

**Study Title: Determining the Relationship Between Financial Hardship and Health Behaviors, Healthcare Utilization, Symptoms and QOL, and Preventive and Screening Practices Among Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)**

**Working Groups:** Cancer Control

**Investigators:**

Neel S. Bhatt	<a href="mailto:nbhatt@fredhutch.org">nbhatt@fredhutch.org</a>
Paul Nathan	<a href="mailto:paul.nathan@sickkids.ca">paul.nathan@sickkids.ca</a>
Claire Snyder	<a href="mailto:csnyder@jhu.edu">csnyder@jhu.edu</a>
Greg Armstrong	<a href="mailto:greg.armstrong@stjude.org">greg.armstrong@stjude.org</a>
Shizue Izumi	<a href="mailto:shizue-izumi@biwako.shiga-u.ac.jp">shizue-izumi@biwako.shiga-u.ac.jp</a>
I-Chan Huang	<a href="mailto:i-chan.huang@stjude.org">i-chan.huang@stjude.org</a>
Anne Kirchhoff	<a href="mailto:anne.Kirchhoff@hci.utah.edu">anne.Kirchhoff@hci.utah.edu</a>
K. Robin Yabroff	<a href="mailto:robin.yabroff@cancer.org">robin.yabroff@cancer.org</a>

Others to be determined

**Background:**

With advancement in childhood cancer therapies, 5-year survival rates now exceed 80%<sup>1</sup> and estimates suggest there are currently half a million survivors of childhood cancer in the United States.<sup>2</sup> As the number of survivors continues to increase, so does our understanding of the life-threatening and life-altering complications these survivors face after completion of therapy. Survivors' treatment exposures not only put them at a higher risk of mortality, but also affect the psychological (emotional distress, depression, anxiety, post-traumatic stress, cognitive dysfunction), social-environmental (educational attainment, employment, income), health care use (adherence to treatment), physical (pain, fatigue, sleep disturbance, sexual dysfunction), and behavioral (risk-taking behaviors, unhealthy diet, physical inactivity) aspects of their lives.

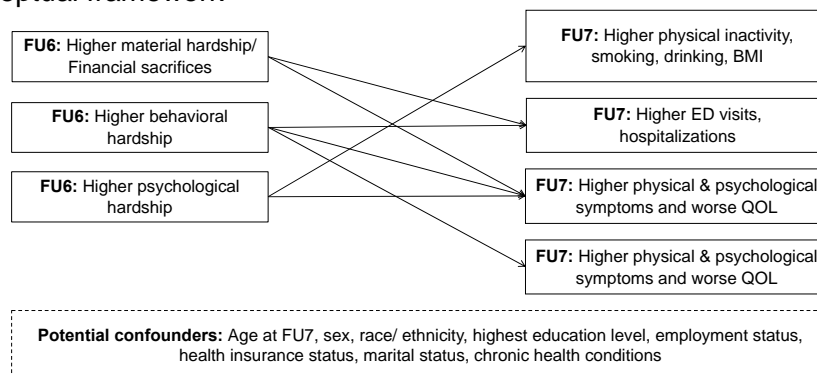
From the prior literature focused on survivors of adult cancers, it is known that compared to people without cancer, survivors have a higher likelihood of developing financial hardship, a term used to describe problems patients have related to the cost of medical care.<sup>3</sup> This increased risk has been reported in material (problems with medical expenses or bills), psychological (worry about medical costs), and behavioral (delaying medical care because of cost) domains.<sup>4-9</sup> Similar findings have been reported by studies focusing on financial hardship among adult survivors of childhood cancers.<sup>10-13</sup> A recent cross-sectional analysis focused on characterization of financial hardship among 3,555 long-term survivors of childhood cancer in the Childhood Cancer Survivor Study (CCSS) compared to 956 siblings.<sup>13</sup> Financial hardship was measured by 21 survey items, which loaded onto three domains through the factor analysis (material hardship or financial sacrifices, behavioral hardship, and psychological hardship) with two additional items not loading onto any domain (a history of being sent to debt collection or of filing for bankruptcy). Survivors reported significantly higher hardship in behavioral (mean standardized domain score 0.51 vs. 0.35,  $p < 0.001$ ), material (0.64 vs. 0.46,  $p < 0.001$ ), and psychological hardship domains (0.69 vs. 0.44,  $p < 0.001$ ) compared to siblings. Additionally, survivors were more likely to report being sent to debt collection (29.9% vs. 22.3%,  $p < 0.001$ ) than siblings. Risk factors for financial hardship included lower educational attainment, lack of private health insurance coverage, and higher anthracycline and chest radiation exposure.

Another analysis focusing on financial hardship among adult survivors of childhood cancer enrolled in the St. Jude Lifetime Cohort (SJLIFE) found a high prevalence of material (22%, 95% confidence interval [CI] 21-24), psychological (51%, 95% CI 49-53), and behavioral (33%, 95% CI 31-35) hardship in this population.<sup>11</sup> As expected, the risk factors for financial hardship included lower household income, lower educational attainment, and evidence of chronic health conditions.

