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Family estimates of risk for neurocognitive late effects following pediatric cancer: From diagnosis through the first three years of survivorship

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Abstract

Background: Families often express a need for additional information about neurocognitive late effects (NCLE) after a pediatric cancer diagnosis. Therefore, we examined: (i) differences in parent, child, and oncologist estimates of risk for NCLE; (ii) whether the estimates of parents and/or children change over time; and (iii) whether estimates are different for children treated with central nervous system (CNS) directed therapies.

Procedure: Mothers, fathers, and children (initial age: 5–17, self-report: >10) from 258 families reported their perceived likelihood of the child developing "thinking/learning problems" on a visual analog scale (0–100%) at 2 months (T1), 1 year (T2), and 3 years (T3) following cancer diagnosis/relapse. Oncologists estimated the likelihood of NCLE at T1. Children were separated into groups based on CNS-directed treatment (n = 137; neurosurgery, intrathecal chemotherapy, and/or craniospinal radiation) or no CNS treatment.

Results: Mother, father, and child estimates of risk for NCLE were similar to oncologists and to one another around diagnosis (T1). Although there were no significant mean differences, a considerable subset of family members either underestimated their child's risk for NCLE (>40%) or overestimated the risk for NCLE (20%) in comparison to oncologists. At T2 and T3, the estimates of mothers were significantly higher than children. Linear growth curves indicated that mothers' estimates for children with CNS-directed treatment significantly increased throughout the first 3 years of survivorship.

Conclusions: Considering that accurate understanding of NCLE is essential to seeking appropriate assessment and intervention, healthcare providers should focus on implementing family-based education early in treatment and throughout survivorship care.

KEYWORDS
neurocognitive late effects, risk, survivorship

1 | INTRODUCTION

Survivors of childhood cancer who receive treatment directed to the central nervous system (CNS), such as neurosurgery, cranial radiation, or intrathecal chemotherapy, are at an increased risk for developing neurocognitive late effects (NCLE) in comparison to other survivors of childhood cancer.[1] These neurotoxic therapies place children with brain tumors and certain other diagnoses (e.g., leukemia) at highest risk for NCLE, with greater impairment associated with being female and younger at diagnosis.[2] Common NCLE include difficulties sustaining attention, problem solving, processing speed, and memory,[1,2] which can have a cascading and lasting impact on development.[3,4] For example, survivors with NCLE demonstrate lower academic achievement,[2–4] have fewer friendships and lower peer acceptance,[5] and are more likely to be unemployed as young adults[6] compared to both normative samples and survivors without NCLE.

Abbreviations: CNS, central nervous system; NCLE, neurocognitive late effects

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Although CNS-directed treatments have the potential for long-term detrimental effects, little is known about whether families are aware of these risks and how their awareness changes throughout treatment and survivorship. Screening for NCLE during routine follow-up often relies partially on the report of parents and survivors regarding potential cognitive problems, as they present in day-to-day functional impairments (e.g., academic or learning problems). However, these might be difficult to detect as NCLE may emerge 2–3 years after diagnosis and manifest in subtle ways.[7–10] Often, children with NCLE fail to make age-appropriate gains, rather than losing skills or previously acquired knowledge.[1,9] Therefore, accurate understanding of the possibility and cause of NCLE is critical for parents and survivors to identify and report concerns to their healthcare team. This enables timely assessment (e.g., neuropsychological testing), school accommodations (e.g., individualized education plans), and intervention (e.g., cognitive remediation).[10]

Many parents of childhood cancer survivors report feeling unprepared for the future late effects their child might encounter and desire more detailed information about these late effects, including NCLE.[11–14] Compared to their oncologist, parents of children newly diagnosed with cancer report more concerns about future NCLE.[15] However, when compared to 5-year outcomes of the child's cognitive functioning as reported by parents, both parents and oncologists initially underestimated the likelihood of NCLE around diagnosis.[14] Furthermore, survivors of childhood cancer themselves may have limited knowledge of their diagnosis, treatment, and common late effects,[16,17] and their perceptions have yet to be compared to that of parents or oncologists. Compared to other diagnosis groups, survivors of brain tumor are least likely to recall the name of their diagnosis and whether they had received chemotherapy.[16] This lack of knowledge is concerning, and it is unclear what factors (e.g., diagnosis, treatment, or age at diagnosis) family members and children consider when estimating the risk for future difficulties and how these estimates change over time.

