

Effect of Psychosocial Factors on Health Outcomes in Autologous BMT Patients

BY

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Abstract

Psychosocial factors have been shown to be indicative of health recovery in cancer populations. However, less is known about Blood and Marrow Transplant (BMT) patients. This paper explores pre-transplant psychosocial factors that may predict poorer health outcomes following autologous transplant (AuBMTs) in patients with hematological malignancies. Participants included 130 cancer patients (51.5% male) who completed a pre-AuBMT evaluation ($M = 58.39$, $SD = 11.71$, range = 21 – 80). Data extracted include information regarding measures for distress (DT), problems in daily life (PPL), depressive symptoms (CES-D) and physical and mental health quality of life (PCS-12 and MCS-12). Health outcomes including cancer-related hospital re-admittance, survival rates, and number of medications prescribed within 12 months post-transplant were also extracted. Results indicated that medications were positively correlated to PPL score, $r(128) = 0.179$, $p < 0.05$, and to CES-D scores, $r(128) = 0.220$, $p < 0.05$, and inversely related to PCS-12 scores, $r(128) = -0.293$, $p < 0.01$. ANOVA and Welch ANOVAs indicated insurance status has a significant effect on mortality rate, depression, and physical and health-related quality of life ($p < .05$). A stepwise multiple linear regression model indicated that approximately 7.9% of the variance of the number of medications used was accounted for by PCS-12. Results suggest that individuals with greater overall problems and depressive symptoms and a poorer physical health quality of life (QOL) were prescribed more medications. Additionally, physical health QOL proved to be a significant predictor for medication use. The impact of insurance status on these outcomes is an area for further exploration. This research supports a relationship between psychosocial variables and health outcomes for BMT patients with a hematological malignancy and may help inform appropriate psychosocial screening and intervention practices for this population.

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Background

Cancer and Blood and Marrow Transplantation

The rate of new cancer diagnoses continues to grow at an exponential rate. Presently, cancer remains the second primary cause of death in the United States, leading to nearly one in four deaths (American Cancer Society Facts and Figures, 2014). In 2014, the incidence rate for hematological malignancies, cancers which originate in the blood-forming tissues, is expected to increase as follows: 24,050 new cases of myeloma, 52,380 new cases of leukemia, and 79,990 new lymphoma diagnoses (American Cancer Society Facts and Figures, 2014). The mortality rate of these diseases is estimated to be 25 to 48% (Howlader, et al., 2013). Given the increasing number of cases and the fairly high mortality rate, medical science is working to establish effective treatments that address the disease and also patients' overall survival and quality of life.

Often, the most effective treatment option for patients with these diagnoses is bone marrow or peripheral blood stem cell transplant (BMT). There are two primary types of stem cell transplant, allogeneic and autologous (Bone Marrow Transplant, 2012). It is important to keep in mind the inherent differences between these two transplant processes, as it may impact individuals uniquely. An allogeneic transplant requires having cells or marrow donated from an outside source, such as a matched sibling or adult volunteer donor from a national or international registry. An autologous transplant involves the treatment, harvest, and storage of one's own stem cells or marrow to be later transplanted back into the body. As of 2006, there were over 15,000 allogeneic and 30,000 autologous transplants completed worldwide (Copelan, 2006). This number has only continued to increase over time.

Following initial treatment and harvest of cells, individuals undergoing an autologous BMT (AuBMT) receive supra-lethal doses of chemotherapy, sometimes accompanied by total

body irradiation, which results in a significantly compromised immune system. Following this intensive treatment, one's own stem cells are then infused into one's own body in order to regenerate normal blood cells. Following AuBMT, it often takes many months for patients to achieve complete immune recovery (Peggs and Mackinnon, 2004; Bone Marrow Transplant, 2012). As such, AuBMT is one of the most aggressive, physically intense and demanding treatments available for cancer patients (Feigin et al., 2000).

Following AuBMT, individuals may experience certain complications such as increased risk of infection (Bone Marrow Transplant, 2012; as cited in Feigin et al., 2000). Infection often occurs within the six weeks after transplant when patients are considered "neutropenic," which is the period of time when white blood cell count is extremely low (American Cancer Society, 2013). While many of these infections may only be a mild concern for individuals with regular immune systems, it is "quite dangerous" for those who have recently received a transplant or who are neutropenic. Engraftment, the period of time when the new bone marrow begins producing white blood cells, generally occurs approximately thirty days post-transplant, and while it is less likely that a patient will develop an infection following engraftment, it may take six to twelve months for a patient's immune system to fully recover (American Cancer Society, 2013).

Bacterial infections are the most common post-transplant complication, but it is also likely that a patient may acquire viral or fungal infections (American Cancer Society, 2013), which may be "life-threatening" (Bone Marrow Transplantation, 2015). One study found invasive fungal infections as a primary concern for morbidity and infection-related mortality among patients receiving BMT (Bhatti, Almyroudis, Segal, 2006). There are particular infections within patients with hematological malignancies, such as fusariosis, a fungal infection,

that have been associated with poor prognosis (Boutati and Anaissie, 1997), and type of transplant (allogenic or autologous) did not seem to make a difference in mortality rate (Barnes & Marr, 2007 as cited in Nucci et al., 2004). Not only do infections directly cause increased risk to the AuBMT patient, but they also cause indirect harm through increasing risk of extended hospital stay or re-hospitalization, and preventing or delaying engraftment or immune recovery (Bone Marrow Transplantation, 2015). Therefore, physicians often prescribe antiviral, antifungal and antibiotic medications to patients post-transplant in order to both prevent and treat these serious infections (Bone Marrow Transplantation, 2015).

In addition to risk of infection, a patients' health outcomes may be governed by type of diagnosis received prior to the transplant. Although many hematological malignancies are treated with AuBMT, characteristics of specific diagnoses are unique and may guide overall treatment outcome as well as interact with a host of other psychosocial factors and health variables.

For the purposes of this paper it is important to differentiate among a few of the specific cancer types that fall under the larger umbrella of "hematological malignancies." One important variation of these forms of cancer is Multiple Myeloma (MM). MM develops from malignant plasma cells. Healthy and normal plasma cells are particularly important to the immune system and can be found in the bone marrow (American Cancer Society, 2014). However, once these healthy cells become cancerous and begin growing more rapidly than normal they can create a tumor called *plasmacytoma*. Once an individual develops more than one plasmacytoma they are diagnosed with multiple myeloma. Some characteristic features of MM include low blood counts, bone and calcium problems, infections, and kidney issues. MM is not curable, but is sometimes very slow growing and with treatment, especially AuBMT, patients can have

remissions of several years. However, the disease will eventually relapse, and patients often have to receive regular treatments of chemotherapy, radiation therapy or other drugs to keep the cancer in check (American Cancer Society, 2014).

Another important diagnoses type is lymphomas, which can be broken into the following two main categories: Non-Hodgkin's Lymphoma (NHL) and Hodgkin's Lymphoma. NHL is a type of cancer that begins in lymphocytes which are located in the lymph nodes as well as other lymphoid tissue (i.e., spleen, bone marrow) and are a crucial part of the immune system. NHL can be even further broken down into specific categories such as B-cell or T-cell lymphomas. B-cell lymphomas make up approximately 85% of NHL diagnoses in the United States while T-cell lymphomas account for the other 15% (Leukemia & Lymphoma Society, 2013). There are various risk factors for NHL such as, age (i.e., getting older), being male, race (i.e., Asian and African Americans), exposure to certain chemicals (i.e., certain herbicides and insecticides, and exposure to certain viruses and bacteria such as the Epstein-Barr virus (Leukemia & Lymphoma Society, 2013; American Cancer Society, 2014). In contrast to MM, many times chemotherapy treatment will completely cure NHL and mortality rates for this disease have been decreasing since the late 1990s (American Cancer Society, 2014).

The second main category of lymphomas is Hodgkin's Lymphoma (HL), previously known as Hodgkin's Disease (HD). The disease name was changed once it was discovered that, similarly to NHL, the disease results from an injury to the DNA of a lymphocyte (Leukemia & Lymphoma Society, 2013). Like NHL, HL also develops within lymphocytes, but how this lymphoma spreads and responds to treatment is different from NHL, so it is important to distinguish between the two. Physicians can distinguish between the two types through examining the cancer cells underneath a microscope or through laboratory tests (American

Cancer Society, 2014). Additionally, HL can be differentiated from other types of lymphoma by the presence of Reed-Sternberg cells (named for the scientist who first discovered them (Leukemia & Lymphoma Society, 2013). In contrast to NHL, HL is most common in early adulthood, predominantly in individuals in their 20s (American Cancer Society, 2014). Another risk factor for HL is previously being infected with the Epstein-Barr virus. Survival rates have increased throughout the past several decades due to improvements in treatment and, currently, the 1-year survival rate is 92% and the 5-year rate is 85%. However, certain factors, such as stage of HL or one's age may alter these rates (American Cancer Society, 2014).

Finally, the success of a patient's recovery from a BMT can be uncertain and dependent upon multiple psychosocial factors, such as age and overall health, type and dosage of chemotherapy or radiation prior to transplant, a range of other complications during and after transplant, and genetic makeup (Bone Marrow Transplant, 2012). It is not uncommon for BMT patients to experience lengthy and/or repeated hospital stays, extended periods of social and physical isolation due to their immunocompromised nature. These types of complications following AuBMT are not only taxing physically, but socially, emotionally, and financially as well (Feigin et al., 2000).

Biopsychosocial Model of Health

When proposing the importance of the biopsychosocial model, Engel (1977) argued that a medical model that only understands biological indices does not suffice. He stated that it is imperative to take the patient, the social context in which they live, along with the physician role and healthcare system into consideration in an attempt to appropriately understand disease, and arrive at rational treatments (Engel, 1977). The biopsychosocial model is the idea that psychological and social factors are reciprocally related to biological processes. For more than

25 years, this model has fueled many new advances in research (Suls & Rothman, 2004). It posits that social, behavioral and psychological dimensions are pertinent to consider, along with biological factors, when understanding the framework of physical health and illness. This framework allows researchers and clinicians to develop a multilevel and multisystem approach to human functioning (Suls & Rothman, 2004). In line with a biopsychosocial framework, this paper will explore certain psychosocial factors such as distress, depressive symptoms, and quality of life to further understand their role in predicting physical health outcomes following an AuBMT.