While these studies have primarily focused on correlates of and risk-factors for financial hardship, it is equally important to study the consequences of financial hardship in this vulnerable population. In the SJLIFE analysis, all of the domains of financial hardship were significantly associated with anxiety, depression, somatization, suicidal ideations, and lower physical and mental quality of life (QOL).<sup>11</sup> In another study using the National Health Interview Survey, Zheng and colleagues reported that adult cancer survivors reporting higher financial hardship intensity were more likely to have emergency room visits (37% vs. 28%,  $p=0.011$ ). In addition, higher financial hardship intensity was also associated with lower utilization of preventive or screening services (influenza vaccination: 46% vs. 52%,  $p=0.036$ ; breast cancer screening: 47% vs. 61%,  $p=0.001$ ). While it is known that a substantial proportion of adult survivors of childhood cancer don't receive survivor-focused care,<sup>14</sup> undergo recommended surveillance for second malignant neoplasms<sup>15</sup> and late cardiovascular sequelae<sup>16</sup>, and perform routine physical exercise<sup>17</sup>, current literature lacks information on the association between financial hardship and healthcare utilization patterns, receipt of preventive or screening services, and health behaviors. It is possible that the development of chronic health conditions and resultant vocational disruption, reduced earning, and lack of employer-sponsored insurance coverage among childhood cancer survivors<sup>18-20</sup> could lead to difficulty accessing healthcare and undergoing preventive surveillance. Additionally, it could lead to difficulty affording basic living needs and subsequent adoption of unhealthy lifestyle. In this proposed analysis, we hypothesize that survivors who report more financial hardship will show significantly higher use of urgent health care resources (e.g. more emergency room visits and inpatient hospitalizations), lower utilization of preventive surveillance and population screening, and higher rates of physical inactivity and unhealthy lifestyle (higher smoking, problematic drinking, abnormal body mass index) compared to those with lower financial hardship scores.

Using longitudinal data collected from CCSS FU6 and FU7, our study will shed light on the relationship between financial hardship and survivors' healthcare access and health behaviors. Results of this study have the potential to inform development and testing of future efforts to prevent and mitigate financial hardship and its sequelae in this population.

**Figure 1:** Conceptual framework



## **Specific Aims:**

The overarching goal of this study is to assess the relationship between financial hardship and health behaviors, healthcare utilization, symptoms and QOL, and preventive and screening practices of adult survivors of childhood cancer.

Data collected from a randomly selected group of 3,555 CCSS participants of the FU6 survey will be utilized to define financial hardship; FU7 will be used to study healthcare utilization, symptoms capturing 10 domains (as per Shin H et al.<sup>26</sup>) and QOL, preventive screening practices, and health behaviors; Patient-, disease-, and treatment-level data will be captured from previously abstracted medical records.

**Aim 1:** To assess the relationship between financial hardship and childhood cancer survivors' health behaviors (physical activity, smoking, alcohol intake) and body mass index

Hypothesis 1: Survivors with higher financial hardship (specifically psychological hardship) scores will report lower moderate and vigorous physical activity as per metabolic equivalent (MET) times/ week, increased likelihood of smoking behavior, and increased problematic drinking behavior.

**Aim 2:** To evaluate the association between financial hardship and healthcare utilization patterns (physician visits, emergency department visits, inpatient hospitalizations, and type of hospitalizations) among childhood cancer survivors

Hypothesis 2: Survivors with higher financial hardship (specifically material and behavioral hardship) scores will report fewer physician visits (primary care and cancer center) and more emergency department visits and inpatient hospitalizations (especially due to ambulatory care sensitive conditions [ACSCs] as defined by the the Prevention Quality Indicators [PQI v2022] developed by the Agency for Healthcare Research and Quality [AHRQ] [[https://qualityindicators.ahrq.gov/measures/PQI\\_TechSpec](https://qualityindicators.ahrq.gov/measures/PQI_TechSpec)]) during the study reporting period.

**Aim 3:** To assess the relationship between financial hardship and symptoms and QOL

Hypothesis 3: Survivors with higher financial hardship (all three domains of hardship) scores will report higher prevalence of physical and psychological symptoms and worse QOL.

**Aim 4:** To examine the relationship between financial hardship and adherence to risk-based and population-based screening recommendations in childhood cancer survivors

Hypothesis 4: Survivors with higher financial hardship (specifically behavioral hardship) scores will report lower adherence to Children's Oncology Group (COG) and applicable standard risk screening guidelines (American Cancer Society) recommended for cardiovascular sequelae, breast cancer, skin cancer, colorectal cancer, and cervical cancer screening.

## **Analysis Framework:**

### **Study Population:**

The study sample will consist of all CCSS cohort members who completed the FU6 (medium) survey and FU7 survey. For Aim 4, we will exclude the survivors who are participating in both

CCSS and SJLIFE cohorts because SJLIFE participants receive late-effect screening/surveillance regardless of their financial status.

### **Outcomes of Interest from FU7:**

#### Aim 1: Health behaviors:

1. Physical activity (M16-21): calculated using the methods from the prior analysis by Scott et al.<sup>24</sup>
  - Total exercise frequency (continuous): the frequency of exercise sessions per week within each intensity category (i.e., moderate or vigorous) multiplied by the average reported duration (in minutes), weighted by an estimate of the metabolic equivalent (MET), summed across both intensities, and expressed as average MET-hours per week. The standard MET weightings and examples for each level of exercise intensity are as follows: moderate (5 METs, e.g., brisk walking, tennis), and vigorous (9 METs, e.g., running, vigorous swimming). From this calculation, categories of MET-hours per week can be defined to examine a potential dose-response relationship. For example, a participant reporting 3 moderate intensity exercise sessions for an average duration of 30 minutes per week would receive a score of 7.5 MET-hours/week [i.e., (3 x 30 x 5)/ 60].
  - Meeting exercise guidelines (dichotomized): the proportion of participants reporting <9 MET-hours/week vs. ≥9 MET-hours/week of vigorous exercise per week; 9 MET-hours/week equates to approximately 150 minutes of moderate to vigorous exercise per week, which are the current national recommendations for adult cancer survivors.
2. Problematic drinking behavior (categorical):
  - During the last 12 months, how often did you have 5 or more (males) or 4 or more (females) drinks containing any kind of alcohol in a single day? (M6)
    - Problematic drinking behavior will be defined as ≥5 days of binge drinking per month
3. Smoking behavior (categorical):
  - Do you smoke cigarettes now? (M9)
  - Have you smoked at least 100 cigarettes in your entire life? (M7)
  - Categorize M7 and M9 as followed:
    - a. Never smokers, M7= No AND M9= No
    - b. Former smokers M7= Yes AND M9= No
    - c. Current Smokers, M7= Yes AND M9=Yes
4. Body mass index (categorical) (A1-2):
  - Underweight <18.5 kg/m<sup>2</sup>
  - Normal 18.5-24.9 kg/m<sup>2</sup>
  - Overweight 25.0-29.9 kg/m<sup>2</sup>
  - Obese ≥30 kg/m<sup>2</sup>

