Psychosocial Predictors of Distress in Parents of Children Undergoing Stem Cell or Bone Marrow Transplantation

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Objective To examine psychosocial predictors of distress (mood disturbance, perceived stress, caregiver burden) in parents of children undergoing stem cell or bone marrow transplantation (BMT). Method Measures of prior illness experiences, premorbid child behavior problems, family environment, social support, and parental coping behavior were obtained from the resident parents of 151 children prior to the children’s admission for BMT. Parents subsequently completed assessments of their mood disturbance, perceived stress, and caregiving burden on a weekly basis through week +6 post-BMT, and then monthly through month +6 post-BMT. Results Significant changes were observed in parental distress across the course of BMT. After correcting for demographic and medical factors, several significant predictors of parental distress trajectories were identified, including prior parent and patient illness-related distress, premorbid child internalizing behavior problems, the family relationship dimensions of the family environment, and parental avoidant coping behaviors. Multivariable models were developed using a hierarchical modeling approach. The best-fit model accounted for approximately 50% of the variance in parental global distress. Conclusions Subgroups of parents at higher risk for increased distress during the acute phase of transplant have been identified. These findings can help target parents who may be in greater need of intervention aimed at reducing transplant-related distress.

Key words bone marrow transplant; parental distress; family environment; avoidant coping.

Despite numerous medical advances that have reduced morbidity and improved outcomes in children undergoing stem cell or bone marrow transplantation (BMT), the procedure remains a prolonged, demanding, and highly stressful one for patients and families (Sanders, 1997; Treleaven & Barrett, 1998). While the responses of the child undergoing BMT have been, appropriately, the focus of some research (Barrera, Pringle, Sumbler, & Saunders, 2000; Parsons, Barlow, Levy, Supran, & Kaplan, 1999; Phipps et al., 1995; Phipps, Dunavant, Garvie, Lensing, & Rai, 2002; Rodrigue, Graham-Pole, Kury, Kubar, & Hoffman, 1995; Stuber, Nader, Yasuda, Pynoos, & Cohen, 1991), there has also been considerable focus on the response of parents to the stresses of BMT. A focus on parental response to BMT has been of interest not only because high levels of stress and psychological symptomatology have been reported in parents of children with cancer (Barakat et al., 1997; Brown et al., 1993; Dahlquist et al., 1993; Kazak et al., 1997; Sawyer, Antoniou, Toogood, Rice, & Baghurst, 1993), but also because of research demonstrating a strong relationship between parental mental health and adjustment to illness among those children (Blotcky, Raczynski, Gurwitch, & Smith, 1985; Brown et al., 1993; Dockerty, Williams, McGee, & Skegg, 2000; Dolgin & Phipps, 1995; Sahler et al., 2002). Moreover, there is some evidence suggesting that parental and family factors may be particularly important predictors of child adjustment to the challenges of BMT (Phipps & Mulhern, 1995).
Many studies of parental response to transplant have been limited to assessment of parental functioning prior to, or at the time of, admission to BMT (Dermatis & Lesko, 1990; Kronenberger et al., 1998; Manne et al., 2001; Rodrigue et al., 1996), while some have focused on the post-BMT functioning in parents of BMT survivors (Heiney, Newberg, Meyers, & Bergman, 1994; Sormanti, Dungan, & Reiker, 1994). A rather wide range of outcomes have been reported, from those that indicate high levels of distress and psychopathology (Dermatis & Lesko, 1990; Manne et al., 2001) to those showing very low levels of stress (Streisand, Rodrigue, Houck, Graham-Pole, & Berlant, 2000). Therefore, the findings do not yet allow for the emergence of a coherent picture of parental functioning during BMT.

In one of the first empiric studies on the topic, Dermatis and Lesko (1990) reported significantly elevated levels of psychological distress in more than 50% of parents, assessed after the process of consenting to their child’s transplant. More recently, Manne et al. (2001) conducted psychiatric interviews with mothers at the time of their child’s admission for transplant using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (Gibbon, Spitzer, & Williams, 1996), and found that more than 20% met DSM-IV criteria for diagnosis of either major depression, panic disorder, or generalized anxiety disorder. In contrast, Barrera et al. (2000), using the Beck Depression Inventory (BDI; Beck, 1978), reported low levels of depressive symptoms in mothers at the time of their child’s admission for transplant, with only 8% reaching a clinical cutoff for mild depression. This group did report mildly elevated levels of anxiety at the time of the child’s admission for BMT, but these had resolved to normative levels when reassessed at 6 months posttransplant. Even more striking were the findings of Streisand et al. (2000) that mothers of children undergoing BMT reported significantly less perceived stress and parenting stress than normative samples, both at admission and at day +21 post-BMT.

Some of the discrepancies in the literature may relate to the philosophical approach to assessment taken in the research design, i.e., whether intended primarily to identify “caseness” in a psychopathology model or, alternatively, to evaluate more normative responses in an adjustment or stress and coping model. These differing models also tend to rely on different methods of assessment; structured diagnostic interviews in a pathology approach, and questionnaires assessing levels of symptomatology in general adjustment studies. For example, the Manne et al. (2001) study was designed to ascertain the incidence of specific psychiatric disorders, and the outcome indicates a high level of problems. Other studies designed to assess issues of adjustment, and predictors of such issues, have reported more benign outcomes (Rodrigue et al., 1996; Streisand et al., 2000). While there are advantages and disadvantages to either approach, the apparent transience of the parents’ psychological symptoms raises some question about the utility of psychopathological labels.

