

Psychosocial and Medical Predictors of Academic and Intellectual Functioning in Childhood Cancer Patients

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Abstract

Background.

Childhood cancer patients experience worse educational and vocational outcomes relative to age-matched peers. Numerous demographics, cancer, and treatment-related variables impact these outcomes. However, they have not been thoroughly explored in initial stages post-diagnosis or in the context of return to school evaluations. The current study seeks to explore the predictive abilities of these variables on intellectual/academic, cognitive, and emotional/behavioral outcomes.

Method.

101 pediatric oncology patients completed neuropsychological evaluations at an academic medical center using validated intellectual, academic, cognitive, and emotional measures as part of standard care within three years of diagnosis. Multiple imputation was utilized to estimate missing data. Linear regression models were conducted for each outcome measure and post-hoc analyses identified risk factors for poorer outcomes.

Results.

Lower intellectual functioning, government or lack of insurance, nervous system focused treatment, less than 250 milligrams of chemotherapy, more than 20 grays of radiation, and presence of premorbid diagnosis or complications were associated with worse outcomes. Evidence regarding sex and radiation type remained mixed.

Conclusions.

Childhood cancer survivors are at risk for poor academic and occupational attainment, which can be impacted by individual demographic and medical variables. Neuropsychological evaluations can help inform individualized intervention and improve survivor outcomes.

Introduction

Globally, an estimated 202,164 new childhood cancer cases and 77,182 deaths occurred worldwide in 2022 (Kudek & Wang, 2026; Li et al., 2026). In the United States, approximately 15,000 children and adolescents are diagnosed with cancer each year, with an estimated 500,000 pediatric cancer survivors as of 2020 (Bhatia et al., 2023; Siegel et al., 2023). With the widespread adoption of multimodal treatment approaches, 5-year survival among children diagnosed with cancer has risen substantially over the past several decades—from roughly 60% in 1970 to more than 85% today (Chow et al., 2020). Despite higher survival rates, childhood cancer patients are at increased risk for somatic, psychosocial, and cognitive late effects due (Erdmann et al., 2021; Friedman & Meadows, 2002; Jacola et al., 2021; Janssen et al., 2021). Evidence shows that regardless of diagnostic category—childhood cancer patients are at elevated risk for cognitive and adaptive functioning deficits. Across all groups, long-term impairments were observed in processing speed, attention, executive functioning, and adaptive skills (Beamish et al., 2025). It is estimated that 35% to 60% of those who survive childhood cancer develop cognitive deficits attributable to the malignancy and/or medical treatment that present years after treatment and persist into adulthood (Cheung & Krull, 2015; Conklin et al., 2012; Hermans et al., 2023; Jacola et al., 2021; Merchant et al., 2023; Olosso et al., 2019; Phillips et al., 2015).

Notable domains of impairment include attention, processing speed, working memory, executive functioning, and verbal memory encoding and retrieval (Child et al., 2021; Hutchinson et al., 2017; Mash et al., 2023; Pierson et al., 2016; Yeo et al., 2019). Academic and intellectual functioning has been highlighted as an area of persistent difficulty for childhood cancer patients and survivors (Brown et al., 1999; Child et al., 2021; Ehrstedt et al., 2018; Haupt et al., 1994; Liguoro et al., 2020; Pulsifer et al., 2018; Wagner et al., 2020). Math, reading, and overall learning abilities are particularly vulnerable to impairment. Several studies suggest that math and reading performance among survivors is significantly lower than control groups and remains lower across the lifespan (Ach et al., 2012; Merchant et al., 2023; Olsson et al., 2019). One study suggests impairments of more than a half (-0.64) standard deviation for math and a third (-0.30) standard deviation for reading, compared to controls (Olsson et al., 2019). Additionally, research indicates that childhood cancer patients tend to have significantly lower intellectual functioning compared to peers (Mavera et al., 2021; Pulsifer et al., 2018; Sleurs et al., 2021; Wagner et al., 2020), with up to one and a half standard deviations lower performance in childhood cancer survivors (Mavera et al., 2021; Wagner et al., 2020). Importantly, poorer performance in these domains is associated with lower educational attainment and lower income in adulthood (Mavera et al., 2021; Olsson et al., 2019; Saatci et al., 2020).

Suggested causes or contributors to academic and cognitive impairments in childhood cancer survivors include frequent absences from school, as well as the adverse effects of medical treatments on the developing brain (e.g., disruption of myelination and white matter topology during critical developmental periods; Hutchinson et al., 2017; Liguoro et al., 2020; Na et al., 2018; Sleurs et al., 2021; Tsimicalis et al., 2017). Given these concerns, neuropsychological and educational evaluations are indicated across childhood cancer populations to identify individual strengths and weaknesses in intellectual functioning, attention, processing speed, memory, executive functioning, and academic achievement. These evaluations can guide individualized educational planning, classroom accommodations, cognitive rehabilitation, and return-to-school or school-reintegration services to facilitate the academic success of pediatric patients, particularly for children exposed to central nervous system-directed therapies or those experiencing academic, behavioral, or cognitive difficulties (Annett et al., 2015; Devine et al., 2022; Jacola et al., 2021).

