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Family Life Events in the First Year of Acute Lymphoblastic Leukemia Therapy: A Children's Oncology Group Report

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Abstract

Background—Despite higher cure rates, childhood acute lymphoblastic leukemia (ALL) may continue to result in considerable family strain. We sought to (i) measure incidence of divorce, reduced career opportunities, changes to work hours, home relocation, and changes to family planning at one year after ALL diagnosis; and (ii) Identify family and patient factors associated with these events.

Procedure—We conducted a prospective cohort study of 159 children with average risk-ALL enrolled and treated on COG protocol AALL0331 at 31 selected sites. Eligibility criteria included age ≥ 2 years and English or Spanish comprehension. Parents completed surveys at three time points during the first 12 months of therapy.

Results—Parents were at significantly increased risk of loss of employment (46% vs. 9.1%, $P = 0.001$) than peers nationally. 13% divorced/separated, 27% relocated homes, 22% decided not to have more children, 51% declined occupational opportunities, and 68% decreased work hours. In adjusted analyses, relocation correlated with less maternal education (OR: 4.27 [95% CI: 1.43–12.82]). Declining parental opportunities associated with family income <\$50,000 (OR: 4.25 [95% CI: 1.50–12.02]) and child <5 years old (OR: 4.21 [95% CI: 1.73–10.25]). Deciding not to have more children correlated with smaller family size 2–3 versus 4–5 (OR: 3.62 [95% CI: 1.10–11.96]).

Conclusion—Families experience a high incidence of major life changes in the first year of ALL treatment. Understanding these burdens helps health care providers to provide appropriate anticipatory guidance and support. No unifying factor was associated with the different family events. Ongoing follow-up is planned to measure long-term outcomes.

Keywords

family coping/functioning; leukemia; pediatric cancer

INTRODUCTION

Over 90% of children with standard-risk acute lymphoblastic leukemia (SR-ALL) become long-term survivors [1]. The duration of therapy is 2–3 years, involving frequent clinic visits, unanticipated hospitalizations, and other therapy-related complications. Children suffer fatigue, nausea, prolonged absence from school, and behavioral changes as side effects of chemotherapy. As such, families experience many financial, psychosocial, and family-management burdens. While these strains have been studied in cohorts with mixed types of pediatric cancer, less is known about children specifically treated for ALL with current treatment regimens.

In addition to inclusion of patients with heterogeneous cancers, past studies of the family burden of childhood ALL were in earlier treatment eras or used retrospective data. Studies of childhood cancer's impact on parental marriages yielded conflicting results, with regards to divorce/separation rates [2–7]. Studies regarding financial burdens likewise showed mixed results though recent studies have utilized prospectively recorded expense-journals [3,8–15]. Even so, at present, there are no studies regarding objective family events, after a childhood ALL diagnosis, in a diverse patient population in the modern era of therapy.

Measuring the family burden of average risk B-precursor ALL (AR-ALL) and its treatment is important because AR-ALL is among the most common and curable of childhood cancers [1]. Pediatric cancer centers already recognize the need for multidisciplinary, family-centered care. However, prospective and representative data regarding critical family outcomes are needed to inform further support interventions.

In this prospective, longitudinal study, our aim was to measure the relational, financial, and psychosocial burdens to families of children treated for newly diagnosed AR-ALL. We recruited patients enrolled on Children's Oncology Group (COG) AALL0331 AR-ALL trial from a predominantly U.S. subset of all COG clinical trial sites. Families were surveyed regarding the incidence of discrete family life events at three time points during the first year of therapy. We sought to (i) measure changes in marital status, parental occupational and educational opportunities, location of home, and family planning; and (ii) identify family and patient factors associated with a greater likelihood of these major family life events.

