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Predictors of physical outcomes in pediatric bone marrow transplantation

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Summary:

The purpose of the present study was to investigate the hypothesis that family factors, in conjunction with clinical factors, are associated with physical outcomes in pediatric BMT. A prospective study of 68 pediatric patients (mean age = 7.5 years; ranging from 4 months to 18 years) undergoing BMT was carried out over a 6.5 year period. Physicians rated initial prognosis on a (0–5) scale which incorporated the child's diagnosis, known risk factors, and type of donor. Both parents individually completed two psychometrically sound questionnaires assessing family well-being and marital satisfaction. Cox proportional hazards survival analyses were performed to determine predictors of death (44% of the patients died). Potential predictor variables included were: initial prognosis, type of transplant, patient's age, socioeconomic status, marital satisfaction and family status, and family stress. Initial prognosis, as estimated by the physician, (RR = 0.62, 95% CI = 0.40, 0.97) was the best predictor of survival. Initial clinical factors are clearly critical in outcomes for pediatric BMT patients. *Bone Marrow Transplantation* (2000) **26,** 553–558.
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BMT in pediatric patients, while no longer an experimental treatment, is often a procedure used as a last resort. It is complicated, costly (both in human and financial terms), and extremely stressful for all involved (ie patient, family, hospital personnel). Initially, research focused on the medical technology and physical health outcomes. Given the high demands of BMT it is not surprising that a second line of research addressed the psychosocial issues for both patients and family members. Most of this latter work was descriptive,[1] outlining the various challenges incurred during the different phases of the procedure. Studies typically were cross-sectional and included small sample sizes. Attention was paid to the impact of BMT on family members' well-being[2] and on the psychiatric aspects of survival.[3] Adjunct programs to assist family members cope with the demands of BMT have been described but not evaluated.[4] (The reader is directed to Phipps'[5] excellent review chapter concerning the psychosocial aspects of pediatric BMT.)

An emerging area of research addresses the determinants of medical complications and survival in BMT patients. One would expect that disease-related variables such as type of transplant and previous medical history would be related to outcomes. A more controversial idea is that psychosocial factors may also impact outcomes.[6] Yet, if one considers the growing literature which links social support to longevity in the general population[7] as well as to survival in other medical conditions (eg breast cancer[8]), then the notion that psychosocial factors may contribute to BMT outcomes does not appear so polemic. Certainly, for psychological adjustment it is clear that family support is critical for pediatric patients in general,[9] and BMT patients, in particular.[10] Moreover, family support has been found to predict survival in other diseases, such as patients being treated with hemodialysis.[11]

In an initial effort to identify variables related to physical outcomes, McConville *et al*[12] conducted a retrospective cross-sectional study of 32 pediatric BMT patients. They found that four factors contributed to 'unexpected' severe medical complications; they were: (1) the child's functional impairment, (2) family dysfunction, (3) geographical dislocation, and (4) paternal psychopathology. With regard to 'unexpected' deaths, the following four factors were found to contribute to this outcome: (1) the child's functional impairment, (2) paternal psychopathology, (3) family dysfunction, and (4) the child's personality (ie perceived as 'likeable and cooperative'). In the former case (ie medical complications) 55% of the variance was accounted for by the four factors whereas in the latter case (ie unexpected death) 36% of the variance was accounted for by the four factors. Yet, this study involved retrospective chart review which may have introduced bias with regard to the variables assessed. Moreover, cases with particularly poor outcomes were selected, compromising external validity.

In a study of psychological factors associated with survival in 71 adult BMT patients, Young and colleagues[13] reported that younger age, autologous (*vs* allogeneic) transplant, higher emotional social support, lower somatic anxiety, and lower future despair scores predicted survival. The methods employed in this study were markedly superior to the McConville *et al*'s study in that patients were tested

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directly using standardized psychological instruments and followed prospectively for 1 year.

