

**Concept Protocol for the Childhood Cancer Survivor Study
(Approval # XXXXXX)**

1. STUDY TITLE

Progression of Late Medical Effects and Impact on Financial Hardship Among Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

2. WORKING GROUPS

Cancer Control and Intervention (Primary) and Chronic Disease (Secondary)

3. INVESTIGATORS

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4. BACKGROUND AND RATIONALE

Survivors of childhood cancer often develop treatment-related late effects including chronic health conditions (CHCs),^{1,2} physical/neurocognitive performance deficits,^{3,4} physical/psychological/somatic symptoms, and poor health-related quality-of-life (HRQOL).^{5,6} Socio-economic consequences of childhood cancer are also considerable as survivors are less likely to graduate from college, assume higher-skilled occupations, or earn incomes comparable to their siblings.⁷⁻⁹ The Childhood Cancer Survivor Study (CCSS) reports that adult survivors of childhood cancer incurred significantly higher out-of-pocket medical expenses vs. siblings.¹⁰ In addition, annual productivity loss in adult survivors of childhood cancer was significantly higher compared to similar adults without a cancer history in national data.¹¹

Financial Hardship and Cancer Survivorship

“Financial hardship” is an emerging concept to describe financial challenges faced by cancer populations. A taxonomy has been recently proposed to study this concept: material conditions (expenses/bills related to medical care), psychological responses (worry/distress due to medical costs), and coping behaviors (skipped medical care or medications due to financial problems).¹² Approximately 30% of **survivors of adult-onset cancers** in the U.S. report financial problems.¹³⁻¹⁵ Key correlates identified from these cross-sectional studies include younger age (18-54 years) at time of survey,^{14,16} female sex,^{14,16,17} minority race/ethnicity,^{14,16-18} lower educational attainment^{15,16,19} and personal income,^{15,16,18,19} unemployment,¹⁸ lack of health insurance coverage, shorter time since diagnosis,^{13,15} treatment with chemotherapy/radiation,¹³ and poor health status.^{15,18,19} Survivors who report financial problems (vs. no problems) have elevated risk of delaying medical care,²⁰ suboptimal HRQOL¹⁴ and bankruptcy.²¹

A recent study evaluating determinants of different financial hardship domains (i.e., material, psychological, and coping/behavioral domains) among **adult survivors of childhood cancer** was published in 2019 based on 2,811 survivors (mean age at evaluation 31.8 years; 23.6 years post-diagnosis) enrolled in St. Jude Lifetime Cohort Study (SJLIFE).²² Among participants, 22.4%, 51.1%, and 33.0% reported having material, psychological, and coping/behavioral hardship. Significant risk factors across the three hardship domains were annual household income ≤\$39,999 and below high school educational attainment. Based on a cross-sectional design, this study specifically found an association between financial hardship and presence of organ-specific CHCs graded by CTCAE (grades 2-4 vs. none/grade 1), with subsequent neoplasm, myocardial infarction, stroke, peripheral neuropathy, seizure, reproductive disorders, upper gastrointestinal diseases, hearing loss, and amputation significantly associated with having financial hardship in any of the three domains. Financial hardship report was associated with higher risk of poor HRQOL, suicidal ideation, and difficulty in planning for retirement.

Late effects/CHCs as Key Determinants of Financial Hardship

Few studies have elucidated how the **dynamic progression of late effects/CHCs** impacts financial hardship. To date, all the CHCs-financial hardship studies in childhood cancer survivors were conducted in an exploratory manner through a cross-sectional design (i.e., CHCs and financial hardship were assessed at the same time point) because the concept of cancer-related financial hardship was emerged in the past few years. **The impact of dynamic progression of late effects/CHCs on financial impact in childhood cancer survivors deserves close attention because the mechanism is likely different from survivors of adult-onset cancer.** A recent CCSS study found that childhood cancer survivors vs. sibling controls had higher cumulative incidence of CHCs which occurred at earlier developmental stages.²³ In contrast to adult-onset cancer, treatment exposures and subsequent medical complications occurring during the early life course might lead to lower endowment, lower rate or lower level of human capital development (i.e., lower educational attainment, lower employment skill/opportunity, and poorer health status), which places childhood cancer survivors at high risk of financial hardship later in their life course. Preventing progression (onset of/worsening) of late effects/CHCs may decrease the financial burden of childhood cancer survivors.