Distress

Even without the added stressor of a transplant, cancer diagnoses are often associated with significant emotional distress. It is important to distinguish the variable *distress* from that of *depression* and *quality of life*, even though they are all correlated. Most definitions describe *distress* as “an aversive, negative state” in which an organism is unable to appropriately cope and adapt in order to return to psychological homeostasis (as cited by Ward et al., 2008). More specifically, in cancer patients, it may be the case that someone is struggling in coping and adapting to a diagnosis or treatment, but is not meeting a clinical depression diagnosis or experiencing any significant depressive symptoms (i.e., loss of appetite, low energy, loss of interest in activities, suicidal ideation). In other words, psychological distress may be used as a more broad term encompassing stress and both mood and anxiety reactions that do not meet clinical criteria. Furthermore, *distress* is distinct from *quality of life* in that one may perceive their quality of life to be low, but not be in as great a state of distress as someone who experiences their quality of life as average. In other words, all individuals may experience

varying levels of distress *in response* to depressive or anxiety-related symptoms and/or changes in their differing quality of life facets.

In cancer patients, the risk of psychiatric distress has been shown to be almost twice that of the general population (Hinz et al., 2010), and previous studies have shown that approximately one-third of all cancer patients will experience a significant level of distress following diagnosis and throughout treatment (see references in Carlson et al., 2004). While emotional distress differs from mood disorders, the two variables may be interconnected. At times, emotional distress can lead to the development of a mood disorder. Following diagnosis and treatment, periods of time that may instill high levels of psychological distress, patients often report experiencing various psychological issues such as depressive and anxiety symptoms (Kvillemo & Branstrom, 2011). Previous research has indicated that approximately 25 to 30% of cancer patients experience clinically significant distress (Baken and Woolley, 2011). High levels of distress have been shown to impact patients' quality of life, satisfaction with care and overall participation in treatment, as well as recovery -- potentially resulting in a prolonged rehabilitation period (Baken and Woolley, 2011; Grassi et al., 2013).

There are many variables that influence a patient's level of distress, and, in turn their quality of life. For instance, distress levels have been found to be greater in cancer patients with a poorer prognosis, and individuals that have an advanced stage of cancer (Carlson & Bultz, 2003). Distress levels have also been found to relate to various demographic factors such as female gender, minority ethnicity, lower income, and younger patients. It is thought that younger patients may suffer higher levels of distress due to a greater disruption in social and familial roles at an earlier developmental stage (Carlson et al., 2004). This disruption may include practical issues such as difficulties establishing one's career and/or raising small children

(Carlson et al., 2004). Patients have been found to experience distress related to a psychological, social or spiritual nature which may interfere with one's ability to cope with a cancer diagnosis (National Comprehensive Cancer Network, 2003).

Also, certain types of distress may be unique to specific types of cancers and treatments, such as BMTs. For instance, an AuBMT may involve its own potential source of distress for hematological cancer patients, as one study found higher levels of emotional distress, in the form of anxiety and depression, when compared to those who received an allogeneic transplant (Meyers et al., 1994). Therefore, distress is not only impacted by the cancer disease itself, but can be unique to the individual type of treatment, and exacerbated by disruptions in a number of other life domains that include one's own practical concerns, and daily hassles that come along with their cancer diagnosis and treatment.

In addition, distress levels during cancer treatment and recovery may be impacted by levels of pre-transplant distress. Pre-transplant distress may vary depending on multiple factors such as prior disease with relapse, treatment history, physical functioning, and psychological, financial, and social resources (McGregor et al., 2013). Pre-transplant distress is an important variable to examine when considering factors that contribute to a patient's recovery trajectory. Several studies have indicated that levels of pre-BMT distress predict certain health-related outcomes. McGregor and colleagues (2013) found that increased levels of pre-transplant distress among 70 AuBMT patients predicted slower white blood cell (WBC) count recovery following transplantation. This is particularly important, as WBC count is a salient indicator of immune function. In another study, Syrjala and colleagues (2004) investigated physical and psychological functioning pre-transplant in a prospective five-year longitudinal study. Results from this study

indicated that cancer patients who had slower physical recovery, as measured by more physical limitations, also had increased levels of depression prior to BMT (Syrjala et al., 2004).

Furthermore, pre-transplant distress levels not only impact health outcomes, but psychological outcomes as well. In a study of 125 cancer patients, Broers and colleagues (2000) found that patients' distress throughout the course of their treatment and during the first three years following BMT varied depending on whether the patient experienced a low or high level of distress pre-transplant. Other studies have shown that pre-transplant emotional distress was correlated with distress at three and twelve months post-transplant (Fife et al., 2000), and that pre-BMT distress levels had a predictive value accounting for 81% of post-transplantation distress (Lee et al., 2005). Therefore, these findings suggest that higher levels of pre-transplant distress may be a risk factor for experiencing increased psychological symptoms even following an AuBMT.

While greater distress has been found to predict poorer health and recovery, other research has found that *decreased* levels of distress may predict *better* mental and physical health outcomes. Some evidence suggests certain forms of coping may be helpful for handling distress. Rodrigue and colleagues (1999) examined psychological variables in 92 patients prior to their BMT and found that increased levels of affective functioning and social support pre-transplant significantly predicted increased quality of life and survival status. In addition to distress, other psychosocial factors, such as age, relationship support, education, mood, and adjustment have been related to a variety of health outcomes, including survival rates, in the BMT population (Hoodin, Kalbfleisch, Thornton, & Ratanatharathorn, 2004). These findings underscore the need for screening and psychological interventions to be employed pre-transplant so that that patients may have a greater likelihood of increased psychological functioning following BMT.

As demonstrated above, research has shown that pre-transplant distress is an important variable to consider in overall treatment and recovery prognosis for cancer patients undergoing BMTs. However, studies specifically investigating pre-transplant distress in AuBMT patients are lacking.

Depression

In addition to examining pre-transplant distress levels, it is also meaningful to consider other psychological variables such as depressive symptoms. Depressive symptoms such as impaired sleep, increased or decreased appetite, and lower energy can have a negative impact on one's overall health. Furthermore, depressive symptoms have been shown to be linked with more severe concerns such as decreased immune system functioning and mortality (see references in Miller, 1998). Within the general population, the association between depressive symptoms and mortality has been well documented (see references in Loberiza et al., 2002). Robust meta-analyses provide strong evidence for this relationship. Harris and Barroclough (1998) conducted a meta-analysis with 19,000 individuals in which they found that, when compared to the general population, people with depression had increased mortality rates from infectious, respiratory, nervous system and circulatory disorders. These harmful effects on one's health may differ depending on the particular population.

While depressive symptoms can be troublesome for individuals in the general population, they can be particularly problematic for those within a cancer population due to the associated health risks, including higher mortality. Evidence suggests a co-occurrence between cancer and depression with bidirectional relationships that may link depression with cancer progression (see references in Giese-Davis et al., 2011). Depression in cancer patients has been associated with various deleterious outcomes, such as increased levels of psychological distress and suicidality,

poorer treatment adherence, greater risk of cancer relapse, and decreased health-related quality of life (Reich, 2008).

The prevalence rate of depression tends to vary by cancer site (Onitilo et al., 2006). Increased rates have been found in patients experiencing greater physical disability, advanced illness, and significant pain (Sellick & Crooks, 1999). For example, in a meta-analysis of studies assessing for mood and adjustment disorders in cancer patients using psychiatric diagnostic interviews, prevalence rates for depressive disorders were estimated at 24.6% among patients treated in palliative-care settings and 20.7% in patients treated in oncology and hematology settings (Mitchell, Chan, Bhatti, Halton, Grassi, Johansen, & Meader, 2011). In a related meta-analysis, researchers examined eight community-based sample studies and 15 studies within cancer patients, and found that depression was related to greater rates of mortality (Chida et al., 2008). Additionally, Satin and colleagues (2009) found that depression predicted higher mortality in cancer patients in their meta-analysis of 25 individual studies. Furthermore, Pinquart and Duberstein (2010) conducted a meta-analysis in which they evaluated results from 76 prospective studies of cancer patients with various diagnoses. Their results indicated that, depression defined either categorically or dimensionally, was associated with elevated risk for mortality in cancer patients.

It is particularly noteworthy to mention that depression seems to have a more negative impact on mortality in individuals with cancer when compared to those without. Onitilo and colleagues (2006) analyzed data on 10,025 individuals, and created four groups based on cancer and depression status including (a) no cancer, no depression, (b) depression, but no cancer, (c) cancer, but no depression, and (d) cancer and depression. Researchers looked at outcome data eight years later and found that the coexistence of cancer and depression is linked to a higher risk

of death from all causes, even if not related with depression or cancer. Furthermore, they found variability within the “cancer and depression” group, in that the relationship between depression and increased risk of death varies depending on cancer site. Researchers found a 0.47 increased risk of death for patients with gastrointestinal cancer, 0.39 for those with lung cancer, 0.07 for patients with skin cancer and 1.13 in patients with other cancers (Onitilo et al., 2006). In this study, patients with hematological cancers were not evaluated individually, but were grouped along with additional cancer diagnoses in the “other” category.

While an examination of research on depressive symptoms within the general cancer population is useful, more literature focusing specifically on pre-transplant depressive symptoms in the hematological malignancy and BMT population is warranted. Overall, there seems to be a paucity of research examining depressive symptoms specifically within this group, and particularly among patients who received AuBMT. However, there have been a few studies that indicate the importance of studying depression among patients within BMT populations, as depressive symptoms have been shown to be predictive of post-transplant outcomes. For instance, study results included within a recent meta-analysis have shown that depression predicted shorter survival time in leukemia and lymphoma patients (Pinquart & Duberstein, 2010). In addition, pre-transplant levels of depression have been associated with higher mortality during the period between 6 and 12 months following BMT. Also, levels of depressive symptoms pre-BMT predicted vulnerability to continued difficulties with depression after BMT (Massie, 2004; Artherholt, Hong, Berry, & Fann, 2014). Given the unique constellation of symptoms and specific difficulties within each cancer diagnosis, it is important not to assume that depressive symptoms function similarly in all patients with cancer, or across all cancer treatments. Therefore, increasing the quantity of studies within the BMT population in patients

who undergo AuBMT would only help further elucidate how depressive symptoms impact these specific patients' health outcomes within the context of this specific treatment.

