Association of environmental characteristics and financial hardships in long-term survivors of childhood cancer

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1. Project Summary and Relevance

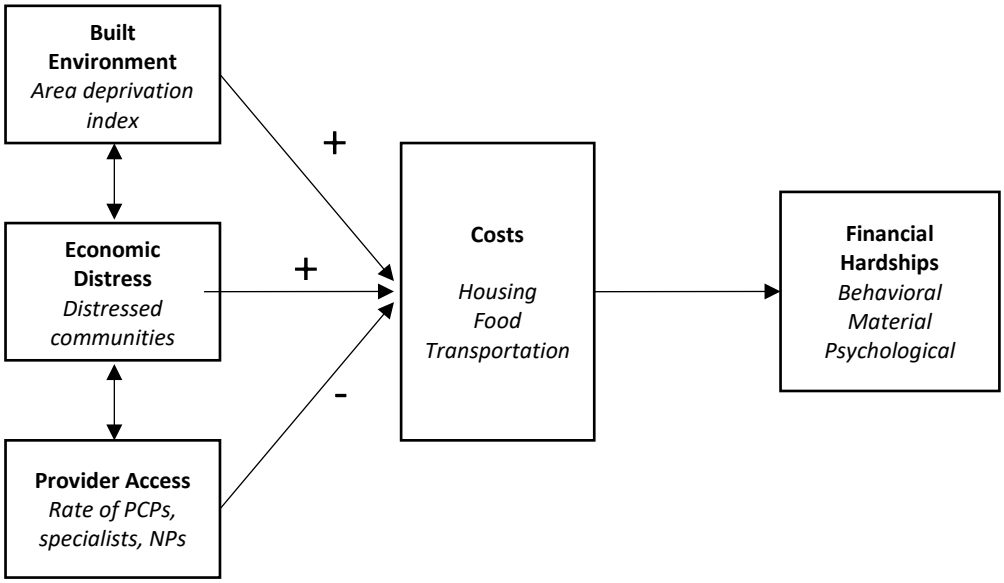
Despite advances in early detection and treatment, a childhood cancer diagnosis can carry substantial long-term clinical and socioeconomic challenges for patients. Financial hardships among long-term childhood cancer survivors represent a complex problem in childhood cancer survivorship. Childhood and young adult cancer survivors report significantly more financial worry and food insecurity than age-matched adults without a cancer history.[1,2] [1,2] Earlier evidence from the Childhood Cancer Survivor Study (CCSS) found that adult survivors of childhood cancer use lifestyle-altering strategies to cope with medical financial hardship such as spending less on food and clothing (57% of sample), borrowing money (54%), and spending emergency savings (50%).[3] Other evidence shows that late treatment effects are associated with disruptions in education and employment, which lead to greater risk of financial hardships later in life.[4,5] Therefore, financial hardships in childhood cancer survivors is priority topic for research, collaboration, and action.

There is a lack of evidence of financial hardship risk factors beyond individual-specific characteristics, such as health insurance enrollment and income.[6] Evidence shows that childhood cancer survivors are slightly less likely to attend college and are more likely to be unemployed and not married.[7] However, research rarely focuses on environmental factors. The built environment, economic stability, and healthcare provider access are environmental characteristics which this project hypothesizes are associated with financial hardship.[8] For example, research has shown that *less deprivation of the built environment* is associated with lower rates of financial burden in cancer patients.[9] Area deprivation has been shown to be positively associated with cancer care crowdfunding.[10] Patients from neighborhoods with higher socioeconomic positions disproportionally receive crowdfunding benefits. In *economically disadvantaged communities*, more individuals experience housing instability, such as moving due to high rent prices, resulting in reduced spending on medical care due to housing costs.[11,12] Impoverished neighborhoods have *lower rates of health care providers,* reducing the likelihood of having a usual source of health care and leads to higher transportation costs when seeking care.[13] Therefore, interventions and policy to improve financial hardships may be ineffective without considering the community's built environment and economic stability among long-term survivors of childhood cancer. Less is known about how this phenomenon manifests in long-term survivors of childhood cancer with financial hardships.

