baseline. Only in those with high levels of social support was cancer-related danger related to less depressed mood at baseline (Figure 15). At low levels of social support (1.39 SDs below the mean), the effect of cancer-related danger on depressed mood is significantly positive ( $b=0.34, p=0.05$ ), such that greater threat associated with cancer danger is related to greater depressed mood at baseline.

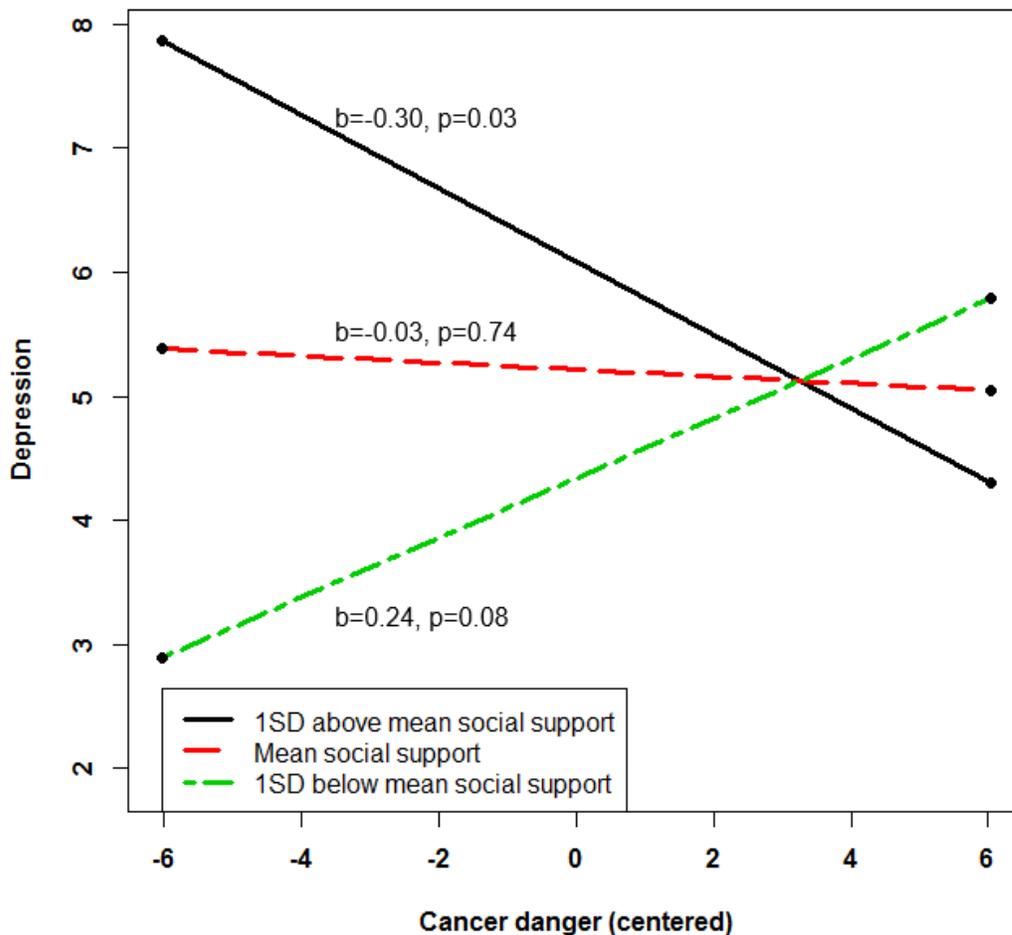


Figure 15. Effect of Cancer Danger on Baseline Depressed Mood at Different Levels of Social Support

Alternatively, only at low levels of social support is greater cancer-related danger related to higher anger at baseline ( $b=0.34$ ,  $p=0.02$ ). At mean levels of social support ( $b=0.09$ ,  $p=0.28$ ) and high levels of social support ( $-0.16$ ,  $p=0.23$ ), the effect cancer danger on baseline anger is not significant (Figure 16). In other words, high levels of social support paired with greater cancer-related danger results in less depressed mood at baseline, while high levels of social support do not impact the effect of cancer-related danger on anger at baseline. Instead, only in those with low levels of social support does cancer-related danger lead to greater anger. Similarly, low levels of social support paired with greater cancer-related danger leads to greater depressed mood at baseline.

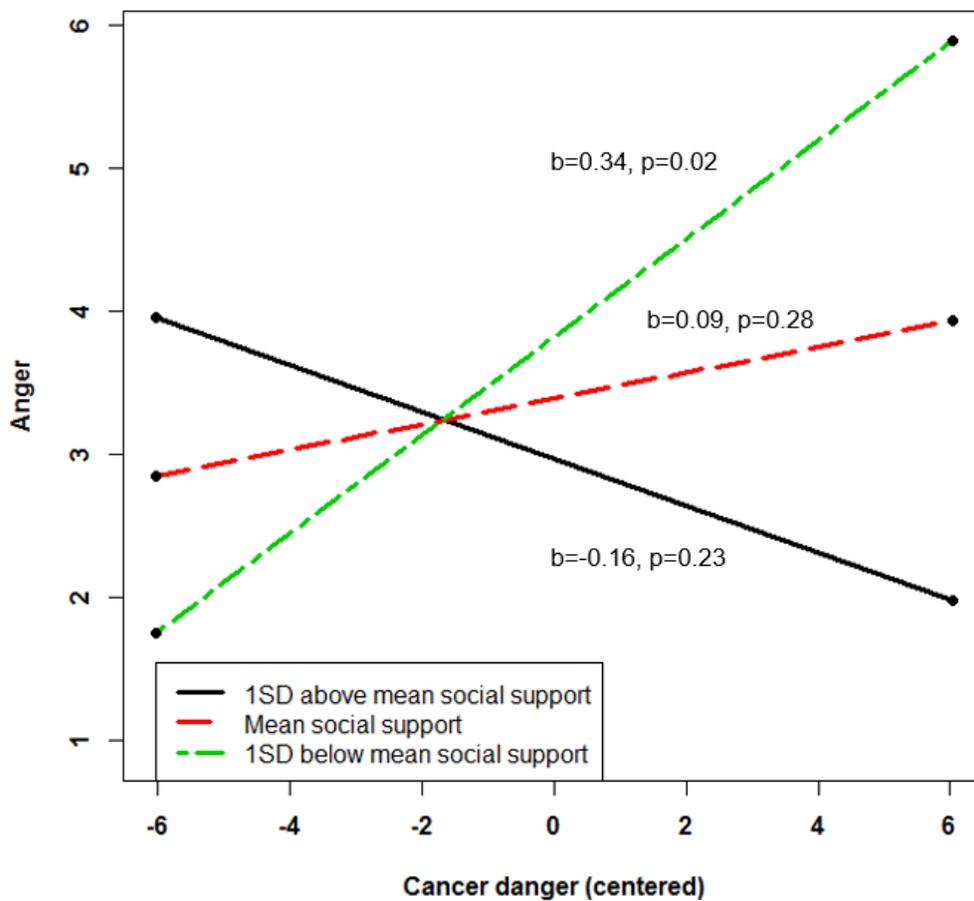


Figure 16. Effect of Cancer Danger on Baseline Anger at Different Levels of Social Support

