Pergamon

European Journal of Cancer Vol. 31A, No. 2, pp. 163–173, 1995

0959-8049/95 $9.50+0.00

0959-8049(94)00464-1

Quality of Life in Adult Cancer Patients Treated with Bone Marrow Transplantation—a Review of the Literature

M.J. Hjermstad and S. Kaasa

There is now an increasing interest in measuring quality of life (QOL) in cancer patients. Information on psychosocial issues and the patients' QOL give a more comprehensive evaluation of the treatment outcome than survival and relapse free intervals alone. Bone marrow transplantation (BMT) has become a standard, curative treatment in haematological diseases such as leukaemia and lymphomas. However, serious physical and psychological side effects are experienced by some patients. A review of the literature on QOL in adult BMT patients shows that the development in post-BMT research on psychosocial factors is slowly progressing. Most studies are retrospective with small sample sizes, and only five of 48 studies fulfilled our preset quality criteria. Identification of factors that are predictive for poor post-BMT outcome might provide a basis for targeted support programmes. This underlines the necessity of undertaking prospective studies using reliable and well-validated methods for measuring QOL in this patient group.

Key words: quality of life, bone marrow transplantation, treatment side effects, functional status, anxiety, depression, psychosocial issues, psychological morbidity
Eur J Cancer, Vol. 31A, No. 2, pp. 163–173, 1995

INTRODUCTION

THERE HAS been an increasing use of bone marrow transplantation (BMT) during the last decade. BMT was initially employed as a treatment for patients with advanced disease who did not respond to conventional therapy. Owing to medical and technological advances, survival rates and the length of relapse free intervals have improved considerably [1]. High dose chemotherapy followed by allogeneic BMT is now a curative treatment modality for malignancies such as acute myelogeneous leukaemia and chronic myelogeneous leukaemia [1–4]. It is also being performed in non-malignant diseases such as severe aplastic anaemia and sickle cell disease [1, 5–7]. Autologous BMT, subsequent to high dose chemotherapy, must still be considered experimental treatment for all malignant diseases [2]. Allogeneic or autologous BMT are also performed for a variety of diseases in children, necessitating extensive follow-up [8, 9].

The increased use of growth factors and peripheral stem cells after intensive chemotherapy will probably reduce the transplant related mortality, morbidity and costs [10, 11]. These are high due to the intensive treatment and highly skilled nursing required, as well as the necessity of a multidisciplinary approach and the long-time follow-up of the individual patient [12–16].

The BMT procedure and the high dose regimens carry significant morbidity. Graft versus host disease (GVHD) is the major complication causing late transplant related morbidity and mortality in allogeneic BMT [17–21]. Haemorrhage, infections, reduced stamina and complications from the lungs as well as cataract and visual and neurological impairment are reported [17, 22–25]. Various psychosocial problems, such as the inability to resume social roles, worry about the future, work-related problems, infertility concerns and fear of relapse in addition to anxiety and depression are evidenced in BMT patients as in other cancer survivors [8, 26–43]. With increasing numbers of long-term BMT survivors, prospective data on the frequency and severity of late side effects, psychosocial sequelae and quality of life (QOL) are important, as in cancer clinical trials [44, 45].

The objective of this article is to give a critical appraisal of the literature on QOL in adult cancer patients treated with BMT. Special emphasis is put on evaluating whether individual papers meet preset criteria. Finally, recommendations for future work in the area will be suggested.

MATERIALS AND METHODS

Applied methods for assessing QOL

In relation to health, QOL is defined as a multidimensional concept consisting of physical, psychological and social phenomena [46–48]. These are all related to the individual's own experiences, and consequently the patient is the most reliable source of information [48, 49]. Several well-validated tools for measuring QOL have been developed. These might be generic such as the Sickness Impact Profile (SIP) [50], the Nottingham Health Profile (NHP) [51], or the SF-36 originating from the Medical Outcomes Study (MOS) [52, 53]. Among the cancer specific inventories, the Rotterdam Symptom Checklist (RSCL)

Correspondence to: M. J. Hjermstad at the Department of Medical Oncology and Radiotherapy, The Norwegian Radium Hospital, Montebello, N-0310 Oslo; S. Kaasa is at the Palliative Medicine Unit, Department of Oncology, University Hospital of Trondheim, Trondheim, Norway.
Revised and accepted 27 Oct. 1994.

[54], the Functional Living Index Cancer (FLIC) [55], the Cancer Rehabilitation Evaluation System (CARES) [56, 57], the EORTC QLQ-C30 from the European Organization for Research and Treatment of Cancer [58] and the Functional Assessment of Cancer Therapy Scale (FACT) [59] are frequently used. When weighing the risks of transplant related mortality and recurrence against the continuing and disabling effects of severe morbidity, BMT will be the right choice of treatment only for selected groups of patients with malignant disorders [60, 61]. Incorporation of QOL assessments in clinical decision making might help the clinician and the patient choose more easily between different treatment options. In explaining which options are available, information on QOL should always be included. A true informed consent could only be obtained when the patient is cognisant of all post-BMT consequences that might occur [26, 30, 62]. Systematic QOL evaluations might enable the clinicians to identify patients and families who are at increased risk of encountering psychosocial problems. Thus, proper intervention strategies could be initiated when necessary [63–65]. In addition, information on the patients' subjective experiences of the health care services and routines might be useful feedback for the multidisciplinary team that takes care of the BMT patient throughout the stay and follow-up period [16, 27, 66].

Approach for identifying existing literature

The publications were identified through literature searches on Medline and Cancerlit using "QOL", "bone marrow transplantation", "psychological", "anxiety" and "depression" as index terms. This search resulted in 113 publications from January 1984 to March 1994 addressing these issues in adult cancer patients. The reference lists of the identified papers and relevant journals were examined, yielding an additional 19 publications. Among these 132 publications, 18 were non-English and are not included in this review, except for two that were Scandinavian [5, 44]. Seventeen of the publications were meeting abstracts, while three were case reports [24, 67, 68]. The majority of the identified publications, 68, did not assess QOL, anxiety or depression. Only 48 were publications presenting studies evaluating these issues in BMT patients. These are listed as an overview in Table 1. By more thoroughly investigating the methodology employed, it became evident that small sample sizes, ambiguous definitions of QOL, lack of appropriate comparison groups and retrospective designs were common. Consequently, only brief comments on the overview from Table 1 will be made. Table 2 gives an overview of the different study designs, as they were labelled by the authors or indexed by Medline. The purpose of this paper was to evaluate these 48 studies with respect to the following four criteria.

(i) published as a journal article;
(ii) a sample size of more than 15 BMT patients;
(iii) a design containing repeated measures;
(iv) employment of standardised measures for assessment of QOL or psychosocial issues.

RESULTS

In Table 1, 37 articles [29–33, 35, 41, 42, 62, 64, 69–95] and 11 abstracts [34, 60, 96–104] are listed presenting studies where QOL, psychological factors or social issues were assessed in BMT patients. To be included in the table, the study had to employ measurement tools that were specifically designed for assessing QOL or psychosocial issues in adult cancer patients. No limits were set on the number of patients or study design. Some authors have reported their patients in multiple publications. Only the most current publications were listed in the table, unless prior results provided additional information.

A wide variety of measures were employed to assess QOL, anxiety and depression and various dimensions of psychosocial morbidity in this patient group. In addition, *ad hoc* questionnaires and interviews were employed.