5. Healthy lifestyle score: to be calculated as a composite of the outcomes 1-4 as per Dixon SB et al<sup>25</sup>. A score of 0 will be considered an unhealthy lifestyle and 4 being a healthy lifestyle.
- Physical activity: 0 MET-hours/week = 0, 3 to 6 MET-hours/week = 0.5 and 9 to 12, or 15-21 MET-hours/week = 1, based on findings from the analysis of Scott et al.<sup>24</sup>
  - Smoking: Ever (current/ former as per outcome 3) = 0 and Never = 1; however, we will examine the distribution of pack-years and consider a 0.5 point for survivors who report very low lifestyle tobacco use
  - Alcohol consumption: problematic drinking = 0, no problematic drinking = 1
  - BMI: Healthy weight defined as BMI 18.5 to <25; No = 0, Yes = 1; however, we will examine the distribution of BMI and consider a score of 0.5 for survivors with a BMI of 25-<30

#### Aim 2: Healthcare utilization patterns

- During the past 2 years, how many times did you see or talk to your primary care doctor or clinician at a cancer center for medical care? (B1a/b) (categorical- 0, 1-2, 3-4, 5-10, 11-20, >20; also dichotomized as high vs. low depending on the data)
- When was the last time you saw a healthcare provider at a cancer survivor clinic or at a cancer center or at the primary care doctor's office (B2a/b/c) (categorical- <1 year, 1-2 years, >2-<5 years, ≥5 years, never; also dichotomized as high vs. low depending on the data)
- During the past 12 months, how many times have you gone to a hospital emergency room about your own health? (T2) (continuous)
- How many times have you been admitted to a hospital in the last 12 months? (U2) (continuous)
- Reason for hospitalization (U3, U3a, U4, U4a)
- Average length of stay during the hospitalization (U3c, U4c)

#### Aim 3: Symptoms and QOL

1. Symptoms: as per Shin H et al<sup>26</sup>
- Cardiac Symptoms
    - i. Item F3- Irregular heartbeat or palpitations?
    - ii. Item F6- Angina pectoris (chest pains due to lack of oxygen to the heart requiring medication such as nitroglycerin)?
    - iii. Item F11-Does exercise cause severe chest pain, shortness of breath, or irregular heart beat?
  - Pulmonary symptoms
    - i. Item H2- Chronic cough or shortness of breath for greater than one month?
    - ii. Item H8- Any other breathing or lung problems?
  - Sensation abnormalities
    - i. Item J8- Decreased sense of touch or feeling in hands, fingers, arms, or legs?
    - ii. Item D4- Tinnitus or ringing in the ears?
    - iii. Item D5- Persistent dizziness or vertigo?
    - iv. Item D12- Problems with double vision?

- v. Item D16- Any other trouble seeing with one or both eyes even when wearing glasses?
- vi. Item D17- Very dry eyes requiring eye drops or ointment?
- vii. Item D21- Abnormal sense of taste?
- viii. Item L12- Numbness or tingling in parts of your body?
- Motor symptoms
  - i. Item J5- Problems with balance, equilibrium, or ability to reach for or manipulate objects?
  - ii. Item J6-Tremors or problems with movement?
  - iii. Item J11- Weakness or inability to move arm(s)?
  - iv. Item J12- Weakness or inability to move leg(s)?
- Nausea
  - i. Item L10- Nausea or upset stomach?
- Pain
  - i. Item J3- Migraine?
  - ii. Item J4- Other severe headaches?
  - iii. Item J9- Prolonged pain in arms, legs, or back?
  - iv. Item L22- Pain in general?
- Fatigue
  - i. Item L2- Faintness or dizziness?
  - ii. Item L14- Feeling weak in part of your body?
- Memory problems
  - i. Item J1- Problems with learning or memory?
- Anxiety
  - i. Item L4- Thoughts of ending your life?
  - ii. Item L6- Feeling lonely?
  - iii. Item L7- Feeling blue?
  - iv. Item L8- Feeling no interest in things?
  - v. Item L13- Feeling hopeless about the future?
  - vi. Item L18- Feelings of worthlessness?
- Depression
  - i. Item L1- Nervousness or shaking inside?
  - ii. Item L5- Suddenly scared for no reason?
  - iii. Item L9- Feeling fearful?
  - iv. Item L15- Feeling tense or keyed up?
  - v. Item L16- Spells of terror or panic?
  - vi. Item L17- Feeling so restless you couldn't sit still?

## 2. QOL:

- SF-36 (N1-8 & O1-3): QOL will be assessed using the self-reported Medical Outcomes Short Form-36 (SF-36) which includes questions regarding general health, well-being, and quality of life over the previous 4 weeks. The SF-36 includes eight subscales of various aspects of well-being where higher scores represent "better" quality of life. Scores will be reported as a continuous variable. Additionally, two summary measures will be used, Physical Component Summary (PCS) and Mental Component Summary (MCS). All eight subscale scores and PCS and MCS

will be scored on a T-metric (mean=50, SD=10) with higher scores indicating better physical and mental QOL.