Using a similar prospective design, Syrjala and colleagues[14] studied 67 allogeneic adult BMT patients for several years. At 1 year post transplant, the physical functioning and psychological adjustment was assessed in 31 survivors. Impaired physical recovery was predicted by more severe chronic GVHD, pre-transplant physical impairment, and family conflict; 41% of the variance was accounted for using multiple regression analysis. Greater emotional distress was predicted by pre-transplant family conflict, non-married status, and development of less severe chronic GVHD; 38% of the variance was accounted for using multiple regression analysis. Interestingly, family relations were tracked throughout the study (ie pre-transplant, 90 days post transplant, and 1 year post transplant) and found to be remarkably stable. This is important because when only one assessment is taken (for example, prior to the transplant) it is often assumed that the result reflects a stable characteristic. This assumption can, apparently, be made with some degree of confidence as Fife *et al*[15] followed 34 families with children diagnosed with acute lymphoblastic leukemia (ALL) over a period of 1 year; families with predominately stable relationships and adequate social support within the family unit coped well whereas those having problems predating diagnosis experienced deterioration in family life.

Neuser[16] followed 35 adult BMT patients between 497 and 754 days. Using survival analyses it was found that patients who scored high on a personality subscale entitled 'strives for recognition and help' were shown to survive the longest. These individuals sought and received social support from their environment. Social support was also a predictor of survival in Colon *et al*'s[17] study of 100 adult patients undergoing allogeneic BMT for acute leukemia. In this study, three variables were found to independently affect outcome: illness status, presence of depressed mood, and the extent of perceived social support (derived from the spouse or family). While the Colon *et al* study has methodological flaws (eg data were based on a retrospective review of clinical data obtained as part of routine psychiatric assessment of patients) its findings corroborate others.

Thus, there is preliminary evidence that a combination of biological and psychosocial factors influence BMT patients' prognosis, although there has not been a prospective study of pediatric patients. The purpose of the present investigation was to extend these early findings and attempt to replicate those reported by McConville *et al* using a prospective design including both parents of the pediatric BMT patient as well as data collected by treating staff.

Materials and methods

Procedures

Parents were informed of the study by their child's physician and invited to participate in the investigation. They were instructed in completing the psychosocial measures by a research assistant who was available to answer questions. Parents were requested to complete the questionnaires individually, without consulting each other. The study was approved by the hospitals' ethics committees prior to commencement.

Baseline assessment

When a child was accepted into the transplantation service the treating physician rated the child's prognosis on a 0 to 5 rating scale whereby 0 = very poor and 5 = excellent. The scale was developed by the first author; physicians were instructed to integrate all previous data pertaining to the case (ie diagnosis, risk factors, type of donor) with current medical knowledge specific to the illness being treated.

General information regarding the demographics of the families (eg, parents' occupation, number of children in the family, years married/separated/divorced/cohabiting, living in Montreal or outside Montreal) was gathered through chart review and interviewing the parents.

Locke–Wallace Marital Adjustment Test: This widely used inventory measures the degree of marital satisfaction by having each partner independently complete 15 questions pertaining to their relationship.[18] The psychometric parameters of the instrument have been studied and its reliability and validity are good.[19] This inventory was administered to intact families (ie, families for whom two parents are living with the children; in the case of reconstituted families (married or not), stepfathers who had lived in the family for at least 1 year were included).

Family Well-Being Assessment: This questionnaire, developed by Caldwell,[20,21] contains the following subscales: family stress, family satisfaction, family support, family cohesion, family adaptation, role conflict, role overload, role ambiguity, role nonparticipation, psychosomatic symptoms, and life satisfaction which can be combined to compute a Total Family Stress score. Individual family members rate each of the 74 items on a six-point Likert scale (a high score indicates poorer functioning for most subscales). Normative data are available from families with chronically ill and healthy children. Findings concerning reliability show that test–retest reliability was 0.88; Chronbach's alpha was 0.90. Content and construct validity were examined and found to be at acceptable levels. Questionnaires were translated into French using the back-translation method.[22]

Outcome variables

Medical charts were reviewed to determine the child's status 4 months following BMT by a research nurse specialized in BMT; she was blinded to the psychosocial baseline data. A standardized form was developed in collaboration with the treating staff (physicians and research nurses) which allowed for documentation of the various medical complications which may follow BMT (eg GVHD, various infections, relapse). Once the type and severity of complications were coded, the nurse made an overall judgment regarding the severity of medical complications on a Visual Analog Scale (VAS) ranging from 0 to 10, where 0 = no

complications and 10 = very serious complications. VASs are widely used with medical patients to assess constructs such as pain, mood, functional capacity, response to and satisfaction with treatment.[23–25] Thus, two physical outcome variables were recorded: death and medical complications.