Furthermore, social support significantly moderated the effect of cancer-related loss on distress over time, such that low levels of social support paired with low levels of cancer loss was related to a decrease in distress over time ( $b=-21.33$ ,  $p=0.003$ ; See Figure 17). High levels of social support paired with high levels of cancer-related loss also resulted in a significant decrease in distress over time ( $b=-19.93$ ,  $p=0.02$ ). The effect of time on distress was not significant at high levels of social support paired with low cancer loss ( $b=-5.60$ ,  $p=0.36$ ) and at low levels of social support paired with high cancer loss ( $b=6.75$ ,  $p=0.35$ ). In other words, only those with low levels of both social support and cancer loss as well as those with both high levels of social support and cancer loss exhibited an improvement in distress throughout the year post-diagnosis.

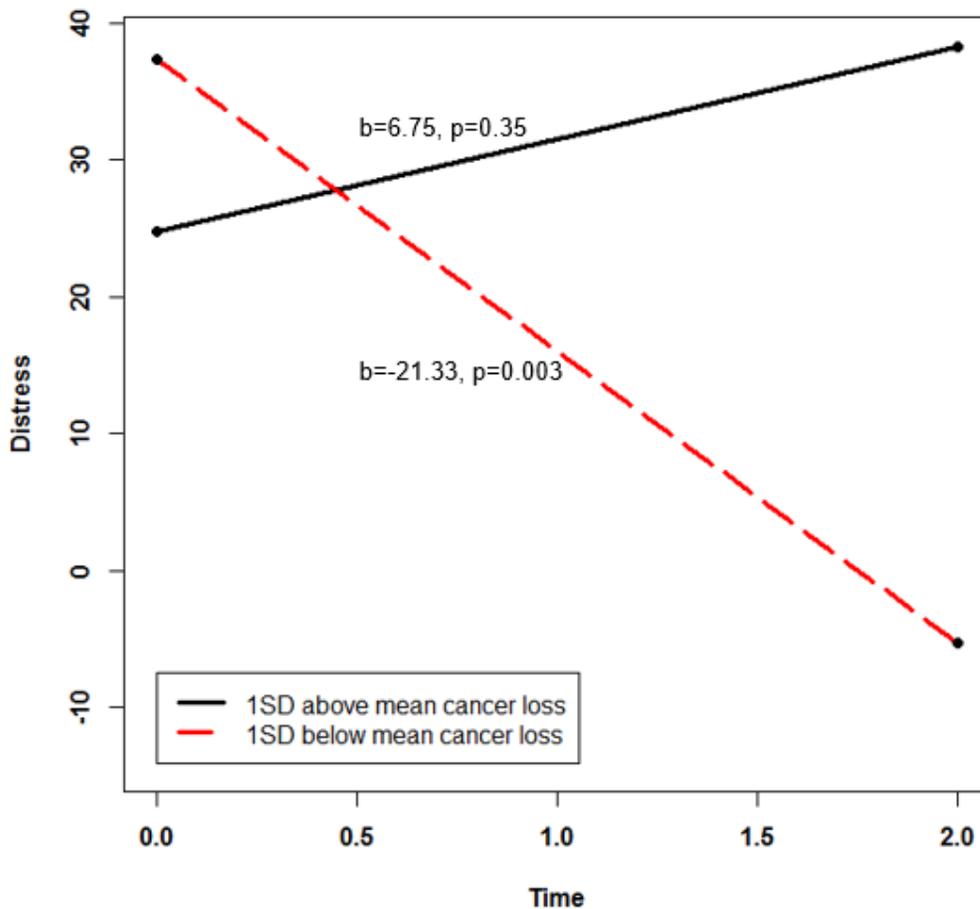


Figure 17. Effect of Time on Distress at Low Levels of Social Support, Paired with Different Levels of Cancer Loss

The only significant mediated moderation effect that was found was the interaction between social support and cancer loss being mediated through self-acceptance. This was significant in predicting baseline distress ( $b=-0.32$ ,  $CI=-0.98, -0.01$ ) as well as baseline depressed mood ( $b=-0.08$ ,  $CI=-0.21, -0.02$ ). The interaction between social support and cancer loss in predicting self-acceptance, with estimates from the distress model, is shown in Figure 18. At high levels of social support, greater cancer loss is associated with greater self-acceptance ( $b=0.69$ ,  $p=0.02$ ). At mean social support ( $b=0.10$ ,  $p=0.57$ ) and 1SD below mean levels of social support ( $b=-0.19$ ,  $p=0.39$ ), the effect of cancer loss on self-acceptance is not significant. However, at 1.5 SDs below the mean of social support, this effect becomes significant, and negative ( $b=0.43$ ,  $p=0.05$ ), such that greater cancer loss paired with low social support is related to lower self-acceptance. These simple slopes, when calculated with estimates from the model predicting depressed mood, were very similar.

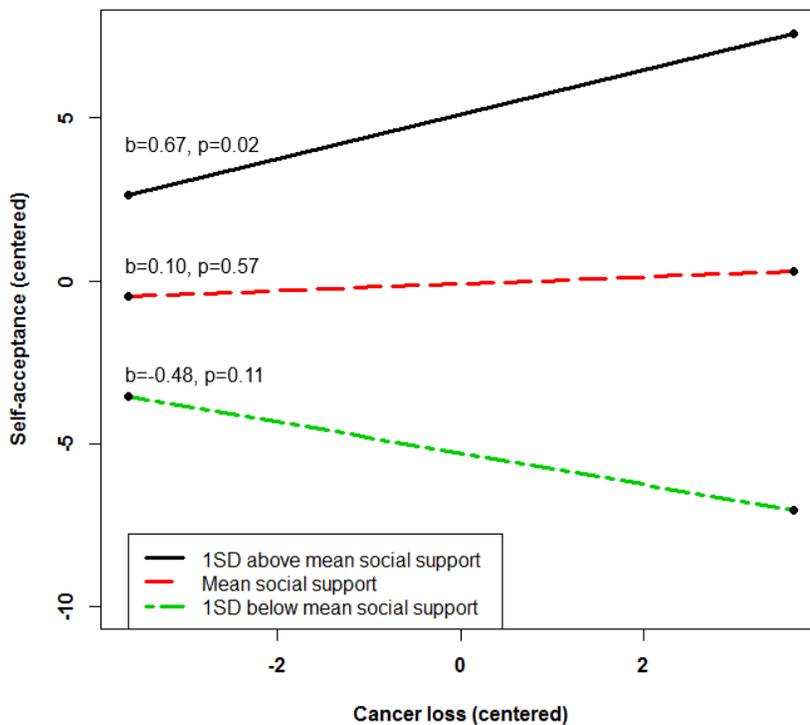


Figure 18. Effect of Cancer Loss on Self-Acceptance at Differing Levels of Social Support