Aim 4: Adherence to recommended surveillance:

- Late cardiovascular sequelae screening (C1a/b)
- Breast cancer screening (C1j/k/l)
- Colorectal cancer screening (C1e/f)
- Skin cancer screening (C1i)
- Cervical cancer screening (C1m)

Organ:	Population at Risk:	Suggested Screening:
Breast	Females who received chest, axilla, or total body radiation with potential impact to the breast	Yearly mammogram and adjunct breast MRI beginning 8 years after radiation or at age 25 (whichever occurs later)
Colorectal	Patients who received abdomen, pelvis, spine (lumbar, sacral, whole), or total body radiation with potential to impact the colon/rectum	Colonoscopy every 5 years or multitarget stool DNA test every 3 years beginning 5 years after radiation or at age 30 (whichever occurs later)
Skin	Patients who received any radiation	Yearly skin examination

Breast	Annual mammogram starting at age 45 (can start at 40 if they wish to do so) until age 54 and then every 2 years and continuing as long as the woman is expected to live 10 more years or longer
Cervical	Cervical pap smears starting at age 21 and then repeated every 3 years from aged 21-29, and every 5 years with an HPV test from age 30-65 with the potential to stop testing at age 65 if the patient meets specific criteria
Colorectal	Starting at age 45, colonoscopy every 10 years, CT colonography every 5 years, or flexible sigmoidoscopy every 5 years up to age 75; for patients between 76-85 years of age, the screening should be based on a person's preference, life-expectancy, overall health, and prior screening history

Anthracycline dose	Radiation dose	Recommended frequency
None	<15 Gy or none	No screening
	≥15- <35 Gy	Every 5 years
	≥35 Gy	Every 2 years
<250 mg/m <sup>2</sup>	<15 Gy or none	Every 5 years

	≥15 Gy	Every 2 years
≥250 mg/m <sup>2</sup>	Any or none	Every 2 years

Table 4: Conversion of Anthracycline Exposures to Doxorubicin Isotoxic Equivalents	
Anthracycline	Doxorubicin Isotoxic Equivalents
Doxorubicin	1
Daunorubicin	0.5
Epirubicin	0.67
Idarubicin	5
Mitoxantrone	4

**Key Independent Variables: Financial hardship from FU6 (medium):**

Using FU6 (medium) data, we will describe the 3 domains (material hardship /financial sacrifices, behavioral hardship, and psychological hardship) among adult survivors of childhood cancer who responded to both FU6 (medium) and FU7 forms. Standardized domain scores will be calculated by adding the item responses and dividing by the standard deviation (SD) among survivors. In addition to the domain scores as an outcome variable, a binary scoring for any affirmative response to the items in the domain will also be used.<sup>13</sup>

**Material Hardship/Financial Sacrifices (8 items – in the past year)**

- Reduced spending on vacation or leisure (C9)
- Reduced spending on large purchases (C9)
- Delayed or reduced spending on home improvement (C9)
- Used savings set aside for other purposes (C9)
- Reduced spending on basics (C9)
- Paying off medical bills over time (C7)
- Made a change to living situation (C9)
- Problems paying medical bills (C5,C6)

**Behavioral Hardship (8 items – in the past year)**

- Forgone any needed medical care (C8)
- Forgone yearly visit to your primary care doctor (C8)
- Forgone specialist (C8)
- Forgone follow-up care (C8)
- Forgone prescription medicine (C8)
- Forgone eyeglasses (C8)
- Forgone mental health counseling (C8)
- Forgone dental care (C8)

**Psychological Hardship (3 items – in the past year)**

- Worry or stress about having enough money to pay rent or mortgage (C17)
- Worry or stress about having enough money to buy nutritious meals (C18)
- Worry or stress about having enough money to pay household utilities, such as water, gas, and electricity (C19)



We will also describe the two individual items (yes/ no):

- History of being sent to debt collection (C29)
- History of filing for bankruptcy (C30)

**Other Dependent Variables/ Covariates from baseline/ FU7:**

- Age at FU7 questionnaire, years (Baseline A1, FU7 Today's date)
- Sex (Baseline A2)
- Race/ ethnicity (Baseline A5)
- Age at diagnosis, years (Medical records)
- Time from diagnosis to FU7 questionnaire, years (Medical records and FU7 Today's date)
- Primary cancer diagnosis (Leukemia, CNS tumors, Hodgkin lymphoma, Non-Hodgkin lymphoma, Neuroblastoma, Wilms' tumor, Bone cancer, Soft tissue sarcoma) (Medical records)
- Therapy (Surgery, Radiation (RT) only, Chemotherapy, Chemotherapy and RT, Chemotherapy, RT, and surgery, RT and surgery, Chemotherapy and surgery) (Medical records)
- Anthracycline exposure and doxorubicin equivalent dose (Medical records)
- Radiation exposure (Any, Chest, Axilla, Abdomen, Pelvis, Lumbar/ Sacral/ Total spine, Total body) (Medical records)
- Highest education level (Less than high school or GED, High school graduate, Some college or higher) (FU7 A6)
- Current employment status (Employed full-time, Employed part-time, Unemployed) (FU7 A7)
- Annual household income (<\$40,000, ≥\$40,000- <\$80,000, ≥80,000) (FU7 A15)
- Health insurance status (Private insurance, Public insurance, None) (FU7 A16) Note: Insurance status of survivors residing in Canada will be classified as private or public based on their age, income, and disability status.
- Marital status (Single, never married, Married/ living with a partner, Divorced/ Widowed/ Separated) (FU7 A10)
- Current living arrangement (With spouse/ partner, with parent(s)/ sibling(s)/ relative(s), with roommates, Alone) (FU7 A9)
- People currently living in the household (A14 a/b)
- Chronic health conditions – using the global burden/ total intensity of chronic health conditions as per Geenen MM et al.<sup>27</sup> Score 0= no chronic health conditions or low burden (≥1 CTCAE grade 1 conditions); Score 1= medium burden (any grade 1 conditions AND ≥1 grade 2 conditions or any grade 1-2 conditions AND 1 grade 3 condition); Score 2= high burden (any grade 1-2 conditions AND ≥2 grade 3 conditions or any grade 1-2 conditions AND 1 grade 4 condition or any grade 1-2 conditions AND 1 grade 3 condition and 1 grade 4 condition); Score 4= very high burden (any grade 1-2 conditions AND ≥2 grade 3 conditions AND 1 grade 4 condition or any grade 1-3 conditions AND ≥2 grade 4 conditions) (FU7 D1-J15)