All studies used multiple measures, such as various questionnaires combined or were supplemented by interviews as a way of gathering data. Information on whether or not these were structured, semi-structured or consisted of open-ended questions was not always provided. Data from the BMT patients were compared with data from a companion comparison group in 11 studies, consisting of heterogeneous chemotherapy patients in respect of diagnoses, stage of disease and types of chemotherapy given [35, 70, 85, 86, 96, 102]. Only one of the comparison groups was matched on age [70]. Data on QOL obtained in normal population samples were also used for comparisons [29, 32, 33, 35, 82, 86, 88, 96, 102]. Time for collecting the data showed considerable variation between studies, ranging from 3 months to 5 years post-transplant. Ten studies reported data obtained prior to the BMT procedure followed by data obtained post-BMT [33, 34, 78, 79, 81, 91, 96, 100, 101, 104]. In 28 studies, the patients were evaluated at a mean or median time extending 12 months post-BMT, demonstrating that most research to date has focused on the late adjustment period.

The major similarity between the studies was the retrospective design employed in 23 studies. Different definitions and vague descriptions of the designs made it difficult to clearly distinguish between what were cohort or longitudinal studies, as opposed to retrospective and cross-sectional studies. A small sample size in most of the studies was prohibitive for making generalisations.

The overall impression from the overview presented in Table 1 was the consistency between studies, in that most patients did remarkably well from a physical point of view, the dominating problematic areas being reduced stamina, sexual problems and work-related difficulties. Reports on return to gainful employment or school within 1 year post-BMT varied from 42 to 82% with an average of 65% in the retrospective, cross-sectional and longitudinal studies, depending on the time of measurement [33, 34, 82, 89, 94, 97, 99, 103]. According to the criteria for a more thorough evaluation of the studies, only five studies fulfilled these. Table 3 gives information on sample size, the use of comparison groups, whether or not performance status was assessed and provides more detailed information on the measurement tools than Table 1.

All studies in Table 3 repeated the measures three to four times in the patient sample. Pre-BMT evaluations of the patients were performed in two studies [33, 81]. The times of measurement varied considerably. In two studies, all were undertaken in the immediate pre/post-transplant period from 2 days pre-BMT to 20 days post-BMT and from day 1 to days 30–34 post-BMT, respectively [81, 84], while the follow-up lasted for 1 year up to 51 months post-BMT in the other three [29, 33, 75]. The sample sizes ranged from 16 to 67 BMT patients. While one study included both allogeneic and autologous BMT [84], the others focused on either allogeneic [29, 33] or autologous [75, 81]. Two studies compared their own data with that obtained from normal healthy subjects or historical data from cancer subjects [29, 33]. In one study, the nurses' perception of their patients' distress was registered and compared to the patients' own assessment of their situation [84].

Table 1. Studies and abstracts assessing quality of life (QOL) and psychosocial issues in adult cancer patients (pts) treated with BMT

Reference	Year*	BMT	No. of pts†	Comparison group	Study design	Time for measuring	Methods of assessment	Performance status	Conclusion
Achard and Zittoun [96]ª	1992	Allo/auto	40	136 chemotherapy pts	Cohort	Before BMT, day 1, 11 and 21 post-treatment	Modified EORTC-QLQ C30, HAD	No	Overall QOL relatively good. Slightly associated with anxiety, and strongly with depression, fatigue and malaise/ vomiting
Aeschelmann *et al.* [69]	1992	Allo	34	No	Retrospective	7–96 mo post-BMT	Interview, modified CJDM	No	Denial was the most common defense mechanism. Cluster analyses gave two groups of pts, one with more self-esteem and satisfaction
Altmaier *et al.* [70]	1991	Allo	12	10 chemotherapy pts	Retrospective	25–41 mo post-BMT (mean 32)	Phone interview on health, functioning	Karnofsky	BMT pts experienced greater difficulties vocationally and sexually. Viewed themselves as equally healthy as the comparison group
Andrykowski *et al.* [30]	1989	Allo	23	No	Cross-sectional	3–52 mo post-BMT (mean 26)	POMS, FLIC	No	Poor functioning after BMT correlated with high age at transplant. More emotional distress than in comparable cancer samples
Andrykowski *et al.* [29]	1989	Allo	16	No	Longitudinal	3 times post-BMT (mean 28, 37, 51 mo)	POMS, FLIC, SIP	No	Many pts had long-term difficulties in psychosocial functioning. Did not seem to change with passage of time
Andrykowski *et al.* [71]	1990	Allo	30	No	Retrospective	12–96 mo post-BMT (mean 47)	POMS, PAIS, SIP	No	Cognitive dysfunction related to increased dose of TBI, involving reduced attention and concentration, and slowed reaction time
Andrykowski *et al.* [72]	1990	Allo	29	29 renal transpl. pts	Retrospective	Minimum 1 year post-BMT (mean 51 mo)	POMS, FLIC, SIP, PAIS	No	Few differences between groups. Neither reported "good QOL". Poorer status correlated with less education, TBI and older age
Baker *et al.* [41]	1991	Allo/auto/syn	135	No	Retrospective	6–149 mo post-BMT (mean 47)	Role checklist, SLDS, CSAL, POMS, BPNAS	Self-rating health scale	Significant correlation between role retention and QOL. Total negative mood inversely related to role retention
Baruch *et al.* [73]	1991	Allo/auto	51	No	Cross-sectional	Minimum 6 mo post-BMT (mean 58)	HAD, questionnaire on health, sexual function	No	Raised prevalence of sexual dysfunction, associated with poor health, significantly correlated with psychological morbidity
Belec [74]	1992	Allo/auto	24	No	Retrospective	12–38 mo post-BMT (mean 23)	Interview, QLI-Cancer, checklist	No	92% of QOL scores rated in the upper half. Most were optimistic regarding the future, mostly concerned about health and work
Chao *et al.* [75]	1992	Auto	58	No	Cohort	1 year follow-up, every 3 mo, from day +90	Phone interview	Karnofsky	88% reported above average to excellent QOL 1 year post-BMT. 14% had sexual problems
Claisse *et al.* [97]ª	1992	Not reported	49	No	Retrospective	BMT performed from 1984–1989	Questionnaire with 30 selected items	No	55% had resumed work after 16 mo (mean). Lack of physical strength the most common complaint
Collins *et al.* [76]	1989	Auto	6	No	Longitudinal	Days 3, 7, 12 and 19 of isolation	Semi-structured interviews	No	Visits from main supports important in coping with the isolation. Physical side effects brought more distress than the isolation itself

