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Review

Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature

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Abstract

***Objective*: This article reviews recent literature on adults' quality of life following hematopoietic stem cell transplantation (HSCT).**

***Methods*: We identified 22 prospective reports with at least 20 participants at baseline through a search of databases (Medline and PsycInfo) and handsearching of articles published from 2002 to October 2007. If longitudinal data were not available or were scarce for a particular topic or time point, cross-sectional studies were reviewed.**

***Results*: Although physical, psychological, and social aspects of quality of life tend to improve during the years following transplantation, a significant proportion of HSCT survivors experience persistent anxiety and depressive symptoms, fatigue, sexual dysfunction, and fertility concerns. Despite ongoing treatment side effects, the majority of HSCT survivors resume their work, school, or household activities.**

***Conclusion*: We conclude that theory-driven research with larger samples is needed to identify subgroups of HSCT survivors with adjustment difficulties. Such research would examine survivors' evolving standards and definitions of quality of life to improve the accuracy and meaningfulness of assessment and incorporate biological, psychological, and contextual factors that may contribute to positive adjustment.**
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Keywords: cancer; oncology; hematopoietic stem cell transplantation; bone marrow; quality of life; psychological adjustment

The number of hematopoietic stem cell transplant (HSCT) survivors is rapidly increasing, as more than 45 000 people receive HSCT annually throughout the world [1]. The term HSCT encompasses bone marrow transplants (BMT), stem cell transplants (SCT) from peripheral blood or umbilical cord blood, and mini/light procedures (with lower toxicity) that are used primarily for hematologic and lymphoid cancers, and also for many other disorders [1]. HSCT involves an initial regimen of high doses of chemotherapy and/or radiation followed by infusions of stem cells to reestablish hematopoietic function. During the initial regimen patients' lymphocytes are destroyed, and the subsequent transplant attempts to restore immune function. During this time the low lymphocyte count may reach the 'nadir', the lowest count, and the person is at great risk for infections, which could be lethal. Although the introduction of novel agents and the use of peripheral blood stem cells instead of bone marrow have improved HSCT outcomes [2], about 40% of advanced cancer patients who undergo allogeneic HSCT die from complications related to the transplant [1]. This review focuses on patients' quality of life following two types of HSCT—allogeneic and autologous transplantation. Allogeneic transplantation uses donor stem cells and therefore may be associated with graft-versus-host disease (GVHD), which involves attacks by donor T lymphocytes on the patient's organs and the potential for severe complications. Autologous transplantation uses the patient's own stem cells; therefore, there is no GHVD risk.

For nearly two decades researchers have examined the quality of life of HSCT recipients [3], including the effects of transplantation on physical function, psychological status, social interactions, and economic and/or vocational status. In this review we examine all of these domains of quality of life following HSCT and conceptualize the patient's life-threatening disease and transplantation as a psychosocial transition. According to Parkes [4], a psychosocial transition is a major life experience that requires individuals 'to restructure [their] ways of looking at the world and

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[their] plans for living in it' (p. 102). Psychosocial transitions can potentially result in simultaneous positive and negative outcomes for the same individual as his or her world view evolves to accommodate the stressful event [4,5]. For example, an HSCT patient may experience career disruption and existential distress and simultaneously experience renewed relationships and a greater appreciation of life. Concurrent reports of personal growth and deficits in physical, social, and emotional well-being among HSCT survivors are consistent with the transition paradigm [5,6].

This review of quality of life following HSCT is limited to articles published from January 2002 to October 2007, though some earlier publications are mentioned. We focus on these more recent studies because they are more likely than older studies to reflect changes in HSCT protocols and because they are generally more methodologically rigorous than earlier studies. Articles were identified through a search of PsycINFO using the following keywords: (bone marrow or stem cell) and transplant$.[1] MEDLINE searches also included the following keywords: psycho$, quality of life, fatigue, or sexual. Use of the terms (mini or light or partial or tandem) and transplant$ in combination with the above-mentioned keywords did not result in any relevant publications. Further pertinent studies were found through searches of reference lists in published articles. The database searches yielded 1513 results, and we reviewed the titles, abstracts, and, if necessary, the full papers in order to extract articles that focused on quality of life, fatigue, sexuality, or distress outcomes (e.g. global distress or mood, negative affect, depressive or anxious symptoms) in adult HSCT survivors. We found 22 articles that met our criteria (see Table 1).

Articles presented in Table 1 had to (1) be published in the English language, (2) include at least one assessment prior to transplant and one assessment after transplant, and (3) include at least 20 participants at baseline. We excluded articles in which pediatric populations were included or original empirical data were not reported. Although we generally excluded articles that focused on psychological interventions for HSCT recipients, we note the intervention literature when providing directions for future research. Although we cite papers that included measures of neuropsychological functioning, we do not discuss the cognitive effects of chemotherapy and radiation and refer the reader to recent reviews [7,8]. Throughout this paper cross-sectional work is only cited if few longitudinal studies with HSCT survivors have examined a particular issue (e.g. posttraumatic stress symptoms), or scarce data are available for a particular time point (e.g. 10-year follow-up data).

This article first reviews the literature on HSCT recipients' self-reported physical well-being with an emphasis on fatigue, a common complaint of HSCT survivors. Second, the psychological distress of HSCT recipients is discussed, including depression, anxiety, and posttraumatic stress symptoms. Third, research on vocational and financial status, social well-being, and sexuality and fertility is reviewed. Finally, methodological and conceptual limitations of prior research are presented along with directions for future research.

Physical well-being

General physical functioning

Toxicity and immunosuppression associated with HSCT can contribute to a range of long-term difficulties with physical functioning. These difficulties are exacerbated by conditions such as chronic GVHD, infections, secondary malignancies, organ damage, endocrine dysfunction, and various physical symptoms (e.g. pain, nausea, fatigue) [9]. In this literature, *physical functioning* has been defined as 'the ability to conduct a variety of activities ranging from self-care to more challenging and vigorous activities that require increasing degrees of mobility, strength, or endurance' [10, p. S32]. *Role functioning* specifically refers to the person's ability to perform occupational or household duties [11]. Some quality-of-life instruments evaluate the respondent's functional limitations (e.g. difficulty engaging in strenuous activities) and physical symptoms (e.g. pain, fatigue), whereas other measures only evaluate quality of life in terms of satisfaction with current functioning and symptom control [11]. Other instruments evaluate both physical status and the respondent's satisfaction with his or her physical health [11]. Thus, it is important to consider the varying definitions of physical well-being when comparing outcomes across modestly correlated quality-of-life instruments [11].

