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HEALTH RELATED QUALITY OF LIFE IN ADULT PATIENTS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANT

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A thesis
Submitted in partial fulfillment of the requirements for
the dual track of Master of Science in Nursing - Community and Public Health Nursing track and Psychiatric Mental Health Clinical Nurse Specialist track
to the School of Nursing
of the Faculty of Medicine
at the American University of Beirut

Beirut, Lebanon
June 2020

AMERICAN UNIVERSITY OF BEIRUT

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ACKNOWLEDGMENTS

I would like to express the deepest and immeasurable appreciation to my committee chair, Professor Laila Farhood; she continually and convincingly conveyed a spirit of belief in my work and efforts.

Special thanks are for my academic advisor, Professor Samar Noureddine for her guidance, support, follow up, and patience. The help and empowerment I continuously receive from her are overwhelmingly positive.

My sincere gratitude is for Professor Ali Bazarbachi who always demonstrates the attitude and the substance of a great mentor; the origin of this work would not have been possible without his inspiration.

Finally, and most importantly, a huge thanks to all the patients who allowed me with trust to provide care for them, during their difficult times as well as during their finest moments. None of what I have become as a nurse was attainable without their trust.

AN ABSTRACT OF THE THESIS OF

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Major: Nursing

Title: Health Related Quality of Life in Adult Patients Following Hematopoietic Stem Cell Transplant

Hematopoietic stem cell transplant (HSCT) is a curative treatment modality for a wide array of malignant and benign hematologic disorders and some solid tumors. Patients receive a conditioning regimen prior to transplant that includes high dose of chemotherapy with or without total body irradiation. The side effects of the preparative regimen, myelosuppression, and the effects of cellular therapy can be detrimental to the patient's health. Health-related quality of life (HRQL) has never been studied in the Lebanese population following HSCT.

A longitudinal study was designed targeting 40 adult patients undergoing autologous or allogeneic HSCT. The subjects were interviewed based on the FACT-BMT tool that contains the four dimensions of quality of life (QoL): physical, social/family, emotional, and functional; in addition to a section of additional questions that addresses general symptoms and concerns. The answers are based on a Likert scale ranging from zero to four. Interviews were taken at points in time that are considered sensitive to the patient's transplant trajectory: baseline (on admission), day +7 post transplant, and the day of discharge, day 30, and day 100.

All subjects reported lower means on all dimensions at day +7, and returned back to near baseline mean on days +30 and +100. Men and women reported the same fluctuations in the means. Women reflect worse QoL than men do, especially on the physical and emotional dimensions. Although the means for allogeneic and autologous patients show the same pattern of change, however autologous patients report a worse QoL than allogeneic at the beginning and towards day +7, yet they return to their baseline on the day +100 assessment better than their allogeneic counterparts do.

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CHAPTER I

INTRODUCTION

Hematopoietic stem cell transplant (HSCT) is one of the curative modalities for a wide array of malignant and benign hematologic disorders (European Blood and Marrow Transplant Group, [EBMT] 2015), in addition to some solid tumors and inherited disorders in adult and pediatric populations (Thomas, 2000). HSCT is either autologous or allogeneic. Autologous transplants take place when the patients are their own donors, whereas an allogeneic transplant is when the patient receives stem cells from a related or unrelated donor (American Cancer Society, 2013). In preparation for the procedure, the patients receive a treatment regimen called conditioning that could be myeloablative (MAC) or of reduced intensity (RIC); conditioning regimens consist of high-dose chemotherapy with or without total body irradiation. The preparative regimen is selected based on several factors, mainly the diagnosis and type of transplant, and other patient characteristics (EBMT, 2012). The purpose of conditioning is to eradicate the disease (Juliusson et al., 2003), for the creation of space for the engraftment of the donor bone marrow (Gratwohl & Carreras, 2012), and to induce immunosuppression for the prevention of a graft-versus-host reaction (GvHD) (Servais, Baron, & Beguin, 2011). As a result, and during the acute course of transplant, patients suffer a spectrum of side effects and toxicities that increase the risk for life-threatening infections and severe sepsis, bleeding, malnutrition, and many distressing symptoms, in addition to social isolation due to prolonged hospitalization and reduced social encounters. After discharge from the hospital, patients suffer a delayed immune reconstitution that puts them at risk for developing community acquired infections, viral reactivation, and acute and chronic graft-versus-host disease. All of the above-mentioned

complications have a tremendous effect on the patient's performance, social functioning, sexuality, as well as on body image that is their overall quality of life.

HSCT has become available to the population and residents of Lebanon in the late 1990s. There are four transplant centers in Lebanon, one of them is exclusive to autologous transplants for adult patients, and the other three accommodate adult and pediatric patients for autologous and allogeneic transplants. One of the centers has received accreditation by the Joint Accreditation Committee – International Society of Cellular Therapy (ISCT) and European Society for Blood and Marrow Transplant (EBMT), as known as JACIE. For the past six years, more than 500 transplants were performed in one Lebanese center (Bazarbachi et al., 2017). The effect of HSCT on the health-related quality of life (HRQL) is still not well-reported for the Lebanese population. The study aims at describing the changes in health-related quality of life (HRQL) in adult recipients of hematopoietic stem cell transplant (HSCT) throughout the continuum of the transplant process.

A. Background and Significance

According to the Lebanese Ministry or Public Health (MOPH), hematologic malignancies such as leukemia, lymphoma, and plasma cell disorders accounted for 10.64 % (1084 cases) of the total cancer incidence in Lebanon for the year 2015. As the population of Lebanon was estimated 5.8 million in the year 2015 (World Bank, 2015), which makes the ratio of hematologic malignancies 18.25 cases in 100.000 of the general population (Shamseddine et al., 2014).

The HSCT program at the American University of Beirut Medical Center (AUBMC) was founded in 1998. By the end of the year 2017, the program has performed 890

transplants, among which 704 transplants were performed on adult patients, and they are distributed according to the initial diagnoses as follows: lymphoma (43.9 %), plasma cell disorders (30.5 %), leukemia and myelodysplastic syndrome (19 %), solid tumors (3 %), benign disorders (2.7 %), and myeloproliferative disorders (1.4 %) (Bazarbachi et al., 2017).

The treatment of hematologic malignancies is usually chemotherapy. In the last 20 years, there has been advances in the cure of such disorders by introducing monoclonal antibodies (Dotan, Aggarwal, & Smith 2010), proteasome inhibitors, and other immunomodulatory therapies (Richardson et al., 2010). However, some of the patients fail to respond to these lines of treatment and stem cell transplant becomes the available curative line of choice (Tan & Chiou, 2016). Moreover, patients with diseases known to have a high-rate of relapse with conventional treatments alone (e.g. acute leukemia with FLT-3 mutation) are candidates for transplants from the time of diagnosis. The stem cells are either harvested from the bone marrow, or mobilized to the peripheral blood with the help of growth factors and/or a mobilizer (e.g. plerixafor). Thus, the terms hematopoietic stem cell transplant (HSCT), historically known as bone marrow transplant (BMT), and BMT are still being used interchangeably.

The choice of conditioning depends on the diagnosis, the type of HSCT, as well as on the patient's age, performance status, co-morbidity, and the status of the disease at the time of transplant. Hence, the duration of the conditioning protocol might vary from one single dose given the day before stem cell infusion, up to two weeks of treatment. During the period of chemotherapy conditioning and for the later periods, patients experience a spectrum of side effects and toxicities from the treatment that range from mild to severe. These toxicities are mainly gastrointestinal: nausea, emesis, decreased appetite, dry mouth, taste changes, diarrhea, and inflamed mucosal lining (from oral cavity to the anus). Other toxicities are

fatigue and energy loss, and infections. Later toxicities and complications include infertility, secondary malignancies, cardiopulmonary toxicities, hepatic and renal insufficiency, and the effects of graft-versus-host disease on the skin, liver, immune system, and the high risk of developing viral and fungal infections (EBMT, 2012.)

Due to a higher-risk of infection because of immunosuppression and late immune reconstitution, patients are given prophylactic treatment for infection as well as reverse isolation. However, the isolation of patients in single rooms with positive air pressure and limited number of visitors, could lead to social isolation, alteration in social functioning and role, sleep disturbances, anxiety, depression, and adjustment disorders (El-Jawhari et al., 2016). All these psychosocial problems could be aggravated by fatigue, hair loss, and changes in body image. Upon discharge, patients are instructed to keep a distance from crowded places for a period of three months after transplant, and use a facemask within their household for almost the same period. A risk assessment regarding their back to work routine is usually done by their primary physician and discussed in their follow up clinic visits. Presentation to the emergency department with fever and other signs of infection among this patient population is not uncommon.

Despite the magnitude of the effect of high dose chemotherapy and radiation therapy, and the long-term complications of cellular therapy, and the number of patients who underwent transplant since 1997 to date, the effect of HSCT on the health-related quality of life (HRQL) is under-studied in the Lebanese population. The purpose of this study is to describe the changes in health-related quality of life (HRQL) in adult recipients of hematopoietic stem cell transplant (HSCT) patients throughout the continuum of the transplant process and to examine the association between HRQL scores and select demographic and clinical variables.

CHAPTER II
LITERATURE REVIEW

This chapter reviews the literature on the complications associated with hematopoietic stem cell transplant, the empirical evidence about the quality of life of patients following this procedure, in addition to the factors associated with their health related quality of life.

A. Complications of HSCT

Investigators found that HSCT has long-term effects on individuals and results in organ-system toxicities (Majahil et al., 2012). Bhatia (2011) found that two-thirds of HSCT survivors develop one chronic health condition, one-fifth develops a severe or life-threatening condition, and survivors after five years of HSCT are at a four- to nine-fold increased risk of late mortality for as long as 30 years from HSCT, producing an estimated 30 % lower life expectancy compared with the general population. Ogonek et al. (2016) found that HSCT patients experience delayed immune reconstitution for up to two years following allogeneic HSCT, a condition that puts patients at higher risk for fatal infections, increased hospital length of stay, and over-use of antimicrobials. Amin et al. (2015) reported the severity of pulmonary toxicities after allogeneic HSCT. In addition, malnutrition associated with chronic graft versus host disease (GvHD) were described in this patient population by Bassim et al. (2014), Petryk et al. (2014), and Philips et al. (2013.)

Different studies elaborated on the long-term effects and toxicities of HSCT on the patients. Oria et al. (2013) described that after the first year of transplant, 90% to 99 % of women and 60 to 90% of men undergoing HSCT had gonadal impairment among other endocrine disorders, including but not exclusive to hypothalamus-pituitary-growth hormone

problems (10 %), hypothalamus-pituitary-thyroid axis disorders (40 %), and hypothalamus-pituitary-adrenal axis disorders (50%.).

B. Quality of Life Following HSCT

Bevans (2010) highlighted the importance of measuring HRQL in HSCT patients as a determinant of their general health. Terrin, Rodday, and Parsons (2015) elaborated that the HRQL trajectories were predictive of transplant-related mortality in pediatric patients, even after adjusting for baseline characteristics of the patients.

1. Changes in HRQL over time in Patients who undergo HSCT

The HRQL of patients who undergo HSCT varies throughout the trajectory of the illness. Grant et al. (2012) found that HSCT patients at discharge from the hospital scored low on their functional status and HRQL. Hacker et al. (2006) found that patients experienced increased fatigue and decreased physical activity following chemotherapy conditioning, as well as diminished functioning and increased symptomatology following HSCT.

Chao et al. (1992) studied HRQL in patients undergoing autologous HSCT (n = 58) at baseline, three months after HSCT, and then every three months up to a period of one year after HSCT. At discharge, fatigue was noticed and the patient's quality of life was the lowest at the 90-day follow up, but was improved at 1-year follow up. At the one-year follow up, patients reported their quality of life to be above average to excellent on a linear visual analogue scale. Similarly, Hjermstad et al. (1999) and Syrjala et al. (1993) showed that it takes about a year for patients following any type of transplant to improve their HRQL to their baseline values. On the other hand, Kopp et al. (1999) have reported that it takes a

period of two years for patients who underwent allogeneic HSCT to report to their baseline values on all dimensions of any quality of life assessment tool. Lee et al. (2001) also reported that a total of 324 patients with autologous and allogeneic HSCT reported back to normal at 2-year follow up (63% in autologous versus 68% of allogeneic HSCT); however, fatigue and difficulties related to sexuality were still perceived as a problem for more 30% of the patients.

Recently, Yasar and Akin (2016) have studied 104 HSCT patients in Turkey over a period of seven months, and concluded that the transplant process was associated with lower scores on all quality of life dimensions. In a study of women with advanced breast cancer undergoing high-dose chemotherapy and autologous HSCT, a questionnaire was administered at seven time points starting at the beginning of treatment, and up to 24-months post enrolment. The investigators found that the short- effects of high-dose chemotherapy followed by autologous transplant in women with breast cancer were back to normal eight weeks after treatment (Conner-Spady et al., 2005). In another study by Le et al. (2010), patients' outcomes were found to be back similar to the normal population five years after transplant.

Lee et al. (2001) found that 53% of the patients undergoing autologous HSCT (n = 93) reported that their life had returned to normal at six months after transplant, and 37% felt that their health was very good or excellent. On the other hand, 112 allogeneic HSCT patients were followed up for six months after transplant, where 31% reported that their life had returned to normal and 33% felt that their health was very good or excellent.

2. *Psychological symptoms following SCT*

Cognitive problems were found to be significant and persistent for patients undergoing HSCT either during hospitalization or after discharge. These include sleep disturbances, fatigue and depression (Cohen et al., 2012; Ghazikhanian et al., 2017; Hacker et al., 2006; Jim et al., 2014; Nelson et al., 2014.) In multiple longitudinal studies by El-Jawhari et al. (2015, 2016), the proportion of patients with depression doubled from baseline in the first two to four weeks after transplant. Post-traumatic stress disorder (PTSD) was found among 43.3 % of patients six months after HSCT, and a decrease in HRQL scores and an increase in symptoms of depression at two weeks from baseline assessment were noted. Artherhold et al. also reported similar results on depression and general distress in 2014, and in a secondary data analysis by Kenzik et al. (2015) and Hobfoll et al. (2015.)

In a study done by Gaston-Johansson et al. (1996), patients with autologous HSCT (n = 24) were assessed to identify the psychological dimension in their quality of life. Assessments were done two weeks prior to transplant, two days prior to the administration of stem cells, and then at days 5, 10, and 20 after transplant. The results showed that poor health and functioning had the most negative impact on quality of life, with a significant negative correlation between depression and quality of life ($r = - 0.79$) and patients experienced higher levels of depression prior to autologous transplant than after the transplant (p-value < 0.05.) In addition, the feelings of fatigue and anxiety during the hospitalization period went back to their baseline assessment scores on discharge. In another study by Artherholt et al in 2014, 228 patients were assessed pre-transplant and 6 to 7 weeks after transplant. The ratio of patients with depression increased to 31% from the pre-transplant initial assessment of 6% indicating that the process of transplant could be a risk factor for depression.

The HRQL score on finding a meaning, and the perception of peace declined at one-month post-transplant; yet it returned to baseline at six months after transplant. Faith has increased from the lowest point on the visual analogue scale in the pre-transplant assessment phase to the highest on the re-assessment that was done six months after transplant (Harris et al., 2015; Leeson et al., 2015; Prince et al., 2015.)