In this study, we examined differences between estimates of risk for NCLE among mothers, fathers, children, and oncologists over time following a new diagnosis or relapse of cancer and tested whether treatment factors influenced these estimates. Families were assessed near diagnosis, as well as 1 and 3 years later. Based on previous research, we hypothesized that mothers and fathers would overestimate their child's risk for NCLE, and thus perceive a greater risk for NCLE than oncologists. We also explored how family members' reports compared to one another. Finally, we hypothesized that the estimates of the risk for NCLE of mothers, fathers, and children would each increase over time, especially for children that received treatments directed toward the CNS (i.e., neurosurgery, intrathecal chemotherapy, and/or craniospinal radiation).

2 | METHODS

2.1 | Procedure

Data for this manuscript are part of a secondary data analysis from a larger, multisite longitudinal study examining family coping and adjustment to pediatric cancer.[18,19] Children with cancer were recruited from the registries of Monroe Carell Jr. Children's Hospital at Vanderbilt and Nationwide Children's Hospital a few weeks after a new cancer diagnosis or relapse (M = 1.3 months, SD = 0.9). Following approval by the Institutional Review Board, eligible families were approached consecutively in the clinic or hospital by a research assistant and introduced to the study. Parents willing to participate provided written informed consent and children (aged 10–17 years) provided written assent. Participants completed a packet of questionnaires at their convenience (i.e., inpatient, at home, outpatient clinic) and returned the questionnaires to the research team at their subsequent visit at approximately 2 months following diagnosis (M = 2.5 months, SD = 2.1 months; T1). Additionally, the child's primary oncologist, who was responsible for managing their care and treatment needs, was invited to participate at T1. Families were contacted again for follow-up questionnaires at 1 year (M = 14.6 months, SD = 3.2 months; T2) and 3 years following diagnosis (M = 41.0 months, SD = 3.8 months; T3). Children who were older than 10 years provided self-report. Each participant was compensated for their participation at each time point.

TABLE 1 Demographic characteristics of parents participating at 2 months postdiagnosis (T1)

	Mother n = 245 M ± SD, range n (%)	Father n = 129 M ± SD, range n (%)
Age (years)	38 ± 8, 23–72	40 ± 8, 25–72
Race		
White	206 (84)	113 (88)
African American	26 (11)	12 (9)
Other	13 (5)	4 (3)
Ethnicity (non-Hispanic)	208 (85)	124 (96)
Education (years)	16 ± 4, 7–24	16 ± 4, 8–24
Marital status (married)	165 (67)	108 (84)
Annual family income		
<$25,000	75 (31)	30 (24)
$25,000–50,000	59 (25)	27 (21)
$50,000–75,000	36 (15)	26 (20)
>$75,000	70 (29)	44 (35)

2.2 | Participants

Eligible participants were as follows: (i) aged 5–17 years, (ii) diagnosed with new or recurrent cancer and patients of the hematology/oncology department, (iii) English speaking, (iv) without a preexisting developmental disorder, and (v) living within 100 miles of the hospital. Approximately 87% (N = 334) of the 385 families approached at T1 agreed to participate.[19] For this manuscript, we included 258 families (245 mothers, 129 fathers, and 78 children) who had at least one family member report on the child's risk for NCLE (see Table 1 for parents' demographic information). There were no significant differences in the demographic factors of children (age, gender, race, or ethnicity) between the larger sample and this subsample.

