Childhood Cancer Survivor Study (CCSS)
Concept Proposal

Title:
Neighborhood Socioeconomic/Environmental Disadvantage and Neurocognitive and Psychosocial Outcomes in CCSS Survivors

Working Group:
Psychology (Primary)
Cancer control (Secondary)
Epidemiology and Biostatistics (Secondary)

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1. Background and Rationale

With the increase in overall 5-year survival rate for childhood cancer, there are over 500,000 adult survivors of childhood cancer currently in the US.[1,2] The advanced treatment modalities (e.g., chemotherapy, radiation therapy, immunotherapy, and biological treatments) and associated supportive care services have significantly improved survival of childhood cancer to above 80%, though survival is often accompanied by late effects.[1,3,4] Survivors are at increased risk of adverse health outcomes compared with siblings or healthy peers.[1] These include higher frequency and severity of chronic health conditions and subsequent malignancies,[3,5,6] higher symptom prevalence (e.g., depression and social withdrawal) and distress,[7] and neurocognitive dysfunction.[4,8,9] Additionally, adult survivors of childhood cancer report poorer overall health or well-being and health-related quality of life (QOL).[8,10] In addition to these direct effects of treatment and physical chronic health conditions neighborhood factors can impact the development or progression of psychosocial and neurocognitive outcomes among survivors of childhood cancer.

In the general population, the role of socioeconomic status on individual outcomes has been well studied, including lower educational attainment, poverty, unemployment, and lack of health insurance.[8,9,11] These adverse factors increase the risk of psychosocial burden and decrease QOL.[12-14] Recent work suggests there could be significant contributions from neighborhood socioeconomic and environmental deprivation (characterized by concentration of impoverished, less educated people, and by poor living conditions[15,16]) to cancer treatment-related outcomes, as well as relapse and second malignancy.[15] The underlying pathways of neighborhood deprivation contributing to adverse cancer outcomes may include material deprivation, physiological/psychosocial stressors, toxic and harmful exposures, limited resources for healthy behaviors, and less access to routine health care.[15,16] Additionally, neighborhood deprivation may promote harmful biological responses, including stress reactivity and inflammation, epigenetics alterations, and shortened telomere length, all of which can lead to poor cancer outcomes.[17]

Area-based measures, such as the Yost index and area deprivation index (ADI), have been used to capture neighborhood deprivation that is distinct from individual-level risk.[18] Although both indexes have limitations, the ADI is used in somewhat wider than the Yost Index.[19] In the adult cancer literature, studies have reported negative associations between adverse neighborhood socioeconomic conditions and cancer incidence (mostly breast and gastrointestinal cancers) [15] and cancer stage.[20,21] Recently, Unger et al.[22] further found that high area-level socioeconomic deprivation (assessed by the ADI) was associated with worse overall, progression-free, and cancer-specific survival, even after adjusting for insurance status, prognostic risk, and rural or urban residency. Adolescent and young adult survivors of Hodgkin lymphoma living in low socioeconomic neighborhoods were found to have higher frequency of respiratory and endocrine diseases.[23] In addition, neighborhood environmental deprivation has wide social, economic, and health implications, particularly indicating geographical inequalities in health.[24-26] For example, air pollution (e.g., fine particulate matter [$PM_{2.5}$], nitric oxide, nitrogen dioxide, and sulfur dioxide) shows the highest environmental risk for the poor [24] or deprived neighborhoods.[27] Both animal[28] and clinical studies[29-31] revealed that air pollution may cause decline of neurocognitive status (e.g., cognition) by triggering neuroinflammations and decreasing integrity tight junction proteins in the blood-brain barrier, as well as influence psychological outcomes (e.g., depressive symptoms and suicidal ideation) among cancer survivors.[32] Neighborhood environmental factors, such as air pollution (i.e., $PM_{2.5}$, nitrogen oxides, and sulfur dioxide), were associated with greater odds of cancers[15,33] and lung health conditions including asthma, respiratory infections, and pulmonary fibrosis.[34,35] Importantly, caregivers worried about potential effects of environmental deprivation (e.g., air pollution) on survivor health and wanted more information.[36] Due to very limited evidence, understanding the impact of neighborhood environmental factors on neurocognitive and psychosocial outcomes is critically needed for childhood cancer survivors.