It may be helpful to clarify that while depression and distress may seem similar, they have important conceptual differences. For example, the broad variable of distress may encompass many other variables such as general stress, spiritual concerns, family problems, or practical issues. In the specific case of a BMT patient, distress may be based on the individual's fear or concern associated with their cancer diagnosis or transplant as it impacts various aspects of life. However, depressive symptoms are usually conceptualized as criteria of a clinical major depressive episode (i.e., lack of interest in activities, low energy, poor appetite, feeling "down" or "depressed"). One could say, patients who are depressed are typically distressed, but not all patients who are distressed are depressed. Therefore, assessing the impact of both of these variables may provide clinicians and researchers with valuable and unique information.

Quality of Life

When an individual is experiencing significant levels of distress and/or depressive symptoms, it may be likely that these symptoms are also impacting their overall quality of life (Vitek, Rosenzweig, Stollings, 2007). In the past couple of decades, medicine has transformed from understanding suffering through focusing solely on the physical manifestations of a disease to also including the psychosocial impact (Armstrong, Lilford, Ogden, and Wessely, 2007). The assessment of quality of life has allowed clinicians and health psychologists to assess both immediate clinical symptoms as well as distal consequences (Armstrong et al., 2007). These distal consequences, assessed through quality of life measures, are comprised of both physical and mental factors. For instance, physical factors may include quality of physical functioning, potential limitations due to physical problems, bodily pain, and general health. Variables that

can impact quality of mental health may be one's level of vitality, social functioning, and role limitations due to emotional or physical problems (Ware, Kosinski, & Keller, 1996). This measurement of quality of life that has emerged over the past few decades has been instrumental in health psychology as it has given clinical symptoms a new and deeper meaning and transformed the patient self-report into the central component of defining health and illness among multiple populations (Armstrong et al., 2007).

Within the general cancer population, quality of life assessment has flourished during the past couple of decades due to improved cancer treatment and survival rates (Ferrell & Grant, 1995). Studies have shown that assessing quality of life in cancer patients can lead to improved treatment and may even be as prognostic as certain medical factors (Montazeri, 2008). Research in quality of life among cancer patients has also been shown to highlight particular directions needed for more efficient and effective treatment. Assessment within a cancer population requires researchers and clinicians to measure unique facets that may not be as critical in the general medical population, such as measuring quality of life for patients in different stages of cancer progression, and among patients in various stages of treatment (i.e., pre-treatment, active stage, post-treatment). Furthermore, various types of cancer and cancer treatments have been studied such as prostate, colon, and lung cancer, with the most research having been done within breast cancer patients (Montazeri, 2008). It is important to consider all of these distinctive variables when assessing quality of life in cancer patients in order to gain the most thorough understanding of each particular population and subgroup.

Specifically, it is important to further understand quality of life factors in the BMT population given the unique impact of this treatment regimen on cancer patients. There have been multiple studies examining the overall quality of life in BMT survivors and various issues

such as fatigue, sexuality concerns, and family distress created by the illness have been reported (Whedon & Millis, 1995). To gain a better understanding of impairments in quality of life specific to a BMT population, some research has examined and compared quality of life in BMT survivors to “healthy” individuals. Hann and colleagues (1997) found that, in comparison to a “healthy” population, BMT patients experienced impairments in physical role functioning, general health, vitality, social functioning, and emotional role functioning. Furthermore, this decreased quality of life was associated with a prolonged hospital stay, lower income, and greater symptom prevalence, severity and distress (Hann et al., 1997).

Other studies have investigated the impact of pre-transplant quality of life on post-transplant outcomes, particularly on survival rates. For example, Andorsky and colleagues (2006) conducted a longitudinal study in which they collected self-reported quality of life data from cancer patients prior to their BMT, and again at six and 12-month follow-up. The quality of life measure consisted of information about patients’ mental and physical health functioning. Results indicated that pre-transplant quality of life data were a strong predictor for post-transplantation self-reported recovery at six months. Furthermore, although the variable disease risk is normally highly predictive of survival; in this study, quality of life scores proved to be more predictive of this benchmark variable.

It is clear that the assessment of quality of life has become an increasingly important aspect in health psychology and oncology research in general. While there have been some studies conducted within a BMT population, few studies have examined the quality of life specifically in individuals with a hematological malignancy who undergo an AuBMT. Given the variability among cancer and treatment types, it is vital that more studies are conducted within

this particular population to better understand the significance of this variable within AuBMT patients.

Financial Burden

Not only is it important to understand how a patient's distress, depressive symptoms and quality of life influence recovery, but also how this recovery process influences other critical factors such as medical costs. Due to a patient's poorer recovery following treatment, patients, healthcare providers, and the health system as a whole may experience increased financial strain. In recent years, cancer treatment costs have increased drastically and created financial burdens for both patients and third-party payers (see references Greenberg, Earle, Fang, Elder-Lassai & Neumann, 2010).

Cancer patients have been shown to have an increased risk of declaring bankruptcy when compared to the general population. Ramsey and colleagues (2013) conducted a study in which they examined the finances of individuals, twenty-one years and older diagnosed with cancer between 1999 and 2009. Cases were identified using the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program and compared to control group data obtained from the LexisNexis data repository, the largest commercial repository for public data in the United States. Their findings suggest that cancer patients were 2.65 times more likely to declare bankruptcy than people without cancer.

With increasing rates of cancer diagnoses, total cancer costs are growing, along with the costs for specific treatment options such as BMT. As of 2009, the total cost of cancer was estimated to be \$216.6 billion; direct medical costs (total of all health expenditure) to be 86.6 billion, and indirect mortality costs, which is the cost of lost productivity due to premature death, to be \$130 billion (American Cancer Society, 2014). As new cases of hematological cancers are

expected to increase in 2014, these total costs are likely to continue to grow. For individuals receiving AuBMT, the cost of the transplant is tremendous, totaling approximately \$360,000 (National Foundation for Transplants, 2010). While insurance may cover some costs for patients, depending on their coverage, BMT patients will still incur a number of other costs, such as lodging for follow-up care, prescriptions, potential childcare, and over-the-counter related medication and medical supply costs. This also fails to capture the loss of productivity and possibly employment that patients face over the long course of illness, treatment, and recovery from AuBMT.

Expenses for patients vary depending on medical and treatment issues specific to one's cancer diagnosis and associated end of life (EOL) costs. Chastek and colleagues (2012) investigated the costs of health care services incurred by patients and health care providers through examining medical and pharmacy claims and enrollment information from the Life Sciences Research Database. Medical claims came from industry-standard forms as well as electronic forms submitted for pharmacy claims. Researchers retrospectively studied end of life (EOL) costs at both six months and one month prior to death, and examined multiple medical outcomes including office visits, ER visits, and outpatient services. These services were deemed cancer-related if a cancer diagnosis appeared in the primary or secondary position of the claim. They evaluated a total of 28,530 patients with cancer who had a medical claim between 2002 and 2009; 9% of those patients had a hematological malignancy. Overall, results indicated that hematological cancer patients had a greater mean EOL cancer-related costs (\$160,361) compared with patients with a solid tumor (\$59,822). Additionally, acute cancer-related inpatient stays were also higher for patients with a hematological malignancy than a solid tumor (\$121,651 v \$27,778). The mean emergency room cost for the entire sample was \$507, for office visits it was

\$4,040, and for hospital outpatient procedures it was \$10,123. Meanwhile, the lymphoma patients, one type of hematological malignancy, had a unanimously higher mean cost for these three variables. The mean costs of 1,459 lymphoma patients were as follows: \$651 for emergency room visit, \$4,095 for office visits, and \$16,565 for hospital outpatient procedures (Chastek et al., 2012).

These higher EOL expenses for hematological cancer patients and their healthcare providers indicate an increased need to understand ways in which to lower post-transplant medical costs. If pre-transplant distress, quality of life and depressive symptoms are associated with recovery and health outcomes, implementing effective psychological screening and interventions prior to transplant may also relieve financial strain that may be associated with poorer recovery.

Insurance Status

The aforementioned cancer treatment costs bring to mind the role of health insurance. The impact of these astronomical costs on one's overall wellbeing is even more salient when the role of insurance status is considered. Previous studies have shown that the insurance status of cancer patients may predict health outcomes (i.e., Rodriguez, Ward, Perez-Stable, 2005; Halpern, Bian, Ward, Schrag, Chen, 2007) even after adjusting for race, age, sex, and zip code estimated income (Chen, Schrag, Halpern, & Ward, 2007; Chen, Schrag, Halpern, Stewart & Ward, 2007; Cokkinides, Bandi, Siegel, Ward, & Thun, 2007; Halpern et al., 2008; Ward et al., 2008 as cited in Kwok et al., 2010). Other studies have shown that individuals who are underinsured or insured by Medicaid are more likely to experience more advanced stages of cancer (Chen et al., 2007). Kwok's study (2010) found that patients with Medicaid or who were uninsured were at increased risk of death from head and neck cancer when compared to patients with private

insurance, after adjustment of a number of demographic factors including treatment, cancer stage and socioeconomic status (SES). These studies suggest that insurance status may be one of the most prominent demographic factors that interacts with a patient's overall health outcomes, and should be considered along with examining other psychosocial variables.

Need for Psychosocial Screening and Intervention

Due to medical advancements, BMT survival rates have improved considerably in the past few decades (Horowitz, 1999). Therefore, with increased survivors, further understanding the course of BMT recovery along with potential risk factors for poorer health outcomes is warranted (Syrjala et al., 2004). Although there is a strong association between the aforementioned pre-transplant variables and post-transplant psychological and medical outcomes, only 33% of patients with cancer who experience comorbid distress are recognized within an oncology setting, and referred to an appropriate intervention (Grassi et al., 2013).

However, the oncology community has begun to appreciate that it is not only important to try to extend the length of, but also to try to increase the quality of a patients' life which can be done through proper psychosocial care (Jacobsen & Wagner, 2012). This is due to an increased recognition that psychosocial care is important in the comprehensive treatment of cancer patients and should be integrated into their routine treatment plan (Jacobsen & Wagner, 2012). Recently, the American College of Surgeons (ACoS) Commission on Cancer (CoC) has implemented a new patient-centered accreditation that requires programs to conduct psychosocial distress screening and referral for psychosocial care (Wagner, Spiegel & Pearman, 2013).

In order for the recently mandated distress screening to be most helpful, there is an increasing need for better understanding of the importance of pre-transplant psychosocial

variables, as well as greater awareness of the predictive significance of these variables upon admission to the hospital or initiation of treatment. If these variables are more readily identified in individuals undergoing AuBMT, is it possible that more of these patients in need of psychological intervention may then be identified? Furthermore, would identifying these variables also improve their health and psychological outcomes, as well as reduce their overall costs of transplant-related health incidences (i.e., infection, re-admission)?