Table 1. Continued

Reference	Year*	BMT	No. of pts†	Comparison group	Study design	Time for measuring	Methods of assessment	Performance status	Conclusion
Colon *et al.* [31]	1991	Allo	100	No	Retrospective	Review ratings of charts obtained prior to BMT	Psychiatric history, DSM III, support	No	Three variables independently affecting duration of survival; stage of illness, depressed mood, extent of perceived support
Curbow *et al.* [77]	1993	Allo/auto/syn	135	No	Cross-sectional	6–149 mo post-BMT (mean 47)	Role checklist, SLDS, CSAL, POMS, BPNAS	Self-rating health scale	No. and direction of personal changes investigated. Positive changes in relationship/existential domains, negative in physical health
Cust *et al.* [42]	1989	Allo	46	No	Retrospective	Minimum 6 mo post-BMT (mean 4.2 years)	Interview, designed questionnaire	No	Sexual function was profoundly affected. Anxiety and reduced self-confidence was common. Almost 50% changed social habits
Decker *et al.* [78]	1989	Allo	12	No	Prospective	One week pre-BMT, 1, 6.5, 12 mo post-BMT	Exercise testing, BDI	Testing	Decreased maximal aerobic capacity compared to pre-BMT test results. Average weight loss: 20 lbs. Positive emotional response
Dermatis and Lesko [62]	1991	Allo/auto	39	No	Longitudinal	Within 48 hours after admission	Questionnaire, BSI, Ways of coping list	No	Pts had significant psychological distress at time of informed consent. Broader symptomatology in men than in women
Ersek [79]	1992	Allo/auto/syn	20	No	Qualitative	Pre-BMT, days 9–12, and 25–28 post-BMT	In-depth qualitative interviews	No	Maintaining hope was vital for managing treatment stressors, no matter what mechanisms were used to keep the hope
Ferrell *et al.* [80]	1992	Allo	119	No	Qualitative	Minimum 100 days post-BMT	BMT-QOLS as an indepth interview	No	Areas where QOL can be improved during BMT: managing uncertainty and treatment failure, negotiating for personal control
Ferro *et al.* [98]‡	1992	Auto	15	No	Retrospective	Minimum 6 mo post-BMT	Interview on psycho-social functioning	No	Pts tended to dedicate more time to family and social environment. 75% reported readjustment of values. Sexual difficulties frequent
Futterman *et al.* [64]	1991	Allo/auto	42	No	Retrospective	Review ratings of pre-BMT charts	Psychiatric history, social support, coping	No	Pts rated as mild, moderate and severe regarding emotional difficulties. Level 3 pts needed more psychiatric interventions
Gaston-Johansson *et al.* [81]	1992	Auto	17	No	Descriptive	2 days pre-BMT, 5, 10 and 20 days post-BMT	PoM, STAI, BDI, MHLC, CSQ	No	Pts had a low-grade, persistent pain they could not control, and mild to moderate anxiety. They used inadequate coping strategies
Grant *et al.* [82]	1992	Allo	179	No	Retrospective	Minimum 100 days post-BMT	QOL-BMT questionnaire	No	Overall QOL scores lower than in healthy controls, but higher than in other cancer pts 29% reported frequent colds, 28% reported weight loss
Hengeveld *et al.* [83]	1988	Allo	17	No	Retrospective	12–60 mo post-BMT (mean 36)	Interview, BDI, SCL-90	Karnofsky	BMT caused severe emotional strain in all pts. Psychological state closely linked to physical condition

Jenkins *et al.* [32]	1991	Allo/auto	33	No	Retrospective	After discharge from BMT unit	Interview, HAD, PAIS, EPQ, CIDL	No	Pts had adjusted comparably to other medical pts. No differences between allo/auto. Depression associated with impaired functioning
Kennedy *et al.* [99][a]	1990	Auto	50	No	Retrospective	13–62 mo post-BMT (median 30)	Phone interview, semistructured	Karnofsky	QOL generally perceived as acceptable. 82% employed or in school. 40% reported reduced sexual function or desire
King [100][a]	1988	Auto/allo	20	No	Descriptive	At time of admission and discharge	NSSQ, BDI	No	No correlation between perceived social support and depression. No difference in depression pre- or post-BMT
Larson *et al.* [84]	1993	Allo/auto	30	28 nurses	Prospective	Day 1 post-BMT, days 7–10, 20–23, 30–34	SDS, POMS	Karnofsky	Incongruence between nurses' and pts' ratings. Pts perceived more distress at day 1 than their nurses thought. Little change in distress
Lesko *et al.* [35]	1992	Allo	21	49 chemotherapy pts	Retrospective	Minimum 5 years from end of treatment	BSI, MHI, IES, SAS, ABCL, DSFI, cohesion	Karnofsky	No difference in psychological and social functioning. Both groups reported greater distress than healthy subjects
Magid *et al.* [101][a]	1988	Auto	26	26 significant others	Prospective	Baseline pre-BMT, 1 mo post-discharge	POMS, FLIC	No	Pts appeared to return to a healthy level of physical well-being/activities. Emotional distress decreased over time
Mashberg [102][a]	1989	Allo	21	19 chemotherapy or standard care pts	Retrospective	Minimum 1 year post-BMT	BSI, DAQ, IES, PAIS, DSFI	Karnofsky	No difference between groups in psychological adjustment or distress. No correlation between age and psychological outcome
McElwain *et al.* [85]	1989	Auto	11	28 chemotherapy pts	Longitudinal	6 mo–3 years	Infection rates, pain	ECOG	Complete remission rate was 50%, associated with very good QOL
Mumma *et al.* [86]	1992	Allo	21	49 chemotherapy pts	Retrospective	Minimum 1 year post-BMT (mean 47 and 64)	Interview, BSI, POMS, DAQ, IES, PAIS, DSFI	Karnofsky	Psychosexual sequelae frequent in leukaemia survivors compared to normal data. No difference between BMT pts and comparisons
Peters *et al.* [87]	1993	Auto	52	No	Retrospective	Minimum 1 year post-BMT (median 2 years)	Phone interviews, FLIC, SDS	No	Sleeping, fatigue and worry were the most commonly reported symptoms. Most patients functioning well, reported good QOL
Rodrigue *et al.* [88]	1993	Allo/auto	51	No	Longitudinal	Pre-BMT (mean 23 days)	BDI, STAI, STAXI, MCMQ, MMPI	No	Normal psychological data pre-BMT. Passive coping style correlated with higher negative affect and psychopathology
Schmidt *et al.* [103][a]	1989	Allo	238	No	Retrospective	Every 3 mo, 3–140 mo (median 3.6 years)	Specifically designed questionnaire	Karnofsky	QOL rated as adequate, 42% were employed, 40% indicated sexual problems, 18% had signs of GVHD
Schmidt *et al.* [89]	1993	Allo	162 adults	No	Retrospective	Minimum 12 mo post-BMT	Phone or personal interviews	Karnofsky	Most survivors did well. GVHD and need for medication more common in older pts. Higher Karnofsky scores in younger pts
Smith *et al.* [90]	1984	Allo	22	22 identical twins	Longitudinal	Pre- or post-BMT, most in the peritranspl. period	Personal interview, SRE	No	No increased life changes pre-BMT in the sick twins. The healthy twins had increased or equivalent life changes after diagnosis