Research has established various medical and treatment factors that can impact cognitive outcomes in childhood cancer patients. In terms of premorbid patient characteristics, neurodevelopmental conditions such as Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder, and some genetic conditions such as Trisomy 21 and certain genetic polymorphisms are associated with poorer cognitive outcomes (Nathan et al., 2007; Ullrich, 2008; Ullrich & Embry, 2012). Additionally, evidence suggests patients with baseline cognitive deficits or pre-existing learning or intellectual disabilities are at greater risk for cognitive impairment (Irestorm et al., 2018). Specific cancer variables are also established prognostic indicators. For instance, those with central nervous system (CNS) or solid tumor cancers experience cognitive deficits at higher rates than those with blood cancers (Beltrami et al., 2022; Maas et al., 2023; Patel et al., 2020). Studies also indicate that higher grade tumors and a higher stage at diagnosis are correlated with increased impairment following treatment (Cámara et al., 2019; Fraley et al., 2019; Moore III, 2005). In addition to cancer variables, medical complications and comorbidities are risk factors for cognitive decline (Cámara et al., 2019; Hardy et al., 2008; Merchant et al., 2023; Willard et al., 2019).

With regard to treatment factors, higher doses of chemotherapy and/or radiation, as well as longer or increased intensity of treatment are associated with worse cognitive impairments (de Ruiter et al., 2013; Moore III, 2005; Olsson et al., 2019). Surgical intervention, especially numerous surgeries, is associated with poor cognitive performance (Fraley et al., 2019; Palmer & Leigh, 2009; Turner et al., 2009; Weusthof et al., 2021; Willard et al., 2019). Additionally, several studies suggest the use of photon instead of proton radiotherapy is a risk factor greater cognitive decline (Child et al., 2021; Mash et al., 2023; Pulsifer et al., 2015). Treatment delivery method can also influence cognition. Research indicates that intrathecal chemotherapy, craniospinal or whole brain radiation, and chemotherapy that crosses the

blood-brain barrier are particularly harmful to cognition (Child et al., 2021; Conklin et al., 2012; de Ruiter et al., 2013; Liu et al., 2023; Maas et al., 2023; Pulsifer et al., 2018). There is some mixed evidence on the impact of time since treatment, with some studies raising concern for late effects and decline while others suggest increased time since treatment may be associated with improved cognitive performance (de Ruiter et al., 2013; Palmer & Leigh, 2009; Phillips et al., 2015; Wagner et al., 2020).

In addition to medical and treatment factors, patient demographic (i.e., sex, age at diagnosis, race) and psychosocial variables (i.e., socioeconomic status) are well-documented correlates of academic and cognitive outcomes. Sex has been associated with outcomes. However, literature is mixed as to whether males or females with childhood cancer are at increased risk for cognitive impairment (Maas et al., 2023; Moore III, 2005; Nathan et al., 2007; Oswald et al., 2021; Zureick et al., 2018). Younger age at diagnosis is associated with greater cognitive deficits and poorer academic outcome (Maas et al., 2023; Moore III, 2005; Palmer & Leigh, 2009; Patel et al., 2020; Pulsifer et al., 2015; Pulsifer et al., 2018; Willard et al., 2019). Additionally, Black and Hispanic patients tend to have worse cognitive outcomes compared to White/Non-Hispanic patients (Beltrami et al., 2022; Olsson et al., 2019). Finally, lower socioeconomic status and lack of insurance or government-issued insurance is associated with a greater risk for cognitive impairments compared to those with more socioeconomic resources or private insurance coverage (Ach et al., 2012; Beltrami et al., 2022; Torres et al., 2021).

Given the established impact of childhood cancer and treatment on academic and intellectual functioning and subsequent impact on educational attainment and income, return to school assessments and recommendations are particularly pertinent aspects of care for childhood cancer patients. Therefore, the current study seeks to better understand how medical, treatment, and demographic variables can impact academic and intellectual performance to inform best practices for return to school (i.e., within three years post-cancer diagnosis).

Methods

Participants

Neurocognitive data for this clinical study was collected by the neuropsychology service on the pediatric hematology/oncology unit at an academic medical center in the Southeastern United States. Participants included 101 individuals with pediatric cancer referred for evaluation to assess academic, cognitive, and emotional/behavioral functioning near the time of return to school. Among these pediatric patients, 36 (35.6%) had brain tumors, 29 (28.7%) had acute lymphoblastic leukemia, 15 (14.9%) had different lymphomas, and 21 (20.8%) had other non-CNS tumors. Inclusion criteria included a diagnosis of cancer prior to age 18, age 18 or younger at time of neurocognitive testing, and completion of neurocognitive measures within three months to three years of initial diagnosis. Participants were excluded if they had less than 50% of neuropsychological test scores available or if performance validity measures indicated poor or suspect test engagement.

Procedure

This study was approved by the university Institutional Review Board. A flexible battery of neurocognitive tests was administered by a licensed psychologist, a supervised licensed psychometrist, or a supervised clinical psychology graduate student as part of standard clinical care. As such, patients did not receive a standard battery. Consistent with prior research using non-standard batteries as part of clinical care, participants needed at least 50% of neurocognitive data for inclusion (Karlson et al., 2020). Patient charts and data compiled via RedCap were reviewed for additional demographic, cancer, and treatment-related variables of interest.

