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Relationship Between Disengagement Coping During Primary Treatment for Non-Metastatic Breast Cancer and Long-Term Depressive Symptoms: The Role of Pain and Fatigue Interference

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UNIVERSITY OF MIAMI

RELATIONSHIP BETWEEN DISENGAGEMENT COPING DURING PRIMARY
TREATMENT FOR NON-METASTATIC BREAST CANCER AND LONG-TERM
DEPRESSIVE SYMPTOMS: THE ROLE OF PAIN AND FATIGUE INTERFERENCE

By

Hannah M. Fisher

A THESIS

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Master of Science

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December 2017

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Relationship between Disengagement Coping
During Primary Treatment for Non-Metastatic
Breast Cancer and Long-Term Depressive
Symptoms: The Role of Pain and Fatigue Interference

Abstract of a thesis at the University of Miami

Thesis supervised by Michael H. Antoni, Ph.D.
No. of pages in text (71)

Breast cancer survivors experience significant symptom burden during active treatment and survivorship. Psychosocial factors, such as coping, may influence the course of treatment-related physical and psychological symptomatology. Disengagement coping in particular, may be relevant to breast cancer survivors' symptom experience. Yet, classification of individual coping responses to comprise a higher order category of disengagement coping remains ambiguous, and research investigating the role of disengagement coping on the trajectory of physical and psychological symptoms in breast cancer survivors has yielded inconsistent findings. This study aimed to test a mediation model elucidating the longitudinal relationship between a latent construct of disengagement coping at the time of diagnosis and depressive symptoms 5 years later via pain and fatigue interference during the initial 12 month period of primary treatment for breast cancer.

Stage 0-III breast cancer patients (N=240) were recruited 4 to 10 weeks post-surgery and completed a baseline (T1) questionnaire measuring coping responses, pain, fatigue, and depressive symptoms. Women were reassessed 6-months (T2) and 12-months (T3) post-study enrollment. A long-term follow-up 5-years post-surgery (T5) was also conducted among available cases to assess depressive symptoms and general health status.

A single factor confirmatory factor analysis was conducted to investigate whether behavioral disengagement, denial, self-blame, and venting share a common variance indicative of disengagement coping. Structural equation modeling was used to test the proposed mediation model.

After taking into account modification indices recommended by the *Mplus* program, a measurement model consisting of behavioral disengagement, denial, self-blame, and self-distraction exhibited good model-data correspondence, suggesting that these coping strategies may constitute a higher order category of disengagement coping. Results from structural equation modeling did not reveal direct effects relating a latent construct of disengagement coping at T1 and long-term depressive symptoms at T5 or pain and fatigue interference at T3, nor was there evidence to suggest mediation between T1 disengagement coping and T5 depressive symptoms via T3 pain and fatigue interference. However, more depressive symptoms at T3 ($\beta = .39$, $SE = .12$, $z = 3.02$, 95% CI [.16, .62], $p < .01$) and receipt of chemotherapy within three weeks of the T3 assessment ($\beta = .30$, $SE = .07$, $z = 4.07$, 95% CI [.16, .43], $p < .001$) were associated with greater depressive symptomatology during survivorship (T5).

Findings from the current study expand upon previous coping research exploring classifications of disengagement coping techniques. Moreover, results highlight the relevance of assessing for depressive symptoms and receipt of chemotherapy 12 months post-diagnosis, as these characteristics may relate to worse psychological functioning well into the survivorship phase. Additional research is warranted to clarify the relationship between disengagement coping, physical symptomatology, and long-term psychological functioning of breast cancer survivors.

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Chapter 1: INTRODUCTION

Breast cancer accounts for 29% of all new cancer diagnoses in women (Siegel, Miller, & Jemal, 2016). Fortunately, earlier detection due to widespread use of mammography screening, improved diagnostic procedures, and advances in systemic and adjuvant endocrine therapies have given rise to a growing number of breast cancer survivors (DeSantis et al., 2014; Pinto & de Azambuja, 2011; Siegel et al., 2016). Since the 1970s, the 5-year survival rate for female breast cancer patients has significantly improved, and it is estimated that there will be nearly 4 million long-term (i.e., 5 years or more post-diagnosis) breast cancer survivors by 2024 (DeSantis et al., 2014).

Although women with breast cancer are living longer, prolonged survival is often associated with new challenges (Harrington, Hansen, Moskowitz, Todd, & Feuerstein, 2010). Many breast cancer survivors report considerable symptom burden following the completion of primary treatment, with concerns such as pain, fatigue, and depressive symptoms continuing to negatively affect physical and mental quality of life well beyond the acute treatment phase (Chopra & Kamal, 2012; DeSantis et al., 2014; Ganz, Rowland, Desmond, Meyerowitz, & Wyatt, 1998; Harrington et al., 2010; Pinto & de Azambuja, 2011; Shi et al., 2011). As such, there is a need to better characterize the trajectory of treatment-related sequelae persisting throughout disease-free survivorship (Ganz et al., 1998; Pinto & de Azambuja, 2011), and to elucidate psychosocial factors (e.g., coping) that exacerbate how these symptoms impair functioning and quality of life across the breast cancer continuum (Shi et al., 2011). Endeavoring to clarify the symptom burden of breast cancer patients throughout disease-free survivorship may improve long-term care guidelines in oncological settings (Chopra & Kamal, 2012).

Treatment Course

Primary treatment for breast cancer involves a combination of surgery, chemotherapy, radiation therapy, and/or hormone therapy (DeSantis et al., 2014). Due to advances in the surgical techniques for removing cancerous breast tissue, conventional practice has shifted away from radical surgical procedures (e.g., mastectomy) in favor of breast-conserving surgeries (BCS: i.e., lumpectomy) that reduce treatment burden (DeSantis et al., 2014). Lymph node removal, axillary lymph node dissection, or less invasive sentinel lymph node dissection may be indicated if the cancer has spread beyond the milk duct of the breast (DeSantis et al., 2014). BCS is not appropriate for all breast cancer patients, particularly when there is evidence of large or multiple tumors (DeSantis et al., 2014). In these cases, removal of the whole breast via mastectomy is recommended (DeSantis et al., 2014). Increasingly, BCS-eligible women are electing to undergo mastectomy procedures due to recurrence and cosmetic concerns (DeSantis et al., 2014).

After receiving BCS, the majority of women with early-stage breast cancer will subsequently undergo adjuvant treatment to reduce the risk of local recurrence (DeSantis et al., 2014; Jung, Herrmann, Griggs, Oaklander, & Dworkin, 2005). While this multimodal treatment regimen may improve survival, it is also associated with prolonged medical intervention, protracted treatment-related sequelae, and poor long-term quality of life (Chopra & Kamal, 2012; Ganz et al., 1998; Harrington et al., 2010). The initial 12 months after diagnosis are particularly stressful for breast cancer patients as the risk for significant symptom burden induced by the cancer and its treatment is especially high during this period (Shi et al., 2011). Accordingly, there is a substantial body of literature

characterizing the trajectory of short- and long-term physical and mental concerns associated with breast cancer and its treatment.

Treatment-Related Physical Sequelae

Secondary complications of surgical procedures and post-operative adjuvant therapy are common. In a study conducted by Janz et al. (2007), female breast cancer patients who were approximately 7 months post-treatment reported a mean number of 7 symptoms (e.g., pain, fatigue, worrying, etc.) that had persisted since the completion of primary treatment (Janz et al., 2007). Pain and fatigue are frequently cited treatment-related concerns for many breast cancer survivors, and have been the focus of much research on the symptom burden associated with breast cancer.

Pain. While individual findings on the prevalence of treatment-related pain are varied, there is consensus in the literature that 20-50% of breast cancer survivors will develop chronic pain after completing primary treatment (Andersen & Kehlet, 2011; Bishop & Warr, 2003; DeSantis et al., 2014; Gartner et al., 2009; Jung et al., 2005; van den Beuken-van Everdingen et al., 2007). It is widely accepted that surgical treatment for breast cancer can result in painful post-surgical syndromes, such as post-mastectomy pain and phantom breast pain (Glare et al., 2014). Similarly, radiation therapy can produce an array of painful conditions due to nerve and/or bone damage (e.g., plexopathies and osteoradionecrosis) (Glare et al., 2014). Yet, the most common pain syndrome associated with breast cancer treatment is chemotherapy-induced peripheral neuropathy (CIPN) (Glare et al., 2014). CIPN pain is characterized as an uncomfortable tingling, burning, or numb sensation that may worsen in the months following completion of chemotherapy (Glare et al., 2014). The prevalence of CIPN cannot be overstated, with incidence rates

near 100% in breast cancer patients undergoing chemotherapy (Cleeland, Farrar, & Hausheer, 2010; Glare et al., 2014).

Treatment-related pain is a complex multidimensional experience (Serlin, Mendoza, Nakamura, Edwards, & Cleeland, 1995). Factor analyses have consistently demonstrated that pain is best explained by two domains believed to correspond with the severity of a person's pain (i.e., pain severity) and the degree to which the pain interferes with a person's functioning and overall quality of life (i.e., pain interference) (Serlin et al., 1995). These interrelated dimensions of pain are relevant within the context of breast cancer since more severe disease and/or treatment-related pain will likely concurrently relate to greater impairment and subsequently worse quality of life throughout disease-free survivorship.

Consistent with two-dimensional conceptualizations of pain, there is research to suggest that many breast cancer survivors report post-treatment pain interference to life roles and responsibilities (e.g., parenting, employment, social relationships, involvement in leisure activities etc.; (Andersen & Kehlet, 2011; Berger, Gerber, & Mayer, 2012; Breivik et al., 2009; Cleeland et al., 2010; Gartner et al., 2010; Glare et al., 2014; Mehnert, 2011; Reddick, Nanda, Campbell, Ryman, & Gaston-Johansson, 2005). In fact, Harrington et al. (2010) report that up to 23% of breast cancer survivors endorse functional limitations due to pain in the 6 to 12 months following diagnosis and primary treatment (Harrington et al., 2010). In a similar study investigating persistent physical symptomatology following completion of primary treatment for breast cancer, Tasmuth and colleagues observed that pain "slightly" affected the daily lives of approximately 50% of women, while nearly 25% reported that their pain "moderately" interfered with

their ability to perform activities of daily living (Tasmuth, von Smitten, Hietanen, Kataja, & Kalso, 1995). Despite an expanding interest in pain interference, the majority of pain research continues to primarily focus on pain severity. To further understand treatment-related pain and its long-term effect on the physical and mental well-being of breast cancer survivors, research should endeavor to clarify the specific role of pain interference, beyond that of pain severity.

Fatigue. In addition to pain, research has also demonstrated the presence of debilitating fatigue in the months following breast cancer treatment (DeSantis et al., 2014). Fatigue is often described as the most common and distressing consequence of primary treatment, and is characterized as a multidimensional construct encompassing subjective feelings of tiredness, weakness, and lack of energy (Bower, 2014). The time-course of fatigue across the breast cancer experience has been well characterized in extant literature (Pinto & de Azambuja, 2011). Approximately one third of breast cancer survivors report fatigue immediately following the completion of primary treatment, while nearly 50% of women who are 6 to 12 months post-treatment endorse persistent fatigue (Andrykowski, Donovan, Laronga, & Jacobsen, 2010; Bower, 2006; Carlson, Waller, Groff, Giese-Davis, & Bultz, 2013; Harrington et al., 2010; Jacobsen et al., 2007; Jacobsen et al., 1999).

Fatigue related to breast cancer and its treatment causes considerable disruption to functioning and overall quality of life (Berger et al., 2012; Bower, 2014; Jacobsen et al., 1999). Jacobsen and colleagues (1999) observed that when compared to age-matched healthy controls, breast cancer survivors reported significantly elevated fatigue severity and frequency, as well as fatigue interference to quality of life after the completion of

primary treatment (Jacobsen et al., 1999). Broadly, fatigue has been related to poorer long-term emotional well-being, yet there is a need for future research to investigate the distinct influence of fatigue interference on quality of life throughout disease-free survivorship beyond the effects of fatigue severity (Berger et al., 2012; Bower, 2014).

Long-Term Psychological Sequelae

For some breast cancer survivors, distressing symptoms can emerge years after the completion of primary treatment (i.e., late effects; DeSantis et al., 2014). Long-term difficulties resulting from breast cancer and its treatment may differ from those experienced during diagnosis and adjuvant therapy; therefore, it is necessary for research to explicate unique symptom experiences across the entire breast cancer trajectory (Chopra & Kamal, 2012; Pinto & de Azambuja, 2011).

