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Contributions of Fatigue, Pain, and Functional Limitation to Future Depression in Cancer Survivors

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Contributions of Fatigue, Pain, and Functional Limitation to Future Depression in
Cancer Survivors

by

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2012

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The undersigned committee,
having examined the attached doctoral research project,
“Contributions of Fatigue, Pain, and Functional Limitation to Future Depression in
Cancer Survivors,” by Thomas Santo Recine, M.S.
herby indicates its unanimous approval.

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Abstract

Contributions of Fatigue, Pain, and Functional Limitation to Future Depression in
Cancer Survivors

By

Thomas Santo Recine, M.S.

Doctoral Research Project Chair: Thomas H. Harrell, Ph.D.

This study expanded upon Green (2014)'s study and examined the unique contributions of fatigue, pain, and functional limitation to future depression (depression measured at a later point in time) in cancer survivors. The findings demonstrate that functional impairment and fatigue are both strongly associated with subsequent depression. These findings follow from and are consistent with Green's (2014) study, and demonstrate that functional impairment and fatigue strongly impact ongoing and future depression, with higher levels of functional impairment and fatigue being associated with higher levels of future depression. As a whole, the findings of this study are commensurate with prior research. This study extends these findings to survivors of cancer, and demonstrates the need for further research related to the development and progression of depression in cancer patients and provided additional empirical support for fatigue management training among cancer survivors.

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Introduction

Cancer is currently the second leading cause of death in the United States (American Cancer Society, 2005). Each year, more than half a million people succumb to cancer, but are plagued by significant physiological and psychological distress prior to their deaths (Jemal, Murray, Samuels, Ghafoor, Ward, & Thun, 2003). Among the 10 million cancer survivors in this country (American Cancer Society, 2005), depression is described as the most common psychiatric condition experienced (Lloyd-Williams, Dennis, & Taylor, 2004). In fact, the prevalence of a major depressive disorder in those with cancer has been reported to be as high as 53% (Alt, Gore, & Ng, 2011). Overall, this is not surprising, as depression is one of the most prevalent mental disorders in the world, impacting nearly 340 million people (Greden, 2001).

Among the many cancer survivors who suffer depression, the symptoms of depression and symptoms related to cancer and its treatment are often highly similar. With cancer and depression, several disabilities tend to coincide with symptoms. These commonly include pain, fatigue and loss of energy, and functional limitation. Pain in cancer patients is often a result of many variables, which can include the stage of cancer, extent of the cancer, and type of treatment. In fact, research has shown that approximately 90% of patients with cancer experience pain. Evidence suggests that many features of pain are also related to

depression (Laird, Boyd, Colvin, & Fallon, 2009). Fatigue, defined as a persistent sense of exhaustion that is not the direct result of a recent action or activity, is also highly prevalent in cancer patients and survivors. In addition to cancer treatment and disease side effects, fatigue is also a prominent symptom of depression (Ettinger, 2009). Research also suggests that a diagnosis of cancer leads to increased susceptibility to depression, at least partially because of the drastic disruption of normal life activities (Zeiss, Lewinsohn, Rohde, & Seeley, 1996) that typically accompanies the disease. This disruption often includes limitations in daily functioning, or functional impairment. Functional impairment typically refers to the loss of ability to independently complete everyday tasks and needs, including both self-care and pleasurable activities. Research also suggests that the loss of ability to complete once common every day tasks or leisurely activities is a significant risk factor for depression (Zeiss et al., 1996).

Prior research examining the relationships between these variables has indicated that fatigue, pain, functional impairment, and depression are interrelated. However, few studies have delineated the independent contributions of fatigue, pain, and functional impairment to depression in cancer survivors, with the exception of Green (2014), who found that fatigue was the greatest contributor to concurrent depression in a sample of cancer survivors.

The purpose of the present study is to examine the unique contributions of fatigue, pain, and functional limitation to future depression in a sample of cancer

survivors. Measures of fatigue, pain, functional impairment, and depression were obtained from cancer survivors who attended a fatigue management training program. Depression was measured again approximately six months after program participation. Regression analyses were used to examine the relationships among these variables. Specifically, the study examined the relative contributions of fatigue, pain, and functional impairment to depression measured six months later. The study results increase our understanding of the temporal relationships between the variables of fatigue, pain, functional impairment, and depression; as well as the role of fatigue, pain, and functional impairment in the development and maintenance of depression in cancer survivors.

Review of the Literature

Cancer Survivorship

Not long ago a diagnosis of cancer was immediately associated with little hope for survival. However, at present, among the 10 million cancer survivors in our country, 62% can anticipate living at least 5 years past their first diagnosis of cancer. This statistic is promising, illustrating an increase in survivorship of over 50% compared to 30 years ago (American Cancer Society, 2005). Conditional survival rates also provide a more comprehensive predication of survival for patients who complete treatment and continue to live for several years after diagnosis (Feuerstein, 2007). Nonetheless, despite these advancements, survivors are still faced with an array of potential risks and problems, which can include behavioral health issues. In fact, research has found that survivors two years from their initial diagnosis of cancer can continue to experience behavioral health problems related to their diagnosis and treatment (Feuerstein, 2007). Additionally, psychosocial difficulties that accompany the survivor can also impact family, friends, and the public (Alt et al., 2011).

Depression in Cancer Patients

Depression is one of the most prevalent mental disorders in the world, impacting nearly 340 million people (Greden, 2001). It is especially problematic for those individuals suffering from chronic illnesses such as cancer (Walker, Sawhney, Hansen, Ahmed, Martin, Symeonides, Murray, & Sharpe, 2013).