Table 1. Continued

Reference	Year*	BMT	No. of pts†	Comparison group	Study design	Time for measuring	Methods of assessment	Performance status	Conclusion
Steeves [91]	1992	Allo	6	No	Descriptive, follow-up	Pre-BMT to day 100	Hermeneutic methods, observation, interaction	No	Pts sought meaning with life by renegotiating their social position, and by trying to reach an understanding of their experiences
Syrjala *et al.* [34][a]	1990	Allo	100	No	Prospective	Pre-BMT and 1 year post-BMT	SIP, BDI, BES, coping style	No	Physical and psychological functioning returned to normal 1 year post-BMT for most pts except for work, recreation and stamina
Syrjala *et al.* [33]	1993	Allo	67	No	Prospective	Pre-BMT, 90 days and 1 year post-BMT	SIP, BSI, BDI, family cohesion, coping style	Karnofsky	Greater distress post-BMT predicted by GVHD, pretransplant family conflict, non-married status. Majority returned to work
Vose *et al.* [92]	1991	Auto	50	No	Retrospective	13–62 mo post-BMT (median 30)	Phone interview on appearance, adjustment	No	Changes in appearance normalised after 1 year. 1/3 had sexual difficulties. Most pts had a positive outlook, would do BMT again
Winer *et al.* [60][a]	1992	Auto	61	No	Retrospective	Minimum 1 year post-BMT (median 28 mo)	FLIC, SDS, PAIS, phone interview	No	Overall QOL acceptable, closely correlated with present disease status. Sexual function a particular problem
Wingard *et al.* [93]	1992	Allo/auto/syn	126	No	Cohort	6–149 mo post-BMT (median 47)	MOS, SLDS, CSAL	Karnofsky	22% reported some dissatisfaction with sexual function. Post-BMT satisfaction not correlated with pre-BMT satisfaction
Wingard *et al.* [94]	1991	Allo/auto/syn	135	No	Cohort	6–149 mo post-BMT (median 37)	Mailed survey, health perception scale	Karnofsky	Most subjects reported good to excellent health and functional status. 75% in school or employed
Wolcott *et al.* [95]	1986	Allo/auto	26	Donor group	Cross-sectional	Minimum 1 year post-BMT (mean 42 mo)	SAS (self report), POMS, Simmons	No	Adequate functioning. 70% rated their health as good or excellent. 25% of the patients had significant physical problems
Zabora *et al.* [104][a]	1990	Allo/auto	43	No	Cohort	Pre BMT, 6–48 mo post-BMT	SI, ICC, SLDS	Physical functioning	Psychosocial factors present before BMT stronger predictors of post-transplant distress than actual BMT complications (GVHD)

*year of publication; †No. of BMT pts.

Abbreviations: a, abstract, ABCL, Achenbach Behaviour Check List; allo, allogeneic; auto, autologous; BDI, Beck's Depression Inventory; BES, BMT Events Scale; BPNAS, Bradburn Positive and Negative Affect Scale; BSI, Brief Symptom Inventory; CJDM, Clinical Judgment of Defense Mechanisms; CSAL, Cantril Self-Anchoring Ladder of Life Scale; CSQ, Coping Strategy Questionnaire; DAQ, Death Anxiety Questionnaire; DSFI, Derogatis Sexual Functioning Scale; DSM III, Diagnostic and Statistical Manual of Mental Disorders; EPQ, Eysenck Personality Questionnaire; EORTC QLQ-C30, European Organization for Treatment and Research of Cancer QOL Questionnaire; FLIC, Functional Living Index Cancer; GVHD, Graft versus Host Disease; HAD, Hospital Anxiety and Depression Scale; ICC, Inventory of Current Concerns; IES, Impact of Event Scale; MCMQ, Medical Coping Modes Questionnaire; MHI, Mental Health Inventory; MHLC, Multidimensional Health Locus of Control; MMPI, Minnesota Multiphasic Personality Inventory; mo, months; MOS, Medical Outcome Survey; NSSQ, Norbeck Social Support Questionnaire; PAIS, Psychosocial Adjustment to Illness; PoM, Pain-o-Meter; POMS, Profile of Mood State; QUALY, Quality Adjusted Life Years; QLI, Quality of Life Index; SAS, Social Adjustment Scale; SCL, Symptom Checklist-90; SDS, Symptom Distress Scale; SI, Screening Instrument; SIP, Sickness Impact Profile; SLDS, Satisfaction with Life Domains Scale; SRE, Schedule of Recent Experiences; STAI, State-Trait Anxiety Inventory; STAXI, State-Trait Anger Expression Inventory; syn, syngeneic; TBI, total body irradiation; normal data, data from healthy controls, population norms.

Table 2. Number of BMT patients and study design in the 48 studies from Table 1

No. of patients/Study design	<20	20–39	40–59	60–79	80–99	100–119	120–139	>140	Total
Cohort			2				2	1	5
Cross-sectional		2	1				1		4
Descriptive	2	1							3
Longitudinal	3	2	1						6
Prospective	1	2		1		1			5
Qualitative		1				1			2
Retrospective	3	8	6	1		1	1	3	23
Total	9	16	10	2	0	3	4	4	48

Table 3. Sample size, use of comparison groups, performance status and information on methods in the five studies

Publication	Sample size	Comparisons	Physical performance	No. of assessments	Pre-BMT assessments	Measurement tools
Andrykowski *et al.* [29]	16	Historical data from patient samples and normal data*	No	3	No	POMS; 65 items, assessing affective state. Yields a total mood disturbance score and subscale scores; FLIC: 22 items, assessing overall functional QOL, yielding a total score and subscale scores; SIP: Measures illness related dysfunction, giving both overall and subscale scores;
Chao *et al.* [75]	58	No	Karnofsky	4	No	Semi-structured telephone questionnaire on QOL and BMT specific issues, developed for the study;
Gaston-Johannson *et al.* [81]	17	No	No	4	Yes	STAI: Two 20 statement scales for evaluating state and trait anxiety; BDI: 21 items describing symptoms of depression, yielding a total score; MHLC: 18 items measuring the subject's perceived control of health outcomes; CSQ: six categories for assessing pain coping strategies; PoM: assessment of the intensity and quality of pain, developed for the study;
Larson *et al.* [84]	30	28 nurses	Karnofsky	4	No	POMS SDS: 13 items assessing distress from physical symptoms. Specific BMT symptoms added
Syrjala *et al.* [33]	67	Normal data*	Karnofsky	3	Yes	SIP, BDI BSI: 53 items assessing nine psychological symptom dimensions and three global scales for psychological distress

* Normal data, data obtained from healthy subjects, population norms.

The measurement tools that were used in the five studies mainly focused on psychological distress and psychosocial issues. Only one study [29] employed a well-known cancer specific QOL questionnaire, the FLIC [55]. Four of the studies used multiple measurement tools in combination for assessing QOL, distress or psychosocial issues [29, 33, 81, 84]. The majority of these were well known with respect to psychometric properties. One of the studies relied on a telephone interview specifically designed for assessment of QOL issues relevant to BMT patients [75], while an inventory for assessment of pain was developed for the purpose of another study [81]. The other studies based the assessment on self-report by mailing the questionnaires to the patients. Information on reliability and validity was provided in all publications.

The presence of physical symptoms and side effects post-BMT was assessed in four studies, while one mainly focused on the assessment of pain [81]. The Karnofsky scale [105] was employed for a physician rating of physical performance in three

studies [33, 75, 84]. When focusing on the immediate post-BMT period, the Karnofsky score showed a significant decline from a mean of 77.2–67.1 between assessment no. 1 and 4, the latter being 30–34 days post-BMT [84]. In the other two studies, physical performance considerably deteriorated at day 90 only to show a marked improvement 12 months post-BMT. After 1 year, the mean and median Karnofsky scores were 87.4 and 100, respectively [33, 75]. Although most patients did well after 1 year, it was also shown that recovery might take years for approximately 40% of the patients [29, 33].

Assessment of psychological distress and anxiety in the immediate post-BMT period showed that the BMT-patients' distress did not seem to decrease during the early post-transplant period contrary to their nurses' assessments [84]. Depression changed little during the time as inpatients with most patients reporting mild to moderate anxiety and depression throughout their hospitalisation [81, 84]. This was correlated with the presence of pain, lasting for a period of 15–20 days [81].