The impact of neighborhood socioeconomic/environmental deprivation on neurocognitive and psychosocial outcomes in adult survivors of childhood cancer has not been systematically evaluated. Current work in adult cancer survivors rarely examines outcomes of associations with cancer therapy; additionally, the directions and magnitudes of associations between neighborhood socioeconomic/environmental deprivation and cancer vary because of differences in study populations, geographic regions, and choice of neighborhood measures and geographic scales.[15] To address these research gaps, we propose using data from the Childhood Cancer Survivor Study (CCSS) merged with ZIP code specific measures of socioeconomic and environmental deprivation to describe the neighborhood socioeconomic/environmental deprivation among adult survivors of childhood cancer and study associations between neighborhood socioeconomic/environmental deprivation and neurocognitive and psychosocial outcomes. **This study will allow us to identify characteristics that place survivors at increased risk and inform strategies to enhance long-term surveillance and care**. Three Specific Aims are proposed:

Aim 1: To describe the neighborhood socioeconomic/environmental deprivation (or disadvantage) in CCSS long-term adult survivors of childhood cancer from **both the original and expansion cohorts**. With the help of GeoLytics, all the neighborhood deprivation indices will be coded by our team by using survivors' home address and ZIP codes.

- **1a:** Describe the neighborhood socioeconomic disadvantage assessed by the area deprivation index (ADI; defined by 17 ADI sub-scores for the theoretical domains of income, education, employment, and housing quality) in CCSS survivors.
- **1b:** Describe the neighborhood environmental disadvantage using NASA Satellite-based measures of fine particulate matter, nitrogen oxides, and sulfur dioxide in CCSS survivors.

Aim 2: To examine cross-sectional associations of neighborhood socioeconomic and environmental deprivation with patient-reported neurocognitive and psychosocial outcomes (i.e., emotional distress and QOL) from **the expansion CCSS cohorts**, adjusting for relevant treatment exposures and other covariates. This aim will also assess associations between neighborhood socioeconomic/environmental deprivation and these patient-reported outcomes. In line with previous research,[12-14] we hypothesize that a

higher neighborhood socioeconomic and environmental deprivation will be associated with poorer neurocognitive, emotional and QOL outcomes.

Exploratory Aim 3: To explore the longitudinal associations between baseline neighborhood socioeconomic/environmental deprivation and patient-reported symptoms (i.e., anxiety, depression, and somatization) using a subset of data (at Baseline and Follow-up 5) from **the expansion CCSS cohorts**, adjusting for relevant treatment exposures.

2. Theoretical Framework

Evidence has supported that neighborhood social (e.g., socioeconomic, crime, resident population) and environmental factors (e.g., pollution) affect health as much as the individual factors of residents themselves.[15,37] Gomez et al. have created a theoretical framework to understand the impact of neighborhood social environment on the cancer continuum.[15] We adapted Gomez et al.'s theoretical framework[15] to study associations between neighborhood socioeconomic/environmental deprivation and neurocognitive and psychosocial outcomes cancer survivors **(Figure 1)**. We will also explore the longitudinal associations between neighborhood socioeconomic/environmental deprivation and patient-reported symptoms using a subset of data from the expansion CCSS cohort.

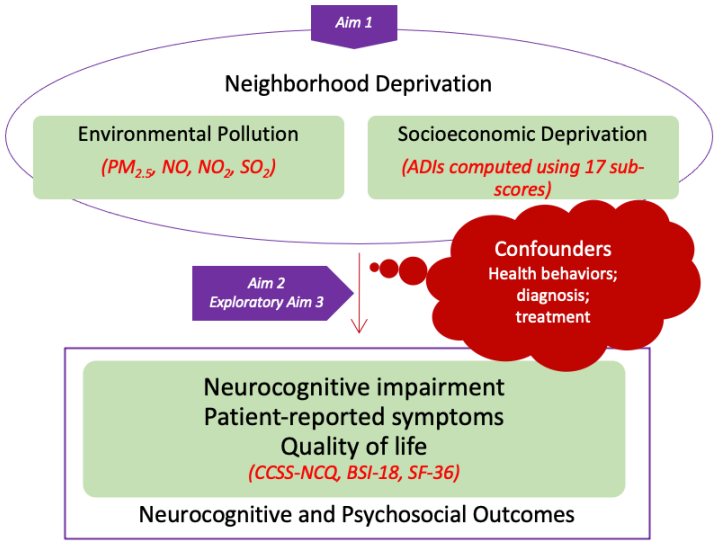

Figure 1. Research Framework

ADI, area deprivation index; BSI, Brief Symptom Inventory; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire; SF-36, Medical Outcomes Short-Form-36