Most ($n = 20$) of the 22 studies in Table 1 include one or more assessments of HSCT patients' physical functioning and/or symptoms. Global physical functioning has been acceptable pre-transplant and 100 days after HSCT [12]. Although HSCT patients have not reported great difficulty engaging in routine activities (e.g. walking, self-care) at these time points, patients have shown a significant decline in physical functioning as their symptoms increase following high-dose chemotherapy [13,14]. In addition, many patients experience long-term side effects of treatment [15]. For example, one study found that physical and role functioning scores were significantly below population norms at 6 months post-transplant, and role

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Table I. Prospective investigations of quality of life following hematopoietic stem cell transplantation

Reference	Sample demographics at baseline	Disease type	Type of transplant	Reported QOL domains[a]	Instruments	Timing of assessments	Results
Jacobsen *et al.*, 2002 [38]	*N* = 70, 76% female, mean age = 48 years	67% breast cancer, 12% leukemia, 13% multiple myeloma, 8% lymphoma	83% autologous BMT, 17% allogeneic BMT	A, D	Coping Responses Inventory, POMS, ISEL-SF, PCL-C	1 month pre-BMT, average of 7 months post-BMT	6–9% had probable cancer-related PTSD, low social support, and high avoidance coping predicted greater PTSD symptoms.
Prieto *et al.*, 2002 [41]	*N* = 220, 58.6% male, mean age = 38.4 years	51.4% leukemia, 20.9% non-Hodgkin's lymphoma, 8.6% Hodgkin's disease, 12.3% multiple myeloma, 6.8% other	58.6% autologous SCT, 41.4% allogeneic SCT	P, A, D	KPS, structured psychiatric interview based on DSM-IV criteria, Bearman Toxicity Scale, Nottingham Health Profile, Psychosocial Adjustment to Illness Scale-self-report, HADS, author-constructed physical and emotional status scales	Baseline (within 48 h of hospital admission), day of transplant (day 0), weekly assessments until discharge or death (day +7, +14, +21, etc.)	An adjustment disorder was diagnosed in 22.7% of patients, a mood disorder in 14.1%, and an anxiety disorder in 8.2%. Diagnosis of any mood, anxiety, or adjustment disorder was associated with a longer length of hospital stay.
Hjermstad *et al.*, 2003 [59]	*N* = 130, 65.4% male, median ages = 35 (allogeneic SCT) and 41 years (autologous SCT)	46.9% leukemia, 53.1% lymphoma	46.9% allogeneic SCT, 53.1% autologous SCT	P, V	CARES-SF, EORTC QLQ-C30	1 month pre-SCT, 2, 6, and 12 months post-SCT	Allogeneic SCT patients reported better physical functioning pre-SCT and better psychosocial scores at 6 and 12 months post-SCT than autologous SCT patients.
Langer *et al.*, 2003 [45]	*N* = 131, 51.1% female, mean age = 42.9 years	55.7% leukemia, 13.0% myelodysplasias, 12.2% lymphoma, 11.0% breast cancer, 7.8% other	18.3% autologous HSCT, 81.7% allogeneic HSCT; 70.2% BMT, 29.8% PBSCT	P, A, D, S	POMS, Dyadic Adjustment Scale, MOS SF-36	Pre-HSCT (2 weeks to 1 day prior to start of chemotherapy or radiation), 6 months and 1 year post-HSCT	With respect to norms, patients reported elevated anxiety at one time point: prior to HSCT. About half of patients became more satisfied with their marital relationship over time, whereas 37% became less satisfied.
El-Banna *et al.*, 2004 [29]	*N* = 27, 56% male, mean age = 49 years	89% non-Hodgkin lymphoma, 11% Hodgkin lymphoma	100% autologous PBSCT	P, D	Revised Piper Fatigue Scale, CES-D	Before chemotherapy initiation, day 2 of chemotherapy, and recovery (day 2, 7, and 14 after PBSCT)	Fatigue and depression changed over time with the highest levels reported at day 7 after PBSCT.
Hjermstad *et al.*, 2004 [17]	*N* = 248, 63.7% male, median ages = 35 (allogeneic SCT), 41 (autologous SCT), and 37 years (combination chemotherapy)	75.4% lymphoma, 24.6% leukemia	24.6% allogeneic SCT, 27.8% autologous SCT, 47.6% combination chemotherapy	P, A, D, S, V	EORTC QLQ-C30, HADS, FQ	EORTC QLQ-C30 and HADS were administered 9 times to SCT patients (2 pre-SCT, 7 in first year post-SCT) and 7 times in 1 year to combination chemotherapy patients. All questionnaires were administered 3–5 years post-SCT.	Despite a faster recovery during the first months post-SCT, allogeneic SCT patients reported poorer functioning and more fatigue than autologous SCT patients after 3 years. All three groups reported more fatigue than the general population on the FQ after 3 years.
Prieto *et al.*, 2004 [47]	*N* = 220, 58.6% male, mean age = 38.4 years	51.4% leukemia, 20.9% non-Hodgkin's lymphoma, 8.6% Hodgkin's disease, 12.3% multiple myeloma, 6.8% other	58.6% autologous SCT, 41.4% allogeneic SCT	P, A, D	KPS, Nottingham Health Profile, Psychosocial Adjustment to Illness Scale-self-report, HADS, author-constructed phy-	Baseline (within 48 h of hospital admission), day of transplant (day 0), weekly assessments until discharge	The reliability and validity of author-constructed scales were demonstrated. Higher education level predicted poorer physical and emotional status at hospital discharge.

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Table I. (*Continued*)