Measures

Demographic/Psychosocial Variables

Age at diagnosis, sex (male/female), race/ethnicity, insurance type (private/public/self-pay), and premorbid variables of interest such as Attention-Deficit/Hyperactivity Disorder (ADHD), genetic conditions, and intellectual/developmental/learning disorders were collected for each participant. Due to sample characteristics, ethnicity was collapsed into White and Black, Indigenous, and Person of Color (BIPOC) categories given prior literature suggesting poorer outcomes for BIPOC patients (Beltrami et al., 2022; Olsson et al., 2019). Further, premorbid concerns were collapsed into a dichotomous yes/no variable.

Medical Variables

Medical and cancer-related variables including diagnosis, stage at diagnosis, time since diagnosis, chemotherapy and radiation dose, type of radiation, location of radiation (CNS-directed or bodily radiation), number of surgeries, and complications and relapses were collected via record review. For analysis purposes, cancer type (CNS/Non-CNS), treatment delivery method (CNS/Non-CNS focused), total chemotherapy dose (none/<250 milligrams/≥ 250 milligrams), and radiation dose (none/<20 grays/20–30 grays/>30 grays), were collapsed into categorical variables based on extant literature (Johnson & Keyes, 2024; Karlson et al., 2020; Noyd et al., 2021). Complications, including presence of seizures and/or relapse, were dummy coded as a dichotomous (yes/no) variable.

Intellectual Functioning

Individuals were administered the Wechsler Abbreviated Scale of Intelligence, first or second edition (WASI; α 's = 0.90-.97; Wechsler, 1999; WASI-II; α = 0.97; Wechsler, 2011), Wechsler Preschool and Primary Scale of Intelligence, fourth edition (WPPSI-IV; α = 0.96; Wechsler, 2012), Wechsler Intelligence Scale for Children, fourth or fifth edition (WISC-IV; α = 0.97; Wechsler, 2003; WISC-V; α = 0.96; Wechsler, 2014), or the Wechsler Adult Intelligence Scale, third or fourth edition (WAIS-III; α = 0.96; Wechsler, 1997; WAIS-IV; α = .87-.98; Wechsler, 2008) to assess intellectual functioning. A Full-Scale Intelligence Quotient (FSIQ) was calculated for each participant.

Academic Functioning

Academic functioning was assessed using the Wechsler Individual Achievement Test third and fourth editions (WIAT-III; Wechsler, 2009; WIAT-4; Breaux, 2020). The WIAT-III and WIAT-4 are commonly used measures of academic achievement. Information was collected from the Word Reading and Numerical Operations subtests as they were the most frequently administered subtests in the sample and consistent with parameters of interest in return to school evaluations (Breaux, 2020; Wechsler, 2005).

Verbal Memory

The California Verbal Learning Test for Children (CVLT-C; Delis et al., 1994) and Second Edition (CVLT-II; Delis et al., 1988) are widely used, well validated measures utilized to assess verbal learning and memory relative to similar-aged peers. List A total recall was used to assess cumulative verbal recall/learning. List A short delay free recall and List A long delay free recall were used to measure immediate and long-delay (20 minute) verbal recall, respectively. Discriminability was utilized to assess recognition of presented words among distractors.

Emotional-Behavioral Functioning

The Child Behavior Checklist for Ages 1.5-5 (CBCL/1.5-5) and the Child Behavior Checklist for Ages 6–18 (CBCL/6–18) were used as parent-report of internalizing and externalizing symptoms (Achenbach & Ruffle, 2000; Achenbach et al., 2003). The Internalizing Problems, Externalizing Problems, and Total Problems *T*-scores were used in analyses. Scores of ≥ 60 indicated Borderline symptom elevation and scores of ≥ 65 indicated Clinically Elevated symptoms.

Data Analysis

All statistics were calculated using SPSS 30.0. Descriptive statistics were calculated as mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Missing data was present for each neurocognitive variable and was estimated using multiple imputation (see below). Correlation and Analysis of Variance (ANOVA) analyses were conducted to initially examine the relationships between predictor and outcome variables. A multiple linear regression was then conducted for each neurocognitive measure using demographic and medical variables as predictors. FSIQ was also added into the regression model for measures of academic achievement, verbal memory, and emotional/behavioral functioning to account for the relationship between intellectual functioning and these variables (Chen et al., 2006; McCoach et al., 2017; Mohn et al., 2014; Rapport et al., 1997; Tong et al., 2010; Vicari et al., 2016). Post hoc analyses were conducted for significant variables in each regression model. For dichotomous variables, regression coefficients were reviewed. Correlations between continuous predictor variables and dependent variables were examined to clarify relationships. For categorical predictor variables with multiple levels, ANOVAs were run to explore group differences and better understand specific predictors for poorer outcomes.

Preliminary Analyses.