METHODS

Study Population

We conducted a prospective, longitudinal study of major life events in families of children with AR-ALL who were enrolled and treated on COG protocol AALL0331 between April 2005 and March 2009 at 31 sites (30 U.S. sites and one Australian site) selected from approximately 200 sites. The 31 sites were selected to represent a broad geographic distribution and both community care and tertiary care centers. Additional eligibility criteria included age ≥ 2 years old at diagnosis and at least one parent with English or Spanish literacy, the languages for which validated surveys were available. AR-ALL is defined as standard risk-ALL by National Cancer Institute criteria (peripheral white blood count $<50,000$ and age between 1.0 and 9.99 years [16]) with no central nervous system or testicular leukemia, bone marrow minimal residual disease $<0.1\%$ at the end of 4 weeks of Induction therapy, and certain molecular features (see <http://www.cancer.gov/clinicaltrials/search/view?cdrid=409589&version=HealthProfessional> for more details).

Clinicians approached and consented all patients' families at the end of induction (about four weeks after diagnosis), which is the time of enrollment in the therapeutic study. AR-ALL patients were randomized in a 2×2 therapeutic trial design to: (i) standard Consolidation (SC) versus intensified Consolidation (IC) therapy that added two doses of cyclophosphamide and peg-asparaginase; and (ii) standard Interim Maintenance (SIM) with oral methotrexate versus augmented Interim Maintenance (AIM) with escalating intravenous (IV) methotrexate as post-Consolidation therapy. Maturation of protocol CCG-1991 data showed that IV methotrexate was superior to oral methotrexate [17]. Therefore, all patients enrolled subsequent to September 29, 2008 received IV methotrexate, and randomization regarding post-Consolidation was closed.

One hundred ninety four patients enrolled in AALL0331 at the participating sites met ancillary study eligibility. Of these, 24 declined participation. Of the 170 who consented, four patients withdrew prior to the first set of surveys, and seven did not receive the first set of evaluations due to administrative errors. The 35 eligible non-participants were similar to the 159 patients who participated (82% of eligible) with regards to gender and age at diagnosis. Participants, compared to non-participants, were more likely to be White ($P=0.01$). Compared to the therapeutic AALL0331 population, participants were more likely to be ≥ 5 years old at diagnosis, White, and randomized to Standard (vs. Augmented) Interim Maintenance (Table I).

The target accrual goal was 154 patients to account for a 20% anticipated lost to follow-up rate to yield the 123 patients required based on sample size calculations. Target accrual was met by March 5, 2009. The study was initially powered for the main outcome of change in health-related quality of life outcomes (which will be reported separately).

Procedures

In addition to the Yale University Human Investigation Committee, institutional review boards of each participating center approved the study. Informed consent and assent, when indicated, were obtained for all participants.

The primary caregiver (child's mother in 84% of instances) completed the required surveys at 3 time points during regularly scheduled clinic visits (day 1 of Consolidation phase [~1 month after diagnosis], end of Delayed Intensification phase [~6 months after diagnosis], and six months after starting maintenance phase [~12 months after diagnosis]). Surveys were completed in clinic to maximize compliance and rates of completion and were completed by one parent because only one parent usually attends clinic.

Measures

Socioeconomic data were obtained using a parent demographic survey, which included questions about race/ethnicity, household income, marital status, maternal education, and family size. Marital status responses of "married" or "living with someone in a marriage-like relationship" were consolidated due to their presumed similar impact on social and financial support and to better reflect current family structures [7].

Incidence of major family life events was quantified by line item responses to the Family Inventory of Life Events and Changes Subset (FILE-S; adapted from McCubbin, Patterson, and Wilson 1991 [18]). The full FILE has α reliability of 0.72; however, there are no specific validation data available for FILE subsets. Parents were asked whether the following events occurred since their child's leukemia diagnosis: "Husband and wife separated or divorced," "Took a second job or worked more hours," "Quit or lost my job," "Worked part-time instead of full-time," "Did not start a job but wanted to," "Did not accept a job promotion or transfer," "Quit or did not start further education/training," "Moved to different home or community," and "Changed plan and decided not to have more children." The content of the FILE was guided by life changes included in previous validated life inventories, as well as clinical and research experiences with families of healthy and ill children [19–22]. Change in marital status has previously been found to be a meaningful indicator of cumulative family strains in the course of a child's chronic illness [19], and, specifically, in children with cancer [6,23,24].