## Statistical Analyses:

Descriptive statistics of the survivors, including socio-demographic characteristics, such as age at FU7 completion, sex, race/ethnicity, and educational attainment as well as disease/ treatment characteristics such as diagnosis, treatment combinations, and time from diagnosis will be provided. Additionally, descriptive statistics of physical activity, alcohol intake, smoking, and body mass index will be provided. We will describe the frequency and percentages of physician (primary care or clinician at a cancer center) visits. We will also evaluate emergency room hospitalizations visits as continuous variables (Table 5). Mean domain scores of material, behavior, and psychological hardship and frequency and percentages of individual items will be provided (Table 6).

**Aim 1:** To assess the relationship between financial hardship and childhood cancer survivors' health behaviors (physical activity, smoking, alcohol intake, body mass index)

Multiple linear regression models (continuous outcome: total exercise frequency) and multivariable logistic regression models (binary outcomes: not meeting exercise guidelines, current smoker, problematic drinking, unhealthy BMI) will be used to study the relationship between domains of financial hardship and health behaviors. Additionally, the relationship between domains of financial hardship and healthy lifestyle score will also be studied. Each of the models will be adjusted for age, sex, and race/ ethnicity. Additional adjustment will be considered for other sociodemographic, disease, treatment, and chronic health condition variables. We will also check for multicollinearity among the independent variables using variance inflation factor (VIF) or generalized variance inflation factor (GVIF).<sup>28</sup> No correction will be performed for multiple testing since the outcomes are treated as separate hypotheses of individual interest. Continuous financial hardship domain scores will be forced in each model (Table 7).

**Aim 2:** To evaluate the association between financial hardship and healthcare utilization patterns (physician visits, emergency department visits, and inpatient hospitalizations) among childhood cancer survivors

To study the association between financial hardship domain scores and different healthcare utilization outcomes, individual models for physician visits, emergency department visits, inpatient hospitalizations, and hospitalizations due to ambulatory care sensitive conditions (ACSC) will be created. To study the hospitalizations due to ACSC, the reasons for hospitalization data from FU7 will be used along with the Prevention Quality Indicators (PQI v2022) developed by the Agency for Healthcare Research and Quality (AHRQ) ([https://qualityindicators.ahrq.gov/measures/PQI\\_TechSpec](https://qualityindicators.ahrq.gov/measures/PQI_TechSpec)). Specifically, we will study the hospitalizations due to diabetes (short-term or long-term complications, uncontrolled diabetes, lower-extremity amputation), chronic obstructive pulmonary disease (COPD) or asthma, hypertension, heart failure, community acquired pneumonia, and urinary tract infection. We will assess the associations using multivariable logistic regression models for binary outcomes or multivariable Poisson regression models for count outcomes, which will be adjusted for age, sex, and race/ ethnicity. Additional adjustment will be considered for other sociodemographic, disease, treatment, and chronic health condition variables. We will also check for multicollinearity among the independent variables using variance inflation factor (VIF) or generalized variance inflation factor (GVIF).<sup>28</sup> No correction will be performed for multiple testing since the outcomes are treated as separate hypotheses of individual interest. Continuous

financial hardship domain scores will be forced in each model (Table 8). Additionally, we will study the correlation between financial hardship domain scores and average length of hospitalization.

**Aim 3:** To assess the relationship between financial hardship and symptoms and QOL

To study the relationship between financial hardship domain scores and symptoms and QOL, multivariable logistic regression models for individual symptom domains and multiple linear regression models for cumulative symptom burden will be created. Additionally, relationship between financial hardship scores and QOL (role emotional, social function, mental health, physical component summary, and mental component summary) will be studied through linear models. Each of the models will be adjusted for age, sex, and race/ ethnicity. Additional adjustment will be considered for other sociodemographic, disease, treatment, and chronic health condition variables. We will also check for multicollinearity among the independent variables using variance inflation factor (VIF) or generalized variance inflation factor (GVIF).<sup>28</sup> Continuous financial hardship domain scores will be forced in each model (Table 9).