Initially, thirteen predictor variables were selected for inclusion in each linear regression model. However, prior literature has established there should be a minimum of ten participants in the sample per predictor variable for regression analyses with more than six predictor variables to have appropriate power (VanVoorhis & Morgan, 2007). Thus, with a sample of 101 participants, the number of predictor variables needed to be reduced to ten. After reviewing preliminary analyses, race/ethnicity, cancer type (CNS/non-CNS), and time since diagnosis were removed from the models. Race/ethnicity was removed as insurance type remained in the model and can be used to capture race-driven disparities that are typically examined with the inclusion of race as a proxy variable. Additionally, cancer type was removed given treatment focus (CNS/non-CNS), a variable with significant overlap, was included in the models and was more consistently associated with outcomes. Finally, time since diagnosis was removed as the sample was already constrained to three months to three years post-diagnosis and the variable was infrequently correlated with outcomes upon preliminary analysis. Therefore, final predictors were age at diagnosis, sex, insurance type, premorbid diagnosis, focus of treatment, chemotherapy dose, radiation dose, radiation type, complications, and FSIQ.

Missing Data.

Missing data was present for each variable (mean = 21.3%; range = 11.9–51.5%). Little's test (1988) was nonsignificant, suggesting the data satisfied the pattern for missing completely at random (MCAR; $\chi^2 [61] = 62.37, p = .43$). FSIQ, Word Reading, and Numerical Operations measures had the most missing data with 22.8%, 48.5%, and 51.5% missingness, respectively. CVLT scores consisted of 15.8–16.8% missing data, and CBCL measures had 11.9% missing data. To address the amount of missing information, multiple imputation was utilized to estimate the missing data points. Historically, it had been cautioned against using multiple imputation in cases with more than 20% missing data or when data is in a configuration aside from missing at random (MAR; Jakobsen et al., 2017; van Ginkel et al., 2020). However, recent literature has argued that multiple imputation can be utilized in cases of MCAR and when there is up to 63% of data missing without introducing additional bias relative to deletion strategies (Hardt et al., 2013; Hayati Rezvan et al.,

2015; van Ginkel et al., 2020). The use of listwise deletion in the current sample would have greatly reduced the sample size in analyses ($n = 50$), thereby limiting the power. As such, multiple imputation was utilized to retain power in current analyses.

Demographic (age, sex, race/ethnicity, insurance, and premorbid characteristics) and medical variables (cancer type, time since diagnosis, chemotherapy dose, radiation dose, radiation type, treatment focus, and complications) were used as predictors for imputation while neurocognitive measures were utilized as both predictors and imputed for missing values. A total of 55 imputations was selected based on a quadratic rule that incorporates percent of missing data (51.5%) and standard error (0.5), allowing for most precise results (Graham et al., 2007; von Hippel, 2019; von Hippel, 2020). Fully conditional specification method was automatically selected by SPSS given data characteristics. Analyses were then conducted on all imputed data sets, allowing for pooled results.

Results

Participants

Demographic information of participants is presented in Table 1. The sample trended towards male (59.4%), middle childhood at diagnosis ($M = 8.71$; $SD = 3.95$), and public insurance (64.4%). Participants were about evenly split between White and BIPOC groups and presence of premorbid diagnoses. In terms of cancer and treatment characteristics, the sample primarily consisted of those with non-CNS cancer (59.4%), stage 1 cancer (36.6%), CNS-directed treatment (48.5%), and cumulative chemotherapy dose of greater than 250 milligrams (40.6%). There were relatively fewer participants who underwent radiation of any focus point (38.6%). The sample was evenly split between individuals with and without complications.

Table 1
Descriptive Statistics for Sample

Participants	M	SD	Range
Age at Diagnosis (Years)	8.71	3.95	2.00–17.00
Time since Diagnosis (Days)	49.47	268.88	94.00-1094.00
	<i>n</i>	%	
Sex			
Female	41	40.6%	
Male	60	59.4%	
Race			
White	49	48.5%	
BIPOC	52	51.5%	
Insurance			
Private	26	25.7%	
Public	65	64.4%	
No Insurance/Self-Pay	10	9.9%	
Premorbid Diagnosis			
Yes	50	49.5%	
No	51	50.5%	
Cancer Type			
CNS	41	47.5%	
Non-CNS	60	52.5%	
Treatment Focus			
No chemotherapy/radiation	25	24.8%	
CNS	27	26.7%	
Non-CNS	49	48.5%	
Chemotherapy Dose			
No chemotherapy	26	25.7.8%	
Less than 250mg	34	33.7%	
250mg or more	41	40.6%	
Radiation Dose			
No radiation	62	61.4%	
Note. BIPOC= Black, Indigenous, Persons of Color, CNS = Central Nervous System, mg = milligrams, Gy = grays.			

Participants	M	SD	Range
Less than 20Gy	8	7.9%	
20-30Gy	8	7.9%	
More than 30Gy	23	22.8%	
Radiation Type			
No Radiation	61	39.6%	
Photon	28	27.7%	
Proton	12	11.9%	
Complications			
Yes	48	47.5%	
No	53	52.5%	

Note. BIPOC= Black, Indigenous, Persons of Color, CNS = Central Nervous System, mg = milligrams, Gy = grays.