Family coping was assessed using the Coping Health Inventory for Parents [25], which has been validated for children with a variety of chronic illnesses. In this 45-item checklist, parents rate how helpful a particular coping behavior is (e.g., "talking over personal feelings and concerns with spouse") on a 4-point scale ranging from "not helpful" to "extremely helpful." The three subscales, (i) Maintaining family integration and optimism; (ii) Maintaining social support and self-esteem; and (iii) Understanding the medical situation, have α reliabilities of 0.79, 0.79, and 0.71. A higher score on each subscale indicates a greater reliance on that coping pattern, but there are no normative scores.

Parental perception of cancer's impact on a child's quality of life was measured using the PedsQL 3.0 Cancer Module Parent Proxy-Report [26]. In this 27-item questionnaire, parents rate each item on a 5-point scale ranging from "never a problem" to "almost always a problem." Of the eight subscales, "Nausea" (α reliability of 0.85) and "Pain and Hurt" (α reliability of 0.89) subscales were analyzed as these physical symptoms are typical treatment complications. A higher score indicates fewer problems or symptoms.

Data Analyses

The family and patient factors of age at diagnosis, gender, and race/ethnicity were summarized and compared between participants and eligible nonparticipants using an exact chi-square test to evaluate the potential for response bias. Data regarding eligible nonparticipants were obtained from the AALL0331 therapeutic study database.

The primary outcomes of interest were changes in marital status, parental working hours, parental work and educational opportunities, moving of residence, and family planning at the three time points after diagnosis. The cumulative incidence of loss of employment, home relocation, and divorce/separation among married couples at one year after diagnosis were calculated after excluding the eight Australian participants to enable comparison with available United States Census data. Logistic regression was used for univariate and multivariate analyses for each outcome. Potential predictors that were nominally significant at P -value of <0.1 in the univariate analyses were included in the multivariate model. In addition, we determined, based on the longitudinal model with repeated measures, whether the incidence of events changed significantly between the three time points. All analyses were performed using SAS[®] software, Version 9.2 (SAS Institute Inc., Cary, NC; 2008).

RESULTS

Characteristics of Study Population

Table I displays characteristics of the 159 enrolled patients and their families. The study population was mostly White (68%) with 16% Hispanic and 7% Black. The majority of parents were married or living in a marriage-like relationship (75%) at diagnosis, comparable to parents of children with other cancers (68–100%) [3,27–29]. The majority of families consisted of 4–5 individuals (59%). Average maternal age at diagnosis was 34 years old.

Cumulative Incidence of Major Family Life Events

Table II displays the cumulative incidence of major family life events in the first year after diagnosis. Key findings were primarily economic burdens. Among parents, 51% declined work or educational opportunities, 18% increased work hours, and 68% decreased work hours (including 46% who reported loss of employment vs. 9.1% from 2010 Census data [30,31], a statistically significant difference).

Among the 120 sets of parents initially married or living together in a marriage-like relationship, 13% divorced/separated by ~12 months after ALL diagnosis. Of those married, 10% divorced or separated (vs. 7.4% annually for married women 20–34 years old from the 2011 U.S. Census American Community Survey [32]). The incidence of moving to a different home was somewhat higher (27% vs. 21% annually for persons 1–4 years old from 2009 Census data [33]). After their child's ALL diagnosis, 22% of parents changed their plans and decided not to have additional children.

As seen in Figure 1, the increase in frequency of major family life events is greatest earlier in treatment but continues to steadily rise. Forty-two percent of parents decreased work

hours from the time of diagnosis to time point 1; at subsequent time points, additional parents decreasing work hours was substantially less. The increases in frequencies of outcomes between time points are statistically significant for all events ($P < 0.05$), except from time point 2–3 for divorce/separation, increased work hours, and decreased work hours.

