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Fatigue Symptom Distress and Its Relationship with Quality Of Life in Adult Stem Cell Transplant Survivors

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Fatigue Symptom Distress and Its Relationship with Quality Of Life in Adult Stem
Cell Transplant Survivors

by

Suzan Fouad Abduljawad, R.N., B.S.N.

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

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DEDICATION

This thesis is dedicated to my outstanding mother, Khadija Elmoujarrad. Her devotion, hard work, and thirst for knowledge inspired my motivation to pursue my Master of Science degree, and the completion of this thesis. Thank you mother, your endless love, support, prayers and encouragement put me on the road to success. To my deceased father, Fouad Abduljawad, who had always encouraged me to learn and dream big, I wish you were here to witness the success of your daughter getting the honor of being the first female to attain the Master's degree in the family. I would like to also dedicate this thesis to my husband, Abdullah Wolkens, for his love, support, and willingness to put my needs before his own. Thank you for believing in me. And last but not least, I dedicate this to my beloved family. Grandmother Aicha El-Eidi and Grandfather Jeloul Elmoujarrad, thank you for your unconditional love and your continuous prayers; my brother Feras, who inspired me with his enthusiasm for higher education and greater knowledge; my brother Fahad and sister Sundus, I appreciate your love and encouragement, I hope you may find this thesis a source for your own inspiration. I am blessed to have each and every one of you in my life.

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Fatigue Symptom Distress and Its Relationship with Quality Of Life in Adult Stem
Cell Transplant Survivors

Suzan Fouad Abduljawad

ABSTRACT

Fatigue is a common problem among cancer patients, especially those who have received chemotherapy and radiation therapy. Stem cell transplant (SCT) patients are at a particular risk of persistent fatigue as they receive more aggressive therapies. This study examined the prevalence of fatigue after completion of SCT. Further, the level of fatigue symptom distress and its relationship with quality of life (QOL) among long term SCT survivors was examined.

The study involved thirty-three patients, 21 males and 12 females, treated with autologous or allogeneic SCT in a comprehensive cancer center in Southwest Florida. Participants' ages ranged from 36 to 70 years, with a mean age of 53 years. All subjects completed the Cancer Related Fatigue Distress Scale and the Functional Assessment of Cancer Therapy-Bone Marrow Transplant questionnaires. All the patients had to be at least six months from transplant.

The results of this study showed that fatigue is quite prevalent among SCT survivors. Ninety-three percent of the patients reported some degree of fatigue, and 15% experienced severe fatigue. Patients who received autologous transplant (24%) reported less fatigue symptom distress (mean= 48, SD= 36.62) compared to the

allogeneic transplant group (mean= 66.2, SD= 54.49). A strong negative relationship was found between fatigue symptom distress and QOL ($r = 0.85, p < 0.0001$) suggesting that patients with the greatest fatigue distress report the worst QOL. The time from transplant factor was significantly positively associated with fatigue symptom distress ($r= 0.46, p= 0.007$) indicating greater distress with the passage of time. A moderate negative relationship was also found between time from transplant and QOL ($r= -0.34, p= 0.052$) suggesting that QOL was less in some patients as time passed; however this was a weak relationship that did not achieve statistical significance.

Although the sample size was small, this study was able to provide a confirmation that fatigue symptom distress and QOL are related to one another. Understanding the relationship between fatigue symptom distress and QOL should encourage interdisciplinary collaboration in planning proper interventions to minimize fatigue. This would improve the outcomes of SCT long term survivors, and would positively impact their overall QOL.

Chapter I

Introduction

Fatigue is a common symptom of cancer that has been demonstrated by research to be one of the most distressing symptoms associated with cancer and all cancer treatment modalities including chemotherapy, surgery, biotherapy, radiation therapy, and bone marrow transplantation. It is reported that 70 to 100% of patients who are undergoing cancer treatment suffer from fatigue at some or all stages of their illness (Flude, Groll, Tranmen, & Woodend, 2007). This distressing symptom can interfere with many aspects of QOL, including physical, psychosocial and spiritual well being. Cancer patients undergoing stem cell transplant (SCT) are subject to receiving high doses of chemotherapy and radiation therapy in bone marrow conditioning regimens prior to transplant. The side effects from this multi-treatment approach often precipitate heightened levels of fatigue (Gielissen et al., 2007). Persistent burden on the physical and psychological status contributes to decreased levels of activity, cognitive ability and the resultant poor sense of well being (Harder et al., 2002). Certainly symptom management is a priority for those who strive to improve patients' outcomes. With growing evidence that SCT patients suffer from persistent fatigue, it should be equally important for the clinicians and researchers to understand this phenomenon and examine its relationship to QOL of SCT survivors.

Statement of the Problem

Fatigue is a common side effect that can be expected in the immediate recovery period of SCT (El-Banna et al., 2004). When the transplantation journey

concludes, the patients hope to regain their pre-diagnosis health status, functional ability, and their psychological, social and spiritual well being, to again lead their lives somewhat normally. Unfortunately, some patients experience a lingering fatigue that begins with their diagnosis of cancer, and continues in some cases for years after the completion of successful therapy. However, the factors contributing to the persistence of this problem and its impact on overall survival remains poorly understood. Thus, this study sought to describe the phenomenon of persistent fatigue, and how fatigue symptom distress is related to quality of life in long term SCT survivors.

Research Questions

The following questions guided the study:

1. What is the prevalence of fatigue and the level of fatigue symptom distress reported by cancer patients at least six months past completing SCT?
2. What do patients report their QOL to be at least six months after SCT?
3. Is there a significant relationship between fatigue symptom distress and QOL of cancer patients at least six months after SCT?
4. Is there a significant relationship between fatigue and time from transplant?
5. Is there a significant relationship between QOL and time from transplant?

Definition of Terms

For the purpose of this paper the following definitions are used.

Fatigue: An unusual, sustained, subjective sense of tiredness, malaise or lack of energy, related to cancer or cancer treatment that interferes with usual functioning (The National Comprehensive Cancer Network [NCCN], 2008).

Fatigue Symptom Distress: It is the distress and suffering that accompanies the experience of the fatigue symptom (Holley, 2000).

Quality of life: Is a subjective multidimensional construct that represents aspects of the individual's satisfaction with well being. It is defined as the difference or gap between the current hopes and expectation of the individual and that individual's present experiences (Frick, Borasio, Zehentner, Fischer, & Bumedner 2004).

Stem cell transplantation: Is a procedure used to restore the stem cells when the bone marrow has been destroyed by disease, radiation or chemotherapy. Depending on the source of the stem cells, this procedure may be called a bone marrow transplant (BMT), a peripheral blood stem cell transplant (PBSCT), or a cord blood transplant (American Cancer Society, 2009).

Autologous stem cell transplantation (ASCT): A procedure in which blood-forming stem cells are harvested from the blood stream, stored, and later transfused back to the same person (American Cancer Society, 2009).

Allogeneic stem cell transplantation (aSCT): A procedure in which a person receives blood-forming stem cells from a genetically similar, but not identical, donor. This is often a sister or brother, but could be an unrelated donor (American Cancer Society, 2009).

Significance to Nursing

Describing the post transplant fatigue phenomenon is of particular significance in improving SCT patients' outcomes. In order to be able to design and achieve optimal management of this distressing symptom, healthcare professionals need to understand the magnitude of the problem. The knowledge of prevalence and severity of fatigue reported by cancer patients after SCT, coupled with examining the quality of life in relation to reports of the fatigue distress should help focus post transplant nursing care. The information obtained from this study can assist nursing clinicians

and researchers, who strive to improve patients' outcomes, in recognizing the impact of fatigue on quality of life. This will further refine the clinicians' timing of supportive interventions and the content of education they provide to patients.

Chapter II

Review of Literature

This chapter presents the review of literature that is associated with fatigue and the quality of life following SCT treatment in patients with hematologic malignancies. First studies of fatigue are reviewed. This is followed by studies of quality of life, and finally the literature is summarized.

Fatigue

In the past two decades, stem cell transplantation, following a conditioning regimen of intensive high dose chemotherapy with or without total body irradiation, has been used increasingly as means for a potential cure of many hematologic diseases and malignancies (Hjermstad et al., 2004). This approach to treatment, despite its effectiveness in decreasing mortality, is often complicated with unpleasant symptoms and side effects that can be extremely daunting and at times even life threatening.