Levels of depressive symptoms are typically highest in the period surrounding diagnosis and active treatment, and then may decline as patients become accustomed to their disease (Vahdaninia, Omidvari, & Montazeri, 2010). Some studies of long-term breast cancer survivors have found post-treatment depressive symptoms at comparable levels to those of the general population (Pinto & de Azambuja, 2011), while others report that 21-34% of breast cancer patients continue to endorse elevated levels of distress 12 months post-diagnosis (Harrington et al., 2010; Knobf, 2007; Vahdaninia et al., 2010). Similarly, literature on the trajectory of depressive symptomatology beyond the first year post-treatment is mixed. In studies that assessed elevated but non-clinical levels of depressive symptoms, rates were 15-32% in breast cancer survivors 2 to 5 years post-treatment (Avis, Levine, Case, Naftalis, & Van Zee, 2015; Avis et al., 2013; Burgess et al., 2005; Harrington et al., 2010; Mols, Vingerhoets, Coebergh, & van de Poll-Franse,

2005). However, Knobf and colleagues (2007) reported that 24% of breast cancer survivors exhibited clinically significant levels of depressive symptoms 2 years after being diagnosed with breast cancer (Knobf, 2007).

These results suggest that for some long-term breast cancer survivors, depressive symptoms may decrease over time, but for others they may persist well into the survivorship phase. Long-term psychological adjustment following a breast cancer diagnosis and treatment regimen is a critical concern for health care professionals in the oncology community. Understanding factors that worsen physical and mental quality of life throughout disease-free survivorship may help to enhance the medical and psychosocial care of breast cancer patients across the disease trajectory.

Pain, Fatigue, and Long-Term Depressive Symptoms

A symptom cluster involving pain, fatigue, and depressive symptoms in breast cancer survivors is well-established in the literature (Beck, Dudley, & Barsevick, 2005; Pud et al., 2008; So et al., 2009). Indeed, pain and fatigue commonly co-occur with depressive symptoms across the entire breast cancer continuum (Bower et al., 2000; Carlson et al., 2013; Pud et al., 2008; So et al., 2009). Moreover, there is evidence to suggest that levels of post-treatment pain and fatigue are related to long-term depressive symptoms in breast cancer patients (Lam, Shing, Bonanno, Mancini, & Fielding, 2012; Reich, Lesur, & Perdrizet-Chevallier, 2008; So et al., 2009; Spiegel & Giese-Davis, 2003; Vahdaninia et al., 2010). In recent longitudinal studies conducted by Avis et al. (2013, 2015), the presence of depressive symptoms in breast cancer survivors more than 2 years post-diagnosis was associated with fatigue and pain, such that decreases in pain and fatigue during active treatment for breast cancer preceded significant decreases in

depressive symptoms in the years following treatment (Avis et al., 2015; Avis et al., 2013).

Despite an abundance of research investigating the relationship between physical concerns (e.g., pain and fatigue) during treatment and depressive symptoms during disease-free survivorship, findings remain largely inconsistent. Several studies have found no relationship between symptoms experienced during primary treatment for early stage breast cancer and depressive symptoms 5 years post-diagnosis (Burgess et al., 2005; Carlson et al., 2013; Mols et al., 2005), and the majority of these studies have focused on levels of pain and fatigue severity, instead of interference. Given prior research demonstrating how pain and fatigue considerably impair activities of daily living, social relations, and general enjoyment of life, it is plausible that levels of pain and fatigue interference (rather than symptom severity) precipitate depressive symptoms in breast cancer survivors up to 5 years post-diagnosis.

Coping with Breast Cancer

Although pain interference, fatigue interference, and depressive symptoms are common throughout the breast cancer trajectory, there remains substantial variability in how women adjust to their disease. Identifying factors that facilitate or impede positive adaptation throughout disease-free survivorship will contribute to the development of more effective psychosocial treatments that address long-term adjustment to the breast cancer experience (Bishop & Warr, 2003; Low, Stanton, Thompson, Kwan, & Ganz, 2006). To this end, models of coping have long been used to explain individual differences in how women with breast cancer adapt to their disease (Bussell & Naus, 2010; Carver & Connor-Smith, 2010; Carver et al., 1993; Carver, Scheier, & Weintraub,

1989; Low et al., 2006; Manne et al., 1994; Osowiecki & Compas, 1998; Rao, 2009; Reddick et al., 2005; Shapiro et al., 1997; Stanton, Danoff-Burg, & Huggins, 2002).

Theories of coping. Coping has traditionally been defined as voluntary or involuntary cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as threatening, hurtful, or distressing (Lazarus & Folkman, 1984). Changes to the conceptualization of coping have advanced how researchers make sense of coping within the context of chronic illnesses such as breast cancer.

Prior to the emergence of Lazarus and Folkman's Transactional Theory, coping was widely believed to reflect an enduring personality trait (Manne et al., 1994). Since then, substantial theoretical development has resulted in altered conceptualizations of coping as a dynamic process that changes in response to particular situations (Lazarus, 1966; Lazarus & Folkman, 1984). The Transactional Theory of stress and coping posits that any given response to stress consists of three processes: Primary Appraisal, Secondary Appraisal, and Coping (Lazarus & Folkman, 1984). Primary appraisal involves the initial perception of threat to oneself and one's goals as a result of situational stress, while secondary appraisal is the process of considering potential responses to this threat (Carver et al., 1989). Using information obtained during primary and secondary appraisal, an individual may select a coping responses depending on motivation to either maintain or abandon progress towards one's goals in light of current stress (Carver et al., 1989).

Widespread adoption of the Transactional Theory has led to growth in situation-specific measurement of coping (Manne et al., 1994). To date, there are several measures that assess coping responses to a particular stressful event (Carver, 1997). These include

the Ways of Coping (Lazarus & Folkman, 1984), Multidimensional Coping Inventory (Endler & Parker, 1990), the Coping Strategies Inventory (Tobin, Holroyd, Reynolds, & Wigal, 1989), as well as the COPE and Brief COPE inventories (Carver, 1997; Carver et al., 1989). These questionnaires allow for a comprehensive examination of coping responses within the context of a salient stressor such as breast cancer (Carver, 1997). Indeed, many of these measures have been applied to chronically ill populations, in an effort to elucidate how individuals cope with highly stressful situations (Bellizzi & Blank, 2006; Bussell & Naus, 2010; Carver et al., 1993; Felton, Revenson, & Hinrichsen, 1984; Reddick et al., 2005; Stanton et al., 2002). In addition to identifying common ways of coping with a chronic illness, many studies have also attempted to utilize these questionnaires to form higher order classifications of coping that may explain both short- and long-term adjustment to stressful diseases (Bellizzi & Blank, 2006; Bussell & Naus, 2010; Stanton et al., 2002).

Classifying coping. Despite considerable progress in the field of coping research, a typology to organize individual coping responses has remained elusive. To address this, Skinner and colleagues (2003) proposed a heuristic that hierarchically distinguishes coping (Skinner, Edge, Altman, & Sherwood, 2003). At the lowest level of the hierarchy are dynamic, real-time instances of coping (e.g., “I tried to figure out what to do,” “I got advice from someone,” etc.) (Skinner et al., 2003). These specific coping responses must be categorized into intermediate levels that represent conceptually clear, mutually exclusive, and exhaustive ways of coping (e.g., problem-solving, rumination, venting, etc.;(Skinner et al., 2003). Lastly, intermediate coping families must themselves be

classified in to higher order categories (Skinner et al., 2003). To achieve this, research has often relied on top-down approaches (Skinner et al., 2003).

Broadly speaking, top-down classification of coping uses higher order categories to organize coping by the function a specific coping response serves in relation to one's goals when threatened (Skinner et al., 2003). One of the most widely cited categorizations of coping is that between engagement and disengagement coping. Engagement coping is characterized by actions that promote continued progress towards goals despite stress (e.g., problem-solving, planning etc.), while disengagement coping often involves behaviors that encourage distraction from and/or abandonment of goals when confronted with a stressor (e.g., behavioral disengagement, self-distractions etc.) (Carver & Connor-Smith, 2010).

Unfortunately, the utility of this distinction remains limited by persistent ambiguity in the boundaries that circumscribe it, making it difficult to aggregate and compare findings throughout the field. Attempts to characterize engagement versus disengagement coping are increasingly ubiquitous in coping research, yet there is a need for further clarification of the lower order coping responses that comprise higher order categories of engagement and disengagement coping within the context of chronic illnesses such as breast cancer.

Defining Disengagement Coping

Clarifying the components of disengagement coping (also known as passive, avoidant, or maladaptive coping) is particularly worthwhile since this style of coping may negatively influence breast cancer survivors' medical recovery and psychosocial adjustment following adjuvant treatment. Theoretical classifications of disengagement

coping have been supported by empirical research utilizing situation-specific measurement of coping responses (Bellizzi & Blank, 2006; Bussell & Naus, 2010; Compas et al., 2006; Danhauer et al., 2013; Lebel, Rosberger, Edgar, & Devins, 2008; Litman, 2006; Luszczynska, Gerstorf, Boehmer, Knoll, & Schwarzer, 2007; Skinner et al., 2003; Stanton et al., 2002; Zuckerman & Gagne, 2003). The majority of these studies have found that coping responses such as behavioral disengagement, denial, self-blame, and venting load positively onto a factor seemingly representative of disengagement coping (Bussell & Naus, 2010; Compas et al., 2006; Danhauer et al., 2013; Skinner et al., 2003; Stanton et al., 2002). However, despite an expanding interest in explicating the components of disengagement coping, there is still a lack of consensus regarding the specific coping responses that represent disengagement coping. In particular, classification of coping responses such as substance use and mental disengagement (i.e., self-distraction) remains inconclusive (Compas et al., 2006; Danhauer et al., 2013; Litman, 2006; Luszczynska et al., 2007; Zuckerman & Gagne, 2003). Furthermore, there is a need to examine how disengagement coping influences the physical and mental quality of life of breast cancer survivors in the months following completion of adjuvant therapy.

Disengagement Coping and Breast Cancer

Although limited clarity regarding the specific coping responses that comprise disengagement coping remains, there is a large body of research focused on understanding the considerable variability with respect to how breast cancer survivors cope with both short- and long-term treatment-related sequelae. Coping is particularly relevant within the context of highly impactful illnesses, such as breast cancer, because it

affects long-term quality of life (Reddick et al., 2005). While some breast cancer survivors may utilize coping strategies that facilitate personal growth as a result of their disease (Bellizzi & Blank, 2006), others may resort to disengagement coping techniques to manage their disease and its treatment (Reddick et al., 2005). Disengagement coping is common among breast cancer survivors and research demonstrates that this type of coping is associated with worse physical symptoms and emotional distress across the entire breast cancer continuum (Andersen & Kehlet, 2011; Bellizzi & Blank, 2006; Bishop & Warr, 2003; Bussell & Naus, 2010; Manne et al., 1994; Osowiecki & Compas, 1998; Reddick et al., 2005).

Disengagement Coping and Treatment-Related Physical Sequelae

There is a growing body of research suggesting that disengagement coping may relate to common physical symptoms (e.g., pain and fatigue) associated with breast cancer treatment (Kenne Sarenmalm, Ohlen, Jonsson, & Gaston-Johansson, 2007; Pinto & de Azambuja, 2011; Reddick et al., 2005). In a study conducted by Shapiro et al. (1997), disengagement coping was a significant predictor of physical concerns (e.g., pain, fatigue, etc.) in women with early stage breast cancer undergoing adjuvant therapy (Shapiro et al., 1997). Bishop and colleagues (2003) observed similar findings in a study investigating the relationship between disengagement coping and adaptation to chronic pain associated with breast cancer treatment (Bishop & Warr, 2003). Disengagement coping responses were associated with greater pain-related disability in breast cancer patients who had completed primary treatment (Bishop & Warr, 2003).

Disengagement coping has also been implicated in the development of fatigue (Pinto & de Azambuja, 2011; Reddick et al., 2005). Research from Andrykowski et al.

(2010) has demonstrated that treatment-related fatigue is associated with reports of disengagement coping at the time of breast cancer diagnosis (Andrykowski et al., 2010). These findings were corroborated by Bower and colleagues (2014) who also observed a relationship between disengagement coping and elevated fatigue well into the survivorship phase (Bower, 2014).

While these findings are provocative, it remains unclear how disengagement coping independently influences pain and fatigue interference, as opposed to pain and fatigue severity. It is plausible that the use of disengagement coping early on in the breast cancer experience may predispose a breast cancer survivor for greater pain and fatigue-related functional impairment post-treatment due to disengagement coping habits. There is a need to test these associations longitudinally across the entire breast cancer trajectory to further clarify the role of coping on symptom burden throughout disease-free survivorship.

Disengagement Coping and Long-Term Depressive Symptoms

Individual differences in coping have also been used to elucidate variation in psychological adjustment throughout the breast cancer experience. There is consensus in the literature that disengagement coping is predictive of heightened psychological distress, in particular, depressive symptomatology (Avis et al., 2015; Avis et al., 2013; Bussell & Naus, 2010; Carver et al., 1993; Kenne Sarenmalm et al., 2007; Li & Lambert, 2007; Low et al., 2006; Manne et al., 1994; Osowiecki & Compas, 1998; Reddick et al., 2005; Stanton et al., 2002). Specific disengagement coping responses most commonly associated with elevated depressive symptoms include denial, behavioral disengagement,

and self-blame (Andreu et al., 2012; Carver, 1997; Carver et al., 1993; Li & Lambert, 2007).