Research has demonstrated that cancer patients and survivors are three times as likely to suffer from depression than those without cancer diagnoses (Bowers & Boyle, 2002). Despite the high occurrence of depressive symptomology in cancer patients, the overall prevalence of depression in cancer patients still remains unclear. More specifically, different researchers have found prevalence rates to be anywhere from 1.5%-50% (McDaniel, Musselman, & Nemeroff, 1997) to as high as 58% or greater (Krebber, 2014). The variability in these prevalence rates can be attributed to several possible factors. These include the use of different assessment and diagnostic measures; using different criteria to define depression; and differences within cancer populations with respect to type, stage, and treatment approaches (Krebber, 2014).

Nonetheless, further research has indicated that depressed cancer patients demonstrate more severe depressive symptoms than those experiencing depression alone. Specifically, in cancer survivors, depressive symptoms impact overall quality of life, as well as exacerbate anxiety and bodily pain (Hopko, Bell, Armento, Robertson, Hunt, Wolf, & Mullane, 2007). Symptoms of depressive disorders not only have both emotional and somatic consequences, but also hinder long-term survival in cancer patients (McDaniel, Musselman, & Nemeroff, 1997). Additionally, while depression can typically be treated effectively within the general population, special considerations must be taken with regard to cancer patients. Walker et al. (2013) argue that it is important to avoid the assumption that

treatments designed for the general population would produce the same benefits in cancer patients. Particularly, traditional antidepressant medications and certain psychological interventions may prove ineffective or detrimental to cancer patients suffering from depression (Walker et al., 2013). Thus, although depression in cancer patients requires swift action, the actions to be taken require careful consideration.

Assessing Depression in Cancer Patients

There are a variety of methods for assessing depression in cancer patients, including brief-screening measures, structured clinical interviews, and self-report measures (Trask & Pearman, 2007). In the clinical setting, self-report measures have proven to be the most effective because they are quick, easy, and inexpensive ways to assess the severity of depressive symptoms in cancer patients (Krebber, 2014). However, most of these tools, including some self-report measures, have been designed to assess depression in the general population and focus on physical symptoms (Meyer, Sinnott, & Seed, 2003). In many cases, some of the measured symptoms may actually be a direct result of the cancer itself rather than indices of depression, especially in advanced stages (Bowers & Boyle, 2002). For example, changes in weight or appetite, disturbed sleep, and psychomotor changes are common symptoms as cancer patients advance through their illness (Meyer, Sinnott, & Seed, 2003), and may be unrelated to depression. Research has found that in these cases, if a particular symptom seems to be caused by a medical

problem such as cancer, it is counterproductive to include it as a diagnostic criterion for depression (Meyer, Sinnott, & Seed, 2003). In other cases, depression may actually be easily overlooked because of these side effects associated with cancer treatments are similar to symptoms of depression (Krebber, 2014). As an alternative, and in effort to help differentiate symptoms, measures such as the Mood Evaluation Questionnaire may be more beneficial because it contains only psychological items (Meyer, Sinnott, & Seed, 2003). Further, the Geriatric Depression Inventory (GDI) is particularly useful because it more independently measures depression, unconfounded by physical symptomology (Sheikh & Yesavage, 1986, Green, 2014). On the GDI, age-related and other physical changes do not alter scores because they are not included in the GDI items (Sheikh & Yesavage, 1986).

Cancer-Related Fatigue

Cancer-Related Fatigue (CRF) is a complex and debilitating symptom that impacts as many as 76% to 99% (Alt, Gore, & Ng, 2011) of all cancer patients. Further research supports that fatigue is the most common symptom reported by cancer patients (Brown et al., 2013). CRF can occur at any stage of treatment but tends to increase at more advanced stages of the disease. In fact, in more advanced stages, it appears to be one of the most troubling, with considerable impact on a patient's overall functional ability (Minton & Stone, 2011). Symptoms of CRF vary to a large degree with respect to severity and impact on activity level. However,

the common element appears to be a persistent and subjective sense of tiredness. This fatigue typically persists despite periods of rest and tends to be more severe than fatigue secondary to intense physical exertion (Alt, Gore, & Ng, 2011). Cancer-related fatigue is not responsive to sleep in the way that exertion-related is ameliorated by rest (Ream & Richardson, 1996). Also, cancer-related fatigue does not vary significantly with mild exertion. Cancer-related fatigue is typically associated with significant decreases in activity level, especially activities that are not essential to daily living and activities that are pleasurable (Levy & Fann, 2008).

As was the case with regard to cancer-related depression, CRF is complex and multidimensional. The presence of CRF may be a result of cancer itself or a side effect of various treatment methods (Brown, et al., 2013). Specifically, studies have demonstrated that CRF is prevalent in nearly 40% of patients upon initial diagnosis, 90% of those receiving radiation treatment, and 80% of those receiving chemotherapy treatments (Hoffman et al., 2007), although the exact cause of CRF is generally unknown (Alt, Gore, & Ng, 2011). In addition to the possibilities that fatigue is secondary to cancer itself and/or treatment side effects, research has also suggested that there are several other medical issues that could account for the presence of CRF. These include electrolyte imbalance, cardiopulmonary distress, chronic pain, hepatic and renal dysfunction, infection, poor nutrition, and drugs that also impact the central nervous system (Mitchell & Berger, 2006). From a physiological perspective, CRF may also be secondary to anemia, cytokine