**Aim 4:** To examine the relationship between financial hardship and adherence to risk-based and population-based screening recommendations in childhood cancer survivors

For the purposes of Aim 4 analysis, survivors who have developed one of the target cancers as a subsequent neoplasm (skin, colorectal, breast, or cervical) will be excluded from the analysis. Similarly, survivors who have developed grade 3 or 4 cardiac toxicity will be excluded from analysis of echocardiogram adherence. Survivors at high-risk or standard risk of cancers or cardiomyopathy will be defined (Table 10). Adherence to each of the outcomes will be assessed using multivariable logistic regression separately (Table 11). Survivors who completed the test within the recommended period will be considered “adherent” to the guidelines. Survivors at high-risk and standard risk will be analyzed separately. Each of the models will be adjusted for age, sex, and race/ ethnicity. Additional adjustment will be considered for other sociodemographic, disease, treatment, and chronic health condition variables. We will also check for multicollinearity among the independent variables using variance inflation factor (VIF) or generalized variance inflation factor (GVIF).<sup>28</sup> Continuous financial hardship domain scores will be forced in each model (Table 12-13).

## References:

1. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. *CA Cancer J Clin.* Mar-Apr 2014;64(2):83-103. doi:10.3322/caac.21219
2. Robison LL, Hudson MM. Survivors of childhood and adolescent cancer: life-long risks and responsibilities. *Nat Rev Cancer.* Jan 2014;14(1):61-70. doi:10.1038/nrc3634
3. NCI Dictionary of Cancer Terms: Financial Hardship. National Cancer Institute. Accessed March 14, 2023. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/financial-hardship>
4. Zheng Z, Jemal A, Han X, et al. Medical financial hardship among cancer survivors in the United States. *Cancer.* May 15 2019;125(10):1737-1747. doi:10.1002/cncr.31913
5. Altice CK, Banegas MP, Tucker-Seeley RD, Yabroff KR. Financial Hardships Experienced by Cancer Survivors: A Systematic Review. *J Natl Cancer Inst.* Feb 2017;109(2)doi:10.1093/jnci/djw205

6. Ekwueme DU, Zhao J, Rim SH, et al. Annual Out-of-Pocket Expenditures and Financial Hardship Among Cancer Survivors Aged 18-64 Years - United States, 2011-2016. *MMWR Morb Mortal Wkly Rep.* Jun 7 2019;68(22):494-499. doi:10.15585/mmwr.mm6822a2
7. Yabroff KR, Dowling EC, Guy GP, Jr., et al. Financial Hardship Associated With Cancer in the United States: Findings From a Population-Based Sample of Adult Cancer Survivors. *J Clin Oncol.* Jan 20 2016;34(3):259-67. doi:10.1200/JCO.2015.62.0468
8. Yabroff KR, Zhao J, Zheng Z, Rai A, Han X. Medical Financial Hardship among Cancer Survivors in the United States: What Do We Know? What Do We Need to Know? *Cancer Epidemiol Biomarkers Prev.* Dec 2018;27(12):1389-1397. doi:10.1158/1055-9965.EPI-18-0617
9. Zheng Z, Han X, Zhao J, et al. Financial Hardship, Healthcare Utilization, and Health Among U.S. Cancer Survivors. *Am J Prev Med.* Jul 2020;59(1):68-78. doi:10.1016/j.amepre.2020.02.016
10. Fair D, Park ER, Nipp RD, et al. Material, behavioral, and psychological financial hardship among survivors of childhood cancer in the Childhood Cancer Survivor Study. *Cancer.* Sep 1 2021;127(17):3214-3222. doi:10.1002/cncr.33613
11. Huang IC, Bhakta N, Brinkman TM, et al. Determinants and Consequences of Financial Hardship Among Adult Survivors of Childhood Cancer: A Report From the St. Jude Lifetime Cohort Study. *J Natl Cancer Inst.* Feb 1 2019;111(2):189-200. doi:10.1093/jnci/djy120
12. Nipp RD, Kirchhoff AC, Fair D, et al. Financial Burden in Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study. *J Clin Oncol.* Oct 20 2017;35(30):3474-3481. doi:10.1200/JCO.2016.71.7066
13. Nathan PC, Huang IC, Chen Y, et al. Financial Hardship in Adult Survivors of Childhood Cancer in the Era After Implementation of the Affordable Care Act: A Report From the Childhood Cancer Survivor Study. *J Clin Oncol.* Feb 10 2023;41(5):1000-1010. doi:10.1200/JCO.22.00572
14. Casillas J, Oeffinger KC, Hudson MM, et al. Identifying Predictors of Longitudinal Decline in the Level of Medical Care Received by Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study. *Health Serv Res.* Aug 2015;50(4):1021-42. doi:10.1111/1475-6773.12282
15. Nathan PC, Ness KK, Mahoney MC, et al. Screening and surveillance for second malignant neoplasms in adult survivors of childhood cancer: a report from the childhood cancer survivor study. *Ann Intern Med.* Oct 5 2010;153(7):442-51. doi:10.7326/0003-4819-153-7-201010050-00007
16. Nathan PC, Greenberg ML, Ness KK, et al. Medical care in long-term survivors of childhood cancer: a report from the childhood cancer survivor study. *J Clin Oncol.* Sep 20 2008;26(27):4401-9. doi:10.1200/JCO.2008.16.9607
17. Florin TA, Fryer GE, Miyoshi T, et al. Physical inactivity in adult survivors of childhood acute lymphoblastic leukemia: a report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev.* Jul 2007;16(7):1356-63. doi:10.1158/1055-9965.EPI-07-0048
18. Gurney JG, Krull KR, Kadan-Lottick N, et al. Social outcomes in the Childhood Cancer Survivor Study cohort. *J Clin Oncol.* May 10 2009;27(14):2390-5. doi:10.1200/JCO.2008.21.1458
19. Kirchhoff AC, Leisenring W, Krull KR, et al. Unemployment among adult survivors of childhood cancer: a report from the childhood cancer survivor study. *Medical care.* 2010;48(11):1015-1025. doi:10.1097/MLR.0b013e3181eaf880 [doi]
20. Bhakta N, Liu Q, Ness KK, et al. The cumulative burden of surviving childhood cancer: an initial report from the St Jude Lifetime Cohort Study (SJLIFE). *Lancet.* Dec 9 2017;390(10112):2569-2582. doi:10.1016/S0140-6736(17)31610-0
21. Lown EA, Hijjiya N, Zhang N, et al. Patterns and predictors of clustered risky health behaviors among adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. *Cancer.* Sep 1 2016;122(17):2747-56. doi:10.1002/cncr.30106