Intellectual Functioning

Multiple linear regression was conducted to examine the accuracy of variables on predicting FSIQ score. The pooled mean FSIQ standard score was 89.08 (SD = 14.62; low average range). The models significantly predicted FSIQ in 36 of the 55 imputation models at the .05 level ($F(9,91) = 1.19-4.44, p < .001-.310$). The significant models accounted for 16.5% to 25.6% of the variance in FSIQ. A summary of pooled regression coefficients is presented in Table 2, which indicated chemotherapy dose was the only variable that consistently contributed to the pooled model. Individual models were reviewed and indicated that complications, radiation dose, insurance type, type of radiation, and premorbid diagnosis also significantly contributed to individual models. Interestingly, review of pooled coefficients of dummy-coded variables suggests presence of complications ($B = 4.91$) and premorbid diagnoses ($B = 2.18$) were associated with higher scores than those without. ANOVAs indicated worse performance among those with no insurance or government insurance ($p < .001$), those who with less than 250 milligrams (mg) of chemotherapy relative to those with more than 250mg ($p < .001$), those who had either type of radiation ($p < .001$), and those who received at least 20 grays (gy) of radiation ($p < .001$).

Academic Functioning

Word Reading

The pooled mean word reading standard score was 87.22 (SD = 22.95; low average range). All models significantly predicted word reading performance ($F(10,90) = 5.44-19.95, p < .001$). The models accounted for 37.7% to 68.9% of the variance in word reading performance. A summary of pooled regression coefficients is presented in Table 2 demonstrating age at diagnosis and FSIQ significantly contributed to the overall model. Review of individual models showed premorbid diagnosis, insurance type, sex, chemotherapy dose, complications, radiation type, and treatment significantly contributed to individual models. Correlations indicate positive correlation with age at diagnosis and FSIQ ($p < .001$). Pooled coefficients indicated worse performance among those with premorbid diagnoses ($B = -7.87$), but slightly better performance among those who experienced complications ($B = 1.58$) and male participants ($B = 5.57$). Significantly worse performance was observed among those with no insurance or government insurance ($p < .001$), those who had less than 250 mg of chemotherapy relative to those with high dose ($p < .001$), those who did not undergo chemotherapy or radiation ($p < .001$) or those who had CNS-directed treatment ($p = .001$) relative to those

with non-CNS focused treatment, and those without radiation treatment or who had photon treatment relative to those with proton treatment ($p = < .001$).

Mathematics

The pooled mean numerical operations standard score was 85.90 ($SD = 18.57$), which falls in the low average range. All models significantly predicted math computation performance ($F(10,90) = 2.82-19.05, p = < .001-.004$). The models accounted for 23.8% to 67.9% of the variance in numerical operations score. A summary of pooled regression coefficients is presented in Table 2 demonstrating age at diagnosis, sex, and FSIQ significantly contributed to the pooled model. Insurance type, premorbid diagnosis, CNS-focused treatment, radiation dose and type, chemotherapy dose, and complications also significantly contributed to individual models. Age at diagnosis and FSIQ were positively correlated with performance ($p = < .05$). Pooled coefficients indicated worse performance among those with premorbid diagnoses ($B = -3.78$) and complications ($B = -.72$) but slightly better performance among male participants ($B = 9.70$). Significantly worse performance was observed among groups with proton treatment ($p = < .001$), more than 30 Gy of radiation ($p = < .001$), less than 250 mgs of chemotherapy ($p = < .001$), any treatment focus relative to no treatment ($p = < .001$), and no insurance ($p = < .001$).

Table 2
Regression Table for Intellectual and Academic Functioning

Variable	FSIQ			Word Reading			Numerical Operations		
	B	SE B	p	B	SE B	p	B	SE B	p
Age	-.18	.44	.683	1.91	.78	.015	1.27	.61	.039
Sex [§]	-1.61	3.36	.631	5.57	.53	.294	9.70	4.57	.035
Insurance	-4.45	2.89	.123	-6.31	5.10	.218	-.26	4.13	.950
Premorbid [§]	2.18	3.64	.549	-7.87	5.18	.130	-3.78	4.77	.430
Treatment	-1.23	2.45	.617	.29	3.61	.936	.49	3.01	.871
Chemo.	5.76	2.45	.019	3.83	3.98	.337	.55	3.31	.869
Radiation	-4.74	3.03	.118	.05	3.96	.990	-6.56	3.87	.092
RadType	2.38	4.15	.567	-3.66	5.87	.534	2.43	5.35	.651
Comp. [§]	4.91	3.46	.156	1.58	5.00	.752	-.78	4.25	.866
FSIQ	--	--	--	.84	.21	< .001	.53	.21	.015
Note. [§] dichotomous variable, Chemo. = chemotherapy dose, Radiation = radiation dose, RadType = type of radiation, Comp. = complications.									

