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Relationship Between Cancer-Related Fatigue and Depression: A Pilot Study

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Relationship Between Cancer-Related Fatigue and Depression: A Pilot Study

by

Gloria Michelle Guess

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science
College of Nursing
University of South Florida

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Dedication

This is dedicated to my wonderful family, who has supported me through the years of achieving my academic and career goals. Danny, all of this hard work has been for us, for our family, for our success; to show our boys that no matter what obstacles you face in life to never lose sight of your goals or aspirations. To my boys, Tyler and Nick, you have grown up with your Mom always working toward higher education. You both are my inspiration, and I appreciate the sacrifices we have made as a family to achieve this dream. Mimi, you and Papa always showed me the importance of hard work and family. Thank you for always believing in me, for being supportive, and for showing me unconditional love. Aunt Sue, thank you for listening, for checking in on me, for offering words of encouragement, for believing in me, and for always being supportive. To my sister, thank you for checking in on me, for believing in me, for listening, and for offering for support. To my parents, thank you for teaching me the importance of hard work, dedication, and for believing in me. I hope I have made you proud. I love and appreciate you all.

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Abstract

Fatigue is one of the most bothersome symptoms reported by patients diagnosed with cancer, and research indicates that the majority of patients receiving chemotherapy report symptoms of fatigue. Fatigue can have an effect on quality of life; therefore, it is essential that healthcare providers gain a better understanding and recognition of fatigue.

Fatigue can also be a symptom of depression. Depression is another prominent symptom reported by patients diagnosed with cancer. Unfortunately, there are similarities between the symptoms of depression and fatigue making it difficult for health care providers to distinguish between the two. This study utilizes the subscale of the Hospital Anxiety and Depression Scale and the Multidimensional Fatigue Scale-Short Form to further investigate the relationship between cancer-related fatigue and depression. The convenience sample consisted of 30 chemotherapy patients being treated at an outpatient infusion center in a comprehensive cancer center in southwest Florida. All participants were between the ages of 26 and 74, and had been receiving chemotherapy for a minimum of three weeks; none had been diagnosed with chronic fatigue syndrome, or were currently being treated with radiation.

The participants in the study self-rated their fatigue on a Likert-type scale of 0-10. The mean score on the self-rated fatigue scale was 4.03 (SD= 2.76). This study supports prior studies in which chemotherapy patients report mild to severe levels of fatigue.

The mean score on the depression subscale of the Hospital Anxiety and Depression subscale was 4.53 (SD=4.2). A statistically significant correlation was noted

between cancer-related fatigue and depression, utilizing the Hospital Anxiety and Depression subscale score and Multidimensional Fatigue Inventory–Short Form total scores ($r=.676$, $p=.000$).

This study provides evidence that tools such as the Hospital Anxiety and Depression Scale and the Multidimensional Fatigue Inventory-Short Form can aid researchers and providers in distinguishing between fatigue and depression. Using these instruments in future research and practice may help avoid the overlap in symptoms of fatigue and depression.

These study results support findings from previous studies indicating a moderate correlation between cancer-related fatigue and depression. This study addresses the correlation between cancer-related fatigue and depression in chemotherapy patients which may improve nursing assessment of fatigue and depression in this population. Findings suggest the need for ongoing research focusing on cancer-related fatigue and depression as well as appropriate pharmacological and non-pharmacological interventions to improve the quality of life of this patient population.

Chapter I. Introduction

The American Cancer Society (2010) estimates that more than 1,529,560 people will be diagnosed with cancer annually. Many patients diagnosed with cancer will be treated with chemotherapy. Hauser, Walsh, Rybicki, and Seyidova-Khoshknabi (2008) estimated that 90% of patients diagnosed with cancer, report cancer-related fatigue. These numbers are significant to health care providers as more people are being diagnosed with and surviving cancer. These persons present with multifaceted symptoms that may be related to the diagnosis of cancer.

One of the most common distressing symptoms reported by patients with cancer is fatigue. Mitchell and Berger (2006) report that 78% of patients with cancer report living with the distressing symptom of fatigue. Cancer patients report fatigue during and soon after cancer treatment has concluded. Fatigue is an important symptom for health care providers to understand and assess as it impacts the patient with multifaceted problems such as weakness, decreased mental concentration, insomnia or hypersomnia, and emotional reactivity. These multifaceted problems could also be identified as symptoms of depression. It is important for the provider to be able to distinguish between cancer-related fatigue and depression as both have a negative effect on the patient. Providers must realize the strong implications of fatigue and depression as both affect the patient's physical, social and vocational functioning, mood, and sleep disturbances as well as affecting family members.

It is important to make an accurate diagnosis of depression in the patient with cancer as a misdiagnosis can have negative clinical consequences (Endicott, 1984). The treatment for depression can increase the somatic symptoms if a misdiagnosis of depression is made. Another consequence of misdiagnosing depression is that fatigue, decreased energy, and change of appetite can be overlooked in the patient with cancer if attributed to a depressive disorder instead of an underlying medical problem. A provider can easily attribute the somatic symptoms associated with cancer and its treatment to depression which can result in over diagnosis of depression (Walker et al., 2007).

Stress from a medical condition such as cancer can lead to somatic symptoms seen also in depression. It can be difficult for a provider to distinguish depression from cancer related symptoms. Jean-Pierre and colleagues, (2007) noted that there is a significant challenge in distinguishing cancer-related fatigue from depression as the measurement of these variables tends to overlap. It is important for the provider to use a tool that would help accurately diagnose symptoms of depression. Zigmond and Snaith (1983) worked to help providers distinguish between anxiety and depression by developing the Hospital Anxiety and Depression Scale (HADS Scale), a tool which assesses mood without including physical symptoms such as tiredness or lack of appetite.

Problem Statement

Numerous studies have been conducted on cancer-related fatigue and depression as separate entities. Limited studies take into consideration the bias introduced by depression measures that include fatigue as an item (Brown & Kroenke, 2009). Chemotherapy is often associated with fatigue and depression. More research is needed to determine whether cancer-related fatigue and depression are correlated using methods

that avoid the overlap in symptoms of fatigue and depression. The purpose of this study was to evaluate the relationship between cancer-related fatigue and depression in patients receiving chemotherapy.

Research Questions

The following research questions are addressed in this study:

1. What is the mean fatigue severity in patients receiving chemotherapy based on the Multidimensional Fatigue Symptom Inventory-Short Form?
2. What is the mean severity of depressive symptoms in patients receiving chemotherapy based on the Hospital Anxiety and Depression Scale: Depression Subscale?
3. Is there a significant positive relationship between fatigue severity and severity of depressive symptoms in patients receiving chemotherapy?

Definition of Terms

For the purpose of this study the following terms are defined:

Fatigue: “persistent and subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning” (Jean-Pierre et al., 2007, p.12).

Minor Depression: “individuals who experience at least two depressive symptoms for two weeks but do not meet the criteria for major depression” (Fauci, 2008, p.2716).