The incidence and intensity of cancer related fatigue in BMT recipients varies over the course of treatment and recovery. In a longitudinal study, El-Banna et al. (2004) described the temporal patterns of depression and the four dimensions of cancer related fatigue including: behavioral, sensory, cognitive and affective meaning. Twenty-seven adult patients with lymphoma undergoing autologous stem cell transplantation (ASCT) were included in this study. Fatigue was measured over multiple time points; at baseline before chemotherapy initiation, on chemotherapy day, and on recovery at days 2, 7, and 14. The authors used the revised Piper Fatigue

Scale (PFS), a multidimensional self-report fatigue instrument, on which high scores indicate higher levels of perceived fatigue. El-Banna et al. (2004) found variations over the two-week period following ASCT. The patients reported significant increase of PFS scores from baseline to day seven for total fatigue and all dimensions of fatigue except the cognitive or mood subscale. The pattern showed a decline after day 14 of transplantation. To measure depression, The Center for Epidemiologic Studies–Depression (CES-D) Scale was used. Total scores on the CES-D scale range from zero (no depression) to 60 (severe depression). A score of 16 or more on the CES-D scale indicates depressive symptoms. The authors also found depression presenting a similar pattern of sharp increase on day seven and a gradual decline afterwards with a high positive correlation between affective fatigue and depression ($p < 0.01$). The findings of this study highlight the importance of continuity of care, measuring fatigue with concurrent assessment for depression, and paying close attention to the immediate recovery period where the peak of these symptoms seems to occur.

From the NCCN definition of fatigue one can find the concept of fatigue rendered with much influence on physical activity and functional ability. In a prospective study, Hacker et al. (2006) sought to examine the feasibility of obtaining real-time fatigue and physical activity data, to describe the patterns of fatigue, physical activity, health status, and quality of life before and after hematopoietic stem cell transplantation (HSCT). Twenty adult patients undergoing autologous or allogeneic HSCT participated in the study. To assess fatigue, two different measures were used, the fatigue subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-core 30 (EORTC QLQ-C30) and the Actiwatch (a wrist actigraph with a subjective event marker which was used as a self report scale to measure real-time fatigue intensity). The Actiwatch was also used

to measure physical activity of the patients as the device consisted of an accelerometer that records motion and speed of the subject.

The Quality of Life Index (QLI) was used to measure life satisfaction related to the domains of family, health and functioning, social and economic, and psychological or spirituality. The majority of the patients were found to experience mild fatigue at baseline, which escalated following HSCT to significantly higher levels ($p < 0.001$). Also after HSCT physical activity markedly decreased by 58% and overall health status became significantly worse. The significant decline in patients' physical, emotional and cognitive functioning seemed to peak in the immediate post-transplant period. The authors also found this decline in functioning and physical activity associated with significant increases in symptoms of fatigue, pain, nausea and vomiting, diarrhea, loss of appetite and sleep disturbance. The QLI scores of socioeconomic and psychological or spiritual subscales showed no significant changes in this study, allowing the authors to support the notion that a lag time exists between actual experiencing of health status changes and assimilating those changes into an appraisal of life's circumstances (Hacker et al., 2006). The study findings suggest that patients experience prolonged fatigue and physical inactivity for at least 7 to 14 days following HSCT. This prolonged inactivity may eventually lead to reduction of muscle mass and loss of strength and functional capacity. The consequences of this diminished functional capacity are of particular concern with patients' ability to maintain or return to their productive roles in society (Hacker et al., 2006). Therefore, maintaining levels of activity may enhance functional capacity and role performance towards improving patient's perception of health status and QOL. This study further calls for effective management of fatigue symptoms experienced during the immediate period following stem cell transplant.

An earlier study by Harder et al. (2002) considered fatigue a main disease and treatment related predictor for cognitive impairment. Harder and colleagues examined the cognitive functioning and quality of life in long-term adult survivors of bone marrow transplant 22 to 82 months post treatment. The sample was comprised of 40 disease-free patients treated with SCT for hematological malignancies, 87% of whom had undergone an allogeneic transplant. A battery of neuropsychological tests was used to assess the mental status and cognitive performance of the subjects. For QOL and mood states measurement the EORTC QLQ-C30 and the brief version of the Profile of Mood States (POMS) were utilized. POMS measures five dimensions of general psychological distress: depression, tension, anger, fatigue, and vigor. The authors found mild to moderate cognitive impairment in 60% of the subjects, especially in the areas of verbal learning, visual memory, selective attention and information processing speed. A substantial correlation was found between cognitive impairment and fatigue symptom on both EORTC QLQC30 ($r= 0.55; p <0.001$) and POMS scales ($r=0.51, p < 0.001$). A significant relationship was also found between fatigue, cognitive functioning and physical functioning. QOL and fatigue were significantly associated with depression measured by POMS.

Fatigue remains a challenge for SCT patients even years after transplant. The findings of this study indicate that fatigue can predict late cognitive deficits in long term survivors. The authors reported that neuropsychological impairments and cognitive complaints were associated with increased absence from work and school. With such decreases in functional status, patients may experience role dissatisfaction and a reduction in quality of life.

Clinicians mostly attribute fatigue to the nature of the cancer illness and the treatment regimens. However, it is not well understood why fatigue persists long after

treatment completion when the patients are disease free or in complete remission years after the transplant. Most recently in the Netherlands, Gielissen et al. (2007) explored this phenomenon of post SCT persistent fatigue in light of the precipitating and perpetuating theoretical model. The authors identified five perpetuating factors that influence the persistence of fatigue symptoms which include insufficient coping, fear of disease recurrence, cognitive dysfunction, sleep disturbance and dysregulation of activity. In a cross-sectional retrospective design, ninety-eight survivors of acute myeloid or lymphatic leukemia, chronic myeloid leukemia and non-Hodgkin's lymphoma who received autologous and allogeneic SCT between 1981 and 2003, participated in the study. All patients had to be in persistent complete remission for at least one year after SCT, those with graft-versus-host disease (GVHD) grade III and IV or with hemoglobin of 10 g/dl and lower were excluded. This was done in order to make the sample less prone to fatigue than the general population of SCT. Several instruments were used to evaluate the prevalence of each of the perpetuating factors identified. Fatigue was measured using the fatigue severity subscale of the Checklist Individual Strength (CIS). A CIS fatigue score equal to or higher than 35 identified severe fatigue. Even long after receiving SCT (mean= 9.3 years) thirty-four patients (35%) met the criteria of severe fatigue and 12% had heightened fatigue scores. The data analysis revealed a very low non-significant correlation between fatigue scores and the length of hospital stay during transplantation. The correlation between CIS fatigue scores and time since transplantation, which ranged from 1 to 15 years, also proved to be low and non-significant. Patients with comorbidities such as hypertension, diabetes, infections and hepatitis C were found to have higher levels of fatigue (Gielissen et al., 2007). The authors also concluded that the perpetuating model explained and highly predicted the severity and the persistence of fatigue,

suggesting that several psychosocial factors, rather than medical factors, were mostly associated with persistent fatigue.

Anderson et al. (2007) assessed symptom burden of patients during the acute phase of autologous transplant. The purpose of their study was to determine the severity of the symptoms experienced by patients and to identify predictors of high levels of symptom burden. The authors hypothesized that symptom intensity and related interference would increase post transplant and be most severe at nadir. The sample consisted of 100 patients with multiple myeloma or non-Hodgkin's lymphoma undergoing autologous stem cell transplantation with matched conditioning regimens for each group. Assessment was carried out at baseline before commencing conditioning regimen, on the third to fourth day of the conditioning regimen, on the day of transplantation, on the day of nadir and on 30 days post-transplant. The subjects were asked to complete the blood and marrow transplantation module of the M. D. Anderson Symptom Inventory (MDASI-BMT), a measure of symptom severity and symptom related interference in daily life, and the Eastern Cooperative Oncology Group Performance Status (ECOG PS), which measures functional status, at each time point. Mood and quality of life were measured on baseline and on day 30 post-transplant using the Profile of Mood States (POMS) and the Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT) scales (Anderson et al., 2007). The authors reported that over half of the patients complained of moderate to severe fatigue which interfered mostly with general activity, mood, walking, and enjoyment of life. The mean scores of symptom severity and symptom interference were significantly greater at nadir compared with baseline levels. Fatigue along with symptoms of weakness, feeling physically sick, disturbed sleep, nausea and vomiting showed the highest intensities. The severity of fatigue had a significant correlation

($p= 0.049$) between the time point and the diagnosis. Patients with non-Hodgkin's lymphoma reported higher levels of fatigue at baseline, on nadir, and on 30 day post-transplant compared to the patients with multiple myeloma. Anderson et al. (2007) related this difference among these two groups to differences in the disease physiology or treatment history and conditioning regimens. Clinicians can help optimize symptom management, as they become aware of the different symptoms' burden and pattern associated with the different diagnoses of SCT population (Anderson et al., 2007).