Factors Potentially Modifying the Association of Late Effects/CHCs and Financial Hardship

It is critical to identify multi-level factors potentially modifiable to mitigate the potential impact of late effects/CHCs on financial hardship. Area (i.e., geographic location of residence) socioeconomic deprivation and rural-urban disparity may additionally contribute

to financial hardship, which is beyond the influence of personal SES.²⁴ Rural cancer survivors often have worse health outcomes than their urban counterparts (e.g., poorer HRQOL, more non-cancer comorbidities, and increased psychological distress),²⁵ in part due to poor cancer knowledge or literacy,²⁶ or difficulty understanding cancer-related information.²⁷ In addition, data from the Medical Expenditure Panel Survey suggests that rural residents spend more on out-of-pocket medical costs than urban residents.²⁸ If the influence of CHC burden on financial hardship is significant, especially if it is stronger among cancer survivors living in higher (vs. lower) socioeconomic deprivation areas, then healthcare policy or community-level interventions (e.g., providing specific financial support or navigation systems from local or state governments for survivors living in disadvantaged areas) are warranted in the future.

Psycho-behavioral factors are another set of factors that could potentially influence the impact of late effects/CHCs on financial hardship. Studies from the SJLIFE cohort have found that childhood cancer survivors having CHCs are at higher risk of psychological distress vs. survivors having no CHCs,²⁹ and psychological distress was significantly associated with financial hardship.²² On the other hand, abstaining from smoking or increasing physical activity is associated with reduced psychological distress.³⁰⁻³³ If the influence of CHC burden on financial hardship is significant, especially if it is stronger among cancer survivors having more psychological distress or unhealthy lifestyle (smoking, physical inactivity), then interventions to improve psychological distress and unhealthy lifestyle are warranted.

5. SPECIFIC AIMS/OBJECTIVES/RESEARCH HYPOTHESES

The overarching goal of this study is to evaluate the degree to which the progression of late effects/CHCs impacts financial hardship in adult survivors of childhood cancer. Data collected from CCSS FU6 (focused on extensive financial hardship issues) and earlier CCSS surveys will be used. Our specific aims and corresponding hypotheses are as follows:

Aim 1: Identify late effects/CHCs that are associated with cross-sectional assessment of financial hardship domains

H₀ 1a: Specific late effect/CHC groups at CCSS baseline are associated with future financial hardship.

H₀ 1b: Individuals with early progression of specific late effect/CHC groups will have higher risk of financial hardship vs. individuals with late progression of the same specific late effect/CHC groups.

Note, progression of specific late effect/CHC groups over time includes 1) onset (from none/G1 of CTCAE grade at baseline to ≥G2 at a recent FU) or 2) worsening (from G2 at baseline to ≥G3 at a recent FU, or from G3 at baseline to G4 at a recent FU); the reference group is persistently no late effects/CHCs over time. Also refer to "4. Definitions for the progression of late effects/CHCs" under the header "Key independent variables: late medical effects/CHCs" for a detailed statement.

H₀ 1c: Individuals with greater intensity/burden (number and severity) of late effects/CHCs will have higher risk of financial hardship compared to individuals with less burden/intensity.

Note, total intensity/burden of late effects/CHCs will be quantified by 3 methods including Geenen et al³⁴ (Method 1), Charlson/Deyo et al^{35,36} (Method 2), and Mukherjee et al³⁷ (Method 3). Will create an ordinal variable to indicate the change of total intensity from baseline to a recent FU with range -3 (least worsening) to +3 (most worsening). Also refer to “3. Measures of total intensity across all late effects/CHCs” under the header “Key independent variables: late medical effects/CHCs” for a detailed statement.

Aim 2: Identify risk factors that influence the impact of late effects/CHCs on cross-sectional assessment of financial hardship

H₀ 2a: Impact of late effects/CHCs on financial hardship will be greater for individuals with lower personal SES status (e.g., lower educational attainment, low family income, inconsistent no health insurance coverage) vs. individuals with higher personal SES status (e.g., higher educational attainment, higher family income, consistent health insurance coverage)

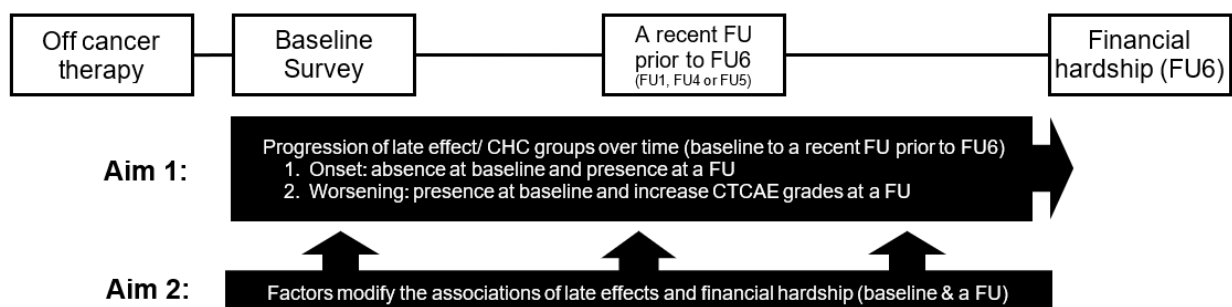
H₀ 2b: Impact of late effects/CHCs on financial hardship will be greater for individuals with more psychological distress (e.g., anxiety, depression) compared to individuals with less psychological distress