Currently, there are no conclusive answers to these questions. While there have been multiple studies investigating associations among psychosocial and physical health factors in cancer patients, little research has been done specifically in BMT patients prior to their transplant, and even less research has been conducted on the even more specialized AuBMT population. It is important to remember that individuals with certain cancer diagnoses may have unique psychological symptoms separate from other cancer types (Lengacher et al., 2012), and that those with hematological cancer may differ in these levels pre-transplant. Additionally, individuals with various cancer diagnoses may respond differently to various psychological assessments. For example, research has indicated a differential response on psychological measures that assess patients with hematological disorders and those with other cancer types, such as breast cancer (Ahles, Tope, Furstenberg, Hann & Mills, 1996).

More specifically, there are noteworthy differences that distinguish an autologous from an allogeneic BMT, such as the auto-harvest of one's own bone marrow or stem cells, and the absence of graft versus host disease risk (Grassi et al., 1996). There also may be differences in treatment-related side effects and mortality between allogeneic and AuBMT patients. For example, one study found that there is a consistent pattern of relapse often seen with prolonged follow-up and a higher rate of disease progression that occurs following an AuBMT, compared

to an allogeneic BMT, in patients with certain types of lymphoma (Verdonck, Dekker, Lokhorst, Petersen, Nieuwenhuis, 1997). These inherent characteristics of AuBMT, and the diseases treated, may uniquely impact the interaction and relationship between pre-transplant psychological functioning and post-transplant health recovery. Further understanding how pre-transplant psychosocial concerns impact physical health outcomes of hematological cancer patients, post-AuBMT, may help in identifying “high-risk” patients in this specific population. With better identification of these concerns, it may be possible to better allocate resources, implement psychological intervention, reduce medical costs, and enhance overall recovery and health.

Aim & Hypotheses

While a significant amount of research has been conducted in the general cancer population regarding psychological symptoms and health outcomes, less is known about BMT patients, and even less about differences between different types of transplant such as allogeneic versus autologous BMT. BMT patients are different from other cancer populations in that they face more lifestyle-limitations with treatment, greater mortality and higher healthcare costs (Chastek et al., 2012). It is important for researchers and clinicians to understand the psychological aspects of care from a whole-person framework in this specialized, high-risk and growing population. Furthermore, in order to better understand these aspects of care, it is critical to differentiate between the two specific categories of BMT, allogeneic and autologous, as each type is associated with its own challenges in recovery as well as physical and psychological functioning. Therefore, this study will specifically aim to investigate the psychological aspects of care associated with AuBMT.

The overall aim of this study is to highlight pre-transplant psychological factors that may predict poorer health outcomes following AuBMT. Increasing knowledge about these pre-transplant psychological variables may be clinically relevant in developing effective psychosocial screenings and interventions for BMT patients. No other study, to date, has examined the effect of pre-transplant distress, depressive symptoms and quality of life on health outcomes in patients with hematological cancers post-AuBMT.

The present study plans to test the following three hypotheses:

- (1) Greater levels of distress, depressive symptoms, and poorer self-reported quality of life (physical health-related quality of life; mental health-related quality of life) will predict greater number of medications (antiviral, antifungal, and antibiotic) used up to twelve months following transplant.
- (2) Greater levels of distress, depressive symptoms, and poorer self-reported quality of life (physical health-related quality of life; mental health-related quality of life) will predict a greater number of re-hospitalizations up to twelve months post-transplant.
- (3) Greater levels of distress, depressive symptoms, and poorer self-reported quality of life (physical health-related quality of life; mental health-related quality of life) will predict mortality up to twelve months after AuBMT.

Methods

Participants

A previous study conducted a retrospective chart review for 254 consecutive patients who completed evaluations at the University of Kansas Cancer Center for bone marrow or peripheral blood stem cell transplant (BMT) between January 2012 and December 2013. Data extracted from medical records included information regarding patient demographics, diagnoses, and

treatment history. Results of three psychosocial measures routinely administered as part of the clinical pre-transplant assessment for the patients' preparation for BMT were also extracted. No identifying information was collected and patients were not separately consented for inclusion in this retrospective study. Patients for the current study were limited to AuBMT patients. Thus, patients were excluded from the original sample of 254 if they were being evaluated for an allogeneic transplant (unrelated donor or matched sibling), or alternative donor transplant (i.e., cord blood or haploidentical donor). The current study and retrospective chart review were both approved by the University of Kansas Medical Center (KUMC) IRB.

Of the 254 cases previously screened for eligibility, 137 met the aforementioned study inclusion criteria. Out of the 137 potential participants, seven were excluded for the following reasons: transplant delayed for personal or medical reason ($n = 3$), medical information not included in KU Cancer Center database ($n = 3$), transplant date did not allow for medical outcome data collection past six months at this time of data extraction ($n = 1$). See Figure A.

The final sample included 130 KU Cancer Center patients (51.5% male), over the age of 18 at the time of pre-transplant evaluation ($M = 58.39$, $SD = 11.71$, range = 21 – 80). Due to this study being conducted as retrospective chart review, data on race/ethnicity was unavailable. All were evaluated for an AuBMT, and completed all clinical assessment measures. All participants had been diagnosed with one or more hematological condition(s) or malignancies including the following: Multiple Myeloma ($n = 86$; 66.2%), Non-Hodgkin's Lymphomas ($n = 32$; 24.6%), Hodgkin's Lymphoma ($n = 11$; 8.5%), and Plasma Cell Leukemia ($n = 1$; < 1%).

Insurance status was also assessed as a demographic variable, as previous studies have shown that the insurance status of cancer patients may predict health outcomes (i.e., Rodriguez, Ward, Perez-Stable, 2005; Halpern, Bian, Ward, Schrag, Chen, 2007). In order to categorize

insurance type, the various types of insurance listed on each patient's electronic medical file were recorded. This included the following: self-pay, Medicare, Blue Cross Blue Shield, commercial, Tricare, and Medicaid. After consulting with an oncology nurse clinician who was knowledgeable about insurance-related patient issues, the following three insurance categories were developed: commercial (n = 49), Medicare (n = 56) and underinsured (n = 25). The commercial group included patients with Blue Cross Blue Shield and Tricare insurance. The underinsured group included patients who "self-paid" or relied on Medicaid. The participants' insurance status is as follows: Medicare (n = 56; 43.1%), commercial (n = 49; 37.7%), and underinsured (n = 25; 19.2%).

Measures

Demographic and clinical information. Participants' gender, age, diagnosis, and treatment history were gathered through the pre-transplant evaluation and/or review of each patient's medical chart.

Distress Thermometer (DT) and Patient Problem List. The DT (National Comprehensive Cancer Network, 2003; Roth et al., 1998) was used to measure the subjective level of a patient's psychological distress. This measure is a single, Likert-scale item in which the patient is asked to indicate how much distress they have experienced in the past 7 days. The thermometer is based on a scale from 0 (*No distress*) to 10 (*Extreme distress*). The DT has been validated in a sample of patients anticipating BMT by comparing its scores with scores on the Center for Epidemiologic Studies Depression Scale (CES-D; Ransom, Jacobsen, & Booth-Jones, 2006). A score of four and above has been found to differentiate between individuals who are experiencing clinically significant distress and those who are not. The specificity and sensitivity found in a robust multicenter validation study also suggest that a score of four or higher indicates

a significant need for further evaluation (Jacobsen et al., 2005). Additionally, a higher score on the DT has been associated with increased anxiety and depression, and worse performance status (Ransom et al., 2006).

The Patient Problem List (National Comprehensive Cancer Network, 2003) is a self-reported checklist of 33 common concerns of cancer patients which typically accompanies the DT on a single sheet. Patients are asked to indicate whether or not each of the problems has bothered them in the past seven days (i.e., “yes”, “no”). Questions on the checklist assess each of the following domains: Family Problems, Practical Problems, Emotional Problems, Spiritual/Religious Concerns, and Physical Problems. These domains have been identified in other papers following established procedure in the field (Jacobsen et al., 2005; Hollingworth et al., 2013; NCCN, 2015). The PPL was created to identify areas in which further evaluation and psychosocial service were needed when the DT cutoff score is four or greater (NCCN, 2003; Jacobsen et al., 2005). One study looked at cumulative problems endorsed across all domains, and found individuals who had increased distress endorsed significantly more PPL items in general (Shim, Shin, Jeon, Hahm, 2008). For this study, the total score of these domains combined were considered as a representation of overall psychosocial difficulties, and this single score was looked at separately from the overall single-item distress thermometer score.

Center for Epidemiologic Studies Depression Scale (CES-D). This widely-used instrument (Radloff, 1977) is intended to measure symptoms of depression. The CES-D is a 20-item, 4-point Likert scale that ranges from 0 (*Rarely or none of the time*) to 3 (*Most or all of the time*) which assesses mostly somatic or emotional symptoms of depression. The psychometric properties of this measure have been consistently supported through research. A score of 16 has

been established as a cutoff point to identify participants who are experiencing clinical levels of depressive symptoms (Myers & Weissman, 1980; Radloff, 1977).

Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12). The SF-12 (Ware et al., 1996) is a 12-item, self-report tool which is a well-validated measure used to evaluate health-related quality of life. The items measure a participant's functioning in the following eight domains: physical functioning, role-physical (i.e., role limitations due to physical problems), bodily pain, general health, vitality, social functioning, role-emotional (i.e., role limitations due to emotional problems), and mental health. Two quality of life scores were determined from these eight domains. The physical health composite scale (PCS-12) is a sum of the initial four domains while the mental health composite scale (MCS-12) is comprised of the last four domain scores. Summary scores are transformed so that the mean population scores are 50 and the standard deviations are 10, with the range of possible scores being 0 to 100. Higher scores indicate more adaptive functioning and quality of life within the two scales.

Procedure

Participants completed study measures, as aforementioned, as part of the standard clinical evaluation in preparation for BMT. A retrospective medical chart review was then conducted to extract the following medical outcomes data for patients' post-AuBMT:

- 1) Rate of re-admittance to the hospital in a twelve-month period.
- 2) Number of antiviral, antifungal, and antibiotic medications used.
- 3) Mortality rate twelve months post-transplant.

Hospital re-admittance was determined based on number of overnight, re-admissions to the hospital following transplant. Re-admissions or E.R. visits that did not include an overnight stay, or regular outpatient office visits were not included in this variable. Hospitalizations were

evaluated both continuously and categorically. The binary outcome variable of hospitalization was defined as “0” (no re-hospitalization) or “1” (any re-hospitalization).