Another possible explanation for some discrepancies in the literature may relate to the timing of assessments, since the few studies that have included assessments at more than one time point have shown significant changes over time (Barrera et al., 2000; Manne et al., 2002; Streisand et al., 2000). In the study by Manne et al. (2002), levels of both depressive symptoms and anxiety declined from admission to 6 months posttransplant. Similarly, in the Barrera et al. (2000) study, symptoms of anxiety declined significantly from pre-BMT to 6 months posttransplant, although a measure of depressive symptoms was unchanged. The declines in distress observed at 6 months posttransplant may occur much earlier. In the only study to include repeated assessments during this time period, Streisand et al. (2000) assessed 22 mothers of children undergoing BMT prior to admission, and then obtained stress ratings weekly from admission through week +3. Stress was highest pretransplant and declined significantly from admission through week +3. Although the overall levels of stress were quite low in this study, the authors concluded that the pre-BMT period is the most difficult for parents.

The current study was designed from a coping and adjustment model, which views the BMT procedure as a major stressful event for parents. As such, our focus is on the range of parental responses to this challenge and on the changes in these responses over time, rather than identification of cases meeting diagnostic criteria or the incidence of specific disorders. This approach assumes that a stressor such as BMT will produce a wide distribution of distress responses, from those who cope exceptionally well and show very low levels of distress to those who have difficulty coping and show higher levels of distress. This framework, which utilizes all of the normal variance of parental responses, also lends itself more readily to identifying predictors of distress and those factors that are associated with more adaptive or maladaptive outcomes.

To date, there have been very few factors identified that are associated with parental adjustment to the stresses of BMT. Kronenberger et al. (1998) found that
avoidant and disengagement forms of coping were associated with maternal depression at the time of admission for BMT, but other personality, family environment, or social variables were not. Manne et al. (2002) found that maternal symptoms of anxiety and depression measured at the time of admission for transplant were associated with symptoms of posttraumatic stress disorder (PTSD) at 6 months post-BMT. They also found that mothers who perceived more criticism from spouses or other family members at admission for BMT reported higher levels of PTSD symptoms at 6 months post-BMT. Aside from these isolated findings, no other significant correlates of parental adjustment response have been identified. The major impediment to this research has been sample-size considerations. Most prior studies have involved samples too small to reliably examine these associations.

The present study was designed to advance our understanding of parental response to BMT in several ways. It utilizes a prospective, longitudinal design, with multiple repeated measures to examine changes in parental distress across the acute phase of BMT, from admission through 6 months post-BMT. This approach allows for a depiction of trajectories of parental stress response across the BMT process, as has been done with acute health-related quality of life outcomes for the child patient (Phipps, Dunavant, Garvie, et al., 2002; Phipps, Dunavant, Lensing, & Rai, 2002). As stated above, it focuses on issues of adjustment rather than pathology, assuming a normative range of adjustment responses to the stresses of BMT. Therefore, parental response is characterized with a triad of measures assessing mood disturbance, perceived stress, and caregiver burden, which compose a comprehensive picture of adjustment. Multiple factors were examined as predictors of parental stress response. This report focuses on psychosocial predictors of parental response, including measures assessing the prior medical experiences of both parent and child, child premorbid behavioral adjustment, family environment, social support available to the parent, and parental coping.

Although this study was designed primarily to develop models, several a priori predictions were also examined. Specifically, we predicted that (1) parents who report greater distress in coping with their child’s prior illness and treatment experiences would demonstrate higher distress trajectories across the BMT process; (2) parental distress would be associated with the child’s premorbid internalizing behavior problems but not externalizing behavior problems, because the intensity of transplant tends to reduce externalizing behaviors (Phipps et al., 1995); (3) parental distress trajectories would be lower in the context of greater perceived family support, that is, in families reporting higher levels of cohesion and expressiveness and lower levels of conflict; (4) parental distress would not be strongly related to measures of instrumental social support, because outside of the family, most parents are separated from their prior sources of support during the acute phase of BMT; and (5) parental distress would not be significantly related to parental use of problem-focused coping strategies, given the largely uncontrollable nature of BMT-related stressors, but would be associated with greater use of avoidant coping.

Methods
Participants
Parents of children scheduled to undergo BMT at a large pediatric cancer program were recruited for participation over a 42-month period. Eligible parents were English speaking and self-identified as being a primary caregiver who would be available throughout the hospitalization period. Of 174 families who were approached, 168 (96.6%) agreed to participate. Our consecutive sampling and this high agreement ensured that our study population was representative of the population undergoing transplant at our institution. A total of 17 patients were unevaluable for a variety of reasons, including a failure to be admitted for transplant, early morbidity or mortality that precluded participation, or early noncompliance with study procedures. The data presented comprise a sample of 151 parents who provided baseline data and at least one additional in-hospital observation.

Participation was based on the concept of the “resident parent.” For each child scheduled for transplant, one parent was identified who was to remain with the child throughout most of the hospitalization and would be used consistently as informant. If both parents were to be equally present, they were given the choice as to which would participate based on their preference/convenience. Investigators indicated no preference as to who this should be, although we anticipated that the majority would be mothers. Using this approach, better than 90% of the resident parents were biological mothers, with only 6% being fathers and the remainder “others” (stepparent, grandparent) (Table I). The very small sample of nonmothers among our resident parents precluded meaningful separate analysis and led us to consider simply reporting the data from mothers only. However, because our intent was to obtain an unbiased sample of primary caregivers regardless of gender, and
because the fathers and “others” had participated in good faith, we felt it was appropriate and ethically justified to include these data. Moreover, analyses of results from the entire sample and from the sample limited to mothers were comparable. Thus, we chose to report here results from the entire sample.