TABLE 2 Child treatment variables

	CNS-directed treatment n = 137 n (%)	Non-CNS-directed treatment n = 121 n (%)
Factors included in CNS categorization		
Intrathecal methotrexate	96 (70)	–
Intrathecal cytarabine	78 (57)	–
Focal brain radiation	13 (9)	–
Total body irradiation	12 (9)	–
Whole brain radiation	9 (7)	–
Craniospinal radiation	6 (4)	–
Neurosurgery	12 (9)	–
Other treatment factors		
Intravenous methotrexate	57 (51)	10 (8)
Intravenous cytarabine	54 (48)	4 (3)
Other focal radiation	4 (3)	44 (36)
Surgery for limb salvage	3 (2)	14 (12)
Bone marrow transplant	27 (20)	8 (7)
Enrolled in Phase I study	4 (3)	2 (2)

CNS-directed treatment was coded to include any cancer treatment within the first year of diagnosis or relapse, including one or more of the following: (i) neurosurgery to resect a brain tumor, (ii) intrathecal chemotherapy using methotrexate or cytarabine, (iii) cranial radiation, including total body irradiation and craniospinal radiation. Note that those children who received bone marrow transplant and who were categorized in the non-CNS-directed treatment group did not receive total body irradiation.

Information including type of cancer, date of diagnosis/relapse, and types of treatment during the first year were obtained from medical records. At T1, the sample of children was on average 10.7 years old (SD = 4.0), 52% (n = 133) male, and 83% (*n* = 213) white. Most families participated at initial diagnosis, whereas a small subset was recruited at relapse (8%; n = 21). Diagnoses included leukemia (40%; n = 102), lymphoma (22%; n = 58), brain tumors (7%; n = 19), and other solid tumors (31%; n = 78).

Based on previous literature about cancer treatment modalities that are most likely related to NCLE,[1,20–22] CNS-directed treatment was coded if the child's treatment within the first year of diagnosis included one or a combination of the following: (i) neurosurgery for tumor resection, (ii) intrathecal chemotherapy with methotrexate and/or cytarabine, or (iii) craniospinal radiation (including total body irradiation).[1,21,22] Other treatment modalities, such as intravenous methotrexate, were not included as they do not directly target the CNS and only pose a significant risk for neurocognitive insult at very high doses.[7,23] Based on these criteria, 137 children (53%) were coded as having CNS-directed treatments (see Table 2 for detailed treatment information).

At 3 years postdiagnosis (T3), 102 mothers, 44 fathers, and 79 children participated, and thus, unfortunately, a portion of families was lost to follow-up by T3. Reasons for not participating included families relocating, having inaccurate contact information (i.e., address or phone number changes), passive declines (i.e., packets mailed but were not returned), and death on study. Families that participated at T1 were reinvited to participate at each subsequent time point (unless they explicitly withdrew from the study). This led to slight inconsistencies in the sample across measures and time points (e.g., mother participated at T1 and T3, but not T2; child did not participate at T1, but aged into providing self-report at T2 and T3). Participants with incomplete data were retained to provide the largest possible sample. Attrition analyses indicated that nonparticipating mothers at T3 were more likely to have older children (t = 2.68, $P = 0.008$), with relapsed disease ($\chi^2 = 8.61$, $P = 0.003$), who died during the study ($\chi^2 = 41.60$, $P < 0.001$), and were rated as more likely to develop NCLE by their oncologist (t = 2.13, $P = 0.03$). Because these factors were related, we included deceased status as a covariate in our analyses to account for disease-related attrition. No other differences were observed between mothers lost or retained at T3 with respect to child's age, gender, secondary malignancy status, CNS-directed treatment status, race, or ethnicity.

3 | MEASURES

3.1 | Cancer information questionnaire

Similar to previous work,[15,24] mothers, fathers, children (over the age of 10), and the child's primary oncologist estimated the chances of the child having "problems with learning and/or thinking (such as difficulty with school work) 5 years from now" on a visual analogue scale. The scale ranged from 0% ("no trouble at all") to 100% ("will definitely have trouble"), with tick marks at each 25% increment. Mothers, fathers, and children reported at T1, T2, and T3, and oncologists provided their estimates at T1. Similar to previous research,[15,24] we used oncologists' ratings as the reference group for the most accurate risk estimation. Agreement with the oncologist was determined if the estimate of the family member was within 10 percentage points of the oncologist, which is consistent with previous studies utilizing similar visual analog scales among adults with cancer.[25–27]

3.2 | Analyses

Descriptive statistics were calculated for the estimates of the risk for NCLE at each time point (T1, T2, and T3) and each informant (mothers, fathers, children, and oncologists). Pearson correlations examined associations between informants. To test for informant differences at each time point, we conducted a mixed linear effects analysis (using PROC MIXED in SAS; version 9.3; SAS Institute, Cary, NC). We also tested for clustering effects by oncologist; however, we ultimately did not control for potential reporter clustering in our models because the groupings were nonsignificant ($ICC_{oncologist} = 0.01$, $P = 0.43$). We report results for pairwise comparisons between informants that reached significance ($P < 0.05$), along with standardized mean differences.