Reference	Sample demographics at baseline	Disease type	Type of transplant	Reported QOL domains[a]	Instruments	Timing of assessments	Results
					sical and emotional status scales, energy-level scale, and systemic symptom scale	or death (day +7, +14, +21, etc.)	Female sex predicted poorer emotional status at discharge.
Syrjala *et al.*, 2004 [18]	*N* = 319, 56% male, mean age = 36 years	79.3% leukemia, 20.7% lymphoma	17% autologous HSCT, 83% allogeneic HSCT	P, D, V	Ambulation subscale of Sickness Impact Profile, BDI, Cancer Treatment Distress Scale, Social Support Inventory (baseline only), self-reported work status	Pre-HSCT, 90 days, 1 year, 3 years, and 5 years post-HSCT	In general, physical recovery occurred earlier than psychological recovery. Only 19% of survivors recovered on all outcomes at 1 year. Among survivors without recurrent malignancy, 84% returned to work by 5 years.
Chang *et al.*, 2005 [40]	*N* = 84, 57% male, mean age = 43.6 years	100% chronic myelogenous leukemia	100% allogeneic HSCT	P, D	FLIC, Quality of Life Index, BDI, Alcohol Use Disorders Inventory, Alcohol Timeline Followback	Time of admission for HSCT, 6 and 12 months post-HSCT	QOL significantly improved at 12 months post-HSCT. Depressive symptoms declined between 6 and 12 months post-HSCT. Alcohol use was lowest at 6 months post-HSCT.
Conner-Spady *et al.*, 2005 [16]	*N* = 52, 100% female, mean age = 44.7 years	100% breast cancer (34.6% stage II, 65.4% stage III) at high risk of relapse	100% autologous SCT with HDC	P, A, D, S	EQ-5D, FLIC, QOL visual analog scale	Baseline (pre-treatment), day 1 of third cycle of conventional chemotherapy, 3 weeks post-HDC, approximately 8 weeks post-HDC, and 12, 18, and 24 months after study enrollment	All three measures showed a similar pattern of change with QOL decreasing following HDC and returning to baseline levels at 8 weeks post-HDC. At 2 years post-study entry, cancer-specific QOL was better than baseline.
Lee *et al.*, 2005 [23]	*N* = 61, 51% male, median age = 49 years	Not reported	44% autologous HSCT, 56% allogeneic HSCT; 10% BMT, 88% PBSCT, 2% BMT and PBSCT	P, A, D	Pre-HSCT: Spielberger State Anxiety Scale, BDI, MOS-SSS, Brief COPE Post-HSCT: BDI, HADS, PHQ, PCL-C, NCCN Distress Thermometer, MOS SF-36, FACT-BMT subscale, Morisky's medication compliance scale	Pre-HSCT, first clinic visit after hospital discharge, and 100 days post-HSCT	Pre-HSCT, elevated levels of anxiety and/or depression were detected in 55% of respondents. Post-HSCT, 44% had at least moderate symptoms of depression, anxiety, or PTSD at either assessment point.
Prieto *et al.*, 2005 [42]	*N* = 220, 58.6% male, median age = 45 years (autologous SCT) and 36 years (allogeneic SCT)	51.4% leukemia, 29.5% lymphoma, 12.3% multiple myeloma, 6.8% other	58.6% autologous SCT, 41.4% allogeneic SCT	P, A, D	HADS, author-constructed physical status scale, energy-level scale, and systemic symptom scale	Baseline (within 48 h of hospital admission), day of transplant (day 0), weekly assessments until discharge or death (day +7, +14, +21, etc.)	Anxiety was highest at hospital admission. Depression and physical health status worsened and then improved at approximately 2 weeks post-SCT. Autologous SCT patients showed better physical, but not emotional functioning relative to allogeneic SCT patients.
Schulmeister *et al.*, 2005 [14]	*N* = 36, 75% female, 31% = 42–49 years, 39% = 50–57 years	31% stage IV breast cancer, 28% stage II–III breast cancer, 19% lymphoma, 14% multiple myeloma, 9% other	100% outpatient autologous SCT	P	FACT-BMT version 4, open-ended questions regarding patients' SCT experiences and satisfaction with the outpatient SCT process	Pre-HDC, 4–6 weeks post-HDC, 6 months post-HDC	QOL decreased post-HDC but increased to levels higher than those found at pretreatment by 6 months. Patients with progressive disease reported worse QOL at 1 and 6 months post-HDC.

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Andorsky *et al.*, 2006 [22]	*N* = 320, 51.9% male, median age = 47 years	48.7% leukemia, 21.9% non-Hodgkin's lymphoma, 18.6% multiple myeloma, 10.7% other	62.8% autologous HSCT, 37.2% allogeneic HSCT	P	Author-constructed assessment of symptoms and health, MOS SF-36	Before hospital admission and 6 and 12 months post-HSCT	Mental health was comparable to population norms, whereas physical health was worse than population norms at all three time points. Pre-HSCT mental and physical health, relapse, and chronic GVHD were associated with QOL after HSCT.
Goetzmann *et al.*, 2006 [15]	*N* = 28, 60.7% male, mean age = 40.5 years	67.8% leukemia, 14.3% multiple myeloma, 7.1% Hodgkin's disease, 10.7% other	100% allogeneic BMT	P, A, D, S	MOS SF-36, Life Satisfaction Questionnaire FLZ, HADS, Social Support Questionnaire	Baseline (during first 2 days of hospitalization), 6 and 12 months post-BMT	At baseline, patients reported worse QOL in almost all domains relative to norms. Twelve months post-BMT, only the role-physical and social functioning subscales of the MOS SF-36 remained below norms.
Hacker *et al.*, 2006 [13]	*N* = 20, 55% female, mean age = 48.7 years	36% leukemia, 23% lymphoma, 12% myelofibrosis	59% autologous HSCT, 41% allogeneic HSCT	P	Actiwatch-Score (an accelerometer), EORTC QLQ-C30, Quality of Life Index	Assessed over a 5-day period before and after HSCT for a total of 10 days	Patients reported significant declines in physical, role, emotional, and cognitive functioning following transplant that coincided with increases in symptoms.
Lee *et al.*, 2006 [24]	*N* = 96, gender of total sample not reported, median ages of patient groups = 45–47 years	Not reported	100% allogeneic HSCT	P	MOS SF-12, trial outcome index of FACT-BMT	Pre-HSCT, 6 and 12 months post-HSCT	The QOL of patients who experienced acute GVHD declined, whereas the QOL of patients without acute GVHD was stable over the first 6 months after HSCT. At 12 months, QOL improved, unless a patient developed chronic GVHD.
Prieto *et al.*, 2006 [30]	*N* = 220, 58.7% male, median age = 38 years	51.4% leukemia, 29.5% lymphoma, 12.3% multiple myeloma, 6.8% other	58.6% allogeneic SCT, 41.4% autologous SCT	P, A, D	Energy loss rated on a 0–100 scale, HADS, items from DSM-IV that assess insomnia and appetite loss, systemic symptom scale (nausea, vomiting, and pain), KPS, Bearman Toxicity Scale	Baseline (within 48 h of hospital admission), day of transplant (day 0), weekly assessments until discharge or death (day +7, +14, +21, etc.)	A number of demographic and medical variables were associated with fatigue. Baseline depression was associated with subsequent fatigue during hospitalization.
Anderson *et al.*, 2007 [21]	*N* = 100, 50% male, mean age = 53.6 years	34% non-Hodgkin's lymphoma, 66% multiple myeloma	100% autologous PBSCT	P, A, D	MDASI-BMT, POMS-30-item short form, FACT-BMT, ECOG PS	MDASI-BMT completed 3 times during PBSCT, all assessments completed at baseline (pre-HDC) and 30 days post-PBSCT	Symptom means were mild at baseline, intensified during PBSCT, and decreased at 30 days post-PBSCT. Symptom patterns varied by cancer type.
Beglinger *et al.*, 2007 [43]	*N* = 30, 66.7% male, mean age = 47.6 years	23.3% leukemia, 43.3% lymphoma, 20.0% myeloma, 13.3% other	50% autologous, 50% allogeneic; 46.7% BMT, 53.3% PBSCT	P, A, D	SCL-90, visual analog scales for rating pain and mood, delirium rating scale, and neuropsychological test battery	Baseline (average = 11.6 days pre-HSCT) and 100 days post-HSCT	At baseline, patients endorsed more psychiatric symptoms and greater symptom severity and distress relative to nonpatient norms. Patients endorsed fewer symptoms of anxiety and depression after HSCT.
Humphreys *et al.*, 2007 [46]	*N* = 242, 54.1% male, age not reported	Not reported	100% allogeneic BMT	D	CES-D, questions from the Sexual History Form and the Sexual Problems Measure	Pre-BMT, 1 and 3 years post-BMT	Highly prevalent sexual difficulties at all three time points with women reporting more sexual concerns than men. Baseline levels of depression were associated with sexual functioning 3 years post-BMT.