3. Analysis Framework

3.1 Study Population

All adult survivors of childhood cancers who completed the Follow-up 2 survey from the original and Follow-up 5 survey from the expansion CCSS cohorts will be included for **Aim 1** *(descriptive analysis)*. All adult survivors of childhood cancers who completed Follow-up 5 survey from the expansion CCSS cohorts will be included for **Aim 2** *(cross-sectional)*. We selected these CCSS cohort data due to its nationally geographic representation of adult cancer survivors of pediatric cancer and the collection of patient-reported outcomes. The subset of adult survivors of childhood cancers with Baseline and Follow-up 5 data from the CCSS expansion cohort will be used for an **Exploratory Aim 3** *(longitudinal)*.

3.2 Data Sources

The Follow-up 2 survey from the original and the Follow-up 5 survey from the expansion CCSS cohorts will be used for a cross-sectional analysis (*Aim 1*). The Follow-up 5 dataset from the expansion CCSS cohorts will be used for *Aim 2*. Baseline and Follow-up 5 dataset from the CCSS expansion cohorts will be used for a subset longitudinal analysis (*Exploratory Aim 3*).[38] The NASA Satellite-based pollution data and the Census data from American Community Survey (ACS) will be obtained, coded, or used to compute neighborhood socioeconomic/environmental deprivation measures using the home address data or ZIP code from the CCSS cohorts.

3.3 Variables and Measures

3.3.1 Independent Variables

3.3.1.1 Neighborhood environmental variable: As an exploratory study, neighborhood environmental deprivation will focus on NASA Satellite-based pollution measures (fine particulate matter [PM 2.5], nitrogen oxides [NOx], and sulfur dioxide [SO_2]). All continuous variables will be obtained

from NASA Socioeconomic Data and Applications Center (SEDAC). Detail resources of data can be found at https://sedac.ciesin.columbia.edu/data/set/aqdh-pm2-5-concentrations-contiguous-us-1-km-2000-2016 [39] and https://www.nature.com/articles/s41597-021-00891-1.[40] The resolution will be at an resolution of 1 km to estimate short- and long-term effects on human health. We will extract the CCSS survey year PM 2.5, NOx, and SO_2 data around the date when Follow-up 2 data were collected in the original cohorts or Follow-up 5 data were collected in the expansion cohorts. For each pollution parameter, we will obtain the maximum, minimum, mean, stand deviation, and variance annually ($PM_{2.5}$) or 3-year average (NOx, and SO_2) based on the survey year. A subset of longitudinal data will also be created using the ZIP code of CCSS expansion cohort. For the survivor lived in different zip codes at times of completion of the Baseline and Follow-up 2 or Follow-up 5 surveys, we will create another category which will be considered in analysis. These environmental indices will be coded by our team member Dr. Qi Zhang, an expert in geospatial data coding and analysis and with great expertise and experience of deriving and using air pollution indicators. All the NASA environmental data coded will align with CCSS survey years.