Major Depression: “individual who has a depressed mood on a daily basis for a minimum duration of two weeks” (Fauci, 2008, p.2716).

Significance to Nursing

Cancer-related fatigue and depression are significant to nursing as each have an impact on quality of life and possibly survival of patients. Nurses must assess for both

fatigue and depression in an effort to provide holistic care to the chemotherapy patient. Research has shown that cancer-related fatigue can last years past the final cancer treatment; therefore early assessment and intervention are necessary.

This study may identify a correlation between cancer-related fatigue and depression. Understanding the relationship between cancer-related fatigue and depression may allow the nurse to offer appropriate interventions. Management of the symptom of fatigue and depression can help improve the quality of life of the patient and perhaps extend the life of the patient diagnosed with cancer and treated with chemotherapy.

Chapter II. Review of Literature

The literature from 1983 to present was reviewed utilizing Ovid, PubMed, CINAHL, and EBSCOhost electronic databases. Key terms used included a combination of the following: fatigue, cancer, cancer-related fatigue, chemotherapy, depression and cancer, depression and cancer-related fatigue. First, research pertaining to fatigue in cancer is reviewed. Second, research focusing on fatigue and cancer is presented. Finally, research relating fatigue and depression is reviewed. The chapter ends with a summary of pertinent variables.

Fatigue in Cancer

Cancer-related fatigue is a symptom that is very disruptive in the life of the cancer patient. It affects patients not only physically, but psychosocially as well, having an impact on the overall quality of life of the patient. Cancer-related fatigue differs from normal fatigue as it is not relieved by rest or sleep and persists over time becoming more intense. This fatigue can last even after cancer treatment has concluded (Morrow, 2007).

Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, and Morrow (2007) identified how fatigue impacted patients with different cancer diagnoses. The researchers found that more than 80% of patients receiving outpatient chemotherapy report fatigue as a significant side effect of treatment. Patients diagnosed with melanoma, prostate, or lung cancer had fatigue lasting more than six months which also affected their functional abilities.

This study provides evidence that cancer-related fatigue is a significant side effect of chemotherapy treatment. Hofman and colleagues, (2007) surveyed 379 patients who had chemotherapy treatment and 76% reported the side effect of cancer-related fatigue in comparison to 54% who reported nausea, 23% who reported depression, and 20% who reported pain. The researchers also found that 88% of patients who had chemotherapy reported that fatigue had affected their activities of daily living.

Jean-Pierre and colleagues, (2007) found that a patient can reliably rate fatigue on a scale from 0 to 10 asking such questions such as, “ How would you rate your fatigue on a scale of 0 to 10 over the past 7 days?” Scores were assigned numerically with a 0 indicating no fatigue, 1 to 3 mild fatigue not requiring intervention, 4 to 6 and 7 to 10 as moderate and severe fatigue which would require further assessment and intervention. These questions are subjective and are based on the patient’s personal experiences.

Hauser, Walsh, Rybicki, and Seyidova-Khoshknabi (2008) examined the affect of fatigue in 171 patients with advanced cancer. The researchers created a fatigue questionnaire to gather clinically significant information on cancer-related fatigue (CRF). This tool evaluated fatigue at present and in the past week with the use of 100 mm visual analog scales (VAS) with one end of the scale labeled as very fatigued and the other end as no fatigue. This study showed a negative correlation between quality of life and fatigue. Persons with lung cancer reported that the affect of fatigue on quality of life is worse than the affects of dyspnea and pain. Researchers also noted that fatigue is related to significant disability to perform daily activities and ability to enjoy relationships (Hauser et al., 2008).

Prue, Rankin, Cramp, Allen, and Gracey (2006) investigated the relationship of fatigue and gynecological cancer using the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF). The researchers collected data from 30 female patients ranging from 31 to 84 years of age. Data showed that 85% of participants reported that tiredness had an affect on their ability to complete activities of daily living. Nausea, vomiting, and pain were also symptoms reported by participants; however, these symptoms did not affect activities of daily living. This study showed that 90% of participants related fatigue to their cancer diagnosis.

Survivors of breast cancer commonly report fatigue as a distressing symptom following adjuvant treatment lasting months to years. Fatigue has an affect on quality of life; therefore, researchers worked to identify demographic, medical, and psychosocial characteristics of 1,957 survivors (Bower et al., 2000). This study provided evidence that there is no difference in level of fatigue in survivors who received different treatment regimens including surgery, radiation, adjuvant chemotherapy, and Tamoxifen. Energy levels remained low one year after treatment. The RAND scale provided evidence that bodily pain is strongly associated with fatigue and is correlated with greater problems with sleep and sleep disturbance. Researchers also found a strong correlation between fatigue and depression. Researchers found the link between fatigue and depression to be complex. Fatigue can be a symptom of depression or it can be associated with symptoms of depression. This data provides evidence of the importance of screening for depression and other disorders in cancer survivors who complain of fatigue.

Depression in Patients with Cancer

It can be difficult for the provider caring for a patient with cancer to diagnose depression when cancer-related fatigue is present because of the overlap in symptoms. Evidence has shown that depression is one of the most significant problems experienced by cancer patients. Reich (2008) reported that oncology patients who are depressed have a higher relapse rate and decreased compliance with treatment.

Singer and colleagues, (2010) studied depression in oncology patients incorporating the HADS. The researchers noted that the severity of the depression is not related to the stage of the cancer but with socio-demographic and psychosocial characteristics. The researchers identified that medical providers typically screen for depression without use of a structured clinical interview tool. The goal of this study was to provide evidence of the importance of implementing a screening tool for diagnosis of depression. In this cross-sectional study of 329 patients, researchers used the HADS questionnaire to identify participants with depression. Twenty-eight (11.75%) patients were identified as having either major or minor depression. Furthermore, in this study the HADS had a sensitivity of 96%. This study provides supportive evidence of implementing a screening tool such as the HADS to help identify, early in the treatment process, patients who may be depressed.

Castelli, Binaschi, Caldera, Mussa, and Torta (2010) conducted a study of 151 subjects newly diagnosed with different cancer pathologies. In this study the researchers provided evidence that a cut off score of eight, instead of eleven, is more accurate in screening for depression when using the HADS. The results of this study also provide evidence of the prevalence of depression in newly diagnosed cancer patients. This study

showed that the HADS can be used in practice to quickly and accurately screen for depression in patients diagnosed with cancer. Krespi-Boothby and colleagues, (2010) also provide evidence that the HADS tool accurately detected major depression as defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) when a cut off score of eight is used. The investigators used the HADS scale in screening 251 patients diagnosed with breast cancer.

Castelli, Binaschim, Caldera, and Torta (2009) recognized the importance of screening for depression in outpatients receiving treatment for cancer. The researchers conducted a study of 53 newly diagnosed lung cancer patients, who had been advised to undergo chemotherapy, to determine the accuracy of the HADS scale in screening for depression. Results showed that the HADS is a fast and accurate screening tool for depression when a cut off score of eight is used. The study also shows evidence of the high prevalence of depression in newly diagnosed lung cancer outpatients (Castelli, Binaschim, Caldera, & Torta, 2009).