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Table I. (*Continued*)

Reference	Sample demographics at baseline	Disease type	Type of transplant	Reported QOL domains[a]	Instruments	Timing of assessments	Results
Schulz-Kindermann *et al.*, 2007 [12]	$N = 39$, 64.1% male, mean age = 46.5 years	53.8% leukemia, 10.3% lymphoma, 10.3% multiple myeloma, 25.6% other	100% allogeneic HSCT	P	EORTC QLQ-C30 and a neuropsychological test battery	Baseline (maximum of 2 weeks before admission for HSCT), follow-up (100 days post-HSCT, range: 80–120 days)	Self-rated physical functioning declined, whereas self-rated cognitive functioning remained stable and in the normal range. Regarding symptoms, only nausea and vomiting increased.

BDI, Beck Depression Inventory; BMT, bone marrow transplantation; CARES-SF, Cancer Rehabilitation Evaluation System—Short Form; CES-D, Center for Epidemiologic Studies Depression Scale; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-Core 30; EQ-5D, European Quality of Life—5 Dimensions; FACT-BMT, Functional Assessment of Cancer Therapy-Bone Marrow Transplantation; FLIC, Functional Living Index for Cancer; FQ, Fatigue Questionnaire; GVHD, graft-versus-host disease; HADS, Hospital Anxiety and Depression Scale; HDC, high-dose chemotherapy; HSCT, hematopoietic stem cell transplantation; ISEL-SF, Interpersonal Support Evaluation List—Short Form; KPS, Karnofsky Performance Scale; MDASI-BMT, M.D. Anderson Symptom Inventory—Bone Marrow Transplantation; MOS SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; MOS SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; NCCN, National Comprehensive Cancer Network; PBSCT, peripheral blood stem cell transplantation; PCL-C, Posttraumatic Checklist—Civilian Version; PTSD, posttraumatic stress disorder; QOL, quality of life; SCT, stem cell transplantation.

[a]QOL domains were coded as follows: P, physical well-being (i.e. physical functioning and/or symptoms); A, standardized measure of anxiety; D, standardized measure of depressive symptoms; S, social well-being; V, vocational status.

functioning scores remained below population norms at 12 months [15].

Several prospective reports have evaluated HSCT survivors' physical functioning and/or symptoms beyond the first year post-transplant (see Table 1) [16–18]. Hjermstad *et al.* [17] found that the physical functioning of three patient groups (i.e. patients undergoing allogeneic HSCT, autologous HSCT, or combination chemotherapy) was comparable to that of the general population at 1 year and 3–5 years after HSCT; however, role functioning declined significantly for both HSCT groups over the same time period. The authors reasoned that impaired role functioning may be related to the pronounced fatigue that HSCT survivors experience. Other studies have found that a significant minority of HSCT patients (range = 18–34.3%) experience major functional limitations (i.e. difficulty with mobility or the performance of usual activities) at follow-ups ranging from 18 months to 5 years post-transplant [16,18].

Cross-sectional studies of HSCT survivors who were at least 10 years post-transplant have found decrements in physical and role functioning relative to the general population or age-, sex-, and race-matched controls [19,20]. Relative to matched controls, 10-year HSCT survivors have reported a greater number of medical problems (3.5 vs 1.7) and more musculoskeletal stiffness, cramps, weakness, and joint swelling [20]. However, HSCT survivors and controls had similar rates of hospitalization and prevalence of other noncancer diseases.

Conclusions and future directions

Despite the rigorous and often toxic nature of HSCT, most studies have found that the majority of survivors report resumption of routine activities at long-term follow-ups [17,18]. However, physical symptoms, especially fatigue, and serious functional limitations affect a sizable proportion of long-term HSCT survivors [16,18–20]. Research is needed in several areas to improve our understanding of physical outcomes following HSCT. First, quality-of-life dimensions (e.g. physical, psychological, and social well-being) are often assessed without an exploration of their interrelationships [14,16,17]. In addition, medical variables (e.g. GVHD, type of transplant) and psychological distress have not been consistently associated with subjective assessments of physical well-being [18,21–24]. Given great variability in physical symptoms and functioning following HSCT, predictors of these outcomes warrant further study. Second, prediction of physical outcomes would be improved by attention to a number of methodological issues. For example, samples are often heterogeneous with regard to disease and treatment history and co-morbid medical conditions, which does not allow for detailed analyses of these

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variables. Significant attrition also limits the utility of many findings. Third, examining daily fluctuations in physical symptoms (e.g. fatigue) and mental well-being would provide a detailed understanding of the recovery process following HSCT. Finally, research is needed to assess changes in patients' standards and definitions of physical well-being or their relative importance as they adapt to long-term treatment side effects [25]. Such research would improve the accuracy and meaningfulness of quality-of-life assessment [26].

Fatigue

Approximately 80–96% of patients receiving chemotherapy endorse some degree of cancer-related fatigue [27]. Although consensus regarding the definition of fatigue is lacking, there is general agreement that it is a subjective and multidimensional phenomenon that can negatively impact quality of life [27,28]. Single-item assessments of fatigue are common in the HSCT literature; only two prospective studies have included multi-item, standardized fatigue measures (see Table 1) [17,29]. Patients' fatigue has been documented before, during, and shortly after HSCT [21,29,30]. For example, one study found that approximately one-third of multiple myeloma and non-Hodgkin's lymphoma patients reported moderate to severe levels of fatigue at baseline and 30 days following SCT, whereas 55% of patients reported moderate to severe fatigue at nadir (the time of lowest white blood cell count) [21]. The pattern of fatigue varied by cancer diagnosis, with non-Hodgkin's lymphoma patients reporting higher levels of fatigue than multiple myeloma patients at multiple time points (i.e. baseline, during the conditioning regimen, and at 30 days post-transplantation). Results may reflect differences in disease or treatment history and conditioning regimens.