[[The central hypothesis for this study is that environmental characteristics are associated with the risk of financial hardship in survivors. Specifically, the hypothesized social characteristics are operationalized as the built environment (area deprivation), economic stability (distressed communities index), and healthcare provider access (rate of providers) in this study. Area deprivation and economic distress are hypothesized to be positively associated with financial hardships because of the higher prevalence of relative cost-related food and housing insecurity.[12] Healthcare provider access is hypothesized to be negatively associated with financial hardship risks due to greater transportation costs.[11] See the conceptual framework for this study (Figure 1), informed from a previous framework by Yabroff and colleagues.[14] Financial hardship research

using only individual-level socioeconomic status measures may not provide sufficient information about the environmental characteristics of health to understand the complex, multilayered interplay of societal forces affecting childhood cancer survivors compared to adults without a cancer history. It is unclear whether these environmental characteristics correlate with financial hardship outcomes in long-term survivors of childhood cancer. **]]**

[[Figure 1. Environmental characteristics of financial hardships in adult survivors of childhood cancer. The project operationalizes built environment, economic distress, and provider access as exposure variables, supported by previous evidence. The distal outcomes are self-reported behavioral, material, and psychological financial hardships. **]]**



Since 1995, the Childhood Cancer Survivor Study (CCSS) has followed approximately 25,000 individuals who survived more than five years after their initial cancer treatment or bone marrow transplantation as children (less than 21 years of age) diagnosed between 1970-99.[15,16] **[[**The unique advantages of the CCSS data for this proposal are (i) available data on the financial, employment, and insurance experiences from a follow-up questionnaire in 2017 (Follow-up 6, "FU6"); and (ii) the ability to utilize previously geocoded data (proposal 20-07) to link questionnaire data with external datasets describing the communities where survivors live. **]]**Therefore, the purpose of this proposal is to examine whether there is an association between environmental characteristics of health and financial hardships reported by long-term childhood cancer survivors in the context of the communities where they live. To achieve this, the investigator (Fauer) proposes to provide area-level databases (see Table I: Data Sources) to CCSS analysts for linkage and analysis of the CCSS questionnaire and address data.

Table I. Data Sources

Number	Data Source	Main Study Construct, Exposure Variable	Description
1	Childhood Cancer Survivor Study (CCSS) Questionnaires & Tracking Resource	Financial Hardships	Cohort study of childhood cancer survivors and their siblings to understand long-term morbidity, mortality and psychosocial outcomes.
2	Neighborhood Atlas	Built Environment, Area Deprivation	National dataset of social mobility information across the US aimed to understand where economic opportunity has been missing and how it affects poverty.
3	Distressed Communities Index (DCI) dataset	Economic Stability, Economic Distress (DCI)	National dataset examining economic well-being at various levels in order to provide a detailed view of economic prosperity in the US.
4	Area Health Resource File	Health care access and quality, Health care provider access	National dataset on access to health care professionals (i.e., physician, nurse practitioner, etc.) at the US county, state, and national-levels.

2. Objective

[[Objective: Determine the relationships between area-level environmental indices and self-reported financial hardships in survivors and siblings.

Research Questions: Are area deprivation and economic distress positively associated with financial hardships in survivors and siblings? Is healthcare provider access negatively associated with financial hardships? What environmental characteristics of financial hardships vary between survivors and siblings? **]]**

Data Transfer and Sharing.

[[*Following concept approval by the CCSS Publications Committee, Dr. Fauer will prepare and clean the external, area-level datasets at the census tract and 9 digit zip code levels. For example, the Neighborhood Atlas (area deprivation) data is provided at the census block group level and will be statistically summarized in the larger census tract. The DCI data is provided at the 9 digit zip code level, which will be linked directly to census tracts.*

Once completed, Dr. Fauer will share the relevant datasets with CCSS investigators via a secure, cloud-based data-sharing network, Box. Therefore, no

investigators outside CCSS will receive any crude, protected health information (PHI) during data management and analysis. Furthermore, the datasets provided to CCSS may be reused for other studies with Dr. Fauer's permission. **]]**

Innovation.

[[The research in this concept proposal is separate from other CCSS projects in three distinct ways. First, the area-level variables in this proposal reflect validated indices for socioeconomic conditions of communities, whereas other proposals have used crude rates of education, employment, and income for this construct (CP 20-07). See links to approved concept proposals in Appendix A. Secondly, this project operationalizes risk factors for financial hardship at the area-level rather than the individual-level (CPs 20-09, 21-12). While CP 20-20 investigates measures of financial hardship, this project uses other validated area-level metrics (economic distress, rates of health care providers. Finally, this project explicitly uses a paradigm of environmental factors contributing to well-being, which is rare for childhood cancer survivorship literature.**]]**

3. Approach

Study Population.