The only types of medications considered in these analyses were antifungal, antibiotic, or antiviral medications. This is because these are the types of medications prescribed by physicians in order to prevent or treat an infection within this population. For analyses, these three types of medications were tallied over the course of 12 months post-transplant, and summed as one “medication” variable. In order to accurately account for the antiviral, antifungal, and antibiotic medications needed following the AuBMT, no medications that were used during the actual transplant process were considered in analyses. For example, if a patient were hospitalized while undergoing their AuBMT, none of the medications prescribed during that initial hospital stay were included. Additionally, inpatient and outpatient medication dosages were tallied differently. If a patient was hospitalized as an inpatient for multiple days, and they received multiple IV doses of a certain antiviral, antifungal, or antibiotic medication, each IV dose prescribed was considered a separate dose of medication, and counted as “one” in the analyses. However, if patient was prescribed an antiviral, antibiotic, or antifungal medication on an outpatient basis, then only one medication dose was counted for that particular prescription bottle for the patient, and tallied as “one” in the analyses. This procedure for tallying medications was consistent across all patients. Medications were calculated in this way in order to best capture greater variability among patients, account for the level of severity of infection, account for the increased concentration in each inpatient IV dose of a particular medication, and maintain consistency across patients in analyses.

Data on mortality were obtained through the use of the KU Cancer Center electronic medical files. If a patient’s file indicated that they were deceased, the file’s notes were checked

to confirm whether or not date of death occurred within 12 months post-transplant. For this study's purpose, patient was not coded as "deceased" if patient passed away after 12 months post-transplant.

Medical Consultation

In order to calculate the number of medications, the list of medications for each patient was retrieved from the KU Cancer Center electronic medical files. Once each file was attained, medical professionals at the KU Cancer Center helped to confirm particular cancer-specific antifungal, antibiotic and antiviral medications prescriptions, on each patients' list, issued within twelve months of the initial transplant procedure.

Statistical Analyses

Data analyses were conducted using IBM SPSS version 22. Two-tailed tests of significance were conducted with the level of significance set at $p < 0.05$ for all analyses.

Descriptive and frequency statistics were examined for the following variables: age, gender, diagnosis code, and insurance type. These statistics were also examined for the three health outcome variables: total medications, number of hospitalizations, and mortality. Furthermore, means were observed for the following predictor variables: Distress score, Total Problems score, CES-D score, and SF-12 (PCS-12 and MCS-12) scores. All descriptive statistics are reported in Tables 1 through 4.

Main analyses consisted of separate stepwise linear regression models and/or logistic regression models to examine whether any of the five following continuous, independent variables (DT score, patient problem list score, CES-D score and PCS-12 and MCS-12 scores) were significant predictors of the health outcome variables (medications used, hospital admissions, and/or mortality within 12-months post-transplant). Specifically, a stepwise linear

regression model using a backward elimination procedure, was used to capture the continuous nature of the variables medications and hospitalizations. All predictors were initially included in the model, and then, through the use of the backward elimination process, predictors that did not account significantly for the outcome variable were discarded (reference Hocking, 1976 for further discussion of this method).

Binary logistic regression was used for mortality as well as hospitalizations as this type of regression can be helpful for modeling the independence of a binary response on an explanatory variable which may be categorical or continuous (Bewick, Cheek, Ball, 2005). Due to the low number of re-hospitalizations per patient ($M = 0.55$; $SD = 0.81$; $Range = 0-4$), both linear and logistic regression analyses were used to accurately assess hospitalization data.

Bivariate correlations between the following variables were computed to assess for significant relationships: gender, age, DT score, PPL score, CES-D score, PCS-12, MCS-12, medications, hospitalizations, and mortality. Due to the exploratory nature of analyses, the bivariate correlations were helpful to determine potentially important relationships and trends among variables that may help inform future research. See Table 6.

Finally, relevant demographic data such as diagnosis and insurance status were assessed to identify if either of these factors independently predicted poorer health outcomes among patients. The Levene's test was used to test for the assumption of homogeneity of variance of the data (Levene, 1960; Glass, 1966). Depending upon the outcome, either a standard one way analysis of variance (ANOVAs), for homoscedastic data, or Welch's ANOVA (Welch, 1947; Welch, 1951), for heteroscedastic data, was conducted in order to compare the differences in means among diagnosis code and insurance for each of the following variables: medications, hospitalizations, mortality, PCS-12, MCS-12, CES-D score, DT score, and PPL score. Under

variance heterogeneity, the Welch procedure provides superior control of Type I errors and better power compared to the standard ANOVA (Tomarken & Serlin, 1986). Following significant F-tests, post hoc comparisons were conducted. In cases where data were homoscedastic, Tukey's HSD was used (Tukey, 1949). Games-Howell was used for data that were heteroscedastic (Games & Howell, 1976).

Results

Preliminary Analyses

Covariates. Preliminary analyses were conducted to identify covariates.

Influence of diagnosis. Either a one-way ANOVA or Welch's ANOVA, depending on each variables' homogeneity of variance, were conducted to compare the effect of diagnosis on the following variables: DT, PPL, CES-D, PCS-12, MCS-12 scores and hospitalizations, medications, and mortality for the diagnoses of MM, NHL and HL. Analyses excluded the PCL group due to the very low subsample size ($n = 1$). No significant differences were found. Means and standard deviations are provided in Table 3.

Influence of insurance status. A series of one-way between subjects ANOVAs and Welch's ANOVA tests were conducted to compare the effect of insurance status on the following variables: DT, PPL, CES-D, PCS-12, MCS-12 scores and hospitalizations, medications, and mortality for commercial, Medicare and underinsured groups. Although mortality rate did not meet the assumption for homogeneity of variance, ANOVA was used in this case as one group had a variance of zero, resulting in the Welch's test being invalid. There was a significant effect of insurance status on mortality, $F(2, 127) = 6.206$, $p = 0.00$, and depression scores on the CES-D, $F(2, 59.651) = 3.281$, $p = 0.044$. Games-Howell post hoc tests revealed that the underinsured group had a marginally higher mortality rate ($p=.055$) and

depression score ($p=.076$) when compared to the commercial insurance group; the Medicare group was not significantly different from the other two insurance groups on either variable. A Welch's ANOVA indicated a significant effect of insurance status on mental health-related quality of life scores on the MCS-12 $F(2, 56.283) = 4.598, p = 0.014$ in which a Games-Howell test indicated significantly poorer mental health quality of life among the Medicare group when compared to the commercial group ($p<.05$); the underinsured group was not significantly different from the other groups. Insurance status significantly impacted scores on the PCS-12, $F(2, 127) = 3.206, p = 0.044$, in which a Tukey's HSD post hoc test revealed the underinsured group had marginally poorer physical health quality of life when compared to the commercial group ($p=.058$) and the Medicare group ($p=.056$). These data can be found in Table 4 and Table 5.

Influence of age and gender. Bivariate correlations were examined for the remainder of the study variables. As shown in Table 6, gender had a significant relationship with several of the predictors, specifically, being female was associated with DT scores, $r(128) = -0.226, p < 0.01$ and being male was positively correlated with MCS-12 score, $r(128) = 0.213, p < 0.05$. There were no differences based on age.

Psychosocial self-report scales. Bivariate correlations indicate a high level of multicollinearity among psychosocial variables. As shown in Table 6, the DT, PPL, CES-D, PCS-12 and MCS-12 are all significantly correlated.

Health outcomes. The health outcome variables of medications, hospitalization, and mortality correlated in the expected direction. For example, medications positively correlated with hospitalizations, $r(128) = 0.531, p < 0.001$ and a higher mortality rate, $r(128) = 0.294, p <$

.01. Also, hospitalizations was positively correlated with mortality, $r(128) = 0.343, p < 0.001$.

See Table 6.

Hypothesis One: Medications

Hypothesis one tested whether the self-reported psychosocial variables (DT, PPL score, CES-D score, PCS-12 and/or MCS-12) predicted medication use in the 12 months following AuBMT. To better understand specific relationships, bivariate correlations among medications and the psychosocial variables were examined. Medications were found to be positively correlated to PPL score, $r(128) = 0.179, p < 0.05$, and also to CES-D scores, $r(128) = 0.220, p < 0.05$. These results suggest that individuals who self-reported greater problems and depressive symptoms were prescribed more medications during the 12 months post-transplant. Also, higher PCS-12 scores were inversely related to number of medications used, $r(128) = -0.293, p < 0.01$. Therefore, patients who reported better physical health quality of life were prescribed fewer medications during 12 months post AuBMT. All correlations are reported in Table 6.

Due to high collinearity among psychosocial variables, a stepwise multiple linear regression model was conducted to identify a unique source of variance that predicted medication use. At step 1 of the analysis, PCS-12 entered into the regression equation as significantly related to medications $F(1, 128) = 12.05, p < 0.01$. The adjusted R^2 was 0.079, indicating that approximately 7.9% of the variance of the number of medications used was accounted for by PCS-12, physical health-related quality of life. Distress ($t = 0.44, p > 0.05$), PPL ($t = 0.78, p > 0.05$), CES-D ($t = 1.50, p > 0.05$), and MCS-12 ($t = -0.80, p > 0.05$), scores were removed from the equation during the following steps of the analysis. Thus, PCS-12 was the only unique predictor of Medication. See Table 7 and Figure C.

Additionally, in order to control for covariates, a second model was completed which included age, diagnosis, insurance status and gender into the model. The inclusion of these potential covariates in the stepwise linear regression model did not significantly change the outcome, and no other variables besides PCS-12, were significant predictors of medications in the first 12-months post-AuBMT.

Hypothesis Two: Hospitalizations

The second hypotheses examined whether the aforementioned self-reported psychosocial variables would predict number of hospitalizations in the 12 months following AuBMT. None of the bivariate correlations were significant correlates of hospitalization. A stepwise multiple linear regression model was conducted to evaluate whether the five psychosocial predictor variables were necessary to predict number of hospitalizations up to twelve months post-transplant. None of the variables were significant predictors. Please see Table 8. Due to the low number of hospitalizations per patient ($M = 0.55$), and low degree of variability ($SD = 0.81$; see Table 2 and Figure B), the outcome of the linear regression was less meaningful. Therefore, a logistic regression model was conducted to more accurately capture the nature of the data. Again, no psychosocial predictors were found to significantly predict the variable, hospitalization.