Patient and Family Factors Associated With Major Family Life Events

Table III displays the univariate analysis of factors associated with major family life events. For family relationships and management, moving was strongly associated with maternal education less than college (OR = 4.63, $P = 0.004$) and non-White race/ethnicity (OR = 2.88, $P = 0.008$). Deciding not to have more children was associated with smaller family size (2–3 vs. 4–5 members; OR = 3.44, $P = 0.02$). Divorce/separation was associated with less maternal education (OR = 4.61, $P = 0.05$). In multivariate analysis (Table IV), moving was substantially associated with lower maternal education (OR = 4.27, $P = 0.009$) but no longer associated with race/ethnicity. The strong association between deciding not to have more children and smaller family size (2–3 vs. 4–5; OR = 3.62, $P = 0.04$) remained.

For economic burdens, in univariate analysis, declining occupational or educational opportunities was associated with lower family income (OR = 3.21, $P = 0.003$), child younger than 5 years at diagnosis (OR = 2.48, $P = 0.008$), and less than college education in the mother (OR = 2.05, $P = 0.05$). A decrease in work hours was predicted by more intensive treatment (IC/AIM vs. SC/SIM; OR = 3.75, $P = 0.04$). Parental perception of the child's pain and nausea and endorsement of parental coping behaviors were generally not associated with the studied outcomes. In multivariate analysis, declining occupational/educational opportunities was associated with lower family income (<\$50,000; OR = 4.25, $P = 0.006$) and younger age of child at diagnosis (OR = 4.21, $P = 0.002$). Randomization to IV methotrexate significantly ($P < 0.05$) reduced the likelihood of parents increasing work hours or declining work/educational opportunities (OR = 0.18 and 0.25, respectively). No unifying patient or family factor correlated with all six major family life events.

DISCUSSION

Our multi-site, prospective study of 159 children undergoing contemporary therapy for childhood average risk acute lymphoblastic leukemia demonstrates that families experience considerable burdens despite the high probability of cure and mostly outpatient chemotherapy. By one year after diagnosis, 46% of the 68% of parents who decreased work hours either quit or lost their jobs, 18% increased work hours, 51% declined educational/occupational opportunities, 27% relocated residences, and 22% changed their family planning regarding additional children. In addition, 13% of parents, who were initially married or living-as-married, divorced or separated. In general, families of all socioeconomic backgrounds were vulnerable to economic stresses, ranging from increases and reductions in work hours to quitting or losing a job. A child's physical symptoms, such as pain and nausea, as well as parental coping behaviors were not associated with studied outcomes. While the burden is considerable, no common patient or family factor was identified that increased the likelihood of all these major life events.

Compared to peers nationally, parents were at significantly increased risk of loss of employment (46% vs. 9.1% [30,31]). For parental divorce (10% vs. 7.4% [32]) and home relocation (27% vs. 21% [33]), our findings were not statistically different from national data. National comparison data were not available for the other outcomes.

This is the first study to quantify the family burden of newly diagnosed childhood ALL in a large, racially and regionally diverse sample in the era of modern therapy. The substantial percentage of patients from previously underrepresented groups (16% Hispanic and 7% Black) and the 31 designated sites enable fair representation of the diversity of children who develop AR-ALL. Our high participation rate of 82% mitigates major selection bias, although there was some bias given the requirement of parental English or Spanish literacy. In contrast to prior studies that mainly used measures of parental strain, coping, or qualitative interviews [2,3,5,34–37] to measure family burden, our study measures distinct family life events. Furthermore, the prospective cohort design decreases the likelihood of recall bias.

Divorce/separation in married parents of children with ALL in the first year after diagnosis was only slightly higher than peers nationally (10% vs. 7.4%). It is difficult to determine the effect of the cancer diagnosis as baseline marriage quality was not assessed. Even so, our results concur with previous studies, which likewise report no impact on divorce rates [6,7,38].

By one year after diagnosis, about 20% of parents had decided to change family planning and not to have more children. This concurs with a retrospective Netherlands study by Van Dongen-Melman et al. [39] wherein 20% of parents decided not to have more children after a child's leukemia diagnosis. Family planning is pertinent to families of children with AR-ALL since the peak age at diagnosis is ~4 years old. Many parents of young children may be in the midst of building their families. Our study found that smaller family size (2–3 vs. 4–5) was predictive of changing family planning. This association may reflect that larger families have completed family building prior to a child's cancer diagnosis. However, interpretation of these results is limited by lack of knowledge of parental rationale.