Another research study addressing the symptom burden by Bevans, Mitchell and Marden (2008) was aimed at describing the symptom characteristics experienced in the post transplant period. Seventy-six adult patients with hematologic disorders undergoing their first matched related allogeneic SCT enrolled in this study. Data were utilized from a prospective study of health-related quality of life (HRQL) in which the participants were already enrolled. Symptom occurrence, distress, and clusters were measured using the Symptom Distress Scale (SDS). Based on the 11 symptoms of nausea, appetite change, insomnia, pain, fatigue, bowel changes, concentration, appearance, worry (outlook), breathing, and cough; each symptom is rated on a 6-point Likert-type scale. Symptom distress was indicated as mild, moderate, or severe. To be considered clustered, symptoms had to at least be moderately and significantly related to one another and simultaneously independent of other SDS symptoms (Bevans et al., 2008). Medical Outcomes Short Form 36 Health Survey (SF-36 version 1) also was used to measure functional health and well being. Data were collected on baseline before conditioning commencement and on days 0, 30, and 100 after allogeneic SCT. Bevans and colleagues reported that fatigue was among the most prevalent symptoms across study time points. Fatigue was reported

by 68% of participants at baseline, 86% of participants on day zero, 90% of participants on day 30 and 81% of participants at day 100 post-transplant. Fatigue occurrence was also prevalent in symptom clusters. At baseline, the most prevalent symptom cluster was fatigue and worry. On days 0 and 30 the symptom cluster consisted of fatigue, bowel change, and insomnia. Fatigue symptom distress was reported by six patients (11%) at day 100, but no symptom cluster was noted. The authors suggested that the extent of symptom distress, prevalence, and occurrence of fatigue in clusters emphasizes the importance of tailoring interventions to target fatigue according to the phase of recovery. Fatigue symptom distress predicts poor functional recovery, general health, and quality of life. Managing symptom distress may provide SCT population with an opportunity for better outcomes (Bevans et al., 2008).

Quality of Life

In a prospective study by Hjermstad et al. (2004), health related quality of life (HRQOL), fatigue, anxiety, and depression were assessed in 248 patients with hematological or lymphocytic malignancies, following treatment SCT. The purpose of the study was to describe the fluctuations of those symptoms and HRQOL of the patients over a period of three years or more after completion of transplant, while comparing assessment scores between allogeneic SCT and autologous SCT groups with patients who received conventional chemotherapy (CT) alone. The EORTC QLQ-C30 questionnaire was utilized by the authors, is a 30-item tool which incorporates five functional scales (physical, role, emotional, cognitive, and social); a three symptom scales measuring fatigue, pain and nausea and vomiting; one scale assessing overall health/global QOL; and six single items to assess symptoms commonly reported by cancer patients such as dyspnea, sleep disturbances, appetite

loss, diarrhea, constipation and financial impact. The EORTC QLQ-C30 was administered nine times throughout the three-year study period. Measurement of physical and mental fatigue was assessed by the Fatigue Questionnaire (FQ). The FQ asks questions about fatigue symptoms experienced during the last month compared with how the subjects felt when they were well. Anxiety and depression symptom distress was measured using the Hospital Anxiety and Depression Scale (HADS).

At baseline, a marked difference was found between allogeneic SCT and autologous SCT patients on the fatigue symptom scale and global QOL scores. The allogeneic SCT group experienced less fatigue and better quality of life at baseline, but greater impairment than autologous SCT patients on second week post transplant with an increase in fatigue symptoms and reduction in functional levels. Gradual improvement in symptomatology occurred at 4 to 8 months until levels returned to baseline at one year. In comparison, the autologous SCT group showed less fluctuation from the baseline scores and a more rapid recovery, as global QOL scores became similar to baseline or even better after four months only. The CT group showed a negative change in global quality of life after 4 to 6 months of treatment, where scores stabilized at a level significantly higher than baseline (Hjermstad et al. 2004).

The authors reported that despite that early recovery of the autologous SCT group they were found to report poorer functioning and more fatigue at three years after transplant. No statistically significant difference was reached for physical and mental FS scores, yet more autologous SCT patients reported chronic fatigue when compared to allogeneic SCT group, CT patients and the general population. There was no significant change in depression or anxiety scores across all groups. The authors also suggested that this pronounced impairment in QOL and the chronic

fatigue complaints of ASCT group, may be attributed to the extensive chemotherapy and radiation those patients received prior to transplant. These findings emphasize the importance of HRQOL assessment of stem cell transplantation recipients with focus on functional status and fatigue symptoms. It is also important to advise patients to maintain a close follow up with their health care providers to optimize the hospital to home environment transition (Hjermstad et al. 2004).

Schulmeister, Quiett, and Mayer (2005) explored the quality of life, quality of care, and patients' satisfaction with outpatient autologous stem cell transplant (ASCT) experience. Forty adult patients undergoing ASCT were interviewed via telephone, three times, over a six-month period. To measure Quality of life, subjects were asked to complete the Functional Assessment of Cancer Therapy–BMT (FACT-BMT) scale during interviews at 4 to 6 weeks after chemotherapy and again at six months post chemotherapy. The FACT-BMT scale measures five dimensions of QOL including: physical, social/family, emotional, functional well-being, and BMT effects.

Telephone interviews guided by open-ended questions were used to explore patients' ASCT experiences and satisfaction with the outpatient ASCT process (Schulmeister et al., 2005). The authors found that patients who reported negative previous healthcare experiences had significantly lower scores on the emotional well-being subscale.

Those who had progressive disease showed lower QOL and significantly more regret for having the transplant. Concentration and memory problems, which interfered with work, household responsibilities, leisure activities, and interpersonal relationships, were experienced by 22% of the patients. FACT-BMT scores were lowest one month post treatment and were highest six months post transplant. Higher QOL and greater satisfaction with care were associated with good clinical outcomes following ASCT.

In general, the majority of the patients had reported a positive outpatient experience.

Although some of the patients reported that the outpatient ASCT experience did not feel personalized, they complained that the recommendations for self care and symptom management booklets, which they received in outpatient clinic, did not address their personal concerns and needs. Many complained that important treatment related issues such as: sexuality and fertility issues, complementary and alternative therapies, and long term side effects were underemphasized. Patients expressed a need for more information on how to maintain their strength and activity tolerance, fatigue, and skin problems management. They also expected post transplant psychosocial support to be offered for patients and families which could have further improved their quality of life (Schulmeister et al., 2005).

One of the strengths of this study was that it included both qualitative and quantitative research methods. The findings indicate the value of constructing individualized interviews with patients where clinicians can personalize the experience of SCT and address the most relevant concerns for each individual. The SCT experience is faced with much uncertainty and thus, as these authors suggested, the nurses should consider providing specific care plans including specific dietary suggestions and exercise prescriptions. Ongoing evaluation of the survivors' needs and concerns would enhance patients' satisfaction with the SCT experience and help optimize the associated quality of life.

Summary

In summation, research has found that SCT related fatigue worsens in the acute post transplant period along with the quality of life (El-Banna et al., 2004; Hacker et al., 2006; Anderson et al., 2007). Many differing phenomena are associated with fatigue in post SCT individuals. These phenomena could be physiological with effects on strength, sleep pattern, and physical activity (Hjermstad et al., 2004), or

they could be cognitive, perceptual, motivational or psychological in nature (Harder et al., 2002). Higher levels of fatigue symptoms distress have been predictive of poor quality of life, poor general health, greater emotional distress, and overall mortality (Gielissen et al., 2007; Schulmeister et al., 2005).

Proper assessment of the fatigue dimensions is essential in combating this condition. Clinicians should be able to identify fatigue symptom distress in each phase of recovery (Bevans et al., 2008) and design appropriate individualized interventions with personalized patient education plans (Schulmeister et al., 2005). Most of the available literature on fatigue in stem cell transplant population focused on the acute recovery period. The current study is proposed to expand the knowledge base related to fatigue intensity, fatigue symptom distress, and their relationship with quality of life of long term adult survivors at least 5 months post stem cell transplantation.

Chapter III

Methods

This chapter presents the research methods and procedures that were used in this study. First the sample selection and setting are described. Second, methods of measurement including description of the Instruments with their validity and reliability are discussed. Third, research procedures are described including the data collection methods. Finally the data analysis plan is discussed. This descriptive, exploratory study used a cross sectional design to describe the relationship between fatigue symptom distress and quality of life (QOL) in stem cell transplant (SCT) survivors.