Sexual health was also examined in a study by Li et al. (2015), who reported that the issue is understudied in HSCT patients due to several obstacles that prevented a proper assessment including conditioning regimens, genital GvHD, and cardiovascular complications. Mosher et al. reported patients' concerns over sexuality, change in appearance, lack of sexual interest, and fatigue in a study in 2011, in which one-third of survivors below the age of 40 years reported their concern about the ability to have children.

3. Factors associated with HRQL following HSCT

In a study done by Hamilton et al. (2013), survivors of HSCT faced economic challenges that were described as chronic stressors capable of reducing the mental and physical well-being of patients. Herzberg et al. (2013) and Wingard et al. (2010) reported that demographic and clinical characteristics of study subjects such as age, employment, gender, education, marital status, family function, social support, co-morbidity, transplant type, intensity of conditioning, time after transplant and acute GvHD were significantly associated with self-reported symptoms. Patients with lower socioeconomic status and lower levels of education reported fewer symptoms on their follow up clinic visits, whereas patients privileged with a steady job, a social support network, and health insurance reported symptoms of decreased optimism. Conversely, Mosher (2012) reported that unemployed survivors and those with lower incomes and worse functional status were more likely to experience poorer scores on

the HRQL in multiple domains. In a different study by Hamilton et al., (2014) there was a focus on age comparing patients below and above the age of 60 years. Patients older than 60 years showed lower scores in social well-being than those who are younger than 60 years.

Pidala et al. (2018) stated that the quality of life of adult patients (N=209) with chronic graft-versus-host disease was associated with the severity of chronic GvHD. Sun et al. (2015) reported a significant association between chronic GvHD and reported quality of life in a scheduled follow ups on 342 patients with chronic ocular GvHD after allogeneic HSCT. Mastropierto et al (2010) followed up 62 patients after their allogeneic HSCT; 25 of them had chronic GvHD and reported significantly lower mean scores on quality of life measurements of parameters of physical well-being, social well-being, emotional well-being, functional well-being ($P < 0.001$) and patient-physician relationship ($P < 0.014$) than their non-GvHD counterparts in the study. Lee et al. (2010) studied 96 patients post their allogeneic HSCT and stratified them into three categories, (1) No GvHD acute or chronic, (2) No acute, but chronic, and (3) acute and chronic. The second and third group scored lower quality of life measurements on 6-months and 1-year follow up (P 0.008) than those patients in the first group.

In summary, whether studies have investigated one or more than one dimension on the quality of life, all studies in their different designs reported a negative impact of hematopoietic stem cell transplant on the HRQL of patients after the procedure. The impact lasts one to two years before patients go back to their baseline level of functioning. Most of the reviewed studies were conducted in the West, and none was found in the Middle East. In addition, only few studies examined the factors that predict HRQL in this patient population, a gap that this study is attempting to fill.

CHAPTER III

CONCEPTUAL FRAMEWORK

Based on the reviewed literature, the specific aims of the study were the following:

1. To describe the changes in HRQL scores from baseline to scheduled time points after transplant: at day +7 following HSCT, discharge, then at days +30 and +100 following HSCT
2. To compare HRQL scores by transplant type (allogeneic vs. autologous) and sex at the four time points following the transplant
3. To describe the associations between demographic and clinical variables, and HRQL scores at days +7 and +30 following the transplant

The World Health Organization (WHO, 2007) defined quality of life (QoL) as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns". The definition encompasses six major domains: physical health, psychological state, level of independence, social relationships, environmental features, and spiritual concerns, including personal beliefs. This definition reflects the multi-dimensional nature of quality of life, and addresses the subjective view of patients regarding the effects of disease and health interventions on their quality of life. The Center for Disease Control and Prevention (CDC) stated in 2016 that Quality of Life (QoL) is "a broad multidimensional concept that usually includes subjective evaluations of both positive and negative aspects of life". The challenge to measure QoL is that it has a different meaning for nearly everyone and every discipline.

Individuals with a life-limiting or life threatening condition have their quality of life affected by such illnesses. As health takes the multiple aspects of physical, psychosocial, and spiritual dimensions, QoL takes on the same dimensions. Thus, the concepts of health and quality of life intersect along these dimensions known as the health-related quality of life (HRQL). In fact, health is a right that is recognized by international laws and the United Nations' Universal Declarations of Human Rights in December 1948. The World Health Organization (WHO) in 1946 has defined health as "a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity". This part of the WHO constitution was re-enforced in several assemblies afterwards, the last in September 15, 2005.

The concept of health-related quality of life (HRQL) has been evolving in the literature since the 1980s to incorporate the aspects of quality of life that are known to affect and be affected by health in all its dimensions. The National Institute of Health (NIH) provided a more specific and focused definition of HRQL: "Health-related quality of life is the value assigned to the duration of life as modified by the impairments, functional state, perceptions and social opportunities influenced by disease, injury, treatment or policy" (Padilla, Frank-Stromborg, & Koresawa, 2004, p. 129). According to this definition, HRQL is restricted to areas in life that are important to evaluate with regard to health and illness.

The conceptual framework of the study is based on the holistic concepts of health and quality of life, and has as its main outcome the health related quality of life (HRQL). The dimensions of HRQL addressed in this study are the physical, emotional, functional and social dimensions. The physical dimension reflects the patient's ability to perform activities of daily life in spite of the illness and the associated physical symptoms. The social/family dimension reflects the person's ability to build and maintain sound relationships and interactions in one's social environment. The emotional dimension reflects the ability to cope with the feelings and perceptions despite the illness and reflects the patient's status of

optimism and anticipation. Finally, the functional dimension studies the patient's competence to assume roles and perform tasks and jobs needed to feel content (Sprangers, 2002, Bowling, 2001).

The figure below shows the interrelations of the health-related quality of life dimensions along with the patients' characteristics. These associations are based on the empirical literature and anecdotal clinical evidence. Because the dimensions of HRQL are inter-related, its measurement cannot be exclusive to one dimension, and cannot ignore the effect of the individual variations related to home, jobs, social support, and emotional status on health. In addition, the patient's clinical characteristics and the underlying illness affect his/her physical QoL and consequently other aspects of his/her HRQL. Hence the selection of the below demographic and clinical characteristics of the patients.

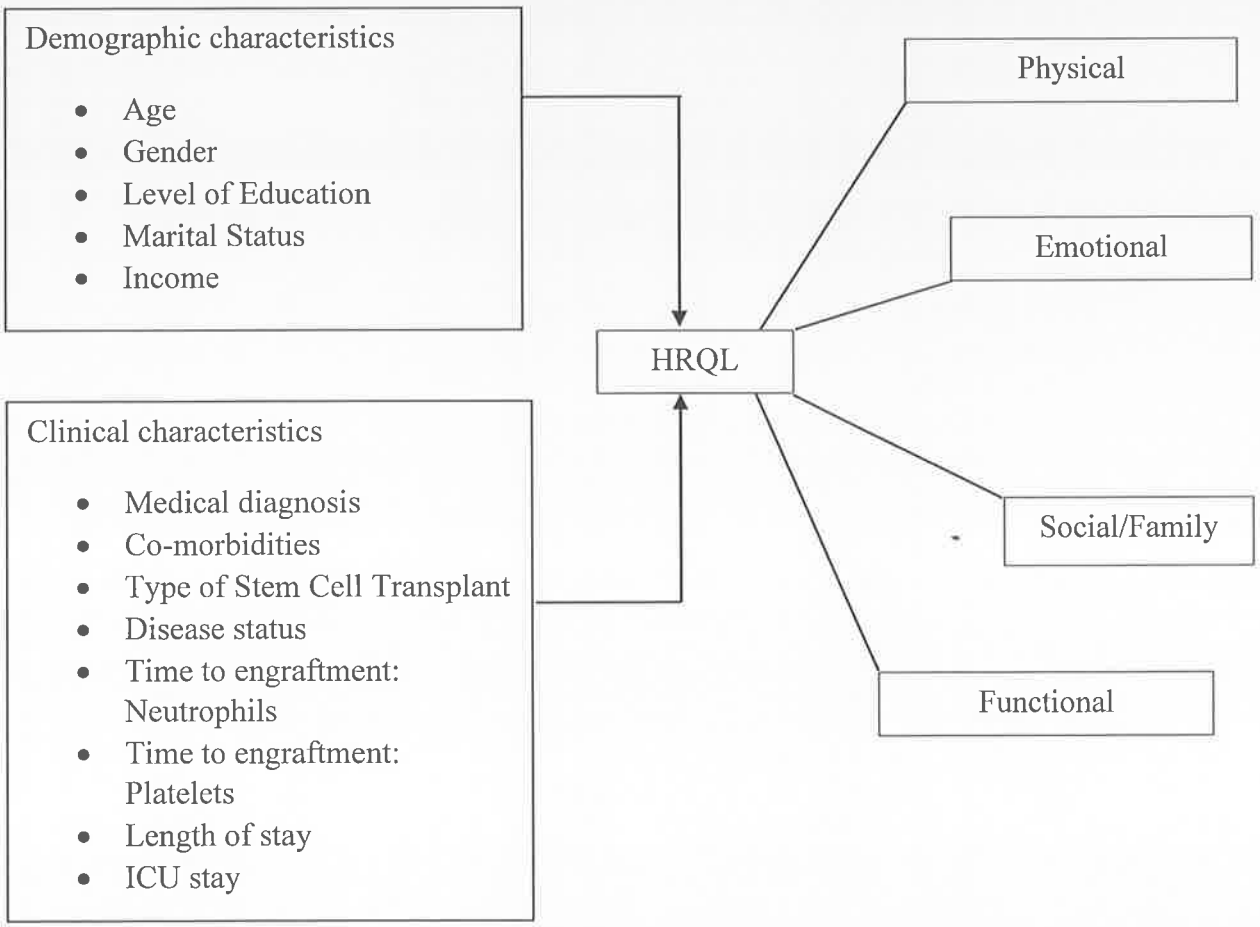

Figure 1: Conceptual Framework of the Study

CHAPTER IV

METHODS

A. Design

The study used a longitudinal observational design. Adult patients who were planned to go through HSCT were interviewed at different stages of the transplant period. Patients undergoing HSCT have significant checkpoints in time, where the evaluation of their disease is done, and hence the results of the transplant are evaluated. The longitudinal design is appropriate for examining changes in HRQL over time. The time points of data collection were chosen as they denote significant milestones in the patient's trajectory.

Day +7 after transplant is the time when patients complete their conditioning regimen. Due to a deep level of myelosuppression, patients are at the utmost risk of developing fatal infections, and at the peak effect of side effects of chemotherapy and/or radiation therapy. During this period, patients have their social encounters limited to phones, video calls, and social media. Hence, the selection of this point in time becomes important in order to capture the perceptions on their health.

At the time of discharge, patients are supposed to take responsibility for their health, and for self-care at home, and so they receive information and education about precautions to be taken among other aspects of care. This period of close monitoring from afar is critical, as patients are still prone to develop infections, viral re-activation, and acute graft-versus-host disease. They are in close contact with their health care team, and the information exchanged during their clinic visits are paramount to their care and follow up. The 30 and 100-day periods after transplant were selected for an interview because this is when a disease

evaluation is usually scheduled, and for the reason where the patients become more independent in managing their care.

B. Sample and Recruitment

The study used a convenience sample of 40 patients consecutively admitted for HSCT to the bone marrow transplant (BMT) unit of the American University of Beirut Medical Center (AUBMC). The sample size represented half the number of patients who undergo this procedure at AUBMC per year. Below are the inclusion and exclusion criteria.

1. Inclusion Criteria

All patients aged 18 years and above scheduled for HSCT at AUBMC, who can and are willing to participate in the study and verbally agree on an informed consent, were included in the study. Both autologous and allogeneic HSCT patients of both sexes were included in the study, regardless of their disease.

2. Exclusion Criteria

Patients who did not agree to sign the informed consent were excluded from the study. In addition, patients with a mental disability or a cognitive dysfunction that hinders them from understanding the informed consent were excluded. In addition, some patients would still have an active disease at the time of transplant, where the disease status is not considered a remission (e.g. blast cells in leukemia patients, active lymph nodes in lymphoma patients). These patients usually have symptoms that can be referred to their disease that might be the same as the side effects of chemotherapy cellular therapy, and thus they were excluded. For the same reason, other patients who might be in relapse during a point in time

where disease evaluation is checked had their participation terminated from the study. However, the data provided by their participation prior to being censored were included in the data analysis.

3. Recruitment

Study subjects are the patients of the HSCT program at AUBMC. Patients planned for HSCT are usually discussed in a weekly planning meeting. The discussion in this meeting includes an overview of brief history and previous treatments, type of transplant, type of donor, admission date, conditioning regimen, estimated length of stay, and anticipated complications, in addition to existing psychosocial conditions including family and/or caregiver issues. The patients who are eligible for inclusion in the study were identified to be recruited as subjects by the study coordinator. The primary attending physician in the specialty clinic introduced patients to the study prior to admission for transplant, where it is a routine to see their primary physician for information on the procedure.

Once admitted, those willing to participate were introduced to the study by a research fellow who explained the study procedures and obtained the informed consent (Appendices A and B). As the coordinator of the study has a direct relationship with the patients and their families in his role of care provider and facilitator, the research assistant/fellow who is a medical doctor involved in the research activity of the program and hired by the HSCT program at AUBMC took the consent. The informed consent was taken for a series of interviews that were done as face-to-face in a private setting (patient's room or a secluded office.)

Fifty-six transplant patients were eligible for inclusion; sixteen refused to participate in the study for several reason that include lack of interest, fatigue, and unwillingness to share individual stories and perceptions. Forty patients were included with a response rate of 71.4 per cent. One patient died in the intensive care setting on day +30 of the transplant, three other patients had a disease relapse before day +100, and one patient withdrew from the study as she was travelling to live abroad. Thus at day +100, there were still 36 patients. One patient was late for the day +100 the follow up, and after data was in process for analysis.

C. Data Collection

The data was collected partly from the patients' medical records, and partly by face-to-face interviews. The interviews were conducted in the patient's room while he/she was hospitalized, and later following discharge from the hospital in a private room in the clinic or in the transplant coordinator's office.

As patients were selected and an informed consent was obtained (Appendices A and B for informed consent form, English and Arabic). Data were taken from the patient's medical record (Appendix C) including demographic data and information related to the diagnosis and the course of transplant. A unique patient number (Appendix D) was given to each patient and was referred to as a "study number". Study Numbers were listed against the patient's initials and the patient's unique hospital medical record number on one excel sheet for future reference and tracking. The study coordinator conducted the interviews as follows:

1. Admission: On admission, or just before starting the conditioning regimen
2. One week after transplant (day +7): At this point, patients start to experience side effects of chemotherapy and they start to have pancytopenia, and this adds to some of

the complications they might have (e.g., febrile neutropenia, fatigue, increased need for transfusion of blood products)

3. Discharge: Acute illness has resolved; residual side effects of chemotherapy might be witnessed
4. Day +30 post-transplant for autologous HSCT: All patients have their disease evaluation checked around this day. The average length of stay at AUBMC for autologous HSCT patients is 12 to 14 days after transplant, and that for allogeneic patients is 20 to 23 days after the day of transplant. However, if a discharge is delayed due to any complicated condition in either allogeneic or autologous HSCT patient, the day +30 survey can be done on discharge
5. Day +100 post-transplant: Addressing any post-transplant complications and the back-to- normal life routine at home, school, work, etc.