Hypothesis Three: Mortality

The third hypothesis investigated whether mortality at twelve months post AuBMT would be influenced by any of the five self-reported psychosocial variables (DT, Total Problems, CES-D score, PCS-12 and/or MCS-12). None of the bivariate correlations were significant. A logistic regression model was conducted to evaluate whether any of the five psychosocial predictor variables were necessary to predict mortality up to twelve months post-transplant.

None of the variables were found to be significant predictors. Please see Table 9. However, only 6% of the sample died within 12 months post-transplant. Therefore, the low 12-month post-AuBMT mortality rate within this sample size may impact one's ability to detect a significant effect.

Discussion

The current study aimed to better understand the impact of pre-AuBMT psychosocial factors (i.e., distress, depression and quality of life) on post-AuBMT health outcomes (i.e., medication use, hospitalizations, mortality) in hematological cancer patients. The panel of psychosocial predictors did not predict hospitalizations or mortality. However, consistent with the study hypotheses, preliminary analyses suggest that psychosocial problems may be significant predictors of antiviral, antifungal, antibiotic medication use throughout the 12 months following transplant. This research, based on objective chart data, suggests that psychosocial factors appear to be meaningfully associated and predictive of medical outcomes including antiviral, antifungal, and antibiotic medication use. Therefore, it may be important to consider psychosocial functioning pre-transplant in order to better understand variables impacting recovery.

Medications

Individuals who self-reported more problems and depressive symptoms were prescribed more antiviral, antifungal, and antibiotic medications during the 12 months post-transplant. Furthermore, preliminary analyses suggest self-reported physical quality of life may be a significant predictor of the number of antiviral, antifungal, and antibiotic medications that a patient used during the 12 months after their AuBMT. Additionally, preliminary analyses suggest that some of the demographic variables such as insurance status, as well as the high level

of collinearity among health outcomes may be important when interpreting these main results. For example, although the other two primary variables regarding hospitalizations and mortality were not associated with significant differences, the zero order correlations between these variables and the primary outcomes were significant (i.e., those who used more medications also had a higher mortality rate and greater number of hospitalizations).

Main results from the study suggest that certain psychosocial variables may have a relationship with post-transplant medication use. For example, results indicate that the greater number of problems and concerns (i.e., family, practical, emotional, spiritual and physical problems) and/or depressive symptoms a patient is experiencing prior to AuBMT, the higher number of antiviral, antifungal and antibiotic medications may be used post-transplant. Additionally, those patients who reported less satisfaction with their physical health quality of life, such as worse physical functioning, lower overall general health, and more bodily pain and limitations due to physical pain prior to transplant reported that they used more medications post-AuBMT, even though the medications monitored for this study are not related to the care of pain. This last finding was also supported by the stepwise linear regression, in which the physical health quality of life score was a significant independent prognostic factor for increased medication use following transplant –the worse one views their physical health quality of life pre-AuBMT, the more medications that were used post-AuBMT.

These findings are important in several ways. First, they address the question of a relationship between psychosocial factors and health outcomes, such as infection treatment, following AuBMT. As previously mentioned, antiviral, antifungal and antibiotic medications are often used in this population in order to prevent and/or treat infections that may be life-threatening due to patient immune limitations post-transplant (Bone Marrow Transplantation,

2015; Bhatti, Almyroudis, Segal, 2006). Infections are more likely to occur prior to a patient's immune system being fully recovered, during the "engraftment" period (American Cancer Society, 2013); therefore, use of these medications may indirectly indicate a poorer immune system, which has the potential to lead to slower recovery. If individuals who view their physical health quality of life as poorer pre-AuBMT are taking more medications post-AuBMT, this may indicate that they are suffering from a poorer immune system, increased infections, and which possible increased risks to their recovery.

Furthermore, the association between greater depressive symptoms and perceived daily problems, which have been shown to be correlated with distress levels (see Table 6; Jacobsen et al., 2005), and greater medication use may indicate a relationship between psychosocial functioning and health outcomes. Depression scores for this population fall within a subclinical range, based on the CES-D measurement (Radloff, 1977); however, based on the standard deviation, scores extend into the clinical range (see Table 2). Therefore, there is a portion of this population suffering from clinical levels of depressive symptoms. Past research has indicated that depression, both subsyndromal and syndromal, directly influences dysregulation of one's immune system, and that depression and stress may lead to prolonged infection or delayed wound healing (Kiecolt-Glaser & Glaser, 2002). Also, other studies have indicated that pre-transplant distress is related to poorer physical health recovery (Syrjala et al., 2004) and immune functioning post-transplant (McGregor et al., 2013). Therefore, increased distress and depression may potentially be increasing risk of infection, which in turn is causing individuals to use more antiviral, antifungal and antibiotic medications in order to treat such infections. These results further indicate that there may be a relationship between certain psychosocial factors and health recovery in AuBMT patients.

Hospitalizations and Mortality

Psychosocial variables were not found to significantly predict hospitalizations or mortality in this study. It is likely that this data does not possess enough sensitivity due to a low hospitalization and mortality rate. Other studies have found that various psychosocial variables can impact health outcomes (McGregor et al., 2013; Satin et al, 2009; Pinquart & Duberstein, 2010; Andorsky et al., 2006). Had patients been followed for a longer period of time, there may have been an increased opportunity to observe significant findings in hospitalization or mortality rate. For example, Prieto and colleagues (2005) followed cancer patients for up to 3 years and found that depression predicted higher 1 and 3-year mortality rates in cancer patients after stem-cell transplantation. Another study, that followed cancer patients for more than a four-year period, found that poorer overall pre-BMT adjustment, mood (i.e., greater depressive symptoms) predicted shorter life spans (Hoodin et al., 2004).

Insurance Status

According to preliminary results, several study variables were found to be significantly related to insurance type, including mortality rate, depressive symptoms, and physical and mental health quality of life. Additionally, medications and distress scores were trending toward significant association with insurance type. If the participant sample had been larger, these trends may have reached significance. These associations between insurance status and health and psychosocial variables are important when considering the critical role that insurance may play in cancer patients' recovery.

When looking further into the means for each of the variables significantly related to insurance type, it was found that, in general, those in the underinsured group experienced more depressive symptoms and poorer physical health quality of life prior to the transplant compared

to the group with commercial insurance status, and had higher rates of mortality at 12 months post-AuBMT. The results regarding individuals with Medicare were less conclusive. However, these findings suggest, overall, that insurance status plays a role in health outcomes which is consistent with previous studies. One study, for example, found that, even when controlling for various other factors such as self-and physician-rated health status, body mass index, leisure exercise, alcohol use, ethnicity/race, and income, a lack of insurance is significantly associated with mortality (Wilper et al., 2009). In addition, there have been multiple studies that have shown an effect of insurance payer on cancer care, screening and long-term outcomes (Roetzheim, Pal, Gonzalez, Ferrante, Van Durme, Krischer, 2000; Hsia, Kemper, Kiefe, 2000; Roetzheim, Pal, Tenant et al., 1999; Ayanian, Kohler, Abe, Epstein, 1993 as cited in Kelz et al., 2004).

In fact, uninsured and underinsured cancer patients have been reported to be at a heightened risk for receiving overall substandard care, impaired access to quality healthcare, and poorer medical treatment (Kelz et al., 2004). Kelz and colleagues (2004) found that uninsured and Medicaid patients with colorectal carcinoma have a greater risk of developing postoperative complications and dying than individuals who are privately insured. Ayanian and colleagues (1993) suggest that uninsured and Medicaid breast cancer patients had worse survival rates than those patients with private insurance. The adjusted risk of death in this study was 49% and 40% higher for uninsured and Medicaid patients, respectively, than for privately insured patients in the 4-7 years post-diagnosis (Ayanian et al., 1993). A more recent study by Bristow and colleagues (2013) found that among all sociodemographic factors evaluated, “not insured payer status” was one of the strongest predictors for a “worse overall survival outcome.” These

previous studies heighten the importance of further understanding the role of insurance status among individuals with hematological malignancies who have had an AuBMT.

Findings also suggest an additional risk to recovery may be one's health insurance status. Those individuals who were underinsured experienced worse psychosocial functioning prior to transplant, such as increased depressive symptoms and decreased physical health quality of life. This is highly concerning given the aforementioned significant relationships between medication use and physical health quality of life and depressive symptoms (Table 6). The current findings of a relationship between insurance status and psychosocial functioning are consistent with previous studies that suggest that people with psychosocial concerns are more likely to be uninsured than those without such issues (Rowan, McAlpine & Blewett, 2013). This fact is concerning when research has shown that, when compared with individuals without a cancer history, cancer survivors are more likely to use mental health services (Hewitt & Rowland, 2002). In a study that examined a nationally representative sample of 95,615 adults in the U.S., researchers found that if all cancer survivors with mental health problems who needed but could not access mental health services due to cost had received such care, mental health service use would have seen a 62% increase (Hewitt & Rowland, 2002).

This association between mental health and cancer health outcomes and insurance status is highly problematic for successful cancer survivorship and the opportunity for patients to thrive post-AuBMT. Future studies should replicate these important results as there were no a priori hypotheses regarding insurance status, and sample size may have not been large enough to detect all significant effects.

Health Care Outcomes and Cost Offset

If there is indeed a link between these psychosocial factors (depression, perceived problems/distress, and perceived physical health quality of life) and increased medication usage, there may be need to further investigate how improving mental health prior to transplant, or throughout recovery post-AuBMT may not only improve the patient's finances, but the financial state of the health care system as well.

While the medication costs to patients may vary depending on the patients' particular insurance provider, and the pharmacy in which the medication was issued, it is worthwhile to examine some examples of average medication costs for this population. Some medications were less costly, such as the common antiviral medication Acyclovir and the antifungal, Diflucan which, for varying strengths of prescriptions of 30 tablets are in the \$30.00 - \$70.00 range. However, one common antibiotic used in this population was Vancomycin. The "cash cost" of this, or the cost without insurance, according to the KU Cancer Center pharmacy representative, is approximately \$793.00 for 30 of the 125 mg tablets or \$1309.00 for 30 of the 250 mg tablets. The amount and strength of tablets prescribed varied widely from patient to patient based on overall health, immunity, and strength of active or potential infection. However, it is important to note that often, patients are already struggling financially to pay for the AuBMT alone, along with doctor and hospital visits, and have potentially had to cease working, pay for extra childcare or household care services, and cover co-pays or out-of-pocket costs for procedures, office visits, and medications on top of all of their other expenses. Financial stressors can play a role in exacerbating other mental health issues such as distress and depression (Sharp, Carsin, Timmons, 2013; Price, Choi, & Vinokur, 2002). Therefore, with the cost of medication usage potentially increasing severity of mental health issues, and results indicating that mental health/psychosocial

functioning is associated with increase in medication usage, results from this study may suggest that there appears to not only be a deleterious relationship between medication usage, psychosocial functioning, and health recovery/disease progression but also between mental health and health care costs/usage, creating a potentially vicious cycle for patients.