These findings are informative as they provide a largely consistent conceptualization of disengagement coping and its influence on psychological adjustment to breast cancer. Yet, there is still inconsistency in the time-course of these effects; some studies reported concurrent associations between disengagement coping and depressive symptoms (Kenne Sarenmalm et al., 2007; Li & Lambert, 2007; Manne et al., 1994; Osowiecki & Compas, 1998; Reddick et al., 2005), while others demonstrated a relationship between disengagement coping and late-onset elevations in depressive symptomatology at 1, 2, and 5 years post-diagnosis (Andreu et al., 2012; Avis et al., 2015; Avis et al., 2013; Bussell & Naus, 2010; Carver et al., 1993; Stanton et al., 2002). Thus, additional research is needed to confirm how disengagement coping influences depressive symptomatology across the entire breast cancer continuum.

Current Study

As research exploring the association between disengagement coping and poorer long-term psychological adjustment to the breast cancer experience continues to grow, a related question is whether pain and fatigue experiences in the months following primary treatment play a role in this association. Based on literature demonstrating links between disengagement coping and short-term pain and fatigue interference, as well as longer-term depressive symptoms, the current study explored the possibility that effects of disengagement coping on depressive symptoms throughout disease-free survivorship are mediated by the magnitude of pain and fatigue interference after completion of primary treatment.

There is limited research exploring mediated pathways involving disengagement coping, treatment-related physical sequelae, and long-term depressive symptoms in breast cancer populations, and the majority of this research hypothesizes that coping may operate as the mediator (Andreu et al., 2012; Carver et al., 1993). Importantly though, the relations between coping and adaptation to chronic illness are likely dynamic and may vary in directionality depending on the stressful situation (Bishop & Warr, 2003). Additionally, there is inconsistency in the coping literature regarding the specific coping responses that comprise a higher order category of disengagement coping.

To address these gaps in the literature, the current study aimed to elucidate the longitudinal relationship between a latent construct of disengagement coping at the time of diagnosis and depressive symptoms 5 years later via pain and fatigue interference during the initial 12 month period of primary treatment for breast cancer.

Specific Study Aims and Hypotheses

Aim 1: Measurement model of disengagement coping. To assess whether a measurement model comprised of post-surgical measures of behavioral disengagement, denial, self-blame, and venting is indicative of a latent variable of post-surgical disengagement coping.

Hypothesis 1: The shared variance among post-surgical behavioral disengagement, denial, self-blame, and venting will positively load onto a latent factor reflecting post-surgical disengagement coping.

Aim 2: Overall model fit of structural model. To examine whether the proposed mediation model fits the data. Direct pathways by which post-surgical disengagement coping relates to post-adjuvant pain and fatigue interference, and long-

term depressive symptoms 5 years post-diagnosis will be examined. Additionally, direct effects relating post-adjuvant pain and fatigue interference with long-term depressive symptoms will be investigated. Indirect pathways will be assessed to determine whether post-adjuvant pain and fatigue interference operate as mediating variables by which post-surgical disengagement coping is related to depressive symptoms 5 years post-diagnosis.

Hypothesis 2: Greater disengagement coping post-surgery will be associated with greater pain and fatigue interference after completion of adjuvant therapy, and greater depressive symptoms 5 years after diagnosis. More pain and fatigue interference post-adjuvant therapy will be associated with more depressive symptoms during survivorship. Higher levels of post-surgical disengagement coping will relate to greater depressive symptomatology 5 years post-diagnosis indirectly via post-adjuvant pain and fatigue interference.

Chapter 2: METHOD

Participants

Women diagnosed with non-metastatic stage 0-III breast cancer were recruited through physician referrals and community advertising and enrolled in a randomized controlled trial between 1998 and 2005. Participants were required to have had surgery for primary breast cancer in the 4–10 weeks prior to enrollment (lumpectomy, mastectomy, or bilateral mastectomy). Exclusion criteria included: (1) a diagnosis of stage IV breast cancer or prior cancer (except minor skin cancers such as squamous or basal cell carcinomas); (2) ongoing neoadjuvant or post-surgical adjuvant treatment; (3) a major medical condition other than cancer; (4) falling outside the age range of 21–75 years of age; (5) non-fluency in English; (6) previous hospitalization for psychiatric conditions; and (7) current psychosis, suicidality, major depressive disorder or panic disorder. The original trial tested the effects of a psychosocial intervention, Cognitive Behavioral Stress Management (CBSM). The study was a single center, single blind, randomized, parallel assignment efficacy trial approved by the Human Subjects Research Office of the University of Miami (UM) Institutional Review Board (IRB; National Institutes of Health Clinical Trial NCT01422551). A detailed description of the original study design is available in previous reports (Antoni et al., 2006; Vargas et al., 2014).

Procedures

From a total screening sample of 502 women, 240 were consented, enrolled, completed a baseline assessment, and were then randomized to CBSM intervention or a 1-day psychoeducational control group. Randomization and assessments were completed by blinded study coordinators. Initial assessments (T1) took place at approximately 4 to 10

weeks post-surgery and prior to the initiation of adjuvant cancer treatment (chemotherapy and radiation). These baseline assessments consisted of blood samples and psychosocial questionnaires measuring coping responses, pain, fatigue, depressive symptoms, and quality of life. All assessments took place prior to randomization to study intervention or control group. In addition to the initial assessment, women were reassessed 6-months (T2) and 12-months (T3) post-study enrollment. A long-term follow-up 5-years post-surgery (T5) was also conducted to assess depressive symptoms and general health status.

Measures

Demographic and medical characteristics. At the time of enrollment in the initial trial, self-reported information was collected regarding demographics (e.g., age, race/ethnicity, and partnered status) and socioeconomic status (e.g., income). Follow-up assessment time points similarly obtained self-reported medical and treatment-related information (e.g., stage of disease, surgical procedure, type of adjuvant treatment received). At 5-year follow-up women reported on breast cancer recurrence and overall medical status. Self-reported medical information was verified with medical chart review.

Pain interference. The 7-item Pain Interference subscale of the Brief Pain Inventory (BPI) was used to assess participants' current pain interference (Cleeland & Ryan, 1994). Women were asked to rate how much their pain affected specific life domains (e.g., general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life) using a scale from 1 = does not interfere to 9 = completely interferes. These ratings were averaged to obtain a pain interference score, ranging from 1 to 9, with higher scores indicating greater pain interference. The BPI has demonstrated adequate reliability and sensitivity in prior studies investigating pain severity and

interference in cancer patients (Cleeland & Ryan, 1994; Kornguth, Keefe, Wright, & Delong, 2000). Reliability for the current sample was high, $\alpha = .95$.

Fatigue interference. Fatigue interference was assessed using the 7-item Perceived Interference subscale of the Fatigue Symptom Index (FSI), which was developed for and validated in cancer patients (D. M. Hann, Denniston, & Baker, 2000; D. M. Hann et al., 1998). Using a scale from 1 = no interference and 9 = extreme interference, the perceived interference subscale assessed the degree to which fatigue in the past week interfered with life activities, concentration, relationships and quality of life (e.g., general level of activity, ability to bathe and dress yourself, normal work activity, ability to concentrate, relations with other people, enjoyment of life, and mood). The total score for this subscale was obtained by averaging the items. Scores range from 1 to 9, with higher scores indicating greater fatigue interference. Reliability for the current sample was high, $\alpha = .94$.

Coping. Coping responses were measured using Carver's (1997) Brief COPE scale, which consists of 28 items grouped into 14 subscales (i.e., self-distraction, active coping, denial, substance use, use of emotional support, use of instrumental support, behavioral disengagement, venting, positive reframing, planning, humor, acceptance, religion, and self-blame) (Carver, 1997). In previous samples, these subscales have had acceptable alpha reliabilities, with 11 of the 14 subscales exceeding .60 and the remaining three (venting, denial, and acceptance) exceeding .50 (Carver, 1997). In the present study, alpha reliabilities ranged from .53 to .92. Participants were asked to rate how they are currently coping with the stress in their life associated with their breast cancer and its treatment. Example responses include "I've been concentrating my efforts on doing something about the situation I am in," "I have been saying to myself, this isn't

real,” and “I’ve been giving up trying to deal with it.” Response choices range from 1 = “I haven’t been doing this at all” to 4 = “I have been doing this a lot.”

Depressive symptoms. The severity of depressive symptoms 5 years post-diagnosis was assessed using the Center for Epidemiologic Studies-Depression Scale (CES-D). The CES-D consists of 20 items that represent major symptoms in the clinical syndrome of depression. Patients were asked to rate a series of statements (e.g., I was bothered by things that usually don’t bother me, I did not feel like eating; my appetite was poor, I had trouble keeping my mind on what I was doing” etc.) for how frequently they were experienced in the past week, using a scale of 0 = rarely or none of the time to 3 = most or all of the time. Item scores were summed to form a measure of depressive symptoms. Scores can range from 0 to 60, with higher scores indicating more depressive symptomatology. The CES-D has well established concurrent and construct validity (Carpenter et al., 1998; Sheehan, Fifield, Reisine, & Tennen, 1995), and has been used previously in breast cancer populations (D. Hann, Winter, & Jacobsen, 1999). Reliability for the current sample was high, $\alpha = .90$.

Analytic Strategy

Preliminary analyses and data screening. Preliminary descriptive analyses were conducted using Statistical Package for the Social Sciences Version 23 (SPSS 23). All variables of interest were screened for outliers, and distributions were inspected for skewness, kurtosis, and multivariate assumptions of normality (Kline, 2005). Subsequent analyses were performed using *Mplus* Version 7 (Muthén & Muthén, 2012). Missing data were estimated using full information maximum likelihood (FIML), which yields population estimates using all observed data to ensure each participant is represented in

the analyses. Four indices were estimated and interpreted for model fit: chi-square test (χ^2) >.05, confirmatory fit index (CFI) >.95, root mean squared error of approximation (RMSEA) <.06, and standardized root mean square residual (SRMR) <.08 (Kline, 2005).

Test of Hypothesis 1. A single factor confirmatory factor analysis (CFA) was conducted to test the measurement component of the model, which estimated whether four indicators (i.e., behavioral disengagement, denial, self-blame, and venting at T1) shared a common variance that can be explained by an underlying construct of disengagement coping at T1. Indices of model fit, as well as unstandardized and standardized factor loadings were examined to determine model-data correspondence and whether these indicators significantly loaded onto the latent disengagement coping construct. Unit loading identification (ULI) was applied whereby the first indicator of the measurement model was specified as the reference variable by setting the unstandardized factor loading at 1.0. This specification assigns the latent factor a scale related to that of the explained variance of the reference variable and allows for the estimation of all other parameters in the measurement model (Kline, 2005). The measurement model was re-specified and re-estimated consistent with suggested modification indices provided by *Mplus* and that were supported by theory.

Tests of Hypothesis 2. The structural component of the model was tested to determine the relationship between the latent variable of disengagement coping at T1 and the observed variables of pain and fatigue interference at T3 and depressive symptoms at T5. The model was specified with T3 pain and fatigue interference, and T5 depressive symptoms regressed on the latent variable of disengagement coping at T1. A path was specified to correlate pain interference with fatigue interference at T3. The model also

specified indirect paths from T1 disengagement coping to T5 depressive symptoms via T3 pain and fatigue interference.

Based on usage in prior literature, demographic (i.e., age) and cancer-related (i.e., stage of disease and type of adjuvant therapy received) factors served as covariates (Stagl, Antoni, et al., 2015; Stagl, Bouchard, et al., 2015). Stage of disease was categorized as noninvasive (Stage 0) or invasive (Stage I, II, or III) (Bouchard et al., 2016). Recent adjuvant therapy (i.e., chemotherapy and/or radiation therapy) was categorized as having received adjuvant therapy within three weeks of the T3 assessment or having not received adjuvant therapy in the three weeks prior to the T3 assessment. The CES-D was not administered at T3; instead, depressive symptoms were assessed via interview with the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960). HDRS scores were used to control for T3 levels of depressive symptoms when investigating the role of pain and fatigue interference on long-term depressive symptoms throughout survivorship. Lastly, as the current sample was part of a larger randomized controlled trial, study condition served as a covariate.

The structural model was estimated both independent of covariates and adjusted for covariates, and was re-specified consistent with suggested modification indices provided by *Mplus*. Indices of model fit were examined for model-data correspondence. The specific direct and indirect effects were interpreted by examining the z-statistic of the unstandardized coefficients at a two-tailed significance level of .05. The standardized coefficients were interpreted as measures of effect sizes and were evaluated at the following levels: .1 = small; .3 = medium; .5 = large (Cohen, 1988).

Finally, in model building it is advisable to consider different explanations for the data; an alternative model was tested to rule out reverse directionality between disengagement coping and physical symptomatology.