D. The study Questionnaire

Many tools are used to measure HRQL. Some of them are generic while others are disease-specific or condition-specific. The Short Form (SF-36) is a non-disease specific generic scale that is used to assess the health-related quality of life in individuals. The tool has a special role in studying HRQL in chronic disease conditions, and has no questions in relation to sickness, income, or social status (https://qolty.com/q/sf-36/, accessed April 27, 2018). The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) is a tool utilized to measure the quality of life in cancer patients and not specifically in patients undergoing HSCT. In a study done by Kopp et al. (2000), the tool was introduced to 56 HSCT patients in Germany and was translated to Arabic and validated by Huijer et al. in 2013.

The Functional Assessment of Cancer Therapy (FACT) tool has been used to measure the magnitude of disease and treatment-related complications and side effects in patients with cancer since the mid-1990s. The FACT-BMT, a version of the FACT, is a valid and reliable tool that has been created to measure the HRQL specific to patients undergoing bone marrow transplant. This tool was first published after validation in 1997 and has been used worldwide to assess the HRQL in HSCT patients. A multidimensional tool assesses the well-being of HSCT patients over five dimensions. These dimensions are physical, social, emotional, functional, and a fifth dimension "additional concerns" that addresses the general side effects of transplant and chemotherapy. Patients rate their answers to each of the 50 questions on a Likert Scale rated from zero to four: Zero = not at all, one = a little bit, two = somewhat, three = quite a bit, and four = very much (McQuellon et al., 1997).

The questionnaire is usually self-administered and patients are asked to recall their symptoms and experiences for the past seven days. Each dimension of the tool has a mean score; a high score on social/family and functional dimension reveals a high quality of life, and a low score on the physical and emotional dimension as well as on the additional question section reveals a high quality of life (Appendices E and F for the FACT-BMT tool, English and Arabic).

FACT-BMT form was designed to measure the quality of life in patients undergoing bone marrow transplantation. It adds transplant-related questions to the FACT-G (general), a widely used tool primarily assessing physical well-being, social and family well-being, emotional well-being, and functional well-being. In a study by Martino et al., (2017), the quality of life in patients with multiple myeloma undergoing autologous HSCT was studied using the FACT-BMT at three points in time, a week before and a week after HSCT, and then at day +30 after transplant. The study compared patients in the inpatient setting to those in the outpatient setting. Inpatients scored higher mean compared to outpatients in physical well-

being. On the other hand, outpatients scored higher mean score than the inpatients on the social and family well-being. Pulewka et al., (2017), used the FACT-BMT tool with a focus on adolescents and young adults in comparison with their older counterparts when both populations had graft-versus-host disease (GvHD). The study reported higher mean scores on the physical well-being and activity for the younger population than those of older adults. La-Nasa et al. also used the tool on patients with thalassemia major 20 years after transplant in a study, in 2013. The authors reported low mean scores on the FACT-BMT tool in patients who had chronic GvHD, and those with comorbidities or living alone.

The tool has a coefficient of internal consistency ranging 0.86 to 0.89 on the various subscales (McQuellon et al., 1997). The tool was translated to Arabic and validated by Soudi et al. in 2009, and used in a research on lymphoma patients undergoing autologous HSCT. The Arabic translation of Soudi et al. (2018) was tested with an internal consistency Cronbach alpha coefficient of 0.90; and a range of 0.67 to 0.91. Cronbach's alpha coefficient for the subscales of social (0.78), emotional (0.67) and functional well-being of (0.88) were reported.

One group of Japanese investigators utilized both the SF-36 and the FACT-BMT version 4 in 36 post-BMT patients (12 allogeneic and 24 autologous), where both questionnaires were administered in a cross-sectional survey. The study indicated the feasibility of using the FACT-BMT in one-time follow-up of quality of life in post-transplant Japanese patients (Imataki, et al., 2010.) In comparison to the EORTC QLC-C30, it was found that the FACT-BMT covers comprehensively the multidimensional construct of quality of life, while the EORTC QLQ-C30 has a better insight on the physical aspects of quality of life.

In addition to the questions listed in the (FACT-BMT) assessment tool, other demographic and clinical variables were collected. These include, but not exclusive to: patient's age, sex, level of education, marital status and income, disease status at transplant, duration from diagnosis to transplant, treatment lines of therapy (chemotherapy, immunotherapy, radiation treatment), as well as type of transplant (autologous versus allogeneic), type of conditioning, type of donor, and the sequence of the current transplant (first or redo). This data were collected using a medical record review while the patient was hospitalized.

E. Ethical Considerations

Approvals from the Institutional Review Board (IRB) of the University and from the administration of the medical center were obtained on May 27, 2019 (Appendix G). Adherence to the rules and regulations of the IRB about recruitment of subjects, informed consent, data collection, patient's privacy and confidentiality and any other measure that mandates the protection of the human subjects participating in this study were maintained.

1. Benefits

There was no direct benefit to the subjects participating in the study. However, as the literature on the Lebanese patients undergoing HSCT has little evidence on the HRQL, the inferences drawn from the data will be used for the benefits of the future HSCT patients.

2. Risks

No more than minimal harm was expected as a risk to study participants. Participants were asked to take the time to decide whether or not participate while they were admitted in the hospital (initial assessment and the week after) and when they came back for their day

+30 and day +100 evaluation. Interview appointments were coordinated during the time a disease evaluation and/or clinic appointments are scheduled. The primary physician, the research fellow obtaining consents have a long experience in conducting research studies with the target population. The study coordinator conducting the interviews has been an oncology/transplant nurse for a period of 23 years and has an experience in approaching patients, and will ensure patients' well-being during the process of informed consent and data collection. None of the research subjects has shown any signs of anxiety during the interviews. The interview tackled mental health aspects of participants along with physical and functional aspects of their health. No adverse events related to the study were noted.

3. Privacy and Confidentiality

Consents were obtained by a research assistant/fellow who is a medical doctor hired by the HSCT program. As their primary physician in the confidential setting of the doctor's clinic introduced patients to the study, an undue influence on the patient was somehow avoided even when the study coordinator had a daily direct relationship with the patient as a care provider/facilitator. Consents were taken for a series of interviews, yet the procedure of the interview was explained at every point in time the questionnaire was administered. Interviews were done by the HSCT research fellow in a private setting (patient's room or secluded office) ensuring minimal interruptions. None of the research subjects was illiterate, hard of hearing, or had any visual impairment.

Patients were given a unique study number. A password-protected electronic record of the patient's unique study number was attached to the patient's initials and hospital medical record number and this record was only used for future references when the questionnaires were administered, or to mark those patients who for any reason withdrew from participation. All data on paper records was transferred into a spreadsheet using Statistical Package for

Social Sciences (SPSS) and then stored in a locked cabinet. On the other hand, electronic records were kept in a password-protected computer that is a property of AUBMC and backed up on a separate record [external disk] that is saved in a locked cabinet/drawer.

F. Statistical Analysis

The data were entered and analyzed in SPSS version 25. Descriptive analyses, using means and standard deviation for continuous variables and frequencies and percent for categorical variables were used to describe the sample characteristics: Diagnoses, age, disease status, type of HSCT and type of donor, length of hospitalization, co-morbidities, all the demographic data and the FACT-BMT scores. Based on the different directions of the items on the additional questions scale, with nine positively worded items and the rest negatively worded, reverse coding was performed to get one direction out of all the questions and the mean calculated accordingly. Due to the small sample size and to the skewness of the data of HRQL, nonparametric statistical tests were used to determine the statistical significance of variation of HRQL scores over time and associations with predictors. Logarithmic transformation of the variables that measured the HRQL dimensions was created to draw the univariate and bivariate analyses because most of these variables were skewed to the right. The level of statistical significance was set at 0.05, for 2-tailed tests.

For study aim # 1, the Friedman test was used to compare variations of the means within the sample across the different time points. Wilcoxon test was used to compare means of the same group (i.e. the whole sample) in a pairwise fashion between the various time points. For these multiple comparisons the significance level was 0.05 divided by the number of tests that is 10, thus $p = 0.005$ was considered statistically significant to account for multiple testing.

For aim # 2, the Mann-Whitney test was used to compare the means of two independent subgroups (sex groups and type of transplant groups) at the various data collection time points, and the Wilcoxon test to compare means within each group.

For aim # 3, univariate and multivariate regression analyses to predict the physical and emotional dimensions at time 2 (day 7 following HSCT), and the social and functional dimensions at time 4 (day 30 post HSCT) using the log transformed outcome variables. Following univariate analyses, those predictors with a p value of 0.25 or below were entered in the multivariable regression analysis.

CHAPTER V

RESULTS

A. Sample Characteristics

The sample included 40 patients, with completed data on the outcome variables on 35 patients at day 100 (due to the 4 subjects who were lost as described above). The majority of the subjects in the sample were autologous HSCT patients (N=26, 65%) whereas allogeneic HSCT patients constituted the rest (N=14, 35%). Thirty subjects (75%) were males and 10 (25%) were females. The distribution of the subjects among their sex and the type of transplant does not differ much from the general transplant population at AUBMC.

The majority of the subjects (95%) were Lebanese and living inside Lebanon with a major concentration in and around Beirut (37.5 %). The mean age for patients at the time of transplant was 50.45 years with standard deviation of 13.75 and a range of (23 – 74 years). The rest of the sample's demographic characteristics are outline in Table 1.

Table 1. Sample Demographic Characteristics (N = 40)

Variable	Frequency	Percentage
Age at transplant (Mean ± Standard Deviation)	50.45 (±13.75)	
Sex		
Males	30	75.0
Females	10	25.0
Nationality		
Lebanese	38	95.0
Palestinian	1	2.5/2.5
Iraqi	1	
Residence		
Beirut	15	37.5
Mount Lebanon	10	25.0
South Lebanon	7	17.5
North Lebanon	5	12.5
Bekaa	2	5.0
Iraq	1	2.5
Marital Status		
Married	30	75.0
Divorced	5	12.5
Single	4	10.0
Widowed	1	2.5
Living Conditions		
With family	36	90.0
Alone	4	10.0
Third-Party (Guarantor)		
NSSF	16	40.0
Private insurance/Self-payer	8/8	20.0/20.0
Government agency	7	17.5
NSSF + Private insurance	1	2.5
Occupation Status		
Self-employed	10	25.0
Paid leave	10	25.0
Retired	7	17.5
Unpaid leave/Unemployed	6/6	15.0/15.0
Employed	1	2.5
Income		
< $500	1	2.5
$500 - $999	11	27.5
$1000 - $1499	6	15.0
$1500 - $1999	9	22.5
≥ $2000	1	2.5
Education		
Basic	13	32.5
High school	10	25.0
University	15	37.5
Vocational	2	5.0

The majority of the study subjects were patients with plasma cell disorders (N=14), followed by patients with lymphoma (N=13), and acute leukemia (N=12.) Three patients were diagnosed with myelofibrosis and myelodysplastic syndrome. Most of the patients (65%) underwent autologous transplant from a matched related donor (71.43%), with an average of 11 days until engraftment of neutrophils and 19 days until platelet engraftment. The average length of stay was 24 days, with only three patients transferred to ICU during hospitalization, and another two admitted to ICU following discharge. Only four patients had history of having undergone prior SCT.

Patients with history of mental illness constituted 20 % of all patients. Other co-morbidities among the subjects included diabetes, obesity, impaired pulmonary function, and dysrhythmias. The co-morbidity index is a score given based on 15 pre-existing conditions that do not carry the same weight as one another. The score is called Sorror score and it is used by HSCT centers when patients are reported to EBMT. The highest score that can be recorded on the co-morbidity index is 26, meaning a higher risk for transplant-related mortality and a lower progression-free survival (Sorror et al., 2005.)

The mean LOS for the autologous subjects 20.6 (± 4.2) days and a range of 15 to 30 days, and 31.6 (± 5.5) days for the allogeneic patients with a range of 26 to 43 days.

For autologous subjects, the mean for ANC engraftment was 10 (± 2.2) days with a range of 8 to 18 days, whereas for platelet engraftment, the mean time was 19.5 (± 6) days with a range of 11 to 38 days. Allogeneic subjects engraft their ANC at a mean of 15 (± 4.5) with a range of 12 to 28 days, and for platelets at 17.3 (± 6.4) days with a range of 8 to 31 days. The rest of the sample's clinical characteristics are outlined in Table 2.

Table 2. Sample Clinical Characteristics (N = 40)

Variable	Mean ± Standard Deviation	
Age at Diagnosis (Years)	48.2 ± 14.59	
Diagnosis to SCT (days)	789.35 ± 1009	
ANC Engraftment (days)	11.5 ±4.03	
Platelet Engraftment (days)	18.82 ±0.18	
Length of Stay	24.48 ±23.5	
LOS in ICU during SCT in days (N=3, 7.5%)	3.67 ± 3.0	
LOS in ICU within 100 days post SCT in days (N=2, 5.0%)	5 ± 2.8	
Variable	**Frequency**	**Percent**
Diagnosis		
PCD	14	35.0
NHL	8	20.0
AML	8	20.0
HL	5	12.5
ALL	4	10.0
Myelofibrosis	2	5.0
MDS	1	2.5
Co-Morbidity Index		
0	20	50.0
1	14	35.0
2	5	12.5
3	1	2.5
History of Mental Illness	8	20.0
Type of SCT		
Autologous	26	65.0
Allogeneic	14	35.0
Type of Donor		
Match related	10	71.43
Mismatch related	4	28.57
Prior SCT	4	10.0
Treatment Lines prior to SCT		
1 lines	13	32.5
2 lines	7	17.5
3 lines	11	27.5
4 lines	5	12.5
5 lines/8 lines	1/1	2.5/2.5
6 lines	2	5.0
Disease Status at SCT		
CR	23	57.5
VGPR	11	27.5
PR/Residual/stable disease	3 /3	7.5/7.5
Acute GvHD	14.3	14.3

Legend: ALL: Acute lymphocytic leukemia; AML: acute myelocytic leukemia; ANC: absolute neutrophil count; CR: Complete Remission; GvHD: Graft versus Host Disease; HL: Hodgkin lymphoma; MDS: Myelodysplastic Syndrome; NHL: Non-Hodgkin Lymphoma; PCD: Plasma Cell disorder; PR: Partial Response/Remission SCT: Stem cell transplant; VGPR: Very Good Partial Response

B. Health Related Quality of Life Trajectory

The means of each dimension on the FACT-BMT were calculated with their standard deviations using SPSS. The below table shows the variations of different means across the different points in time where the interviews were conducted with the patients. The data are presented as means ± standard deviation.