Findings regarding fatigue in HSCT recipients have been discrepant across studies, which may reflect sample heterogeneity as well as variation in the measurement of fatigue [6,16,17,31]. For example, Conner-Spady *et al*. [16] found that the greatest fatigue occurred after high-dose chemotherapy with 75% of breast cancer patients scoring in the negative half of a visual analog scale (score < 70 on a scale from $0 =$ *worse* to $140 =$ *better*). This percentage markedly decreased (5.6% to 22.2%) at four follow-up assessments from 6 to 24 months post-enrollment. Conversely, another study found that a significant minority of SCT patients (30–44%) were bothered a lot or extremely bothered by their fatigue at 6, 12, and 24 months post-transplant [31]. A third study documented fatigue among survivors of SCT and conventional chemotherapy that either paralleled or exceeded population norms across fatigue measures at 3–5 years post-treatment [17]. Finally, a cross-sectional survey found significantly higher levels of fatigue among long-term HSCT survivors (mean = 7 years post-HSCT) relative to an age- and sex-matched healthy comparison sample [6].

Conclusions and future directions

Evidence suggests that many HSCT patients experience fatigue following receipt of chemotherapy and are dissatisfied with their energy level at long-term follow-ups [21,31]. Prior to drawing definitive conclusions regarding the course and severity of fatigue in HSCT survivors, a number of important issues warrant further conceptual and empirical attention. First, given the absence of a common definition of fatigue and its dimensions, a variety of self-report measures have been used, some of which provide minimal information [28,30]. Second, the high correlations between continuous measures of fatigue and depression when administered concurrently to cancer patients indicate potential problems with discriminant validity [32]. As diagnostic criteria for cancer-related fatigue syndrome are being refined [33], it will be important to distinguish between fatigue associated with cancer and its treatment and fatigue associated with mood disturbance. Third, researchers are just beginning to demonstrate the feasibility of conducting ecological momentary assessment of fatigue (i.e. real-time assessment of fatigue in naturalistic settings) with HSCT patients [34]. This real-time data capture is important for understanding the temporal course of fatigue and overcoming the limitations of retrospective reporting. Other limitations that should be addressed in future research include the reliance on small, convenience samples, and high rates of missing data [29]. Finally, cancer-related fatigue most likely involves the dysregulation of several interrelated physiological, biochemical, and psychological systems [35]. Proposed mechanisms underlying cancer-related fatigue include cytokine and serotonin neurotransmitter dysregulation, alterations in muscle and adenosine triphosphate metabolism, hypothalamic–pituitary–adrenal axis dysfunction, vagal afferent activation, and circadian rhythm disruption [35]. Identifying the mechanisms that produce fatigue and the extent to which neoplastic disease, cancer therapies, and comorbid conditions (e.g. anemia, cachexia, sleep disorders, depression) contribute to fatigue is a considerable challenge for future research [35].

Psychological well-being

Anxiety and depressive symptoms

A number of prospective reports on the adjustment of HSCT recipients ($n = 15$) have included standardized assessments of anxiety and/or depressive

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symptoms (see Table 1). Research indicates that HSCT survivors may face intrusive recollections of noxious treatments [36–38], distressing physical and cognitive side effects [12], and fear of relapse and death [39]. Difficulty resuming former roles, a sense of isolation and stigmatization, and financial insecurity also may precipitate distress [39].

Although most prospective studies have assessed distress during the post-transplantation period [17,23,40], some studies have examined psychological adjustment during transplantation [29,41,42]. Prieto *et al*. [42] found that the proportion of probable anxiety cases decreased from the point of hospital admission for SCT (22.7%) until 14 days post-admission (8.0%), whereas the proportion of probable depression cases increased over the same time period (11.4 vs 16.6%). The researchers also administered structured psychiatric interviews on a weekly basis and found that the most common diagnoses during transplantation were adjustment disorders (22.7%), mood disorders (14.1%), and anxiety disorders (8.2%) [41].

Other studies have documented anxiety and depression among HSCT patients up to 2 years post-transplant [16,23,40,43]. Approximately 26–36% of patients reported moderate to severe depressive symptoms during the first year following HSCT [23,40], and a lower proportion of patients (18%) endorsed moderate to severe anxiety within the first 100 days after HSCT [23]. In a study of Norwegian cancer patients treated with autologous SCT, allogeneic SCT, or standard chemotherapy, levels of anxiety and depression generally did not differ across the three patient groups during the first year after SCT and were higher than those of the Norwegian general population at the 1-year follow-up [44]. Across patient groups, cases of anxiety ranged from about 10 to 30% of patients, whereas cases of depression were more variable (5% to over 40% of patients) over the first year post-transplant. Finally, psychological distress has been reported at 2 years post-HSCT, with a significant minority (33%) of breast cancer patients indicating at least moderate problems with anxiety or depression [16].

Other studies have not found elevated levels of anxiety and depression relative to normative samples following transplantation [15,45]. Among allogeneic BMT patients, levels of anxiety and depression did not differ from population norms before BMT [15]. Levels of anxiety continued to be consistent with population norms at 6 and 12 months post-BMT, whereas levels of depressive symptoms were significantly below norms over the same time period. Results should be cautiously interpreted due to attrition and the relatively small sample size ($n = 28$). Another study with a larger sample ($n = 131$ at baseline) found that patients who enrolled in a psychological intervention trial following HSCT did not report elevated levels of depressive symptoms relative to healthy controls before transplant and at 6 and 12 months after transplant [45]. Psychological outcomes did not vary as a function of intervention condition. Patients only showed elevated anxiety relative to controls before transplant and then reported a dramatic decline in anxiety at 6 months following HSCT. Patients may have experienced anxiety related to the cancer diagnosis and impending treatment followed by relief when they perceived that the cancer had been effectively treated.

With respect to long-term HSCT survivors, studies have found levels of psychological distress that are comparable to those of the normative population at 3 or more years post-transplant [17,19]. For example, one study found that anxiety decreased during the first 8 months following HSCT, and then levels of anxiety, depression, and emotional well-being did not differ from those of the general population at 3–5 years post-HSCT [17]. Another study found that 19% of 5-year HSCT survivors reported depressive symptoms with most survivors endorsing mild depressive symptoms [18]. At 10 or more years post-transplant BMT survivors' self-reported psychological health has been comparable to that of the general population [19] and case-matched controls [20].

Predictors of psychological distress among HSCT survivors have been identified. Better pre-transplant psychological functioning [23], better post-transplant physical and sexual functioning [46], and less fatigue [30] have been associated with less psychological distress. Mixed associations have been found between demographic (e.g. age, gender, marital status) and medical variables (e.g. type of transplant, relapse, GVHD) and psychological distress [18,23,24,42,47]. Although reduced-intensity conditioning allotransplantation is less toxic than traditional HSCT, distress has not varied as a function of transplant type [48].