[[This study will use all available data from survivors and sibling controls in FU6. The CCSS investigators distributed this survey to approximately 33% of the eligible survivors and sibling cohorts. Survivors and siblings have completed the FU6 questionnaire between 2017 and 2019.**]]** In the FU6 questionnaire, responses were received from 3,349 survivors and 976 siblings who were older than 26 years of age. Additionally, 29% (n = 1080) survivors and 55% (n = 536) of siblings were $\geq$ age 45. The CCSS study began enrolling survivor and sibling participants from 1970 to 1999. Therefore, statistical adjustments for age and marital status are warranted.

[[The study requires validated address information for eligibility. We will only use the most recent latitude and longitude information on file (available from proposal 20-07.) for this cross-sectional analysis. **]]**

Data Sources.

CCSS Data (Outcome Variables). The CCSS FU6 questionnaire data contains demographic, treatment, and financial hardship variables. From work by Dr. Nathan and Dr. Yabroff, financial hardship will be operationalized from the FU6 survey into the following domains: behavioral hardship, material hardship/financial sacrifices, and psychological hardship. The domains have been identified by a previous principal components analysis. The behavioral, material, and psychological hardship domains are subscales of multiple survey items. The domains are standardized and summed in statistical analyses.

Please see **Appendix A** for a sample of the CCSS FU6 questionnaire for survivors. Additionally, **Appendix B** contains descriptions of which survey items are included in the financial hardship domains.

Exposure measures. The area-level datasets for this proposal include the Neighborhood Atlas, DCI database, and the Area Health Resource File.[17] Dr. Fauer will provide CCSS with an analytic dataset the Neighborhood Atlas, DCI, and Area Health Resource File for linkage with the participant's census tract. Please see Table II for exposure measures to be retrieved for analysis.

Table II. Exposure Measures.

Exposure Measures			
Construct	Variables, indices, or rates	Source, **Years, Level**	Type
Environmental characteristics	Area Deprivation Index	Neighborhood Atlas**, 2015 data file, census block group level**	Continuous
	Distressed Communities Index ("Economic Distress")	Distressed Community Index dataset **2017 data files, 9 digit zipcode**	"
	Rate of primary care physicians at the county-level	Area Health Resource File	"
	Rate of specialist physicians at the county-level	"	"
	Rate of nurse practitioners at the county-level	"	"
Individual risk factors, CCSS FU6	Marital Status/Partnership	CCSS	Ordinal
	Living arrangement	"	Categorical
	Education	"	Ordinal
	Recurrence	"	Categorical
	Insurance status	"	Categorical

Area Deprivation Index (ADI): a composite measure created in part by the Health Resources & Services Administration and Kind and colleagues.[18] The ADI is available for public download at no cost. The measure captures socioeconomic disadvantage in terms of education, income/employment, housing, and household characteristics, see Table III below.

Table III. ADI components in the composite measure.[19]

ADI components	*Variables*
Education	*% Population aged 25 years or older with less than 9 years of education*
	% Population aged 25 years or older with at least a high school diploma
	% Employed population aged 16 years or older in white-collar occupations
Income/employment	*Median family income in US dollars*
	Income disparity
	% Families below federal poverty level
	% Population below 150% of federal poverty level
	% Civilian labor force population aged 16 years and older who are unemployed
Housing	*Median home value in US dollars*
	Median gross rent in US dollars
	Median monthly mortgage in US dollars
	% Owner-occupied housing units
	% Occupied housing units without complete plumbing
Household characteristics	*% Single-parent households with children younger than 18*
	% Households without a motor vehicle
	% Households without a telephone
	% Households with more than 1 person per room

The ADI provides a continuous summary score from 0 “least disadvantage” to 10 “high disadvantage” as well as a percentile ranking (0 to 100) **[[** for individual states and national percentiles, respectively**]]**. Kind and colleagues organized the measure at the census block group level. This study will cluster ADI values for block groups within the county- and zip code-levels for dataset linkage. **[[**We prefer to operationalize the ADI at the national percentile because CCSS participants come from across the US.**]]**

Distressed Communities Index (DCI): a 7-item composite index used to classify geographic variations in economic prosperity at the zip-code level.[20] In these analyses, the DCI is referred to as “economic distress.” The DCI incorporates variables from counties with at least 500 residents in the Census American Community Survey.

The DCI combines socioeconomic indicators to a single score that depicts how economic activity in a geographic area compares to its peers. The metrics include: Percent of county residents without high school diploma; poverty rate; adults not working; housing vacancy rate; median household income; change in employment; change in establishments. The DCI score reflects the percentile rank of each measure combined, then normalized to a final score that ranges from 0 (most prosperous) to 100 (most distressed). Communities are sorted into quintiles of economic well-being: prosperous,

comfortable, mid-tier, at risk, and distressed. **A DCI score of 80 or greater in univariate analysis represents a distressed community.**

Health care provider access. We operationalize access to primary care physicians, specialist physicians, and nurse practitioners with a continuous rate of from the Area Health Resource File. The denominator for health care provider access is per 1,000 residents at the county level, calculated with the most recent population estimates.