Demographic and medical variables are presented in Table I. Patients ranged in age from less than 1 year to 20 years, with a mean age of 8.9 years, and there was a slight excess of male patients. There was a wide distribution of patients across socioeconomic strata as determined by the Hollingshead four-factor index (Hollingshead, 1975). The majority of patients were transplanted for leukemia, with a smaller number of patients with solid tumors or nonmalignant disorders. Approximately two thirds of the patients underwent allogeneic BMT, with the majority of those involving unrelated donors, and the remaining third received autologous transplants. Multiple BMT treatment protocols are represented using different conditioning regimens and posttransplant prophylaxis. A total of 57% of patients received total body irradiation as part of their conditioning regimen.

**Measures**

**Parental Distress**

Measures for assessing parental functioning across the acute phase of transplant were chosen based on three factors. First, we wished to depict the magnitude of symptoms of distress rather than specific diagnostic cut-offs, since we assumed that the incidence of psychopathology would be relatively low but that there would be considerable variability in levels of distress both between parents and across time. Second, since we planned to obtain measurements repeatedly, we were interested in brief measures that could be completed quickly and easily to reduce participant burden. Finally, we felt that the distress of parents in this setting would reflect a complex and dynamic composite of factors that would be difficult to capture in a single measure. Thus, we chose a triad of brief instruments assessing mood disturbance, perceived stress, and magnitude of caregiver burden, as follows:

1. **Profile of Mood States (POMS) Short Form.** Mood disturbance was assessed with a short form of the POMS (McNair, Lorr, & Droppleman, 1971), a widely used self-report instrument whose reliability and validity is firmly established. Several short forms have been shown to correlate highly with the total mood disturbance score of the full measure (Cella et al., 1987; Shacham, 1983). A 15-item form was adapted for this study, designed to best depict the range of negative mood states likely for parents in the BMT setting. Across the 13 observation points in the current study, the median internal reliability (Cronbach’s α) of the short form was .92, and in a small subset of observations (n = 21), the correlation between the short-form and full-scale total mood disturbance was \( r = .93 \).

2. **Perceived Stress Scale (PSS).** The PSS (Cohen, Kamarck, & Mermelstein, 1983) is a 14-item self-report instrument that measures the degree to which situations in one’s life are perceived to be unpredictable, uncontrollable, and overwhelming. It is a unidimensional scale that has demonstrated excellent reliability and validity. Median internal reliability (α) across the 13 observation points in this study was .91.

<table>
<thead>
<tr>
<th>Table I. Demographic and Medical Breakdown of Study Participants</th>
<th>n</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Resident parent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>139</td>
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</tr>
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<td>Father</td>
<td>9</td>
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</tr>
<tr>
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<tr>
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<td>6–12 years</td>
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</tr>
<tr>
<td>&gt;12 years</td>
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<tr>
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<tr>
<td>AML</td>
<td>40</td>
<td>26.5</td>
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<tr>
<td>Other leukemia</td>
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<tr>
<td>Neuroblastoma</td>
<td>16</td>
<td>10.6</td>
</tr>
<tr>
<td>Other solid tumor</td>
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<td>10.6</td>
</tr>
<tr>
<td>Nonmalignancy</td>
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<td>17.2</td>
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<tr>
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<tr>
<td>Type of donor</td>
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<tr>
<td>MSD</td>
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<tr>
<td>MUD</td>
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<tr>
<td>Mismatched</td>
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<td>7.3</td>
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<tr>
<td>Autologous</td>
<td>50</td>
<td>33.1</td>
</tr>
</tbody>
</table>

SES = socioeconomic status; ALL = acute lymphoblastic leukemia; AML = acute myelogenous leukemia; HD = Hodgkin’s disease; NHL = non-Hodgkin’s lymphoma; MSD = matched sibling donor; MUD = matched unrelated donor.
3. Caregiver Burden Scale (CBS). This 14-item, unidimensional instrument measures the burden a parent experiences in caring for the patient. It was adapted from a measure designed for use with families providing care to elderly relatives suffering from Alzheimer’s disease or other dementia (Poulshock & Deimling, 1984) but is applicable to any situation in which a family member is caring for a chronically ill loved one. The original instrument included measures of cognitive impairment, burden, and impact, and items from the latter two areas were adapted for more generic use. In the current study, median internal reliability (α) across the 13 observation points was .85.

Each of this triad of measures provides a unique outcome, but there is also considerable overlap among them. The median intercorrelations of the measures across the 13 observation points (representing over 1,100 observations) were as follows: POMS-PSS, r = .78; POMS-CBS, r = .62; PSS-CBS, r = .66. Given this level of common variance, we also took a simple sum of the scores on the three instruments, which we labeled global distress.

Predictive Measures
A number of baseline psychosocial predictor measures were obtained by parent report prior to admission for BMT. These included:

Prior Illness Experiences Scale (PIES). This is a 17-item parent-report scale developed for this study. It assesses previous parent and child experiences with cancer therapy and inpatient hospitalization. Each item is answered on a 5-point Likert scale. Three subscales were derived by factor analysis: child distress (6 items, α = .78; example: “In the past month, how often has your child complained of illness/treatment-related pain or discomfort?”), child cooperation/compliance (8 items, α = .72; example: “In the past month, how often have you had difficulties getting your child to take oral medications or do mouth care?”), and parental distress (3 items, α = .81; example: “In the past month, how often have you felt anxious or worried about your child’s illness?”).