Setting and Sample

The research data were collected at Moffitt Cancer Center, a National Cancer Institute (NCI) designated comprehensive cancer center in southwest Florida. The target population for this study was adult SCT survivors who were at least six months following completion of SCT procedures including chemotherapy, total body irradiation therapy and stem cells transfusion. Inclusion criteria included: (1) being an adult over 18 years of age at the time of transplant, (2) incomplete or partial remission of underlying disease, (3) being able to read and understand English, and (4) willingness to participate in the study. Exclusion criteria for this sample included (1) active cancer treatment with chemotherapy, radiation, or immunotherapy in the past 6 months, (2) hospitalization at the time of the study, (3) a history of chronic fatigue syndrome, fibromyalgia, or any comorbidity related fatigue history, and (4) a current

psychiatric diagnosis or neurological deficit that may impede the subject's ability to comprehend the study. A sample of 50 adult BMT outpatients was sought.

Instrumentation

Three Instruments were used for this study, (1) The Cancer Related Fatigue Distress Scale (CRFDS), (2) The Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) version 4, and (3) a Demographic Data/Health Information Form.

Cancer Related Fatigue Distress Scale

The Cancer Related Fatigue Distress Scale (CRFDS) was used to collect data on fatigue symptom distress (Appendix A). The summated rating scale of 20 items addresses cognitive, physical, psychological, social and spiritual distress. The CRFDS items have similar stem and response structure. Each item begins with: "The fatigue or tiredness I am having causes me distress because it..." followed by an item from distress categories (e.g., "Makes me too tired to eat"). The study participants were asked to rate their distress on an 11-point scale, ranging from 0 (no distress) to 10 (severe distress). The CRFDS scores are based on how the subject has felt over the last week, therefore, lending itself to a more accurate reporting of one's overall fatigue distress experience. The total possible scores of the scale ranges from zero to 200, the higher the score, the greater the level of fatigue symptom distress. The CRFDS also includes three 0-10 fatigue intensity scales that measure "fatigue now" "usual fatigue in the past week," and "worst fatigue in the past week." Zero represents no fatigue and ten as the most severe fatigue. The participants' performance status was measured using the Karnofsky Performance Status (KPS) Scale, to determine the participants' ability to perform daily activities (Holley, 2000).

Validity and Reliability. The CRFDS has strong content validity and high reliability. The items of this scale were constructed from 23 audio taped interviews with 17 patients who experienced cancer related fatigue (CRF). Patients' input in developing the scale supported its construct validity. Factor analysis was used to assess construct validity which confirmed all items loaded on one factor, indicating that all items assessed CRF distress. Using a conservative standard of 0.70, 20 of the 23 items met the standard and were retained. Factor loadings ranged from 0.589-0.913. The measure also has shown significant pre to post score changes ($p < 0.001$). Reliability for internal consistency estimate of this measure is very high, with coefficient alpha of 0.98 (Holley, 2000).

Functional Assessment of Cancer Therapy–Bone Marrow Transplant

The Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT–BMT) is a 39-item scale that measures five dimensions of QOL in BMT recipients including: physical (7 items), social/family (7 items), emotional (6 items), functional (7 items) well-being and a 12 item BMT-subscale. BMT specific items were designed to assess QOL content specific to the BMT process (Appendix B). Patients are asked to rate themselves on how they feel today and over the past 7 days. A 5-point Likert-type scale is used to rate each item of the questionnaire from 0 (not at all) to 4 (very much). Higher scores are associated with higher levels of satisfaction with QOL. The total scores for the FACT-BMT can range from 0–148. The FACT-BMT was further expanded to include 23 items in the BMT subscale, resulting in FACT-BMT (Version 4) which more specifically measures the unique effects of BMT on QOL. Items that were added to the subscale included ability to concentrate, ability to remember things, experiencing blurry eyesight, experiencing frequent colds or infections, noting food taste changes, having tremors, experiencing shortness of

breath, having skin problems, experiencing bowel trouble, illness hardship on family members, and the cost of treatment (McQuellon et al., 1997). These items are considered experimental, with ongoing psychometric evaluation and currently are not included in the scoring. This data was not reported. Respondent's burden of this 50-items scale is considered minimal as the average time to completion is 5-10 minutes (McQuellon et al., 1997).

Validity and Reliability. The FACT-BMT underwent a three-step validation process which involved testing of overall measures with subscales correlation and internal consistency calculations. Items of BMT subscale were selected from a list produced by seven oncology experts and 15 patients which enhances its construct validity. The BMT subscale demonstrated sensitivity to change over time at baseline, post-transplant, upon discharge and 100 days post transplant (McQuellon et al., 1997). Coefficients of reliability and validity for the entire scale are high. The authors found no significant difference between autologous or allogeneic SCT patients, or patients with Graft Versus Host Disease (GVHD) compared to those without GVHD. This supports more generalizability of this tool for the BMT population.

Demographic Data/Health Information form

Demographic and personal characteristics of the subjects were collected using the Demographic Data/Health Information Form (Appendix C). The data included in this form are: age, gender, ethnicity, educational background, marital status, and employment status. Questions were asked about underlying cancer diagnosis, type of transplant received and months from transplant completion, status of their cancer, and whether they received any cancer treatment in the past 6 months. These data were used to determine whether type of transplant and/or time from transplant influence the experience of persistent fatigue.

Procedures

Approvals

The principle investigator was responsible for assuring the research was implemented safely and effectively in accordance with the regulations of the Institutional Review Board (IRB) of the University of South Florida. Before obtaining the research approval of IRB, a behavioral research application was filed with the Scientific Review Committee of MCC. The benefit-risk ratio was assessed for this study, indicating the study design had minimal risk to subjects and important benefits. Informed consent (Appendix D) was designed to be easily understood and contained no coercive language. Upon approval of MCC (Appendix E) the proposal was submitted to IRB. Approval letter was obtained from IRB (Appendix F) along with approved consent stamped with IRB approval and expiration date.

Data Collection

A research flyer was used to advertise the study and was distributed around the BMT outpatient clinic, treatment center, and the clinic waiting areas at MCC. The Principle investigator's (PI) phone number was provided in the flyer for interested individuals to contact and inquire about the study. The healthcare providers and support staff of BMT clinic also identified potential participants, initiated the contact, and referred them to the study. Upon visiting the outpatient clinic for scheduled BMT follow up appointments, patients met with the PI and the study was explained. If patients agreed to join the study, they completed a screening form which determined their eligibility to participate.

The PI assessed potential participants using the inclusion/exclusion criteria. When sample criteria were met, written consent to participate was collected from patients and a copy of the signed informed consent was given to the participants to

keep. Patients participating in other MCC fatigue or quality of life studies were not asked to participate. Participants were taken to a private consult room, the study was explained to them, and they were instructed on how to complete the three questionnaires. Subjects were given the opportunity to ask questions about the research and the PI was available in the area for clarification. Forms were reviewed for completeness of response, staff and patients were thanked for their participation. Data were gathered from 33 subjects. The raw data collected and original consent forms were stored in a locked file drawer in the principle investigator's locked office and will be kept for five years after completion of study and then shredded.

Data Analysis

Descriptive statistics were performed for all variables. Tests were two-sided and a p value of 0.05 or less was considered statistically significant. All data were analyzed using the Statistical Package for Social Sciences (SPSS) for windows version 18 software. Demographic data were reported with frequencies, percentages, means, standard deviations, and ranges; which are presented in the sample characteristics table (Table 1).

The research questions provided direction for this data analysis. For research question #1: What is the prevalence of fatigue and the level of fatigue symptom distress reported by cancer patients at least six months past completing SCT? The mean ratings of each item on the CRFDS were used to evaluate the levels of fatigue Intensity and fatigue distress described by the participants.

Similarly, for research question #2: What do patients report their quality of life to be at least six months after SCT? Mean quality of life scores of FACT-BMT were calculated overall and among subscales.

For research question #3: Is there a significant relationship between fatigue symptom distress and quality of life of cancer patients at least six months after SCT? Pearson's correlation coefficient (r) was utilized.

Similarly, for research questions 4 and 5, the Pearson correlation was used to assess the association between time from transplant and fatigue symptom distress and quality of life.

Chapter IV

Results, Discussion and Conclusion

The following chapter presents the findings of this study. First, the sample is described. Next, the research questions are addressed. The results, strengths and limitations of the study are discussed. The chapter also includes recommendations for nursing practice, nursing education, and nursing research.