The economic impact of a child's diagnosis of AR-ALL is likewise substantial during the first year of therapy: 68% of parents decreased work hours, 18% increased work hours, and 51% declined occupational/educational opportunities. In the first year of treatment, 46% of families reported that one or more parents resigned from or lost their jobs. This is over five times the national annual incidence of unemployment among previously employed individuals. Our data indicated that more than half of parents decreased work hours and that the economic impact was felt most acutely at treatment onset. Prior studies, using prospective family expense journals [8,9] and population data analysis [12], similarly recognized the economic impact of a cancer diagnosis and its treatment on families, noting 25–60% decreases in weekly income and large proportions of costs (56%) attributed to travel expenses [14,15]. Our results showed lower age of child (age <5) at diagnosis and lower family income (<\$50,000) were associated with decreased occupational/educational opportunities. These associations may reflect the greater amount of supervision required for

younger children and the greater burden of unexpected medical costs to lower income families.

Intravenous methotrexate, compared to oral methotrexate, was associated with a lower likelihood of parents declining work/educational opportunities or increasing work hours. This may be due to possible differences in toxicities between the treatment arms. From the CCG 1991 trial in which there was also an oral vs. escalating IV methotrexate randomization, more hepatic toxicity was observed in the oral methotrexate arm [17] due to the combination of oral methotrexate with 6-mercaptopurine. Toxicity outcomes have not yet been reported for the current study (AALL0331) so we cannot confirm if differences were observed in our sample with regards to methotrexate randomization.

This study should be understood in the setting of potential limitations. Because families were enrolled after the diagnosis of ALL, data regarding baseline family relationships and plans prior to diagnosis are not available. It will be important for follow-up studies to include more detailed in-person interviews to elicit qualitative changes to parental relationships. For home relocation, it would be helpful to clarify whether families moved for work, treatment, to be closer to extended family, or for reasons unrelated to the leukemia.

Given the dynamic nature of family planning, it is possible that families, who decided not to have more children, will choose to have more children upon completion of AR-ALL treatment. As such, analysis of later time points is needed to clarify whether changes to family planning were temporary or permanent.

For most families, the surveys at all time points were completed by the primary caregiver. However, at some time points, another caregiver was present and completed the study survey. The difference in reporter is a potential limitation; nonetheless, the survey questions were worded to elicit reporting of objective, discrete life events, rather than subjective feelings thereby limiting inter-reporter variability.

Another potential limitation is the completion of surveys by the child's primary caregiver, which may lead to under reporting of certain outcomes, such as changes to work hours.

We chose U.S. Census data for populations that were age-matched for our study cohort. Our use of Census data can only provide a rough comparison group as other potential contributing factors were not available. A potential source of bias is the recession in 2008, which overlapped with our period of enrollment and likely influenced the financial stability and choices of participating families. Even so, our observed frequency of job loss was about five-fold higher than national figures.

Of the 194 families eligible for study enrollment, 169 chose to participate and were enrolled in the study. We recognize that there is a potential selection bias as families experiencing the greatest burden may be least inclined to participate. However, the eligible participants who withdrew possessed demographic features/characteristics that were no different than our cohort.

While there have been considerable advances in the treatment of childhood ALL, this study emphasizes the great burdens that the disease places on the family in the first year after a child's diagnosis. Understanding the impact on the entire family is essential as a family's adaptation impacts a child's adjustment to cancer [40,41]. Discussion of anticipated family burdens as well as expected treatment and disease-related symptoms allows physicians to prepare parents for their role as caretakers.

Our study highlights the substantial economic cost to the family as evidenced by altered work hours and opportunities. In addition to mentally preparing parents for these economic burdens, the care team can advocate for greater work flexibility and financial resources from public and/or philanthropic organizations. For children actively undergoing treatment, the Affordable Care Act's (ACA) policy regarding insurance coverage despite pre-existing conditions may allow for more parental employment flexibility. Since the closing of enrollment for our study in 2009, the ACA has been implemented. It remains to be seen how these policy changes will affect our study cohort.