3.3.1.2 Neighborhood socioeconomic variable: Neighborhood socioeconomic deprivation will be assessed using the area deprivation index (ADI), calculated from the American community survey (ACS). Singh et al. created a composite measure of neighborhood socioeconomic deprivation for the United States - the ADI.[41,42] Compared with the Yost Index (using 7 sub-scores), the ADI is a factor-based index which uses 17 U.S Census income, education, employment, and housing indicators **(see Table right)** to characterize Census-based regions. It has been associated with a number of health outcomes, including cardiovascular diseases, childhood mortality, and adult cancer prevalence.[41-43] It has been rigorously tested, is inclusive of all US neighborhoods and is regularly updated. The ADI measure is scored from 0 to 100, with higher scores indicating greater neighborhood socioeconomic deprivation. According to Kind's work,[44] we will extract the 17 ADI sub-scores based on ACS 5-year summary data. We will align census data with survey years of CCSS participants. The ADI indicators will be coded by Geolytics and then the ADI will be calculated by our team at Emory. All the calculated ADIs will be matched with patients' ZIP codes. We have a protocol to extract the ACS data and compute the ADI variable based on our completed project.[45] For these already existing ADIs for 2015 and 2019, we will use them if they match with our data collection timepoints (e.g., Follow-up 5) based on personal communication with Drs. Kiri Ness and Carrie Howell (PI of the CCSS concept proposal 20-07). Based on recent studies, the ADI measure will be split into quintiles; and the most deprived patients are defined as those in the highest ADI quintile (81%-100%) and the most affluent were patients in the lowest ADI quintile (0%-20%).[46-48] A higher neighborhood percentile means more disadvantaged neighborhood.

Area Deprivation Index
1. % of the block group's population aged ≥ 25 years with < 9 years of education
2. % aged ≥ 25 years with greater than or equal to a high school diploma
3. % of employed persons ≥16 years of age in white-collar occupations
4. Median family income
5. Income disparity †
6. Median home value
7. Median gross rent
8. Median monthly mortgage
9. % owner-occupied housing units (home ownership rate)
10. % of civilian labor force population ≥ 16 years of age unemployed
11. % of families below the poverty level
12. % of population below 150% of the poverty threshold
13. % of single-parent households with children < 18 years of age
14. % of occupied housing units without a motor vehicle
15. % of occupied housing units without a telephone
16. % of occupied housing units without complete plumbing (log)
17. % of occupied housing units with more than one person per room (crowding)
† Income disparity defined by Singh as the log of 100*ratio of number of households with <$10K income to number of households with $50K+ income.

3.3.2 Dependent Variables - Patient-reported outcomes (Aims 2 and 3)

3.3.2.1 Neurocognitive impairment will be assessed with the Childhood Cancer Survivor Study Neurocognitive Questionnaire (CCSS-NCQ). The CCSS-NCQ was developed to screen for neurocognitive impairments in the CCSS population.[49] Participants rated 19 items on a Likert scale with three possible responses: "Never a problem" (score = 1), "Sometimes a problem" (score = 2) and "Often a problem" (score = 3). Four factor scores were derived from these items, including Task Efficiency, Emotional Regulation, Organization, and Memory. The neurocognitive impairment is defined as T-score ≥ 63.

3.3.2.2 Psycho-physiological symptoms will include pain, anxiety, depression, and somatization. The last 3 domains will be based on the Brief Symptom Inventory–18 (BSI-18).[50] Each item is scored using a five-point scale to measure how much they have been bothered by the symptom in the past week. Scores on the 18 items are summarized on the Global Severity Index (GSI). The BSI-18 includes three domains: somatization (6 items), depression (6 items), and anxiety (6 items). Raw scores on the BSI-18 are converted to T-scores based on gender-specific normative data from community-dwelling US adults.[51] All the symptom scores will be reported as a continuous variable. Additionally, the BSI-18 scales of anxiety, depression, and somatization (impairment defined as T-score ≥ 63) will be examined in separate models.

3.3.2.3 QOL will be measured using the Medical Outcomes Short-Form-36 (SF-36),[52] including questions regarding general health/well-being and QOL over the past 4 weeks. The SF-36 yields eight subscales and two summary scores: mental component summary (MCS) and physical component summary (PCS) (impairment defined as T-score ≤ 40). The summary T-scores have a mean = 50 and SD = 10, where higher T-scores represent poorer health.

3.3.3 Covariates

3.3.3.1 Sociodemographic variables: Sex (male vs female); race/ethnicity (White non-Hispanic [NH], Hispanic, African American NH, others); age at diagnosis (0-4 yrs., 5-9 yrs., 10-14 yrs., and 15-20 yrs.); age at follow-up (<25 yrs., 25-34 yrs., 35-44 yrs., 45-54 yrs., ≥55 yrs.); years since diagnosis; health insurance status (Yes vs No); Household Income in $ (<20,000, 20,000-39,999, 40,000-59,999, 60,000-79,999, 80,000-99,999, ≥100,000); Educational attainment (< college degree vs ≥ college degree); Marital Status (Never married vs Ever married); Lives independently (Yes vs No); Employment (Unemployed vs Employed). A category of "NA" will be created for some of these variables not appropriate for participants younger than 25 years.