22. Tonorezcos ES, Ford JS, Wang L, et al. Impact of exercise on psychological burden in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. *Cancer*. Sep 1 2019;125(17):3059-3067. doi:10.1002/cncr.32173
23. Yan AP, Chen Y, Henderson TO, et al. Adherence to Surveillance for Second Malignant Neoplasms and Cardiac Dysfunction in Childhood Cancer Survivors: A Childhood Cancer Survivor Study. *J Clin Oncol*. May 20 2020;38(15):1711-1722. doi:10.1200/JCO.19.01825
24. Scott JM, Li N, Liu Q, et al. Association of Exercise With Mortality in Adult Survivors of Childhood Cancer. *JAMA Oncol*. Oct 1 2018;4(10):1352-1358. doi:10.1001/jamaoncol.2018.2254
25. Dixon SB, Liu Q, Chow EJ, et al. Specific causes of excess late mortality and association with modifiable risk factors among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. *Lancet*. Apr 5 2023;doi:10.1016/S0140-6736(22)02471-0
26. Shin H, Dudley WN, Bhakta N, et al. Associations of Symptom Clusters and Health Outcomes in Adult Survivors of Childhood Cancer: A Report From the St Jude Lifetime Cohort Study. *J Clin Oncol*. Jan 20 2023;41(3):497-507. doi:10.1200/JCO.22.00361
27. Geenen MM, Cardous-Ubbink MC, Kremer LC, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. *JAMA*. Jun 27 2007;297(24):2705-15. doi:10.1001/jama.297.24.2705
28. Fox J, Monette G. Generalized Collinearity Diagnostics. *Journal of the American Statistical Association*. 1992;87 (417):178–183.

**TABLE 5:** Characteristics of the Adult Survivors of Childhood Cancer who responded to both FU6 (medium) and FU7 questionnaires

<b>Variable</b>	<b>Survivors</b>
<b>Age at survey (FU7) completion, N (%)</b> 18-20 20-29 30-39 ≥40	
<b>Sex, N (%)</b> Male Female	
<b>Race/ethnicity, N (%)</b> Non-Hispanic White Non-white	
<b>Education, N (%)</b> High school (HS) or below HS Some college College graduate and above	
<b>Marital Status, N (%)</b> Married/ living with partner Divorced/separated Never married	
<b>Disease Diagnosis, N (%)</b> Leukemia CNS tumors Hodgkin lymphoma Non-Hodgkin lymphoma Wilms' tumor Neuroblastoma Soft tissue sarcoma Bone cancer	
<b>Age at diagnosis, N (%)</b> 0-4 5-9 10-14 ≥15	
<b>Treatment combinations, N (%)</b> No surgery, chemotherapy, or radiation Surgery only Chemotherapy only Radiation only Surgery + chemotherapy Surgery + radiation Chemotherapy + radiation Surgery + chemotherapy + radiation	
<b>Chronic Health Condition burden, N (%)</b>	

Score 0 Score 1 Score 2 Score 3	
<b>Total moderate/ vigorous exercise frequency (metabolic equivalent-hours/ week),</b> Median (range)	
<b>Meeting exercise guidelines, N (%)</b> <9 MET-hours/ week ≥9 MET-hours/week	
<b>Problematic drinking behavior, N (%)</b>	
<b>Smoking, N (%)</b> Never smoker Former smoker Current smoker	
<b>Body mass index, N (%)</b> Underweight <18.5 kg/m <sup>2</sup> Normal 18.5-24.9 kg/m <sup>2</sup> Overweight 25.0-29.9 kg/m <sup>2</sup> Obese ≥30 kg/m <sup>2</sup>	
<b>Type of physician visits over a 2-year period, N (%)</b> Primary care doctor Clinician at a cancer center	
<b>Last physician visit, N (%)</b> <1 year 1-2 year >2-<5 years ≥5 years Never	
<b>Number of physician visits over a 2-year period, N (%)</b> None 1-2 3-4 5-10 11-20 >20	
<b>Emergency room visits over a 12-month period</b> Median (range)	
<b>Hospitalizations over a 12-month period</b> Median (range)	

**TABLE 6:** Financial Hardship Domain Specific Scores for Survivors

Financial Hardship Domain	Survivors Mean Domain Score (95% CI)
<b>Material Hardship/ Financial Sacrifices Domain</b> <b>Behavioral Hardship Domain</b> <b>Psychological Hardship Domain</b> <b>Sent to debt collection*</b> <b>Filing for bankruptcy*</b>	
	<b>Percent (95% CI)</b>
<b>Any Material Hardship/ Financial Sacrifices</b> <b>Any Behavioral Hardship</b> <b>Any Psychological Hardship</b>	

\*Percent values will be reported for the two items (sent to debt collection and filing for bankruptcy as they are binary (yes/no)).