Statistical models for the mediated moderation effects on distress and depressed mood are shown in Figures 19 & 20. The effects of self-acceptance on distress ( $b=-1.09$ ) depressed mood at baseline ( $b=-0.25$ ) are negative such that greater self-acceptance is associated with lower distress/depressed mood. Thus, high levels of social support in the context of cancer loss can act as a protective factor by increasing self-acceptance, which is related to lower overall distress and depressed mood. Additionally, low levels of social support in the context of high cancer loss is a risk factor, as it reduces self-acceptance and, thus, increases distress/depressed mood.

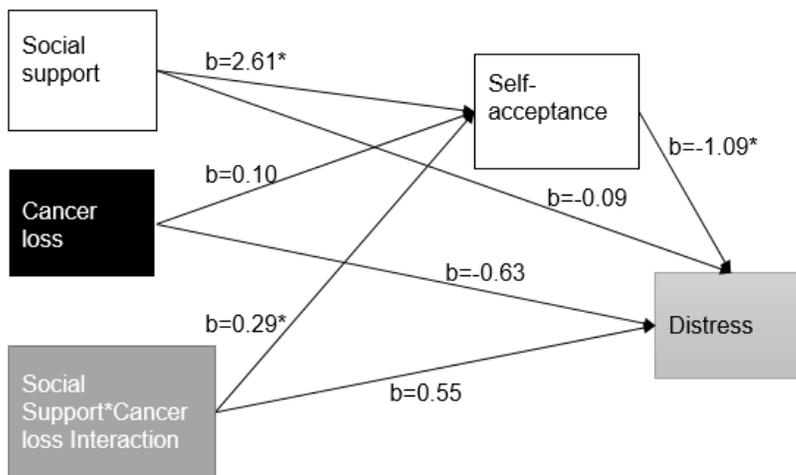


Figure 19. Statistical Model of Significant Mediated Moderation Effect Predicting Distress

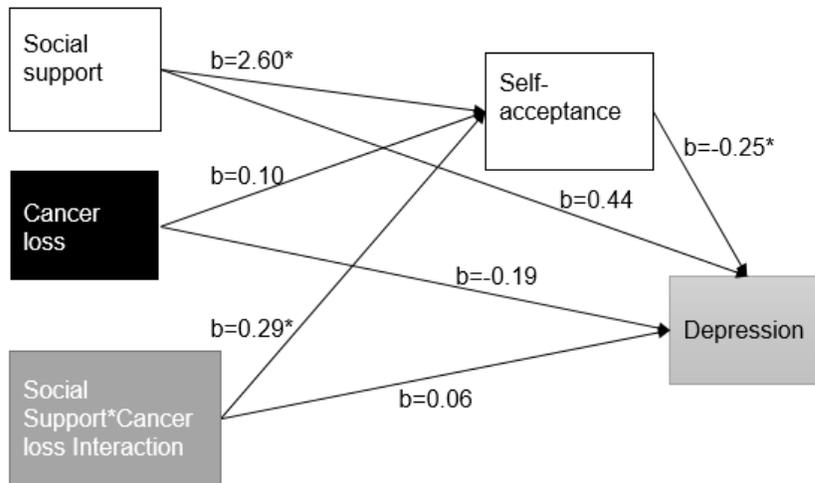


Figure 20. Statistical Model of Significant Mediated Moderation Effect Predicting Depressed Mood

**Comparison of models of psychosocial resources.** Fit statistics for each model, as well as all following models of protective resources, are displayed in Tables 24-27. For the outcomes of distress, depressed mood, and anger, the mediated moderation model was the only model of protective resources to have significant effects when including all stressors. Thus, while it did not have the best fit compared to the other models according to the BIC (when tends to favor parsimonious over more complex models), it was the most predictive model of psychosocial resources in the context of all stressors, and also had good fit to the data.

In examining psychosocial resources in the context of major stressors, all models examining distress as an outcome fit the data well, with the mediated moderation model being the only one to find no significant effects. Not surprisingly, the independent effects model fit the data the best according to BIC, followed by the multiple moderator model. Similarly, only the independent effects model and multiple moderator model found significant relationships between psychosocial resources and major stressors when examining depressed mood as an outcome. The multiple moderator model was the only model examining anger to find significant effects. Lastly,

when fatigue was the outcome of interest, only the independent effects model fit the data well and found significant effects of psychosocial resources.

Table 24. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Overall Distress

<b>Outcome</b>	<b>Model</b>	<b>Chi-square</b>	<b>RMSEA</b>	<b>CFI</b>	<b>TLI</b>	<b>SRMR</b>	<b>BIC</b>	<b>Significant effects</b>
<b>All stressors</b>	Independent effects	9.31 (df=16), p=0.90	0	1	1.21	0.02	2879.13	None
	Multiple moderators	105.05 (df=36) p<0.01	0.12	0.68	0.11	0.02	3023.44	Not examined due to poor model fit.
	Multiple mediators, one moderator	95.99 (df=62) p=0.004	0.07	0.92	0.86	0.09	5255.30	Not examined due to poor model fit.
	Mediated moderation	34.61 (df=33), p=0.39	0.02	1	0.99	0.03	4823.31	- Social support moderating cancer loss (slope) -Social support moderating cancer loss through effect on self-acceptance (intercept)
<b>Major stressors</b>	Independent effects	9.09 (df=16), p=0.91	0	1	1.12	0.02	2877.60	Mastery (intercept)
	Multiple moderators	32.83 (df=36), p=0.62	0	1	1.04	0.02	3005.07	Social support moderating major cancer danger (intercept)
	Multiple mediators, one moderator	87.32 (df=62), p=0.02	0.06	0.95	0.91	0.08	5982.86	Social support moderating major non-cancer danger (slope)
	Mediated moderation	35.27 (df=33), p=0.36	0.02	1	0.99	0.04	5489.99	None

Note: Models examining all stressors included both minor and major stressors.