Mood disturbances and psychosocial problems were greater in BMT survivors than in historical cancer or normal subjects, with 25–33% of the patients scoring at least 1 standard deviation above the population norms for psychological distress [29, 33]. However, consistent findings reported no association between time since transplant and the degree of psychological and social problems [29, 33].

Family relationships were found to be important determinants of physical and emotional recovery, showing that family conflict and low family cohesion pre-transplant were predictors of psychosocial problems after the transplant [33].

DISCUSSION

At first glance, there seemed to be a fair amount of research on QOL and psychosocial issues in BMT patients. However, only five studies fulfilled our criteria for a more thorough evaluation, in spite of setting the requirement for sample size as low as 15 patients. This demonstrates that the research in this field has mainly focused on the life and functioning of survivors after BMT by employing a retrospective, cross-sectional design with only one assessment point. Retrospective results have been reviewed elsewhere [106, 107]. Little attention has been paid to the first year post-transplant, when returning to normal life and functioning is crucial to prevent deleterious psychosocial adjustment. Some studies, however, have focused on the peri-transplant period. These were studies mostly undertaken by nurses, the reason being that this might seem especially relevant for nursing care and practice. Nevertheless, no studies presented any intervention strategies or the evaluation of support programmes. We identified only one journal publication presenting prospective data on physical and psychological functioning of BMT patients before and after transplant [33]. Another longitudinal, prospective study is currently being undertaken, but only cross-sectional data have been published from this research so far [41, 77, 93, 94, 108].

Based on what has been demonstrated in the previous sections, it seems that many of the studies in BMT patients are hampered by methodological weaknesses. This is partly related to inconsistencies in the definition of QOL and the fact that only a few domains of QOL are addressed, i.e. anxiety and/or depression, social functioning. Based on the definition of health as stated by the WHO [109], and QOL being a multidimensional concept, a more holistic approach is warranted. Some QOL measurement tools allow for summary scores of the different dimensions. This facilitates comparisons between groups of patients. There is controversy, however, on the utility of summary scores, because important information on specific domains might be lost. Such a global approach could be regarded as contradictory to QOL being a multidimensional concept [110]. As demonstrated in Table 1, a wide array of well-known and *ad hoc* QOL questionnaires has been used, rendering interpretation and valid comparisons between studies difficult.

There is also a lack of comparison groups in most of the studies. Comparisons with population norms might only be valid provided that the demographic, socio-economic and cultural factors are equal. Most studies are retrospective or cross-sectional in nature with small sample sizes, and consequently prohibitive for making generalisations. This is further complicated by the great variability in the number of assessment points as well as the time of measurement in relation to the transplant. The timing of the assessment is important in capturing critical periods in the time of psychosocial adjustment.

The elevated levels of psychological distress reported in the BMT patients must be seen in the context of the study population, the study design and the methodology employed. This is consistent with findings in retrospective and cross-sectional studies, indicating that BMT patients experienced severe emotional distress [27, 31, 32, 35, 62, 72, 83, 101, 111]. Whether this can be attributed to the suffering from cancer, to the intensive treatment with high dose chemotherapy followed by a BMT rather than to personality variables, requires further investigation. In studies among patients with advanced cancer, psychological problems are reported with a prevalence from 47 to 67% [36, 38]. The most commonly assessed symptoms when investigating psychological morbidity in cancer patients are anxiety and depression ranging from 13 to 30% in different studies [37, 40, 111]. It is important to distinguish between a normal transient condition related to having a life-threatening illness as opposed to persistent psychopathological morbidity. The diagnostic criteria for diagnosing psychiatric morbidity must always be considered when interpreting such results.

Some results were nevertheless supported by similar findings in different studies. Many patients seemed to do well after treatment with BMT. Although this was consistent across studies, it was also evidenced that up to 25% of the BMT survivors reported moderate to severe problems post-BMT. This means that there might be different subgroups of long-term survivors; those who adapt reasonably well shortly after the transplantation, those for whom the readjustment might take from 1 to 2 years and those who continue to have long-term psychosocial problems. The identification of these subgroups early in the treatment could lead to therapeutic intervention for the individuals at risk. Findings from psychiatric consultation literature give reason to believe that people who have experienced stressful life events, who have a prior history of mental disease, or a history of problems with compliance to treatment will be more susceptible than others [39, 112, 113]. Clinical experience and research findings emphasize the importance of social functioning and social support of cancer patients [31, 111, 114]. This is consistent with results in follow-up studies evaluating family functioning pre- and post-BMT as well as in other samples of cancer patients [40, 43, 104]. Pre-transplant psychosocial problems were the strongest predictive factors for experiencing greater distress and more problems post-transplant [33, 104]. There is also a paucity of studies assessing family relationship and the impact of intensive treatment like BMT on family cohesion and dynamics [64, 108, 115, 116]. Validated QOL tools that are used prior to the transplant might prove useful for

predicting poor outcomes in terms of psychosocial problems. This is supported by a systematic follow-up of BMT patients offering psychiatric consultation as part of the routine care [111]. Methods for screening psychiatric morbidity supplemented with psychiatric interviews might be useful in identifying patients with signs of anxiety or depression or who have a prior psychiatric history at the time of admission. Questionnaires like Beck's Depression Inventory (BDI) [117] and the Hospital and Anxiety Depression scale (HAD) [118] have been used with success in that respect [37, 104]. What must be kept in mind is how the sensitivity and specificity of the different methods and their ability to truly differentiate between groups of people might have influenced the percentages that were reported. Furthermore, these subgroups might not be directly comparable between studies due to differences in study design, sample size and methodology as well as on national, cultural and racial characteristics.

Descriptions of QOL differences between groups in cancer clinical trials, predictions of post-BMT outcomes and initiation of support programmes, have so far been the clinical utility of QOL measures. There is still a gap between the existing knowledge on QOL and its application in medical decision making, in general. It is a major challenge for medical researchers and researchers who are particularly interested in QOL to incorporate such measures in clinical work, to disseminate the results and to build databases for use in decision making and practical work.

In spite of the increasing use of BMT, there has been little research on QOL in long-term survivors. However, QOL research is still a relatively young field and the reported findings provide a basis and indicate the directions for future research in this field. This particular patient group is ideally suited for such research, due to the multidisciplinary approach which is already a traditional part of their care.

Prospective studies are now warranted, preferably with extended follow-up periods. This is due to the long-term side-effects caused by the preparative regimens in particular, which might not become manifest until a decade after the transplantation. Screening patients for psychological factors that might predict a need for targeted interventions might be particularly beneficial in helping the patients overcome psychological morbidity after treatment. The use of reliable and well-validated methods for measuring QOL and rehabilitation needs are important. These should be selected based on their psychometric properties, sensitivity, specificity and the ability to predict poor outcomes. Thus, it might be possible to compare groups of patients on an international level, i.e. in multicentre clinical trials, provided that the questionnaires yield sufficient cross-cultural validity. This will expand the understanding of specific problems that are unique for the BMT patients, and proper intervention strategies could be implemented. Hopefully this will enhance our knowledge and improve the routines for medical follow-up and care of this patient group.