The Relationship between Fatigue and Depression in Cancer

Cancer-related fatigue is one of the most common symptoms reported by patients undergoing cancer treatment that is often unrelieved. This fatigue can have an effect on quality of life affecting physiological, psychological, and behavioral aspects (Goldstein et al., 2006). Fatigue is reported with many medical and psychological conditions including major depression. Fatigue continues to be ongoing in over 75% of patients after treatment is completed. Goldstein and colleagues, (2006) hypothesized that fatigue will vary in the presence of other variables, such as psychological symptoms, and that most cases will improve over time.

Two-hundred and twelve women ages 26 to 85 who were treated for stage one or two breast cancer were asked to participate in the study if they had adjuvant treatment in the last twelve months. Researchers used the Somatic and Psychological Health Report (SPHERE) questionnaire to screen for any significant fatigue states and mood disorders (Goldstein et al., 2006). The SPHERE tool assesses somatic and psychological symptoms, assessment of fatigue following infectious illness, and in patients following adjuvant treatment for cancer. The Brief Disability Questionnaire was also used by researchers to determine social and occupational role impairment due to fatigue.

Data from this study showed that 48% of the subjects reported clinically significant fatigue; 36% reported depression or anxiety and 81% of those were also cases of fatigue (Goldstein et al., 2006). Further data shows that functional status is impaired in persons with fatigue who reported difficulty walking up stairs (40%) whereas those who did not report fatigue only 10% reported difficulty walking up stairs. The researchers found 48% of subjects had a significant fatigue state post cancer treatment, and 33% reported significant psychological distress. Only 1% of cases were found to be solely fatigue, with no accompanying psychological disorder whereas 52% of cases were found to have both disorders. Goldstein and colleagues, (2006) found that psychological distress was the only risk factor associated with post-cancer fatigue ($p < 0.00001$).

This study provides evidence of the prolonged effect of cancer-related fatigue. Evidence from the study shows that fatigue lasts beyond the end of cancer treatment as long as 48 months. Prior studies have shown that fatigue can last up to ten years post cancer treatment (Goldstein et al., 2006). The SPHERE tool is beneficial in showing the correlation of poor mental health and fatigue. This study also provides evidence that

fatigue is not related to a mood disorder such as depression. The study does, however, indicate the relationship of fatigue and mood disorders in the majority of the cases, and both problems are sustained over time.

Jean-Pierre and colleagues, (2007) noted that there is a significant challenge in distinguishing cancer-related fatigue from depression as the measures of each variable correlate highly. In a study of 724 cancer patients, one week after completing chemotherapy, there was an overlap identified in depression and fatigue in multi-item measures of fatigue. Questions such as “to what degree have you experienced fatigue in the past week?” were found to have a high correlation on multi-item and single-item measures of fatigue and depression.

It is important that providers not only recognize the symptom of cancer-related fatigue but know how to assess it as well. Jean-Pierre and colleagues, (2007) provide evidence that unidimensional and multidimensional measurements of CRF are both reliable scales to assess cancer-related fatigue. More importantly the researchers found that the unidimensional scale for fatigue is just as reliable and valid as a more complex multidimensional tool. The researchers also showed that patients are capable of self-reporting cancer-related fatigue and can reliably complete questionnaires which ask subjective questions on cancer-related fatigue. It is important however for the provider to remember the strong correlation between fatigue and depression when measuring on both single and multi-item scales.

The patient diagnosed with cancer not only has to cope with the disease but with the multiple symptoms associated with the disease and with its treatment. Barsevick and colleagues, (2006) recognized the symptoms of fatigue and depression in cancer patients.

The researchers tested a hypothesis about the direct and indirect relationships between fatigue and depressive symptoms and functional status. Previous studies have shown a relationship of symptom clusters showing that one symptom can influence another symptom, and even affect a third symptom (Barsevick et al., 2006).

Researchers conducted a clinical trial of 396 patients being treated for different forms of cancer including breast, gynecologic, testicular, lung, advanced prostate cancer, or lymphoma. Persons with a diagnosis of anemia, or having a psychiatric disorder, or treatment for depression in the last three weeks were excluded from this study. Data was collected from all subjects at times noted to be correlated with highest levels of fatigue in both the chemotherapy and radiation group. Subjects were assigned to intervention groups either, energy conservation and activity management, or a control intervention consisting of information on a healthy diet (Barsevick et al., 2006). A secondary analysis was conducted by the researchers to determine direct and indirect relationships between fatigue and depressive symptoms. These investigators hypothesized that fatigue would influence depressive symptoms and that as fatigue increased functional status was expected to worsen which would cause an increase in depressive symptoms.

Researchers found that functional status after cancer therapy affected the relationship between fatigue and depressive symptoms (Barsevick et al., 2006). Researchers found that when functional status was controlled, the relationship between fatigue and depressive symptoms was reduced ($p < .001$). For the energy conservation and activity management group fatigue was found to be associated with depressive symptoms and related to functional status. In this group the intervention changed the role of functional status but did not reduce fatigue and depressive symptoms.

This study shows the correlation of fatigue and depression and its effect on functional status. This study provides further evidence of the correlation of fatigue and depressive symptoms. This research shows that changing functional status can have an affect on fatigue and symptoms of depression. Barsevick and colleagues, (2006) reinforced that fatigue is an expected symptom in cancer patients and can be correlated with depression.

Summary

Cancer-related fatigue is one of the most common symptoms experienced by chemotherapy patients; yet health care providers may offer no assessment or intervention to help improve the symptoms of fatigue or depression which may affect the quality of life of the chemotherapy patient. The review of literature provided evidence of the correlation of cancer-related fatigue and depression. Jean-Pierre and colleagues, (2007) noted that there is a significant challenge in distinguishing cancer-related fatigue from depression as the measures of each variable correlate highly. The research by Barsevick and colleagues, (2006) provides evidence of the direct and indirect relationships between fatigue and depression symptoms. Goldstein and colleagues, (2006) provide evidence that fatigue lasts up to 48 months after cancer treatment has concluded. The aim of this study is to further evaluate the correlation of cancer-related fatigue and depression in patients undergoing chemotherapy treatment by methods that avoid the overlap in symptoms of fatigue and depression.

Chapter III. Methods

The purpose of this study is to determine whether there is a significant relationship between cancer-related fatigue and depression in cancer patients receiving chemotherapy. This chapter outlines the research methods. First the sample and setting are described. The instruments included in the study are then discussed. Then, data collection procedures are outlined, and finally, data analysis information is provided.

Setting and Sample

The sample consisted of patients from Moffitt Cancer Center Infusion Center currently undergoing chemotherapy treatments. To achieve adequate power (.80) for a moderate effect size, with alpha set at .05, a sample of 60 was needed.