Child Behavior Checklist (CBCL). This widely used, well-validated inventory (Achenbach & Edelbrock, 1983) is designed to measure child social competence and behavior problems as reported by parents. The CBCL includes 40 social competence items and 118 behavior problem items. A wealth of normative data are available, and separate T scores are provided according to age and gender. The CBCL provides scores in the two broad domains of internalizing and externalizing behavior problems, as well as several specific subscales within each domain. Reliability is well documented, with Cronbach’s α in the .80–.90 range for the broad domains. Family Environment Scale (FES). This widely used measure of family environment (Moos & Moos, 1986) consists of 90 true/false items. The FES provides scores on 10 family environment dimension subscales, although the first 3 subscales—cohesion, expressiveness, and conflict, which compose the Family Relationship Index (FRI)—have been the most widely studied and were thought to be the most salient here. Analyses were limited to these 3 subscales and the composite FRI (summing cohesion and expressiveness, and subtracting conflict). Internal reliability estimates for the subscales range from .61 to .78. Test-retest reliabilities from 2-month to 12-month intervals range from .52 to .91.

Inventory for Socially Supportive Behaviors (ISSB). This scale measures the frequency with which people are the recipients of particular supportive actions (Barrera, Sandler, & Ramsay, 1981). A time frame of the past month is used, and respondents rate how often they have received specific supports (e.g., were provided transportation, were helped to understand the situation they were in) on a 5-point scale from not at all to almost daily. Internal reliability is reported at .94 and 2-day test-retest reliability at .88.

Ways of Coping Questionnaire (WOC). This self-report adult coping measure (Folkman & Lazarus, 1988) has been widely utilized with a number of different adult populations. It contains 66 items in eight subscales, labeled confrontive coping, distancing, self-controlling, seeking social support, accepting responsibility, escape-avoidance, planful problem solving, and positive reappraisal. Internal consistencies for the subscales range from .61 to .79. These measures have been shown to predict emotional distress in adult cancer patients (Dunkel-Schetter, Feinstein, Taylor, & Falke, 1992). For this study, parents were asked to consider the most stressful aspect of their child’s illness thus far and to indicate their coping behaviors accordingly.

Procedure
Patients scheduled to undergo BMT and their parents were identified and recruited consecutively for participation 2 to 3 weeks prior to their admission date. At that time, a resident parent was identified. After providing informed consent according to institutional guidelines, resident parents completed the battery of predictive measures. Following hospital admission, the parental distress measures were administered in a repeated
manner to assess stress responses across the acute phase of BMT. Parental distress data were obtained only from the resident parent, and there was no substitution of respondents. If the resident parent was unavailable for a specific observation, that observation was considered missing. Measures were completed on a weekly basis from time of hospitalization (week −1) to week +6. Weekly data collection was timed to occur on a multiple of the transplant day (i.e., week +1 = day +7; week +2 = day +14; etc.). Data collection then continued on a monthly basis through month +6 for a total of 13 observations throughout the entire assessment period (weeks −1 through +6, and months +2 through +6).

Every effort was made to gather data on the prescribed days as scheduled. However, at times this was not possible. If data were missed on the prescribed day, attempts were made to collect it on the following day. If it was not possible to gather the data by the following day, the data were considered missing for that specified time point. Missing observations were encountered for a variety of reasons, including unavailability of the resident parent, simple noncompliance, and the high level of illness and ultimately death of the child patient. Six patients had died by week +6, and a total of 35 expired through month 6 (22.9%). Most participants had occasional missing observations distributed intermittently through the 6-month study period. Only 11 participants completed all possible observations. The median number of completed observations per participant was 8. The number of observations obtained at each time point is presented in Table II. Through week +3, during which time most patients were in hospital, 647 out of 755 possible observations were obtained (86%). After week +6, the frequency of missing data was increased, due to increasing logistical difficulties as patients moved to an outpatient setting. It should be noted, however, that the missing data indicate only a missed assessment point and not attrition from the study. Across the entire study period a total of 1,194 observations were obtained from parents.

Distress variables were examined using an unbalanced mixed-model repeated-measures analysis. A random subject effect and an autoregressive correlation structure were used to account for correlation between measurements taken from the same subject. Because of the greater frequency of missing data during the final assessments at weeks +16, +20, and +24, these final observations were averaged, with the final measurement point labeled weeks 16–24. Data were analyzed using the MIXED procedure in SAS, with the Satterthwaite option for computing degrees of freedom (SAS Institute, Inc., 1999). Missing and mistimed data were handled in a manner consistent with prior longitudinal studies of health-related quality of life in oncology settings (Fairclough, Peterson, Cella, & Bonomi, 1998; Qian et al., 2000). First, a simple model was examined assessing change over time, with time point (i.e., weeks pre- or post-BMT) treated as a categorical variable. Next, demographic and medical variables (age, gender, socioeconomic status (SES), type of transplant, diagnosis) were each singly included in the model along with time point (these analyses will be reported elsewhere). Then, for the purposes of this report, a series of repeated-measures analyses were run, each with a single psychosocial predictor and after adjusting for all demographic and medical variables, which are included in the model as covariates. The predictors were initially modeled as continuous variables, including both a linear and a quadratic term. Subsequently, to facilitate interpretation of the findings and a graphical depiction of the results, selected continuous predictor variables were made discrete using a tertile split to create a three-level variable. The models included only main effects for time point and the independent variables of interest and did not include interactions.