Nurses also rated the children's quality of life 120 and 365 days following the BMT using Lansky *et al*[26] Play Performance status ratings. This scale is similar to the Karnofsky scale used to rate adult cancer patients' functional status. The Play Performance scale ranges from 0 (unresponsive), 50 (gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities), to 100 (fully active, normal). While it may have been preferable to have physicians rate these outcomes, it was not feasible.

Data analyses

Descriptive analyses were created for all study variables using means, standard deviations, medians, ranges, and percentages where appropriate. A Cox proportional hazards model was used to investigate the relationship between risk factors and survival following BMT. The index date was considered to be the date of transplant. Risk factors investigated included the initial prognosis as evaluated by the physician, the sex and age of the patient, the Locke–Wallace marital adjustment scores for both mothers and fathers (for intact families), family stress as rated by both parents, and the occupational status of the mother or father (higher score was used). Missing data were corrected for using multiple imputation techniques.[27] For each missing item, we created a regression model that predicted the item from non-missing information for that patient. For example, we predicted the family stress score from a missing item in the father's data from the score of the mother. Since these items are not generally predicted with high accuracy from the information available, we used 10 imputations of each item, which covered the range of feasible values. In doing this, we in effect create 10 different 'complete' data sets, each of which differs from the other nine data sets in the missing data only. By performing each analysis 10 times while carefully accounting for both the within-analysis variance (sampling variance) and between-analyses variance (variance due to the imputation of missing data), final results are created that fully reflect all inherent uncertainty in the data while not being forced to omit cases with one or more missing items from the analyses. Therefore, we maximize power without exaggerating the accuracy of our missing data imputations. Moreover, we created an indictor variable for family status (single, two-parent) and included that term in the model along with its interaction with the Locke–Wallace score. In this way we were able to include both types of families into the survival analyses without having to omit subjects from the analyses. The relationship of the same risk factors to future medical complications was investigated via linear regression. Similar imputations to those described above were carried out for these analyses as well. In all cases, final models were selected using the BIC[28] model selection criterion. The BIC improves over the conventional backwards or forwards model selection techniques in that the model need not be nested, and the final model is selected independent of the order in which they are estimated.

Table 1 Sample baseline characteristics (n = 68)

Child	
Mean age at transplant (years)	7.53 (s.d. = 5.31) range = 4 months to 18 years
Sex (%)	
Girls	33.8
Boys	66.2
Diagnosis (%)	
Lymphoblastic leukemia	27.9
Myeloid leukemia	23.5
Lymphoma	8.8
Aplastic anemia	7.3
Neuroblastoma	5.9
Others	26.4
Type of transplant (%)	
Autologous	29.4
Allogeneic	70.6
Mean initial prognosis	2.59 (s.d. = 0.90)
Parents	
Mean age (years)	
Mother (n = 66)	36.59 (s.d. = 6.33)
Father (n = 68)	37.61 (s.d. = 8.29)
Occupational status	
Mother (n = 58)	Median = 36, range = 0 to 71.60
Father (n = 66)	Median = 41, range = 0 to 101.32
Family status (%) (n = 68)	
Intact	80.9
Non-intact	19.1
Mean marital satisfaction	
Mother (n = 60)	102.98 (s.d. = 25.31)
Father (n = 49)	105.24 (s.d. = 24.53)
Mean total family stress	
Mother (n = 67)	2.62 (s.d. = 0.54)
Father (n = 52)	2.56 (s.d. = 0.52)