For inclusion in the study, the patients had completed any prior chemotherapy regimen for a minimum of three weeks prior, were receiving chemotherapy treatment lasting longer than two hours, had any cancer diagnosis, were at least 18 years of age, male or female, and were able to speak, read, and write English. Those who were undergoing their first chemotherapy treatment were excluded, as was any patient currently on antidepressant therapy, or with a history of chronic fatigue syndrome. Any patient whose treatment time was less than two hours was excluded from the study.

Instruments

The Hospital Anxiety and Depression Scale. The work by Zigmond and Snaith (1983) provides evidence that the HADS Scale (Appendix A) is a reliable instrument that can be used to screen for anxiety and depression in a non-psychiatric setting. Research

also demonstrated that this scale is reliable for assessing severity of depression and can be used on multiple occasions to determine patient progress. This scale encourages the removal of somatic symptoms such as insomnia, fatigue, and pessimism about the future when diagnosing depression. Zigmond and Snaith (1983) found that once they removed the emotional and somatic illness, then the results of the scale were not affected by physical illness. This scale is useful in assessing the presence or absence of depression and its severity in the patient diagnosed with cancer as it removes the somatic symptoms enabling the provider to make a more accurate and confident diagnosis.

The Hospital Anxiety and Depression Scale (HADS) is a screening tool which assesses depression (Zigmond & Snaith, 1983). This instrument was chosen because it is a simple tool which allows for screening of depression symptoms over the past week. The HADS also excludes somatic symptoms, which could be attributed to cancer and its treatment (Walker et al., 2006). There are a total of seven items pertaining to symptoms associated with depression. It is a four-point Likert-type scale ranging from zero to three, with varying response categories, which applies to the previous week. For the depression subscale, a score ranging from 0 to 21 is calculated: scores less than eight are deemed “non-cases”. Scores of eight, nine, ten are rated borderline; and scores of eleven or more are indicative of the probable presence of psychological distress. The questionnaire is written on a seventh grade reading level, can be self-administered, and takes three to five minutes to complete (Walker et al., 2006).

Reliability. Reliability of the depression subscale was tested with a 1% false positive, 1% false negative whereas the anxiety subscale had a 5% false positive and 1% false negative. Researchers then determined that the findings of both the anxiety and

depression subscales could be used to indicate the severity of depression and anxiety ($p < 0.001$). The researchers also found that the subscale scores of anxiety and depression were not affected by physical illness.

Alpha coefficients for the depression subscale of the HADS is 0.86 (Olsson, Mykletun, & Dahl, 2005). A study by Walker and colleagues, (2007) found that the HADS tool was reliable when used as a screening tool for depression in mixed cancer outpatients. The depression subscale of the HADS had a sensitivity of 0.90 (95% CI, 0.74-0.97) with a specificity of 0.88 (95% CI, 0.84-0.91) (Walker et al., 2007).

Validity. Walker and colleagues, (2007) compared the HADS specifically to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV). The researchers found when using the HADS total score to identify cases of major depressive disorder (MDD) the area under the receiver operating characteristic (ROC) curve was 0.94. Walker and colleagues, (2007) found that when screening for MDD in cancer patients a cut-off score of ≥ 15 to be optimal with a 95% CI, (0.70-0.95) and a specificity of 0.85 (95% CI, 0.81-0.89). This reduces misclassifications of MDD at 0.65 for true negative cases and 0.01 for true positive cases. The study by Walker and colleagues, (2007) validated that the HADS tool is an adequate screening tool for major depressive disorder in mixed cancer outpatients with the areas under the ROC curve close to 1.00 which indicate a good overall performance and good levels of sensitivity and specificity.

Multidimensional Fatigue Symptom Inventory-Short Form. The Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) is a Likert-type scale consisting of 30 questions (Jean-Pierre et al., 2007). The MFSI-SF instrument (Appendix B) was chosen as it has been validated in patients with cancer and does not

assume the presence of fatigue. This scale, like the HADS scale, inquires about patients symptoms over the past week. This instrument consists of 5 subscales: general fatigue, physical fatigue, emotional fatigue, mental fatigue and vigor (Stein, Jacobsen, Blanchard, & Thors, 2004). Possible responses to the 30 questions assessing fatigue include 0=not at all, 1= a little, 2= moderately, 3=quite a bit, 4=extremely. Higher scores indicate a higher level of fatigue.

Reliability. Reliability was evaluated with internal consistency coefficients. The alpha coefficients were 0.85-0.96 (Stein et al., 2004).

Validity. Construct validity of the MFSI-SF was determined by correlating the instrument with the Fatigue Symptom Inventory (FSI) and the SF-36 Vitality Scale [$r = -0.21$ to 0.82] (Stein et al., 2004). Researchers found correlations among the five subscales of the MFSI-SF and two measures of fatigue demonstrated excellent concurrent validity, whereas correlations with a measure of physical well-being provided support for convergent validity [$r = 0.50-0.65$] (Lin et al., 2009).

Demographic Data Form. The demographic data form (Appendix C) was developed to describe the sample. Age, gender, and type of cancer are data included on the form.

Procedures

Approval for the study was first requested from the Scientific Review Committee at Moffitt Cancer Center & Research Institute (Appendix D). Following approval by the Moffitt Committee, the proposal was submitted next to the University of South Florida Institutional Review Board (Appendix E). Following approval the investigator began accruing patients for the study.

The investigator went to the Infusion Center at Moffitt Cancer & Research Institute and introduced herself to patients at the infusion center and explained the purpose of the study. Privacy was maintained during the interview by speaking with the patients in their individual treatment bays of the infusion center. The investigator answered any questions and if the patient chose to participate in the study, verbal consent (Appendix F) was obtained, with a copy of the consent form given to the patient. The investigator kept a record of how many patients were approached to participate in the study, how many patients consented, and how many patients refused to participate. Eligibility was confirmed prior to consent. The investigator asked the patient for demographic data as she did not access the patient's chart. A unique numbering system was used. The questionnaires were completed by the patients while they were receiving chemotherapy. Each subject was asked to complete the HADS and the MFSI-SF one time while receiving chemotherapy on the day of data collection. The investigator remained with the patients to answer questions while the forms were being completed. If patients were unable to write because of weakness, or an intravenous line in the arm, the investigator completed the forms by interviewing the patients. All data was stored in a locked file cabinet. The investigator assumes that subjects responded truthfully to questions.

Data Analysis

Demographic data was analyzed to describe the sample. Frequencies, percentages, means and standard deviations were used to analyze these data. Data was analyzed with means and standard deviations to answer the following research questions:

1. What is the mean fatigue severity in patients receiving chemotherapy based on the Multidimensional Fatigue Symptom Inventory-Short Form?
2. What is the mean severity of depressive symptoms of patients receiving chemotherapy based on the Hospital Anxiety and Depression Scale: Depression Subscale?