The mixed linear effects technique was also used to examine CNS group differences, time effects, and CNS group by time interactions. We fit linear growth curves over time, allowing for random intercepts, random slopes, and covariation between these individual growth curve parameters. This procedure uses maximum likelihood estimation to account for data that are missing at random across measures and time

TABLE 3 Group comparisons for the estimates of the risk for neurocognitive late effects (NCLE) at 2 months postdiagnosis (T1), 1-year postdiagnosis (T2), and 3 years postdiagnosis (T3)

	Mother (M)	Father (F)	Child (C)	Oncologist (O)	Pairwise Comparison	*P*	d
T1 (2 months postdiagnosis)							
Total	20.7 (29.1)	21.0 (29.5)	16.5 (24.8)	23.2 (21.1)	O > C	0.072	0.29
Non-CNS	20.5 (30.0)	23.8 (31.8)	15.3 (24.0)	18.3 (18.4)			
CNS	20.9 (28.4)	18.5 (27.4)	18.9 (26.5)	26.8 (22.3)			
T2 (1-year postdiagnosis)							
Total	24.6 (30.6)	21.4 (32.0)	13.3 (22.3)	–	M > C	0.001	0.42
Non-CNS	24.6 (31.5)	24.0 (37.2)	8.9 (16.7)	–			
CNS	24.6 (30.0)	19.0 (26.8)	19.0 (27.1)	–			
T3 (3 years postdiagnosis)							
Total	30.8 (33.0)	27.2 (34.4)	20.3 (25.1)	–	M > C	0.012	0.36
Non-CNS	20.3 (25.4)	26.0 (33.7)	17.6 (25.9)	–			
CNS	40.1 (36.3)	28.3 (35.7)	23.6 (24.0)	–			

The visual analog scale ranged from 0 to 100%, with higher percentages indicating a higher risk for NCLE. CNS-directed treatment was coded to include any cancer treatment within the first year of diagnosis or relapse, including one or more of the following: (i) neurosurgery to resect a brain tumor, (ii) intrathecal chemotherapy using methotrexate or cytarabine, (iii) cranial radiation, including total body irradiation and craniospinal radiation. Means, standard deviations, and Cohen's d values reflect raw data. Pairwise comparisons are based on data derived from models using maximum likelihood estimation. Only significant (and marginally significant) results are displayed. Independent samples *t*-tests indicated that only oncologists' estimates differed by the CNS group at T1, $t(156) = -2.59$, $P = 0.01$, d = 0.42.

points.[28,29] To ameliorate the effects of data not missing at random, we included deceased status as a covariate in our analyses due to the identified disease-related attrition.

4 | RESULTS

Contrary to our hypothesis, oncologist report of the risk for NCLE at T1 was similar to mothers, fathers, and children (see Table 3 and Fig. 1). There was a significant, but small, correlation between mothers' and oncologists' estimates of NCLE at T1, $r(150) = 0.18$, $P = 0.03$. However, there was no association between the estimates of fathers and oncologists [$r(75) = 0.09$, $P = 0.44$] or children and oncologists [$r(52) = 0.15$, $P = 0.30$]. Furthermore, a subset of mothers, fathers, and children were discrepant from the estimates of their oncologist (i.e., >10 percentage points). Over 40% of mothers, fathers, and children underestimated the child's risk for NCLE in comparison to their oncologist, and about 20% overestimated the risk. Discrepancies between family members and oncologists indicated that family members, on average, underestimated their child's risk for NCLE by several points (mothers: M = 4.27, SD = 31.07, range 0–85; fathers: M = 2.78, SD = 31.95, range 0–100; children: M = 2.44, SD = 26.06, range 0–87). Additionally, independent samples *t*-tests indicated that only oncologists' ratings differed between CNS-directed and non-CNS-directed treatment groups at T1, $t(156) = -2.59$, $P = 0.01$, d = 0.42.