### Results
Significant changes in parental distress over time were observed on the POMS, $F(10, 668) = 2.0, p < .05$, and the CBS, $F(10, 602) = 4.3, p < .0001$, but did not reach significance on the PSS. Significant variation over time was also observed on the omnibus variable of global distress, $F(10, 624) = 2.4, p < .01$. The pattern of change was similar across all measures, indicating a relatively high level of parental distress at admission, which increased slightly, peaking at approximately week +2. Distress levels fluctuated but remained high through week +6 and then began a steady decline that continued.
through week +24. Given the overlap of measures and similar pattern of responses obtained with each, subsequent analyses of psychosocial predictors focused on global distress as the outcome.

**Predictors of Parental Distress Trajectories**

The effect of each predictor, modeled independently as a continuous variable after adjusting for demographic/medical variables (i.e., age group, gender, SES, BMT type), was examined for each of the parental distress outcomes as well as for the omnibus global distress measure. The results for global distress are presented in Table III. Linear and quadratic terms were investigated for each predictor variable. However, the quadratic term was significant in only one case, so that the results are presented for the models with only a linear term. A number of significant predictors were identified from the measures of prior illness experiences, premorbid child adjustment, family environment, and parental coping. To facilitate interpretation of these findings, predictors that were significant when modeled as continuous variables were transformed into discrete groups using a tertile split. These results are presented graphically for selected predictors that demonstrated the largest effects.

**Prior Illness Experiences**

Using the PIES measure created for this study, parental ratings of the child’s prior level of distress associated with medical treatment was predictive of subsequent parental distress, \( F(1, 127) = 4.84, p = .030 \). The group of parents whose children experienced the lowest levels of medically related distress prior to transplant reported lower levels of distress throughout the course of transplant, differing from both the high, \( t(125) = 2.2, p = .032 \), and intermediate groups, \( t(124) = 3.5, p < .001 \). Likewise, the PIES cooperation/compliance measure was also associated with parental global distress, \( F(1, 130) = 8.35, p = .004 \). Not surprisingly, the PIES subscale showing the largest effect on parental distress outcomes was parents’ reports of their own prior distress, \( F(1, 128) = 35.9, p < .0001 \). The group of parents reporting the highest levels of prior distress associated with their child’s illness differed significantly from both the intermediate, \( t(127) = 3.1, p = .002 \), and low distress groups, \( t(127) = 5.2, p < .001 \). This result is depicted graphically in Figure 1.

**Child Premorbid Behavior Problems**

Child premorbid internalizing behavior problems, as measured by the CBCL, were significantly predictive of all parental distress outcomes. For global distress, \( F(1, 98) = 5.86, p = .0174 \). Post-hoc comparisons indicated that parents whose children had lower internalizing scores experienced the lowest distress and differed significantly from both the intermediate, \( t(95) = 3.1, p = .002 \), and high internalizing groups, \( t(94) = 2.3, p = .025 \). In light of this positive finding, we further examined the

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<th>Variable</th>
<th>( N )</th>
<th>( \text{Estimate} )</th>
<th>( \text{Standard Error} )</th>
<th>( F )</th>
<th>( p )</th>
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<td>14.2</td>
<td>.0002</td>
</tr>
<tr>
<td>WOC–confrontive coping</td>
<td>135</td>
<td>2.067</td>
<td>3.055</td>
<td>0.46</td>
<td>.4998</td>
</tr>
<tr>
<td>WOC-distancing</td>
<td>135</td>
<td>5.854</td>
<td>3.494</td>
<td>2.82</td>
<td>.0963</td>
</tr>
<tr>
<td>WOC–sell-controlling</td>
<td>135</td>
<td>5.917</td>
<td>3.357</td>
<td>3.10</td>
<td>.0804</td>
</tr>
<tr>
<td>WOC–seek social support</td>
<td>135</td>
<td>2.567</td>
<td>2.884</td>
<td>0.79</td>
<td>.3752</td>
</tr>
<tr>
<td>WOC–accept responsibility</td>
<td>135</td>
<td>4.436</td>
<td>3.002</td>
<td>2.19</td>
<td>.1402</td>
</tr>
<tr>
<td>WOC–escape-avoidance</td>
<td>135</td>
<td>19.476</td>
<td>3.225</td>
<td>36.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>WOC–planful problem solving</td>
<td>135</td>
<td>−0.768</td>
<td>2.963</td>
<td>0.07</td>
<td>.7959</td>
</tr>
<tr>
<td>WOC–positive reappraisal</td>
<td>135</td>
<td>1.234</td>
<td>2.847</td>
<td>0.18</td>
<td>.6654</td>
</tr>
<tr>
<td>ISSB</td>
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<td>−0.141</td>
<td>0.083</td>
<td>2.89</td>
<td>.0922</td>
</tr>
</tbody>
</table>

PIES = Prior Illness Experiences Scale; CBCL = Child Behavior Checklist; FES = Family Environment Scale; FRI = Family Relationship Index; WOC = Ways of Coping questionnaire; ISSB = Inventory of Socially Supportive Behaviors.
internalizing subscales of withdrawn, anxious/depressed, and somatic symptoms. None of these subscales individually were significantly predictive of parental distress. However, the predictive power of such analyses is limited because of the curtailed distribution of the CBCL subscales, which have a basal level of 50 on the calculated T scores. In contrast to the findings on internalizing problems, and as predicted, parental ratings of child externalizing behavior problems were generally not predictive of subsequent parental distress. The exception to this was parental burden on the CBS, where a marginally significant result was obtained, $F(1, 95) = 4.37, p = .0396$.