Results

Sample

Thirty- nine (n = 39) BMT outpatients were approached to participate in the study. Four declined participation due to feeling tired, and thirty-five (n = 35) agreed to participate. Two of the completed questionnaires were discarded for incomplete information. Twenty-one males and 12 females participated in this study (N = 33) (Table 1). The mean age was 53 (SD = 9.79) with a range between 36 and 70 years. Of the 33 participants, 24 (73%) were married, 5 (15%) were single, 3 (9%) were divorced, and 1 (3%) was widowed. A majority of the patients were Caucasian (79%), followed by Hispanic (15%), and African American (6%). Seventy-six percent (n = 25) of the recipients received allogeneic stem cell transplantation and the remainder underwent autologous SCT (n = 8). The mean length of time from transplant for surviving patients was 19.24 months (SD = 17.78; range = 6–84 months, n = 33). Among the participants the most frequently occurring diagnoses were non Hodgkin's lymphoma (24%), followed by acute myeloid leukemia (21%), and acute lymphocytic leukemia (18%) (Table 2).

Table 1

Demographics and Clinical Characteristics of Patients

| Variable | Frequency | Percentages |
|----------------------------|-----------|-------------|
| Gender | | |
| Male | 21 | 64 |
| Female | 12 | 36 |
| Race/ethnicity | | |
| Caucasian | 26 | 79 |
| Hispanic | 5 | 15 |
| African American | 2 | 6 |
| Education | | |
| 0–11 | 2 | 6 |
| High school | 10 | 30 |
| Some college | 11 | 33 |
| College graduate | 8 | 24 |
| Post graduate | 2 | 6 |
| Marital status | | |
| Married | 24 | 73 |
| Single | 5 | 15 |
| Separated/divorced | 3 | 9 |
| Widowed | 1 | 3 |
| Occupational status | | |
| Disability/unemployed | 15 | 45.4 |
| Employed | 13 | 39.4 |
| Retired | 5 | 15.2 |

Table 2

Diagnoses and Type of Transplant

| Variable | Frequency | Percentages |
|-------------------------------|-----------|-------------|
| Diagnosis | | |
| Non-Hodgkin lymphoma | 8 | 24.2 |
| Acute myeloid leukemia | 7 | 21.2 |
| Acute lymphocytic leukemia | 6 | 18.2 |
| Multiple myeloma | 5 | 15.2 |
| Myelodysplastic syndromes | 3 | 9.2 |
| Chronic lymphocytic leukemia. | 1 | 3 |
| Chronic myeloid fibrosis | 1 | 3 |
| Chronic myeloid leukemia | 1 | 3 |
| Small Cell Lung Carcinoma | 1 | 3 |
| Type of transplant | | |
| Allogeneic | 25 | 76 |
| Autologous | 8 | 24 |

Fatigue Intensity and Symptom Distress

Research question 1: What is the prevalence and level of fatigue distress reported by cancer patients at least six months past completing SCT? Thirty-one participants (93.9%) reported persistent fatigue and five (15%) rated their fatigue 10 out of 10 at its worst. The mean value of current fatigue reported by allogeneic transplant participants was 2.56 (SD= 2.33), and mean= 2.38 (SD= 1.69) for the autologous transplant subjects, for both groups combined the mean was 2.52 (SD= 2.17). The mean usual fatigue of all participants was 2.85 (SD= 1.97), for allogeneic transplant participants the mean usual fatigue was 2.84 (SD= 2.07) and 2.88 (SD= 1.73) for autologous transplant participants. The mean worst fatigue for all subjects

was 4.79 (SD= 3.07), 4.56 (SD= 3.09) for allogeneic transplant participants and 5.50 (SD= 3.07) for autologous transplant participants (Table 3). The ratings of CRFDS were summed for each participant, the total scores ranged from 0–195, with a mean value of 61.8 (Table 4).

Table 3

Means, Standard Deviations and Ranges of Fatigue Intensity Scores

| Variable | n | Minimum | Maximum | Mean | SD |
|-------------------------|----|---------|---------|------|------|
| KPS scale | 33 | 50 | 100 | 85 | 13.5 |
| Total Fatigue intensity | | | | | |
| Usual | 33 | 0 | 7 | 2.85 | 1.97 |
| Current | 33 | 0 | 8 | 2.52 | 2.17 |
| Worst | 33 | 0 | 10 | 4.79 | 3.07 |
| Allogeneic | | | | | |
| Usual | 25 | | | 2.84 | 2.07 |
| Current | 25 | | | 2.56 | 2.33 |
| Worst | 25 | | | 4.52 | 3.09 |
| Autologous | | | | | |
| Usual | 8 | | | 2.38 | 1.69 |
| Current | 8 | | | 2.88 | 1.73 |
| Worst | 8 | | | 5.50 | 3.07 |

Note. n= number of subjects, SD= Standard Deviation.

Research question 2: What do patients report their quality of life to be at least six months after SCT? Total scores of the FACT-BMT ranged from a minimum of 57 and a maximum of 145 with the mean of 113.78 (Table 4).

Table 4

Means, Standard Deviations, and Ranges of Total Scores of CRFDS and FACT-BMT

| | n | Minimum | Maximum | Mean | SD |
|----------------|----|---------|---------|--------|-------|
| CRFDS total | 33 | 0 | 169 | 61.89 | 50.82 |
| FACT-BMT total | 33 | 57 | 145 | 113.78 | 25.66 |

Relationship between Fatigue Symptom Distress and QOL

Research question 3: Is there a significant relationship between fatigue symptom distress and quality of life of cancer patients at least six months after SCT? Pearson's product-moment correlation coefficient (r) was used to calculate the relationship between the total scores of fatigue symptom distress levels from CRFDS and the total scores of QOL from FACT-BMT. A strong negative correlation ($r = -.86$, $p < .0001$) was found, which was statistically significant (Table 5).

Relationship between Fatigue Symptom Distress and Time from Transplant

Research question 4: Is there a significant relationship between fatigue and time from transplant? To assess the association between time from transplant and fatigue symptom distress, Pearson's product-moment correlation coefficient (r) was used. A moderate positive relationship was found between CRFDS total and the time from transplant ($r = .46$, $p = .007$). This finding was statistically significant (Table 5).

Relationship between QOL and Time from Transplant

Research question 5: Is there a significant relationship between quality of life and time from transplant? The Pearson correlation coefficient was used to examine the relationship between QOL and time from transplant. A moderate negative correlation was found ($r = -.34$, $p = .052$) which did not reach statistical significance (Table 5).

Table 5

Pearson Correlation Coefficients between Fatigue Symptom Distress, Quality of Life, and Time from Transplant

| Variable | Fatigue Symptom Distress | | | Quality of Life | | |
|----------------------|--------------------------|------|--------|-----------------|------|------|
| | n | r | p | n | r | p |
| Quality of life | 33 | -.86 | <.0001 | 33 | 1 | — |
| Time from Transplant | 33 | .46 | .007 | 33 | -.34 | .052 |

Discussion

Sample

In this study, a convenience sample of 33 men and women was accrued at the comprehensive cancer center MCC. When the participants came to the BMT clinic for post transplant follow up visits they met with the PI and completed the consent form meeting all institutional, state, and federal guidelines. They also completed the CRFDS and FACT-BMT with an attached demographic data form. The tools took approximately 20 minutes to complete. A minimal respondents' burden is of a particular importance when measuring fatigue in individuals who may already have attentional deficits, lack of energy, and feelings of tiredness.

A limitation of the sample is that it did not represent the SCT types accurately for the BMT population. The majority of the participants underwent allogeneic stem cell transplant, and only eight of them had autologous SCT. In addition, although participation criteria were nonexclusive of ethnicity groups or racial backgrounds, minorities were not well represented in this sample. There were also more men than women participants. Strength of the sample is the diversity of the underlying diagnosis which included eight different types of cancer, which is a good representation of the SCT population.

Fatigue, Symptom Distress, and Quality of Life

This study identified that fatigue is widely prevalent among BMT long term survivors; approximately 93% of the subjects experience some degree of fatigue according to the fatigue intensity scale of CRFDS. The literature reviewed in this study supports this finding. Gielissen et al. (2007) reported that side effects of BMT often precipitate heightened levels of fatigue. In this study, 5 participants (15%) rated their fatigue 10 out of 10 at its worst. This finding is in agreement with the assumption that patients with more aggressive treatments such as BMT are more at risk for persistent fatigue. The CRFDS total scores ranged from 0–195, with a mean of 61.8. The mean of fatigue symptom distress is considered somewhat low. A possible explanation for the inconsistency between the literature reviewed and this study finding is the diversity of underlying diagnoses and the difference in the type of BMT. Also, it should be considered that CRFDS measures the distress and suffering that accompanies the experience of fatigue symptom. Although fatigue symptom was quite prevalent among the participants, fatigue intensity can occur in variable levels that are not necessarily altogether distressful.