At T1, family member comparisons revealed that mother, father, and child reports did not significantly differ from one another (see Table 3). However, at both T2 and T3, mothers perceived a higher risk for NCLE compared to children, T2: $t(130) = 3.33$, $P = 0.01$, d = 0.42; T3: $t(84) = 2.56$, $P = 0.01$, d = 0.36. There were no mean differences at T2 or T3 between fathers and children nor between mothers and fathers.

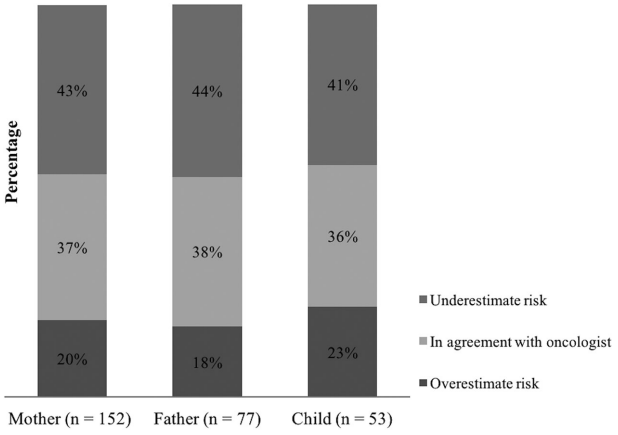

FIGURE 1 Association between family members (mother, father, and child) and oncologist estimates of the likelihood of future NCLE approximately 2 months postdiagnosis (T1). Note: "In agreement with oncologist" indicates agreement within less than 10 percentage points of their oncologist's estimate. One-way ANOVAs indicated no significant group differences by child age or parent education (years). Similarly, correlations with discrepancy scores (oncologist estimates vs. family member estimates) and child age/parent education were not significant

We then examined the correlations among family members' estimates. At T1, mothers' estimates were significantly correlated with the estimates of both fathers, $r(118) = 0.48$, $P < 0.001$, and children, $r(71) = 0.30$, $P = 0.01$, while the estimates of fathers and children were unrelated, $r(39) = 0.04$, $P = 0.79$. At T2, parent estimates were not significantly correlated with child estimates, but at T3, both mother and father estimates were moderately correlated with child estimates, $r(71) = 0.53$, $P < 0.001$ and $r(32) = 0.35$, $P = 0.04$, respectively. Mother and father estimates were correlated with one

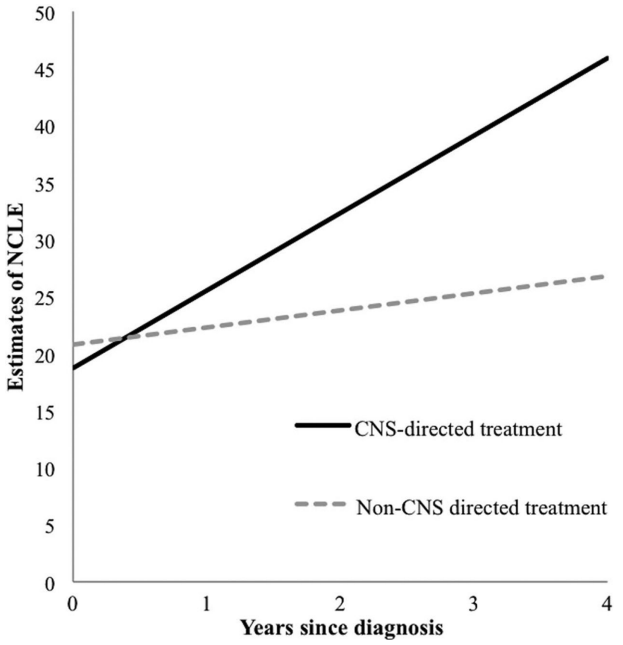

FIGURE 2 Mothers' estimates of the risk for neurocognitive late effects over time since diagnosis (CNS group by time interaction)

another at both T2, r(62) = 0.46, $P < 0.001$ and T3, r(39) = 0.57, $P < 0.001$.