**Family Environment**

Across all parental distress measures, the FES domains of cohesion and conflict were strongly predictive of outcome. For global distress, the effect for cohesion was $F(1, 127) = 12.0, p = .0007$, and for conflict $F(1, 129) = 12.7, p = .0005$. In contrast, the FES domain of expressiveness did not significantly predict any of the parental distress outcomes. To simplify the interpretation of family environment effects, these variables were combined into the FRI by adding the cohesion and expressiveness scores to the inverse of the conflict score. This FRI variable was also predictive of all parental distress outcomes. For global distress, $F(1, 127) = 14.2, p = .0002$. Post-hoc analysis of the grouped variable indicates that all three groups differed significantly from each other. This result is depicted graphically in Figure 2. Parents who reported the most supportive family environment reported the lowest levels of distress throughout the transplant process.

**Social Support**

Social support available to the resident parent, as measured by the ISSB, was not significantly related to any parental distress outcome.

**Parental Coping**

Contrary to prediction, more active, problem-focused coping was not associated with lower parental distress. None of the WOC subscales of confrontive coping, planful problem solving, or seeking social support were significantly related to any parental distress outcomes. There was clear evidence to support the prediction that parental use of avoidant coping strategies would be associated with greater distress. The WOC escape-avoidance subscale was strongly predictive of all parental distress outcomes. For global distress, $F(1, 127) = 36.5, p < .0001$. Post-hoc analysis again indicated that all three coping groups differed significantly from each other. This is illustrated in Figure 3. In addition, the WOC distancing subscale was significantly predictive of parental burden on the CBS, $F(1, 127) = 4.1, p = .0451$. Similarly, the WOC subscale of self-controlling behaviors, which includes items reflecting avoidance of expressions of distress, was also significantly predictive of parental distress on the POMS, $F(1, 127) = 4.8, p = .0312$. 

![Figure 1. Trajectories of global parental distress as a function of the Prior Illness Experiences Scale (PIES) parental distress subscale measured prior to admission for stem cell or bone marrow transplant (BMT). Parents reporting greater distress related to their child’s prior illness experiences also report greater distress across the acute phase of BMT.](image-url)
Multivariable Models

Multivariable models were explored using the same unbalanced mixed-model repeated-measures analysis, with random person effect and autoregressive correlation structure, and global distress as the dependent outcome. Adopting a strategy similar to that of a hierarchical multiple regression, variables were entered into the model according to three levels of hierarchy: (1) demographic/medical (age group, gender, SES, and BMT type), (2) premorbid adjustment (CBCL and PIES), and (3) family and parental coping (FES, ISSB, and WOC). Variables that were significant (at a conservative level of $p < .10$) from models investigating them individually were included in the model first. Then the model was

Figure 2. Trajectories of global parental distress as a function of the Family Relationship Index (FRI) of the Family Environment Scale (FES). Higher scores reflect a more supportive family environment (higher cohesion and expressiveness, lower conflict). Parents whose families are perceived as more supportive report lower distress across the acute phase of stem cell or bone marrow transplant (BMT).

Figure 3. Trajectories of global parental distress as a function of escape-avoidant coping on the Ways of Coping questionnaire (WOC). Parents who reported greater use of avoidant coping prior to admission experience greater distress throughout the acute phase of stem cell or bone marrow transplant (BMT).
checked by reducing one variable at a time. Akaike's information criterion (Bozdogan, 1987) was used to determine the best model from competing models. Additionally, prior nonsignificant variables were tried in the resulting model one at a time (none were ultimately included). This was done at each level. Since the CBCL was not administered to patients younger than 2 years, the sample size for this variable was considerably reduced. Thus two best models were constructed, with and without the CBCL variables. These two best models including all hierarchical levels are presented in Table IV.

The two multivariable models were very similar, with the only difference being the inclusion of the CBCL internalizing score. For the non-CBCL model, the best model at level 1 produced an $R^2$ of .11. With inclusion of level-2 variables, the $R^2$ increased to .32, and after level 3, it reached .43. For the smaller group that completed the CBCL, the $R^2$ for the final model was .50. The variables included in both best models included time (weeks), age group, SES, PIES parental distress, FRI, and WOC escape-avoidance. Because these models are not least-squares, the resulting $R^2$ values are general ones for the maximum likelihood setting (Nagelkerke, 1991).

### Discussion

The present findings provide support for most of the primary study hypotheses while identifying several psychosocial variables significantly associated with parental adjustment to the demands of BMT, with relationships in the predicted direction. The significant determinants of parental distress include prior parent and patient experiences of distress associated with the child's illness, the child's premorbid history of internalizing behavior problems, the support dimensions of the family environment, and a parental tendency toward avoidant coping behaviors. Factors that were not found to be significantly associated with parental distress outcomes include the premorbid level of instrumental social support available to the parent, and the parents' use of problem-focused coping behaviors.