production, altered hypothalamic-pituitary-adrenal (HPA) activation, cachexia, and neuromuscular dysfunction (Green, 2013; Mitchell & Berger, 2006; Ng, Alt, & Gore, 2007). Lastly, CRF can also be secondary to psychological difficulties such as depression and anxiety, which may manifest through symptoms of sleep disturbance, tension, and cognitive disturbance as well as via changes in emotional state (Ng, Alt, & Gore, 2007). Many of these symptoms alone can contribute to increased fatigue. Until there is an understanding of the underlying mechanisms of CRF, there will not be any definitive method of determining what causes CRF (Ng, Alt, & Gore, 2007). However, we can examine the relationships between CRF and other variables associated with chronic illness (Ng, Alt, & Gore, 2007). CRF has been measured at the individual level with regard to frequency, severity, duration, association with “distress,” and the degree to which it impacts pain, depression, and functional impairment. Although multidimensional measures are commonly used, it is important that all aspects of fatigue measurement be independent of any other variables used in a given study. For example, many CRF measures incorporate questions regarding impact on activity, but this prevents a clear examination of the independent relationship of functional impairment to CRF or CRF consequences such as depression (Ng, Alt, & Gore, 2007).

Pain and Cancer

Research suggests that pain in cancer patients is a prominent problem. In fact, pain is frequently the first sign of cancer (Mantyh, 2006) and can be described

as the most distressing symptom for many cancer patients and survivors (Sun, Borneman, Piper, Koczywas, & Ferrell, 2008). Over the last several decades, many studies have examined the interplay of pain and cancer-related symptoms. Not surprisingly, prior research has shown that 40% of adult patients in intermediate stages and 60% to 80% of those in advanced stages of cancer experience disease-related pain (Jay, Elliot, & Varni, 1986). Current research also supports this finding. A study by Chang and Sekine (2007) found that pain was experienced as a symptom of 20%-50% of cancer patients (Fischer, Villines, Kim, Epstein, & Wilkie, 2010). The percentage of cancer patients in significant pain can be as high as 75% for cancer patients in advanced stages (Sun, Borneman, Piper et. al, 2008).

Cancer-related pain may be present during any time of the disease and can arise from different processes. These include post-surgery pain (biopsies or resectioning), tumor infiltration, or therapeutic side effects such as toxicity from radiation or chemotherapy (Mantyh, 2006). Since cancer-related pain has so many dimensions, managing it may pose as a challenge to patients. As discussed by Green (2014), Jacobson et al. (2009) identified several patient factors that lead to these difficulties. Patients were found to be reluctant to report their pain, not adhere to treatments, experience cognitive or affective related difficulties limiting them from reporting pain, fear medication dependence, or be solely focused on curing their cancer as opposed to relieving pain (Jacobsen, Liubarskiene, Moldrup, Christrup, Sjogren, & Samsanaviciene, 2009). Treatment providers also experience

difficulty in assessing cancer-related pain due to its complex nature. Providers may fail to assess pain or use pain-measuring instruments routinely and possess inadequate knowledge about pain management. Green (2014) also discussed providers having concern regarding opioid dosing and side effects such as addiction (Jacobsen et al., 2009). These difficulties in assessing and managing cancer-related pain may also pose further impairment to patients in that if untreated, cancer-related pain may contribute to mood disturbance, distress, or disability (Marcus, 2011). In fact, research has shown that through use of quality of life surveys, researchers were able to identify a relationship between pain and a decreased quality of life with decreased functioning (Chang & Sekine, 2007). Cancer-related pain has also been found to be persistent in long-term cancer survivors (Marcus, 2011). This illustrates that similar to fatigue experienced by cancer patients and survivors, the negative impacts of cancer and/or treatment may continue to impact functional impairment (Green, 2014).

Functional Impairment

Functional impairment refers to “the loss of ability to meet everyday needs independently in the areas of work, self-care, or important leisure activities” (Zeiss, Lewinsohn, Rohde, & Seely, 1996). Research has shown that having a physical or chronic disease increases the likelihood of functional impairment (Zeiss, et al., 1996). As previously described, depression, pain, and chronic illness have been shown to be persistent symptoms in patients diagnosed with cancer. Interestingly,

the interrelations among these symptoms has been found in some cases to be mediated by functional impairment. Specifically, Williamson and Schulz (1992) found that pain and illness contribute to overall functional impairment and that functional impairment typically contributes to the development of depressed mood or psychiatric illness such as depression. Zeiss et al. (1996) also found that disease does not consistently predict depression. Rather, this study found depression is most related to a serious decline in functional impairment (Zeiss et al., 1996). Overall, research has demonstrated that functional impairment commonly contributes to reduced life satisfaction and may exacerbate other symptoms associated with cancer.

In cancer patients, functional impairment has been associated with a shorter survival time (Wedding et al., 2007), treatment-related toxicity, and overall survival rate (Buccheri et al., 1996). Better functional status and lower levels of depressive symptom have been associated with better health-related quality of life (Pinquart et al., 2006). Pinquart et al. (2006) found that in cancer patients with low and average levels of depressive symptoms, poorer functional status was related to lower health-related quality of life, but that this relationship did not hold true for cancer patients with high levels of depressive symptoms.

Statement of Purpose

As the literature indicates, depression is prominent in individuals with chronic illness. However, cancer patients appear to be among the most severely impacted by depression. Further, cancer patients with depressive symptoms experience more severe depressive symptoms than those experiencing depression alone. This is due in part to an overall decrease in quality of life related to the various physical symptoms associated with cancer, including pain and fatigue. Since many of these symptoms do overlap, cancer-related depression may also be difficult to diagnose. Additionally, cancer treatments may contribute to depression; although when depression arises during treatment, symptoms are more often linked to treatment side effects rather than depression specifically. In many cases cancer-related depression symptoms may go unrecognized, and therefore the condition is frequently untreated or misdiagnosed.