Research Question three was:

3. Is there a significant positive relationship between fatigue and severity and severity of depressive symptoms in patients receiving chemotherapy? A series of Pearson correlation coefficients were reported.

Chapter IV. Results, Discussion, and Conclusions

This chapter presents the findings of the study. Included in this chapter are the study results, discussion of the results, conclusions, and suggestions for future research.

Results

Demographic Data. Forty-two patients were approached and 30 enrolled and completed the study. The following are reasons for exclusion: two patients refused to participate, four were currently on antidepressant therapy, five had been receiving treatment less than three weeks, and one was currently receiving radiation. The sample consisted of 30 participants, 18 male and 12 female, ranging in age from 26 to 74 with a mean age of 59.5 (SD=12.4). The largest number of participants reported the following cancer diagnoses: gastrointestinal (29.9%), gynecological (20%), genitourinary cancer (19.9%), hematologic cancer (13.2%), and thoracic (9.9%) (Table 1). All participants had been receiving chemotherapy for a minimum of three weeks; none had been diagnosed with chronic fatigue syndrome, or were currently being treated with radiation.

Descriptive Data. On the demographic data form, participants self-rated their current levels of fatigue on a scale of 0 to 10 (*No Fatigue-Worst Fatigue*) with a mean of 4.03 (SD=2.76) (Table 2), indicating a moderate level of fatigue. The Multidimensional Fatigue Symptom Inventory–Short Form (MFSI-SF) was used to measure participants' fatigue. The mean score for the total scale on MFSI-SF was 14.8 (SD=22.1) and patient scores ranged from -20.00 to 62.00. Since scores may range from 0 to 96 with higher scores indicating more severe fatigue, participants in this study reported low levels of

fatigue. Subscales were further analyzed to determine the various types of fatigue (Table 3).

Table 1 *Frequency and Percent of Reported Cancer Diagnosis*

| Type of Cancer | Frequency | Percent |
|-----------------------|------------------|----------------|
| Gastrointestinal | 9 | 29.9 |
| Gynecological | 6 | 20.0 |
| Genitourinary | 6 | 19.9 |
| Hematologic | 4 | 13.2 |
| Thoracic | 3 | 9.9 |
| Head and Neck | 2 | 6.6 |

Table 2 *Frequency and Percent of Participants' Perceived Fatigue Based on 0-10 Scale*

| Fatigue Variable | Frequency | Percent |
|-------------------------|------------------|----------------|
| None (0) | 3 | 10 |
| Mild (1-3) | 10 | 33.3 |
| Moderate (4-6) | 9 | 30 |
| Severe (7-10) | 8 | 26.7 |

Depression was assessed using the Hospital Anxiety and Depression Scale (HADS). The mean score on the HADS was 4.53 (SD = 4.2) and scores ranged from 0-17 (Table 4). A score of seven or less on the depression subscale indicates a non-case of depression; scores of 8 to 10 indicate a borderline case of depression, whereas a score of 11 or more is indicative of a more probable case of depression. In this study, four

participants' scores indicated borderline cases of depression, and three indicated probable cases of depression (Table 4).

Table 3 *Means and Standard Deviations for Subscales of MFSI-SF*

| Subscale | Mean | Standard Deviation |
|--------------------------|-------------|---------------------------|
| General Scale Score | 10.2 | 6.9 |
| Physical Scale Score | 5.7 | 5.7 |
| Emotional Scale Score | 5.2 | 5.1 |
| Mental State Score | 5.4 | 4.1 |
| Vigor Scale Score | 11.6 | 5.6 |
| Total Scale Score | 14.8 | 22.1 |

Table 4 *Frequency and Percent of Participants' HADS Depression Subscale Scores*

| Depression | Frequency | Percent |
|-------------------|------------------|----------------|
| Non-Depression | 23 | 76.6 |
| Borderline | 4 | 13.3 |
| Probable | 3 | 9.9 |

Correlations. Subscales were further analyzed using Pearson Correlations to determine the relationship between cancer-related fatigue and depression (Table 5). A statistically significant correlation was found between cancer-related fatigue and depression utilizing the HADS Depression scores and MFSI-SF total scores ($r=.676$, $p=.000$).

General fatigue was assessed to further analyze both physical and psychological aspects of fatigue. Mental fatigue was assessed to further analyze cognitive functioning, including difficulty concentrating. Physical fatigue was assessed to analyze physical sensations related to fatigue. Emotional fatigue was assessed to further analyze reduced activity due to the influence of physical and psychological factors on activity. Vigor was assessed to further determine how reduced motivation related to lack of motivation in starting any activity, with a negative correlation noted. Focusing on MFSI-SF subscale scores, all correlations with HADS Depression subscale scores were significant except the mental and physical fatigue scale scores (Table 5).

Table 5 *Correlation Between Cancer-Related Fatigue and Depression*

| Scale | HADS Depression Scores | |
|--------------------------|------------------------|-------------|
| | r | p |
| Fatigue | .379 | .039 |
| General Scale Score | .594 | .001 |
| Physical Scale Score | .345 | .062 |
| Emotional Scale Score | .719 | .000 |
| Mental State Score | .344 | .062 |
| Vigor Scale Score | -.659 | .000 |
| Total Scale Score | .676 | .000 |

Discussion

Demographic Data. A limitation of the study was the small sample size. However, in spite of the small sample, significant relationships were found between fatigue and depression. The age range of patients participating in the study was 26 to 74

years of age with a mean age of 59.5, which is similar to earlier studies of cancer patients (Delgado-Guay et al., 2008). The sample was mostly Caucasian with few Hispanics and African American subjects. This also is a limitation of the study.

Another limitation of this study is the inclusion of different types of cancer which can contribute to fatigue or depression. For example, pancreatic tumors can be associated with depressive disorders due to the secretion of neuropeptides and neurohormones in addition to the secretion of growth hormones. Interferons and Interleukines used to treat renal cell cancer, melanoma, and chronic myelogenous leukemia have been associated with fatigue and depression (Jacobsen, Donovan, & Weitzner, 2003). Data from the participants' medical records was not available so it was not possible to evaluate possible relationships between medical treatment and cancer-related fatigue and depression.

A cross-sectional study was conducted from February through March 2011. Future research should include a longitudinal study perhaps following the participants from early diagnosis through treatment to identify when the fatigue and/ or depression symptoms begin and to correlate with treatment. This is of importance as Laugsand and colleagues, (2010) noted that providers underestimated fatigue and depression. Patients rated their own fatigue and depression symptoms higher than their health care providers did. Patients rated fatigue on a scale of 0 to 100 as a 71 while their providers rated it as 54 and rated depression as 31 while their providers rated depression as 17 (Laugsand et al., 2010). Participants in this study rated their own level of fatigue on a scale of 0 to 10 on the demographic data form for further comparison of results and correlations with the instruments used in the study.