One of the strongest predictors of parental distress outcomes was the PIES, a brief measure created for this study. The PIES was designed to very specifically survey past medical experiences likely to be relevant to a BMT population. Its predictive power speaks to the ecological validity of the measure and reflects the oft-repeated adage that the best predictor of future behavior is past behavior. Not surprisingly, prior parental distress demonstrated the clearest relationship to parental BMT-related distress outcomes, but prior child distress and prior problems with cooperation were also significant predictors. Perhaps the fundamental implication of these findings for clinicians is that pretransplant screening is best focused more proximally on past illness and treatment-related issues than on more global aspects of child and parent functioning. Particularly in situations where time may be limited, a circumscribed focus on past coping with medical demands may be sufficient and provide the most salient information.

As predicted, the child's pretransplant history of internalizing behavior problems as measured by the CBCL was predictive of parental distress. This finding is undoubtedly impacted by a true relationship between children's anxious/depressed, dysphoric, or withdrawn behavioral tendencies and child maladjustment to transplant, which in turn increases parental stress. However, it is possible that these findings are also reflective of the strong influence of somatic symptoms on the internalizing score, and thus reveal a different phenomenon: the impact of the physical state of the child prior to admission; that is, parents of sicker children experience greater distress. Although none of the internalizing subscales were significantly predictive of parental distress, the somatic symptom subscale showed the strongest trend toward significance and appears to account for much of the observed effect. The CBCL and comparable measures have been rightly criticized as potentially biased or misleading when used with chronically ill populations, and the undue influence of somatic symptoms is identified as one of the primary factors for this (Perrin, Stein, & Drotar, 1991). Ironically, the contribution of somatic complaints, which in this instance may reflect medical
status rather than a true internalizing syndrome, may add to the predictive strength of the scale in this setting.

In contrast, the externalizing scale of the CBCL was unrelated to most parental distress outcomes, with the exception of a marginally significant relation to caregiver burden. This was predicted based on previous findings suggesting that the demands and burden of the acute phase of BMT serve to generally diminish externalizing behaviors (Phipps et al., 1995). Children are often too sick to act out a great deal in this setting, even those with a premorbid tendency to do so. Parents of children with a history of externalizing behaviors may even get a respite during this period. Adherence difficulties, which might be considered a component of externalizing behavior, are a common problem in this setting that would increase the demands on parents (Phipps & Barclay, 1996; Phipps & Decuir-Whalley, 1990). This effect may be seen in the significant relationship between CBCL externalizing behaviors and the CBS. However, the CBCL does not appear to have the same sensitivity as the PIES cooperation scale. The relationship identified between the PIES cooperation scale and parental burden reflects the specificity of that measure, in contrast to the more general nature of the CBCL, which may be less relevant to this medical setting (Perrin et al., 1991).

The significance of the family environment as a determinant of parental distress during BMT was confirmed. The importance of the family environment to the adjustment of parents of children with serious illness has been long recognized, and the present findings are consistent with this line of research (e.g., Kronenberger & Thompson, 1992; Noll et al., 1994). However, given that the patient and resident parent are often separated from the remainder of the nuclear family during much of the acute period of BMT (Phipps, 1994; Phipps & Barclay, 1996), the magnitude of the influence of the premorbid family environment on parental response during this period might be somewhat surprising. Perhaps the unique demands of BMT are so intensely stressful for the family that parental distress is a direct reflection of this. This effect would be magnified for parents coming from a less supportive or more conflicted family. The clinical implications of this are not fully clear, as intervening at the level of the family is not always feasible in the transplant setting. At minimum, parents from less supportive family systems could be identified as high risk and as candidates for increased levels of monitoring and support during the acute phase of BMT.

Parental distress was not related to measures of instrumental social support despite sufficient power to detect such effects. This was predicted and is consistent with prior studies demonstrating both the importance of family factors and the absence of an effect of social support for parents of children with serious or chronic illness (Kronenberger & Thompson, 1992; Noll et al., 1994). The nominal effect of social support may be even more mitigated in the setting of BMT, given the typical separation of parents from many of their usual systems of support. This finding may also reflect our choice of social support measure, with a focus on instrumental support that may be less relevant in this setting. Given the largely uncontrollable nature of many of the stressors faced by parents of children undergoing BMT, there may be less value in instrumental support and a greater need for more purely emotional forms of support, which may be difficult to maintain in the face of medically enforced isolation. The medical staff often become the primary support system in these circumstances. Substituting a measure of perceived support from hospital staff in lieu of a generic social support measure might represent a fruitful approach for future research.

Recent studies have called into question the checklist approach to assessment of coping and have suggested that the most commonly used distinctions in such measures (e.g., problem-focused vs. emotion-focused coping, approach vs. avoidant coping, cognitive vs. behavioral coping) should no longer be used at all (cf. Skinner, Edge, Altman, & Sherwood, 2003). However, avoidant coping, as measured by the WOC escape-avoidance subscale, was among the strongest predictors of parental distress in this setting. The present finding that higher distress was associated with greater use of avoidant coping is consistent with numerous prior reports in both adults (Cohen, 2002; McCaul et al., 1999; Miller, Manne, Taylor, Keates, & Dougherty, 1996) and children (Compas, Worsham, Ey, & Howell, 1996; Steele, Forchard, & Armistead, 1997). However, these studies generally report only a concurrent measurement of coping and distress, which does not allow for any inference regarding the direction of causality. Although it has typically been assumed that avoidant coping is less adaptive and will lead to higher levels of distress, it could reasonably be argued that higher levels of distress lead individuals to adopt more avoidant coping strategies. Longitudinal designs such as the present study provide insight into the relationship of coping with distress as it proceeds over time. When an earlier measure of coping behavior is associated with later measures of distress, there is at least a reasonable suggestion of causality. In the current study, parental coping measured prior to admission for transplant was associated with multiple measures of distress obtained repeatedly
throughout the transplant process, indicating that avoidant coping leads to increased distress (or to less reduction in distress) and that individuals who use more avoidant coping are likely to continue to experience greater distress in the future. This is one of only a few studies to show such a finding (Dew et al., 1996; Pakenham, 1999), and to our knowledge the first in the setting of parental coping with a child’s illness.