Covariates: The study will use the following CCSS measures in descriptive analyses: Gender, tumor type, recurrence, age at follow-up, race and ethnicity, and smoking status. We will also investigate chemotherapy and radiation exposure data with dosage(s) for descriptive purposes.

Statistical Analyses.

[[Summary. This project will evaluate the relationship between the area deprivation index, distressed communities index, and rates of healthcare providers with self-reported financial hardships in survivors and siblings. Dr. Fauer will provide geocoded area deprivation index, distressed communities index, and healthcare provider data to the CCSS statisticians. The investigators will triangulate participants' address information with the census block group and 9 digit zip codes from the exposure measures. Dr. Fauer will work iteratively with statisticians while the CCSS team incorporates the FU6 questionnaire data and conducts analyses.

To model financial hardship risks, we will use the composite measures from Dr. Yabroff and Dr. Nathan's previous principal components analyses as the primary outcome measures: behavioral hardship, material hardship & financial sacrifices, and psychological hardship. The financial hardship scores are calculated by standardizing the scores and summing the items. The composite measures described previously have demonstrated satisfactory internal consistency reliability.

Demographic characteristics. A demographic table will contrast survivors and siblings (see Table 1A) with bivariate statistical tests.

Environmental characteristics. Comparisons of area deprivation, economic distress, and healthcare provider access will be compared with bivariate statistical tests (see Table 1B).

Financial hardships. This study involves cross-sectional statistical modeling with multiple linear regression models for the financial hardship factor scores (see Table 1C panels 1 through 3). Financial hardships will be assessed by visualizing the data with histograms and scatter plots to understand outliers and distributions. This first step is essential because introducing all area-level risk factors into regression models may lead to multicollinearity.

Linear models will constructed regressing the standardized financial hardship scores on the composite area deprivation, composite economic distress, and healthcare provider access measures. If a significant relationship is found between the composite area deprivation and economic distress measures, then the investigators will consider a sensitivity analysis investigating the index measures as exposures instead of the composite measure.

Separate models will be constructed for each financial hardship outcome among survivors and siblings (i.e., six models total). Estimating the effects of environmental characteristics in separate models will allow the investigators to compare the magnitude of coefficients and fit statistics (r-square and adjusted r-square). Since there will be multiple comparisons with each linear model, a Bonferroni correction will be necessary to avoid a Type I error. Proper construction of multiple linear models require a relatively large sample size and non-independence, which are met with the FU6 data. **]]**

Limitations.

[[Several limitations of this project must be noted. As previously noted from CCSS secondary analyses, survivors were recruited for the cohort study as early as 1970. Financial hardships reported by survivors may not necessarily be attributed to their cancer diagnosis. The area-level metrics were retrieved from third-party sources and there are slim, but possible, chances the metrics were calculated in error. We are unable to generalize our findings to a broader population because the sample represents patients who were treated at CCSS sites. The statistical design is cross-sectional and is not intended to demonstrate a causal relationship. The study is also limited due to the unmatched sibling controls (i.e., not all survivors and siblings were matched). **]]**

Impact.

In light of the limitations, this study will generate new evidence for environmental characteristics of financial hardships in adult survivors of childhood cancer and hypotheses for future research. The investigator will present findings to stakeholder groups to assist with the interpretation and scale-up of future research.

Proposed Timeline.

The study timeline is proposed in Table IV. Dr. Fauer anticipates that the research will result in at least one empirical manuscript upon completion of the project. Dr. Fauer will lead preparation of research abstracts for the American Society for Clinical Oncology (ASCO).

Table IV, Timeline.

Task	2021 Q4	2022 Q1	Q2	Q3	Q4
Obtain approval from CCSS (after submitting protocol)	x				

Obtain human subjects exemption (IRB)	x				
Statistical analyses - CCSS	x	x	x		
Statistical analyses - Fauer	x	x			
Area-level data transfer to CCSS (non-PHI)	x	x			
Prepare manuscript(s)			x	x	x
Identify key stakeholders and include with dissemination of findings	x	x	x	x	x

4. References

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Table Shell 1A**,** descriptive statistics of survivor and siblings individual factors.