Table 3. Changes in HRQL Scores of all Subjects over Time

Dimension/Time	Admission	Day +7	Discharge	Day +30	Day +100
N	40	40	39	39	30
Physical	0.11 ± .26	1.16 ± .89	0.40 ± .46	0.23 ± .36	0.30 ± .35
Social/Family	3.54 ± .34	3.30 ± .23	3.30 ± .24	3.36 ± .23	3.53 ± .29
Emotional	0.78 ± .19	0.98 ± .31	0.82 ± .22	0.87 ± .27	0.95 ± .28
Functional	3.37 ± .47	2.54 ± .55	3.02 ± .40	3.23 ± .42	3.28 ± .44
Additional	1.36 ± .15	1.45 ± .17	1.41± .13	1.38 ± .20	1.38 ± .19

In order to decide on the normal distribution of the sample, the skewness of each variable was divided over its standard error. The results of all dimensions except for the social/family dimension showed a result above 2.0, which indicated skewness of the data of the HRQL dimensions. Hence, nonparametric statistical tests were used.

A Friedman test was then conducted to determine the significance of the variation of the means of the scales of the FACT-BMT over the four time points. There were statistically significant changes ($P = 0.000$) in the means over time for the four dimensions (physical, emotional, social and functional), but not the additional questions scale ($P = 0.283$). The means of each domain were ranked against one another by using Wilcoxon test. Statistically significant changes were noted, with day +7 results showing the worse quality of life on all four dimensions. Linear graphs were done to show the changes of the means over time for

each dimension. These are shown in the graphs below.

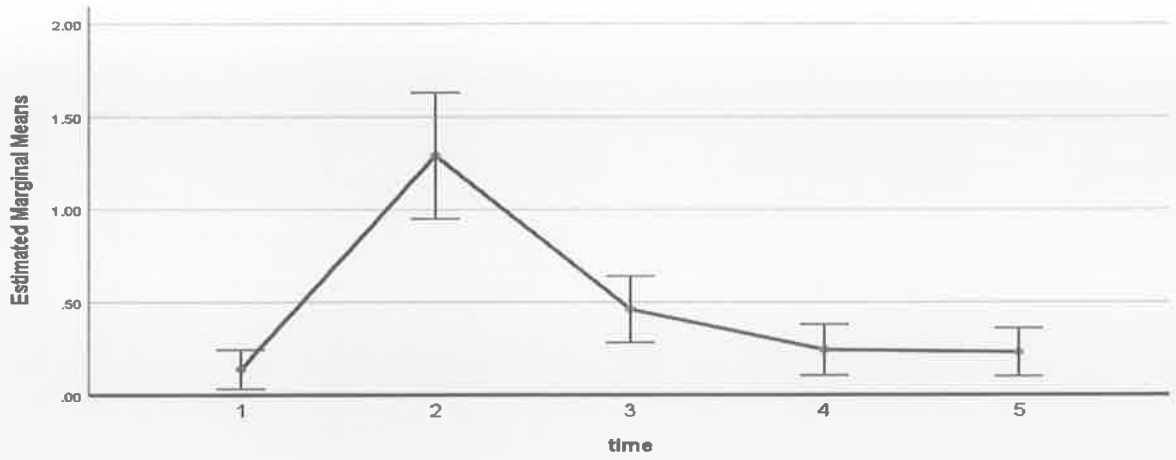

Figure 2. Variation of the physical dimension scores across time

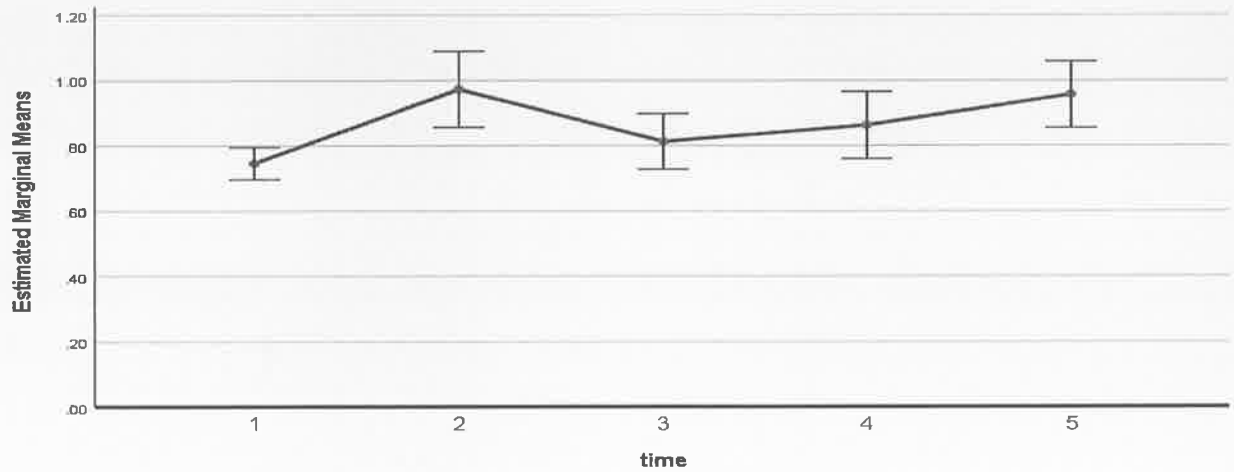

Figure 3. Variation of the emotional dimension scores across time

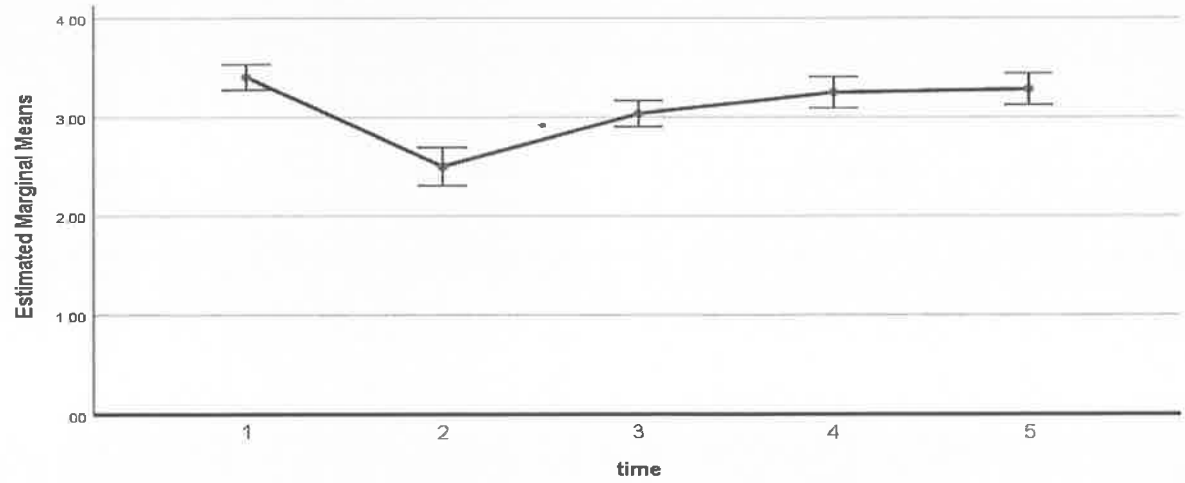

Figure 4. Variation of the social/family dimension scores across time

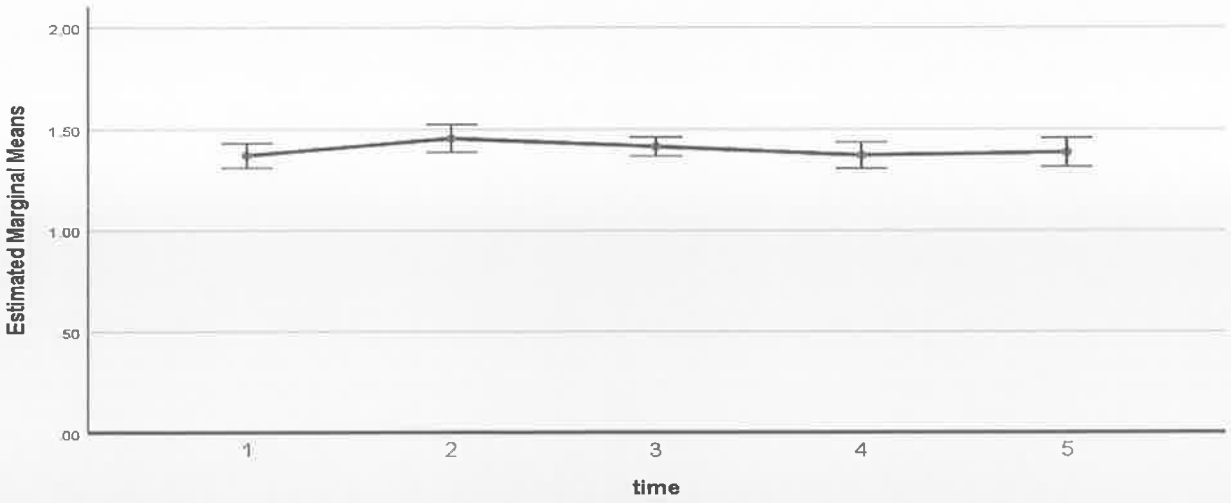

Figure 5. Variation of the functional dimension scores across time

It was noticed that there is a common trend among all groups, where quality of life is shown as worse on day +7 following the transplant.

It was noted in Figure 2 that there is an increase in the HRQL mean (worse QoL) for the physical and emotional dimensions from the baseline assessment to peak on day +7, then it starts to drop on discharge until days +30 and +100, at which point the mean does not return to its baseline value. On the social/family and functional dimension (Figures 3 and 5), a drop in the mean (worse QoL) from baseline to day +7 is noted, then the mean starts to rise after the day of discharge and continues to rise on day +100, but it does not return to its baseline value. A similar trend is noted in emotional dimension (Figure 4).

However, to trend these values in a statistically sound method, a Wilcoxon Test was run in SPSS. A statistically significant difference was shown between the mean on day +7 and the rest of the means of the physical dimension: baseline, the day of discharge, and day + 30, and day +100 with (P = 0.000 for all the comparisons). A statistically significant difference was also noted between the baseline mean and that on the day of discharge (P = 0.000). On the social and family dimension, a statistically significant difference was found between the baseline intake and that of day +7, the day of discharge (P = 0.000) and day +30

(P = 0.003). Another significant difference was also found between the day of discharge and day +100 (P = 0.002). On the emotional dimension a significant difference was noted between the mean at baseline, that of day +7 (P = 0.000) and day +100 (P = 0.000), as well as between day +7 and the day of discharge (P = 0.002). On the functional dimension, the significant difference was noted between the mean recorded on day +7 and the rest of the means (P = 0.000). Finally, there were no significant changes in the means of the additional questions scale across time.

C. HRQL Variation by Sex

For better understanding of the variations between the different groups within the sample, the data was split between the two major independent groups divided by sex and HSCT type. Means and standard deviation for each subgroup were calculated using Friedman's Test. Each group's means were ranked to detect variation within the group using Wilcoxon Test on SPSS. Again, the changes over time were overall significant for all the dimensions except the additional questions scale

To answer aim # 2, the mean of all dimensions were compared between the two groups using Mann-Whitney test at each of the various data collection time points. Statistically significant differences between males and females were shown only on the physical dimension on all time points (P = 0.009 for baseline assessment, P = 0.022 for day +7, and P = 0.024 for the day of discharge) except for day +30 (P = 0.165) and day +100 (P = 1.000). Although the trends of means for both groups took the same fluctuation on the social/family, emotional, and functional domains, there were no statistically significant difference when men and women were compared.

The figures below (Figures 6, 7, 8 and 9) show the means of the various dimensions for males and females over time. As can be seen in the figures, the patterns of changing

means for the male and female subjects did not differ from that of the whole group in terms of trending the means across time. The means for all dimensions reflected the worse quality of life at day 7, and an improvement on day +30 and day +100.