Another limitation of this study is the reliability of data. Many participants were unable to recall the number of treatments they had received or the origin of their cancer prior to metastasis. Participants also were concerned about the stigma of depression; therefore, future studies should use test-retest to ensure reliability of results.

Depression. Depression was assessed using the depression subscale of the Hospital Anxiety and Depression Scale. An advantage of the HADS scale noted by researchers is that its subscales do not include any physical symptoms that could interfere with the measurement of fatigue (Brown & Kroenke, 2009). The mean score on the HADS was 4.53 (SD =4.2). Twenty- three percent of participants scored eight or higher on the HADS indicating possible case of depression. Pirl (2004) noted that major depressive disorder affects 10 to 25 % of cancer patients. Walker and colleagues, (2007) noted when using the depression subscale of the HADS to identify cases of depression that a cut-off of ≥ 7 is optimal (95% CI, 0.74-0.97). Walker and colleagues, (2007) also noted that the HADS depression subscale is an adequate screening tool for mixed cancer outpatients as were used in this study. More significant findings may have resulted from a larger sample size. Many participants verbalized concern over being labeled as depressed; therefore the results may have been skewed due to patient bias.

Karakoyun-Celik and colleagues, (2009) noted that socio-demographic features such as income, age, marital status, and education may significantly affect depression levels. Income and education were not assessed in this study and no correlations were calculated between age and marital status with either depression or fatigue, which is a limitation of this study.

Fatigue. The results of this study confirm that the majority of patients receiving chemotherapy report fatigue (90%) with 57.7% rating fatigue as ≥ 3 on a scale of 0 to 10. Similar findings by Hwang and colleagues, (2003) have previously been reported with 80% of chemotherapy patients reporting fatigue and rating fatigue as ≥ 3 .

An advantage of the MFSI-SF is the instrument does not assume the presence of fatigue and evaluates participants fatigue over a one week time frame (Stein, Martin, Hann, & Jacobsen, 1998). The mean total score on the MFSI-SF was 22.1 (SD=14.8). Hofman and colleagues, (2007) report that cancer-related fatigue rates vary depending on the type of cancer from 37 to 78% for patients with lung cancer and 28-91% in breast cancer, and 15% in those with prostate cancer. The researchers further noted that the severity of cancer-related fatigue peaks within four or five days of completion of treatment. Stein and colleagues, (2004) noted that the MFSI-SF is a valuable tool for multidimensional assessment of cancer-related fatigue following the fourth cycle of chemotherapy for mixed cancer diagnosis.

Correlations. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) refers to assessing a major depressive disorder by having the presence of four or more symptoms in a two week period in addition to a depressed mood or loss of interest in pleasure in usual activities. Fatigue and loss of energy are also symptoms of depression according to the DSM-IV (Jacobsen, Donovan, & Weitzner, 2003). In this present study participants self-rated their perceived level of fatigue on a 0 to 10 scale which showed a significant correlation between cancer-related fatigue and depression ($r=.379$, $p=.039$). Browne and Kroenke (2009) noted the average correlation between fatigue and depression was 0.56 (95% CI: 0.54-0.58). Next, the

total scores of the MFSI-SF were analyzed which showed a significant correlation between cancer-related fatigue and depression ($r=.676$, $p=.000$). To further evaluate relationships between cancer-related fatigue and depression, the MFSI-subcales were analyzed. The MFSI consists of five subscales: general fatigue, physical fatigue, emotional, fatigue, mental fatigue, and vigor. Jacobsen and colleagues, (2003) found a significant correlation between cancer-related fatigue and depression in chemotherapy patients. Prior studies have noted an overlap in symptoms of fatigue and depression in cancer patients; this study used instruments which eliminate the overlap in symptoms and allow for correlation of cancer-related fatigue and depression.

Using the MFSI-SF allows the researcher to focus on specific types of fatigue such as emotional fatigue. The MFSI-SF asks the participant specific questions which can be correlated with depression such as: “*I feel upset, I feel nervous, I feel sad, I feel depressed, I feel tense, and I feel distressed*”. Emotional fatigue has been defined in prior research as reduced activity due to the influence of physical and psychological factors on activity. In this study the emotional fatigue subscale strongly correlated with depression ($r=.719$, $p=.000$).

Implications for Nursing. The findings of this study have several implications for nursing. This study supports prior research findings that there is a significant correlation between cancer-related fatigue and depression even with physical indicators of depression eliminated from the scale. Prior research has shown an overlap in symptoms of fatigue and depression in chemotherapy patients.

Assessment of depression and fatigue in chemotherapy patients should be emphasized in oncology nursing. Research has shown that providers inaccurately assess

levels of depression and fatigue in oncology patients (Laugsand et al., 2010). It is essential that assessment and intervention be incorporated into oncology nursing curriculum.

There are no current tools for assessing both fatigue and depression. Currently, researchers are assessing each independently using separate tools and then making correlations. Nursing research should focus on developing a tool to assess both fatigue and depression to reduce patient burden. Further nursing research is needed.

Conclusions

There is a significant, moderately strong relationship between cancer-related fatigue and depression. This study with a small sample size consisted of a mixed cancer population in an outpatient infusion center. This study supports prior studies which show a significant correlation between cancer-related fatigue and depression; however, there is limited research which focuses on assessment and intervention.

Recommendations for Future Research. Future studies should include a larger sample size, with greater geographic diversity. More studies should focus on determining when the fatigue or depression began to strengthen the correlation between fatigue and depression. Both fatigue and depression have an impact on quality of life; therefore, it is essential that future research focus on development of assessment tools and interventions. Studies should also focus on specific tumors such as pancreatic tumors to correlate with depressive disorders and fatigue. Depression and fatigue in this population can strongly affect quality of life; therefore, it is essential that research continues so providers can successfully assess and intervene to improve the quality of life chemotherapy patients.

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Appendices

Appendix A: The Hospital Anxiety and Depression Scale: Depression Subscale

The Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983)

Read each item and circle the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

1. I still enjoy the things I used to enjoy:

| | |
|--------------------|---|
| Definitely as much | 0 |
| Not quite so much | 1 |
| Only a little | 2 |
| Hardly at all | 3 |

2. I can laugh and see the funny side of things:

| | |
|----------------------------|---|
| As much as I always could | 0 |
| Not quite so much now | 1 |
| Definitely not so much now | 2 |
| Not at all | 3 |

3. I feel cheerful:

| | |
|------------------|---|
| Not at all | 3 |
| Not often | 2 |
| Sometimes | 1 |
| Most of the time | 0 |

4. I feel as if I am slowed down:

| | |
|---------------------|---|
| Nearly all the time | 3 |
| Very often | 2 |
| Sometimes | 1 |
| Not at all | 0 |

5. I have lost interest in my appearance:

| | |
|---------------------------------------|---|
| Definitely | 3 |
| I don't take so much care as I should | 2 |
| I may not take as much care | 1 |
| I take just as much care as ever | 0 |