	Survivors (n=XXX) Mean (SD) or N (%)	Siblings (n=XXX) Mean (SD) or N (%)	p-value from t-test or chi-square
Age (at FU6), years			
Sex			
Race			
Hispanic or Latino			
US Region			
Household Income			
Age at diagnosis or enrollment (sibling)			
Marital status (FU6)			
Education			
Insurance coverage			
Age at diagnosis		n/a	
Diagnosis		n/a	
Total anthracycline dose		n/a	
Total alkylating agent dose		n/a	
BMT		n/a	
Total radiation dose (site)		n/a	

Table Shell 1B, descriptive statistics of survivor and siblings individual factors.

	Survivors Mean (SD) or median (IQR) or N(%)	Siblings Mean (SD) or Median (IQR) or N (%)	*p*-value from t-test or chi-square
Low disadvantage area (ADI= 1-4)			
High disadvantage area (ADI= 5-9)			
Distressed community (DCI >80)			
Rate of primary care physicians at the county-level			
Rate of specialist physicians at the county-level			
Rate of nurse practitioners at the county-level			
…			

Table 1C, panel 1. Multiple unadjusted and adjusted linear regression models, regressing behavioral hardship on area-level social risk factors.

	Unadjusted		**Covariate-adjusted**		**p-value**	**r-square (adjusted r-square)**
Models, Behavioral Hardship	**β**	**(SE)**	**β**	**(SE)**		
(Constant)						
Area deprivation (composite score)						
(Constant)						
Economic distress (DCI score)						
(Constant)						
Rate of primary care physicians at the county-level						
Rate of specialist physicians at the county-level						
Rate of nurse practitioners at the county-level						

Separate models will be constructed for survivors and siblings.

Table 1C, panel 2. Multiple unadjusted and adjusted linear regression models, regressing material hardship/financial sacrifices on area-level social risk factors.

	Unadjusted		Covariate-adjusted		p-value	r-square (adjusted r-square)
Models, Material Hardship/ Financial Sacrifices	**β**	**(SE)**	**β**	**(SE)**		
(Constant)						
Area deprivation (composite score)						
(Constant)						
Economic distress (DCI score)						
(Constant)						
Rate of primary care physicians at the county-level						
Rate of specialist physicians at the county-level						
Rate of nurse practitioners at the county-level						

Separate models will be constructed for survivors and siblings.

Table 1C, panel 3. Multiple unadjusted and adjusted linear regression models, regressing psychological hardship on area-level social risk factors.

	Unadjusted		Covariate-adjusted		p-value	r-square (adjusted r-square)
Models, Psychological Hardship	**β**	**(SE)**	**β**	**(SE)**		
(Constant)						
Area deprivation (composite score)						
(Constant)						
Economic distress (DCI score)						
(Constant)						
Rate of primary care physicians at the county-level						
Rate of specialist physicians at the county-level						
Rate of nurse practitioners at the county-level						

Separate models will be constructed for survivors and siblings.

Appendix A. Childhood Cancer Survivor Study (CCSS) Details.

Link to 2017 follow-up questionnaire (i.e., follow-up 6)

Link to approved CCSS concept proposals.

Appendix B. Financial hardship questionnaire items.

Financial Hardship Domain	Questionnaire Item	Response
Behavioral Financial Hardship	Forgone Any needed medical	Yes
		No
	Forgone Yearly visit to your primary care doctor	Yes
		No
	Forgone prescription medicine	Yes
		No
	Forgone mental health care/counselling	Yes
		No
	Forgone dental care	Yes
		No
	Forgone eyeglasses	Yes
		No
	Forgone Specialist	Yes
		No
	Forgone follow-up care	Yes
		No
	Any behavioral hardship	Yes
		No
Material Financial Hardship/Financial sacrifices	Reduced spending on vacation or leisure	Yes
		No
	Reduced spending for large purchases	Yes
		No
	Reduced spending on basics	Yes
		No
	Delayed or reduced spending on home improvement	Yes
		No
	Used savings set aside for other purposes	Yes
		No
	Made a change to living situation Made a change to living situation	Yes
		No
	Any Financial sacrifices	Yes
		No
Psychological Financial Hardship	Worry or stress about having enough money to pay rent or mortgage	Always/usually/sometimes worry
		rarely/not worry
	Worry or stress about having enough money to buy nutritious meals	Always/usually/sometimes worry
		rarely/not worry
	Worry or stress about having enough money to pay household utilities, such as water, gas, and electricity	Always/usually/sometimes worry
		rarely/not worry
	Any psychological hardship	Always/usually/sometimes worry
		rarely/not worry