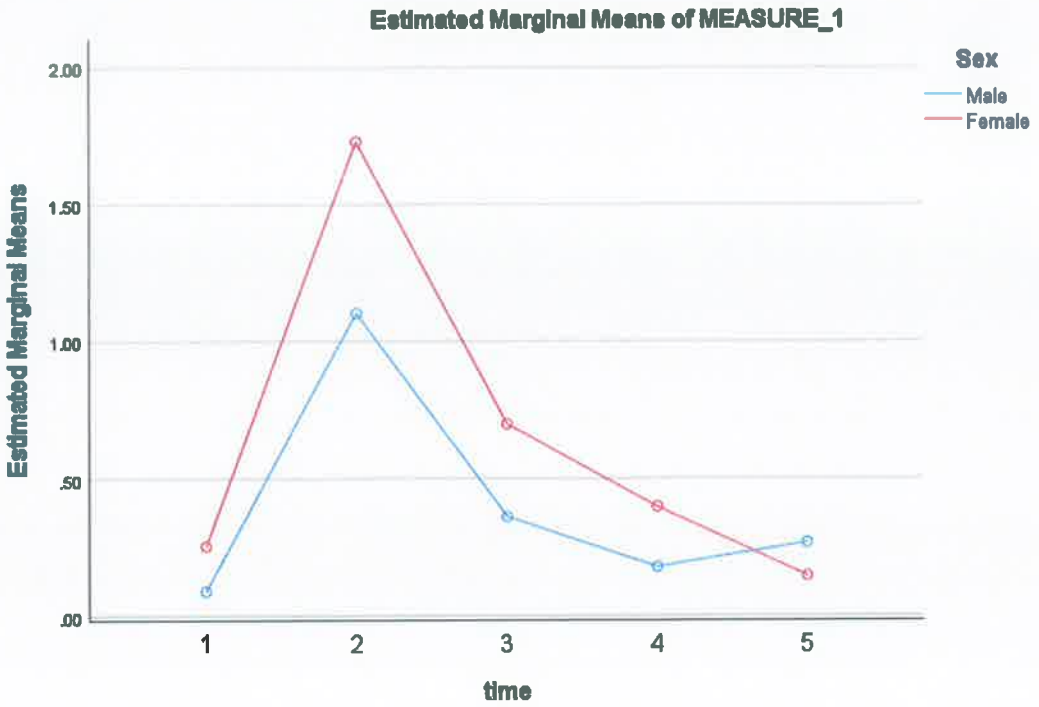

Figure 6. Changes in the HRQL Physical dimension over time for males and females

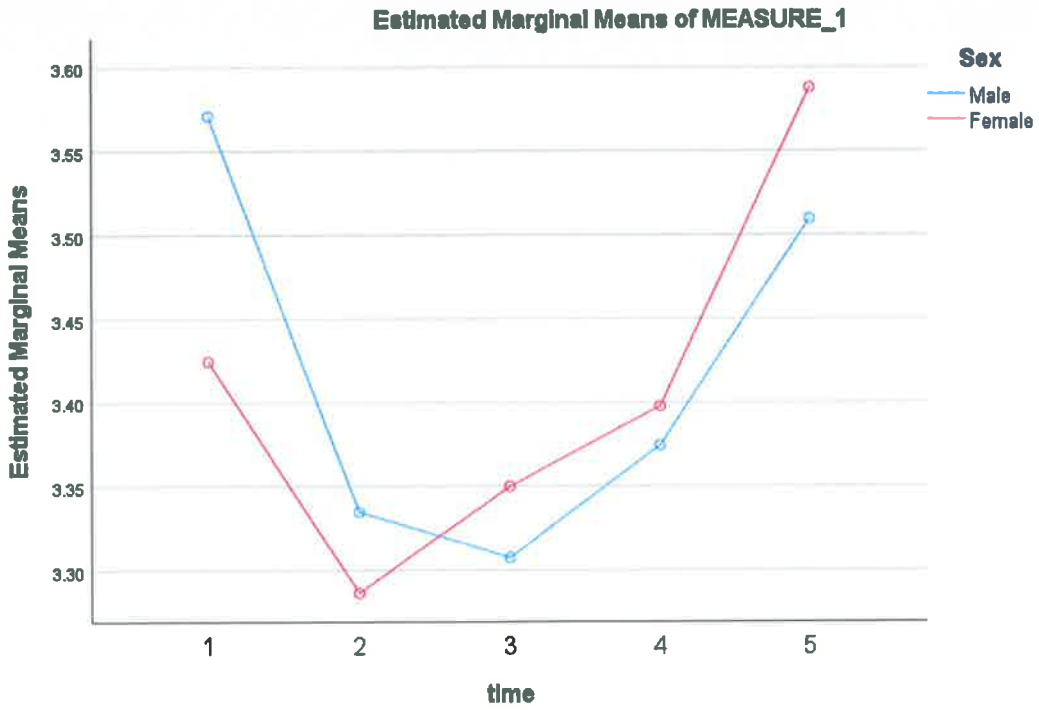

Figure 7: Changes in the HRQL Social dimension over time for males and females

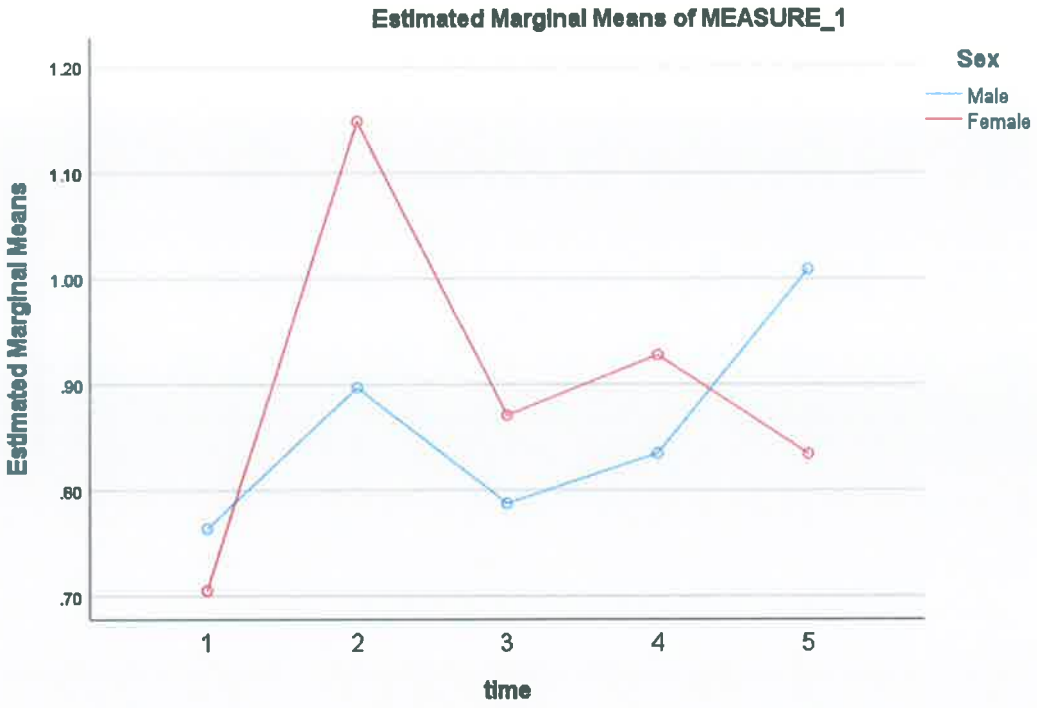

Figure 8: Changes in the HRQL Emotional dimension over time for males and females

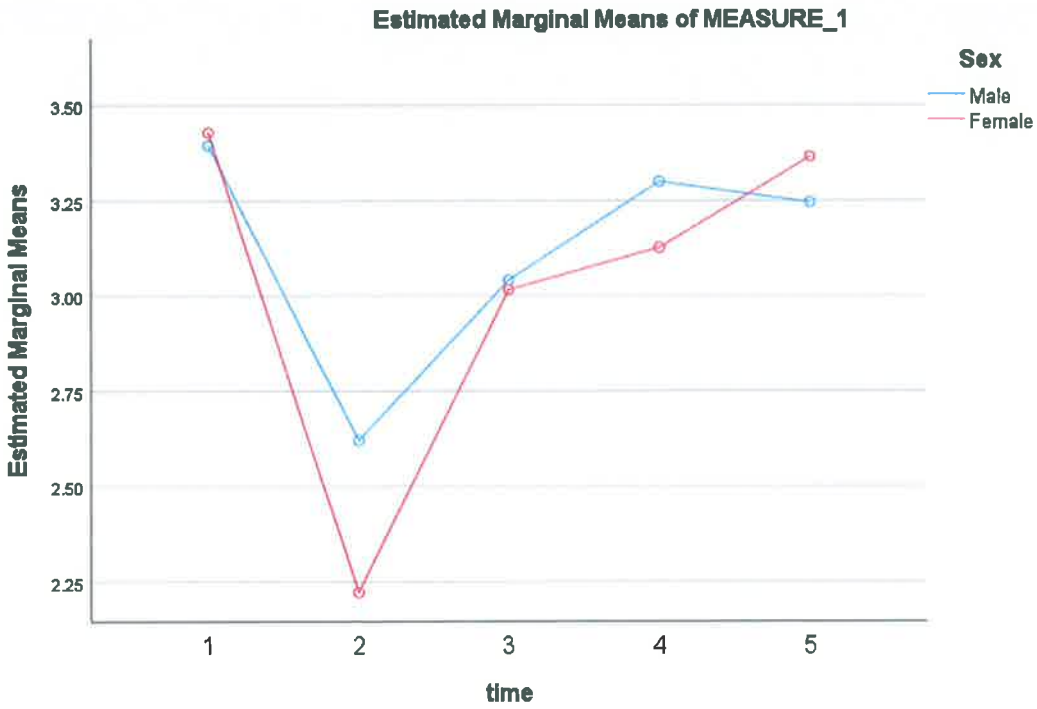

Figure 9. Changes in the HRQL Functional dimension over time for males and females.

We examined next trends within each group separately and the values of the means for all dimensions for males is shown in Table 4 below.

Dimension/Time	Admission	Day +7	Discharge	Day +30	Day +100	P-value
N	30	30	29	29	21	
Physical	0.07 ± .24	0.98 ± .79	0.31 ± .39	0.18 ± .29	0.26 ± .41	0.000
Social/Family	3.58 ± .32	3.31 ± .20	3.30 ± .21	3.35 ± .22	3.50 ± .31	0.001
Emotional	0.80 ± .21	0.93 ± .27	0.80 ± .21	0.86 ± .26	1.00 ±.30	0.001
Functional	3.40 ± .47	2.66 ± .52	3.05 ± .37	3.27 ± .41	3.24 ± 0.50	0.000
Additional	1.39 ± .16	1.44 ± .15	1.41 ± .13	1.41 ± .19	1.42 ± .18	0.754

Table 4. HRQL mean scores of male subjects across time

For males, there was a statistically significant difference in the physical dimension between the baseline mean and that of day +7 (P = 0.000) and between the baseline and the day of discharge (P = 0.003), as well as between day +7 and the day of discharge (P = 0.000), day +30 (P = 0.000) and day +100 (P = 0.002). On the social and family dimension, a significant difference was found between the baseline mean and that of day +7, as well as between the means at baseline and the day of discharge (P = 0.000). On the emotional dimension, significant differences were shown between the means at baseline and day +7 (P = 0.001), and between baseline and day +100 (P = 0.001). Finally, significant differences were noted on the functional dimension between day +7 and the rest of the other time points (P = 0.000).

The same analysis was made for the group of females and results are show in Table 5. Below are the results for the female group. Similar to the group of male patients, the changes over time were significant except for the additional questions scale.

Dimension/Time	Admission	Day +7	Discharge	Day +30	Day +100	P-value
N	10	10	10	10	9	
Physical	0.29 ± .28	1.70 ± .98	0.67 ± .53	0.37 ± .51	0.14 ± .14	0.000
Social/Family	3.42 ± .37	3.26 ± .33	3.30 ± .31	3.38 ± .26)	3.58 ± .22	0.021
Emotional	0.72 ± .07	1.15 ± .39	0.88 ± .26	0.90 ± .33	0.83 (± .18)	0.006
Functional	3.30 ± .49	2.18 ± .46	2.90 ± .50	3.11 ± .45	3.36 ± .26	0.000
Additional	1.29 ± .13	1.48 ± .23	1.40 ± .12	1.27 ± .20	1.30 ± .20)	0.121

Table 5. HRQL scores of female subjects across time

Results were similar for the male and female groups. On the physical dimension, the mean on day +7 was significantly different from those at the rest of the time points (P = 0.005). The means at discharge and at day +100 were also significantly different with P-value of 0.028.

D. HRQL Variation by Type of Transplant

The same analysis was made to compare the autologous and allogeneic transplant groups regarding their means HRQL scores in the various dimensions at the various data collection points. . When the means for both groups of autologous and allogeneic subjects were compared using Mann-Whitney Test on SPSS, there were no statistical significant difference between the mean scores of any dimension at any time point. However, the reporting of worse QoL on all domains was shown on day +7 for both groups. . The fluctuation of the means on all dimension is shown in Figures 10, 11, 12, 13 below.

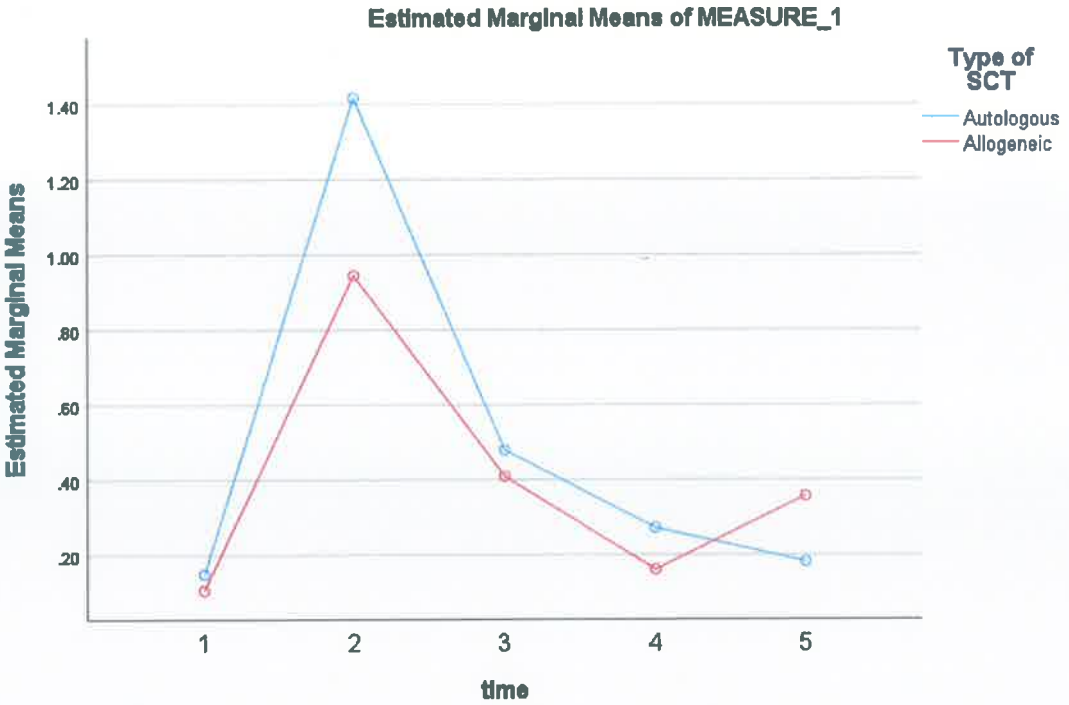

Figure 10. Changes in the HRQL Physical Dimension scores over time for the autologous and allogeneic Groups

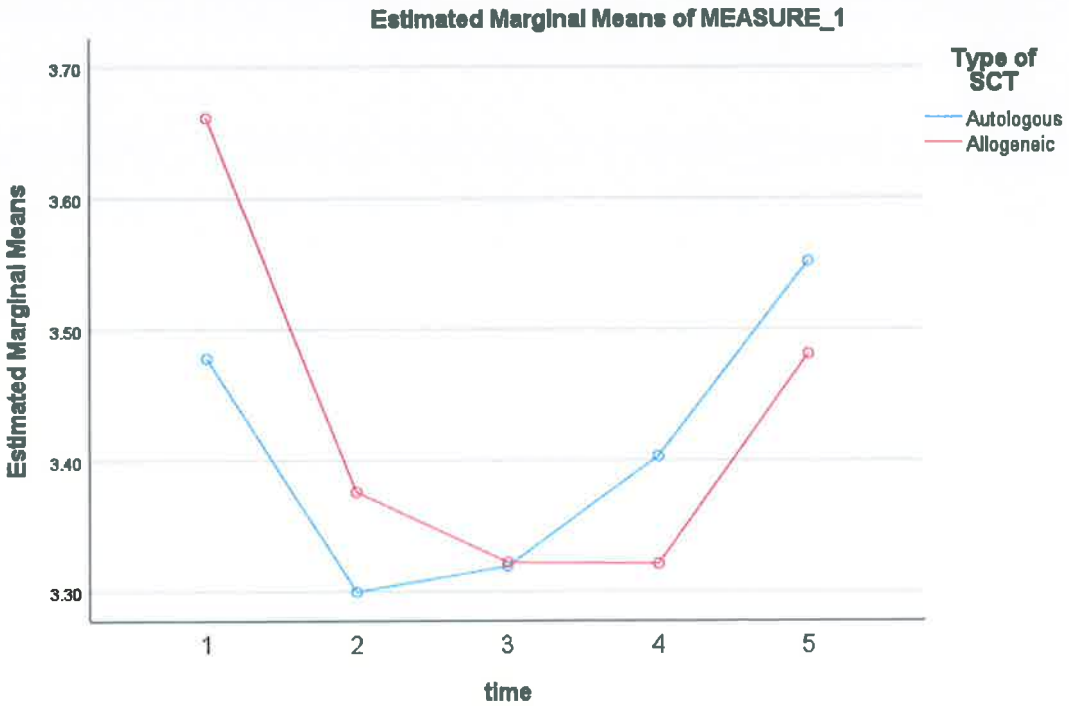

Figure 11. Changes in the HRQL Social Dimension scores over time in the autologous and allogeneic groups.