Table 25. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Depressed Mood

<b>Outcome</b>	<b>Model</b>	<b>Chi-square</b>	<b>RMSEA</b>	<b>CFI</b>	<b>TLI</b>	<b>SRMR</b>	<b>BIC</b>	<b>Significant effects</b>
<b>All stressors</b>	Independent effects	8.11 (df=15), p=0.92	0	1	1.17	0.02	1943.29	None
	Multiple moderators	55.97 (df=35), p=0.02	0.07	0.78	0.64	0.02	2076.01	Not examined due to poor model fit
	Multiple mediators, one moderator	86.89 (df=57), p=0.01	0.07	0.92	0.86	0.09	4441.61	Not examined due to poor model fit.
	Mediated moderation	25.47 (df=29), p=0.65	0	1	1.03	0.03	4010.27	- Social support moderating effect of cancer danger (intercept). -Social support moderating cancer loss through effect on self-acceptance (intercept)
<b>Major stressors</b>	Independent effects	7.24 (df=15), p=0.95	0	1	1.18	0.02	1937.09	Mastery (intercept)
	Multiple moderators	31.23 (df=35), p=0.65	0	1	1.06	0.01	2063.77	Social support moderating major cancer danger (intercept)
	Multiple mediators, one moderator	75.87(df=57) p=0.05	0.05	0.95	0.92	0.07	5050.91	None
	Mediated moderation	25.90 (df=29), p=0.63	0	1	1.03	0.03	4559.03	None

Note: Models examining all stressors included both minor and major stressors.

Table 26. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Anger

<b>Outcome</b>	<b>Model</b>	<b>Chi-square</b>	<b>RMSEA</b>	<b>CFI</b>	<b>TLI</b>	<b>SRMR</b>	<b>BIC</b>	<b>Significant effects</b>
<b>All stressors</b>	Independent effects	19.13 (df=17), p=0.32	0.03	0.98	0.94	0.02	1931.43	None
	Multiple moderators	65.57 (df=38), p=0.004	0.08	0.86	0.62	0.02	2040.40	Not examined due to poor model fit
	Multiple mediators, one moderator	106.48(df=67)p =0.002	0.07	0.90	0.83	0.08	4390.92	Not examined due to poor model fit.
	Mediated moderation	42.77 (df=37), p=0.24	0.04	0.99	0.96	0.03	3960.66	Social support moderating effect of cancer danger (intercept)
<b>Major stressors</b>	Independent effects	17.92 (df=17), p=0.39	0.02	0.99	0.97	0.02	1935.04	None
	Multiple moderators	45.98 (df=38), p=0.18	0.04	0.96	0.89	0.04	2037.48	- Self-acceptance moderating major non-cancer danger (intercept) - Mastery moderating major entrapment (intercept)
	Multiple mediators, one moderator	98.57 (df=67), p=0.01	0.06	0.93	0.88	0.08	4987.90	Not examined due to poor model fit.
	Mediated moderation	45.26 (df=37), p=0.17	0.04	0.98	0.94	0.04	4498.08	None

Note: Models examining all stressors included both minor and major stressors.

Table 27. Fit Statistics and Significant Effects for Growth Curve Models of Protective Psychosocial Resources Predicting Fatigue

<b>Outcome</b>	<b>Model</b>	<b>Chi-square</b>	<b>RMSEA</b>	<b>CFI</b>	<b>TLI</b>	<b>SRMR</b>	<b>BIC</b>	<b>Significant effects</b>
<b>All stressors</b>	Independent effects	22.24 (df=18), p=0.22	0.05	0.96	0.89	0.04	2254.66	- Self-acceptance (intercept) - Social support (intercept)
	Multiple moderators	80.99 (df=38), p<0.001	0.10	0.77	0.36	0.03	2384.63	Not examined due to poor model fit.
	Multiple mediators, one moderator	107.80 (df=73), p=0.01	0.07	0.89	0.82	0.09	4601.72	Not examined due to poor model fit.
	Mediated moderation	38.73 (df=38), p=0.44	0.01	1	0.99	0.04	4190.31	None.
<b>Major stressors</b>	Independent effects	24.77 (df=18), p=0.13	0.06	0.92	0.81	0.04	2265.81	Social support (intercept)
	Multiple moderators	63.36 (df=38), p=0.01	0.08	0.86	0.63	0.03	2387.27	Not examined due to poor model fit.
	Multiple mediators, one moderator	95.44 (df=73), p=0.04	0.05	0.93	0.89	0.08	5170.56	Not examined due to poor model fit.
	Mediated moderation	33.04 (df=38), p=0.70	0	1	1.04	0.03	4706.59	None.

Note: Models examining all stressors included both minor and major stressors.

**Specific Aim #3: To examine the associations between loss, danger, and entrapment on cancer progression.**

*A priori* covariates in analyses examining cancer progression included age and cancer stage. Correlations between the censored variable of days to progression and clinical and demographic variables were examined to determine additional covariates. Cancer grade, success of tumor debulking, tumor histology, medication use, BMI, history of cigarette use, history of psychiatric treatment, presence of comorbidities, histology, education, and ethnicity were all examined as potential covariates. Of these, only tumor debulking was related to progression ( $r=-0.28$ ,  $p=0.002$ ), such that suboptimal debulking was related to faster progression. Thus, this was included as an additional covariate in all progression analyses.

A total of 86 women experienced a cancer progression (63.7%), while 45 did not (33.3%). One patient with persistent disease was removed from analyses, and progression status for 4 patients was unable to be determined. In a multivariate Cox model with control variables, suboptimal debulking (HR=0.74, 95%CI=0.58-0.84,  $p=0.01$ ), advanced stage (HR=0.41, 95%CI=0.27-0.62,  $p<0.001$ ), and age (HR=1.02, 95%CI=1.00-1.04,  $p=0.04$ ) were all related to faster progression. Life stress variables were used as additional predictors in separate multivariate Cox models including these control variables. Estimates of hazard ratios from these analyses are shown in Table 28. Contrary to predictions, no life stress variable was significantly related to progression.

Table 28. Effects of Life Stress on Progression

Variable	HR	95% CI	P
<b>All stressors</b>			
Loss (non-cancer)	1.01	0.98-1.04	0.69
Cancer loss	0.95	0.88-1.03	0.19
Danger (non-cancer)	1.01	0.97-1.04	0.80
Cancer danger	1.01	0.97-1.06	0.55
Entrapment	1.91	0.96-1.07	0.65
<b>Major stressors</b>			
Loss (non-cancer)	0.97	0.92-1.02	0.23
Cancer loss	0.95	0.88-1.02	0.16
Danger (non-cancer)	1.03	0.97-1.09	0.33
Cancer danger	1.02	0.97-1.08	0.44
Entrapment	1.02	0.96-1.08	0.60

Note. Models examining all stressors included both minor and major stressors. Each model included age, stage, and tumor debulking status as control variables.