Conclusions and future directions

Overall, evidence suggests that a significant minority of patients (5% to over 40%) experience high levels of anxiety and/or depressive symptoms before, during, and after HSCT [18,42]. HSCT survivors generally report decreased distress over time, with most research indicating that mean levels of distress are within normative limits at 3 or more years post-transplant [17,19]. Although progress has been made with regard to understanding the course and severity of distress among HSCT recipients, further research is needed to address a number of methodological and conceptual issues. First, structured clinical interviews have rarely been administered to HSCT survivors, and, thus, our knowledge is limited with regard to rates of psychiatric diagnoses [49]. Overlap between physical aspects of mood disturbance and common

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treatment side effects should be considered when interpreting the results of psychiatric interviews and questionnaires. Second, commonly used self-report measures may not fully capture the fears and concerns of HSCT recipients because they were not developed for use with cancer populations. Inclusion of measures of cancer-related distress (e.g. fear of recurrence and late effects) would expand our knowledge of psychological adjustment among HSCT recipients. Third, identifying predictors of distress within and across studies is challenging due to measurement variance, attrition, and small samples with diverse medical histories. Future research should examine the interactive influence of environmental (e.g. social support, discrimination) and individual characteristics (e.g. treatment history, cancer type, coping efforts, perceived personal growth) on distress in larger samples as well as the relationship between distress and adherence to medical regimens. Preliminary evidence suggests that post-transplant distress is related to medication nonadherence [23]. Finally, given that a large proportion of distressed HSCT recipients do not receive mental health services [23], barriers to service use deserve empirical attention.

Posttraumatic stress disorder

To date, nine published studies have documented posttraumatic stress disorder (PTSD) symptoms related to cancer and its treatment in HSCT survivors. Of the seven studies that reported the participants' disease type, two studies focused on breast cancer patients [49,50] and five studies included patients with a range of cancer types (e.g. lymphoma, leukemia, breast cancer) [36–38,51,52]. The majority of studies used cross-sectional designs to assess PTSD over a period ranging from 2 months to 12 years after HSCT.

The incidence of probable PTSD has ranged from 5 to 19% of HSCT survivors [23,37,38, 50,52,53]. The rates of PTSD are comparable to those in studies of cancer patients who did not undergo HSCT [54]. One longitudinal study found that 45% of participants had high levels of cancer-related intrusive thoughts before HSCT, whereas only 7–8% of participants reported high levels of intrusive thoughts during the first year after HSCT [51]. A decline in avoidance symptoms also was observed over this time period.

Two studies used structured clinical interviews to determine the incidence of PTSD following HSCT [49,52]. Among breast cancer patients who were assessed at least 100 days after HSCT, no one endorsed current symptoms that met the criteria for cancer-related PTSD [49]. However, the incidence of lifetime cancer-related PTSD was 41.2%, which did not significantly differ from that of breast cancer patients without a history of HSCT (30%). In a sample of men and women who underwent HSCT an average of 20 months previously, 5% of participants met the criteria for current PTSD [52].

Although there is scarce longitudinal research on PTSD symptoms in HSCT survivors, researchers have assessed a range of potential correlates of these symptoms. A history of psychological disturbance [49], current psychological distress [38,50,53], reduced physical functioning [36,50,53], reduced social support [38,52], greater use of avoidance coping [38,52], and negative life events [36] have been associated with greater PTSD symptomatology. In addition, a positive correlation between PTSD symptoms and positive life events has been found for HSCT survivors with reduced physical functioning [36]. These results suggest that any life transition may be taxing for individuals with limited physical resources.

With regard to the relation of PTSD symptoms to sociodemographic and medical variables, no findings have been replicated across studies with HSCT survivors. For example, Jacobsen *et al*. [50] found that less education, more advanced disease, and longer hospital stays were associated with greater PTSD symptom severity among breast cancer patients who underwent HSCT, whereas other studies did not find these associations [36–38,52]. Interestingly, gender has not been associated with PTSD symptoms among HSCT survivors [36,37,52,53], which contrasts with strong evidence from noncancer populations that women are more likely than men to develop PTSD [55]. However, most correlates of PTSD symptoms among HSCT survivors (e.g. reduced social support, greater avoidance coping, history of psychological disturbance) have been similar to those found in the population at large [55,56].

Conclusions and future directions

Taken together, studies suggest that trauma and PTSD may be a useful framework for understanding the experience of a minority of HSCT survivors. To date, only one prospective study and one retrospective report have examined PTSD symptoms before and after HSCT [49,51], and, thus, little is known regarding changes in PTSD symptoms over this time period. The potentially distinctive features of PTSD in cancer patients who undergo HSCT or other therapies warrant further study [54]. First, the assessment of intrusive thoughts would be improved by attention to the content and temporal focus of these thoughts. Cancer may involve a number of aversive events (e.g. diagnosis, noxious treatments, and their side effects) that trigger past-oriented and future-oriented intrusions. For example, the decrease in cancer-related intrusive thoughts following HSCT (45% pre-HSCT vs 7–8% post-HSCT) may reflect a decrease in posttraumatic stress responses to the

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cancer diagnosis or HSCT-related fears [51]. In addition, it is important to distinguish between PTSD responses, grief reactions [54,57], and normative cognitive processing of cancer-related stressors. Finally, PTSD symptoms overlap with a number of common treatment side effects, such as concentration deficits, insomnia, and irritability [58], and avoiding reminders of the stressor may be difficult due to internal (e.g. nausea, pain) and external cues (e.g. medication regimens, medical appointments). All of these differential diagnostic issues require careful consideration in future research.

Vocational and financial status

Four prospective reports have documented HSCT recipients' change in employment status (see Table 1) [17,18,31,59]. Overall, evidence suggests that many HSCT survivors return to work, even though physical and psychological symptoms may persist [20,60]. One study found that the majority (61% of autologous HSCT survivors and 58% of allogeneic HSCT survivors) had returned to work, school, or homemaking at 1 year following HSCT [31]. At 2 years a greater proportion of this sample had returned to work, school, or homemaking (70% of autologous HSCT survivors and 67% of allogeneic survivors). Among 5-year HSCT survivors without recurrent malignancy and with a pre-transplant history of work or school outside of the home, 84% returned to full-time work or school [18]. Finally, a survey of 10-year HSCT survivors found that their rate of full-time employment (72%) did not differ from age-, sex-, and race-matched non-HSCT controls (74%) [20].

Researchers have documented a number of factors associated with HSCT survivors' employment status. Although the employment rates among HSCT survivors have not shown consistent associations with gender [18,60,61], younger age and higher levels of education have been associated with a higher probably of re-employment [31,61]. Unemployed HSCT survivors have shown poorer physical, cognitive, and social functioning and greater pain, sleep disorders, and distress than their employed counterparts [60,61]. Although cognitive and physical limitations may contribute to unemployment, other potential causes that deserve empirical attention include survivors' concerns regarding infection and discrimination due to cancer history or cancer-related physical limitations. Although cancer survivors have generally reported little overt job discrimination [62], this experience is important to assess among HSCT recipients due to their protracted treatment and recovery period.