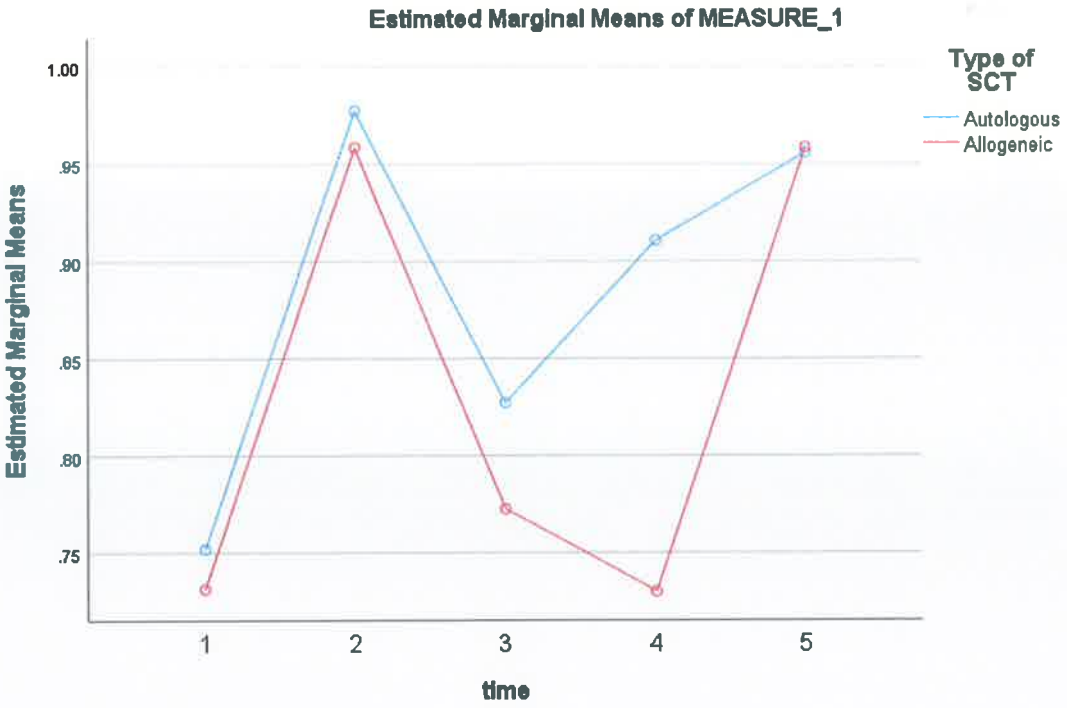

Figure 12. Changes in the HRQL Emotional Dimension scores over time in the autologous and allogeneic groups.

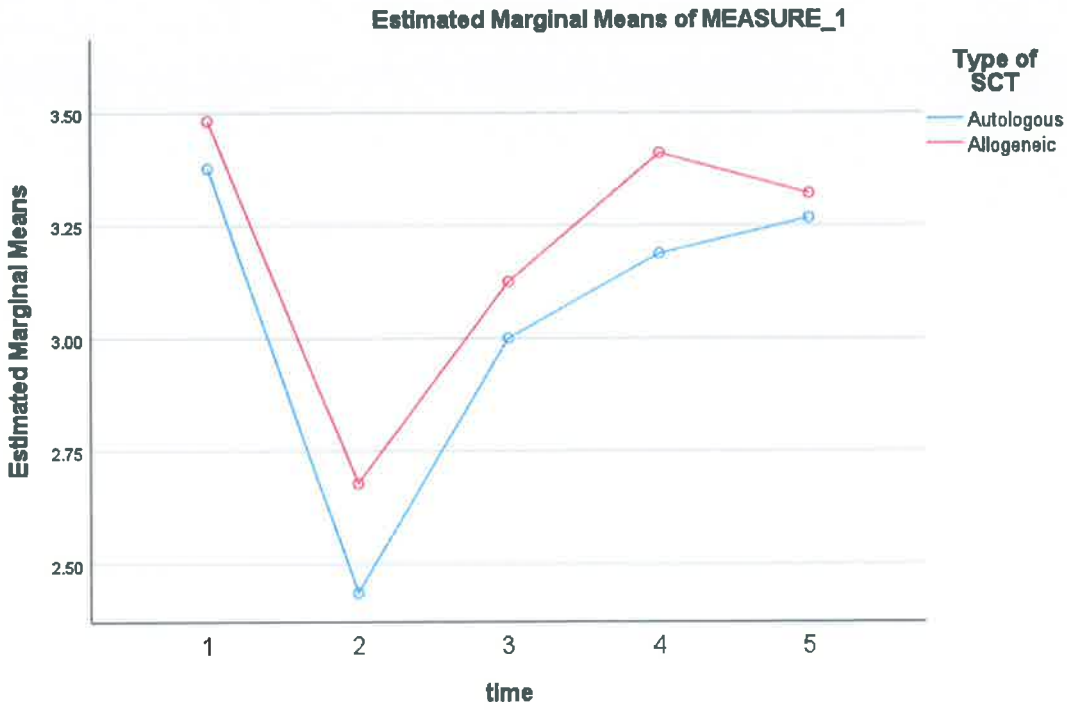

Figure 13. Changes in the HRQL Functional Dimension scores over time in the autologous and allogeneic groups.

The same trends were noticed when the data were examined for the autologous and allogeneic subjects. The values of the mean scores for all the dimensions at the five data collection points for the autologous and allogeneic group are shown in Tables 6 and 7, respectively.

Dimension/Time	Admission	Day +7	Discharge	Day +30	Day +100	P-value
N	26	26	26	26	22	
Physical	0.13 ± .29	1.30 ± 1.01	0.42 ± 50	0.26 ± .40	0.18 ± .29	0.000
Social/Family	3.51 ± .3	3.30 ± .25	3.31 ± .27	3.39 ± .23	3.35 ± .28	0.000
Emotional	0.76 ± .14	0.95 ± .34	0.81 ± .24	0.89 ± .30	0.95 ± .28	0.007
Functional	3.31 ± .51	2.48 ± .59	2.96 ± .44	3.17 ±.49	3.26 ± .45	0.000
Additional	1.35 ± .17	1.45 ± .19	1.41 ± .14	1.38 ± .23	1.37 ± .19	0.281

Table 6. HRQL scores of autologous subjects across time

Dimension/Time	Admission	Day +7	Discharge	Day +30	Day +100	P-value
N	14	14	13	13	8	
Physical	0.81 ± .20	0.91 ± .52	0.36 ± .36	0.17 ± .26	0.36 ± .49	0.001
Social/Family	3.60 ± .30	3.28 ± .21	3.29 ± .15	3.28 ± .22	3.48 ± .32	0.990
Emotional	0.82 ± .25	1.03 ± .26	0.84 ± .17	0.83 ± .23	0.95 ± .29	0.013
Functional	3.48 ± .37	2.66 ± .46	3.12 ± .32	3.34 ± .21	3.32 ± .43	0.001
Additional	1.38 ± .11	1.44 ± .13	1.40 ± .10	1.38 ± .14	1.41 ± .21	0.946

Table 7. HRQL scores of allogeneic subjects across time

In the autologous transplant group, the mean on day +7 for the physical dimension was significantly different from the rest of the means (P = 0.000), yet the trend was not

significant between baseline and the day of discharge (P = 0.132) nor between baseline and day +100 (P = 0.674). Moreover, the changes over time were significant for all dimensions except the additional questions scale.

The same thing can be said about the allogeneic group, where day +7 means were significantly different from the rest of the means on the other time points for the physical dimension; however, the mean did not trend back to baseline on day +30 (P = 0.173) and day +100 (0.293). For the rest of the dimensions, the means on day +7 were statistically significant from the rest of the means on the other time points. One exception is the social/family that did not show significant differences in the changes of the means over time (p=0.990). Finally, there were no significant changes in the additional questions means in neither the autologous nor the allogeneic group.

E. Factors associated with HRQL at Day +7 and Day +30

The means of all dimensions except for the social/family were skewed. A logarithmic transformation was done to ensure a normal distribution of the outcomes variables, i.e. the scores on the physical, emotional, social and functional scales, in order to draw inferences about the correlations and test the predictor(s) for each dimension. The additional questions scale was not included in these analyses because it is multidimensional and the small sample size does not allow factor analyses to be made so subscales of this scale can be analyzed.

One point in time was taken from each domain to identify the possible predictors of that domain. Because of the limited sample size, and to avoid multiple testing, initial correlations between the scales at each time point were done, and many significant ones were found. For instance, the social and emotional HRQL scores were significantly associated at all the data collection time points; the same was true for significant correlations between the

physical and the functional scales at all data collection time points. The decision was to select the outcome variables to be tested for predictors according to the following considerations.

First, during the hospital stay, the physical dimension was shown to be worse on day +7 and so was the emotional domain. Hence the selection of those two dimensions was made for correlational analyses at day +7 following transplant. Moreover, on day +100, most patients reported scores reflecting a good quality of life. However, due to censorship of the patients who died and relapsed after transplant, and because of missing data on the last five patients on day +100, it was decided to take the social/family dimension as well as the functional dimension scores at day +30. Thus, we examined predictors of the physical and emotional dimensions at day 7, and the predictors of the social and functional dimensions at day 30 following the transplant. After the univariate regression analyses were completed with all demographic and clinical variables, every selected dimension was found to have several predictors that had p value < 0.25, and these were entered in the multivariate analysis.

The correlates of the physical dimension on day +7 were sex, co-morbidity index, and disease status at transplant. When these were entered in the multiple regression analysis, the model explained 20.2% of the variance in the physical dimension as per the adjusted R^2 ($P=0.012$) as shown in Table 8. The only significant predictor was sex, with women predicting higher scores on the physical dimension.

	Unadjusted analysis		Adjusted analysis				
Predictor	B	P value	B	Standardized Beta	95% CI for B		P value
					Lower Bound	Upper Bound	
Sex	0.273	0.022	0.234	0.314	0.004	0.463	**0.046**
Disease Status	-0.119	0.014	-0.085	-0.278	-0.204	0.043	0.195
Co-morbidity Index	-0.086	0.200	-0.080	-0.196	-0.180	0.010	*0.078*

Table 8. Linear regression for the physical dimension on day +7. CI: confidence interval

As for the emotional dimension on day +7, the correlates were sex, presence of mental illness, disease status at transplant, length of stay and engraftment of absolute neutrophil count (ANC). When entered in the multiple regression, the model explained 13.2% of the variance in emotional QOL (p=0.079), with none of the predictors significant. There was a trend for women to maintain higher scores than men as shown in Table 9.

	Unadjusted Analysis		Adjusted Analysis				
Independent Variable	B	P value	B	Standardized Beta	95% CI for B		P-value
					Lower Bound	Upper Bound	
Sex	0.088	0.064	0.088	0.297	-0.012	0.187	*0.082*
Disease Status	-0.026	0.190	-0.003	-0.024	-0.044	0.038	0.888
Mental Illness	0.071	0.169	0.013	0.259	-0.026	0.192	0.131
ANC Engraftment	0.008	0.145	0.007	0.369			
Length of Stay	0.005	0.085	0.000	0.024			

Table 9. Linear regression for the emotional dimension on day +7. CI: confidence interval

The correlates of the social and family dimension on day +30 were type of HSCT and engraftment of platelets. When entered in the multiple regression, the model explained only 4.2% of the variance (p=0.173) and none of the predictors was significant as shown in Table 10 below.

	Unadjusted analysis		Adjusted Analysis				
Predictor	B	P value	B	Standardized Beta	95% CI for B		P-value
					Lower Bound	Upper Bound	
SCT Type	-0.014	0.175	-0.012	-0.185	-0.033	0.009	0.260
Platelet Engraftment	0.001	0.133	0.001	0.212	-0.001	0.003	0.196

Table 10. Linear regression for the social/family dimension on day +30. CI: confidence interval

The correlates of the functional dimension on day +30 were age, type of HSCT, and engraftment of ANC. On the assessment of the functional dimension on day +30, it was found that 13.4 % of the variance of that mean was explained by the independent variables (P = 0.045). In the multivariate analysis, age was a significant predictor of functional QOL.

	Unadjusted Analysis		Adjusted Analysis				
Predictor	B	P value	B	Standardized Beta	95% CI for B		P-value
					Lower Bound	Upper Bound	
SCT Type	0.027	0.207	0.009	0.069	-0.042	0.060	0.723
Age at SCT	0.002	0.036	0.002	0.349	0.000	0.003	**0.027**
ANC Engraftment	0.005	0.082	0.005	0.250	-0.003	0.012	0.206

Table 11. Linear regression for the functional dimension on day +30. CI: confidence interval.

CHAPTER VI

DISCUSSION

The study provides data taken for the first time in Lebanon on the HSCT patient population about their HRQL before, during, and after transplant. The study also provides information on the fluctuation of the means of all dimensions of QoL across time. It may be of importance for health care professionals to self-prepare with knowledge, skills, and attitudes ahead of time while providing care for transplant patients, as well as for patients to have a glance on the perceptions of other patients while mentally and emotionally getting ready for their own procedure.

Transplant patients in this study were interviewed to assess the dimensions of QoL before, during, and after transplant at points that were considered sensitive in the trajectory of the physical and emotional symptoms. All dimensions were assessed and followed over time. The Health related quality of life significantly decreased in all patients during the first two weeks of the study in all the dimensions, as reflected by the difference between initial assessment and that done on day +7. All patients had their HRQL scores return near their initial baseline assessment in one to three months after transplant.

The patterns of fluctuation were the same between men and women at all dimensions, however women reported more severity of symptoms than men did. The fluctuations followed the same pattern between allogeneic and autologous subjects; however, there has not been much of a difference between these two groups when it came to comparing the means of each dimension.

A. HRQL Changes over Time

Comparison of our findings to the literature was challenging because of the limited number of studies, variation in the tools used to measure HRQL, and the varied time points used for data collection. Moreover, most of the published prospective studies discussing QoL in the HSCT setting were addressing one aspect of the patient's QoL and not all the dimensions. All of the patients in the study have had anti-cancer treatment with chemotherapy, radiation therapy, and/or immunomodulators, and had their QoL already affected prior to transplant. This could add to the immediate side effects of the conditioning regimen, and consequently justifies the major turn in the means to reflect the worse quality of life on all dimensions, especially that of day +7. This is consistent with the findings of Grant (2012) where patients in his studies manifested increased levels of fatigue following the preparative regimen (around day +7) and low scores on the functional dimension at the time of discharge (Hacker, 2006). On the other hand, Hjermstad (1999), Syrjala (1993), and Chao (1992) showed that the back-to-baseline scores took a minimum of six months and up to 2 years. The follow up on this study, however was up to day +100 post-transplant only.

For the emotional dimension, the findings in this study were consistent with Cohen Ghazikhanian (2017), Jim (2014), Nelson (2014), Cohen (2012), Hacker (2006), Conner-Spady (2005), and Gaston-Johnson (1996) who individually showed that the rates of depression had doubled between the first week of transplant and the day of discharge, and went back to baseline 3 months after transplant. The studies of Yasar and Akin (2016), Lee (2010), Le (2001), and Kopp (1999), showed that the scores were near the baseline was at seven months after the post-transplant and up to five years.

The scores on the social/family dimension were high on all patients at all time-points in this study. One possible explanation is the strong family ties and social support provided

by the family within the Lebanese culture, as well as the health professionals in the transplant unit during the relatively long hospitalization of these patients. This could also be related to social desirability to respond to an outside surveyor in a manner they see expected by the surveyor.

B. Factors associated with HRQL

Several analyses that yielded an incongruence with the review of the literature can be attributed to the size of the sample. Whilst the sample was taken as a whole, the fluctuation of the means across time were showing a statistical significance that can be interpreted from the clinical perspective; however, analyses by groups such as disease status, marital status, and diagnoses could not be done because of the small number within these groups. Has the sample size been larger, the tests might have shown more relevant results.