Chapter 3: Results

Participant Characteristics

Women were an average of 50.3 ($SD = 9.0$) years old, with the majority of women being partnered (62.5%). Over one third of the total sample was a member of a racial or ethnic minority group (36.4%). Additional demographic characteristics are reported in Table 1.

At the time of the T1 assessment, women were approximately 41 days post-surgery, and 50.8% had elected to undergo a lumpectomy procedure. Most women were diagnosed with Stage I and II disease, 37.8% and 38.2% respectively. Receipt of post-surgical adjuvant therapy was common, with nearly 60% reporting having undergone radiation therapy. At 5-year follow-up, the majority of women had remained cancer free (89.2%). Further descriptive information regarding medical characteristics of the sample are reported in Table 1.

Mean levels of pain and fatigue interference at T3, as well as depressive symptomatology at T5 are reported in Table 2. Overall, women in the current sample reported minimal pain and fatigue interference one year after diagnosis. On average, long-term depressive symptoms assessed using the CES-D indicated non-clinical levels of depression 5-years post-diagnosis.

Results of Hypothesis 1

A single factor CFA was tested to determine whether behavioral disengagement, denial, self-blame, and venting at T1 share a common variance explained by an underlying construct of disengagement coping. The specified model (Figure 1) was not a good fit for the data; $\chi^2(2) = 8.76, p = .01$; RMSEA = .12 (90% CI = [.05, .21]); CFI =

.91; SRMR = 0.05. Upon inspection of factor loadings, it was observed that behavioral disengagement ($B = 1.80$, $\beta = .53$, $SE = .08$, 95% CI [.38, .69], $p < .001$, $R^2 = .29$), denial ($B = 1.00$, $\beta = .37$, $SE = .08$, 95% CI [.21, .53], $p < .001$, $R^2 = .14$), self-blame ($B = 2.40$, $\beta = .80$, $SE = .14$, 95% CI [.59, 1.00], $p < .001$, $R^2 = .34$), and venting ($B = .65$, $\beta = .24$, $SE = .08$, 95% CI [.08, .39], $p < .001$, $R^2 = .06$) all significantly correlated with the latent factor of disengagement coping, such that disengagement coping accounted for 29%, 14%, 34%, and 6% of the variance of each indicator respectively. However, using an established cut-off to suggest strong indicators of a latent construct ($\beta > .4$), venting was determined to be a poor indicator of disengagement coping (Kline, 2005).

The measurement model was re-specified by replacing venting with substance use, a theoretically supported disengagement coping response (Figure 2; (Bellizzi & Blank, 2006). Although this measurement model exhibited good model-data correspondence, $\chi^2(2) = 0.02$, $p = .99$; RMSEA = .00 (90% CI = [.00, .00]); CFI = 1.00; SRMR = 0.002, the standardized factor loading for substance use fell below the established cut-off ($\beta = .06$, $SE = .08$, 95% CI [-.09, .21], $p = .43$, $R^2 = .004$), indicating that disengagement coping only explained .4% of the variance of substance use.

A third measurement model was re-specified to determine whether behavioral disengagement, denial, self-blame and self-distraction are indicators of a latent factor of disengagement coping (Figure 3). Self-distraction has been previously shown to positively load onto a latent factor suggestive of disengagement coping (Litman, 2006; Luszczynska et al., 2007). This measurement model was a good fit for the data, $\chi^2(2) = 3.50$, $p = .17$; RMSEA = .06 (90% CI = [.00, .15]); CFI = .98; SRMR = 0.03. Factor loadings for behavioral disengagement ($B = 1.26$, $\beta = .55$, $SE = .07$, 95% CI [.41, .69],

$p < .001$, $R^2 = .30$), denial ($B = .71$, $\beta = .39$, $SE = .07$, 95% CI [.24, .53], $p < .001$, $R^2 = .15$), self-blame ($B = 1.57$, $\beta = .77$, $SE = .08$, 95% CI [.61, .92], $p < .001$, $R^2 = .60$), and self-distraction ($B = 1.00$, $\beta = .43$, $SE = .07$, 95% CI [.28, .57], $p < .001$, $R^2 = .18$) were either at or above the established cut-off suggestive of strong indicators. All indicators were significantly correlated with the latent factor of disengagement coping, such that disengagement coping explained 30%, 15%, 60%, and 18% of the variance of each indicator respectively. Thus, based on model fit indices that demonstrated good model-data correspondence and positive standardized factor loadings that suggested shared variance among the indicators and latent construct, this measurement model was retained for subsequent analyses.

Results of Hypothesis 2

To assess proposed relationships between T1 disengagement coping and pain and fatigue interference at T3, as well as long-term depressive symptoms at T5, a structural model was tested (Figure 4). The model was first estimated unadjusted for covariates. Results indicated that the specified model was consistent with the data as indicated by the non-significant overall chi-square value ($\chi^2(11) = 14.32$, $p = .22$), an RMSEA value less than .06 (RMSEA = .04, 90% CI = [.00, .08]), a CFI greater than .95 (CFI = .98), and a SRMR less than .10 (SRMR = .04).

Pain and fatigue interference at T3 were highly correlated ($r = .45$, $p < .001$), suggesting that elevations in pain interference are associated with elevations in fatigue interference, and vice versa. Examination of the unstandardized and standardized coefficients revealed that the regression of depressive symptoms at T5 on fatigue interference at T3 was significant, such that greater fatigue interference post-adjuvant

therapy was related to more depressive symptomatology 5-years post-diagnosis ($B = 2.29$, $\beta = .42$, $SE = .08$, $z = 4.86$, 95% CI [.26, .58], $p < .001$). Pain interference at T3 was not related to long-term depressive symptoms at T5. Moreover, there was no evidence of mediation as both the total direct ($B = -.74$, $\beta = -.03$, $SE = .09$, $z = -.31$, 95% CI [-.21, .15], $p = .75$) and indirect ($B = -.25$, $\beta = -.01$, $SE = .04$, $z = -.22$, 95% CI [-.10, .08], $p = .83$) effects linking T1 disengagement coping with T5 depressive symptoms were non-significant. Furthermore, specific indirect effects relating T1 disengagement coping with depressive symptoms at T5 via T3 pain interference ($B = -.26$, $\beta = -.01$, $SE = .01$, $z = -.73$, 95% CI [-.04, .02], $p = .46$) and T3 fatigue interference ($B = .01$, $\beta = .001$, $SE = .04$, $z = .01$, 95% CI [-.07, .07], $p = .99$) were also not significant.

The structural model was then re-estimated with each covariate added sequentially into the model. The final model (Figure 5) was specified by regressing both mediating variables (i.e., T3 pain and fatigue interference) and long-term depressive symptoms at T5 on all covariates of interest (i.e., age, stage, adjuvant treatment received, condition, and T3 depressive symptoms). Taking into account modifications indices suggested by *Mplus*, correlations were specified between T3 depressive symptoms and concurrent pain interference, as well as fatigue interference. This analysis was conducted with 183 women, due to missing data values for the control variables. After adjusting for these covariates, the model exhibited good correspondence with the data, $\chi^2(42) = 55.80$, $p = .08$; RMSEA = .04 (90% CI = [.00, .07]); CFI = .95 SRMR = 0.05. However, the path relating T3 fatigue interference to T5 depressive symptoms was no longer significant, and all other direct paths relating T1 disengagement coping to T3 pain and fatigue interference and depressive symptoms at T5 were also not significant. Inspection of

covariates revealed a significant relationship between depressive symptoms at T3 and long-term depressive symptoms at T5 ($B = .64$, $\beta = .39$, $SE = .12$, $z = 3.02$, 95% CI [.16, .62], $p < .01$), indicating that more depressive symptoms one year post-diagnosis is related to more depressive symptomatology well into the survivorship phase (i.e., 5-years post-diagnosis). Additionally, both pain and fatigue interference at T3 were correlated with concurrent depressive symptoms ($r = .34$, $p < .001$; $r = .52$, $p < .001$, respectively).

Receipt of chemotherapy within three weeks of the T3 assessment was also significantly related to depressive symptoms at T5 ($B = 7.45$, $\beta = .30$, $SE = .07$, $z = 4.07$, 95% CI [.16, .43], $p < .001$), suggesting that treatment with chemotherapy within three weeks of the T3 assessment was related to more depressive symptoms 5 years after diagnosis.

Mediation was not supported as both the total direct ($B = .80$, $\beta = .03$, $SE = .09$, $z = .38$, 95% CI [-.14, .20], $p = .70$) and indirect ($B = .13$, $\beta = .005$, $SE = .02$, $z = .24$, 95% CI [-.04, .05], $p = .81$) paths linking disengagement coping at T1 with long-term depressive symptoms were not significant. Specific indirect effects relating disengagement coping at T1 with long-term depressive symptoms at T5 via T3 pain interference ($B = .03$, $\beta = .001$, $SE = .01$, $z = .12$, 95% CI [-.02, .02], $p = .90$) and T3 fatigue interference ($B = .09$, $\beta = .04$, $SE = .01$, $z = .28$, 95% CI [-.02, .03], $p = .77$) were also non-significant. Model parameters are reported in Table 3.

To test for reverse directionality an alternative model was specified regressing T5 depressive symptoms on disengagement coping at T3 and T1 pain and fatigue interference (Figure 6). Without adjusting for covariates, this model exhibited good model-data correspondence, $\chi^2(11) = 18.17$, $p = .08$; RMSEA = .06 (90% CI = [.00,

.11]); CFI = .97 SRMR = 0.05. Similar to T1, indicators of behavioral disengagement ($B = 1.09$, $\beta = .66$, $SE = .06$, $p < .001$, $R^2 = .44$), denial ($B = .71$, $\beta = .66$, $SE = .05$, $p < .001$, $R^2 = .44$), self-blame ($B = 1.20$, $\beta = .81$, $SE = .05$, $p < .001$, $R^2 = .65$), and self-distraction ($B = 1.00$, $\beta = .68$, $SE = .05$, $p < .001$, $R^2 = .46$) at T3 strongly correlated with the latent construct of disengagement coping. Examination of direct paths revealed a significant relationship between pain interference at T1 and T3 disengagement coping ($B = .07$, $\beta = .22$, $SE = .10$, $z = 2.23$, $p < .05$), such that greater pain interference at T1 is associated with more disengagement coping at T3. The relationship between pain interference at T1 and long-term depressive symptoms at T5 was suggested a trend towards significance ($B = .87$, $\beta = .19$, $SE = .11$, $z = 1.62$, $p = .10$), suggesting that greater pain interference at T1 may relate to more depressive symptomatology well into survivorship. After adjusting for age, stage, adjuvant treatment received (i.e., chemotherapy and/or radiation therapy), condition, and T3 depressive symptoms, the model was no longer a good fit for the data ($\chi^2(43) = 74.28$, $p < .01$; RMSEA = .07 (90% CI = [.04, .09]); CFI = .87 SRMR = 0.07), and previously significant relationships relating T1 pain interference to T3 disengagement coping and T5 depressive symptoms were no longer significant.

Chapter 4: DISCUSSION

The present study examined the longitudinal relationship between a latent construct of disengagement coping at the time of diagnosis and depressive symptoms 5 years later via pain and fatigue interference during the initial 12 month period of primary treatment for early-stage breast cancer. Broadly, the current findings contribute to existing literature characterizing disengagement coping and its influence (or lack thereof) on physical and psychological symptomatology throughout the breast cancer experience. This line of research warrants further attention, as it may facilitate the development of psychosocial interventions that target disadvantageous coping strategies negatively affecting the physical and mental health of long-term breast cancer survivors.

Re-Defining Disengagement Coping

Clarifying the specific coping strategies that comprise a higher order category of disengagement coping is particularly relevant to the psychosocial care of breast cancer survivors, since this style of coping has been previously linked to worse physical and psychological functioning across the breast cancer continuum (Andersen & Kehlet, 2011; Bellizzi & Blank, 2006; Bishop & Warr, 2003; Bussell & Naus, 2010; Manne et al., 1994; Osowiecki & Compas, 1998; Reddick et al., 2005). Yet, classification of disengagement coping remains somewhat inconsistent. To further elucidate prior research on the specific lower order coping responses subsumed under a higher order disengagement coping category, a confirmatory factor analysis was conducted to determine whether coping techniques such as behavioral disengagement, denial, self-blame, and venting share a common variance that is suggestive of disengagement coping

(Bussell & Naus, 2010; Compas et al., 2006; Danhauer et al., 2013; Skinner et al., 2003; Stanton et al., 2002).

Notably, this measurement model of disengagement coping was investigated during the post-surgical phase, a particularly vulnerable time for breast cancer patients (Hodges, Humphris, & Macfarlane, 2005; Mitchell et al., 2011). Understanding how post-surgical disengagement coping may relate to short- and long-term physical and psychological functioning of breast cancer survivors builds upon previous coping literature in breast cancer populations, which has primarily focused on the role of coping at the time of surgery and during adjuvant treatment (Andreu et al., 2012; Low et al., 2006; Stanton, 2006; Stanton et al., 2002). If post-surgical disengagement coping plays an enduring role in the trajectory of physical and psychological symptoms, this may encourage earlier dissemination of psychosocial interventions in the months immediately following surgery to curb deleterious coping.