1. Armitage JO. Bone marrow transplantation. *New Engl J Med* 1994, **330**, 827–838.
2. International consensus conference on intensive chemotherapy plus hematopoietic stem cell transplantation in malignancies. Conclusion of the jury, Lyon. *Ann Oncol* 1994, **4** (suppl 1), 1–81.
3. Gluckman E. Allogeneic bone marrow transplantation in acute myeloid and lymphocytic leukemia. *Curr Opin Oncol* 1993, **5**, 255–261.
4. Miller JS, McGlave PB. Therapy for chronic myelogenous leukemia with marrow transplantation. *Curr Opin Oncol* 1993, **5**, 262–269.
5. Ljungman P, Aschan J, Bolme P, *et al.* Bone marrow transplantation or antithymocyte globulin in aplastic anemia? Both therapeutic alternatives result in good quality of life. *Lakartidningen* 1991, **88**, 2308–2311.
6. Hinterberger W, Gadner H, Hocker P, *et al.* Survival and quality of life in 23 patients with severe aplastic anemia treated with bone marrow transplantation (BMT). *Blut* 1987, **54**, 137–146.
7. Kodish E, Lantos J, Siegler M, Kohrman A, Johnson FL. Bone marrow transplantation in sickle cell disease: the trade-off between early mortality and quality of life. *Clin Res* 1990, **38**, 694–700.
8. Sanders J, Sullivan K, Witherspoon R, *et al.* Long term effects and quality of life in children and adults after marrow transplantation. *Bone Marrow Transplant* 1989, **4**, 7–29.
9. Sanders JE. Long-term effects of bone marrow transplantation. *Pediatrician* 1991, **18**, 76–81.
10. Demetri GD, Antman KH. Granulocyte-macrophage colony-stimulating factor (GM-CSF): preclinical and clinical investigations. *Semin Oncol* 1992, **19**, 362–385.
11. Blume E. Investigators, insurers consider marrow transplant issues. *J Natl Cancer Inst* 1991, **83**, 1136–1138.
12. Nims JW, Strom S. Late complications of bone marrow transplant recipients: nursing care issues. *Semin Oncol Nurs* 1988, **4**, 47–54.
13. Eilers J. Coordinated team essential to decrease impact of bone marrow transplantation (BMT) (Meeting abstract). *Oncol Nurs Forum* 1988, **15**, 155.
14. Ford R, Eisenberg S. Bone marrow transplant. Recent advances and nursing implications. *Nurs Clin North Am* 1990, **25**, 405–422.
15. Chielens D, Herrick E. Recipients of bone marrow transplants: making a smooth transition to an ambulatory care setting. *Oncol Nurs Forum* 1990, **17**, 857–862.
16. Larson PJ, Viele C, Cebulski C, Coleman S. Care needs of bone marrow transplant patients (Meeting abstract). *Oncol Nurs Forum* 1991, **18**, 344.
17. Sullivan KM, Mori M, Sanders J, *et al.* Late complications of allogeneic and autologous marrow transplantation. *Bone Marrow Transplant* 1992, **10** (suppl 1), 127–134.
18. Bacigalupo A, Van Lint MT, Frassoni F, *et al.* Late complications of allogeneic bone marrow transplantation. *Med Oncol Tumor Pharmacother* 1991, **8**, 261–263.
19. Atkinson K. Clinical spectrum of human chronic Graft-VS-Host disease. *Hematology* 1990, **12**, 569–586.
20. Atkinson K. Treatment of extensive human chronic Graft-VS-Host disease. *Hematology* 1990, **12**, 681–690.
21. Vogelsang GB. Graft-versus-host disease. *Curr Opin Oncol* 1990, **2**, 285–288.
22. Deeg HJ. Delayed complications and long-term effects after bone marrow transplantation. *Hematol Oncol Clin North Am* 1990, **4**, 641–657.
23. Andrykowski MA, Schmitt FA, Gregg ME, Brady MJ, Lamb DG, Henslee Downey PJ. Neuropsychologic impairment in bone marrow transplant candidates. *Cancer* 1992, **70**, 2288–2297.
24. Noll RB, Kullarni R. Complex visual hallucinations and cyclosporine. *Arch Neurol* 1984, **41**, 329–330.
25. Ozsahin M, Belkacemi Y, Pene F, *et al.* Total-body irradiation and cataract incidence: a randomized comparison of two instantaneous dose rates. *Int J Radiat Oncol Biol Phys* 1994, **28**, 343–347.
26. Brown HN, Kelly MJ. Stages of bone marrow transplantation: a psychiatric perspective. *Psychosom Med* 1976, **38b**, 439–446.
27. Wolcott DL, Fawzy FI, Wellisch DK. Psychiatric aspects of bone marrow transplantation: a review and current issues. *Psychiatr Med* 1986, **4**, 299–317.
28. Patenaude AF. Psychological impact of bone marrow transplantation: current perspectives. *Yale J Biol Med* 1990, **63**, 515–519.
29. Andrykowski MA, Henslee PJ, Barnett RL. Longitudinal assessment of psychosocial functioning of adult survivors of allogeneic bone marrow transplantation. *Bone Marrow Transplant* 1989, **4**, 505–509.
30. Andrykowski MA, Henslee PJ, Farrall MG. Physical and psychosocial functioning of adult survivors of allogeneic bone marrow transplantation. *Bone Marrow Transplant* 1989, **4**, 75–81.
31. Colon EA, Callies AL, Popkin MK, McGlave PB. Depressed mood and other variables related to bone marrow transplantation survival in acute leukemia. *Psychosomatics* 1991, **32**, 420–425.
32. Jenkins PL, Linington A, Whittaker JA. A retrospective study of