The multiple regression analyses showed that women tend to have poorer quality of life at day 7 following the transplant on the physical and emotional dimensions. On the other hand, at day 30, age predicted better functional quality of life. None of the studies reviewed reported sex differences in quality of life in this population. On the other hand, Hamilton et al. (2014) reported worse social function in those older than 60 years of age than their younger counterparts did. In this study, age was associated with functional status in a positive way, probably because the sample is younger, with 70% of patients younger than 60 years.

C. Limitations

There are a number of limitations that warrant caution in interpreting the results:

1. ***Sample***

- The sample was drawn from one medical center, and may not represent the whole population of Lebanese patients who undergo bone marrow transplant.
- The small sample size limited the types of data analyses and comparisons that could be made. The sample was diverse in relation to sex and type of transplant, yet there was a limitation in making inferences to the subcategories of the allogeneic subjects into the different types of conditioning, as well as in categorizing autologous subjects by diagnosis where patients with plasma cell disorders receive one day of conditioning versus 6 days for patients with lymphoma. The sample was representative in its composition between allogeneic and autologous transplant patients, yet the size did not permit to stratify allogeneic patients who received myeloablative conditioning in comparison with those who received the non-myeloablative regimens. The same comment can be made in relation to the type of donor (match related vs. match unrelated vs. mismatch related) and the source of stem cells (bone marrow vs. peripheral blood).
- Only two patients in the sample have developed acute GvHD, an issue that makes it challenging to account for these patients in the analysis. The same thing can be said about the two patients who were transferred to an intensive care setting.
- As the sample size gets bigger with continued recruitment, more information can be collected about the patients who receive post-transplant maintenance, where the physical symptoms can be related to the targeted/immune therapy they receive.

2. ***Tool/Questionnaire***

- Another limitation relates to the questionnaire used in this study, which was not validated in the Lebanese population of BMT patients. The FACT-BMT is a validated tool for assessing HRQL in transplant patients; however, the additional questions

address different aspects of QoL. The same domain addresses financial issues, social support and interactions, relationships with nurses, and physical symptoms. This may explain why all analyses pertaining to this scale were non-significant. With a larger sample, factor analysis can be conducted and the analysis streamlined accordingly. Some of the questions addressing family support, social networks, optimism, and acceptance were all answered towards the best, and almost exclusively creating a ceiling effect that affected the results of the correlational analyses.

D. Clinical Implications

This is the first study in Lebanon to document the quality of life in HSCT patients. The transplant activity in Lebanon has shown an exponential growth in the last ten years in terms of number of patients. When the sample size is bigger and more analysis of the outcomes can be drawn, inferences can be taken into account for patients, caregivers, and health care providers. It is also recommended to extend the follow up to one year following transplant in order to capture the needs of these patients. Expanding data collection to other transplant centers in the country can improve generalizability of the findings.

The role of a clinical nurse specialist in the setting of HSCT and malignant hematology is substantial to address the needs of this patient population, preparing them for a successful transplant in terms of patient and family education and support, as well as for post-transplant triaging and follow up. The findings of this study can inform advanced nursing practice for including assessment of HRQL of patients during hospitalization and follow up visits in order to identify health issues holistically and provide interventions tailored to the patients' needs. As some of the transplant patients return to their referring physician after a short period of follow up with the transplant physician, it is necessary for the referring health

care team to understand the trajectory of transplant, the potential complications, and the needed follow-ups for the HSCT patients.

E. Recommendations

This is the first study that addresses the HRQL of HSCT patients in Lebanon. Knowing that the transplant activity is growing, there has been improvement in the overall survival of transplant patients, which requires more studying of the needs of these patients. The sample size used for this study could start a cohort of patients that could also be assessed over a longer period than day +100 post-transplant to extend up to two years after transplant. The FACT-BMT tool can be further studied to meet the needs of the different research questions that could change over time, and to be validated for the Lebanese population. Assessment of HRQL is recommended to be integrated in the care plan of these patients as part of clinical practice, with the transplant coordination of clinical nurse specialist utilizing the findings to develop an outreach program for these patients so that their health care needs are met and subsequently their quality of life is improved. Additional variables that can be included in future studies are the side effects and symptoms reported, which could explain the sex difference in some of the dimensions of health related quality of life in this study.

F. Conclusion

Transplant patients have health needs that require to be met ahead of time, prior to the transplant, during the hospitalization, and extending to the community for years to come. These needs are not merely physical, and they are to be addressed by a health care team that is holistic and multidisciplinary.

APPENDIX

Appendix (A): Consent Form (English)

Consent Form

Consent to Participate in a Research Study

Health-Related Quality of Life (HRQL) in Adult Patients Following Hematopoietic Stem Cell Transplant

Investigator Dr. Laila Farhood

Address American University of Beirut, Cairo Street, Beirut – Lebanon

Phone Number: 01-350000, extension 5975

Site where the study will be conducted: American University of Beirut Medical Center

Dear Participant,

You are being asked to participate in a clinical research study conducted at the American University of Beirut. Please take time to read the following information carefully before you decide whether you want to take part in this study or not. Feel free to ask your doctor if you need more information or clarification about what is stated in this form and the study as a whole.

My name is Ali Ibrahim; I am a research fellow working for the Bone Marrow Transplant (BMT) Unit at the American University of Beirut Medical Center (AUBMC.) Based on conversation with your physician indicating your approval to be approached for this research project, you are invited to participate in a clinical research study. You are one of 40 patients who will be recruited for the study. The aim of this research is to describe health related quality of life in patients undergoing hematopoietic stem cell transplant.

The investigators of the study are Professor Laila Farhood, Professor Samar Noureddine, Professor Ali Bazarbachi. The study coordinator of the study Mr. Ammar Zahreddine, is a registered nurse in the BMT Unit at AUBMC and he will be conducting a study to assess and monitor the health-related quality of life in patients undergoing hematopoietic stem cell transplant. Other information will be taken from your medical record and includes your age, general health information, co-morbidities, time of diagnosis, and previous treatment; and for patients having allogeneic transplant, information on donors in regard to kinship and the degree of matching will also be collected from the medical record.

The study includes all adult patients aged 18 years and above who are undergoing a transplant, regardless of their disease and regardless the type of transplant. The study excludes patients who have a progressive disease at the time of transplant. The study also excludes later on any patient who has a disease relapse during their participation.

If you agree to participate, you will be interviewed on admission, one week following the transplant, around the time of discharge, one, and three months after transplant when you come for the follow up; and additional data collection point: at 6 months, one and two years' post-transplant. The estimated time to answer the interview questions is about 20 minutes.

Your privacy will be highly maintained during the interviews as they will be conducted in your room or in a private office. The forms where your answers are documented will be kept in a locked cabinet and only the investigators of the study will have access to them.

Your name and phone number as well as other identifying information will be removed before analyzing the data and presenting the results. Names and phone numbers will not be entered on any computer software and will only be found on a separate sheet linked to the questionnaire by a code number. Hard copies of the questionnaire will be stored in a locked cabinet in the office of one of the investigators. Our records will be audited by the Institutional Review Board while assuring confidentiality.

Although you will not receive any direct benefit from this study, the information you provide may benefit other patients as it will enable us to better understand the needs of patients undergoing stem cell transplant.

The study is purely for research purposes. Your participation is voluntary. If you decline participation in this study or if you decide to withdraw from participation at any time during the study, we assure you that the care you receive at AUB will never be compromised. You can accept or decline to participate knowing that refusal will not affect your relationship with AUB/AUBMC nor the care you will receive. You can also drop out from the study at any time you want.

There will be no financial or in kind compensation for those who participate.

If you have any questions, you are free to ask them now. If you have questions, concerns, or complaints about this research study, you may contact the primary investigator Dr. Laila Farhood on 01-350000, extension 5975, or by e-mail at lf00@aub.edu.lb

If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about research or your rights as a participant, please contact the AUB Biomedical Sciences Institutional Review Board (IRB) at AUB on 01**350000**, extension 5445, or by e-mail at irb@aub.edu.lb

Thank you

Investigator's Statement

I have reviewed, in detail, the informed consent document for this research study with _____ (name of patient, legal representative, guardian), the purpose of the study and its risks and benefits. I have answered all the patient's questions clearly. I will inform the participant in case of any changes to the research study.

_____	_____	_____
Name of investigator or designee	Signature	Date and Time

Patient's Participation

I have read and understood all aspects of the research study and all my questions have been answered. I voluntarily agree to be part of this research study and I know that I can contact Dr. Laila Farhood at 01350000, extension 5975 or any of her designee involved in the study in case of any questions. If I feel that my questions have not been answered, I can contact the Institutional Review Board for human rights at 013**50000**, extension 5445, or by email to irb@aub.edu.lb. I understand that I am free to withdraw this consent and discontinue participation in this project at any time, even after signing the form, and it will not affect my care or benefits. I know that I will receive a copy of this signed informed consent.

_____	_____	_____
Name of patient or legal representative or guardian	Signature	Date and Time

_____	_____	_____
Name of witness (if patient cannot read or write)	Signature	Date and Time

Appendix (B): Consent Form (Arabic)

موافقة مستنيرة

موافقة للإشتراك في البحث العلمي

مقياس نوعية وجودة الحياة عند المرضى الذين خضعوا/اللواتي خضعن لزرع الخلايا الجذعية/نقي العظم

الباحث الدكتورة ليلى فرهود

العنوان الجامعة الأمريكية في بيروت، شارع القاهرة، بيروت - لبنان

هاتف: 01-350000 مقسم: 5975

مكان إجراء البحث: الجامعة الأمريكية في بيروت المركز الطبي

عزيزي المشارك/عزيزتي المشاركة،

أنت مدعو(ة) للمشاركة ببحث علمي سريري سيجرى في الجامعة الأمريكية في بيروت. الرجاء أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بتأن قبل أن تقرر(ين) إذا كنت تريد(ين) المشاركة أم لا. بإمكانك طلب ايضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الإستمارة أو عن هذه الدراسة ككل من طبيبك.

إسمي علي ابراهيم وأنا طبيب وباحث لدى برنامج زرع نقي العظم في المركز الطبي في الجامعة الأميركية في بيروت. وبناء على ما تم التحدث عنه مع طبيبكم آنفا، أود أخذ موافقتكم على الإشتراك في هذا البحث العلمي.

انت شخص من حوالى 40 مريض يعالجون عن طريق زرع نقي العظم والذين نرمي إلى إستهدافهم للمشاركة في هذا البحث. إن الهدف من هذا البحث هو دراسة ومعرفة نوعية الحياة عند المرضى الذين خضعوا/اللواتي خضعن لزرع الخلايا الجذعية/نقي العظم.

سوف يتم إجراء البحث تحت إشراف الدكتورة ليلى فرهود، الدكتورة سمر نورالدين، والدكتور علي بازرباشي. ونحن نسعى إلى الكشف عن ومراقبة نوعية حياة المرضى الذين خضعوا/اللواتي خضعن لزرع الخلايا الجذعية/نقي العظم. منسق هذا البحث هو عمار زهرالدين وهو ممرض مجاز في قسم زرع نقي العظم في المركز الطبي للجامعة الأميركية في بيروت. سوف يتم الإطلاع على سجلكم الطبي في المستشفى بهدف الحصول على بعض المعلومات المتعلقة

بصحتكم، على سبيل المثال: العمر، تاريخ التشخيص، العلاجات السابقة، أمراض أو حالات صحية أخرى. عند الأشخاص الذين يتلقون الزراعة الخيفية (من متبرع) سوف يتم جمع بعض المعلومات من السجل الطبي للمتبرع/ة بما يتعلق بدرجة القرابة ونسبة المطابقة.

يتم إدخال جميع المرضى الذين أتموا الثامنة عشرة من العمر والموافقين على المشاركة، وبصرف النظر عن التشخيص أو نوع العملية. يستثنى من هذه الدراسة المرضى الذين يصلون الى مرحلة زرع نقي العظم مع نسبة عالية من المرض، او الذين يعانون من ارتكاس للمرض خلال وقت الدراسة.

في حالة موافقتكم على المشاركة سوف يتم إجراء مقابلات على مراحل محددة من فترة العلاج: عند الدخول إلى المستشفى، بعد زرع الخلايا الجذعية بحوالى الأسبوع، عند الخروج من المستشفى، بعد زرع الخلايا الجذعية بمدة شهر، ثلاثة أشهر، ستة أشهر, سنة واحدة، وسنتين. سوف يتم الإتصال بكم أثناء إجراء تحاليل المتابعة أو أثناء زيارتكم لعيادة الطبيب.

لا يتعدى وقت إجراء المقابلة مدة العشرون دقيقة.

سوف يتم الحفاظ على خصوصيتكم من خلال إجراء المقابلات في غرف مغلقة للحفاظ على سرية مشاركتكم كما على خصوصية اجوبتكم. وحدهم الأشخاص المشرفون على البحث سيتم لهم الإطلاع على أجوبتكم.

سوف يتم أخذ اسمائكم وارقام هواتفكم وحفظها على مستند منفصل عن لائحة الأسئلة والإجابات، وسيتم إستخدامها فقط عند الحاجة للإتصال بكم. وسوف يتم ربط لائحة الأسماء باستمارات الإسئلة والأجوبة من خلال رمز يعطى لكم عند أخذ موافقتكم على المشاركة وإجراء المقابلة الأولى. سوف تحفظ جميع اوراق البحث بما فيها أجوبتكم أو أسمائكم أو أرقام هواتفكم في خزانة مقفلة عند أحد الباحثين الرئيسيين، كذلك الأمر بالنسبة لملفات الكمبيوتر التي تفتح فقط عبر كلمة مرورخاصة.

لحماية خصوصيتكم أثناء إجراء هذا البحث وللحفاظ على نزاهة البحث وحماية المشاركين (ات) يجري مجلس مراجعة الأبحاث في الجامعة الأميركية في بيروت عمليات مراجعة للمقابلات وحفظ المستندات على الأبحاث.

إن هذه الدراسة هي محض علمية ومشاركتكم بها طوعية، ولن يكون هناك أي بدل مادي مقابل هذه المشاركة. لكن المعلومات المعطاة من قبلكم سوف يتم الإستعانة بها لمرفة الإحتياجات الصحية لمرضى زراعة الخلايا الجذعية مستقبلا.

كذلك نود إعلامكم بأن عدم رغبتكم في المشاركة لن ينعكس سلبا وبأي شكل من الأشكال على جودة الرعاية الصحية التي تتلقونها في المركز الطبي للجامعة الأميركية في بيروت. كما باستطاعتكم سحب وتعليق مشاركتكم في الدراسة في

أي وقت ودون ان ينعكس قراركم سلبا على جودة الرعاية الصحية التي تتلقونها في المركز الطبي للجامعة الأميركية في بيروت.

في حال موافقتكم على المشاركة في هذا البحث سيبقى اسمكم طي الكتمان، ولن يكون لأي شخص باستثناء الباحثين الرئيسيين الواردة اسماؤهم/اسمائهن أعلاه ولجان الأخلاق المهنية المستقلة، ومفتشين الإدارات المنظمة حق الإطلاع على سجلكم الطبي.