Our findings as well as results from previous studies suggest that the steepest incidence of family burdens occur at diagnosis and the initiation of treatment [8,11]. Therefore, social workers and other members of the multidisciplinary oncology team should help families anticipate these challenges and develop coping strategies soon after diagnosis. There are promising screening tools for at-risk families, such as the Psychosocial Assessment Tool, but more research is required for effective interventions [42]. Our study is ongoing and will prospectively follow children and their families until 2 years after the end of therapy. These results will be valuable in determining the family impact through the later stages of ALL treatment and survivorship.

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Fig. 1.

Cumulative incidence of family life events in the first year of treatment of ALL. **(A)** Work Hours. **(B)** Marital Status and Family Planning. **(C)** Declined New Occupational/Educational Opportunities. **(D)** Moved to Different Home. The increase in frequencies of outcomes between time points are statistically significant for all events at a significance level of $P < 0.05$, except for frequency changes from time point 2–3 for divorce/separation, increased work hours, and decreased work hours. *Among those married or living together as married prior at diagnosis.

TABLE I
Characteristics of Participants, Eligible Nonparticipants, and Therapeutic Study Cohort

	Participants (n=159)	Eligible nonparticipants (n=35)	P-value	Therapeutic AALL0331	P-value
Age at diagnosis: n (%)			0.13		0.002
2.0–4.99 years	86 (54%)	24 (69%)		3294 (66%)	
5.0–9.99years	73 (46%)	11 (31%)		1666 (34%)	
Gender: n (%)			0.58		0.63
Female	76 (48%)	19 (54%)		2299 (46%)	
Male	83 (52%)	16 (46%)		2661 (54%)	
Race/Ethnicity: n (%)			0.01		0.03
White, non-Hispanic	108 (68%)	16 (46%)		2917 (59%)	
Black, non-Hispanic	11 (7%)	1 (3%)		262 (5%)	
Hispanic	26 (16%)	9 (26%)		1005 (20%)	
Other	14 (9%)	9 (25%)		776 (16%)	
Average maternal age (years)	34				
Marital status: n (%)					
Married	105 (66%)				
Living as married	15 (9%)				
Not married (separated, divorced, widowed, never married, refused)	30 (19%)				
Missing	9 (6%)				
Maternal education: n (%)					
Less than college (training school, high school grad, some HS, grade school)	92 (58%)				
At least some college (some college, college grad, post-grad)	55 (35%)				
Missing	12 (7%)				
Family size: n (%)					
2 – 3 individuals	26 (16%)				
4 – 5 individuals	93 (58%)				
6 or more individuals	31 (20%)				
Missing	9 (6%)				

	Participants (n=159)	Eligible nonparticipants (n=35)	P-value	Therapeutic AA11.0331	P-value
Family income: n (%)					
Less than \$50,000	72 (45%)				
\$50,000–\$79,000	25 (16%)				
\$80,000 or more	30 (19%)				
Missing	32 (20%)				
Treatment: n (%)					<0.001
Standard Consolidation, Standard Interim Maintenance	37 (23%)			198 (15%)	
Standard Consolidation, Augmented Interim Maintenance	42 (26%)			445 (34%)	
Intensified Consolidation, Standard Interim Maintenance	41 (26%)			201 (16%)	
Intensified Consolidation, Augmented Interim Maintenance	39 (25%)			446 (35%)	
Peds QL: score (SD)					
Pain and Hurt ^a	49.4 (25.76)				
Nausea ^b	81.3 (17.24)				
CHIP: score (SD)					
CHIP subscale 1: Maintaining Family Integration, Cooperation, and an Optimistic Definition of the Situation	42.9 (9.37)				
CHIP subscale 2: Maintaining Social Support, Self Esteem, and Psychological Stability	25.6 (10.39)				
CHIP subscale 3: Understanding the Health Care Situation through Communication with Other Parents and Consultation with the Health Care Team	17.3 (4.90)				

^aNormative Pain and Hurt subscale score is 74.7.

^bNausea subscale normative score is 77.8, based on the responses of 333 patients with all types of cancer. Higher scores indicate better functioning.