3.3.3.2 Cancer diagnosis and treatment exposures: Cancer diagnosis will include leukemia; Hodgkin lymphoma; non-Hodgkin lymphoma; brain tumor; soft tissue sarcoma; bone tumor; neuroblastoma; and Wilms' tumor. Treatment exposures will include specific chemotherapy agents (yes vs no for MTX, Cytarabine, Anthracyclines, Alkylating agents; CNS radiation therapy (yes vs no); other radiation therapy (yes vs no).

3.3.3.3 Other clinical variables*:* BMI (underweight < 18.5 kg/m2, normal 18.5–24.9 kg/m^2, overweight 25.0–29.9 kg/m^2, Class 1 obese 30–34.9 kg/m^2, Class 2 obese 35–39.9 kg/m^2, Class 3 obese ≥ 40 kg/m^2); physical activity (meeting CDC requirements for weekly moderate/strenuous activity, Yes vs No); smoking (never, past, current). Clinical variables will be extracted following the same timepoints of outcome variables.

3.4 Analytic Approaches

All analysis will be carried out using the SAS statistical software version 9.4 (SAS Institute, Cary, NC) and R studio. Missing data will be excluded: if the proportion of missing is high, we will either include a "missing" category or use multiple imputation methods employed in the CCSS studies previously to minimize bias. **Table 1** will provide descriptive statistics of the study population including sociodemographic characteristics, such as age at survey, sex, race/ethnicity, BMI, physical activity, marital status, household income, health insurance status, living independently, employment, and educational attainment. **Table 2** will display the diagnosis and treatment-related variables including diagnosis, radiation therapy and chemotherapy.

3.4.1 Aim 1: Descriptive statistics will be used for the ADI continuous scores and categories (the most disadvantaged 20% vs. the remaining 80%), and continuous pollution measures (PM2.5, NO, NO_2,

and SO_2), see **Table 3.** Based on Kind's study,[44] the most disadvantaged neighborhoods will make up the top 20% of the ADI distribution. The remainder of 80% neighborhoods will be grouped into a comparison category. The ADI will be analyzed by quintiles as well. The associations between different levels of ADI score (top 20% vs the remaining 80%) and sociodemographic and clinical variables will be explored using analysis of variance (ANOVA) and Chi-square tests, see **Table 4**.

3.4.2 Aim 2: Neurocognitive and Psychosocial outcomes will be continuous and binary variables. **Table 5** will provide descriptive statistics of outcomes among the survivors at Follow-up 5. Multiple linear regression analysis will be used with the overall symptoms score as a dependent variable. **Table 6 a-d** will describe the linear regression models of CCSS-NCQ domains, including Task Efficiency **(6a)**, Emotional Regulation **(6b)**, Organization **(6c)**, and Memory **(6d)**, respectively. Logistic regression will be used for suicidality, BSI-18 (T score ≥63 vs. T score <63), SF-36 (T score ≤40 vs T score >40) and CCSS-NCQ (T score ≥63 vs T score <63) outcomes, see **Table 7. Tables 8 a-d** shows the linear regression models of patient-reported symptoms: pain **(8a)**, somatization **(8b)**, anxiety **(8c)**, and depression **(8d)**. **Table 9 a-b** will describe the linear regression models of QOL MCS **(9a)** and PCS **(9b)** scores. Independent variables will include ADIs, $PM_{2.5}$, NO, NO_2, and SO_2. Covariates will include treatment exposures (e.g., radiation therapy, alkylating agents), BMI, age at diagnosis, sex, and race. Collinearity diagnostics will be conducted by means of the variance inflation factor (VIF) for each independent variable. The VIF will be used to determine whether individual models will be run for ADI and pollution indices.

3.4.3 Exploratory Aim 3: Linear regression analysis of the changes in the patient-reported symptoms (i.e., pain, GSI, and three domains of BSI-18) from Baseline to Follow-up 5 in the expansion CCSS cohort will be used to explore associations between baseline socioeconomic and environmental deprivation and longitudinal changes of symptoms. Similarly, the VIF will be used to determine whether individual models will be run for ADI and pollution indices.