Predictors of unemployment following HSCT warrant further study, as job loss may contribute to psychosocial distress and financial difficulties. The considerable expense associated with HSCT (at present, generally exceeding $80 000 for autologous HSCT and $150 000 for allogeneic HSCT) [1] may also contribute to financial strain among HSCT survivors and their family members. One study found that a significant minority (11–27%) of HSCT survivors in the United States were bothered a lot or extremely bothered by financial problems at 6, 12, and 24 months post-transplant [31]. Austrian individuals who had survived at least 5 years after HSCT provided significantly worse ratings of their financial situation compared with age- and sex-matched healthy controls [63]. Norwegian HSCT survivors reported significantly greater financial problems than the general population at about 2.5 and 4.5 years after transplant [64]. Finally, 24% of 10-year HSCT survivors in the United States reported a history of health insurance denial, whereas no one in the age-, sex-, and race-matched non-HSCT control sample reported this history [20]. A history of life insurance denial also was common (27%) among 10-year HSCT survivors relative to controls (3.7%). Individuals of lower socioeconomic status have been underrepresented in this research; thus, further work is needed to adequately document the financial burden associated with HSCT and its impact on long-term psychological adjustment and quality of life.

Social well-being

Social well-being may fluctuate as HSCT patients confront a range of stressors associated with their life-threatening illness and treatment. Some measures of social well-being assess participation in routine social activities, whereas other measures define social well-being more broadly, including receipt of support, feelings of closeness, and perceived communication with a partner and other loved ones. As patients experience bothersome side effects during a prolonged period of hospitalization and recovery, their ability to engage in social activities is at least temporarily disrupted. For some patients and their caregivers, intimacy may fade over time as support provision becomes burdensome or the demands of the recovery process exceed expectations. Conversely, many patients report interpersonal growth during the recovery period as they reconstruct their life goals [5].

Five prospective studies have documented change in patients' social well-being up to 5 years following HSCT (see Table 1) [15–17,31,45]. One study found that HSCT patients' marital satisfaction did not change from pre- to 6-months post-transplant [45]. Among women receiving autologous SCT for breast cancer, social well-being declined following high-dose chemotherapy, but

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then returned to baseline levels at 8 weeks post-chemotherapy, which paralleled the pattern of physical well-being [16]. Among allogeneic BMT recipients, general social participation was significantly below population norms from baseline until 12 months after transplant [15]. Another study found comparable levels of social impairment relative to population norms among cancer patients undergoing allogeneic HSCT, autologous HSCT, or combination chemotherapy during the period before HSCT [17]. Clinically significant improvement in social well-being was observed over the first year across all patient groups. Lastly, a higher percentage of autologous BMT patients were able to enjoy socializing with family and friends compared with allogeneic BMT patients at a 6-month follow-up (75 vs 52%), but this difference was not found at 12-month and 24-month follow-ups [31].

Few studies have documented the social well-being of survivors who are at least 10 years post-transplant [19,20]. In a study of patients with chronic myeloid leukemia who had survived more than 10 years after allogeneic BMT, social well-being did not differ from population norms [19]. A study of 10-year HSCT survivors with heterogeneous transplant and disease histories also found levels of social well-being that were comparable to those of the general population; however, social well-being was lower than that of age-, sex-, and race-matched nontransplant controls [20].

Conclusions and future directions

As the above-mentioned studies illustrate, social well-being may vary according to the reference group, patient population, and assessment point. An underlying problem in this area of research is the lack of consensus regarding the conceptualization of social well-being. In addition, many studies report results from heterogeneous samples with respect to medical diagnosis and treatment and significant attrition over time [15,17,20,31]. Subgroup analyses with larger samples would further our understanding of the social aspects of particular medical regimens and disease trajectories. Although global measures of social well-being provide some useful information, a more detailed analysis of social issues faced by HSCT survivors may inform intervention development. For example, the extent to which HSCT survivors experience mutually beneficial emotional exchanges with others has yet to be fully explored.

Sexuality and fertility

Sexual outcomes

For a significant proportion of HSCT survivors, intimacy may decline as they experience alterations in sexual functioning and satisfaction [65]. Research has documented a range of sexual concerns among HSCT survivors, including decreased libido, infertility, erectile and ejaculatory dysfunction, premature menopause, vaginal alterations (e.g. dryness, narrowing, fibrosis), and dyspareunia [46,65]. Radiation and chemotherapy may result in damage to the gonads and hypothalamic–pituitary–gonad axis that disrupts the sexual response cycle [66]. Fatigue and decreased physical stamina also may contribute to sexual dysfunction [65]. Psychosocial factors that may affect sexual functioning include body image changes, anxiety, depression, concurrent stressful life events, and concerns about disease recurrence or infertility [65,67]. For some HSCT survivors these physiological and psychological changes may precipitate long-term sexual problems that adversely affect their quality of life [46].

Researchers have examined a range of sexual outcomes among HSCT recipients. One study found that decreased sexual interest was a problem for about one-third of breast cancer patients up to 2 years following autologous HSCT and was related to younger age and being married or living with a partner [16]. Chemotherapy may cause premature ovarian failure in younger patients, thereby inducing a sudden onset of menopausal symptoms and decreased sexual desire [68]. A study of BMT survivors found that sexual activity generally declined over time, and depression and gender predicted sexual difficulties at 1 and 3-year follow-ups [46]. Women reported more sexual problems relative to men, and, at the 3-year follow-up, women continued to endorse more sexual concerns (e.g. concerns about body appearance and painful intercourse) than they did before the transplant. Other studies have found that male and female long-term HSCT survivors reported greater sexual problems than nontransplant controls [20,69].

Although sexual dysfunction is a common long-term side effect of treatment, many patients indicate that their health care provider did not discuss the potential effects of HSCT on sexual health [46,70]. For example, about half of BMT recipients reported no discussion of sexuality with their health care provider before BMT and at 1 and 3 years after BMT [46]. At 3 years post-transplant, patients who had discussed transplant effects on sexuality with their health care provider reported fewer difficulties with sexual functioning.

Conclusions and future directions

Evidence strongly suggests that sexual dysfunction is one of the most prevalent and persistent long-term problems after HSCT [65]. Recent research on sexuality among HSCT survivors has begun to address the limitations of prior studies, such as

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small sample sizes, cross-sectional designs, and the use of minimal, unvalidated assessments. However, scarce prospective research has been conducted that includes long-term follow-ups and standardized assessments of sexual functioning [46]. Although demographic and medical variables have been included as predictors of sexual dysfunction [65], psychosocial predictors of sexual outcomes, such as qualities of participants' intimate relationships, deserve further empirical attention. Finally, research with ethnoculturally diverse samples would inform the development of culturally sensitive interventions for enhancing sexual well-being and patient–provider communication regarding sexual concerns.