We will consider showing the mean financial hardship domain score comparison by key study outcomes (Health Behaviors, Healthcare Utilization, Symptoms and QOL)



**TABLE 7:** Relationship between financial hardship scores and health behaviors in childhood cancer survivors

<b>Variables</b>	<b>Lower physical activity (continuous)</b>	<b>Physical activity &lt;9 MET- hours/week vs. ≥9 MET-hours/week</b>	<b>Problematic drinking behavior (Yes vs. No)</b>	<b>Current smoker vs. never/former smoker</b>	<b>Unehealthy BMI vs. healthy BMI</b>	<b>Healthy lifestyle score 2.5-4 vs. 0-2</b>
	<b>Estimate (95% CI)</b>	<b>OR (95% CI)</b>	<b>OR (95% CI)</b>	<b>OR (95% CI)</b>	<b>OR (95% CI)</b>	<b>OR (95% CI)</b>
<b>Hardship scores</b> Material hardship Behavioral hardship Psychological hardship						
<b>Age at survey (FU7) completion, N (%)</b> 18-20 20-29 30-39 ≥40						
<b>Sex, N (%)</b> Male Female						
<b>Race/ethnicity, N (%)</b> Non-Hispanic White Non-white						
<b>Additional adjustment</b> <b>TBD</b>						

MET= metabolic equivalent of energy; BMI= body mass index; OR= odds ratio; CI= confidence interval

**TABLE 8:** Associations between financial hardship scores and healthcare utilization in childhood cancer survivors

<b>Variables</b>	<b>Physician visits (high vs. low)</b>	<b>Emergency room visits (continuous)</b>	<b>Hospitalizations (continuous)</b>	<b>Hospitalization due to ACSC (yes vs. no)</b>
	<b>OR (95% CI)</b>	<b>Estimate (95% CI)</b>	<b>Estimate (95% CI)</b>	<b>OR (95% CI)</b>
<b>Hardship scores</b>				
Material hardship				
Behavioral hardship				
Psychological hardship				
<b>Age at survey (FU7) completion, N (%)</b>				
18-20				
20-29				
30-39				
≥40				
<b>Sex, N (%)</b>				
Male				
Female				
<b>Race/ethnicity, N (%)</b>				
Non-Hispanic White				
Non-white				
<b>Additional adjustment TBD</b>				

OR= odds ratio; CI= confidence interval; ACSC= ambulatory care sensitivity condition



Variables	Quality of life									
	Physical function	Role physical	Pain	General health	Energy Fatigue	Role emotional	Social function	Mental health	PCS	MCS
	Estimate (95% Confidence Interval)									
<b>Hardship scores</b> Material hardship Behavioral hardship Psychological hardship										
<b>Age at survey (FU7) completion, N (%)</b> 18-20 20-29 30-39 ≥40										
<b>Sex, N (%)</b> Male Female										
<b>Race/ethnicity, N (%)</b> Non-Hispanic White Non-white										
<b>Additional adjustment TBD</b>										

Note: A forest plot will also be created to show the relationship between symptoms/ QOL and financial hardship scores

**TABLE 10:** Risk group of childhood cancer survivors

<b>Characteristic</b>	<b>N (%)</b>
<b>Breast cancer risk</b> COG high risk ACS standard risk Not at risk	
<b>Colorectal cancer risk</b> COG high risk ACS standard risk Not at risk	
<b>Skin cancer risk</b> COG high risk Not at risk	
<b>Cervical cancer risk</b> ACS standard risk Not at risk	
<b>Cardiac dysfunction risk group</b> None 2 year 5 year	

COG= Children's Oncology Group; ACS= American Cancer Society

**TABLE 11:** Adherence to suggested surveillance interventions in childhood cancer survivors

<b>Characteristic</b>	<b>High risk survivors</b>	<b>Standard risk survivors</b>
	<b>N (%)</b>	<b>N (%)</b>
<b>Breast cancer testing</b> Had test within recommended period Had test, but not within recommended period Never had test Don't know		
<b>Colorectal cancer testing</b> Had test within recommended period Had test, but not within recommended period Never had test Don't know		
<b>Skin cancer testing</b> Had test within recommended period Had test, but not within recommended period Never had test Don't know		
<b>Cervical cancer testing</b> Had test within recommended period Had test, but not within recommended period Never had test Don't know		
<b>Cardiac dysfunction testing</b> Had test within recommended period Had test, but not within recommended period Never had test Don't know		

**TABLE 12:** Associations between financial hardship scores and adherence to surveillance in high-risk childhood cancer survivors

<b>Variables</b>	<b>Breast cancer</b>	<b>Colorectal cancer</b>	<b>Skin cancer</b>	<b>Cardiac dysfunction</b>
	<b>Odds Ratio (95% Confidence Interval)</b>			
<b>Hardship scores</b> Material hardship Behavioral hardship Psychological hardship				
<b>Age at survey (FU7) completion, N (%)</b> 18-20 20-29 30-39 ≥40				
<b>Sex, N (%)</b> Male Female				
<b>Race/ethnicity, N (%)</b> Non-Hispanic White Non-white				
<b>Additional adjustment TBD</b>				

**TABLE 13:** Associations between financial hardship scores and adherence to surveillance in standard-risk childhood cancer survivors

<b>Variables</b>	<b>Breast cancer</b>	<b>Colorectal cancer</b>	<b>Cervical cancer</b>
	<b>Odds Ratio (95% Confidence Interval)</b>		
<b>Hardship scores</b>			
Material hardship			
Behavioral hardship			
Psychological hardship			
<b>Age at survey (FU7) completion, N (%)</b>			
18-20			
20-29			
30-39			
≥40			
<b>Sex, N (%)</b>			
Male			
Female			
<b>Race/ethnicity, N (%)</b>			
Non-Hispanic White			
Non-white			
<b>Additional adjustment TBD</b>			