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Table 1. Sociodemographic and Clinical Characteristics (n =)

	n (%) or Mean (SD)
Sex, n (%)	
Male	
Female	
Race/Ethnicity, n (%)	
White, NH	
Black, NH	
Hispanic	
Others (e.g., Asian, Native American/Pacific Islander)	
Unknown	
Age at diagnosis in year, mean (SD)	
Age at diagnosis, n (%)	
0-4	
5-9	
10-14	
15-20	
Year of diagnosis, n (%)	
1970-79	
1980-89	
1990-99	
Age at follow-up in year, mean (SD)	
Age at follow-up, n (%)	
<25	
25-34	
35-44	
45-54	
≥55	
Marital Status	
Never married	
Ever married	
NA	
BMI, mean (SD)	
BMI, n (%)	
Underweight	
Normal	
Overweight	
Obesity Class	
Physical activity based on CDC criteria	
Yes	
No	
Smoking	
Never	
Past	
Current	
Socioeconomic status, n (%)	
Health Insurance status	
Yes	

No	
Household Income ($)	
<20,000	
20-39,999	
40-59,999	
60-79999	
80-99999	
≥100,000	
Living independently	
Yes	
No	
NA	
Employment	
Unemployed	
Employed	
NA	
Educational attainment	
≥ college degree	
< college degree	
NA	

Table 2. Diagnosis and Treatment Characteristics (n =)

	n (%)
Diagnosis, n (%)	
Leukemia	
Brain tumor	
Hodgkin lymphoma	
Non-Hodgkin lymphoma	
Wilms' tumors	
Bone tumor	
Sarcoma	
Neuroblastoma	
Other tumors	
CNS radiation therapy received, n (%)	
None	
0 to <20 Gy	
20 to <30 Gy	
30 to <50 Gy	
≥50 Gy	
Other radiation therapy	
Yes	
No	
Chemotherapy, n (%)	
None	
MTX	
Cytarabine	
Anthracyclines	

Alkylating agents	
Chemotherapy + Radiation Therapy, n (%)	
Yes	
No	

Table 3. Descriptions of Neighborhood Socioeconomic/Environmental Deprivation (n =)

	Follow-up 2 (n =)	Follow-up 5 (n =)
ADI Score		
Mean (SD)		
20% vs. 80% (Mean [SD])		
Environmental Deprivation		
PM 2.5 (Mean [SD])		
NO (Mean [SD])		
NO_2 (Mean [SD])		
SO_2 (Mean [SD])		

ADI, Area Deprivation Index; SD, standard deviation

Table 4. Associations between Levels of National ADI Ranking and Sociodemographic and Clinical Variables (n =)

	ADI Grouping of the Survivors' Neighborhood of Residence		
	Follow-up 2 or Follow-up 5		
Demographic and Clinical Variables	Least Disadvantage 80% (n=) %	Most Disadvantage 20% (n=) %	P
Sex, n (%)			
Male			
Female			
Race/Ethnicity, n (%)			
White, NH			
Black, NH			
Hispanic			
Others (e.g., Asian, Native American/Pacific Islander)			
Unknown			
Age at diagnosis, n (%)			
0-4			
5-9			
10-14			
15-20			
Year of diagnosis, n (%)			
1970-79			
1980-89			
1990-99			

Marital Status			
Never married			
Ever married			
NA			
BMI, n (%)			
Underweight			
Normal			
Overweight			
Obesity			
Physical activity based on CDC criteria			
Yes			
No			
Smoking			
Never			
Past			
Current			
Socioeconomic status, n (%)			
Health Insurance status			
Yes			
No			
Household Income ($)			
<20,000			
20-39,999			
40-59,999			
60-79999			
80-99999			
≥100,000			
Living independently			
Yes			
No			
NA			
Employment			
Unemployed			
Employed			
NA			
Educational attainment			
≥ college degree			
< college degree			
NA			

ADI, Area Deprivation Index; NA, not applicable

Table 5. Description of Cognitive Impairment, Symptoms, and QOL (n =)

	Follow-up 5
CCSS-NCG	
Task Efficiency	
Emotional Regulation	
Organization	

Memory	
Total CCSS-NCG Score	
CCSS-NCG category, n (%)	
≥ 63	
<63	
Symptoms, mean (SD)	
Somatization	
Anxiety	
Depression	
Pain	
BSI category, n (%)	
≥ 63	
<63	
QOL	
Physical Component Summary	
Physical Component Summary	
Total QOL Score	
QOL category, n (%)	
>40	
≤40	

BSI, Brief Symptom Inventory; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire;

QOL, quality of life; SD, standardized deviation.