Next, we examined whether each family member's estimates of the risk for NCLE changed over time (measured in days since diagnosis) and whether change over time differed by the CNS treatment group (CNS-directed treatment vs. non-CNS-directed treatment). Although the estimates of fathers and children did not change over time and did not differ by the CNS treatment group, linear growth curves indicated that the group by time interaction was significant for mothers ($b = -0.01$, t = −2.65, $P = 0.009$). Specifically, mothers' estimates of risk for NCLE increased over time if their child received CNS-directed treatment (b = 0.02, t = 4.96, $P < 0.001$), whereas the estimates of mothers of children without CNS-directed treatment did not significantly change over time (b = 0.004, t = 1.03, $P = 0.31$; see Fig. 2). At T1, on average, mothers of children who received CNS-directed treatment estimated a 19.88% chance that their child would have NCLE and by T3, their estimates increased to 38.84%. In contrast, mothers of children without CNS-directed treatment estimated a 22.27% chance at T1, which was similar to their estimate at T3 of 25.21%. Similar analyses examining whether mothers estimates of risk changed depending on diagnosis type (i.e., leukemia, lymphoma, brain tumor, other solid tumor) were not significant, b = 0.007, $F = 1.96$, $P = 0.16$.

5 | DISCUSSION

Survivors of childhood cancer may be at risk for neurocognitive problems as a result of their cancer treatment, and family members' knowledge about the risk has important implications for monitoring, assessing, and treating these potential problems. Our study is the first to directly assess and compare multiple family members' estimates of a child's risks for NCLE to one another and over time, as well as to their oncologist's estimates near diagnosis. Our results indicated that family members' estimates were similar to the estimates of their oncologist. In comparing family members to one another, mothers were more pessimistic about NCLE than children at both T2 and T3. Furthermore, mothers' estimates of risk increased over time, but only if their children received CNS-directed treatment.

Contrary to our hypotheses, there were no significant mean differences between the estimates for NCLE for mothers, fathers, children, or oncologists 2 months postdiagnosis (T1). However, a substantial number of family members were not in agreement with the estimates of their oncologist (i.e., over 40% underestimated, about 20% overestimated). This was unexpected since a previous study indicated that about 40% of caregivers reported higher estimates of NCLE than their oncologist.[15] One possible explanation is that it may have been more difficult for families in our study to assess the long-term impact of treatment considering that the baseline assessment of our study occurred closer to diagnosis, which is often a time focused on cure. Another possible explanation is that may be demographic differences between the two study samples, or differences in the education around late effects between institutions. Overall, our results indicate that although there are no overall mean differences between oncologist and family ratings, healthcare providers should be aware of considerable variability in familial estimates (as estimates ranged from 0 to 100%), when communicating about future late effects with families.

Although mothers, fathers, and children did not differ significantly from one another at T1, mothers' estimates of NCLE were significantly higher than their children's estimates at both T2 and T3. This discrepancy indicates that mothers may be more concerned about NCLE, and perhaps more informed, since mothers' estimates were significantly correlated with oncologists. Interestingly, the estimates of both mothers and fathers were not correlated with their child's estimates at T2 but were moderately correlated at T3, suggesting that family members' perceptions were related to one another in early survivorship. We speculate that families may be having more discussions about survivorship and potential late effects with one another at 3 years postdiagnosis, which may influence agreement of individual perceptions about the risk for NCLE. Although these results are promising, our findings provide further support that, in general, survivors of childhood cancer may have limited knowledge about late effects of their cancer treatment in comparison to mothers, or are less concerned than their mothers.[16,17] The healthcare team should include children in discussions regarding potential late effects and continue to build on these discussions as is developmentally appropriate. This knowledge is especially important as survivors begin to manage their own care and transition into adolescence and young adulthood.[30]

Our study prospectively examined how family members' estimates of NCLE may change over time from diagnosis through 3 years of survivorship. Only mothers' estimates of risk for NCLE for children with CNS-directed treatments increased significantly over time, which may indicate that mothers noticed the child's emerging cognitive deficits (or difficulties achieving developmental milestones) by 3 years postdiagnosis. However, we were unable to examine whether or not mothers' estimates of risk for NCLE were concurrent with their child's

actual cognitive decline. Previous studies have compared parent estimates of risk for NCLE around diagnosis to parent reports of cognitive deficits during survivorship.[14] However, research comparing parent reports of NCLE to actual neurocognitive functioning on standardized assessments is limited to survivors of brain tumor, and this work should be expanded in a broader set of survivors, such as survivors of leukemia, who receive neurotoxic treatments and are also at risk for NCLE. This information would help inform the appropriate allocation of services and timing of interventions for survivors of childhood cancer with apparent NCLE or who are at risk for NCLE.