### Discussion

The results of the current study shed light on the rarely examined relationship between life stressors and their impact on psychological functioning in women after receiving a diagnosis of ovarian cancer. Given that the diagnosis of cancer itself is a stressor, the first primary aim of this study was to examine the role of additional life stressors on psychological adjustment. Additionally, as specific mood states are adaptive and are often a response to a particular context (Price, 1972), different types of stressors may elicit distinct psychological responses. Thus, loss, danger, and entrapment stressors were examined separately in these analyses for a more nuanced understanding of life stress. To the author's knowledge, this is the first study to examine how these particular dimensions of stressors may be related to psychological well-being in patients with cancer.

The functional impact of several protective psychosocial factors (social support, mastery, self-acceptance, and purpose in life) on the relationship between specific stressors and

psychological outcomes was examined as a second major aim of the current study. Though these protective factors have been theorized to influence the relationship between stress and psychological outcomes, much more remains to be discovered about the nature of these relationships. Lastly, given the potential impact of stress on tumor progression pathways, this study examined how specific life stressors may be related to cancer recurrence, which has rarely been studied. Specific findings along with potential explanations, directions for future research, limitations of the current study, and clinical implications are discussed below.

### **The Impact of Life Events on Psychological Outcomes**

**Loss.** Stressors that entail loss have been related to both depressive and anxiety symptoms (Gilbert, 2006; Marks & Nesse, 1994). Thus, it was hypothesized that loss (both non-cancer and cancer-related) would be related to all psychological outcomes examined in the current study. In fact, loss was directly related to overall distress, depressed mood, and fatigue, while unrelated (directly) to anger. Furthermore, though it was hypothesized that both cancer-related loss and non-cancer losses would be independently related to outcomes, these subsets of stressors were significantly related to different outcomes. Cancer losses, including events such as receiving test results, being told of a cancer diagnosis, or being told surgery is needed, were related to greater distress over time. Interestingly, this effect was only significant when including all stressors, rather than when examining only major stressors. In other words, though it has previously been hypothesized severe life events are strongly related to onset of depression (Kessler, 1997), the current results suggest that, for some outcomes such as depressed mood as measured by scales such as the CES-D and POMS, the cumulative threat of both minor and major stressors may matter more than the impact of major stressors alone. However, this is not true for all outcomes. In predicting depressed mood over time, both the total threat of all cancer

losses, as well as the threat of only major cancer losses were significant. It may be that major stressors uniquely predict depressive symptoms, while minor stressors elicit generalized distress captured in the broader mood measurement. However, distress as measured in this study is likely highly correlated with depressive symptoms in this sample, as distress included all items that were in the depressed mood scale.

It may be that cancer-related losses, even relatively minor ones, such as a visit to the doctor focused on treatment planning, can have a bigger impact on overall distress and depressed mood than non-cancer losses because they evoke significant existential concerns and aspects of an individual's identity (Bertero & Wilmoth, 2007; Weisman & Worden, 1976). In the context of cancer, non-cancer stressors that are minor may seem relatively less threatening in comparison. Interestingly, non-cancer losses (both all losses, and only major losses) were only related to significantly higher fatigue, while controlling for age, stage, cancer grade, and use of pain medications. This supports previous research that has found that cumulative life stress is a risk factor for cancer-related fatigue (Bower, Crosswell, & Slavich, 2014). Additionally, this result may reflect the enhanced effort that is used to cope with non-cancer losses in the context of cancer. In other words, individuals may be employing strategies to minimize the impact of non-cancer losses on psychological outcomes such as distress, depressed mood, and anger. This may result in a greater sense of fatigue and explain why non-cancer related losses were only related to this outcome, which included primarily physical complaints. This effort may be akin to the concept of "ego depletion," as acts of self-control and choice draw from a limited resource (Baumeister, Bratslavsky, Muraven, & Tice, 1998). In fact, self-regulatory fatigue and physical fatigue may have overlapping neurological mechanisms (Evans, Boggero, & Segerstrom, 2015)

and mental fatigue has been related to both physical endurance and perception of effort in experimental studies (Pageaux & Lepers, 2016).

Stressful life events can impact lead to increased vulnerability for experienced distress after subsequent events due to the cumulative effects of stressors (Fava et al., 2010; McEwen & Seeman, 1999). Thus, it was also hypothesized that the interaction between cancer-related loss stressors and non-cancer-related loss stressors would be significant in predicting all outcomes, such that high levels of both would be related to the worst psychological functioning. However, this interaction was only significant in predicting depressed mood over time (both all losses and only major losses) as well as anger at baseline (only when minor losses were included in addition to major losses). Only patients experiencing low levels of both cancer-related losses and non-cancer losses exhibited significant decreases in depressed mood over time. Thus, the combined effects of cancer and non-cancer losses together constitute a risk factor for poorer psychological adjustment over time. At first glance, this appears to support the theory that effects of stress are cumulative, as patients high in both types of stressors did not improve over time. However, it also highlights the significance of having high levels of either cancer-related or non-cancer related losses on depressed mood, as individuals with either of these also did not improve over time. Rather than high levels of stressors being a vulnerability, low levels of stressors appears to be a protective factor.

On the other hand, only patients experiencing low levels of cancer loss exhibited a significant positive relationship between non-cancer loss and anger at baseline. This appears to support the previous hypothesized explanation that cancer-related losses may hold greater weight than non-cancer losses, and that only when cancer loss is low does non-cancer loss have an impact on anger.

**Danger.** Life events that entail a sense of danger have most commonly been related to anxiety, as it serves to help one respond to potential threats. Thus, it was hypothesized that danger stressors would be related to anxiety symptoms. However, in this sample, anger emerged as a reliable construct as opposed to anxiety. Anger may be thought of as an aggressive defense associated with anxious arousal, the “fight” part of “fight or flight” (Marks & Nesse, 1994). Interestingly, both cancer-related and non-cancer-related danger stressors were unrelated to anger as predicted. Instead, only major non-cancer danger stressors, such as a spouse becoming ill and staying in the hospital and visiting a doctor for other health concerns unrelated to cancer, independently predicted higher overall distress at baseline. Furthermore, the hypothesized interaction between cancer and non-cancer danger was significant in predicting higher distress at baseline, such that the effect of major non-cancer danger was significant only when cancer-related danger was low. This again supports the hypothesis that non-cancer stressors only have an impact when threat due to cancer-related stressors, which hold more salience, is low.

Cancer inherently entails a sense of danger and threat to one’s health and life. However, it may ultimately be losses that are most important rather than the threat of potential loss. Additionally, a potential explanation for why danger was unrelated to anger is that anger may be functionally distinct from anxiety, particularly in the context of life stress. Furthermore, individuals may feel more able to cope with danger than with loss, as potential threats may leave room for hope and for an individual to use coping strategies to prepare.