The proposed measurement model in Aim 1 exhibited good model-data correspondence, suggesting that post-surgical behavioral disengagement, denial, self-blame, and venting share a common variance that is likely indicative of a higher order category of disengagement coping. However, venting demonstrated a weak standardized factor loading, which is symptomatic of poor model specification. Although some research has categorized venting as a disengagement coping technique (Bussell & Naus, 2010; Skinner et al., 2003; Stanton et al., 2002), the need for re-specification in the current study underscores persisting ambiguity in the classification of this coping strategy. It is plausible that this coping technique is more indicative of engagement coping since it often addresses the stressor directly, as well as its impact on personal

goals (Skinner et al., 2003). The present study provides further support for the notion that venting may not be best characterized as a method of disengagement coping, and highlights the need for future research to explore the classification of this coping response as an engagement coping technique.

Similar to venting, categorization of substance use has varied. Some studies have classified substance use as a disengagement coping strategy, while others have found this particular coping technique is best classified individually, outside of established higher order categories (Compas et al., 2006; Danhauer et al., 2013; Litman, 2006; Luszczynska et al., 2007; Zuckerman & Gagne, 2003). Congruent with these findings, the re-specified measurement model including behavioral disengagement, denial, self-blame, and substance use revealed a weak standardized factor loading for substance use, despite good model fit. This problematic model specification may suggest that similar to venting, substance use is not best classified as a disengagement coping technique. Rather, it may be indicative of something unique, beyond disengagement or engagement coping. This has been observed in earlier reports on coping in breast cancer populations and warrants further investigation (Bellizzi & Blank, 2006; Bussell & Naus, 2010; Stanton et al., 2002).

The measurement model was further re-specified by replacing substance use with self-distraction. Self-distraction techniques have been previously evidenced to positively load on to a latent factor of disengagement coping (Litman, 2006; Zuckerman & Gagne, 2003), yet research has been largely mixed, with some studies classifying self-distraction as an engagement coping technique (Danhauer et al., 2013). To address these inconsistencies, the measurement model was re-estimated using behavioral

disengagement denial, self-blame, and self-distraction as indicators. The resulting model fit was good and the standardized factor loadings were strong, with disengagement coping accounting for nearly 20% of the variance in self-distraction. This suggests that self-distraction techniques, measured by responses to statements such as “I’ve been turning to work or other activities to take my mind off things” and “I’ve been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping” are best categorized as forms of disengagement coping in the current sample.

While largely congruent with theoretical classifications of disengagement coping, namely the inclusion of coping techniques such as behavioral disengagement, denial, and self-blame (Bussell & Naus, 2010; Compas et al., 2006; Danhauer et al., 2013; Skinner et al., 2003; Stanton et al., 2002), the final measurement model of disengagement coping provides novel information regarding the classification of previously ambiguous coping responses such as substance use and self-distraction. These findings can be used to inform future research investigating higher order classifications of coping, and perhaps aid in the identification of a more stable typology of coping more generally. However, application of this particular classification of disengagement coping should be tested in other populations to confirm external validity across various medical conditions, age groups, and gender.

Disengagement Coping, Pain and Fatigue Interference, and Depressive Symptoms

Despite adequate model fit, structural equation modeling did not yield significant associations between post-surgical disengagement coping and pain and fatigue interference after the completion of adjuvant therapy, as well as depressive symptoms

throughout survivorship. Moreover, there was no evidence of mediation between post-surgical disengagement coping and long-term depressive symptoms via post-adjuvant pain and fatigue interference.

Without covariates, the regression of long-term depressive symptoms on post-adjuvant fatigue interference was significant, suggesting that greater fatigue interference after the completion of adjuvant therapy was related to more depressive symptomatology 5 years post-diagnosis. This finding has been previously demonstrated in breast cancer populations (Avis et al., 2015; Avis et al., 2013), and speaks to the relevance of physical symptoms in the long-term psychological functioning of breast cancer survivors. However, this association became non-significant upon addition of post-adjuvant depressive symptoms as a covariate.

Entry of post-adjuvant depressive symptoms as a covariate improved model fit and is theoretically supported; it is well-established in the literature that pain and fatigue experiences are often associated with depressive symptoms, and that depressive symptoms after completion of adjuvant therapy are predictive of worse depressive symptomatology throughout survivorship (Avis et al., 2015; Avis et al., 2013; Donovan, Gonzalez, Small, Andrykowski, & Jacobsen, 2014; Lam et al., 2012; Reich et al., 2008; So et al., 2009; Spiegel & Giese-Davis, 2003; Stanton et al., 2015; Vahdaninia et al., 2010). Accordingly, the final structural equation model revealed significant correlations between pain and fatigue interference with concurrent depressive symptoms.

These findings add to a substantial body of literature revealing a symptom cluster involving pain, fatigue, and depressive symptoms throughout the breast cancer continuum (Beck et al., 2005; Pud et al., 2008; So et al., 2009). However, the present study expands

upon these findings by providing evidence that such a symptom cluster occurs not only with pain and fatigue severity, but also pain and fatigue interference. Research on symptom clusters in oncology patients is still growing, and findings presented here provide valuable information regarding a common clustering of symptoms in a homogenous population of breast cancer patients who are post-adjuvant treatment. Prior research has commonly focused on a clustering of the most prevalent and distressing symptoms (e.g., pain severity, fatigue severity, and depression) characteristic of the breast cancer experience (Dodd, Cho, Cooper, & Miaskowski, 2010), yet the current study demonstrates that breast cancer survivors may also exhibit a unique cluster of pain interference, fatigue interference, and depressive symptoms in the post-adjuvant phase. This suggests that perceptions of how one's pain and fatigue interfere with daily functioning is associated with depressive symptoms, and vice versa. Such information may improve post-adjuvant symptom management via promotion of psychosocial protocols that utilize cognitive-behavioral techniques (e.g., cognitive restructuring, activity cycling etc.) to address distorted perceptions regarding impairment due to physical symptoms. Future research should seek to clarify how symptom clusters involving pain and fatigue severity versus interference are different, and whether they are pervasive throughout the entire breast cancer experience, or unique to certain phases of the disease continuum.

Consistent with prior research, a significant relationship between depressive symptoms post-adjuvant therapy and long-term depressive symptoms during survivorship was observed (Donovan et al., 2014; Stanton et al., 2015), suggesting that breast cancer survivors who endorse elevated depressive symptomatology at completion of adjuvant

therapy may endure persistent depressive symptoms during the survivorship phase. This speaks to the relevance of assessing for depressive symptomatology after active treatment, as these symptoms may relate to worse psychological functioning up to 5 years post-diagnosis. Moreover, as previously mentioned, depressive symptoms post-adjuvant therapy were related to concurrent pain and fatigue interference. This highlights the clinical relevance of assessing for physical symptomatology at the post-adjuvant time point, as heightened pain and fatigue interference may relate to heightened depressive symptomatology, which may in turn predict worse mental health throughout survivorship.

Subsequent research should explore how the timing of psychosocial intervention deployment influences symptom burden throughout survivorship; it is plausible that psychosocial protocols are most effective longitudinally when deployed 12 months post-diagnosis, as physical and psychological symptomatology in the post-adjuvant phase may impact long-term functioning up to 5 years later. Several studies have examined the efficacy of interventions aimed at promoting physical and mental well-being as women transition from active treatment to survivorship, and broadly, these interventions have shown promise in reducing cancer-specific distress and depression (Allen, Savadatti, & Levy, 2009). However, the extent to which these gains can be maintained up to 5 years post diagnosis, remains unclear.

Upon further inspection of covariates, it was observed that receipt of chemotherapy within three weeks of the one year post-diagnosis time point was related to more depressive symptoms during survivorship. Although this relationship has been demonstrated in prior literature (Donovan et al., 2014; Shi et al., 2011), there is also research suggesting that medical variables (e.g., stage of disease, characteristics of

treatment regimen, etc.) do not predict subsequent psychological functioning (Bower, 2008; Schlegel, Manning, Molix, Talley, & Bettencourt, 2012). Results from the current study demonstrate that such a relationship exists, and in fact, persists well into the survivorship phase (i.e., 5 years post-diagnosis). This finding is pertinent to the long-term psychosocial care of breast cancer survivors. Health care providers should be aware that undergoing chemotherapy 12 months post-diagnosis may be related to heightened depressive symptomatology during survivorship.

A possible mechanism accounting for the relationship between receipt of chemotherapy and long-term depressive symptoms is inflammation. There is research to suggest that common chemotherapies promote expression of inflammatory genes such as TNF- α , IL-1, IL-6, and IL-8 (Vyas, Laput, & Vyas, 2014). Many of these inflammatory markers have also been shown to correlate with concurrent depressive symptoms in breast cancer populations, as well as community and clinically depressed samples (Bouchard et al., 2016; Howren, Lamkin, & Suls, 2009). Yet, support for a longitudinal relationship between inflammatory genes and subsequent depressive symptomatology is weak, with the majority of reports failing to demonstrate a relationship between inflammatory markers and depressive symptoms in long-term breast cancer survivors (Bower, Ganz, Aziz, & Fahey, 2002; Bower et al., 2011). Additional research is needed to clarify whether protracted chemotherapy regimens (i.e., lasting 12 months post-diagnosis) catalyze inflammatory events that promote depressive symptomatology during long-term survivorship.

Although the present study focused primarily on the potential mediating role of post-adjuvant pain and fatigue interference, an alternative structural equation model was

assessed to determine whether a latent construct of post-adjuvant disengagement coping may operate as a mediator relating post-surgical physical symptomatology and subsequent psychological functioning during survivorship. To test this possibility, an alternative structural equation model was specified by regressing long-term depressive symptoms 5 years post-diagnosis on a latent variable of post-adjuvant disengagement coping and observed variables of pain and fatigue interference post-surgery.

The measurement model of disengagement coping post-adjuvant therapy was specified with the same indicators as previously utilized at the post-surgical time point (i.e., behavioral disengagement, denial, self-blame, and self-distraction). Notably, this measurement model exhibited good model fit, suggesting a consistent categorization of disengagement coping at the post-surgical and post-adjuvant time points. Despite different challenges across the unique phases of the breast cancer continuum, this finding offers preliminary support for a stable categorization of disengagement coping to include coping techniques such as behavioral disengagement, denial, self-blame, and self-distraction. This information may inform future research investigating a stable categorization of disengagement coping and its role on physical and mental health throughout the breast cancer trajectory.

Without controlling for covariates, the alternative structural equation model yielded a significant relationship between post-surgical pain interference and disengagement coping after the completion of adjuvant therapy, such that greater pain interference after surgery is associated with more disengagement coping once adjuvant therapy has been completed. Additionally, the relationship between post-surgical pain interference and long-term depressive symptomatology was trending towards

significance, indicating that greater pain interference post-surgery may relate to more depressive symptomatology throughout survivorship. However, there was no evidence of mediation between post-surgical pain and fatigue interference and long-term depressive symptom via post-adjuvant disengagement coping, and once covariates were added to this model, all significant direct effects were lost.

In contrast to the initial hypothesis that pain and fatigue interference mediate the relationship between post-surgical disengagement coping and long-term depressive symptoms, this alternative model provides another plausible explanation for the relationship between physical symptomatology, disengagement coping, and long-term psychological functioning. An association between physical symptoms and subsequent disengagement coping has been previously reported in the literature (Andreu et al., 2012) and it is conceivable that disengagement coping may also relate to psychological functioning during survivorship, although this association was not observed in the current study. While post-adjuvant disengagement coping did not relate to long-term depressive symptoms, future research should seek to elucidate associations between disengagement coping after completion of adjuvant therapy and other outcomes of interest throughout survivorship (e.g., persisting physical symptoms such as pain and fatigue, and/or emotional, social, physical, and functional quality of life). Support for these inferences may clarify the mechanistic role of disengagement coping in the relationship between physical and psychological symptoms experienced by breast cancer survivors.

It is important to note that the current study was conducted in the context of a randomized clinical trial testing the efficacy of a CBSM intervention, specifically designed to improve coping throughout the breast cancer experience. In light of this

overarching goal, it is reasonable to assume that disengagement coping after the completion of adjuvant therapy (i.e., post-CBSM) may be influenced by group assignment. It will likely be worthwhile to pursue future analyses investigating the interaction between post-surgical physical symptoms and intervention condition in predicting subsequent coping and psychological functioning.