TABLE II

Cumulative Incidence of Major Family Life Events

Time point ^a	Total number respondents	Number with outcome	Frequency of outcome (%)
Parents divorced or separated among married/living together			
1	120	3	3
2	110	7	6
3	106	14	13
Parents divorced or separated among married			
1	105	3	3
2	97	5	5
3	91	9	10
Parents decreased work hours			
1	151	63	42
2	148	90	61
3	144	98	68
Parents increased work hours			
1	156	11	7
2	144	18	13
3	138	25	18
Declined occupational and/or educational opportunities			
1	154	31	20
2	144	56	39
3	144	73	51
Moved residence			
1	156	14	9
2	144	26	18
3	139	38	27
Changed family planning by deciding not to have more children			
1	157	13	8
2	146	21	14
3	138	30	22

^aTime point 1, 2, and 3 are approximately 1, 6, and 12 months after diagnosis. The increases in frequencies of outcomes between time points are statistically significant for all events at a significance level of $P < 0.05$, except for frequency changes from time point 2–3 for divorce/separation, increased work hours, and decreased work hours.

TABLE III

Univariate Association of Patient and Family Factors With the Six Outcomes at Time Point 3 (~12 months after diagnosis)

	Divorced Separated OR(95% CI)	Decreased Work Hours OR(95% CI)	Increased Work Hours OR(95% CI)	Declined Opportunities OR(95% CI)	Relocated Home OR(95% CI)	Changed Family Planning OR(95% CI)
Age at diagnosis: Pre-school (2–4 years old) vs. School-age (5–9 years old)	1.47 (0.50–4.28)	0.70 (0.34–1.42)	0.49 (0.20–1.19)	2.48 (1.26–4.86)	1.03 (0.49–2.19)	2.17 (0.91–5.16)
Race/Ethnicity: Other vs. White, non-Hispanic	2.40 (0.84–6.90)	2.28 (0.99–5.29)	1.25 (0.51–3.12)	1.83 (0.90–3.73)	2.88 (1.33–6.29)	1.14 (0.48–2.70)
Family Income: Less than \$50,000 vs. \$50,000 or more	4.33 (0.91–20.1)	0.95 (0.43–2.07)	0.97 (0.36–2.63)	3.21 (1.49–6.94)	1.57 (0.65–3.76)	0.80 (0.32–1.98)
Maternal Education: No college vs. At least some college	4.61 (1.00–21.28)	1.64 (0.78–3.43)	1.25 (0.49–3.19)	2.05 (1.00–4.20)	4.63 (1.65–12.99)	1.17 (0.48–2.88)
Marital Status: Other vs. Married or live together		0.83 (0.33–2.06)	2.01 (0.73–5.56)	1.66 (0.71–3.88)	0.72 (0.25–2.12)	0.33 (0.07–1.49)
Family size:						
2–3 vs. 4–5	0.71 (0.14–3.51)	2.13 (0.66–6.90)	1.20 (0.35–4.13)	1.40 (0.56–3.48)	1.61 (0.57–4.57)	3.44 (1.17–10.10)
6 or more vs. 4–5	1.05 (0.30–3.64)	0.58 (0.25–1.38)	1.85 (0.68–5.05)	1.94 (0.82–4.61)	1.38 (0.54–3.51)	1.46 (0.49–4.33)
Pain and Hurt subscale	0.97 (0.95–1.00)	1.00 (0.99–1.01)	1.00 (0.99–1.02)	1.01 (0.99–1.02)	1.00 (0.98–1.01)	1.01 (0.99–1.03)
Nausea subscale	1.00 (0.97–1.04)	0.98 (0.95–1.00)	1.00 (0.97–1.03)	0.99 (0.97–1.01)	0.97 (0.95–1.00)	1.01 (0.98–1.04)
Maintaining family integration coping behaviors (CHIP subscale 1)	0.95 (0.90–1.00)	0.96 (0.92–1.01)	0.97 (0.93–1.02)	0.98 (0.94–1.02)	0.99 (0.95–1.04)	0.95 (0.91–1.00)
Maintaining social support coping behaviors (CHIP subscale 2)	0.99 (0.94–1.05)	0.99 (0.95–1.02)	1.06 (1.01–1.11)	1.00 (0.97–1.03)	1.03 (0.98–1.07)	0.97 (0.93–1.01)
Understanding the medical situation coping behaviors (CHIP subscale 3)	0.90 (0.82–1.00)	0.99 (0.91–1.06)	0.98 (0.89–1.07)	1.02 (0.95–1.09)	1.03 (0.95–1.11)	0.96 (0.89–1.05)
Treatment ^a :						
IC/AIM vs. SC/SIM	0.54 (0.12–2.48)	3.75 (1.05–13.34)	0.58 (0.18–1.84)	0.74 (0.28–1.98)	1.56 (0.52–4.69)	1.65 (0.56–4.89)
SC/AIM vs. SC/SIM	0.48 (0.11–2.18)	0.83 (0.32–2.19)	0.20 (0.05–0.79)	0.34 (0.13–0.89)	1.08 (0.37–3.15)	0.35 (0.10–1.31)
IC/SIM vs. SC/SIM	0.88 (0.23–3.34)	0.66 (0.25–1.74)	0.45 (0.14–1.40)	0.44 (0.17–1.14)	1.16 (0.39–3.40)	0.70 (0.22–2.21)