**Entrapment.** Interestingly, entrapment stressors, or ongoing difficulties which entail a sense of hopelessness or uncontrollability (e.g., being a caregiver for an ill family member) were not related to any psychological outcomes, either at baseline or over the year after diagnosis. This is in contrast to a previous finding in breast and prostate cancer patients that chronic strain

was related to worse depressive symptoms (Lehto et al., 2008). This finding may be more evidence for the importance of cancer-related stressors. Cancer as a stressor may resemble entrapment stressors, as it is often perceived as uncontrollable and typically has long-lasting impacts (Kangas, Henry, & Bryant, 2002; Sumalla, Ochoa, & Blanco, 2009). Cognitive adaptation theory posits that self-enhancing distortions about one's control over events can help promote adjustment to stress (Taylor, 1983). In fact, studies in breast cancer patients have found this idea to be supported, as women with higher perceptions of control over their cancer tend to have better psychological outcomes (Bárez, Blasco, Fernández-Castro, & Viladrich, 2007; Henselmans et al., 2010). However, no work has examined this in patients with ovarian cancer, which has worse survival rates. It may be that patients are more likely to experience this diagnosis as an entrapment stressor which takes precedence over other chronic stressors in their lives.

### **The Role of Protective Resources**

The second primary aim of this study was to examine the relationships between protective psychosocial resources and life stress in predicting psychological functioning. Several models were examined to assess these relationships, including an independent effects model, multiple moderator model, a model with multiple mediators, and a mediated moderation model.

**Independent effects.** Though the models examining independent effects all fit the data well and had the best fit according to BIC, few significant independent effects were found. Mastery was only related to distress and depressed mood at baseline when including major stressors as control variables, such that greater mastery was related to lower distress and depressed mood. Additionally, self-acceptance and social support significantly predicted fatigue at baseline, when including all stressors as control variables. Self-acceptance was related to

lower fatigue. This effect may be mediated by stress-related inflammation, as individuals high in self-compassion had less of a physiological response to stress compared to those low in self-compassion (Breines et al., 2014).

On the other hand, social support was related to higher fatigue. There may be several mechanisms underlying this relationship. Most simply, patients may receive an outpouring of support after being diagnosed with cancer. If this support is greater than an individual is used to, it may cause a “social burnout” due to the enhanced effort, which then increases feelings of fatigue. Additionally, individuals who are emotionally close to the patient may be more likely to offer unsolicited advice (Feng & Magen, 2015), which may or may not be helpful. In particular, informational support from family and friends is seen as unhelpful in patients with cancer (Helgeson & Cohen, 1996). In response to unhelpful or unwanted support, an individual may need to draw upon more internal coping strategies to manage the relationship and emotional responses this unsolicited advice engenders, leading to a sense of ego depletion and fatigue as previously described.

**Protective psychosocial resources as moderators.** It was predicted that only social support would emerge as a significant moderator of life stress on psychological outcomes, as it has often been studied as a buffer of life stress. Only in models predicting distress, depressed mood, and anger and including did social support moderate the effect of life stress. In these models, social support moderated the effect of cancer loss on slope of distress over time, as well cancer danger on depressed mood and anger at baseline.

At low levels of social support, greater threat associated with major cancer danger is related to higher anger and distress at baseline. Thus, low social support acts as a risk factor in these relationships. This finding supports previous studies that have found unsupportive

environments are related to worse distress and anxiety (Butler et al., 1999; Koopman et al., 1998). At high levels of support, cancer danger is unrelated to anger and distress at baseline. In other words, social support protects against the deleterious effects of major cancer danger on overall distress, which is in line with the “buffering” hypothesis of social support (Cohen & Wills, 1985). Interestingly, in the context of major cancer danger and non-major cancer danger predicting depressive symptoms, high levels of social support not only buffer the effects of life stress, but act as a potent protective factor, in that more threat due to stressors in the context of high support is related to less depressive symptoms.

The moderation of major non-cancer danger and cancer loss in predicting distress over time was less intuitive. Distress over time decreased when both stress threat and social support are either low or high. When either social support or threat due to stressors is low, while the other is high, distress does not decrease over time. This suggests that social support does not always simply act as a buffer, and that lack of social support is not always a risk factor. Social support may protect most against overall distress over time when it is meeting the particular needs of the individual (assuming that in a high stress environment, more support is needed and in low stress, less support is needed).

These findings again highlight the importance of context, particularly in terms of the impact of social support as a protective factor. Though social support acted as a buffer in some contexts, lack of social support was a more significant risk factor in others. Furthermore, in some contexts, social support interacts with stressors such that their effect on depressive symptoms is not only buffered or unrelated to depressed mood, but related to significantly less depressed mood. As previously described, social support was related to greater fatigue in the independent effects model. Thus, though it may be initially counterintuitive, social support may not always be

beneficial. This is in contrast to many models of social support that highlight the potential positive impacts of support (Cohen, 1988).

Some of the current results suggest that it may be a match between perceived needs and received support that leads to the beneficial effects often observed in studies examining social support. For example, one qualitative study found that women with breast cancer, a theme of support needs was the balance between distance and closeness (Drageset, Lindstrøm, Giske, & Underlid, 2012). Other lines of research have shown that the match between needed and received support is important. For example, in married couples, overprovision of social support was more strongly related to declines in marital satisfaction over 5 years than under-provision of support (Brock & Lawrence, 2009). The match between needed and received support can even impact physiological recovery after a stressor (Priem & Solomon, 2015). Additionally, in a large national sample, in the context of low perceived partner responsiveness, high received emotional support was actually related to an increased risk of mortality (Selcuk & Ong, 2013).

Mastery, self-acceptance, and purpose in life have been examined relatively less in regards to their relationship with life stress, particularly in patients with cancer. Though it was not predicted, self-acceptance moderated major non-cancer danger stressors on anger at baseline, and mastery moderated major entrapment on anger at baseline. However, these results were in unexpected directions. At low levels of self-acceptance, major cancer danger was related to less anger. Similarly, at low levels of mastery, major entrapment was related to less anger. It may be that those with lower levels of self-acceptance and mastery utilize suppression of emotional responses as a coping strategy. In fact, it has been posited that denial, which can include suppression of emotional responses associated with illness, can be beneficial in coping with stress when an individual has little control to improve the situation (Livneh, 2009).

**Mediating relationships of protective psychosocial resources.** Interestingly, the models examining social support as a moderator, with mastery, self-acceptance, and purpose in life as mediators generally did not fit the data well. Further, no significant mediating effects were found in the two models with fairly good fit to the data. Surprisingly, mastery and purpose in life were not significant mediators of any effects. Thus, the deterioration model, or the idea that stressors reduce resources, which mediates effects on psychological outcomes, was not supported in this study (Thoits, 1986).