In this study, the majority of patients (76%) received allogeneic SCT. Those who received autologous transplant (24%) reported less fatigue symptom distress with mean= 48.0 (SD= 36.62), compared to the allogeneic transplant group (mean= 66.2, SD= 54.49). Although this difference did not reach statistical significance ($p= 0.71$) it is considered clinically significant. A possible explanation of this difference is that autologous SCT patients underwent a shorter hospital stay during transplant, had fewer complications and had no risk for GVHD compared to allogeneic transplant patients. In this sample of patients it was also found that fatigue symptom distress in allogeneic transplant subjects have been more severe. Harder et al. (2007) also related

that to their exposure to acute and chronic GVHD and other complications related to immunosuppression or immunosuppressive therapy. However, this finding should not distract from the fact that some autologous transplant participants did report fatigue symptom distress which should still be addressed on individual bases.

The total FACT-BMT scores ranged from 57-145. The mean score was 113.78. This study found moderate levels of QOL. Schulmeister, Quiett and Mayer (2005) reported that higher QOL and greater satisfaction were associated with good clinical outcomes following transplant though there were lingering fatigue effects. Gielissen et al. (2007) also reported that fatigue persists long after treatment had ended.

Relationship between Fatigue Symptom Distress and QOL

A strong significant negative correlation ($r = -.85, p < .0001$) was found between reported levels of fatigue symptom distress and QOL in this sample. The greater the levels of fatigue symptom distress, the poorer the quality of life. This negative correlation was an expected finding, and it supports the idea that persistent fatigue has a detrimental consequence on QOL of BMT long term survivors. However, a correlational study does not confirm cause and effect. This study supports the findings of Hjermstad et al. (2004) who reported an inverse relationship between fatigue, cognitive or social function and QOL.

Relationship between Time from Transplant, Fatigue Symptom Distress and QOL

A significant moderate positive correlation was found between CRFDS total scores and the time from transplant ($r = .46, p = .007$). This correlation may be precipitated by emotional rather than physical distress; that is, those who had the longest survival seemed more distressed by fatigue. This relationship may occur because they expected a resolution of their symptoms and a sooner return to

normalcy. For patients closer to the time of transplant, there is reason to be hopeful that fatigue symptoms will fade away when they return to their normal functional levels and regain their full strength.

A moderate negative relationship was found between QOL and time from transplant, supporting the idea that lingering fatigue does affect the quality of life. Although a shorter time from transplant correlated with higher QOL levels ($r = -.34$, $p = .052$) this finding did not reach statistical significance. It should also be noted that the most well-functioning transplant patients completed the questionnaires, while the most ill, most fatigued patients declined participation. Approximately 10% of these patients stated upon request that they did not feel well, they felt tired, and that was why they did not want to take part in the study. The failure of these patients to participate might have biased the study results in some important ways.

Conclusions

Implications for Nursing

This study supports the importance of addressing fatigue symptoms in patients who have undergone BMT as a possible approach to improving overall QOL. The study findings reflect that approximately 93% of the participants in this study experience some degree of fatigue after transplant. Also, it demonstrated a significant negative relationship between fatigue symptom distress and quality of life. This is relevant to nursing care and patient education. It would be highly advisable to inform the patients prior to transplant of the potential of developing some persistent fatigue that they may find to be distressing. The consequences of this can be diminished functional capacity which is of particular concern with patients' ability to maintain or return to their productive roles in society (Hacker et al. 2006). Therefore, it is equally important to maintain levels of activity to enhance functional capacity and role

performance towards improving patient's perception of health status and QOL.

Understanding the relationship between fatigue symptom distress and QOL should encourage interdisciplinary collaboration in planning proper interventions to minimize fatigue. This would improve the outcomes of BMT long term survivors and would positively impact their overall quality of life.

Implications for Research

A limitation of this study is that the patients with the worst BMT experience probably were not accessible because of their fatigue. Future studies with larger sample size should evaluate the specific chemotherapeutic agents or dosages used in BMT conditioning protocols and determine whether they impact the occurrence, frequency and persistence of fatigue. Similarly, the cross sectional design of this study lacks pre-treatment baseline assessment which precludes definite conclusions about a change in fatigue and QOL over time. A longitudinal cohort study using a comprehensive psychosocial test to investigate the effects of BMT treatment on the QOL of adult long term survivors is warranted.

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Appendices

Appendix A: Cancer Related Fatigue Distress Scale (CRFDS)
CANCER RELATED FATIGUE DISTRESS SCALE
(CRFDS)

Sandra Holley, PhD, ARNP

Instruction:

Below and on the next 3 pages is a list of problems people sometimes have because of their cancer related fatigue. Please read each one carefully. Please circle the number that best describes **HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST 7 DAYS, INCLUDING TODAY**. Circle only one number for each problem and do not skip any items. If you change your mind, erase your first mark carefully. Read the example before beginning, and if you have any questions please ask them now.

Please complete all 20 items and the 3 additional items on the last page.

The fatigue or tiredness I am having causes me distress because it:

1. Makes it difficult for me to concentrate.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | | Severe distress |

2. Makes me feel that I must accept more help from others.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | | Severe distress |

3. Makes me feel that I am more than just tired.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | | Severe distress |

4. Makes me feel frustrated when I can't do what I used to do.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | | Severe distress |

5. Makes my body feel as though it doesn't want to function.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | | Severe distress |

Appendix A (Continued)

The fatigue or tiredness I am having causes me distress because it:

6. Makes it difficult for me to form whole thoughts.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

7. Makes me feel like my physical abilities are being worn away.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

8. Makes me feel that I am still tired after sleeping.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

9. Makes me feel guilty when I can't do the things that are my usual jobs to do.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

10. Makes me too tired to eat.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

11. Makes me limit my family and social activities.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

12. Makes me feel tired more quickly than typical fatigue.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|------------------------|----------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | Severe distress | | |

Appendix A (Continued)

The fatigue or tiredness I am having causes me distress because it:

13. makes me feel uncertain about my future.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

14. Makes me feel totally exhausted.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

15. Makes me feel like I am a different person.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

16. Makes me stay at home more.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

17. Makes me feel a loss of control over my life.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

18. Makes it difficult for me to remember things.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

19. Makes me feel as if I have no energy.

How much distress does this cause you?

| | | | | | | | | | | |
|--------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------------|-----------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | | | | | Severe distress | |

Appendix A (Continued)

The fatigue or tiredness I am having causes me distress because it:

20. Makes me feel like I am losing interest in things.

How much distress does this cause you?

| | | | | | | | | | | |
|-------------|---|---|---|---|-----------------|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No distress | | | | | Severe distress | | | | | |

Please circle the number that most describes your fatigue.

Fatigue level **now** **No fatigue** **Severe fatigue**
0 1 2 3 4 5 6 7 8 9 10

Worst fatigue level
this past 7 days 0 1 2 3 4 5 6 7 8 9 10

Usual fatigue level
for the past 7 days 0 1 2 3 4 5 6 7 8 9 10

Please circle the one number below that best describes your situation now

KARNOFSKY PERFORMANCE SCALE

| | |
|-----|---|
| 100 | Normal; no complaints; no evidence of disease |
| 90 | Able to carry on normal activity; minor signs of symptoms of disease |
| 80 | Normal activity with effort; some sign or symptoms of disease |
| 70 | Cares for self; unable to carry on normal activity or do active work |
| 60 | Requires occasional assistance, but is able to care for most personal needs |
| 50 | Requires considerable assistance and frequent medical care |
| 40 | Disabled; requires special care and assistance |