psychosocial morbidity in bone marrow transplant recipients. *Psychosomatics* 1991, **32**, 65–71.
33. Syrjala KL, Chapko MK, Vitaliano PP, Cummings C, Sullivan KM. Recovery after allogeneic marrow transplantation: a prospective study of predictors of long-term physical and psychosocial functioning. *Bone Marrow Transplant* 1993, **11**, 319–327.
34. Syrjala KL, Georgiadou F, Hazelwood L, Donaldson G. Recovery from marrow transplantation (BMT): physical and psychological functioning at one yr post-transplant (Meeting abstract). *Exp Hematol* 1990, **18**, 660.
35. Lesko LM, Ostroff JS, Mumma GH, Mashberg DE, Holland JC. Long-term psychological adjustment of acute leukemia survivors: impact of bone marrow transplantation versus conventional chemotherapy. *Psychosom Med* 1992, **54**, 30–47.
36. Derogatis LR, Morrow GR, Fetting J, *et al.* The prevalence of psychiatric disorders among cancer patients. *JAMA* 1983, **249**, 751–757.
37. Hopwood P, Howell A, Maguire P. Psychiatric morbidity in patients with advanced cancer of the breast: prevalence measured by two self-rating questionnaires. *Br J Cancer* 1991, **64**, 349–352.
38. Kaasa S, Malt U, Hagen S, Wist E, Moum T, Kvikstad A. Psychological distress in cancer patients with advanced disease. *Radiother Oncol* 1993, **27**, 193–197.
39. Folsom TL, Popkin MK. Current and future perspectives on psychiatric involvement in bone marrow transplantations. *Psychiatr Med* 1986, **4**, 319–329.
40. Fobair P, Hoppe RT, Bloom J, Cox R, Varghese A, Spiegel D. Psychosocial problems among survivors of Hodgkin's disease. *J Clin Oncol* 1986, **4**, 319–329.
41. Baker F, Curbow B, Wingard JR. Role retention and quality of life of bone marrow transplant survivors. *Soc Sci Med* 1991, **36**, 697–704.
42. Cust MP, Whitehead MI, Powles R, Hunter M, Milliken S. Consequences and treatment of ovarian failure after total body irradiation for leukaemia. *Br Med J* 1989, **299**, 1494–1497.
43. Kornblith AB, Anderson J, Cella DF, *et al.* Hodgkin disease survivors at increased risk for problems in psychosocial adaptation. The Cancer and Leukemia Group B. *Cancer* 1992, **70**, 2214–2224.
44. The SBU report on bone marrow transplantation: there are obvious ethical problems. *Lakartidningen* 1991, **88**, 3278.
45. Johnson JR, Temple R. Food and drug administration requirements for approval of new anticancer drugs. *Cancer Treat Rep* 1985, **69**, 1155–1157.
46. Ware JE. Standards for validating health measures: definitions and content. *J Chronic Dis* 1987, **40**, 473–480.
47. Aaronson NK. Quality of life research in cancer clinical trials: a need for common rules and language. *Oncology* 1990, **4**, 59–66.
48. Aaronson NK. Methodologic issues in assessing the quality of life of cancer patients. *Cancer* 1991, **67**, 844–850.
49. Cella DF, Tulsky DS. Measuring quality of life today: methodological aspects. *Oncology* 1990, **4**, 29–37.
50. Bergner M, Bobbitt R, Carter W, Gilson B. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care* 1981, **14**, 787–805.
51. Hunt SM, McKenna SP, McEwan J, Williams J, Papp E. The Nottingham Health Profile: subjective health status and medical consultations. *Soc Sci Med* 1981, **15A**, 221–229.
52. Stewart AL, Hays RD, Ware JE. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988, **26**, 724–735.
53. Ware JE. *SF 36 Health Survey Manual and Interpretation Guide.* Boston, New England Medical Center, 1993.
54. Haas JCJM de, Knippenberg FCE van, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br J Cancer* 1990, **62**, 1034–1038.
55. Schipper H, Clinch J, McMurray A, Levitt M. Measuring the quality of life of cancer patients: the functional living index—cancer: development and validation. *J Clin Oncol* 1984, **2**, 472–483.
56. Schag CA, Heinrich RL, Ganz PA. The cancer inventory of problem situations: an instrument for assessing cancer patients' rehabilitation needs. *J Psychosoc Oncol* 1983, **1**, 11–24.
57. Schag CA, Ganz PA, Heinrich RL. Cancer rehabilitation evaluation system-short form (CARES-SF): a cancer specific rehabilitation and quality of life instrument. *Cancer* 1991, **68**, 1406–1413.
58. Aaronson NK, Ahmedzai S, Bergman B, *et al.* The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993, **85**, 365–376.
59. Cella DF, Tulsky DS, Gray G, *et al.* The functional assessment of cancer therapy scale: development and validation of the general measure. *J Clin Oncol* 1993, **11**, 570–579.
60. Winer E, Lindley C, Hardee M, *et al.* Quality of life (QL) assessment in patients with breast cancer surviving 12 mo or more following high-dose chemotherapy with autologous bone marrow transplant (HDC-ABMT) (Meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1992, **11**, A1328.
61. Hillner BE, Smith TJ, Desch CE. Efficacy and cost-effectiveness of autologous bone marrow transplantation in metastatic breast cancer. Estimates using decision analysis while awaiting clinical trial results. *JAMA* 1992, **267**, 2055–2061.
62. Dermatis H, Lesko LM. Psychosocial correlates of physician–patient communication at time of informed consent for bone marrow transplantation. *Cancer Invest* 1991, **9**, 621–628.
63. Rappaport BS. Evolution of consultation-liaison services in bone marrow transplantation. *Gen Hosp Psychiatry* 1988, **10**, 346–351.
64. Futterman AD, Wellisch DK, Bond G, Carr CR. The Psychosocial Levels System. A new rating scale to identify and assess emotional difficulties during bone marrow transplantation. *Psychosomatics* 1991, **32**, 177–186.
65. Neuser J, Grigelat G, Quabeck K, Beelen DW, Schaefer UW. Principles of supportive psychological care for patients undergoing bone marrow transplantation. *Hamatol Bluttransfus* 1990, **33**, 583–586.
66. Haberman MR. Psychosocial aspects of bone marrow transplantation. *Semin Oncol Nurs* 1988, **4**, 55–59.
67. Kaehler SL, Goodwin JM, Young LD. Bone marrow transplantation: mastering the experience despite psychological risk factors. *Psychosomatics* 1989, **30**, 337–341.
68. Jenkins PL, Roberts DJ. Suicidal behaviour after bone marrow transplantation. *Bone Marrow Transplant* 1991, **7**, 159–161.
69. Aeschelmann D, Schiwilk C, Kachele H, Pokorny D. Defense mechanisms in patients with bone marrow transplantation: a retrospective study. *Isr J Psychiatry Relat Sci* 1992, **29**, 89–99.
70. Altmaier EM, Gingrich RD, Fyfe MA. Two-year adjustment of bone marrow transplant survivors. *Bone Marrow Transplant* 1991, **7**, 311–316.
71. Andrykowski MA, Altmaier EM, Barnett RL, Burish TG, Gingrich R, Henslee Downey PJ. Cognitive dysfunction in adult survivors of allogeneic marrow transplantation: relationship to dose of total body irradiation. *Bone Marrow Transplant* 1990, **6**, 269–276.
72. Andrykowski MA, Altmaier EM, Barnett RL, Otis ML, Gingrich R, Henslee Downey PJ. The quality of life in adult survivors of allogeneic bone marrow transplantation. Correlates and comparison with matched renal transplant recipients. *Transplantation* 1990, **50**, 399–406.
73. Baruch J, Benjamin S, Treleaven J, Wilcox AH, Barron JL, Powles R. Male sexual function following bone marrow transplantation. *Bone Marrow Transplant* 1991, **7**, 52.
74. Belec RH. Quality of life: perceptions of long-term survivors of bone marrow transplantation. *Oncol Nurs Forum* 1992, **19**, 31–37.
75. Chao NJ, Tierney DK, Bloom JR, *et al.* Dynamic assessment of quality of life after autologous bone marrow transplantation. *Blood* 1992, **80**, 825–830.
76. Collins C, Upright C, Aleksich J. Reverse isolation: what patients perceive. *Oncol Nurs Forum* 1989, **16**, 675–679.
77. Curbow B, Somerfield MR, Baker F, Wingard JR, Legro MW. Personal changes, dispositional optimism, and psychological adjustment to bone marrow transplantation. *J Behav Med* 1993, **16**, 423–443.
78. Decker WA, Turner McGlade J, Fehir KM. Psychosocial aspects and the physiological effects of a cardiopulmonary exercise program in patients undergoing bone marrow transplantation (BMT) for acute leukemia (AL). *Transplant Proc* 1989, **21**, 3068–3069.
79. Ersek M. The process of maintaining hope in adults undergoing bone marrow transplantation for leukemia. *Oncol Nurs Forum* 1992, **19**, 883–889.
80. Ferrell B, Grant M, Schmidt GM, *et al.* The meaning of quality of life for bone marrow transplant survivors. Part 1. The impact of bone marrow transplant on quality of life. *Cancer Nurs* 1992, **15**, 153–160.
81. Gaston-Johansson F, Franco T, Zimmerman L. Pain and psycho-