6. I look forward with enjoyment to things:

| | |
|--------------------------------|---|
| As much as ever I did | 0 |
| Rather less than I used to | 1 |
| Definitely less than I used to | 2 |
| Hardly at all | 3 |

7. I can enjoy a good book or radio or TV program:

| | |
|-------------|---|
| Often | 0 |
| Sometimes | 1 |
| Not often | 2 |
| Very Seldom | 3 |

Appendix B: The Multidimensional Fatigue Symptom Inventory –Short Form
The Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF)
(Stein, Jacobsen, Blanchard, & Thors, 2004)

Below is a list of statements that describe how people sometimes feel. Please read each item carefully, then circle the one number next to each item which best describes how true each statement has been for you in the **past seven days**.

| | | Not at all | A little | Moderately | Quite a bit | Extremely |
|-----|-----------------------------------|-----------------------|-----------------|-------------------|------------------------|------------------|
| 1. | I have trouble remembering things | 0 | 1 | 2 | 3 | 4 |
| 2. | My muscles ache | 0 | 1 | 2 | 3 | 4 |
| 3. | I feel upset | 0 | 1 | 2 | 3 | 4 |
| 4. | My legs feel weak | 0 | 1 | 2 | 3 | 4 |
| 5. | I feel cheerful | 0 | 1 | 2 | 3 | 4 |
| 6. | My head feels heavy | 0 | 1 | 2 | 3 | 4 |
| 7. | I feel lively | 0 | 1 | 2 | 3 | 4 |
| 8. | I feel nervous | 0 | 1 | 2 | 3 | 4 |
| 9. | I feel relaxed | 0 | 1 | 2 | 3 | 4 |
| 10. | I feel pooped | 0 | 1 | 2 | 3 | 4 |
| 11. | I am confused | 0 | 1 | 2 | 3 | 4 |
| 12. | I am worn out | 0 | 1 | 2 | 3 | 4 |
| 13. | I feel sad | 0 | 1 | 2 | 3 | 4 |

| | | | | | | |
|-----|--|---|---|---|---|---|
| 14. | I feel fatigued | 0 | 1 | 2 | 3 | 4 |
| 15. | I have trouble paying attention | 0 | 1 | 2 | 3 | 4 |
| 16. | My arms feel weak | 0 | 1 | 2 | 3 | 4 |
| 17. | I feel sluggish | 0 | 1 | 2 | 3 | 4 |
| 18. | I feel run down | 0 | 1 | 2 | 3 | 4 |
| 19. | I ache all over | 0 | 1 | 2 | 3 | 4 |
| 20. | I am unable to concentrate | 0 | 1 | 2 | 3 | 4 |
| 21. | I feel depressed | 0 | 1 | 2 | 3 | 4 |
| 22. | I feel refreshed | 0 | 1 | 2 | 3 | 4 |
| 23. | I feel tense | 0 | 1 | 2 | 3 | 4 |
| 24. | I feel energetic | 0 | 1 | 2 | 3 | 4 |
| 25. | I make more mistakes than usual | 0 | 1 | 2 | 3 | 4 |
| 26. | My body feels heavy all over | 0 | 1 | 2 | 3 | 4 |
| 27. | I am | 0 | 1 | 2 | 3 | 4 |

| | | | | | | |
|-----|--------------------|---|---|---|---|---|
| | forgetful | | | | | |
| 28. | I feel tired | 0 | 1 | 2 | 3 | 4 |
| 29. | I feel calm | 0 | 1 | 2 | 3 | 4 |
| 30. | I am distressed | 0 | 1 | 2 | 3 | 4 |

Administration and Scoring:

The MSFI-SF can be completed in a wide variety of settings in about 5 minutes. Items are rated on a 5-point scale indicating how true each statement was for the respondent during the last week (0 = Not all; 4 = extremely). Scoring instructions for the MFSI-SF are as follows:

1. General scale score = sum of items 10, 12, 14, 17, 18, and 28
2. Physical scale score = sum of items 2, 4, 6, 16, 19, and 26
3. Emotional scale score = sum of items 3, 8, 13, 21, 23, and 30
4. Mental state score = sum of items 1, 11, 15, 20, 25, and 27
5. Vigor scale score = sum of items 5, 7, 9, 22, 24, and 29
6. Total scale score = sum of scales 1-4 minus the Vigor scale score

Appendix C: Demographic Data Form

1. What is your current age? _____
2. Which gender are you? (Circle one) male/female
3. What type of cancer are you being treated for (breast, colon, lymphoma, etc.)? _____
4. What do you understand the goal of the chemotherapy is (check one answer below)?
 cure
 prevention of recurrence
 slowing down the growth of the cancer
 relief of symptoms
 not sure
5. How many chemotherapy treatments have you had, not including today? _____
6. Have you ever been diagnosed with chronic fatigue syndrome? (Circle one) yes/no
7. Are you currently taking any antidepressant medication? (Circle one) yes/no
- 7a. Did you begin taking antidepressant medication before or after your cancer diagnosis? (Circle one) Before/After
8. Marital Status (check one).
 Single
 Married
 Divorced
 Separated
 Widowed
9. On the scale below circle the number that corresponds with your current level of fatigue.
No fatigue The Worst Fatigue
0 1 2 3 4 5 6 7 8 9 10
10. Are you currently being treated with radiation? (Circle one) yes/no

Appendix D: Moffitt SRC Approval

December 15, 2010

Gloria Guess, RN, BSN
H. Lee Moffitt Cancer Center & Research Institute
University of South Florida
12902 Magnolia Drive
Tampa, FL 33612

Dear Ms. Guess:

The Behavioral Subcommittee of the Scientific Review Committee (SRC) has reviewed your response for your research protocol entitled, "Correlation of Cancer-Related Fatigue and Depression: a Pilot Study" (MCC16520).

The revised protocol version dated 12/10/10 is approved as written for use at the Moffitt Cancer Center pending approval of the Institutional Review Board (IRB) and satisfaction of institutional operational and financial review requirements.

Please be aware that after you receive IRB approval, you must request study activation before you commence any study activities. The Protocol Review and Monitoring System will ensure that all applicable institutional reviews have been completed. You will then be issued an activation letter. Upon receipt of the activation letter, you will be able to conduct your study. Please contact Diane Martinez, Manager, Protocol Support Office, at 813-745-8349 to request study activation.

It is your responsibility to ensure that all Moffitt staff (nursing, pharmacy, data management, etc.) are informed and aware of the details of the project. The committee encourages the use of in-services for those projects that are complex or require special attention.

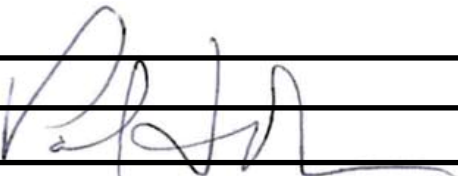
All changes made to protocols approved by the SRC must be submitted to the Protocol Review and Monitoring System office. Changes made to the protocol document require SRC review and approval. Minor changes (i.e. changes to personnel, non-scientific changes, changes that do not affect patient participation) will be expedited through the SRC review process.