Results

Sample characteristics

Sixty-eight consecutive pediatric BMT patients were accrued over a 6.5-year period in the principal urban center to offer BMT to children in Quebec, Canada. Characteristics of the sample are summarized in Table 1. The average age was 7.53 years; two-thirds were boys; and 80.9% of the patients lived in two-parent families. The mean for initial prognosis was 2.59 (s.d. = 0.90). As shown in Figure 1,

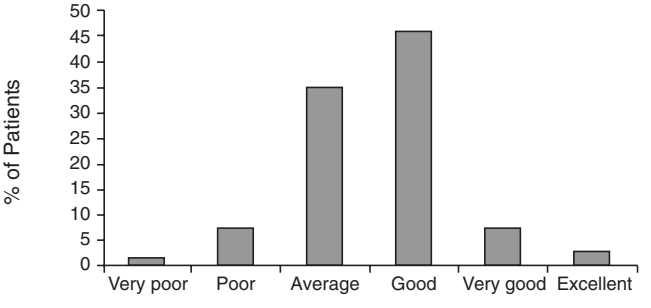

Figure 1 Physicians' ratings of initial prognosis at baseline assessment.

the scores tended towards the middle range, with 80.9% of the patients being scored as average or good prognosis. Forty-eight (70.6%) of the BMTs were allogeneic, with 22 related donors (45.8%) and 26 unrelated donors (54.2%); the balance (ie $n = 20$ or 29.4%) were autologous BMTs. The donors were A, B and molecular DR related and unrelated.

There was a wide range of occupations with mothers and fathers reporting median scores of 36 and 41, respectively. According to Blishen *et al*[29] scores are a composite index of income and education; 42.74 (s.d. = 13.28) represents the mean of 514 occupations classified. Table 1 shows that both parents, on average, reported normal levels of marital satisfaction (100 = average in a nonclinical population, 10 = 1 s.d.; 90 indicates some problems, 80 indicates serious marital problems). Family stress, as indicated by both parents (mothers' mean = 2.62 (s.d. = 0.54); fathers' mean = 2.56 (s.d. = 0.52)), was higher than families with healthy children (based on data provided in Caldwell[21]).

Survival analyses

Thirty of the 68 patients died following BMT. The mean survival time was 1.82 years (s.d. = 1.71; median = 1.19). Table 2 presents the results from the Cox proportional hazards model. The physicians' initial prognostic score was the best predictor of future survival, with each increase of one point in the scale resulting in a relative risk reduction of 0.62 (95% CI = 0.40, 0.97). The confidence intervals for family stress and marital satisfaction as perceived by both mothers and fathers were wide and included the null value of 1. Therefore, this study did not find an effect of family stress or marital satisfaction on survival. Figure 2 shows the results of the survival analysis graphically using initial prognosis as a predictor. The percent of patients alive over the 6.5 years period is shown for those patients with very poor, moderate, good, and very good/excellent prognoses.

Medical complications/causes of death

As shown in Table 3, at 4 months following BMT, 7.4% of the patients had rejected the transplant (three related, two unrelated donors); 32.2% of those with allogeneic BMTs had GVHD. Nurses' global assessment of medical complications ranged from 0 to 10, with an average score of 4.91 (s.d. = 2.53). Causes of death are listed in Table 3. Twelve patients relapsed and 18 patients died of treatment-related events.

Table 2 Cox proportional hazards model of survival

Variable	*Relative risk*	*95% confidence interval*
Initial prognosis	0.62	(0.40, 0.97)
Locke–Wallace – mother (10 point change)	0.91	(0.75, 1.09)
Locke–Wallace – father (10 point change)	0.89	(0.72, 1.10)
Family stress – mother	0.92	(0.62, 1.37)
Family stress – father	0.96	(0.67, 1.36)