Limitations

There are several limitations of this study that should be acknowledged. First, despite the use of robust statistical methodology, a two factor CFA examining the latent constructs of disengagement, as well as engagement coping may provide a better estimation of lower order coping responses that uniquely comprise these higher order classifications of coping. Furthermore, a two-factor measurement model would likely reveal pertinent information regarding how these two coping habits relate to each other. Future research should endeavor to utilize such an approach to confirm whether the coping techniques reported in the present study (i.e., behavioral disengagement, denial, self-blame, and self-distraction) load most strongly onto a latent factor of disengagement coping in other populations, and more importantly, whether they may be alternatively classified under a different coping style (e.g., engagement coping).

Second, this study relied primarily on self-report measures to assess coping, pain and fatigue interference, and depressive symptoms. Self-report questionnaire data are vulnerable to reporting bias, which may have contributed to low levels of pain and fatigue interference observed in the current sample. It is possible that lack of variation in these measures facilitated a floor effect and limited predictive power of long-term depressive symptoms. Although objective measures of pain and fatigue interference have

not been cited in the literature, a CFA specifying multiple indicators of latent pain and fatigue interference constructs (e.g., accelerometer-based physical activity, social engagement, return to work status etc.) may be a novel way in which to obtain a more valid index of pain and fatigue interference, free from measurement error.

Another potential limitation of the current study was the use of the Hamilton Rating Scale for Depression as a covariate indexing depressive symptoms at the post-adjuvant therapy time point. This measure includes one item that concerns somatic manifestations of depressed mood, including fatigue. This item was retained in the scale score for analysis, however, it should be noted that this item potentially overlaps with measures of fatigue interference and may explain why addition of this variable as a covariate eliminated observed effects of fatigue interference on depressive symptoms during survivorship.

Use of anti-depressants and/or pain medication, receipt of additional psychotherapy in the years following adjuvant treatment, and medical comorbidities during survivorship were not utilized as covariates in current model. This decision was due to sample size and literature suggesting that as control variables are added to structural equation models, parameter estimates become less stable (Kline, 2005). Since the current study was limited to a modest sample size of 183, inclusion of covariates was restricted to age, stage, adjuvant treatment received, condition, and T3 depressive symptoms. Future studies with larger sample sizes should include covariates such as anti-depressant and pain medication use, receipt of psychotherapy or other alternative interventions during survivorship, general medical comorbidities experienced in the years following completion of adjuvant treatment, and recurrence status, when examining

similar models of disengagement coping, physical symptomatology, and long-term psychological functioning.

Lastly, these data were collected in a university-based study comprised of white, highly motivated, and well-educated middle class women in Miami, Florida, and results may not generalize to other samples. Furthermore, study attrition was such that nearly half the original sample was lost at 5-year follow-up (46.7%). This is a major limitation of the present sample as it further limits generalizability and likely impacted parameter estimates. Future research investigating whether demographic, physical, and psychosocial variables at the post-adjuvant time point predict attrition at long-term follow-up may offer insight into this bias and inform how future longitudinal research addresses participant retention.

Clinical Implications

The current findings highlight a potential categorization of disengagement coping within the context of breast cancer treatment that includes behavioral disengagement, denial, self-blame, and self-distraction coping techniques. It is notable that this classification was consistent at two unique phases of the breast cancer trajectory (i.e., post-surgery and after the completion of adjuvant treatment) and as such, may inform future attempts to define disengagement coping throughout the entire breast cancer experience. Although the current study did not reveal significant relationships between disengagement coping habits and physical and psychological functioning across the breast cancer continuum, future research should further inspect this model to elucidate whether relationships are present between coping styles and subsequent physical, as well as psychological symptom burden using other outcomes of interest (e.g., Functional

Assessment of Cancer Treatment-Breast Cancer; FACT-B). This line of research will likely be instrumental in the development of efficacious psychosocial interventions that target coping techniques that are deleterious to breast cancer survivors' physical and mental health.

Despite a lack of evidence to support direct effects relating post-surgical disengagement coping with pain and fatigue interference after adjuvant treatment and depressive symptoms during survivorship, significant relationships were observed between post-adjuvant depressive symptoms and receipt of chemotherapy with depressive symptomatology 5 years post-diagnosis. These findings are relevant to the psychosocial care of breast cancer survivors. Women who experience protracted adjuvant therapy regimens, involving receipt of chemotherapy at one year post-diagnosis may be at elevated risk for developing depressive symptoms well into the survivorship phase. Likewise, breast cancer survivors who endorse more depressive symptoms 12 months following diagnosis may experience greater depressive symptomatology 5 years later. It is critical that depressive symptoms be monitored during and after primary treatment, as these may signal an undesirable trajectory of psychological functioning, above and beyond physical symptom burden (e.g., pain and fatigue interference). Similarly, health care professionals should be aware that women receiving chemotherapy well into the breast cancer experience may need additional psychosocial intervention to cope with treatment demands.

Future research should also consider the alternative model presented here specifying disengagement coping as a mediator between physical symptoms and psychological functioning later in the breast cancer trajectory. Results from the current

study provide preliminary support for such a hypothesis, although mediation was not supported. If it is revealed that disengagement coping habits operate as a mechanism by which physical symptomatology relates to long-term psychological symptoms, health care professionals will be better equipped to effect change by addressing such disadvantageous coping techniques earlier in the breast cancer experience. Support for these relationships in subsequent research may promote consistent assessment of coping, pain and fatigue interference, and depressive symptoms throughout active treatment and well into survivorship. Additionally, psychosocial interventions utilizing cognitive-behavioral techniques such as behavioral activation, problem-solving, and communication/assertiveness training may attenuate disengagement coping.

Although significant findings from the current study are limited, tentative support for a consistent classification of disengagement coping across unique phases of the breast cancer continuum is noteworthy. Additionally, preliminary evidence of relationships between post-surgical physical symptomatology, post-adjuvant disengagement coping, and long-term depressive symptoms as observed in the alternative model presented here, warrants further exploration, as this research may optimize how the oncological community approaches psychosocial care of breast cancer survivors across the entire breast cancer experience.

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Table. 1 Sample characteristics

Variable	<i>M (SD)</i>	<i>N (%)</i>
Age at T1 (in years)	50.34 (9.03)	
Race/Ethnicity		
White		152 (63.6)
Hispanic		61 (25.5)
Black		21 (8.8)
Asian		5 (2.1)
Annual Income (in thousands of dollars)	79.62 (67.08)	
Partnered Status at T1		
Partnered		150 (62.5)
Not Partnered		90 (37.5)
Stage of Disease		
Stage 0		38 (16.0)
Stage I		90 (37.8)
Stage II		91 (38.2)
Stage III		19 (8.0)
Surgical Procedure Type		
Lumpectomy		122 (50.8)
Mastectomy		118 (49.2)
Days from Surgery to Baseline	40.64 (23.03)	
Treatment Received		
Chemotherapy		127 (55.2)
Radiotherapy		134 (59.3)
Hormone Therapy		161 (70.6)
Breast Cancer Recurrence at T5		
No, remained cancer free		116 (89.2)
Yes, recurrence		6 (4.6)
New primary		7 (5.4)
Unsure if new primary or recurrence		1 (.8)
Charlson Comorbidity Index at T5	1.18 (2.07)	

Table 2. Descriptive statistics of study variables

	M (SD)
T3 Pain Interference	1.73 (1.49)
T3 Fatigue Interference	2.52 (1.63)
T5 Depressive Symptoms	9.51 (8.98)

N = 183; missingness due to covariates.

Table 3. Mediation model results

	T3 Pain Interference			T3 Fatigue Interference			T5 Depressive Sx		
	<i>B</i>	<i>p</i>	β	<i>B</i>	<i>p</i>	β	<i>B</i>	<i>p</i>	β
Disengagement Coping	.05	.90	.01	.11	.77	.03	.79	.70	.03
T3 Pain Interference	--	--	--	--	--	--	.64	.23	.12
T3 Fatigue Interference	--	--	--	--	--	--	.83	.13	.16
Covariates									
Age	-.01	.74	-.03	-.01	.62	-.04	.11	.17	.11
Stage	.31	.28	.08	.49	.07	.11	-.99	.59	-.04
Chemotherapy	.34	.36	.07	.51	.14	.11	7.45	<.001***	.29
Radiation	-.15	.71	-.03	-.25	.49	-.05	--	--	--
Condition	.21	.34	-.07	-.29	.16	-.09	-1.44	.27	-.09
T3 Depressive Sx	--	--	--	--	--	--	.64	<.01**	.39

Sx = Symptoms; Unstandardized (*B*) and standardized estimates (β); p-values for unstandardized estimates; ***p<.001, **p<.01, *p<.05.

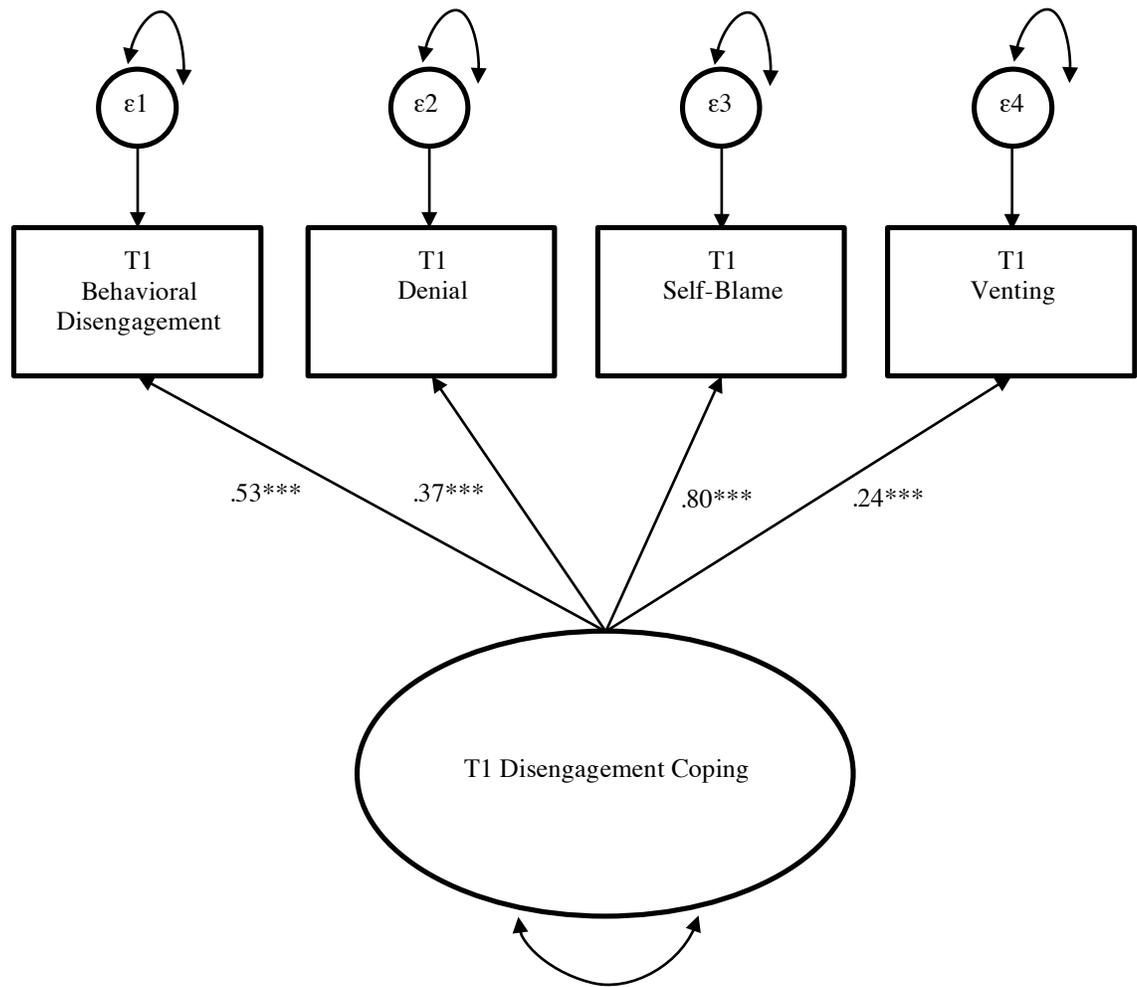


Figure 1. Proposed measurement model of disengagement coping. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