If this project is not being managed by the Clinical Trials Office or Clinical Research Unit, then it is your responsibility to follow through with all requirements for submission to the IRB. All IRB approvals are required to be

documented in Oncore, and all associated regulatory documentation (signed applications, IRB approval letters and IRB approved consent forms, etc.) are to be saved in the appropriate study folder in the e-binders directory at J:\ebinders.

Oncore is the Cancer Center's mechanism for required submission and review of materials requiring IRB review as well as items requiring review by the Scientific Review and Protocol Monitoring Committees. If you are not currently reporting the necessary research activities, such as patient accrual, changes in procedure, adverse events and continuing reviews in Oncore, please contact Jeryl Madden, Oncore Coordinator, at 745-6964 for direction.

Sincerely,

A handwritten signature in black ink, appearing to read 'P. Jacobsen', is written over three horizontal black lines.

Paul Jacobsen, PhD
Chair, Behavioral Subcommittee
Scientific Review Committee

Appendix E: USF IRB Approval



DIVISION OF RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
(813) 974-5638 • FAX (813) 974-5618

January 28, 2011

Gloria Guess
College of Nursing

RE: **Exempt Certification** for IRB#: Pro00003031
Title: Correlation of Cancer-Related Fatigue and Depression: a
Pilot Study

Dear Gloria Guess:

On 1/27/2011, the Institutional Review Board (IRB) determined that your research meets USF requirements and Federal Exemption criteria as outlined in the federal regulations at 45CFR46.101(b):

- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
- (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

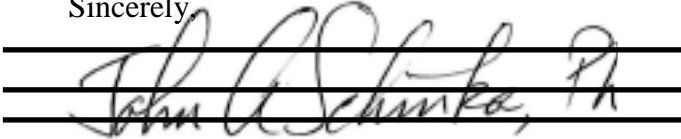
As the principal investigator for this study, it is your responsibility to ensure that this research is conducted as outlined in your application and consistent with the ethical principles outlined in the Belmont Report and with USF IRB policies and procedures. Please note that changes to this protocol may disqualify it from exempt status. Please note that you are responsible for notifying the IRB prior to implementing any changes to the currently approved protocol.

The Institutional Review Board will maintain your exemption application for a period of five years from the date of this letter or for three years after a Final Progress Report is received, whichever is longer. If you wish to continue this protocol beyond five years, you will need to submit a continuing review application at least 60 days prior to the exemption expiration date. Should you complete this

study prior to the end of the five-year period, you must submit a request to close the study.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

A handwritten signature in black ink, reading "John A. Schinka, PhD", is written over three horizontal black lines. The signature is cursive and appears to be a personal or official signature.

John Schinka, PhD, Chairperson
USF Institutional Review Board

Cc: Various Menzel, CCRP, USF IRB Professional Staff

Appendix F: Informed Consent



UNIVERSITY OF
SOUTH FLORIDA

Informed Consent to Participate in Research Information to Consider Before Taking Part in this Research Study

IRB Study # _____ 3031 _____

You are being asked to take part in a research study. Research studies include only people who choose to take part. This document is called an informed consent form. Please read this information carefully and take your time making your decision. Ask the researcher or study staff to discuss this consent form with you, please ask him/her to explain any words or information you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

We are asking you to take part in a research study called: Correlation of Cancer-Related Fatigue and Depression

The person who is in charge of this research study is Gloria Michelle Guess. This person is called the Principal Investigator. However, other research staff may be involved and can act on behalf of the person in charge. She is being guided in this research by Dr. Susan McMillan.

The research will be conducted at Moffitt Cancer Center Infusion Center.

Purpose of the study

The purpose of this study is to:

- The purpose of this study is to determine whether or not a relationship exists between cancer-related fatigue and depression in cancer patient's receiving chemotherapy.
- This study is being done as part of a thesis.

Study Procedures

If you take part in this study, you will be asked to

- Complete three brief questionnaires, while you are at the infusion center receiving your chemotherapy. The time it will take to complete these questionnaires should be less than 30 minutes. You will only be asked to complete the questionnaires during one visit.
- One questionnaire will ask basic demographic information such as age, gender, diagnosis, and number of chemotherapy treatments completed.

- The second questionnaire is a seven question, written depression scale, used to assess how you are feeling.
- The third questionnaire is a thirty question written fatigue scale to assess if you may be having any symptoms of fatigue.

Total Number of Participants

About 60 individuals will take part in this study at USF.

Alternatives

You do not have to participate in this research study.

Benefits

The potential benefits of participating in this research study include increasing our knowledge of cancer-related fatigue and depression in cancer patients on chemotherapy.

Risks or Discomfort

This research is considered to be minimal risk. That means that the risks associated with this study are the same as what you face every day. There are no known additional risks to those who take part in this study.

Compensation

You will receive no payment or other compensation for taking part in this study.

Cost

There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further.

Privacy and Confidentiality

Other than meeting you in person during the data collection process I will not be recording any identifiers or linking at any of your medical records or other documentation containing your Protected Health Information. Moffitt Cancer Center will not be releasing any of your identifiers to me to conduct this research.

We will keep your study records private and confidential. Certain people may need to see your study records. By law, anyone who looks at your records must keep them completely confidential. The only people who will be allowed to see these records are:

- The research team, including the Principal Investigator and faculty advisor.
- Certain government and university people who need to know more about the study. For example, individuals who provide oversight on this study may need to look at your records. This is done to make sure that we are doing the study in the right way. They also need to make sure that we are protecting your rights and your safety.
- Any agency of the federal, state, or local government that regulates this research. This includes the Department of Health and Human Services (DHHS) and the Office for Human Research Protection (OHRP).
- The USF Institutional Review Board (IRB) and its related staff, who have oversight responsibilities for this study, staff in the USF Office of Research and

Innovation, USF Division of Research Integrity and Compliance, and other USF offices who oversee this research.

We may publish what we learn from this study. If we do, we will not include your name. We will not publish anything that would let people know who you are.

Voluntary Participation / Withdrawal

You should only take part in this study if you want to volunteer. You should not feel that there is any pressure to take part in the study. You are free to participate in this research or withdraw at any time. There will be no penalty or loss of benefits you are entitled to receive if you stop taking part in this study. The decision not to participate/terminate participation will have no effect on medical treatment the participant is receiving.

You can get the answers to your questions, concerns, or complaints

If you have any questions, concerns or complaints about this study, or experience an adverse event or unanticipated problem, call Gloria Michelle Guess at 727-359-9312.

If you have questions about your rights as a participant in this study, general questions, or have complaints, concerns or issues you want to discuss with someone outside the research, call the USF IRB at (813) 974-5638. Moffitt Cancer Center Division of Research Integrity and Compliance at (813) 632-1869.

I verbally agree to participate and I have been given a copy of this document.