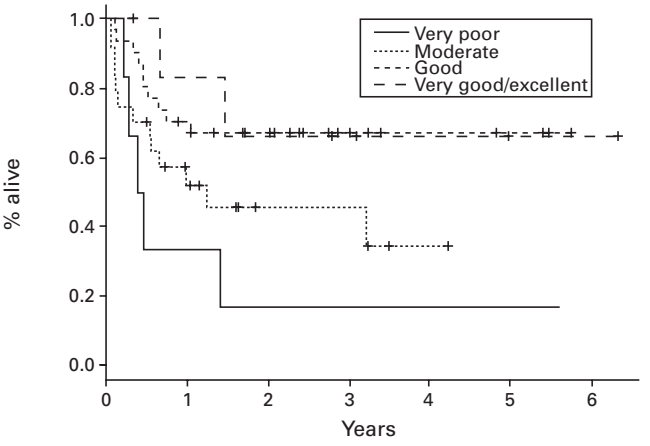

Figure 2 Survival analysis using initial prognosis as a predictor.

Table 3 Medical complications

Mean VAS score	
120 days	4.91 (s.d. = 2.53)
365 days	2.33 (s.d. = 3.14)
Mean Play Performance score	
120 days	80.18 (s.d. = 18.22)
365 days	89.85 (s.d. = 9.31)
GVHD (allogeneic only; %)	
120 days	
Yes	32.2
No	33.9
365 days	
Yes	54.5
No	24.2
Rejection (% yes)	
120 days	17.5
Causes of death (%)	
Relapse ($n = 12$)	40.0
Treatment-related ($n = 18$)	60.0

Sample sizes were 57 at 120 days, 36 at 365 days.
VAS = global score recorded on the Visual Analog Scale; s.d. = standard deviation.

According to the BIC criterion, there were no predictors of medical complications in our data set, in that the best model is simply a constant. Of course, this does not necessarily mean that none of our predictors are potentially important, but rather reflects a lack of power in our study. Eleven subjects died before this variable could be evaluated, meaning that analyses could only be carried out on 57, rather than 68 subjects.

The average Play Performance score average at 120 days was 80.18 (s.d. = 18.22). According to the BIC criterion, there were no important predictors of this measure in our data set. Again, given that data were available for only 57 patients, these results may reflect a lack of power in our study.

Finally, although the study was not designed to be carried out to 1 year, we were able to obtain medical data for 36 survivors. As shown in Table 3, 54.5% of those with allogeneic BMTs had GVHD. A much smaller percentage of patients had infections compared to 4 months following

BMT. Nurses' global assessment of medical complications ranged from 0 to 10, with an average score of 2.33 (s.d. = 3.14). Play Performance score average was 89.85 (s.d. = 9.31).

Discussion

The results of this prospective study do not support the only other investigation published to date including psychosocial variables in a pediatric BMT sample. McConville *et al*[12] reported that the patient's functional impairment (ie biological factor), paternal psychopathology, family dysfunction, and the child's personality (ie psychosocial factors) predicted 'unexpected' deaths. In the present study, initial prognosis, as estimated by the treating physicians, was the only significant predictor of survival.

The finding that initial prognosis was the best predictor of death warrants further discussion. First, as is evident in Figure 1, physicians tended to respond in the middle zone of the VAS; this may reflect the cases they treated or it may indicate an unwillingness to endorse extreme scores. In other words, is the VAS reliable and valid? There is sufficient evidence to indicate that the psychometric properties of VASs are good. For example, Scott and Huskisson[24] found a high correlation between pain severity measured with a VAS and a simple descriptive pain score ($r = 0.90$, $P < 0.01$) when both measures were administered at the same time. Similarly, Rider *et al*[30] compared physician-rated disease activity scores of juvenile idiopathic inflammatory myopathies using VAS and five-point Likert scales. High correlations were found using Spearman rank correlation (0.89) and intraclass correlation coefficients (0.85). Thus, it appears that physicians are skilled in assessing prognosis. Psychosocial findings are not predictors of physical outcomes. Even without considering the confidence interval, the effect of the Locke–Wallace score on survival is small, with a relative risk decrease of only 0.90 for a 10 point decrease in marital satisfaction. However, while not predictors of physical outcome, the data indicate that some families are having difficulty coping with the demands of BMT, and that the children with the worst prognosis are found in the most dysfunctional couples.