Fertility

Research suggests that many patients may benefit from further communication with their health care providers as they cope with long-term fertility-related concerns [71]. Recent data indicate that 25% of autologous transplants and over 60% of allogeneic transplants are performed on patients younger than 40 years of age [72]. HSCT survivors have an almost certain risk of infertility (>98%) secondary to the gonado-toxic myeloablative chemotherapy with or without total-body irradiation that they receive prior to HSCT [73,74]. One study examined 10-year HSCT survivors and controls who were matched on sex, age, ethnicity, and education level [71]. Of 137 HSCT survivors, only four persons (all male) conceived after completing cancer treatment, and only one was an unassisted conception. One quarter of survivors had moderate to high levels of concern regarding infertility compared with 7% of controls, and no sex differences were found with regard to survivors' degree of concern. The majority (54%) of HSCT survivors younger than 40 years of age reported elevated infertility concern. Fertility-related concerns among HSCT recipients have rarely been reported in the literature on quality-of-life outcomes [75], and, thus, descriptive studies, including those that focus on doctor–patient communication, are needed in this area.

Limitations of past research and directions for future research

Methodological critique

Although a number of prospective, longitudinal studies have measured quality of life before and at multiple time points after hospitalization for HSCT, this design has rarely been used to assess some aspects of functioning (e.g. sexual functioning, existential well-being). In addition, many studies have small sample sizes and considerable attrition. These relatively small samples often consist of patients with various diagnoses who have received autologous and allogeneic forms of HSCT as well as patients who have received total body irradiation and those who have not been irradiated. Furthermore, patients who have received different pre-HSCT courses of radiation or chemotherapy are often grouped together. Different diseases and treatment regimens may be associated with distinct physical and/or emotional difficulties that impact quality of life. Researchers studying samples with diverse patient populations should consider reporting the effects of different diagnoses and treatments (e.g. autologous vs allogeneic transplantation) on outcomes. However, as diagnostic procedures and cancer treatments concurrently occur, it may be difficult to disentangle the psychological impact of cancer diagnosis, disease progression, and cancer treatments.

Although study samples of HSCT patients have been diverse with regard to age and gender, most participants are White and middle- to upper-class. Given the considerable expense associated with HSCT and the frequent denial of health insurance for HSCT recipients in the United States [20], it is important to assess the psychosocial and economic impact of HSCT on patients with limited financial resources. Ethnicity has been associated with socioeconomic status, conceptualizations of illness [76], doctor–patient communication [77], and health-related coping strategies [78]; thus, cross-cultural explorations of adjustment following HSCT remain a fruitful area for future research.

Documenting the temporal trajectory of concerns after HSCT in culturally diverse populations is critical to the development of interventions to enhance quality of life. To date, physical exercise and mindfulness-based interventions have shown promise in reducing the negative physical and psychological effects of cancer and HSCT [79,80]. However, little published research has examined cognitive-behavioral approaches to managing the physical and psychological sequelae surrounding HSCT.

Conceptual critique

Most studies on quality of life following HSCT lack a theoretical framework. Exceptions to this trend include research on the HSCT experience within a stress and coping [52] or psychosocial transition paradigm [5,6]. The psychosocial transition paradigm assumes that HSCT is a traumatic event that may precipitate long-lasting positive or negative changes, either simultaneously or sequentially, in the same individual [4,5]. From this perspective a number of factors may contribute to alterations in world views or future plans among HSCT patients. Contextual factors include the sociocultural context (e.g. age, gender, socioeconomic status), the temporal context (e.g. disease stage), the situational context (e.g. unemployment,

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denial of health insurance), and the interpersonal context (e.g. social support network) [81]. Although including all aspects of context in research is impractical, consideration of the entire context should lead to inclusion of relevant variables. For example, with regard to the temporal context, many HSCT patients are young or middle-aged adults for whom a life-threatening illness and treatment may be particularly unexpected or 'off schedule' in the life cycle [82]. Off-schedule illness provides patients with few age peers who have faced similar issues and affords no opportunity for planning ahead in anticipation of illness. Thus, social support, role restructuring (e.g. child-care arrangements, leave from work), and future-oriented fears may be especially important to assess when conducting research with HSCT recipients.

In addition to adopting a contextual perspective, it is important to explore patients' views of quality of life in order to account for paradoxical findings in the literature. For example, how can researchers explain the replicated finding that the majority of HSCT recipients report acceptable or even enriched quality of life despite ongoing physical and psychosocial morbidities [3]? According to Taylor's [83] theory of cognitive adaptation, many people who face personal tragedies engage in efforts to enhance the self, such as finding personal benefit in the experience. This process of self-enhancement as well as efforts to gain a sense of meaning and mastery over the experience may contribute to positive perceptions of quality of life [83].

Sprangers and Schwartz [25] proposed a related theoretical model to elucidate changes in quality of life as a result of interactions between the following factors: (a) a catalyst, or change in health status; (b) antecedents, defined as stable or enduring characteristics of the individual (e.g. socioeconomic status, personality); (c) mechanisms, including behavioral, cognitive, or affective processes that may facilitate or hinder adaptation to the catalyst (e.g. altering priorities, engaging in social comparisons); and (d) response shift, or changes in the meaning of self-reported quality of life as a function of changes in internal standards of measurement, values, and conceptualization of quality of life. For example, HSCT survivors may engage in downward social comparisons, thereby altering their internal evaluative scale to account for worse outcomes [84], or develop a new sense of meaning in life that informs their conceptualization of quality of life. Methodological approaches to response shift assessment are beyond the scope of this paper and have been reported elsewhere [26]. Incorporating response shift assessment into research with HSCT survivors would improve the accuracy and meaningfulness of quality-of-life assessment and inform a patient-centered approach to health care.

Finally, as theory-driven research is conducted to elucidate the biological, psychological, and social processes that affect quality of life following HSCT, it will be imperative to assess the individual and contextual characteristics that foster positive sequelae (e.g. personal growth, improved relationships). Clinicians have long observed that many HSCT survivors report good to excellent quality of life despite various health problems and state that their current condition 'beats the alternative' [3, p. 137]. As HSCT recipients compare themselves with those who did not survive the disease or treatment, an active coping process of positive reappraisal may emerge that facilitates adjustment. Thus, for many HSCT survivors, the definition of quality of life may simply be life itself.

Notes

1. The dollar sign ($) is a truncation character that allows one to retrieve all possible variations of a root word. For example, the search psycho$ retrieves words such as 'psychological' and 'psychosocial'.

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