Appendix B: Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

| <u>PHYSICAL WELL-BEING</u> | Not at all | A little bit | Some what | Quite a bit | Very much |
|---|-------------------|---------------------|------------------|--------------------|------------------|
| I have a lack of energy | 0 | 1 | 2 | 3 | 4 |
| I have nausea | 0 | 1 | 2 | 3 | 4 |
| Because of my physical condition, I have trouble meeting the needs of my family | 0 | 1 | 2 | 3 | 4 |
| I have pain | 0 | 1 | 2 | 3 | 4 |
| I am bothered by side effects of treatment | 0 | 1 | 2 | 3 | 4 |
| I feel ill | 0 | 1 | 2 | 3 | 4 |
| I am forced to spend time in bed | 0 | 1 | 2 | 3 | 4 |

| <u>SOCIAL/FAMILY WELL-BEING</u> | Not at all | A little bit | some what | Quite a bit | Very much |
|---|-------------------|---------------------|------------------|--------------------|------------------|
| I feel close to my friends | 0 | 1 | 2 | 3 | 4 |
| I get emotional support from my family | 0 | 1 | 2 | 3 | 4 |
| I get support from my friends | 0 | 1 | 2 | 3 | 4 |
| My family has accepted my illness | 0 | 1 | 2 | 3 | 4 |
| I am satisfied with family communication about my illness | 0 | 1 | 2 | 3 | 4 |
| I feel close to my partner (or the person who is my main support) | 0 | 1 | 2 | 3 | 4 |

Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box and go to the next section.

| | | | | | |
|---------------------------------|---|---|---|---|---|
| I am satisfied with my sex life | 0 | 1 | 2 | 3 | 4 |
|---------------------------------|---|---|---|---|---|

Appendix B (Continued)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

| <u>EMOTIONAL WELL-BEING</u> | Not at all | A little bit | Some -what | Quite a bit | Very much |
|---|-------------------|---------------------|-------------------|--------------------|------------------|
| I feel sad | 0 | 1 | 2 | 3 | 4 |
| I am satisfied with how I am coping with my illness | 0 | 1 | 2 | 3 | 4 |
| I am losing hope in the fight against my illness | 0 | 1 | 2 | 3 | 4 |
| I feel nervous | 0 | 1 | 2 | 3 | 4 |
| I worry about dying | 0 | 1 | 2 | 3 | 4 |
| I worry that my condition will get worse | 0 | 1 | 2 | 3 | 4 |

| <u>FUNCTIONAL WELL-BEING</u> | Not at all | A little bit | Some -what | Quite a bit | Very much |
|--|-------------------|---------------------|-------------------|--------------------|------------------|
| I am able to work (include work at home) | 0 | 1 | 2 | 3 | 4 |
| My work (include work at home) is fulfilling | 0 | 1 | 2 | 3 | 4 |
| I am able to enjoy life | 0 | 1 | 2 | 3 | 4 |
| I have accepted my illness | 0 | 1 | 2 | 3 | 4 |
| I am sleeping well | 0 | 1 | 2 | 3 | 4 |
| I am enjoying the things I usually do for fun | 0 | 1 | 2 | 3 | 4 |
| I am content with the quality of my life right | 0 | 1 | 2 | 3 | 4 |

Appendix B (Continued)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

| <u>ADDITIONAL CONCERNS</u> | Not at all | A little bit | Some what | Quite a bit | Very much |
|---|---------------|--------------------|--------------|----------------|--------------|
| I am concerned about keeping my job (include work at home) | 0 | 1 | 2 | 3 | 4 |
| I feel distant from other people | 0 | 1 | 2 | 3 | 4 |
| I worry that the transplant will not work | 0 | 1 | 2 | 3 | 4 |
| The effects of treatment are worse than I had imagined | 0 | 1 | 2 | 3 | 4 |
| I have a good appetite | 0 | 1 | 2 | 3 | 4 |
| I like the appearance of my body | 0 | 1 | 2 | 3 | 4 |
| I am able to get around by myself | 0 | 1 | 2 | 3 | 4 |
| I get tired easily | 0 | 1 | 2 | 3 | 4 |
| I am interested in sex | 0 | 1 | 2 | 3 | 4 |
| I have concerns about my ability to have children | 0 | 1 | 2 | 3 | 4 |
| I have confidence in my nurse(s) | 0 | 1 | 2 | 3 | 4 |
| I regret having the bone marrow transplant | 0 | 1 | 2 | 3 | 4 |
| I can remember things | 0 | 1 | 2 | 3 | 4 |
| I am able to concentrate | 0 | 1 | 2 | 3 | 4 |
| I have frequent colds/infections | 0 | 1 | 2 | 3 | 4 |
| My eyesight is blurry | 0 | 1 | 2 | 3 | 4 |
| I am bothered by a change in the way food | 0 | 1 | 2 | 3 | 4 |
| I have tremors | 0 | 1 | 2 | 3 | 4 |
| I have been short of breath | 0 | 1 | 2 | 3 | 4 |
| I am bothered by skin problems (rash, itching) | 0 | 1 | 2 | 3 | 4 |
| I have trouble with my bowels | 0 | 1 | 2 | 3 | 4 |
| My illness is a personal hardship for my close family members | 0 | 1 | 2 | 3 | 4 |
| The cost of my treatment is a burden on me or my family | 0 | 1 | 2 | 3 | 4 |

Appendix C: Demographic Data/Health History Information Form

Part A: Demographic data

1. Age ___ (Please, do NOT provide your date of birth)
2. Gender: Male ___ Female ___
3. Ethnicity/Race (check one)
 American Indian/Alaska Native Arab American
 Asian American/Pacific Islander Black/African American
 Caucasian/White/Anglo Hispanic/Latino
 Other
4. Educational background _____ (Highest grade completed)
5. Marital status: Single ___ Married ___ Widowed ___ Separated ___ Divorced ___
6. Employment status:
 Self employed Employed outside the house
 Disability ___ no ___ yes, specify: _____

Part B: Health History Information

- Underlying Cancer diagnosis: _____
- Type of Transplant received: (Check one)
- Bone Marrow Transplant Blood/Stem Cell Transplant Cord Blood
 Allogeneic Transplant (from a donor) Autologous Transplant (from self)
- Number of months from Transplant completion _____
- Are you in complete or partial remission? Complete ___ Partial ___ I don't know ___

Appendix D: Informed Consent

Subject's Name _____
Medical Record # _____

MCC # _____
IRB # _____

Informed Consent to Participate in Research and Authorization to Collect, Use and Share Your Health Information

Moffitt Cancer Center (MCC) / University of South Florida (USF)
Information to Consider Before Taking Part in this Research Study

| | |
|---------------------|---------|
| IRB Approval | |
| FWA 00001669 | |
| IRB Number: | 108313I |
| From | 8-31-09 |
| Thru | 8-30-10 |

Researchers at the University of South Florida (USF) and Moffitt Cancer Center (MCC) study many topics. To do this, we need the help of people who agree to take part in a research study. This form tells you about this research study.

We are asking you to take part in a research study that is called: **Fatigue Symptom Distress and its Effect on Quality of Life in Adult Stem Cell Transplant Survivors.**

The person who is in charge of this research study is **Suzan Abduljawad**. This person is called the Principal Investigator (PI). This study is being conducted as a part of a thesis and is being supervised by Dr. Susan McMillan. This person is called the Co-Investigator.

The research will be done at the bone marrow transplant clinics of Moffitt Cancer Center.

Your participation in this study is entirely voluntary. Please read the information below and ask questions about anything you do not understand, before deciding whether or not to participate.

Why is this research being done?

The purpose of the study is to explore the nature of fatigue experienced after bone marrow or stem cell transplantation, and to assess how it affects the quality of life of adult bone marrow/stem cell transplant long term survivors.

What will happen during this study?

If you volunteer to participate in this study the PI will ask you to:

- Complete a **Screening Form** which will ask questions about certain aspects of your person such as: do you understand English? Are you over 18 years old? Did you receive bone marrow transplant? And other health information that are required to determine your eligibility to participate in the study.

If you are eligible to participate in the study, a meeting with the Principle Investigator will be arranged during your visit to Moffitt BMT clinic. The PI will discuss with you in detail the study aims, methods, anticipated benefits, potential hazards or discomforts, and alternatives and will answer any questions you may have about the study to your satisfaction. If you agree to participate you will be asked to sign this consent form.

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Appendix D (Continued)

Subject's Name _____
Medical Record # _____

MCC # _____
IRB # _____

The principle investigator will then ask you to:

1. Complete a **Demographic Data/Health Information Form**. The term Demographic Data refers to a selected population characteristics such as: Age, gender, ethnicity, marital status; it is used in research to describe the group of participants who joined the study. In this study, this information will be used to determine the commonalities and differences between participants, and to find out if those factors affect the experience of fatigue and the reports of quality of life. The health information part asks questions about your cancer diagnoses and the type of transplant you received.
2. Fill out two questionnaires, the Cancer Related Fatigue Distress Scale and the Functional Assessment of Cancer Therapy-Bone Marrow Transplant.

You will be asked to do this only once during the study. The screening form takes less than 2 minutes to complete, the demographic data form takes less than 2 minutes to complete, and each questionnaire takes from 5 to 10 minutes to complete. The total time of your participation is estimated to be 35 minutes including the time spent with the PI for the informed consent process.