Verbal Memory

Initial Learning

The pooled mean CVLT List A total T-score was 42.69 ($SD = 13.10$; low average range). All models significantly predicted verbal learning and recall ($F(10,90) = 2.24-6.05, p = < .001-.022$). The significant models accounted for 19.9% to 40.2% of the variance in List A total score. A summary of pooled regression coefficients is presented in Table 3 demonstrating sex and FSIQ significantly contributed to the pooled model. Radiation dose and type, chemotherapy dose, premorbid diagnosis, and insurance status were significant contributors to individual models. There was a

positive correlation between FSIQ and List A total T-score ($p < .001$). Pooled coefficients indicated worse performance among male participants ($B = -5.77$) and those with premorbid diagnoses ($B = -3.18$). Significantly worse performance was observed among those with government insurance ($p < .01$), those who experienced more than 30 Gy of radiation ($p < .001$), and those who underwent proton radiation ($p < .001$). No statistically significant differences were observed between varying levels of chemotherapy dose ($p = .473$), likely given this variable was at the cusp of significantly contributing to a few models.

Immediate Recall

The pooled mean CVLT short-delay free recall z-score was $-.70$ ($SD = 1.25$; low average range). The models significantly predicted verbal learning and recall for only eight of the models at the $< .05$ level ($F(10,90) = .78-2.67$, $p = .007-.606$). The significant models accounted for 17.7% to 22.9% of the variance in short-delay free recall score. A summary of pooled regression coefficients is presented in Table 3 demonstrating no single variable significantly contributed to the pooled model. However, review of individual significant models indicated FSIQ and age significantly contributed to the individual models. Correlations indicate positive correlation with FSIQ ($p < .05$), but negative correlation with age at diagnosis ($p < .05$).

Delayed Recall

The pooled mean CVLT long-delay free recall z-score was $-.61$ ($SD = 1.27$; average range). Twelve of the models significantly predicted delayed recall at the $< .05$ level ($F(10,90) = .68-2.66$, $p = .007-.738$). The significant models accounted for 18.4% to 22.8% of the variance in long-delay free recall score. A summary of pooled regression coefficients is presented in Table 3 demonstrating no single variable contributed to the pooled model. Review of individual significant models indicate FSIQ was the only significant contributor across models. FSIQ was positively correlated with CVLT long-delay z-score ($p < .001$).

Discriminability

The pooled mean CVLT discriminability z-score was $-.53$ ($SD = 1.65$; average range). Forty-three models significantly predicted discriminability at the $< .05$ level ($F(10,90) = 1.34-4.88$, $p < .001-.221$). The significant models accounted for 17.7% to 35.2% of the variance in discriminability score. A summary of pooled regression coefficients is presented in Table 3 demonstrating chemotherapy dose and FSIQ significantly contributed to the pooled model. Insurance type, treatment focus, age at diagnosis, and premorbid diagnosis also significantly contributed to individual models. Correlations indicate significant positive correlation FSIQ ($p = .002$), but non-significant negative correlation with age at diagnosis ($p = .435$). Pooled coefficients indicated worse performance among those with premorbid diagnoses ($B = -.309$). Significantly worse performance was observed among those with government insurance ($p < .001$), those who received less than 250mg of chemotherapy relative to higher dose ($p < .001$), and those who did not undergo chemotherapy or radiation or those who had CNS-directed treatment relative to those with non-CNS focused treatment ($p = .001$).

Table 3
Regression Table for Verbal Memory

Variable	Total			CVLT Short			CVLT Long			CVLT Discrim.		
	B	SE B	p	B	SE B	p	B	SE B	p	B	SE B	p
Age	.28	.39	.466	-.06	.04	.154	-.00	.04	.910	-.01	.05	.803
Sex [§]	-5.77	2.91	.047	-.19	.29	.551	-.08	.30	.793	-.19	.38	.612
Insurance	1.46	2.51	.560	-.10	.25	.678	.05	.26	.843	.12	.32	.712
Premorbid [§]	-3.18	2.96	.283	-.14	.29	.617	.08	.30	.791	-.31	.39	.425
Treatment	1.46	2.18	.503	.04	.23	.869	.01	.23	.958	-.31	.27	.250
Chemo.	-2.39	2.34	.307	.14	.24	.570	.10	.24	.691	.62	.29	.033
Radiation	-3.32	2.41	.169	-.02	.24	.922	.16	.25	.518	.02	.31	.954
RadType	5.03	3.31	.129	-.20	.32	.528	-.34	.33	.307	-.09	.41	.821
Comp. [§]	.26	2.95	.929	-.05	.30	.871	-.21	.31	.498	.24	.37	.515
FSIQ	.38	.12	.001	.01	.01	.317	.03	.01	.052	.03	.02	.034
Note. [§] dichotomous variable, Chemo. = chemotherapy dose, Radiation = radiation dose, RadType = type of radiation, Comp. = complications, CVLT Discrim. = CVLT Discriminability Score.												