Cancer patients also typically complain of fatigue, pain, and functional limitation in addition to depressive symptoms. Although research suggests there is no definitive method of determining what causes cancer-related fatigue (CRF), when examining the relationships among CRF and other variables associated with chronic illness, fatigue is typically regarded as a predictor of depression both during and after treatment. The reasons for this relationship are not fully understood. Both pain and functional impairment are also common in cancer patients. Associations between pain and functional impairment in relation to

depressive symptoms have been found both during and after cancer treatment. Thus, each of these factors have been linked to depressive symptoms and depression in cancer patients.

Although multiple studies has separately examined the relationships between fatigue, pain, functional impairment, and depression, few studies have examined all of these variables at the same time and delineated the independent contributions of fatigue, pain, and functional impairment to depression in cancer survivors. Green (2014), in a sample of cancer survivors, did examine each of these variables, and found that when the independent contributions of fatigue and functional limitation were examined, both were strongly related to depression measured at the same point in time. In her study, Green (2014) also determined fatigue was the strongest relative contributor to concurrent depression, followed by functional impairment, whereas pain was not significantly related to depression. No previous studies have simultaneously examined the unique contributions of fatigue, pain, and functional limitation to future depression (depression measured at a later point in time) in cancer survivors. This is important in establishing the temporal relationship between depression and the presumed predictors of fatigue, pain, and functional impairment. In order to examine the impact of fatigue, pain, and functional impairment on future depression, the proposed study will reexamine these relationships in Green's sample of cancer patients, using depression scores obtained six months following the initial assessment of functional impairment,

pain, and fatigue. Based on the findings of the literature review, it is hypothesized that fatigue and functional impairment will be significantly and positively related to future depression, and that cancer-related fatigue will demonstrate the strongest relationship with future depression when the factors are examined independently. Fatigue is hypothesized to be the more significant variable because it cannot be reliably relieved or diminished by rest or methods of energy conservation, and because there are no effective medical treatments for cancer-related fatigue; thus, fatigue and its effect on daily life is less easily compensated for or managed. The model proposed is one in which fatigue and functional limitation both contribute to future depression, and the analyses will examine the relative and unique contribution of each factor to the degree of depression reported six months later.

The specific hypotheses are:

1. Cancer-related fatigue will be significantly and positively correlated with future depression.
2. Functional limitation will be significantly and positively correlated with future depression.
3. When independent effects are considered, cancer-related fatigue will account for a greater degree of variance in depression, relative to functional impairment.

Method

Participants

This study utilized a sample of subjects who voluntarily participated in the Cancer Fatigue research project at Florida Tech either by attending a Fatigue Management Training program or by simply completing the packet of questionnaires. Participants were recruited for participation from the general community (including local senior centers, independent and assisted living facilities, cancer treatment facilities, community cancer support groups, and retirement communities in East Central Florida), via newspaper announcements, and via health fairs.

Eligibility criteria for the participants included: (a) a prior medical diagnosis of cancer; (b) the ability to read and complete the questionnaires; and (c) willingness to participate, including understanding and signing the informed consent form. Participants did not receive any compensation for their participation. Potential participants were considered ineligible for inclusion in the study if they met any of the following criteria: (a) the presence of significant cognitive impairment or (b) language, speech, or hearing problems that would preclude informed interaction with experimenters.

The total sample used for the study consisted of 74 participants. Demographic characteristics of the obtained participants are described in the Results section.

Instruments

Demographics: Demographic measures included age, gender, marital status, education, current living status, ethnic background, religion, and employment status.

Cancer-Related Variables: Measures obtained from the sample included length of time elapsed since cancer diagnosis, methods used to treat cancer (i.e., surgery, radiation, chemotherapy, hormone therapy, other), and whether or not participants were currently taking medication to treat their cancer. Participants were asked to list both current treatment they were receiving and treatment they had previously received. For previous treatments, participants were asked to describe the number of months elapsed since receiving the treatment. Other variables asked participants about other medical aspects, such as health status. Participants were asked to describe their current health, on a 5-point likert-type scale, as *excellent* (1), *very good*, *good*, *fair*, or *poor* (5), and to compare their health to that of other people their age, with the following response options: *much better* (1), *somewhat better*, *about the same*, *somewhat worse*, and *much worse* (5). Participants were also asked to rate their overall satisfaction with their health, on a

5-point likert-type scale, as *very satisfied* (1), *somewhat satisfied, not sure*, *somewhat unsatisfied*, and *not at all satisfied* (5).

Pain: The degree of cancer-related pain was measured with a 5-point likert-type scale ranging from 1 (*no pain*) to 5 (*severe pain*). Participants were asked to rate the overall cancer-related pain typically experienced. Single item measures of pain remain the most widely used measures of pain in cancer research, as a single item is most often included in cancer-related quality of life measures.

Functional Limitation: The Health Assessment Questionnaire (HAQ) (Fries, Spitz, Kraines, & Holman, 1980) measures physical impairment in activities of daily living among persons with impairment. Activities are rated on a four-point scale ranging from 0 (*no difficulty*) to 3 (*unable to do*). The HAQ has demonstrated good validity and reliability as a measure of physical impairment (Ramey, Raynauld, & Fries, 1992) and HAQ scores have been correlated with independent observations of physical performance (Fries et al., 1980; McDowell & Newell, 1996). Because of the demonstrated relationship with independent observations, the HAQ is widely used as an objective measure of functional impairment in adults. As the items cover all the primary activities of daily living, the HAQ and has been used in studies examining a diverse range of medical conditions.