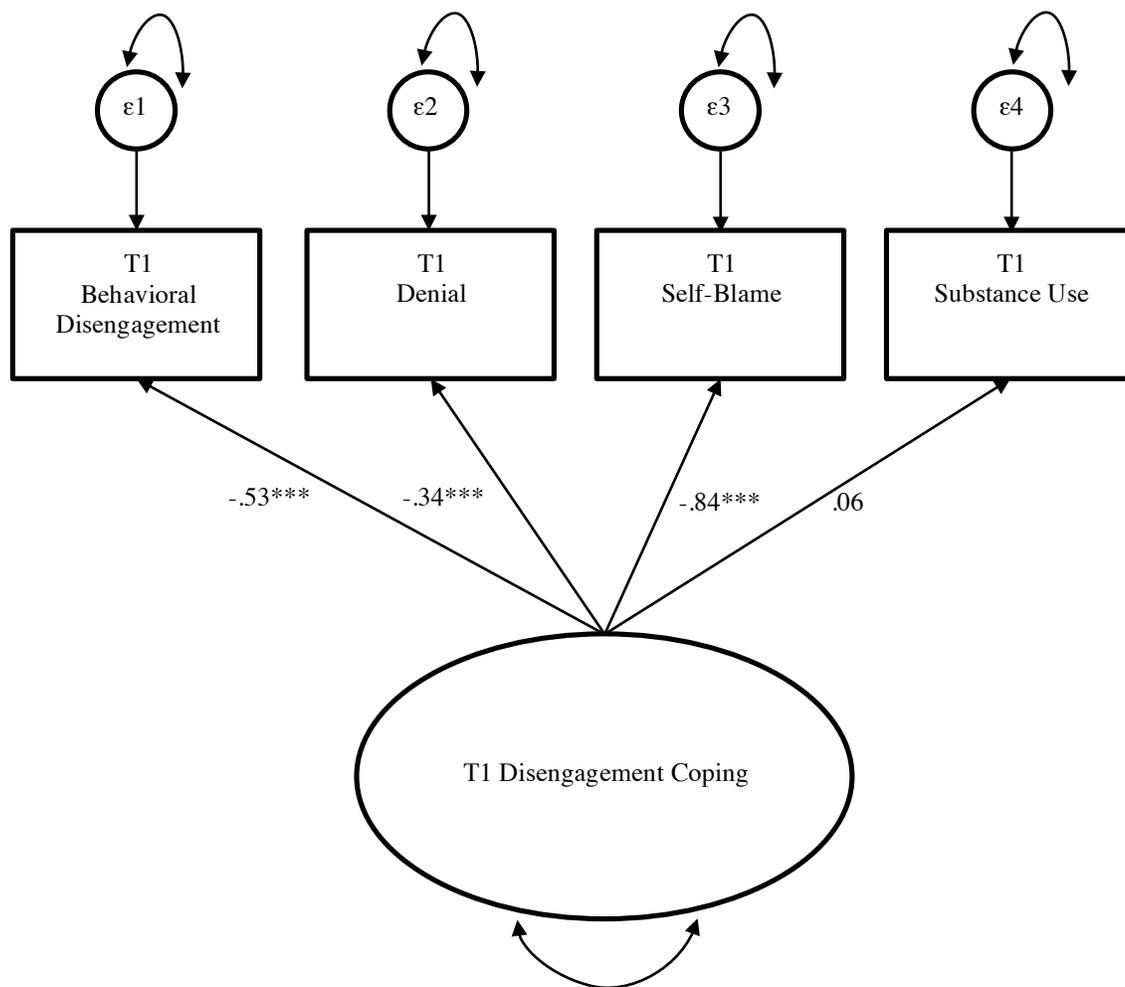


Figure 2. Re-specified measurement model of disengagement coping with substance use. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

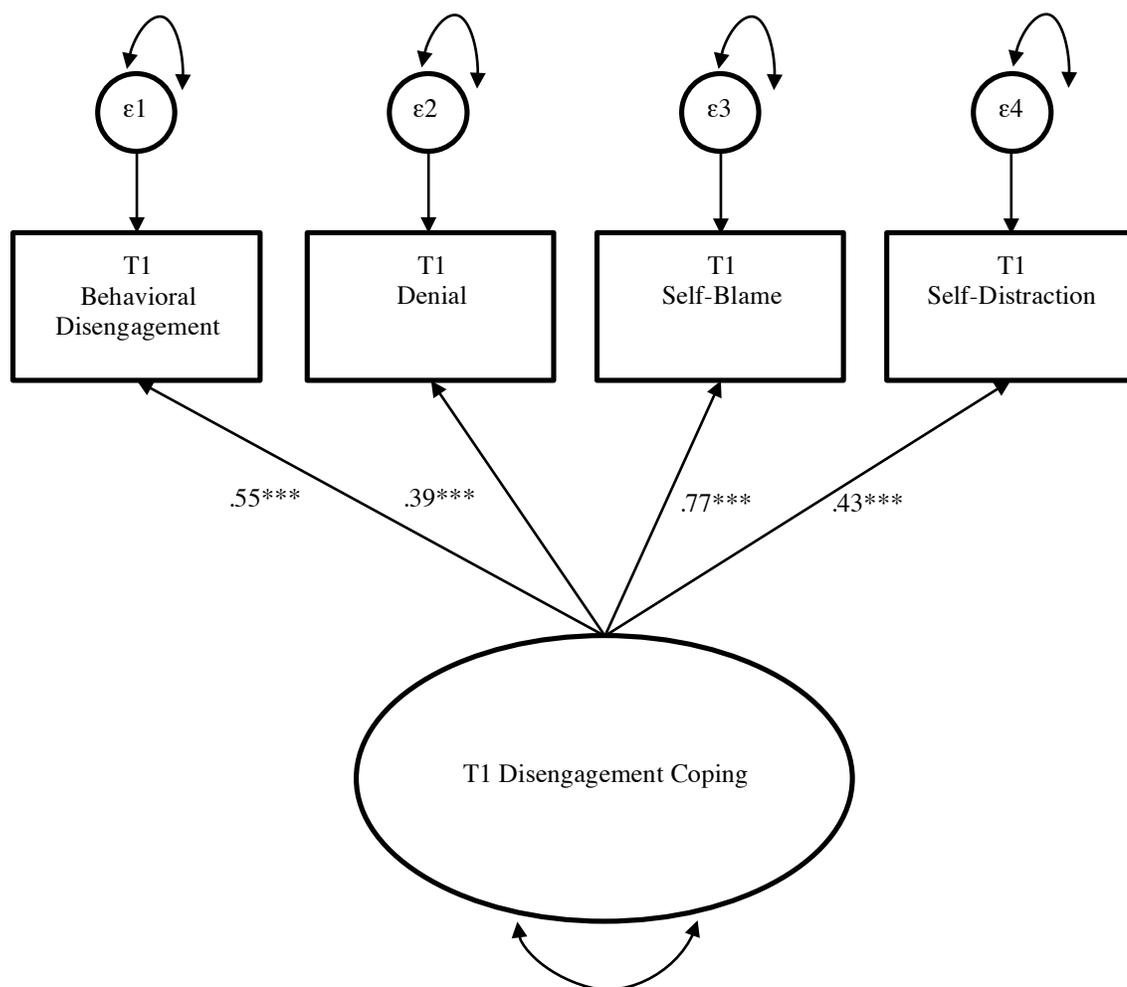


Figure 3. Re-specified measurement model of disengagement coping with self-distraction. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

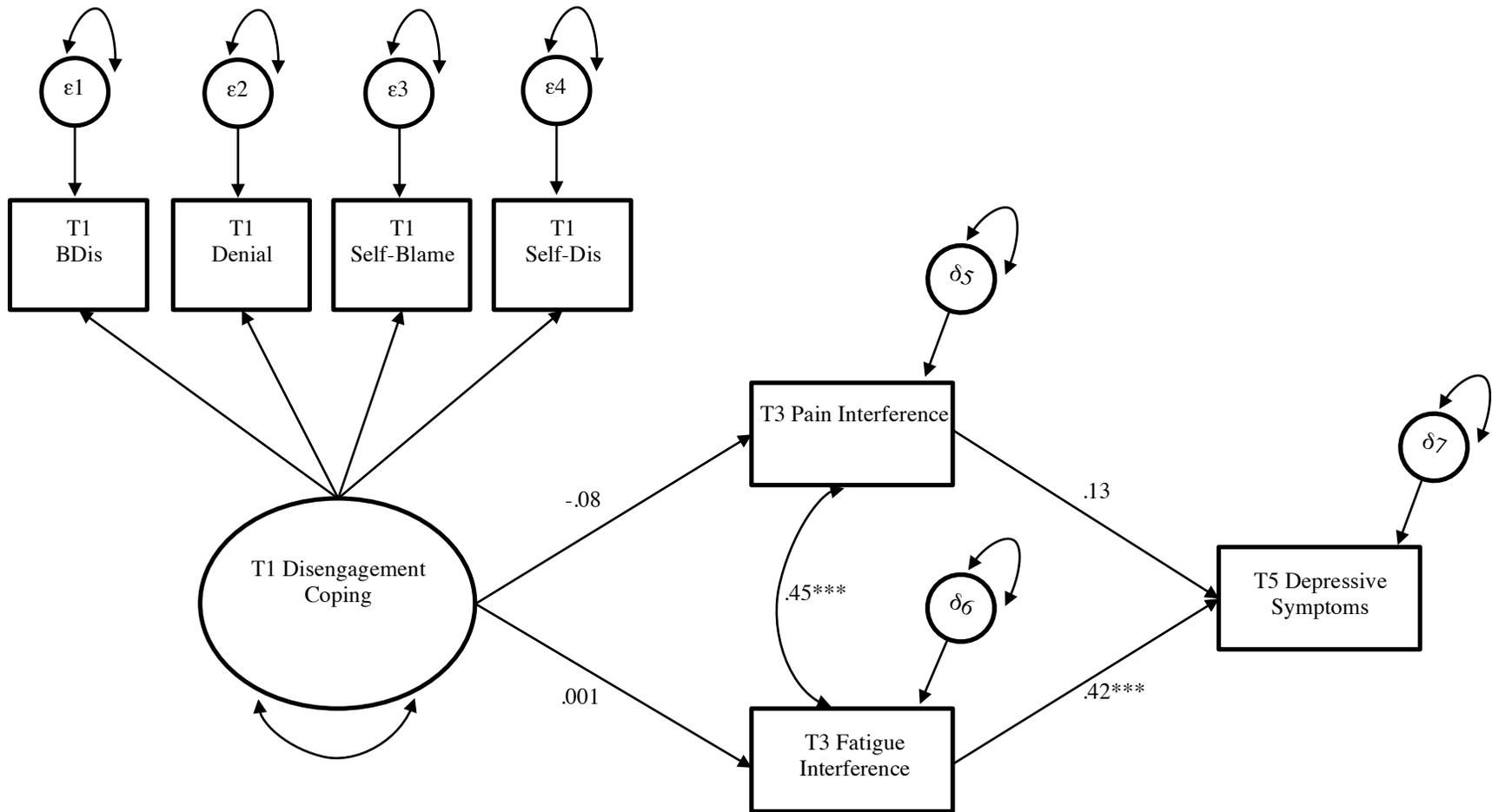


Figure 4. Structural equation model estimated without covariates. BDis=Behavioral Disengagement. Self-Dis=Self-Distracton. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

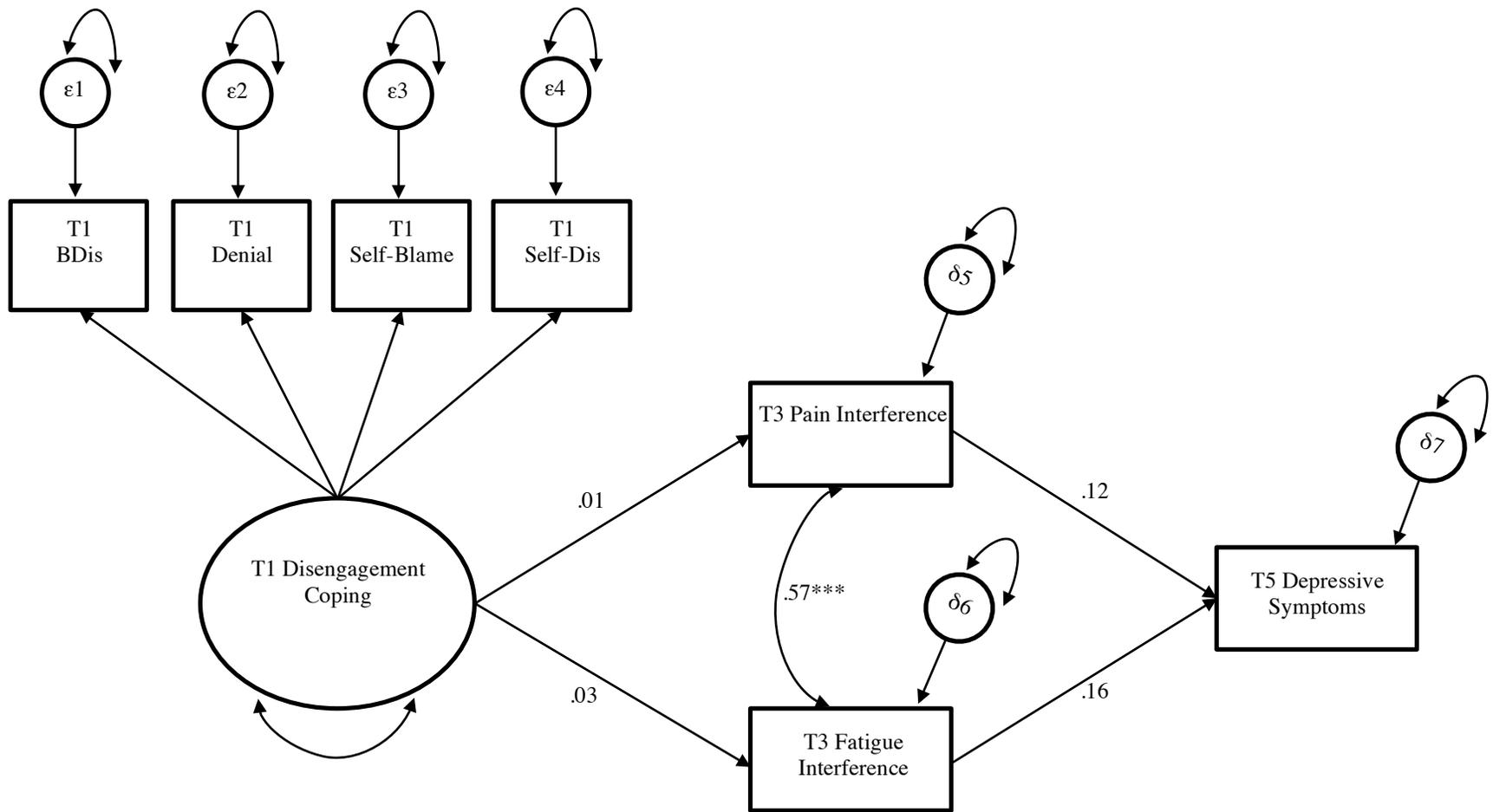


Figure 5. Structural equation model estimated with covariates. Covariate paths not shown for simplicity. BDis=Behavioral Disengagement. Self-Dis=Self-Distraction. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