Table 6. Linear Regression to Predict Neurocognitive Impairment at Follow-up 5

a. CCSS-NCQ-Task Efficiency

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						
Chemotherapy + Radiation Therapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire; CI, confidence interval; SD, standardized deviation.

b. CCSS-NCQ-Emotional Regulation

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						

CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						
Chemotherapy + Radiation Therapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire; CI, confidence interval; SD, standardized deviation.

c. CCSS-NCQ-Organization

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire; CI, confidence interval; SD, standardized deviation.

d. CCSS-NCQ-Memory

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						
Chemotherapy + Radiation Therapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; CCSS-NCQ, Childhood Cancer Survivor Study Neurocognitive Questionnaire; CI, confidence interval; SD, standardized deviation.

Table 7. Logistic Regression models to Predict Impairments of Neurocognitive Outcomes, Symptoms, and QOL

	BSI (T score <63 vs. T score ≥ 63)			SF-36 (T score ≤40 vs. T score >40)			CCSS-NCQ (T score <63 vs. T score ≥ 63)		
Variable	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
ADI Score									
Least Disadvantaged 80% (n=)	1.00		ref	1.00		ref	1.00		ref
The Other Most Disadvantaged 20% (n=)									
PM 2.5 (continuous)									
NO (continuous)									
NO_2 (continuous)									
SO_2 (continuous)									
Sex									
Male (n=)	1.00		ref	1.00		ref	1.00		ref
Female (n=)									
Race/Ethnicity, n (%)									
White, NH	1.00		ref	1.00		ref	1.00		ref
Black, NH									
Others (e.g., Asian, Native American/Pacific Islander)									
BMI, n (%)									
Underweight									
Normal	1.00		ref	1.00		ref	1.00		ref
Overweight									
Obesity									
Physical activity based on CDC criteria									
Yes	1.00		ref	1.00		ref	1.00		ref
No									
Smoking									

Never	1.00		ref	1.00		ref	1.00		ref
Past									
Current									
Radiation therapy									
Chemotherapy									
Chemotherapy + Radiation Therapy									

Table 8. Linear Regression to Predict Emotional Symptoms at Follow-up 5

a. Pain

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						
Chemotherapy + Radiation Therapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; BSI, Brief Symptom Inventory; CI, confidence interval; SD, standardized deviation.

b. Somatization

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						
Chemotherapy + Radiation Therapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; BSI, Brief Symptom Inventory; CI, confidence interval; SD, standardized deviation.

c. Anxiety

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; BSI, Brief Symptom Inventory; CI, confidence interval; SD, standardized deviation.

d. Depression

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2

ADI score (20% vs 80%)
PM 2.5 (continuous)
NO (continuous)
NO_2 (continuous)
SO_2 (continuous)
CNS Radiation therapy (yes vs no)
Other Radiation therapy (yes vs no)
Chemotherapy (yes vs no)

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; BSI, Brief Symptom Inventory; CI, confidence interval; SD, standardized deviation.

Table 9. Linear Regression to Predict QOL at Follow-up 5

a. Mental Component Summary Score

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						

b. Physical Component Summary Score

Variable	Standardized β	SD	*p*	95% CI	ΔR^2	*p* for ΔR^2
ADI score (20% vs 80%)						
PM 2.5 (continuous)						
NO (continuous)						
NO_2 (continuous)						
SO_2 (continuous)						
CNS Radiation therapy (yes vs no)						
Other Radiation therapy (yes vs no)						
Chemotherapy (yes vs no)						

Note: Model: R^2=, F (,) =, p<

ADI, Area Deprivation Index; CI, confidence interval; QOL, quality of life; SD, standardized deviation.