Fatigue: The Fatigue Impact index score was intended as a measure of the overall impact of fatigue on survey participants that was also independent

from functional impairment with regard to item content. Many fatigue measures include items related to the impact of fatigue on function. However, because this study was designed to examine the independent contributions of fatigue and impairment, it was necessary to use a fatigue measure that did not include functional impairment items. The Fatigue Impact score was calculated by combining three items about fatigue frequency, three fatigue severity ratings, and one item examining the degree to which fatigue has caused the participant distress. Good internal consistency was established in this sample and similar measures have been used in a number of prior studies (Belza, 2006), although the most commonly used fatigue scales are confounded with functional limitation.

Depression: The 15-item short form of the Geriatric Depression Scale (GDS) (Sheikh & Yesavage, 1986) was used to assess depressive symptoms. Responses are provided on a four-point scale (1= *strongly disagree*; 4 = *strongly agree*) and are based on respondent's feelings over the previous week. The advantage of the GDS is the lack of item overlap with somatic symptoms, which can be a significant confound in assessing depression among individuals with chronic medical problems. The GDS contains fewer items concerning somatic symptoms than other depression measures. The short form of the GDS has been demonstrated to be a reliable and valid measure of depression among both younger and older adults and has been used in a wide range of settings.

Procedure

All participants completed a questionnaire packet that included the research measures described above. Participants who were obtained via their participation in the fatigue management-training program completed the questionnaires prior to program participation and again six months after.

Results

Participant Demographics

The sample size for this study was 74 participants. Not all participants responded to every item, therefore some there is some missing data on some variables. In these cases, the number of participants was less than 74. The mean age of the sample was 66.01 years ($SD = 11.67$), with a range of 28 to 85 years of age. The overall sample was inclusive of a representative range of individuals. Table 1 summarizes the demographic characteristics of the sample. The sample consisted primarily of female participants, which equated to 77.0% of the sample. The sample appeared to be adequately representative of marital status in the U.S. 50% of participants indicated they were married, 20% indicated they were divorced, 16.2% were widowed, and 10.8% were single and never married. Approximately 72% of the sample reported having some college or graduating from college. The sample appeared to somewhat underrepresent minority groups, with 85.1% being Caucasian. However, it did include respondents from multiple ethnic groups, including Hispanics (9.5%) and African Americans (4.1%). With regard to religion, the sample appeared to be adequately representative of diverse groups including 28% Protestant, 24% Catholic, 2.7% Jewish, and 27.0% indicated other religion or faith.

With respect to employment and economic variables, 18.9% of the participants were currently employed, 58.5% were retired, and 8.1% identified

themselves as disabled. Participant financial status also varied, with 56.7% reporting an annual income that they categorized as 'adequate' or 'more than adequate' to their needs. The remaining 43.2% of the sample reported an annual income that was 'less than adequate' or 'just barely adequate' to their needs. This demonstrates a sample with large variation with regard to annual income. In addition, 97.3% of the sample was living with a parent, friend, or relative while only 1.4% were living in a retirement community.

Other Important Characteristics of the Sample

Participants were asked to specify if they had any disabilities. Disabilities, for the purpose of this study, were defined as medical problems that continually interfere with ability to function, other than cancer. Nearly one-half (48.6%) of the sample indicated they had disabling conditions other than cancer, and 47.3 % indicated they had no other disabling conditions. Therefore, the sample was representative of individuals with, and without, medical conditions other than cancer that interfere with ability to function. The mean number of disabling conditions other than cancer was 1.66 (SD = 1.32). This number is not surprising when given the average age of 66 in this sample since disability generally increases with age. Only 10.5% of the sample indicated they had five disabling conditions other than cancer. With regard to the other types of disability, responses included: cardiovascular (n = 7), pulmonary (n = 3), neurological (n = 4), orthopedic (n = 14), endocrine (n = 2), psychological (n = 2), other (n = 6).

Perceived health was measured with responses to three health perception items embedded in the questionnaire. Each item was rated on a 5-point likert-type scale. Participants were asked to describe their current health status as *excellent* (1), *very good*, *good*, *fair*, or *poor* (5), and to compare their health to that of other people their age, with the following response options: *much better* (1), *somewhat better*, *about the same*, *somewhat worse*, and *much worse* (5). Participants were also asked to rate their overall satisfaction with their health as *very satisfied* (1), *somewhat satisfied*, *not sure*, *somewhat unsatisfied*, and *not at all satisfied* (5). The mean perceived health score was 2.95 (SD = .94). This suggests that on average, perceived health was considered to be good. However, the distribution of scores indicated 28.8% of the sample perceived their health as only fair or poor.

Among the participants, the mean length of time since diagnosis was 54.51 months (SD = 72.16), approximately 4.5 years. The standard deviation indicated a significant degree of variation in length of time since diagnosis in the sample.

Prior and Current Cancer Treatment

Information regarding the prior and current cancer treatment of the sample is summarized in Table 2. Respondents frequently left these questions blank. Rather than infer a blank was indicative of “no” in Table 2, we identified blanks as “not known.” Almost half of the sample, 45.9%, indicated they currently take medications related to their cancer history, and 35.1% indicated they did not. The majority of the sample was not currently receiving either radiation therapy (91.9%)

or chemotherapy (74.3%). However, most of the sample had previously received treatment for their cancer, such as radiation therapy (44.6%), chemotherapy (37.8%), or surgery (39.2%).