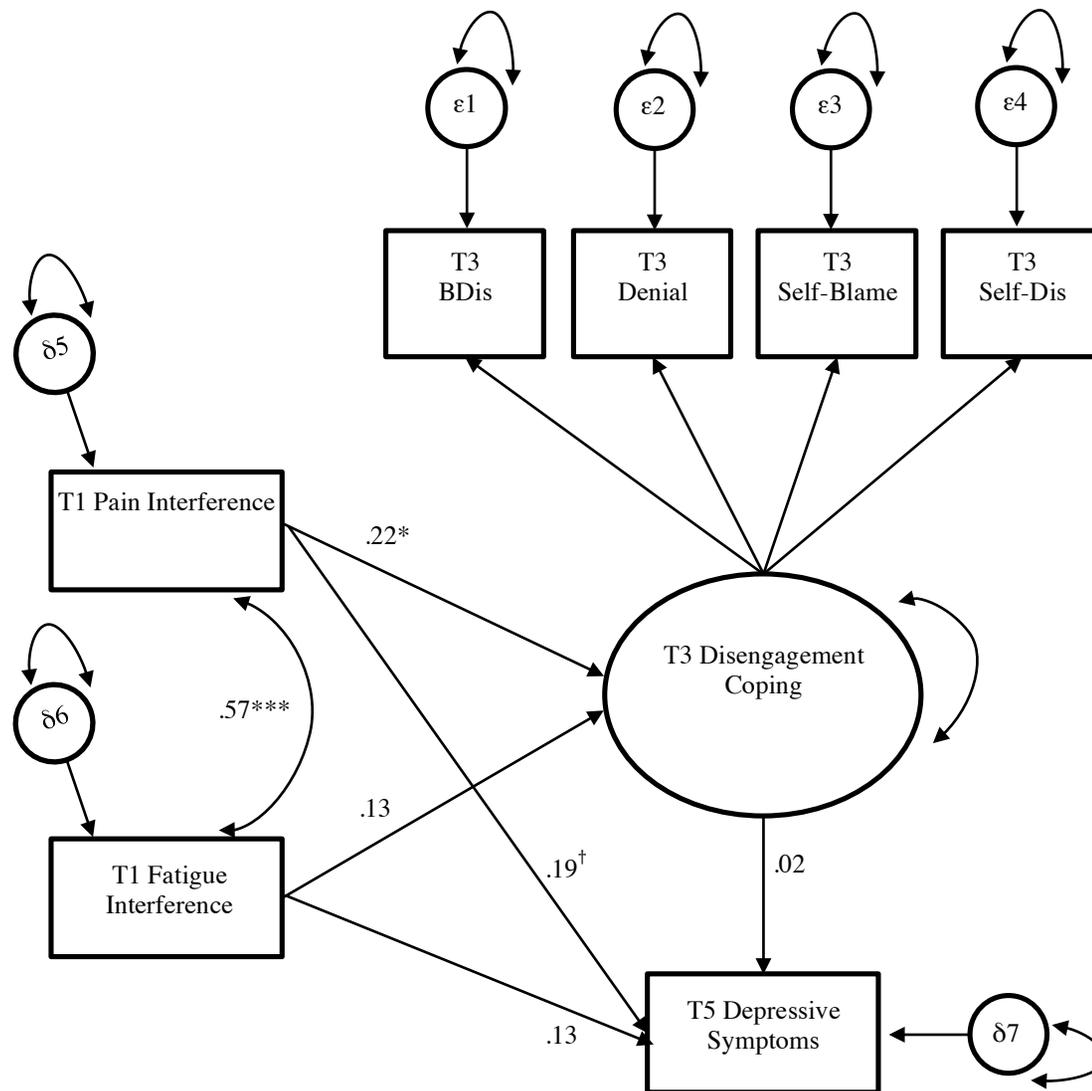


Figure 6. Alternative structural equation model. Covariates not shown for simplicity. BDis=Behavioral Disengagement. Self-Dis=Self-Distracton. Standardized parameter estimates (β) are shown. * $p < .05$. ** $p < .01$. *** $p < .001$.

Appendix A: Measures

Pain Interference subscale from Brief Pain Inventory (BPI)

Instructions: Indicate the one number that describes how, during the past 24 hours, pain has interfered with your:

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

- A. General activity
- B. Mood
- C. Walking Ability
- D. Normal Work (includes both work outside the home and housework)
- E. Relations with other people
- F. Sleep
- G. Enjoyment of life

Brief COPE

Instructions: Using the response options below, please rate the following statements based on the time since your surgery.

- 1 = I haven't been doing this at all
- 2 = I've been doing this a little bit
- 3 = I've been doing this a medium amount
- 4 = I've been doing this a lot

1. I've been turning to work or other activities to take my mind off things.
2. I've been concentrating my efforts on doing something about the situation I'm in.
3. I've been saying to myself "This isn't real".
4. I've been using alcohol or other drugs to make myself feel better.
5. I've been getting emotional support from others.
6. I've been giving up trying to deal with it.
7. I've been taking action to try to make the situation better.
8. I've been refusing to believe that it has happened.
9. I've been saying things to let my unpleasant feelings escape.
10. I've been getting help and advice from other people.
11. I've been using alcohol or other drugs to help me get through it.
12. I've been trying to see it in a different light, to make it seem more positive.
13. I've been criticizing myself.
14. I've been trying to come up with a strategy about what to do.
15. I've been getting comfort and understanding from someone.
16. I've been giving up the attempt to cope.
17. I've been looking for something good in what is happening.
18. I've been making jokes about it.
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.
20. I've been accepting the reality of the fact that it has happened.
21. I've been expressing my negative feelings.
22. I've been trying to find comfort in my religion or spiritual beliefs.
23. I've been trying to get advice or help from other people about what to do.
24. I've been learning to live with it.
25. I've been thinking hard about what steps to take.
26. I've been blaming myself for things that happened.
27. I've been praying or meditating.
28. I've been making fun of the situation.

Center for Epidemiologic Studies-Depression Scale (CES-D)

Instructions: Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	Most or all of the time (5-7 days)

1. I was bothered by things that usually don't bother me.
2. I did not feel like eating; my appetite was poor.
3. I felt that I could not shake off the blues even with help from my family or friends.
4. I felt I was just as good as other people.
5. I had trouble keeping my mind on what I was doing.
6. I felt depressed.
7. I felt that everything I did was an effort.
8. I felt hopeful about the future.
9. I thought my life had been a failure.
10. I felt fearful.
11. My sleep was restless.
12. I was happy.
13. I talked less than usual.
14. I felt lonely.
15. People very unfriendly.
16. I enjoyed life.
17. I had crying spells.
18. I felt sad.
19. I felt that people dislike me.
20. I could not get going.

Hamilton Rating Scale for Depression (HAM-D)

Instructions: For each item, write the correct number on the line next to the item. (Only one response per item).

1. DEPRESSED MOOD

(Sadness, hopeless, helpless, worthless)

0 = Absent

1 = These feeling states indicated only on questioning

2 = These feeling states spontaneously reported verbally

3 = Communicates feeling states non-verbally—i.e., through facial expression, posture, voice, and tendency to weep

4 = Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. FEELINGS OF GUILT

0 = Absent

1 = Self reproach, feels he has let people down

2 = Ideas of guilt or rumination over past errors or sinful deeds

3 = Present illness is a punishment. Delusions of guilt

4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. SUICIDE

0 = Absent

1 = Feels life is not worth living

2 = Wishes he were dead or any thoughts of possible death to self

3 = Suicidal ideas or gesture

4 = Attempts at suicide (any serious attempt rates 4)

4. INSOMNIA EARLY

0 = No difficulty falling asleep

1 = Complains of occasional difficulty falling asleep — i.e., more than 1/2 hour

2 = Complains of nightly difficulty falling asleep

5. INSOMNIA MIDDLE

0 = No difficulty

1 = Patient complains of being restless and disturbed during the night

2 = Waking during the night—any getting out of bed rates 2 (except for purposes of voiding)

6. INSOMNIA LATE

0 = No difficulty

1 = Waking in early hours of the morning but goes back to sleep

2 = Unable to fall asleep again if he gets out of bed

7. WORK AND ACTIVITIES

0 = No difficulty

1 = Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies

2 = Loss of interest in activity; hobbies or work—either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)

3 = Decrease in actual time spent in activities or decrease in productivity

4 = Stopped working because of present illness

8. RETARDATION:PSYCHOMOTOR

(Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)

0 = Normal speech and thought

1 = Slight retardation at interview

2 = Obvious retardation at interview

3 = Interview difficult

4 = Complete stupor

9. AGITATION

0 = None

1 = Fidgetiness

2 = Playing with hands, hair, etc.

3 = Moving about, can't sit still

4 = Hand wringing, nail biting, hair-pulling, biting of lips

10. ANXIETY (PSYCHOLOGICAL)

0 = No difficulty

1 = Subjective tension and irritability

2 = Worrying about minor matters

3 = Apprehensive attitude apparent in face or speech

4 = Fears expressed without questioning

11. ANXIETY SOMATIC:

Physiological concomitants of anxiety, (i.e., effects of autonomic overactivity, "butterflies," indigestion, stomach cramps, belching, diarrhea, palpitations, hyperventilation, paresthesia, sweating, flushing, tremor, headache, urinary frequency).

Avoid asking about possible medication side effects (i.e., dry mouth, constipation)

0 = Absent

1 = Mild

2 = Moderate

3 = Severe

4 = Incapacitating

12. SOMATIC SYMPTOMS (GASTROINTESTINAL)

0 = None

1 = Loss of appetite but eating without encouragement from others. Food intake about normal

2 = Difficulty eating without urging from others. Marked reduction of appetite and food intake

13. SOMATIC SYMPTOMS GENERAL

0 = None

1 = Heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability

2 = Any clear-cut symptom rates 2

14. GENITAL SYMPTOMS

(Symptoms such as: loss of libido; impaired sexual performance; menstrual disturbances)

0 = Absent

1 = Mild

2 = Severe

15. HYPOCHONDRIASIS

0 = Not present

1 = Self-absorption (bodily)

2 = Preoccupation with health

3 = Frequent complaints, requests for help, etc.

4 = Hypochondriacal delusions

16. LOSS OF WEIGHT

A. When rating by history:

0 = No weight loss

1 = Probably weight loss associated with present illness

2 = Definite (according to patient) weight loss

3 = Not assessed

17. INSIGHT

0 = Acknowledges being depressed and ill

1 = Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.

2 = Denies being ill at all

18. DIURNAL VARIATION

A. Note whether symptoms are worse in AM or PM. If NO diurnal variation, mark none

0 = No variation

1 = Worse in A.M.

2 = Worse in P.M.

B. When present, mark the severity of the variation. Mark "None" if NO variation

0 = None

1 = Mild

2 = Severe

19. DEPERSONALIZATION AND DEREALIZATION

(Such as: Feelings of unreality; Nihilistic ideas)

0 = Absent

1 = Mild

2 = Moderate

3 = Severe

4 = Incapacitating

20. PARANOID SYMPTOMS

0 = None

1 = Suspicious

2 = Ideas of reference

3 = Delusions of reference and persecution

21. OBSESSIVE AND COMPULSIVE SYMPTOMS

0 = Absent

1 = Mild

2 = Severe