Emotional and Behavioral Functioning

Externalizing Behaviors

The pooled CBCL Externalizing T-score was 51.36 ($SD = 12.42$; normal range). Forty-two models significantly predicted parent-reported externalizing symptoms at the $< .05$ level ($F(10,90) = 1.24-3.31, p = .001-.275$). The significant models accounted for 17.8% to 26.9% of the variance in CBCL Externalizing score. A summary of pooled regression coefficients is presented in Table 4 demonstrating no single variable significantly contributed to the pooled model. FSIQ, premorbid diagnosis, sex, insurance type, age at diagnosis, chemotherapy dose, treatment focus, and complications were significant contributors to individual models. Correlations indicate non-significant positive correlation with FSIQ ($p = .170$) and non-significant negative correlation with age at diagnosis ($p = .078$). Pooled coefficients indicated increased complaints among those with premorbid diagnoses ($B = 4.50$) and male participants ($B = 4.54$), and fewer among those with complications ($B = -3.55$). Significantly more symptoms were reported among those with no insurance ($p = .011$), and those who experienced any amount of chemotherapy ($p = < .001$) or CNS-focused treatment ($p = < .01$).

Internalizing Symptoms

The pooled mean CBCL Internalizing T-score was 54.54 ($SD = 13.27$; normal range). Ten of the models significantly predicted internalizing symptoms at the $< .05$ level ($F(13,87) = 1.19-2.30, p = .019-.306$). The significant models accounted for 17.8% to 20.4% of the variance in CBCL Internalizing score. A summary of pooled regression coefficients is presented in Table 4 demonstrating that no single variable significantly contributed to the pooled model. FSIQ and insurance status significantly contributed to individual models. There was a non-significant positive correlation with

FSIQ and Internalizing score ($p = .073$) and significantly more symptoms were reported among those with no insurance ($p = < .001$).

Table 4
Regression Table for Emotional and Behavioral Functioning

Variable	External			Internal			Total Problems		
	B	SE B	p	B	SE B	p	B	SE B	p
Age	– .54	.37	.147	.24	.40	.545	– .12	.41	.770
Sex [§]	4.54	2.79	.104	2.91	2.95	.324	3.91	3.04	.199
Insurance	4.32	2.33	.060	4.49	2.51	.073	3.91	2.56	.127
Premorbid [§]	4.50	2.67	.092	3.46	2.92	.237	5.52	2.97	.063
Treatment	-2.50	2.07	.228	-3.32	2.23	.137	-4.29	2.27	.059
Chemo.	2.50	2.12	.240	3.60	2.27	.113	3.66	2.33	.116
Radiation	.81	2.47	.742	2.12	2.67	.427	.99	2.69	.712
RadType	-1.15	3.20	.718	-2.34	3.56	.512	-1.69	3.56	.635
Comp. [§]	-3.55	2.77	.201	-2.76	3.06	.399	-4.28	3.11	.168
FSIQ	.12	.11	.295	.12	.12	.317	.12	.12	.329
Note. § = dichotomous variable, Chemo. = chemotherapy dose, Radiation = radiation dose, RadType = type of radiation, Comp. = complications.									

Total Problems

The pooled mean CBCL Total Problems T-score was 53.08 ($SD = 13.69$; normal range). Thirty-eight of the models significantly predicted emotional and behavioral problems at the $< .05$ level ($F(10,90) = 1.40–2.63$, $p = .007–.193$). The significant models accounted for 17.7% to 22.6% of the variance in CBCL Total Problems score. A summary of pooled regression coefficients is presented in Table 4 demonstrating no single variable significantly contributed to the pooled model, though treatment focus and premorbid diagnosis approached significance. Treatment focus and premorbid diagnosis, as well as sex, insurance status, chemotherapy dose, complications, and FSIQ significantly contributed to individual models. There was a non-significant positive correlation with FSIQ ($p = .073$). Pooled coefficients indicated increased complaints among those with premorbid diagnoses ($B = 5.52$) and male participants ($B = 3.91$) and fewer complaints among those who experienced complications ($B = -4.28$). Significantly more symptoms were reported among those with no insurance ($p = < .001$), more than 250mg of chemotherapy ($p = < .001$), or non-CNS treatment ($p = < .001$).

Discussion

The current study examined the predictive ability of demographic, cancer, and treatment variables on intellectual, academic, cognitive, and emotional/behavioral outcomes within the first three years of a childhood cancer diagnosis. Consistent with existent literature, mean scores across all domains fell in the low average to average or non-clinical range. Among intellectual, academic, and cognitive measures, cancer and treatment-related variables were often predictive, whereas demographic variables appeared to more frequently predict emotional/behavioral outcomes. Of note, our sample had a slightly lower mean FSIQ ($M = 89.08$; $SD = 14.62$) compared to other published samples that

tend to have an average intellectual ability around the low 90's. Nonetheless, FSIQ was the primary driver of predictive ability across models, particularly for models of academic and verbal memory abilities, which is consistent with prior literature. Specifically, FSIQ was negatively correlated with performance on cognitive and academic measures but positively correlated with emotional/behavioral symptoms.

Among demographic variables, age, sex, insurance type, and premorbid diagnosis contributed to models, though less consistently than FSIQ, which is consistent with the mixed literature regarding the impact of these variables. These findings might offer insight and explain why some studies demonstrate significant findings while others report null results. Potentially, since these variables account for a small amount of the variance, impacts such as increased error variance, sampling variability, and reduced power to detect true effects, can lead to inconsistent findings across studies (Cohen, 1988; Kline, 2011).