Pain

Participants were asked to rate the overall cancer-related pain they experienced, responding on a 5-point likert-type scale ranging from 1 (*no pain*) to 5 (*severe pain*). A mean pain level of 2.59 (SD = 1.31) was obtained; indicating most of the sample experienced 'very mild' to 'mild' pain. However some of the sample (6.8%) indicated typically experiencing 'severe' pain.

Depression

Participants were asked to assess their depressive symptoms on the Geriatric Depression Scale, based on their feelings over the previous week. A mean of 2.16 (SD = .44) was obtained from the sample, indicating a relatively low average level of depression. Participant's responses ranged from 1.07 to 3, which is demonstrative of varying levels of depressive symptoms within the sample. Participant's responses were normally distributed within the obtained range. Approximately half the sample (51.5%) indicated they experienced mild levels of depressive symptoms over the previous week. 14.7% of the sample indicated experiencing moderately severe depressive symptoms over the previous week. Although no responses were indicative of more severe levels of depressive symptoms, this is not surprising given the debilitating nature of severe depression.

Symptoms of severe depressive symptoms would likely impact functions necessary for completing the questionnaire and/or attending the fatigue management training program, thus deterring them from participating in the study.

Functional Limitation

Functional limitations were assessed by asking respondents to indicate to what degree their fatigue affected their ability to carry out activities of daily living over the past week. Activities of daily living assessed included the following: dressing, standing up from a straight chair, getting in and out of bed, cutting food, climbing up five steps, washing and drying their body, getting on and off the toilet, bending down to pick up clothing from the floor, opening a car door, opening a previously opened jar, turning faucets on and off, running errands and shopping, getting in and out of a car, doing chores and visiting/socializing. Ability to carry out activities was rated on a four-point scale ranging from 0 (*no difficulty*) to 3 (*unable to do*). A functional limitation index score was calculated for each participant by summing their responses to the 15 items and dividing the sum by 15. A mean score of .44 (SD = 0.38) was obtained, indicating that on average, respondents experienced relatively minimal impairment in completing these types of tasks. Although 9.6% of respondents reported they experienced some difficulty in completing daily tasks over the past week, most respondents indicated they experienced no or minimal difficulty.

Fatigue Characteristics and Measures

The Fatigue Impact scores, based primarily on frequency and severity of fatigue, averaged 3.88 ($SD = 1.27$), with an obtained range of 1.29 to 6.14. Tables 3 and 4 summarize the results of fatigue characteristics and measures. Generally, the sample as a whole demonstrated low but persistent levels of fatigue, which is typical of the ongoing fatigue experience over time by cancer survivors. The distribution of the scores was relatively normal within the obtained range.

Relationship Between Fatigue, Functional Impairment, Pain, and Depression Measured Six Months Later

The relationships between pain, functional limitation, fatigue, and subsequent depression were initially investigated using Pearson correlation coefficients. The analyses were first conducted using the actual depression score obtained six months after the other measures. The analyses were repeated using the difference score obtained by subtracting the depression score obtained at Time 2 from the depression score obtained at Time 1. The difference score reflected change in depression level rather than a specific depression value.

The distribution for the depression scores at Time 2 ranged from 0.93 to 2.71, with a mean of 1.87 ($SD = 0.44$). The distribution was relatively normal and not significantly skewed. The difference score ranged from 0.0 to 1.36, with a mean of 0.41 ($SD = 0.34$). As expected, the difference scores were significantly

skewed, with 59.0% of the scores less than or equal to 0.50, thus the distribution of scores departed significantly from a normal distribution.

Table 5 displays the correlation matrix that included the depression score obtained six months later. Subsequent depression was significantly correlated with all of the other variables, and the obtained correlations were within the moderate range of those typically found with psychological variables. Thus, hypotheses 1 and 2 were supported, as both fatigue and functional limitation were significantly positively correlated with future depression.

None of the correlations between absolute change in depression level and the other variables were significant. Combined with the finding that the difference score demonstrated a non-normal distribution, the ability to use the difference scores as dependent variable in a regression equation was suspect. Thus, a direct regression of depression score differences on the other variables was conducted solely in order to examine the collinearity diagnostics output by the statistical software. The obtained indices indicated the assumptions of regression analysis were significantly violated and therefore the difference score was not further utilized as a criterion variable.

Regression Analyses of the Impact of Fatigue, Functional Impairment, Pain and Valued Activity Impairment on Subsequent Depression

The variables were further examined to explore the unique relationship of fatigue, functional limitation, pain, and valued activity impairment with depression.

A set of hierarchical multiple regression analyses were performed in which subsequent depression was regressed on the independent variables: fatigue, functional limitation, and pain. In the first analysis, all predictor variables were entered simultaneously. The model was significant, $[F(4, 55) = 4.04, p < .01]$, and the total R for the model was .490, indicating a combination of the variables were significantly related to subsequent depression.

In order to examine the degree of predictor relationship that was unique to each variable, and thereby reveal the relative impact of the predictors on subsequent depression, a stepwise regression was conducted, in which predictor variables were entered into the equation based on their relative strength of association with subsequent depression. The final derived model was significant, $[F(4, 55) = 5.81, p < .002]$, and the total R for the model was .494. Standardized beta weights and the percent of variance accounted for associated with each independent variable are displayed in Table 6. Functional limitation accounted for the greatest amount of variance in depression (17.2%), followed by fatigue (13.5%). Neither pain nor valued activity impairment were significantly related to later depression. Therefore, hypothesis 3 was not supported, because functional impairment accounted for a significantly greater amount of variance in future depression than cancer-related fatigue. However, fatigue did account for 13.5 percent of the variance in later depression.