logical distress in patients undergoing autologous bone marrow transplantation. *Oncol Nurs Forum* 1992, **19**, 41–48.
82. Grant M, Ferrell B, Schmidt GM, Fonbuena P, Niland JC, Forman SJ. Measurement of quality of life in bone marrow transplantation survivors. *Quality Life Res* 1992, **1**, 375–384.
83. Hengeveld MW, Houtman RB, Zwaan FE. Psychological aspects of bone marrow transplantation: a retrospective study of 17 long-term survivors. *Bone Marrow Transplant* 1988, **3**, 69–75.
84. Larson PJ, Viele CS, Coleman S, Dibble SL, Cebulski C. Comparison of perceived symptoms of patients undergoing bone marrow transplant and the nurses caring for them. *Oncol Nurs Forum* 1993, **20**, 81–87.
85. McElwain TJ, Gore ME, Meldrum M, Viner C, Judson IR, Malpas JS. VAMP followed by high dose melphalan and autologous bone marrow transplantation for multiple myeloma. *Bone Marrow Transplant* 1989, **4**, 109–112.
86. Mumma GH, Mashberg D, Lesko LM. Long-term psychosexual adjustment of acute leukemia survivors: impact of marrow transplantation versus conventional chemotherapy. *Gen Hosp Psychiatry* 1992, **14**, 43–55.
87. Peters WP, Ross M, Vredenburgh JJ, *et al.* High-dose chemotherapy and autologous bone marrow support as consolidation after standard-dose adjuvant therapy for high-risk primary breast cancer. *J Clin Oncol* 1993, **11**, 1132–1143.
88. Rodrigue JR, Boggs SR, Weiner RS, Behen JM. Mood, coping style, and personality functioning among adult bone marrow transplant candidates. *Psychosomatics* 1993, **34**, 159–165.
89. Schmidt GM, Niland JC, Forman SJ, *et al.* Extended follow-up in 212 long-term allogeneic bone marrow transplant survivors. Issues of quality of life. *Transplantation* 1993, **55**, 551–557.
90. Smith CK, Harrison SD, Ashworth C, Montano D, Davis A, Fefer A. Life change and onset of cancer in identical twins. *J Psychosom Res* 1984, **28**, 525–532.
91. Steeves RH. Patients who have undergone bone marrow transplantation: their quest for meaning. *Oncol Nurs Forum* 1992, **19**, 899–905.
92. Vose JM, Kennedy BC, Bierman PJ, Kessinger A, Armitage JO. Long-term sequelae of autologous bone marrow or peripheral stem cell transplantation for lymphoid malignancies. *Cancer* 1992, **69**, 784–789.
93. Wingard JR, Curbow B, Baker F, Zabora J, Piantadosi S. Sexual satisfaction in survivors of bone marrow transplantation. *Bone Marrow Transplant* 1992, **9**, 185–190.
94. Wingard JR, Curbow B, Baker F, Piantadosi S. Health, functional status, and employment of adult survivors of bone marrow transplantation. *Ann Intern Med* 1991, **114**, 113–118.
95. Wolcott DL, Wellisch DK, Fawzy FI, Landsverk J. Adaptation of adult bone marrow transplant recipient long-term survivors. *Transplantation* 1986, **41**, 478–484.
96. Achard S, Zittoun R. Determinants of quality of life (QOL) during intensive chemotherapy (IC) or bone marrow transplantation. (Meeting abstract). *Quality Life Res* 1993, **2**, 67.
97. Claisse JP, Hirsch I, Gluckman E. Quality of life after bone marrow transplantation. (Meeting abstract). *Quality Life Res* 1993, **2**, 68.
98. Ferro N, Kusminsky G, Dictar M, *et al.* Assessment of psychosocial aspects influencing quality of life following autologous bone marrow transplantation (ABMT) (Meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1992, **11**, A1422.
99. Kennedy B, Vose J, Nelson J. Nursing assessment of quality of life in lymphoma patients after autologous bone marrow transplantation (ABMT) (Meeting abstract). *Oncol Nurs Forum* 1990, **17**, 154.
100. King SR. Social support and depression in bone marrow transplant patients (Meeting abstract). *Oncol Nurs Forum* 1988, **15** (suppl 2), 109.
101. Magid DM, Barker C, Browning A, Williams S, Bitran J. Psychosocial adjustment (PA) of patients (PTS) and their significant other (SO) to high dose chemotherapy and autologous bone marrow reinfusion (HDC-ABMR) (Meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1988, **7**, A1210.
102. Mashberg DE. Psychological adjustment of patients with chronic leukemia. *Diss Abstr Int B* 1989, **50**, 2629.
103. Schmidt GM, Fonbuena PP, Chao NJ, *et al.* Quality of life in survivors of allogeneic bone marrow transplantation (BMT) for malignant disease (Meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1989, **8**, A1211.
104. Zabora JR, Seddon CF, Wingard JR, Baker F. Predicting psychosocial distress following bone marrow transplantation (BMT) (Meeting abstract). *Proc Annu Meet Am Soc Clin Oncol* 1990, **9**, A1189.
105. Karnofsky DA, Abelmann WH, Craver LF, Burchenal JH. The use of the nitrogen mustards in the palliative treatment of carcinoma. *Cancer* 1948, **1**, 634–656.
106. Lesko LM. Psychiatric aspects of bone marrow transplantation: Part 1: special issues during pre-transplant assessment and hospitalization. *Psycho-Oncology* 1993, **2**, 161–183.
107. Lesko LM. Psychiatric aspects of bone marrow transplantation: Part 2: life beyond transplant. *Psycho-Oncology* 1993, **2**, 185–193.
108. Zabora JR, Smith ED, Baker F, Wingard JR, Curbow B. The family: the other side of bone marrow transplantation. *J Psychosoc Oncol* 1992, **10**, 33–45.
109. The Constitution of the World Health Organization. Geneva, WHO Chronicle, 1947.
110. Kaasa S. Measurement of quality of life in clinical trials. *Oncology* 1992, **49**, 289–294.
111. Lesko LM. Surviving hematological malignancies: stress responses and predicting psychological adjustment. *Prog Clin Biol Res* 1990, **352**, 432–437.
112. House RM, Thompson TL. Psychiatric aspects of organ transplantation. *JAMA* 1988, **260**, 535–539.
113. Holland JC, Rowland JH. Psychiatric, psychosocial and behavioral interventions in the treatment of cancer. In Weiss SM, Herd A, Fox B, eds. *Perspectives on Behavioral Medicine*. New York, Academic Press, 1981, 235–260.
114. Wortman CB. Social support and the cancer patient; conceptual and methodological issues. *Cancer* 1984, **53**, 2339–2362.
115. Woolery-Antill M. The effects of bone marrow transplantation (BMT) on family dynamics (Meeting abstract). *Oncol Nurs Forum* 1988, **15** (suppl 2), 145.
116. Wolcott DL, Wellisch DK, Fawzy FI, Landsverk J. Psychological adjustment of adult bone marrow transplant donors whose recipient survives. *Transplantation* 1986, **41**, 484–488.
117. Beck AT, Ward CH, Mendolson M, *et al.* An inventory for measuring depression. *Arch Gen Psych* 1961, **4**, 561–571.
118. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression scale. *Acta Psych Scand* 1983, **67**, 361–370.

Acknowledgements—The first author is a research fellow employed by the Norwegian Cancer Society, financial support by grant no. 93094. We acknowledge the valuable advice from S.A. Evensen and S.O. Kvaloy in the preparation of this manuscript.