In mediated moderation models, the interaction between social support and cancer loss was significantly mediated through self-acceptance. In the context of high levels of cancer loss, higher level of social support is related to greater self-acceptance, which is associated with lower distress and depressed mood at baseline. On the other hand, low levels of social support in the context of high cancer loss is a risk factor, as it reduces self-acceptance and, thus, increases distress/depressed mood. This supports models that suggest social support impact health through increasing a positive view of the self, most commonly examined as self-esteem (Cohen, 1988; Symister & Friend, 2003). However, the current findings give credence to a relatively newer body of literature examining self-acceptance and self-compassion as unique constructs that may be more related to psychological well-being, and less related to narcissism than self-esteem (Leary, Tate, Adams, Allen, & Hancock, 2007). Self-compassion may increase the use of effective coping strategies, including increasing cognitive restructuring while decreasing avoidance and escape strategies (Allen & Leary, 2010). The current finding supports previous research that has found self-compassion to be related to lower distress and depressive symptoms in cancer patients (Pinto-Gouveia et al., 2014; Przewdzicki et al., 2013). To the author's

knowledge this is the first study to examine how self-acceptance impacts the effect of life stress in patients with cancer.

### **The Impact of Life Events on Recurrence**

A final aim of the current study was to assess the differential impact of loss, danger, and entrapment stressors on cancer recurrence. Given the pathophysiological pathways underlying both stress and cancer progression (Armaiz-Pena et al., 2013; Lutgendorf & Andersen, 2015; Reiche et al., 2004), it was hypothesized that higher levels of life stress would be related to a more rapid recurrence. However, none of the life stressors that were examined significantly predicted time to cancer recurrence in this sample.

It may be that chronic stressors play a potentially greater role in recurrence than short-term stressors and thus the shorter term stressors captured by the LEDSS do not have a role in recurrence. Chronic stress tends to have greater effects on the immune system (Segerstrom, 2010), and immune processes in the tumor microenvironment have been implicated in tumor progression (Costanzo, Sood, & Lutgendorf, 2011). Given that entrapment stressors were unrelated to all psychosocial outcomes examined in previous analyses, it is not surprising that these stressors did not exhibit a significant relationship with recurrence. Again, this may highlight the fact that the cancer itself may be perceived as a significant entrapment stressor, and the chronic nature of stress due to cancer may not have been captured in the cancer-related loss and danger stress variables.

Furthermore, given that a variety of psychosocial factors may influence cancer progression, it may be that more complex models including protective influences, life events, and other contextual variables are likely to show significant results. In fact, social support has been related to survival in patients with cancer (Nausheen, Gidron, Peveler, & Moss-Morris, 2009),

including ovarian cancer patients (Lutgendorf et al., 2012). Additionally, coping strategies have been related to survival in patients with breast cancer, while presence of non-cancer life stressors was not (Lehto et al., 2006). Though this was beyond the scope of the current study, future research should continue to examine the interplay between life stress and protective psychosocial factors and how this impacts cancer progression.

Another potential explanation for the lack of significant relationships of life stress to cancer progression is that, though specific life stressors elicit different psychological responses, the underlying physiological processes that are implicated in tumor progression may have significant overlap. In fact, different negative emotions, including depressed mood, anxiety, and anger/hostility have all been shown to impact morbidity and mortality in patient populations (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002). It may be that the extent (severity) of life stress in general, as opposed to specific types of life stressors, is related to cancer recurrence in patients with ovarian cancer.

Lastly, the reason for lack of findings regarding progression may be due to the fact that we examined progression free survival, rather than overall survival, to improve statistical power to detect significant effects, as recurrence is easier to track in the short term as opposed to overall survival. However, overall survival is the most commonly examined and valid end-point in studies examining progression of cancer. It may be that stressful life events impact overall survival in ways not reflected in tumor progression and recurrence. In fact, studies have found that psychosocial factors can influence overall survival in women with recurrent disease, even when controlling for length of disease-free interval (Levy, Lee, Bagley, & Lippman, 1988). Additionally, in the current sample, the correlation between days to recurrence and days to survival was 0.65, which has been classified as a low correlation in criteria proposed for

evaluating surrogate endpoints for overall survival (Institute for Quality and Efficiency in Health Care, 2011) and suggests that other factors may be operative in terms of progression.

### **Directions for Future Research**

The current findings highlight the need for further research into the complex relationships between certain life stressors and psychological outcomes in patients with cancer, as well as the role of protective resources. While stage of cancer was a control variable in all analyses, this sample of ovarian cancer patients generally had late-stage cancer. Much of the research in women with cancer is done with samples of breast cancer patients. Future research should examine the above relationships in other samples of patients with cancer to determine if the current findings are specific to women with ovarian cancer. For example, it may be that, in patients with earlier stage cancers, the effect of non-cancer life events have a greater impact and different functional relationships with cancer-related stressors.

Several studies have shown differential effects of stressful life events in patients with cancer, which may be in part due to the methodological differences in measurement timing relative to stage of treatment (Golden-Kreutz et al., 2005; Lehto et al., 2008; Lutgendorf et al., 2013). The findings that cancer-related stressors were more commonly related to psychological measures around the time of diagnosis suggest that, during this stage of treatment, cancer takes focus, and additional life stressors may impact more at a later time. In a study of cancer patients with mixed diagnoses, those who have recently been treated were more likely to report their illness as chronic and having drastic consequences in their lives (Hopman & Rijken, 2015). Thus, future research should examine the presence of non-cancer loss and danger, as well as entrapment, further out from cancer diagnosis and treatment. In fact, some research has shown that events prior to cancer diagnosis can impact well-being years later (Beatty et al., 2009), even

though most research examining life stress and psychopathology has found that acute events predict onset of disorders soon after the event occurrence (Tennant, 2002).

In the current study, support functioned as a moderator of stressors, but in a variety of different ways. Lack of social support was a risk factor for distress and anger at baseline, social support acted as a buffer of stress on depressed mood, and the match between needed support (assumed based on presence of stressors) and reported support was predictive of overall distress throughout the year after diagnosis. The pattern of findings related to social support highlight the complex ways in which support may influence well-being. Research should continue to examine the contexts in which social support results in harmful effects, as well as the particular mechanisms (Uchino et al., 2012).

Additionally, though outside of the scope of this paper, future research should directly evaluate the utility of examining particular life stressors. For example, a study comparing models which collapse all types of stressors together with models that delineate particular characteristics of life stressors as the current study did. Similarly, the psychological outcomes in this study were determined using methodologically sound methods to ensure replicability of constructs over time. The pattern of results between overall distress as an outcome and facets of mood as outcomes (depressed mood and anger) indicate that examining both general and specific aspects of mood may be useful. Future work should continue to examine which measurement of psychological well-being is most meaningful in patients with cancer.