While results did not directly support the hypotheses that psychosocial factors predicted hospitalizations or mortality post-transplant, it is important to note that this may be due to some experimental design limitations which will be discussed in the following section.

Limitations and Future Directions

Based on current literature searches, this is the first study that has examined the effect of psychosocial functioning on health outcomes in the specific population of AuBMT patients. While a significant relationship was found between medication use and psychosocial factors, there were less supportive data for that relationship with mortality and hospitalizations. These results raised a number of other questions which are currently limitations of this research, but potential avenues for future research.

One limitation is that this is a retrospective chart review study. Therefore, there were some limitations as to what information could be collected about patient demographics and health outcomes, for example, there was incomplete data regarding patient ethnicity for the sample. There were data to suggest that a patient's ethnicity may impact certain factors studied, such as psychosocial variables and health outcomes during cancer survivorship (Janz, Friese, Li, Graff, Hamilton & Hawley, 2014; Advani et al., 2014; White, Pollack, Smith, Thompson, Underwood, & Fairley, 2013). Therefore, future studies would benefit from replicating aspects of this study, but collecting ethnicity data and including such information in analyses to control for variability.

Also, because this was a retrospective chart review study, it was difficult at times to determine exact medication dosage. Dosages for inpatient and outpatient use were calculated differently. If a patient was hospitalized as an inpatient for several days, and they received multiple IV doses of a certain medication, each IV dose prescribed was considered a separate dose. Yet, for outpatients, one bottle of medication was tallied as one medication dose, regardless of number of tablets in the bottle. This method was instilled to create consistency across both types of patients and to control for dose potency as the IV dose for inpatients tended to be much stronger than those given in pill/tablet form to outpatients. Moreover, because this was chart review study, it was not possible to control for adherence to outpatient medications. Future studies would highly benefit from investigating medication usage more thoroughly by controlling and measuring medication dosage more accurately, or possibly separating inpatient and outpatient medication use, as well as developing a system to measure adherence for medications prescribed on an outpatient basis. Adherence measures may help address a separate question of whether or not low adherence is related to psychosocial factors, or whether adherence contributes to increased infections post-transplant.

Additionally, due to the retrospective nature of the study as well as the broad use of antiviral, antifungal, and antibiotic medications, it was difficult to disentangle age-related complications and cancer infection-related complications contributing to medication use. The potential confounding variable of age-related complications was also evident when considering mortality rate. Future studies tracking medication use or mortality rate as health outcomes within this population would benefit from thorough documentation to better understand the driving factor behind these two variables.

Also, while we found that insurance status seems to play a role in one's overall well-being pre-transplant and potentially in one's survival rates post-transplant, it would be important for future studies to more closely investigate other mediating variables associated with a lower insurance status. For example, many studies indicate that those who are underinsured or who do not have insurance have limited access to preventive services, have less ability to seek timely care, and/or are less likely to receive recommended treatment (Halpern et al., 2007; DeVoe, Fryer, Phillips, & Green, 2003; Powell-Griner, Bolen, & Bland, 1999). These other factors may be important variables to examine in understanding the importance of insurance status in this population.

Another limitation is that this study only tracked and measured health outcomes of patients for 12 months post-transplant. In order to gain more comprehensive data regarding health outcomes it would be helpful to collect and analyze data for a longer post-transplant time period, at least up to 24 months post-transplant. Research shows that even with the most favorable hematological malignancy prognoses, net survival tends to decrease over time (Monnereau et al., 2013; American Cancer Society, 2015). It could be particularly helpful to better understand the relationship between psychosocial variables and mortality rates over time within this specific population. For example, when cleaning data it became apparent that multiple individuals passed away after the 12-month time point, but these data were unable to be captured within the current study parameters.

An additional limitation was the operationalization of the hospitalization variable. Hospitalization re-admission rates were lower than expected. Following chart review, it became apparent that tracking hospitalization re-admissions solely based on whether or not patients were admitted overnight posed a limitation in being able to fully capture the range of health care

usage. For instance, many patients were hospitalized in the E.R., but did not stay overnight, therefore, that data were exempt from analyses. Also, many patients utilized additional outpatient services, such as office visits, to address any additional issues or concerns that arose following transplant such as neutropenic fevers or other transplant-related symptoms. There is currently a push within the AuBMT population to transition care from an inpatient to outpatient basis (Graff et al., 2015; Leger et al., 2006; Meisenberg, Ferran, Hollenbach, Brehm, Jollon, Piro, 1998; Gluck et al., 1997). This may be why only the most severe cases or complications appeared to have led to patients being hospitalized overnight. Also, the overnight hospitalizations ranged from a few days to a few weeks, and the exact number of days per hospitalization not fully captured or used in the current analyses. It may be that not analyzing overnight hospitalizations, but the rather the number of days hospitalized, would have allowed for greater variability and perhaps would have led to more accurate or conclusive results for this health outcome variable.

Another concern that may be addressed in future studies is the high multicollinearity found among this study's psychosocial variables. For example, the distress thermometer score was significantly correlated with each of the four other psychosocial variables, indicating potential overlap in content that each scale measures. While this is consistent with previous research data, particularly when looking at distress scales (Vodermaier, Linden, & Siu, 2009), this high level of correlation among variables may present a problem when interpreting the stepwise linear regression models. This multicollinearity suggests a need for future studies to replicate current findings with this particular population, while employing different statistical techniques, such as Structural Equation Modeling (SEM) (Muthen & Muthen, 1998). This would allow all of the highly correlated psychosocial predictors to be examined as a latent

variable (i.e., psychosocial functioning). A latent variable can be simply described as an underlying cause of multiple observed behaviors or an important construct that is measured indirectly through multiple indicators that capture different aspects of the construct (Muthen, 2002).

In addition to using SEM analytic techniques, future studies may benefit from utilizing mediation techniques. Some findings from this current study might indicate possible mediating factors that could come to light given a larger sample and/or a longer time frame post-transplant.

While this study found significant results indicating self-reported physical health quality of life predicts medication usage, future research may choose to take these findings a step further and investigate what psychotherapeutic or other clinical steps or services could be taken to improve physical health quality of life prior to transplant in order to potentially decrease medication usage and/or infection and reduce health care costs to patients, the health care system, and insurance companies.

Conclusion

In summation, findings from this sample of patients with hematological malignancies who undergo AuBMT suggested that there is a link between psychosocial functioning and health care outcomes. Those patients who self-reported an increase in problems such as Family Problems, Practical Problems, Emotional Problems, Spiritual/Religious Concerns, and Physical Problems and/or depressive symptoms were prescribed more medications during the 12 months after their transplant. Furthermore, self-reported physical quality of life proved also to be a significant predictor of the number of medications that a patient used during the 12 months after their AuBMT. Additionally, insurance status accounted for differences in individuals' mortality rate, depressive symptoms, and physical and mental health quality of life.

Patients completing AuBMT are a high-risk population for suffering from mental health concerns due to their marked lifestyle limitations as part of the treatment and recovery process. They are forced to be socially isolated during treatment and recovery, in order to prevent further complications to their already compromised immune systems. Additionally, they may undergo changes in a variety of settings in a short period of time such as occupational, financial, family, social, and leisure. These changes not only impact these patients' physically, but also emotionally, and they may suffer from a great amount of distress due to these changes. Additionally, the impact of insurance status across all of the psychosocial and health outcomes is an important area for further exploration as it could serve as an impediment to overall recovery. There is much literature investigating mental health outcomes and cancer survivorship in general cancer populations, but less is known about this relationship in a population of individuals with hematological malignancies who have undergone AuBMT. Due to each cancer diagnosis and treatment being unique and varied, it is important to address the specific needs in each population. Through continuing to investigate the important questions addressed in this study with this particular population, we will be able to further increase and expand our knowledge regarding the best way to care for patients prior to and following an AuBMT.

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Table 1
Descriptive and Frequency Characteristics of Demographic Variables

Variable	N	%	Min-Max	Mean	Std. Deviation
Age (years)	-	-	21-80	58.39	11.71
Male	67	51.5			
Diagnosis					
MM	86	66.2			
NHL	32	24.6			
HL	11	8.5			
PCL	1	0.8			
Insurance Status					
Medicare	56	43.1			
Commercial	49	37.7			
Underinsured	25	19.2			

Note. MM= Multiple Myeloma; NHL= Non-Hodgkin's Lymphoma; HL= Hodgkin's Lymphoma; PCL= Plasma Cell Leukemia

Table 2
Descriptive and Frequency Characteristics of Outcome Variables

Variable	N	%	Min-Max	Mean	Std. Deviation
DT			0-10	3.19	2.86
PPL			0-23	6.35	5.26
CES-D			0-41	10.29	8.48
PCS-12			13.06-58.31	36.55	11.57
MCS-12			28-68	52.67	8.90
Medications			0-69	13.98	11.83
Hospitalizations			0-4	.55	.81
Hospitalizations*	52	40			
Mortality Rate	8	6.2			

Note. DT=Distress Thermometer; PPL=Patient Problem List; CES-D= Center for Epidemiologic Studies Depression Scale; PCS-12 = Physical Health Composite Scale-12; MCS-12= Mental Health Composite Scale-12

*This is the categorical version of the variable (0=no hospitalizations,1=hospitalization(s))

Table 3
Means and Standard Error of Variables by Diagnosis Type

Variable	MM	NHL	HL
DT	3.22 (.30)	2.72 (.55)	4.55 (.68)
PPL	6.69 (.57)	4.88 (.81)	8.09 (1.96)
CES-D	10.58 (.91)	9.41 (1.48)	11.09 (3.00)
PCS-12	36.09 (1.28)	38.98 (1.97)	32.62 (3.06)
MCS-12	52.82 (.94)	52.89 (1.71)	50.17 (2.58)
Medications	14.28 (1.41)	12.16 (1.34)	18.00 (3.55)
Hospitalizations	.50 (.08)	.63 (.15)	.73 (.33)
Mortality	.02 (.02)	.13 (.06)	.18 (.12)

Note. No significant differences found among means.