Findings in the literature regarding the relationship between active, problem-focused coping and distress outcomes have been more mixed, with some showing an inverse relationship, but perhaps an equal number showing null findings (Epping-Jordan et al., 1999; Pakenham et al., 1999). In the setting of BMT, where there is a high degree of uncontrollability for parents, it is perhaps not surprising that problem-focused coping was not found to be a significant predictor of parental distress. Alternatively, the null findings regarding problem-focused coping in the present study may be a reflection of the shortcomings of the checklist approach to coping assessment and to the inadequacy of common categorical distinctions such as problem- vs. emotion-focused coping (Coyne & Gottlieb, 1996; Skinner et al., 2003).

There are several methodological aspects of the study that deserve comment. First is the specification of the resident parent as informant. Given that the more available parent in the transplant setting tends to be the mother in the majority of cases, it is more common to focus only on mothers in the research design (e.g., Manne et al., 2001, 2002; Streisand et al., 2000). This allows for more straightforward and perhaps “cleaner” analyses but excludes fathers from participation and eliminates the minority of cases in which the mother is not available. Alternatively, one can attempt to obtain data from all available parents, but this adds undue analytic complexity and, in a repeated-measures design, can significantly increase the amount of missing data. Our approach was a compromise that is not without problems but simplifies analysis with a single informant for each patient and allows the parent who is most available and most invested in the study to participate, which also helps to reduce missing data. Because of well-documented problems with cross-informant consistency, we chose to not substitute if the resident parent was unavailable. Our earlier pilot work suggested that we might obtain 10–15% fathers and another 5% others, but our final sample revealed a much smaller percentage of nonmothers, such that it was not practical to look at this group separately. If this pattern of participants were to remain consistent in future studies, limiting such studies to mothers might be a reasonable approach. However, excluding fathers from child/pediatric studies has been an ongoing concern, may be considered ethically questionable, and is now likely to be deemed inappropriate by federal funding agencies.

Another methodological issue involves our approach to assessment of parental outcomes from a coping and adjustment model, rather than a psychopathology model. A potential drawback of this approach is a more limited perspective on the magnitude of the problem, in terms of the number of cases, or prevalence of psychiatric illness. This decision was based in part on our expectation that the incidence of frank pathology would be relatively low and that parental function during the acute phase of transplant would be in a continuous state of change. This influenced our repeated-measures design and choice of weekly assessments. In addition, in the absence of a reasonable control group (to be discussed further below), definitive inference about the incremental magnitude of pathology is not possible. Use of an adjustment model also influenced our choice of outcome measures, utilizing a triad of brief surveys that encompass the domains of mood disturbance, perceived stress, and perceived caregiver burden, to obtain a more global picture of parental distress. In some respects, this battery is an attempt to reflect the quality of life for parents whose children are in a demanding medical circumstance. This contrasts with a pathology approach, though they need not be mutually exclusive, and future study designs could include both.

Our data-analytic strategy, examining and reporting the main effects of each predictor variable separately in isolation from other psychosocial predictors first, before proceeding to multivariable modeling, might be viewed as redundant, and perhaps in reversed direction. However, we felt that this approach would allow for better clarity, illustration, and ease of interpretation regarding the direction of effects of the predictor variables of interest. Moreover, since our approach was to include in the multivariable models only those predictors that showed significant effects when modeled individually, the order of presentation reflects our statistical approach.

Missing outcome data represent another limitation to the current study. With a longitudinal, repeated-measures design, some degree of missing data is inevitable. Our data analysis is based on the assumption (which cannot be proven) that data are missing at random. However, our statistical approach has been used previously in similar contexts and has been found to be fairly robust (Fairclough et al., 1998; Qian et al., 2000). Another limitation is that the data set, although large, was generated from a single institution. Thus, the
generalizability of the findings is uncertain. This would best be addressed via multisite studies, which is our planned approach in the future. Finally, the study is limited by the absence of a control group. In our repeated-measures design, participants served as their own control, but the absence of a control group limited conclusions about the comparative value of the outcomes obtained. Although normative data are available for comparison on some outcomes, there is no control for the effect of the repeated measures and whether changes over time might reflect some degree of reactance, or “drift,” from repeated use. Few studies have utilized control groups in this setting, and it is not clear who would represent an appropriate control. Parents of children with other illnesses, such as those with leukemia not undergoing transplant, are a common comparison group, though not necessarily the most appropriate. Given that our primary objectives were not comparative, but rather involved identification of psychosocial predictor variables, the inclusion of a comparison group was thought to be unnecessary.

In summary, a number of significant predictors of parental distress across the acute phase of transplant have been identified. The variables producing the strongest effects include the parents’ prior history of distress associated with their child’s illness, the FRI, and parental use of avoidant coping. Since the majority of parents of children undergoing transplant adjust relatively well, with only a small percentage experiencing pathological responses, the predictors identified here could help serve to target the subset of parents at highest risk of experiencing difficulties with transplant-related distress.

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References


Predictors of Parental Distress in BMT