Discussion

The purpose of this study was to examine the relative and unique contributions of fatigue, pain, and functional limitation to future depression in cancer survivors. It was hypothesized that cancer-related fatigue would be significantly and positively correlated with future depression; functional limitation would be significantly and positively correlated with future depression; and when independent effects are considered, cancer-related fatigue would account for a greater degree of variance in depression relative to functional impairment. This study utilized the same sample as Green (2014), who examined the impact of fatigue, function impairment, and pain on depression measured at the same time as the other variables. In the current study, the relationship between fatigue, functional impairment, and pain with depression measured six months later was examined. The discussion will describe the findings of this study and compare them with Green's (2014) results.

As in Green's (2014) study, the 74 adults in the sample used in this study were representative of the general population with regard to age (range= 28-85). It was also diverse in terms of marital status, religion, and socioeconomic status. However, some limitations to the sample diversity include an underrepresentation of males, Hispanics, and African Americans. Despite this underrepresentation, these populations were included in the study. Additionally, half the sample indicated having other disabling conditions other than cancer that interfered with

their daily functioning. Consequently, the sample was also representative of individuals with and without disabilities other than a diagnosis of cancer. Participants, on average, perceived their health to be good. However, participants' perceptions of their health were considerably varied. Specifically, approximately one-quarter of participants perceived their health as only "fair" or "poor." There was also variability with regard to the length of time since diagnosis of cancer ($M=4.5$ years). Further, the majority of the sample was not currently receiving treatment for cancer (radiation or chemotherapy), however indicated they were taking medications related to their cancer history. As with Green's (2014) study, overall, the sample was representative of a wide range of previous cancer treatments. However, it was not representative of cancer survivors currently receiving treatment other than medication. Lastly, pain levels also demonstrated considerable variation with most indicating they experience a very mild, to mild pain.

For the sample as a whole, there was a low average level of future depression, with most participants' responses falling in the mild range. Approximately 16% indicated experiencing moderately severe depressive symptoms over the previous week, and overall the responses to depression items were normally distributed with a good range. On average, respondents experienced relatively minimal limitations in completing tasks of daily living. A relatively small percentage of respondents experienced mild to moderate difficulty in completing tasks, whereas most indicated they experienced no or minimal

difficulty. This distribution was also normally distributed. With regard to levels of reported depression, fatigue and functional limitation, the sample appeared to be relatively representative of the population of cancer survivors, and therefore the findings should be widely applicable.

In Green's (2014) study the relationships between pain, functional limitation, fatigue, and concurrent depression were initially investigated using Pearson correlation coefficients. There were positive correlations between all of the independent variables and concurrent depression. In the present study, there were also positive correlations between all of the independent variables and future depression. The additional significance of this finding is that the measurement of the independence variables months before depression was measured demonstrates a temporal order, in which the variables of pain, functional limitation, and fatigue precede depression, and thus may be further examined to determine if they are predictive of depression, which was via measurement sequence established as subsequent to the independent variables.

Green's (2014) found that cancer-related fatigue accounted for a significant amount of variance in concurrent depression (16.2%), followed by functional limitation (9.8%). In the current study, regression of subsequent depression on the predictor variables indicated that functional impairment accounted for the greatest amount of variance (17.2%), followed by fatigue (13.5%).

Overall, the current study's findings demonstrate that functional impairment and fatigue are both strongly associated with subsequent depression. These findings follow from and are consistent with Green's (2014) study, and demonstrate that functional impairment and fatigue strongly impact ongoing and future depression, with higher levels of functional impairment and fatigue being associated with higher levels of future depression. As the relative importance of functional impairment and fatigue on depression differed depending on whether depression was measured concurrently or at a later time, further research is needed to determine whether the difference between the current results and those of Green (2014) are simply measurement artifacts, or in fact represent the possibility that the impact of functional impairment on depression actually increases over time whereas the impact of fatigue diminishes. Measurement of all variables at multiple points in time over a period of several months would be necessary to examine this question.

Of considerable significance is the degree to which functional impairment and fatigue together contribute to depression over time. In combination, the two variables accounted for nearly one-third of the variance in depression. These findings demonstrate that treatment of depression in cancer survivors must address the depressogenic implications of functional limitation and fatigue, and should in many patients include techniques for better managing functional impairment and fatigue. Although well-researched programs for managing illness-related fatigue

and limiting the impact of functional impairment have been developed, they are rarely introduced to cancer patients when undergoing treatment or in the early stages of remission following treatment. The findings of the current study emphasize the need to better educate medical care providers about the impact of fatigue and functional impairment, as well as in the importance of treating these elements of cancer concurrently with medical interventions. At least a portion of both fatigue and functional limitation in many cancer survivors are iatrogenic to chemotherapy, and therefore medical care providers need to take greater responsibility for helping patients address these inadvertent side effects of their interventions.

The findings of this study are congruent with prior research regarding the impact of fatigue and functional limitation on depression in patients with other chronic illnesses. As discussed in the review of the literature, illness-related fatigue and functional limitation have been clearly related to depression across a range of illnesses, with increased fatigue and functional impairment associated with higher levels of depression. This study extends these findings to survivors of cancer, and demonstrates the need for further research related to the development and progression of depression in cancer patients.