Table 4
Means and Standard Error of Variables by Insurance Status

Variable	Commercial	Medicare	Underinsured
⁺ DT ^b	2.49 (.35)	3.39 (.39)	4.12 (.64)
PPL ^a	5.41 (.66)	6.46 (.71)	7.96 (1.20)
*CES-D ^b	8.16 (.94)	10.88 (1.19)	13.16 (2.01)
*PCS-12 ^a	37.84 (1.74)	37.74 (1.54)	31.38 (1.82)
*MCS-12 ^b	55.32 (.81)	51.30 (1.28)	50.54 (2.28)
⁺ Medications ^a	12.08 (1.55)	13.43 (1.31)	18.96 (3.24)
Hospitalizations ^b	.51 (.11)	.48 (.11)	.76 (.19)
*Mortality ^b	.00	.05 (.03)	.20 (.08)

Note. ⁺= variable is approaching significance (p=.05); * = variable has significant difference between means (p<.05); ^a=equal variances, used ANOVA; ^b=unequal variances, used Welch ANOVA

Table 5
Paired Comparisons Among Insurance Status Groups

	Commercial- Underinsured	Commercial- Medicare	Medicare- Underinsured
CES-D^a	p= .076		
PCS-12^b	p=.058		p=.056
MCS-12^a		*p<.05	
Mortality^b	p=.055		

Note. ^a=Games-Howell post hoc test; ^b=Tukey's HSD post hoc test

Table 6
Bivariate Correlations of Psychosocial Variables, Health Outcomes, and Individual Differences

	DT	PPL	CES-D	PCS-12	MCS-12	Meds	Hosp.	Mor.	Gen.
DT	1								
PPL	.655***	1							
CES-D	.612***	.685***	1						
PCS-12	-.202*	-.404***	-.348***	1					
MCS-12	-.705***	-.648***	-.657***	.108	1				
Meds	.096	.179*	.220*	-.293**	-.099	1			
Hosp.	.065	.009	.072	-.078	.014	.531***	1		
Mortality	.050	-.060	.048	-.127	.006	.294**	.343***	1	
Gender	-.226**	-.052	-.112	-.098	.213*	.005	-.107	-.072	1
Age	-.084	-.123	.021	.007	.016	-.075	-.108	.107	-.020

Note. * p<.05, **p<.01, ***p<.001;

Table 7
Stepwise Linear Multiple Regression for Medication Use

<i>Independent Variables</i>	<i>Beta (β)</i>	<i>Significance</i>
PCS-12	-.293**	.001
DT	.038	.661
PPL	.072	.437
CES-D	.061	.500
MCS-12	-.068	.427

Note. ** $p < .01$; $F(1, 128) = 12.05$, $p < 0.01$;
 Total adjusted $R^2 = .079$

Table 8
Stepwise Linear Multiple Regression for Hospitalizations

<i>Independent Variables</i>	<i>Beta (β)</i>	<i>Significance</i>
PCS-12	-.246	.013
DT	-.060	.645
PPL	.002	.990
CES-D	.168	.199
MCS-12	-.003	.984

Note. $F=2.88$; $F(1,128)=.611$, $p =.655$;
 Total adjusted $R^2 = .068$

Table 9
Logistic Regression for Mortality Rate

<i>Independent Variables</i>	<i>Beta (β)</i>	<i>S.E.</i>	<i>Significance</i>
PCS-12	-.068	.041	.095
DT	.189	.191	.324
PPL	-.242	.127	.058
CES-D	.038	.060	.526
MCS-12	-.002	.063	.977

Note. S.E.=standard error

Figure A

Flow Chart for Patient Inclusion in Present Study

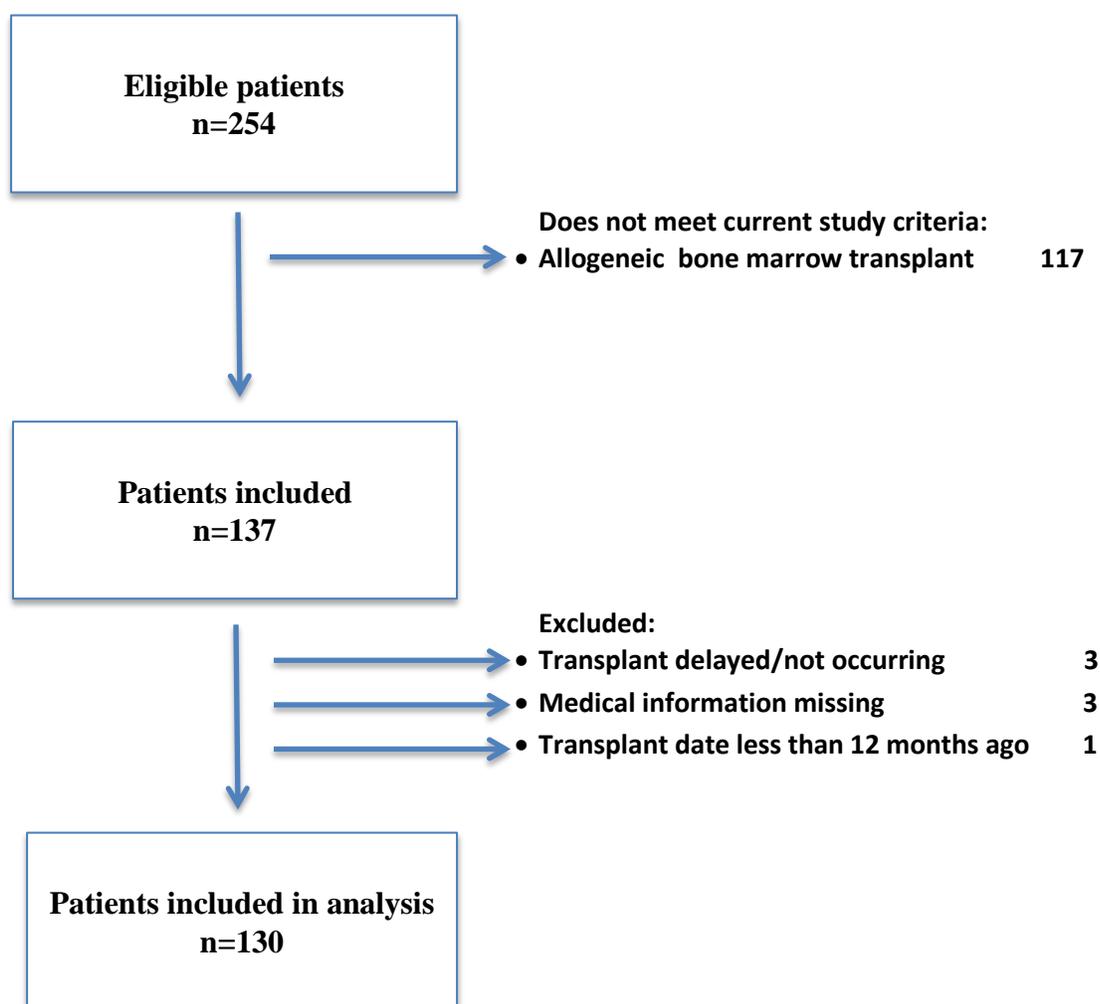


Figure B

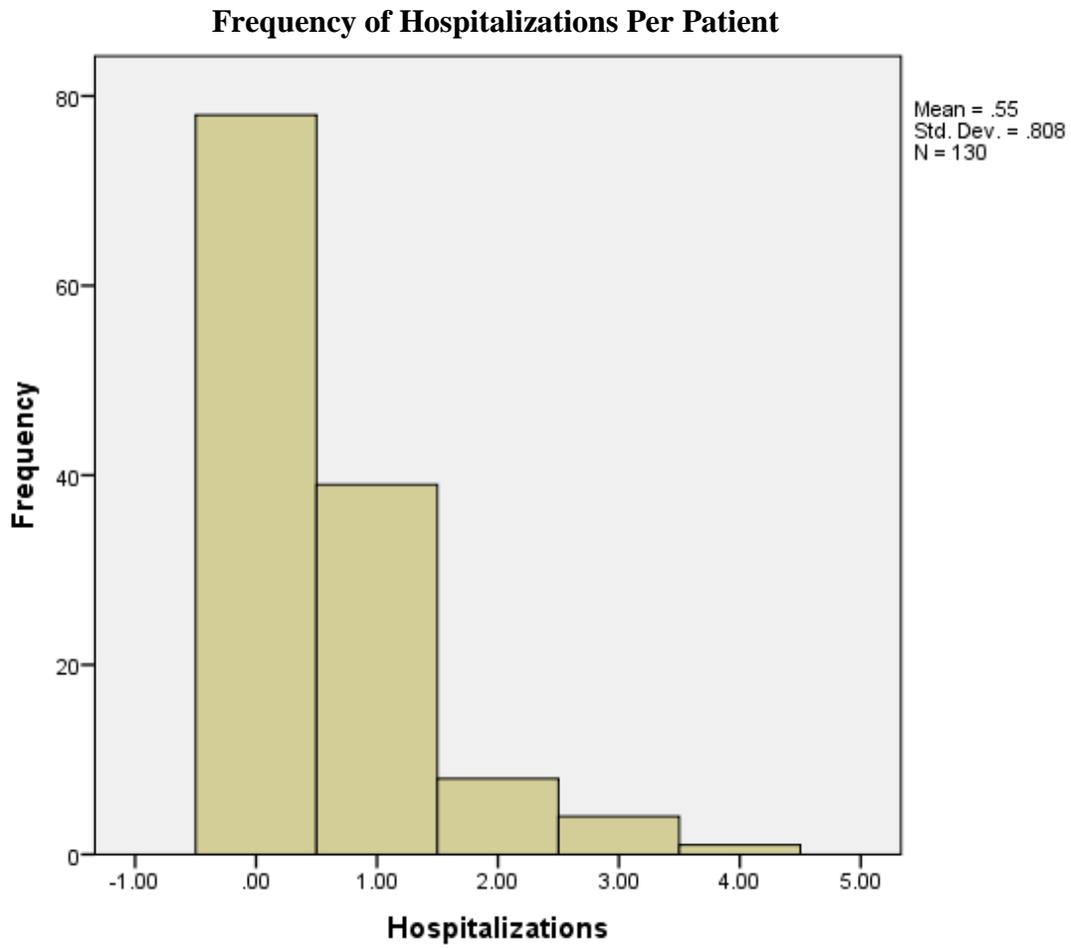


Figure C

Path Diagram for Stepwise Linear Regression Model for Medication Use