However, in the current study, multiple imputation was used to fill in missing values and allow for the inclusion of all 101 participants. This method is a statistical strength and addresses several of the noted impacts of small variance of demographic variables. Primarily, the inclusion of all participants enhanced statistical power and reduced bias in the sample. Further, these benefits can increase the ability to detect true effects. Additionally, the use of 55 imputed datasets reduces the impact of sampling variability and accounts for missing data (Rubin, 1996). Further, by considering variability and missing data, the influence of measurement error is averaged across datasets (Graham, 2009; Little & Rubin, 2019). Together, these allow for more stable and reliable results.

In this sample, older age at diagnosis was related to better academic outcomes but was less frequently correlated with fewer emotional/behavioral symptoms and poorer verbal memory performance. Sex was also mixed in terms of neurocognitive outcomes but consistently indicated more emotional/behavioral concerns among males. Insurance type also played a less frequent role across models, but lack of insurance or government insurance indicated worse outcomes when significant. In contrast, at least one premorbid diagnosis was frequently associated with poorer outcomes across domains.

In terms of cancer and treatment-related variables, chemotherapy dose was most consistently associated with outcomes. Interestingly, 250mg or less of cumulative dose was associated with poorer cognitive outcomes, but more than 250mg was associated with worse emotional/behavioral outcomes. More uniformly, more than 20 Gy of radiation dose was associated with poorer cognitive performance. However, the impact of type of radiation was infrequently predictive and remained mixed, consistent with extant literature. The focus of treatment was variably predictive of outcomes. Notably, either lack of treatment or CNS-directed treatment was associated with poorer cognitive performance, while the impact of non-CNS directed treatment was less salient. Finally, the presence of complications was inconsistently predictive of worse outcome. Paradoxically, there were fewer reported externalizing and total emotional and behavioral complaints among those with complications. This could potentially be explained by the severity of health consequences negatively impacting a child's ability to interact with peers and the environment but remains an area for research.

Limitations

Despite several strengths, including use of multiple imputation, a diverse sample, and novel exploration of outcomes within three months to three years post-diagnosis, there are limitations to the current study. First, the current study used archival data from a clinical dataset without standardized test battery or administration time. Therefore, concern could be raised for selection bias and reduced generalizability as well as the limitations imposed by cross-sectional retrospective data. The use of archival data from a clinical dataset also resulted in some variables, particularly academic achievement, missing significant amounts of data. Although missing data was addressed using multiple

imputation in a manner supported by prior research, this could reduce the reliability of the results. Additionally, given the number of predictor variables included in the analyses, several of the variables were collapsed into combined categorical variables. These variables were combined in accordance with prior literature, but this approach could have reduced the sensitivity and analyses and ability to explore nuance. Additionally, the only measurement of emotional and behavioral functioning was parent-report, which could be biased.

Clinical Implications and Future Directions

These findings reinforce the need for evaluations for childhood cancer patients planning to return to school. However, given the busyness of a clinical setting, there is emphasis on the need for efficiency and maximized utility. As indicated by current findings and prior research, intellectual ability largely drives school performance. Additionally, an abbreviated measure can be administered in 30 minutes or less and can serve as a valuable screening tool in fast-paced clinical settings. Therefore, clinicians may wish to prioritize brief intellectual assessments in these situations.

Furthermore, it has been well-established that childhood cancer survivors have poorer educational and vocational outcomes relative to their peers. As such, interventions to minimize the negative impact and lead to more equivalent outcomes between patients and their peers are needed. Given the current findings, cognitive evaluations for survivors planning to return to school is strongly indicated. Such assessments are crucial to informing appropriate interventions for children based on their unique strengths and weaknesses, allowing for the development of a personalized Individualized Education Plan or 504 Plan. In turn, this additional, individualized support may allow the child to be more successful throughout their schooling and lead to improved long-term outcomes. Therefore, to address gaps in outcomes, clinicians across disciplines should advocate for childhood cancer patients to receive back-to-school cognitive evaluations and subsequent accommodations as part of the standard of care.

Future research could seek to replicate these findings in a larger sample to explore these outcomes with increased power and precision. Further studies may utilize a longitudinal approach to further elucidate the impact of the examined predictor variables on outcomes and provide insight into the comparison between evaluation and actual classroom performance and behavior. These findings could also inform creation of guidelines for standardized return to school assessments and planning. Finally, given the continued uncertainty of which aspects of variables are more harmful and novel findings regarding the impact of chemotherapy dose, complication, premorbid diagnosis, and focus of treatment, continued study of these variables in long-term follow-up could clarify these relationships and risk factors for poor outcome.

Declarations

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Ethical Approval

Informed Consent Statement

Specific Consent for Publication

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

Author Contribution

All authors contributed to the study conception and study design. Lauren Frick: Conceptualization, Methodology, Investigation, Formal Analysis, Writing – Original Draft. Julie Schumacher: Data Curation, Methodology, and Writing – Review & Editing and Supervision. Dinan Noor: Conception, Formal Analysis, Writing- Review and Editing. Cynthia Karlson: Supervision, Project Administration, Writing – Review & Editing. All authors approved the final manuscript.

Data Availability Statement

To protect participant privacy, study data are not publicly available. However, data access and analytical code requests sent to the corresponding author will be considered and honored to the extent possible.

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