^a SC-standard consolidation; IC-intensified consolidation (additional cyclophosphamide and peg-asparaginase); SIM- standard interim maintenance (oral methotrexate); AIM-augmented interim maintenance (escalating intravenous methotrexate).

TABLE IV

Multivariate Analyses for the Association of Patient and Family Factors With the Six Outcomes at Time Point 3 (~12 months after diagnosis)

	Divorced Separated OR(95% CI)	Decreased Work Hours OR(95% CI)	Increased Work Hours OR(95% CI)	Declined Opportunities OR(95% CI)	Relocated Home OR(95% CI)	Changed Family Planning OR(95% CI)
Age at diagnosis: Pre-school (2–4 years old) vs. School-age (5–9 years old)				4.21 (1.73–10.25)		1.72 (0.63–4.66)
Race/Ethnicity: Other vs. White, non-Hispanic		2.40 (0.93–6.24)		0.71 (0.26–1.97)	1.93 (0.79–4.74)	
Family Income: Less than \$50,000 vs.\$50,000 or more	3.16 (0.52–19.23)			4.25 (1.50–12.02)		
Maternal Education: No college vs. At least some college	1.72 (0.28–10.64)			1.52 (0.57–4.05)	4.27 (1.43–12.82)	
Family size:						
2–3 vs.4–5		1.82 (0.52–6.37)				3.62 (1.10–11.96)
6 or more vs.4–5		0.44 (0.16–1.18)				1.54 (0.44–5.36)
Pain and Hurt subscale						
Nausea subscale	0.97 (0.95–1.00)				0.97 (0.94–0.99)	
Maintaining family integration coping behaviors (CHIP subscale 1)	1.02 (0.93–1.11)					0.95 (0.90–1.00)
Maintaining social support coping behaviors (CHIP subscale 2)			1.06 (1.01–1.12)			
Understanding the medical situation coping behaviors (CHIP subscale 3)	0.90 (0.75–1.07)					
Treatment ^a :						
IC/AIM vs.SC/SIM		3.45 (0.89–13.30)	0.40 (0.10–1.59)	0.84 (0.24–2.86)		1.18 (0.32–4.35)
SC/AIM vs.SC/SIM		1.44 (0.48–4.26)	0.18 (0.04–0.80)	0.30 (0.09–1.02)		0.34 (0.08–1.42)
IC/SIM vs.SC/SIM		0.99 (0.33–2.93)	0.48 (0.14–1.69)	0.25 (0.07–0.87)		0.46 (0.12–1.81)

^a SC-standard consolidation; IC-intensified consolidation (additional cyclophosphamide and peg-asparaginase); SIM- standard interim maintenance (oral methotrexate); AIM-augmented interim maintenance (escalating intravenous methotrexate).