The present study failed to replicate McConville *et al*'s findings for medical complications as well. Plausible reasons for the descrepancies between the two studies are as follows. First, McConville *et al*[12] included cases with 'unexpected' complications, whereas we assessed almost all BMT patients in the province of Quebec during the study period. It is likely that this biased their sample by selecting the extreme cases. Second, our data were collected 4 months post BMT whereas theirs was based on recall and chart review. It is likely that raters were influenced by their knowledge of the child's outcome. Third, while our sample size (n = 57–68, depending on the analyses) was typical of studies of the population, we had too little statistical power to rule out effects. While unanticipated, the results of the present study emerge from a strong research design (ie prospective, using standardized measures completed by each parent) indicating that predictors of medical complications remain unknown.

What, if any, are the clinical implications of these findings? First, treating physicians may be interested in knowing that they are skilled in assessing prognosis. As for the psychosocial findings, while not predictors of physical outcomes, the data indicate that some families are having difficulty coping with the demands of BMT as reflected by their reports concerning their marriage and home lives. In a previous study[31] where we compared three groups: (1) families with a child being treated for ALL ($n = 19$); (2) families with a child undergoing BMT ($n = 25$, a subset of the present sample); (3) controls, ie families with a healthy child ($n = 24$), we noted that, on all psychosocial measures the BMT families were fairing the worst. There were significant differences for marital satisfaction with BMT parents scoring the lowest, and control families scoring the highest. Likewise, for family stress, the pattern was the same, with a significant difference between mothers and fathers, with mothers reporting more stress than fathers. Two indices of vulnerability recorded on the Family Well Being Assessment (psychosomatic symptoms and life satisfaction) were the worst for the BMT families. This may reflect the burden of disease history as most BMT patients and their families have gone through numerous phases of illness leading to transplantation as a last resort. Thus, support for the supporters (ie parents) may need to be part of the overall treatment plan, especially for families with problems which predate the BMT.

This study is not without its limitations. While the sample size was large for a pediatric BMT study, we may not have had enough power to investigate many of the effects of interest. In many cases, while the 95% confidence intervals for risk factor effects included the null value of 0, they also did not rule out clinically interesting effects. We felt, however, for the amount of time required to accrue more subjects (with an average of about 10 per year) that it was time to report the results as they are. Second, we did not assess the children undergoing the BMT directly. This was intentional so as not to burden the sick patients. Moreover, given the wide age distribution (4 months to 18 years) uniform psychosocial testing across different age groups was untenable. Nonetheless, perhaps the patient's perception of social support is critical and assessing parent's perceptions may not be capturing the variable of interest. It is recommended that future research select children old enough to respond directly and that the investigation takes place in a number of treatment centers to accrue a sufficient sample size.

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References

1 Pot-Mees CC, Zeitlin H. Psychosocial consequences of bone marrow transplantation in children: a preliminary communication. *J Psychosocial Oncol* 1987; **5**: 73–81.