Principal limitations of this study include the small sample size and underrepresentation of males, Hispanics, and African Americans. Thus, suggestions for further research include better representation of these groups to

determine whether there are gender and/or ethnic differences that are related to the impact of fatigue and functional limitation on depression. Further, the relationships among these variables should be examined in a sample with more moderate to severe levels of depression, and possibly in samples representing survivors of specific types of cancer, as differences may exist due to the nature of medical interventions, duration of medical treatment, and/or levels of functional impairment associated with the specific cancer.

Over the last few years, programs have been developed to target fatigue and functional impairment in chronic illness through psychoeducation and cognitive behavioral techniques. Emerging research, including the results of this study, support the underlying assumption that improved management of fatigue can improve overall psychological functioning and quality of life, as well as reduce the impact of functional limitations. The current study highlights the potential importance of fatigue management interventions, and the need to help medical professionals recognize the importance of addressing fatigue in cancer patients and survivors.

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Table 1

Demographics of Sample

	<u>n</u>	<u>%</u>
<u>Gender</u>		
Male	17	23.0
Female	57	77.0
<u>Marital Status</u>		
Single, never married	8	10.8
Married	37	50.0
Separated	2	2.7
Divorced	15	20.3
Widowed	12	16.2
<u>Education</u>		
Less than high school	1	1.4
High school graduate	13	17.6
Some college	30	40.5
College graduate	24	32.4
Graduate degree	6	8.1
<u>Ethnicity</u>		
Caucasian	63	85.1
African American	3	4.1
Hispanic	7	9.5
<u>Religion</u>		
Protestant	28	37.8
Catholic	24	32.4
Jewish	2	2.7
Other	20	27.0

Table 1, continued

Demographics of Sample

	<u>n</u>	<u>%</u>
<u>Employment Status</u>		
Working	14	18.9
Retired	44	59.5
Homemaker	5	6.8
Disabled	6	8.1
Looking for employment	4	5.4
<u>Annual Income</u>		
Less than adequate to needs	14	18.9
Just barely adequate to needs	18	24.3
Adequate to needs	34	45.9
More than adequate to needs	8	10.8
<u>Residence</u>		
Home owner	72	97.3
Retirement apartment	1	1.4

Table 2

Prior and Current Cancer Treatment

	<u>n</u>	%
Currently taking medications for cancer		
Yes	34	45.9
No	26	35.1
Not Known	14	19.0
Currently receiving radiation		
Yes	6	8.1
No	68	91.9
Not Known	0	0.0
Previously received radiation therapy		
Yes	33	44.6
No	24	32.4
Not Known	17	23.0
Currently receiving chemotherapy		
Yes	19	25.7
No	55	74.3
Not Known	0	0.0
Previously received chemotherapy		
Yes	28	37.8
No	24	32.4
Not Known	22	29.7
Currently receiving surgery		
Yes	3	4.1
No	25	33.8
Not Known	46	62.1
Previously received surgery		
Yes	29	39.2
No	8	10.8
Not Known	37	50.0

Table 2, continued

Prior and Current Cancer Treatment

	<u>n</u>	%
Currently receiving hormone therapy		
Yes	8	10.8
No	21	28.4
Not Known	45	60.8
Previously received hormone therapy		
Yes	9	12.2
No	19	25.7
Not Known	46	62.1
Currently receiving other treatment		
Yes	12	16.2
No	21	28.4
Not Known	41	55.4

Table 3

Fatigue Characteristics

	<u>n</u>	%
Frequency of fatigue over past month		
Every Day	17	23.0
Occasionally but not most days	22	29.7
Most, but not all days	29	39.2
Hardly any days	4	5.4
Fatigue Severity		
Mild	23	31.1
Moderate	36	48.6
Severe	11	14.9
Very Severe	4	5.4
Fatigue considered a disability		
Yes	28	37.8
No	36	48.6
I Don't Know	9	12.2
Frequency of fatigue over past week		
Hardly any days	4	5.4
Occasionally, but not most days	16	21.6
Most, but not all days	17	23.0
Every day	32	43.2
Degree to which health status is affected by fatigue		
Very affected	27	36.5
Somewhat affected	28	37.8
Not Sure	11	14.9
Somewhat unaffected	5	6.8
Very unaffected	1	1.4

Table 4

Fatigue Measures

	<u>n</u>	%
Days unable to work in past 6 months due to fatigue	36.19	47.37
Episodes of severe fatigue in past month	3.26	1.47
Fatigue Index	3.88	1.27

Table 5

Correlations among Impairment, Fatigue, and Subsequent Depression

Measures

	Depression At Time 2	Functional Limitation	Valued Activity Impairment	Fatigue
Pain	-.01	.17	.33*	.31*
Depression Time 2		.40**	.18	.47**
Functional Limitation			.68**	.53**
Valued Activity Impairment				.59**

Note: Depression was measured six months after the predictor variables were assessed. The obtained depression score, evaluated six months after the other measures, was used in this analysis.

* $p < .05$ ** $p < .01$

Table 6

Multiple Regression Analysis Examining The Impact of Fatigue, Functional Impairment, Valued Activity Impairment, and Pain on Subsequent Depression in Cancer Survivors

Predictor	[Depression]	
	Beta	r_{part}^2
Fatigue	.579	.172**
Functional Impairment	.435	.135**
Valued Activity Limitation	.125	.010*
Pain	.034	.001

Notes. Depression was measured six months after the predictor variables were assessed. The obtained depression score was used in this analysis. Beta values represent unique effects for each variable. The r_{part}^2 is the proportion of variance accounted for when controlling for all other predictors in the equation.

* $p < .05$. ** $p < .01$.