في حال لديكم اسئلة أو استفسارات، يرجى التحدث بها الآن، او توجيهها الى الباحث الرئيسي للدراسة الدكتورة ليلى فرهود على الرقم 01-350000 مقسم: 5975 أو عبر البريد الألكتروني lf00@aub.edu.lb

في حال عدم رضائكم عن كيفية إدارة البحث أو لتعليقاتكم وملاحظاتكم حول حقوقكم كمشاركين/مشاركات يرجى الإتصال بمجلس مراجعة البحوث في الجامعة الأميركية في بيروت (Institutional Review Board, IRB) على الرقم 01-350000 مقسم: **5445** أو بارسال بريد الكتروني إلى irb@aub.edu.lb

شكرا جزيلا

إفادة الباحث

لقد شرحت بالتفصيل للمشارك/ة _____ (اسم المشارك/ة، أو الممثل القانوني، أو الوصي) طبيعة البحث ومجرياته وتأثيراته، ولقد أجبت عن جميع الأسئلة بوضوح على خير ما أستطيع. وسوف أعلم المشارك/ة بأي تغيرات في مجريات هذا البحث او تأثيراته السلبية أو فوائده في حال حصولها أثناء البحث.

_____ _____ _____

اسم الباحث (أو الشخص المخول الحصول على الموافقة على المشاركة) التوقيع التاريخ والساعة

إفادة (موافقة) المشترك/ة

لقد قرأت إستمارة القبول هذه وفهمت مضمونها. ولقد تمت الإجابة عن جميع اسئلتي، وبناء عليه فانني حرا/ة مختارا/ة، أجيز إجراء هذا البحث وأوافق على الإشتراك فيه، وإني أعلم أن الباحث الدكتور ليلى فرهود والزملاء/الزميلات المعاونين/ات سيكونون على استعداد للإجابة على أسئلتي، وانه باستطاعتي الإتصال بهم على

الرقم 01-350000 مقسم: 5975 أو عبر البريد الألكتروني lf00@aub.edu.lb. وإذا شعرت لاحقا ان اسئلتي تحتاج إلى المزيد من الإيضاح فسوف أتصل بأحد أعضاء بمجلس مراجعة البحوث في الجامعة الأميركية في بيروت

(Institutional Review Board, IRB) على الرقم 01-350000 مقسم: 5445 أو بارسال بريد الكتروني إلى irb@aub.edu.lb. كما أدرك تماما بأن لي الحق بالإنسحاب من مشاركتي في هذا البحث متى شئت وحتى بعد التوقيع على الموافقة، وبدون أن يؤثر ذلك على الرعاية الصحية المقدمة لي.

كما أني أعلم انني سأحصل على نسخة موقعة من هذه الموافقة.

_____	_____	_____
اسم المشارك/ة، أو الممثل القانوني، أو الوصي	التوقيع	التاريخ والساعة
_____	_____	_____
اسم الشاهد/ة (عند تعذر المريض/ة عن القراءة أو الكتابة)	التوقيع	التاريخ والساعة

Appendix (C): Demographic and Medical Record Data

Research Study Number:			Admission date:		Discharge date:		
Sex:	☐ Female	☐ Male	Nationality:		Residence:		
Marital Status:			Living with:	☐ Alone	☐ Family	☐ Friends	☐ Roommate
Guarantor(s)	Occupation Status:	☐ Employed	☐ Paid Sick leave	☐ Unpaid Sick Leave	☐ Retired	☐ Disabled	Income (monthly)
Date of Diagnosis		Age at Diagnosis		Date of HSCT		Age at HSCT	
Diagnosis		Co-morbidities/Co-morbidity Index:					
Type of HSCT		☐ Autologous		☐ Allogeneic			
HSCT #		☐ 1		☐ 2		☐ ≥ 3	
HSCT # more than 1, previous HSCT is		☐ Autologous		☐ Allogeneic			
Type of Donor		☐ Match Related		☐ Match Unrelated		☐ Mismatch Related	
Stem Cell Source		☐ Bone Marrow		☐ Peripheral Blood			
Conditioning		☐ Myeloablative		☐ Non-myeloablative			
Number of lines of Treatment pre-HSCT							
Disease Status	☐ CR1	☐ CR2	☐ ≥ CR3	☐ PR1	☐ PR2	☐ ≥ PR3	☐ VGPR
Time for WBC engraftment		Time for platelet engraftment			Length of Stay		
ICU transfer during HSCT hospital stay		☐ Yes		☐ No	☐ Number of days in ICU		
Re-admission with ICU transfer		☐ Yes		☐ No	☐ Number of days in ICU		
Acute Graft-versus-Host Disease		☐ Yes		☐ No	☐ Time of aGvHD		
Chronic Graft-versus-Host Disease		☐ Yes		☐ No	☐ Time of cGvHD		
Patient's history of Mental Illness		☐ No		☐ Yes (describe)			

Appendix (D): Tracking Sheet

Research Number (code)	Medical Record Number	Initials	Phone Number (1)	Phone Number (2)
001				
002				
003				
004				
005				
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007				
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040				

Appendix (E): FACT-BMT (Version 4) English

FACT-BMT (Version 4)

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 seven days

	PHYSICAL WELL-BEING	Not at all	A little bit	Some what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with my family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4

Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer please mark the box* ☐ *and go to the next section*					
GS7	I am satisfied with my sex life	0	1	2	3	4

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope with the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some what	Quite a bit	Very much
GF1	I am able to work (including work at home)	0	1	2	3	4
GF2	My work (including work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

	ADDITIONAL CONCERNS	Not at all	A little bit	Some what	Quite a bit	Very much
BMT1	I am concerned about keeping my job (include work at home)	0	1	2	3	4
BMT2	I feel distant from other people	0	1	2	3	4
BMT3	I worry that the transplant will not work	0	1	2	3	4
BMT4	The side effects of treatment are worse than I had imagined	0	1	2	3	4
C6	I have a good appetite	0	1	2	3	4
C7	I like the appearance of my body	0	1	2	3	4
BMT5	I am able to get around by myself	0	1	2	3	4
BMT6	I get tired easily	0	1	2	3	4
BL4	I am interested in sex	0	1	2	3	4
BMT7	I have concerns about my ability to have children	0	1	2	3	4
BMT8	I have confidence in my nurse(s)	0	1	2	3	4
BMT9	I regret having the bone marrow transplant	0	1	2	3	4
BMT10	I can remember things	0	1	2	3	4
Br1	I am able to concentrate	0	1	2	3	4
BMT11	I have frequent colds/infections	0	1	2	3	4
BMT12	My eyesight is blurry	0	1	2	3	4
BMT13	I am bothered by a change in the way food tastes	0	1	2	3	4
BMT14	I have tremors	0	1	2	3	4
B1	I have been short of breath	0	1	2	3	4

BMT15	I am bothered by skin problems	0	1	2	3	4
BMT16	I have trouble with my bowels	0	1	2	3	4
BMT17	My illness is a personal hardship for my close family members	0	1	2	3	4
BMT18	The cost of my treatment is a burden on me or my family	0	1	2	3	4
	DO YOU HAVE ANY ADDITIONAL CONCERNS?					

Appendix (F): FACT-BMT (Version 4) Arabic

FACT-BMT (Version 4)

هذه قائمة بعبارات واسئلة ذكرها أشخاص بحالتكم أنها مهمة وجديرة بالذكر. من فضلك ضع (ي) دائرة أو علامة على الرقم في السطر المقابل للسؤال (العبارة) لبيان مدى انطباق إجابتكم على حالتكم خلال الأيام السبعة السابقة

	الكفاءة الجسمانية	ليس على الإطلاق	مرات قليلة	نوعا ما	غالبا	كثيرا جدا
GP1	أنا أشعر بالوهن	0	1	2	3	4
GP2	أنا أشعر بالغثيان	0	1	2	3	4
GP3	بسبب حالتي الصحية، لدي صوبة في تلبية إحتياجات أسرتي	0	1	2	3	4
GP4	أشعر بألم	0	1	2	3	4
GP5	أشعر بالضيق من الآثار الجانبية للعلاج	0	1	2	3	4
GP6	أشعر أنني مريض	0	1	2	3	4
GP7	أنا مضطر لملازمة الفراش	0	1	2	3	4

	الكفاءة الإجتماعية والأسرية	ليس على الإطلاق	مرات قليلة	نوعا ما	غالبا	كثيرا جدا
GS1	أشعر أنني قريب من أصدقائي	0	1	2	3	4
GS2	أحظى بدعم عاطفي من أسرتي	0	1	2	3	4
GS3	اجد دعما من اصدقائي	0	1	2	3	4
GS4	أجد أن اسرتي قد تقبلت مرضي	0	1	2	3	4

GS5	أنا راض عن طرق التواصل بيني وبين أسرتي حول مرضي	0	1	2	3	4
GS6	أشعر بقربي من الشريك (أو الشخص الذي اتلقى منه الدعم الرئيسي)	0	1	2	3	4
Q1	بغض النظرعن نشاطك الجنسي حاليا، يرجى الإجابة عن السؤال التالي. إذا كنت لا ترغب في الإجابة يرجى وضع علامة في المربع ☐ ثم الإنتقال إلى القسم الذي يلي عن الكفاءة العاطفية					
GS7	انا راض عن حياتي الجنسية	0	1	2	3	4

	الكفاءة العاطفية	ليس على الإطلاق	مرات قليلة	نوعا ما	غالبا	كثيرا جدا
GE1	أشعر بالحزن	0	1	2	3	4
GE2	أنا راض عن طريقة تعاطي/تأقلمي مع مرضي	0	1	2	3	4
GE3	أفقد الأمل في مقاومتي لمرضي	0	1	2	3	4
GE4	أشعر بالتوتر	0	1	2	3	4
GE5	أنا قلق من فكرة الموت/من أن أموت	0	1	2	3	4
GE6	أشعر بالقلق من فكرة أن تسوء حالتي	0	1	2	3	4

	الكفاءة الوظيفية	ليس على الإطلاق	مرات قليلة	نوعا ما	غالبا	كثيرا جدا
GF1	أنا قادر على العمل (بما فيه العمل في المنزل)	0	1	2	3	4
GF2	أشعر بأن عملي (بما فيه العمل في المنزل) يرضيني	0	1	2	3	4

GF3	أنا قادر على الإستمتاع بالحياة	0	1	2	3	4
GF4	لقد تقبلت مرضي	0	1	2	3	4
GF5	أنا أنام جيدا	0	1	2	3	4
GF6	أنا أستمتع بالأعمال/النشاطات التي أقوم بها عادة بهدف التسلية/الترفيه	0	1	2	3	4
GF7	أنا سعيد/راض عن نوعية حياتي	0	1	2	3	4

	إهتمامات/شؤون إضافية	ليس على الإطلاق	مرات قليلة	نوعا ما	غالبا	كثيرا جدا
BMT1	أنا قلق بشأن الحفاظ على عملي (بما فيه العمل في المنزل)	0	1	2	3	4
BMT2	أشعر بأنني بعيد عن الآخرين	0	1	2	3	4
BMT3	أنا قلق بأن زراعة الخلايا الجذعية لن تكون ناجحة	0	1	2	3	4
BMT4	أجد بأن الآثار الجانبية للعلاج هي أسوأ مما كان بالحسبان	0	1	2	3	4
C6	أجد بأن لدي شهية جيدة	0	1	2	3	4
C7	أنا راض عن شكلي الجسدي	0	1	2	3	4
BMT5	لدي القدرة على التحرك والتنقل بمفردي	0	1	2	3	4
BMT6	أشعر بالتعب بسرعة	0	1	2	3	4
BL4	أنا مهتم بممارسة الجنس	0	1	2	3	4
BMT7	أشعر بالقلق من قدرتي على الإنجاب	0	1	2	3	4
BMT8	لدي الثقة بالطاقم التمريضي الموكل الرعاية بي	0	1	2	3	4

BMT9	أشعر بالندم لإجرائي عملية زرع الخلايا الجذعية	0	1	2	3	4
BMT10	أنا أستطيع أن أتذكر الأشياء/الأحداث	0	1	2	3	4
Br1	أنا قادر على التركيز [مثالا: القراءة]	0	1	2	3	4
BMT11	لدي التهابات متكررة [رشح، نزلة برد]	0	1	2	3	4
BMT12	لدي غشاوة في البصر	0	1	2	3	4
BMT13	أشعر باللإنزعاج من طعم الأشياء [تغيير في طعم الأكل]	0	1	2	3	4
BMT14	لدي إرتعاش في الجسم/الأطراف Tremors	0	1	2	3	4
B1	لدي ضيق في التنفس	0	1	2	3	4
BMT15	أشعر بالإنزعاج من تغيرات في الجلد [حكة، طفرة، تغيير في لون البشرة]	0	1	2	3	4
BMT16	لدي إضطراب في الأمعاء	0	1	2	3	4
BMT17	أشعر بأن مرضي يشكل عبء/مشقة على أفراد أسرتي	0	1	2	3	4
BMT18	تشكل كلفة العلاج عبء/مشقة علي/على أفراد أسرتي	0	1	2	3	4
	هل لديكم أي إضافات أو تعليقات تودون الإفصاح عنها					

Appendix (G): AUB Institutional Review Board – Approval of Research

APPROVAL OF RESEARCH

May 27, 2019

Dr. Laila Farhoud
American University of Beirut
01-350000 Ext. 5975
lf00@aub.edu.lb

Dear Dr. Farhoud,

On May 27, 2019, the IRB reviewed the following protocol:

Type of Review:	Initial, Expedited
Project Title:	Health-Related Quality of Life in Adult Patients Following Hematopoietic Stem Cell Transplant
Investigator:	Laila Farhoud
IRB ID:	SBS-2019-0048
Funding Agency:	None
Documents reviewed:	Received April 11, 2019: Email Response, Amended IRB Application, Amended Proposal, Amended Consent Form (Arabic and English versions), Demographic Data and Medical Record Data Variables, FACT BMT Tool (Arabic and English versions).

The IRB approved the protocol from **May 27, 2019** to **May 26, 2020** inclusive.
Before March 26, 2020 or within 30 days of study close, whichever is earlier, you are to submit a completed "FORM: Continuing Review Progress Report" to request continuing approval or study closure.

If continuing review approval is not granted before the expiration date of **May 27, 2020** approval of this research expires on that date.

Please find attached the stamped approved documents:

- Proposal (received April 11, 2019),
- Consent Form Arabic and English versions (received April 11, 2019),
- Demographic Data and Medical Record Data Variables (received April 11, 2019),
- FACT BMT Tool (Arabic and English versions (received April 11, 2019).

Only these IRB approved consent forms and documents can be used for this research study.

Thank you.

The American University of Beirut and its Institutional Review Board, under the Institution's

Federal Wide Assurance with OHRP, comply with the Department of Health and Human Services (DHHS) Code of Federal Regulations for the Protection of Human Subjects ("The Common Rule") 45CFR46, subparts A, B, C, and D, with 21CFR56; and operate in a manner consistent with the Belmont report, FDA guidance, Good Clinical Practices under the ICH guidelines, and applicable national/local regulations.

Sincerely,

Michael Clinton, PhD
Co-Chairperson IRB Social & Behavioral Sciences

Cc:

Fuad Ziyadeh, MD, FACP, FRCP
Professor of Medicine and Biochemistry
Chairperson of the IRB

Ali K. Abu-Alfa, MD, FASN, FAHA
Professor of Medicine
Director, Human Research Protection Program
Director for Research Affairs (AUBMC)

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