2 Sormanti M, Dungan S, Rieker PP. Pediatric bone marrow transplantation: psychosocial issues for parents after a child's hospitalization. *J Psychosocial Oncol* 1994; **12**: 23–42.
3 Stuber ML, Nader K, Yasuda P *et al*. Stress responses after pediatric bone marrow transplantation: preliminary results of a prospective longitudinal study. *J Am Acad Child Adolesc Psychiat* 1991; **30**: 952–957.
4 Atkins DM, Patenaude AF. Psychosocial preparation and follow-up for pediatric bone marrow transplant patients. *Am J Orthopsychiat* 1987; **57**: 246–252.
5 Phipps S. Bone marrow transplantation. In: Bearison DJ, Mulhern RK (eds). *Pediatric Psychooncology: Psychological Perspectives on Children with Cancer*. Oxford University Press: New York, 1994, pp 143–170.
6 Dobkin PL, Poirier RM, Bonny Y. Family factors affecting bone marrow transplantation: case report. *Psychother Psychosom* 1995; **64**: 102–108.
7 House JS, Landis KR, Umberson D. Social relationships and health. *Science* 1988; **241**: 540–545.
8 Spiegel D, Bloom JR, Kraemer HC, Gottheil E. Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* 1989; **14**: 888–891.
9 Wallander JL, Varni JW. Social support and adjustment in chronically ill and handicapped children. *Am J Commun Psychol* 1989; **17**: 185–201.
10 Phipps S, Mulhern RK. Family cohesion and expressiveness promote resilience to the stress of pediatric bone marrow transplant: a preliminary report. *Devel Behavioral Pediatr* 1995; **16**: 257–263.
11 Christensen AJ, Weibe JS, Smith TW, Turner CW. Predictors of survival among hemodialysis patients: effects of perceived family support. *Health Psychol* 1994; **13**: 521–525.
12 McConville J, Steinchen-Asch P, Harris R *et al*. Pediatric bone marrow transplants: psychological aspects. *Can J Psychiatr* 1990; **35**: 769–775.
13 Young LD, McQuellon RP, Craven B *et al*. Psychological factors associated with survival following bone marrow transplantation. *Third International Congress of Behavioral Medicine* 1994; 138.
14 Syrjala KL, Chapko MK, Vitaliano PP *et al*. Recovery after allogenic marrow transplantation: prospective study of predictors of long-term physical and psychosocial functioning. *Bone Marrow Transplant* 1993; **11**: 319–327.
15 Fife B, Norton J, Groom G. The family's adaptation to childhood leukemia. *Soc Sci Med* 1987; **24**: 159–168.
16 Neuser J. Personality and survival time after bone marrow transplantation. *J Psychosom Res* 1988; **32**: 451–455.
17 Colon EA, Callies AL, Popkin MK, McGlave PB. Depressed mood and other variables related to bone marrow transplantation survival in acute leukemia. *Psychosom* 1991; **32**: 420–425.
18 Locke HJ, Wallace KM. Short Marital-Adjustment and prediction tests: their reliability and validity. *Marriage Family Living* 1959; **21**: 251–255.
19 Kimmel D, Van Der Veen F. Factors of marital adjustment in Locke's Marital Adjustment Test. *J Marriage Family* 1974; **36**: 57–63.
20 Caldwell SM. Family communication patterns, siblings, and insulin-dependent diabetic children. Vanderbilt University, 1983.
21 Caldwell SM. Measuring family well-being; conceptual model, reliability, validity, and use. In: Waltz CF, Strickland OL (eds). *Measurement of Nursing Outcomes: Measuring Client Outcomes*. Springer Publishing: New York, 1988, pp 396–416.
22 Haccoun RR. Une nouvelle technique de vérification de l'équivalence de mesures psychologiques traduites. *Revue Quebecoise de Psychologie* 1987; **8**: 30–39.
23 Scott J, Huskisson EC. Graphic representation of pain. *Pain* 1976; **2**: 175–184.
24 Scott PJ, Huskisson EC. Measurement of functional capacity with visual analogue scales. *Rheum Rehab* 1977; **16**: 257–259.
25 Streiner DL, Norman GR. *Health Measurement Scales. A Practical Guide to Their Development and Use*. Oxford University Press: New York, 1995, pp 1–230.
26 Lansky SB, List MA, Lansky LL *et al*. The measurement of performance in childhood cancer patients. *Cancer* 1987; **60**: 1651–1656.
27 Rubin D. *Multiple Imputation for Nonresponse in Surveys*. Wiley: New York, 1987.
28 Kass RE, Raftery AE. Bayes factors. *J Am Stat Assoc* 1995; **90**: 773–795.
29 Blishen BR, Carroll WK, Moore C. The 1981 socioeconomic index for occupations in Canada. *Canadian Rev Sociol Anthropol* 1987; **24**: 465–488.
30 Rider LG, Feldman BM, Perez MD *et al*. Development of validated disease activity and damage indices for the juvenile idiopathic inflammatory myopathies. I. Physician, parent and patient global assessments. *Arthritis Rheum* 1997; **40**: 1976–1983.
31 Dobkin PL, Poirier R-M, Robaey P. Comparing treatment impact on families of children with leukemia to those with bone marrow transplants. *Ann Behav Med* 1994; **16** (Suppl.) E105 (Abstr.).