### **Limitations**

The current analyses have several limitations which merit consideration. First, the sample utilized in this study primarily consisted of well-educated Caucasian women, which may limit the generalizability of the current findings. Furthermore, though there was variability in

endorsement of stressors across types, it may be that a more diverse sample endorses even further variability which may yield itself to more powerful analyses.

Additionally, aside from entrapment, which inherently entails chronicity, the short-term and long-term effects of stressors were combined to evaluate total cumulative threat. Some research has found that both acute life events and chronic stressors may lead to detrimental psychological outcomes, with different patterns of results (Bower et al., 2014; Lehto et al., 2008). However, the emphasis of the current study was examining the psychological aspects of stress, rather than chronicity.

Despite the analytical strengths of this study, there are a number of methodological limitations. A goal of this study was to look at both baseline levels of psychological outcomes as well as changes in psychological well-being over time. However, in some of the examined models, psychological outcomes did not significantly change over time, which limits potential relationships that can be examined. For example, in the multiple moderator models, some interaction effects predicting slope were significant, though the average slope was not significant. Additionally, unconditional models did not exhibit substantial variability between individuals in changes over time. However, when adding predictors into the model, power to detect differences was increased. It may be that, in a larger sample, and over a longer measurement period, variability in changes over time become more apparent in unconditional models. Furthermore, given that there were many analyses included in this study, these results bear replication.

Lastly, the current study is limited by small sample size, which may have impacted the power to detect significant effects. Additionally, given the small sample size, psychological outcomes were unable to be examined within one model. It may be that including fatigue along

with the mood outcomes impacts the results, as this would allow the correlation between mood and fatigue to be modeled and corrected for. In fact, fatigue and sleep disturbance are common in cancer patients and survivors, and have been related to depressive symptoms and quality of life (Bower, 2008; Clevenger et al., 2013). Additionally, they may even have similar underlying neuroendocrine and immune pathways (Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008). However, in the current study, and particularly in more complex models, this was not able to be examined, as the number of parameters begins to exceed the sample size. Future research should examine the extent to which the correlation between fatigue and mood measures changes the relationships between life stress and protective factors on these outcomes.

### **Clinical Implications**

**Distress screening.** The results of this study highlight the need for measurement of distress in cancer patients particularly around the time of diagnosis. Though distress screening has become more prevalent (Carlson & Bultz, 2003), improvements can continue to be made. For example, previous research has shown that oncologists are more likely to recommend supportive counseling in patients with more progressive disease and less denial, and that this recommendation for counseling is unrelated to patients' distress and perceived social support (Söllner et al., 2001). The current findings also suggest that the assessment of non-cancer life stressors is particularly important in those without high levels of stress related to cancer, which may at first seem counterintuitive. Similarly, in individuals with low levels of life stress, unsolicited social support may be deleterious, though it is often assumed as beneficial.

The current findings also highlight the need for distress screening not just when patients are finally diagnosed with cancer, but at all doctor visits. A common theme from a qualitative study of women with ovarian cancer is that many felt they had symptoms prior to diagnosis, but

that their diagnosis of cancer was delayed (Ferrell, Smith, Cullinane, & Melancon, 2003). The frequency of cancer-related stressors in the current sample is consistent with this idea, as many women experienced multiple stressful events related to the eventual diagnosis of their cancer, including many visits to the doctor and procedures such as blood tests, ultrasounds, CT scans. However, one study showed that women who were initially diagnosed with depression or told their symptoms were stress were more likely to have greater delays in diagnosis (Goff, Mandel, Muntz, & Melancon, 2000), so, though screening for distress is important, presence of distress should not rule out the diagnosis of ovarian cancer.

**Interventions.** The current findings suggest that patients would benefit from improving ability to manage stress, particularly when faced with significant threat associated with either cancer or non-cancer stressors, and especially cancer-related losses in particular. In fact, psychological interventions for patients with cancer often contain a stress reduction component, and one meta-analysis showed that self-help interventions including stress management showed greater effects on mental health than those without (Matcham et al., 2014). Furthermore, Cognitive-Behavioral Stress Management has been shown to improve quality of life and psychological well-being in women with breast cancer, with many effects being mediated by improved confidence in one's ability to relax (Antoni et al., 2001). Other interventions, including positive psychology interventions (Casellas-Grau, Font, & Vives, 2014) and mind-body interventions such as yoga (Smith & Pukall, 2009) have been shown to reduce stress and improve quality of life in cancer patients. Additionally, in patients with significant cancer-related stress, interventions focused on existential and spiritual concerns may be particularly helpful (Hench & Danielson, 2009).

The current findings also suggest that interventions that increase self-compassion may be particularly helpful for those who experience cancer loss and have low social support. Interventions such as Compassionate Mind Training, guided imagery, Mindfulness Based Stress Reduction, Dialectical Behavioral therapy, and Acceptance and Commitment Therapy may all increase self-compassion (Barnard & Curry, 2011). Future work on psychosocial interventions in cancer patients should examine the comparative effectiveness of these interventions in the context of life stressors, as well as the mechanisms underlying effectiveness. For example, research has shown that Mindfulness-Based Stress Reduction may offer multiple pathways that increase psychological well-being in cancer patients, as it has been shown to increase self-acceptance and directly improve quality of life and biomarkers of stress (Carlson et al., 2007).

## **Conclusion**

This study utilized methodologically rigorous methods of examining life stress as well as psychological outcomes in women with ovarian cancer. The current findings highlight the psychological impact of the experience of cancer itself, as cancer-related losses were the most predictive stressor. Additionally, the interactions found between cancer-related stressors and non-cancer related stressors suggest that, only in the presence of low cancer-related stress do other stressors have an impact on psychological well-being. The only direct effect of non-cancer stressors was the finding that non-cancer loss was related to greater fatigue at baseline, which suggests that fatigue is a particularly important measure of well-being that is most susceptible to the impact of non-cancer life stress.

The current study also examined a variety of potential functional impacts that psychosocial protective resources of social support, self-acceptance, mastery, and purpose in life may have on the relationship between stress and psychological well-being. Social support was

found to be the most predictive moderator of threat due to life stressors, though this relationship varied in different contexts. Additionally, in predicting distress and depressed mood at baseline, this moderation effect was mediated by increases in self-acceptance, a factor which has rarely been studied in patients with cancer.

Ultimately, the strengths of the current study offer a greater understanding of life stress and protective psychosocial resources in patients with ovarian cancer. The conclusions that can be drawn from this study can inform future research, with clinically significant implications particularly for distress screening and interventions. Future research should continue to examine the psychological impact of different stressors in the context of patients with cancer, as well as how social support and other protective resources may play a role in psychological well-being.

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