Although our study contributes novel insights to the literature regarding families' perceptions of late effects, there are several limitations that should be considered when interpreting our findings. First, given competing demands on their time, oncologists' estimates were collected only at T1. Additionally, families with higher oncologist estimates for NCLE at T1 were more likely to be lost to follow-up at T3. Although this is most likely associated with deceased status (i.e., higher NCLE estimates, more progressive disease), future studies should collect oncologists' estimates at multiple time points in order to compare family members to oncologists over time. Second, we dichotomized the treatment variable (CNS-directed vs. non-CNS-directed), which might be an oversimplification. Our categorization was intentionally conservative to include only children with direct insult to the brain and at the highest risk for NCLE. Therefore, we did not abstract or include other neurotoxic treatment factors that have inconsistent or dose-specific links to NCLE (i.e., high-dose intravenous methotrexate).[7,23] We also were unable to examine treatment modalities in isolation due to the number of potential combinations, and consequently, limited samples within each subgroup. There are likely dose-related effects of treatment on cognitive abilities, such that more intense treatments (e.g., higher dose chemotherapy or radiation) produce more severe neurocognitive deficits.[23,31] However, additional research is needed to establish cut-points for the intensity of each CNS-directed treatment, as well as the potential additive effect of corticosteroids (i.e., dexamethasone and prednisone), which can be detrimental to a child's future cognitive functioning.[32,33] We were also unable to evaluate whether children had previously received neuropsychological assessment and/or treatment for NCLE and how these services may have influenced estimates of NCLE. Finally, the sample included a relatively small number of brain tumor survivors and was relatively homogenous regarding family demographics (i.e., mostly white two-parent households).

Some of the limitations in our design were due to the nature of this secondary data analysis and our findings should be regarded as preliminary. Future prospective research should further delineate subgroups of survivors most at risk for NCLE and examine the accuracy of family members' estimates. Ideally, these estimates could be directly compared to oncologists and objective neuropsychological assessment and conducted at regular intervals over time. Future studies should also examine other potential moderators that might explain discrepancies between reporters such as the quality of oncologist communication, sources of medical information, family functioning, parental anxiety, health literacy, or other demographic factors that may be related to NCLE, such as the child's gender.[2,13,15,24,34]

Considering that family members' understanding of the risk for NCLE is crucial in identifying and reporting late effects during survivorship, healthcare providers should ensure thorough communication and education with families about the likelihood, presentation, and timing of potential late effects.[12] Providers should consider discussing late effects more frequently and more comprehensively (perhaps in multiple formats: verbal, written, and online), since past studies indicate that oncologists only mention the possibility for NCLE during 20% of informed consent conferences.[35] Furthermore, many parents of survivors wish they had more information about late effects.[11–14] Still providers should be flexible about the timing of these discussions, as some families prefer to receive more information close to diagnosis, while others prefer this detailed information only during survivorship care.[11] In particular, families of children who receive neurotoxic chemotherapies (e.g., children with leukemia) may have a need for additional information about NCLE in comparison to families whose child received craniospinal radiation.[11] Considering that only mothers recognized increased risks for NCLE over time, providers should consider educating each family member during the transition to survivorship. This may be especially important for the child because of survivors' suboptimal adherence to long-term survivorship care.[30]

Ideally, and as suggested by the Psychosocial Standards of Care in Pediatric Oncology, communication and screening for emerging late effects should be an ongoing process involving multidisciplinary teams that help children through the transitions to survivorship, as well as during key school transitions (e.g., middle school to high school).[36] Providers should also make appropriate referrals for a comprehensive neuropsychological assessment if any concerns are identified to ensure that potential late effects are addressed in a timely manner.[10] By gaining a better understanding about how families perceive information and estimate children's risk for late effects, family education, referrals, and interventions can be optimized to benefit survivors of childhood cancer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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