All the information gathered from these forms will be calculated into numbers and ranges and transformed into statistical data and then will be documented in the study.

You will be provided with a copy of this informed consent document, and we will obtain your signature for consent; a copy of the consent will be provided for scanning into your electronic medical record at Moffitt, and a copy will be given to you to keep.

How many people will take part in this study?

Approximately fifty individuals will take part in this study at Moffitt Cancer Center.

What other choices do you have if you do not participate?

You have the choice not to participate in this research study.

What are the risks if you take part in this study?

A possible risk is the inevitable loss of privacy as we gain knowledge of your health information, otherwise, there are no known risks or any unpleasant or harmful side effects associated with this study. There are no costs to you for participating in the study. Neither you, nor the hospital, or the University of South Florida, will be charged or incur any expense or compensation for your participation.

What are the potential benefits if you take part in this study?

We cannot tell whether you may benefit directly by taking part in this study, but the information learned from this research should provide more general benefits because the knowledge gained would contribute to the science of nursing and medicine, by further expanding the literature on fatigue related to bone marrow or stem cell transplant. It could help health care professionals

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Appendix D (Continued)

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IRB #

identify fatigue symptom distress in specific phases of recovery, and recognize its impact on the quality of life. A better understanding of this fatigue might lead to appropriate individualized care designed to manage fatigue and help BMT patients recover to their fullest.

Will you be paid for taking part in this study?

No, we will not pay you for the time you volunteer while being in this study.

The use and disclosure of your personal health information

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment, we must obtain your written authorization before we use or disclose your information for this study. This form provides that authorization and helps you understand how your information will be used or disclosed.

Research at Moffitt Cancer Center is undertaken jointly with the University of South Florida or other persons or entities under an organized health care arrangement. By signing this form you are permitting the Moffitt Cancer Center to use personal health information collected about you for research purposes within its organized health care arrangements.

What information will be used and/ or disclosed?

By signing below, you authorize the use and disclosure of your entire study record and any medical or other records held by Moffitt Cancer Center/University of South Florida. We may publish what we learn from this study. If we do, we will not let anyone know your name. We will not publish anything else that would let people know who you are.

How are we going to protect your confidentiality?

By Federal law we must keep your study records as confidential as possible. We will keep the records of this study, including the demographic data collected and your completed questionnaire forms, in the Principal Investigator's locked office. All study data will be collected by the PI, stored in a secure place, and will not be shared with any other party without your permission. Your identity will not be revealed while the study is being conducted except to the PI, doctors, and nurses caring for you. Although your physician or nurse practitioner is not an investigator he or she will be informed of your participation.

After completion of the study data collection the completed questionnaires, demographic sheets and the original consent forms will be safeguarded by keeping them in a locked file drawer at the Principal Investigator's locked office for 5 years, and then will be shredded and discarded safely by the Principle Investigator.



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Appendix D (Continued)

Subject's Name _____
Medical Record # _____

MCC # _____
IRB # _____

Who will disclose, receive, and/or use your information?

People who need to know more about the study may need to see your study records. By law, anyone who looks at your study records must keep them completely confidential. The people who will be allowed to see these records are:

- The Principal Investigator and the Co-Investigator.
- Every member of the Moffitt Cancer Center and University of South Florida workforce who provides services in connection with this study.
- Certain government agents from the Department of Health and Human Services (DHHS) can review all research records.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards, Privacy Boards, Data and Safety Monitoring Board and their related staff that may have oversight responsibilities for this study.

All of these people may not be known now, they will be sought 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. The purpose for the uses and disclosures you are authorizing is to conduct the study explained to you during the informed consent and research authorization process and to ensure that the information relating to that study is available to all parties who may need it for this research purposes. If you would like to have more specific information about this at any time during the study, you may ask the PI and your questions will be answered.



What happens if you decide not to take part in this study?

You are free to participate in this research or withdraw at any time. 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, to please the investigator or the research staff. There will be no penalty or loss of benefits you are entitled to receive if you stop taking part in this study. Any information that has been collected before you withdraw your authorization from the study will continue to be used for research purposes.

Where can you get the answers to your questions, concerns, or complaints?

- If you have any questions or concerns or complaints about this research, please contact the Principal Investigator: Suzan Abduljawad at (985) 710-0461.
- If you have questions about your rights as a participant in this study, complaints, concerns or issues you want to discuss with someone outside the research, call the Division of Research Integrity and Compliance of the University of South Florida at (813) 974-9343.
- If you have questions about your rights as a research patient at Moffitt Cancer Center, call the Division of Research Compliance in the Corporate Compliance at the Moffitt Cancer Center (813) 745-1869.
- If you experience an unanticipated problem related to the research call Suzan Abduljawad at (985) 710-0461.

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Appendix D (Continued)

Subject's Name _____
Medical Record # _____

MCC # _____
IRB # _____

Consent to Participate in Research and Authorization for the Collection, Use and Disclosure of Health Information

It is up to you to decide whether you want to take part in this study. If you want to take part, please sign the form, if the following statements are true.

Statement of Participation in Research and Authorization for the Collection, Use and Disclosure of Health Information

I understand that by signing this form I am agreeing to take part in research. I have read the consent form which included information about this study I am participating in. I understand the procedures described above. I understand that I am to rely on the investigator for information regarding the nature and purpose of the research study, and I have been given an opportunity to discuss my concerns and ask any questions. My questions have been answered to my satisfaction, and I **freely give my consent to take part in this study**. I have received a copy of this form to take with me.

Signature of Person Taking Part in Study

Date

Printed Name of Person Taking Part in Study

Statement of Person Obtaining Informed Consent / Research Authorization

I have carefully explained the study and consent to the person as signed above. I have taken part in the consent process prior to the patient's signature and discussed in detail the study aims, methods, anticipated benefits, potential hazards or discomforts, and alternatives. I have answered any and all questions the patient and/or family have asked. No study procedures were initiated prior to consent.

Signature of Person Obtaining Informed
Consent/ Research Authorization

Date

Printed Name of Person Obtaining Informed
Consent/ Research Authorization



[Original Approval Date: 02/20/09] Version # 2 revised 08/31/09
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August 14, 2009

Suzan Abduljawad
H. Lee Moffitt Cancer Center & Research Institute
University of South Florida
12902 Magnolia Drive
Tampa, FL 33612

Dear Ms. Abduljawad:

The Behavioral Subcommittee of the Scientific Review Committee (SRC) has reviewed your response for your research protocol entitled, "**Fatigue Symptom Distress and Its Relationship with Quality of Life in Adult Stem Cell Transplant Survivors**" (MCC 16029). The revised protocol version dated 08/11/2009 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.

It is your responsibility to ensure that all Moffitt staff (nursing, pharmacy, data management, etc.) is 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. 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

Appendix E (Continued)

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,



Paul Jacobsen, PhD
Chair, Behavioral Subcommittee
Scientific Review Committee

Appendix F: Institutional Review Board Approval



UNIVERSITY OF
SOUTH FLORIDA

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

September 3, 2009

Suzan Abduljawad
College of Nursing
Tampa FL 33612

RE: **Expedited Approval** for Initial Review

IRB#: 108313 I

Title: *Fatigue Symptom Distress and its Effect on Quality of Life in Adult Stem Cell
Transplant Survivors*

Study Approval Period: 08/31/2009 to 08/30/2010

Dear Ms. Abduljawad:

On August 31, 2009, Institutional Review Board (IRB) reviewed and **APPROVED** the above protocol **for the period indicated above**. It was the determination of the IRB that your study qualified for expedited review based on the federal expedited category number **five (5) and seven (7)**.

Approval included with the Moffitt Adult Informed Consent Form.

Please note, if applicable, **only use the IRB-Approved and stamped consent forms for participants to sign**. The enclosed informed consent/assent documents are valid during the period indicated by the official, IRB-Approval stamp located on page one of the form. Make copies from the enclosed original.

Please reference the above IRB protocol number in all correspondence regarding this protocol with the IRB or the Division of Research Integrity and Compliance. In addition, you can find the Institutional Review Board (IRB) Quick Reference Guide providing guidelines and resources to assist you in meeting your responsibilities in the conduction of human participant research on our website. Please read this guide carefully. It is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB.

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 813-974-2036

Sincerely,

Krista Kutash, Ph.D., Chairperson
USF Institutional Review Board

Cc: Various Menzel/cd, USF IRB Professional Staff
Susan McMillan PhD