H₀ 2c: Impact of late effects/CHCs on financial hardship will be greater for individuals with an unhealthy lifestyle (e.g., consistently physically inactive, consistently smoking) compared to individuals with a healthy lifestyle (e.g., consistent physically active, consistent non-smoking)

H₀ 2d: impact of late effects/CHCs on financial hardship will be greater for individuals residing in more disadvantaged areas (e.g., higher area SES deprivation, rural areas) vs. individuals residing in less disadvantaged areas (e.g., lower area SES deprivation, urban areas)

6. METHODS

Conceptual Framework



Participants

This study will evaluate the natural progression of late effects/CHCs in associations with financial hardship among adult survivors of childhood cancer. Financial hardship data are from the FU6 survey and late effects/CHCs are from baseline and other follow-up surveys

prior to FU6. In total, 4,153 survivors completed FU6, including 2,266 from the original cohort and 1,887 from the expanded cohort. The inclusion and exclusion criteria to identify potential participants for use in statistical analyses are as follows:

1. Inclusion criteria
 - a. All pediatric cancer diagnoses
 - b. Age at FU6 completion: ≥ 18 years of age
 - c. Completion of baseline and FU6 surveys

Note, testing hypothesis 1a will rely on survivors who completed baseline and FU6 surveys, and testing other hypotheses will rely on survivors who completed baseline, FU6 and other surveys collected between baseline and FU6 (FU1, FU4 or FU5).

2. Exclusion criteria
 - a. In conjunction with inclusion criteria

Outcomes of interest: financial hardship in FU6

1. Direct effect of medical conditions on financial hardship
 - a. Effect over past week (C11)
 - b. Effect over past year (C12)
2. Material hardship (domain 1)
 - a. Problems paying medical bills (C5, C6)
 - b. High out-of-pocket medical spending ($>10\%$ of family income) (C10, C21)
 - c. History of being sent to debt collection (C29)
 - d. History of filing for bankruptcy (C30, C31)
3. Psychological hardship (domain 2)
 - a. Worries about not being able to pay upcoming medical bills (C16)
 - b. Concern about being able to pay mortgage, afford food, or pay for household utilities (C17, C18, C19)
4. Coping/behavioral hardship (domain 3)
 - a. Inability to afford medical/paramedical care or delay/foregoing of medical care (C8)
5. **Intensity of overall financial hardship** over three domains
 - a. Consistent with the methods used in the FU6 “master” concept (Lead: Nathan)
 - b. Method 1: total number of hardship domains
 - Calculate the number (0, 1, 2 or 3) of three financial hardship domains in which survivors reported ≥ 1 measure of hardship.
 - c. Method 2: weighted intensity over three hardship domains
 - Perform factor analysis to measure financial hardship intensity that allows for incorporating relative weights of individual hardship items (i.e., factor loadings) into the calculation of hardship intensity scores.
 - First, perform principal component factor analysis with the multiple items of each hardship domain to generate a factor score for each participant. Specific items with low factor loadings (e.g., standardized loading <0.3) may be

removed from the score calculation after reviewing the content appropriateness. Second, sum the standardized factor scores derived from each of three domains, and trichotomize by Z-scores <-1 , -1 to 1 , and >1 (or per score distribution across all study participants) for measuring the overall intensity as low, moderate, high level.

6. Other financial hardship-related measures from FU6 at the item level (for exploratory purpose to test associations with progression of late effects/CHCs)
 - a. Financial sacrifices
 - Financial sacrifices because of medical debt (C9)
 - b. Employment/job or position change
 - Employment – full/part-time (C13)
 - Job or position change (C14)
 - c. Assets/debts
 - Home ownership/values/mortgages (C22, C23, C24, C25, C26)
 - Other debts (C27, C28, C29)

Key independent variables: late medical effects/CHCs

1. Timepoints:
 - a. Baseline and a recent FU survey prior to FU6 (either FU1, FU4 or FU5)
 - b. The most recent available FU that was closest to FU6 will be selected
2. Measures of specific **late effect/CHC groups**:
 - a. Individual late effects/CHCs will be grouped in 13 organ system-based groups, including hearing, vision, speech, endocrine, respiratory, cardiac, gastrointestinal, renal, musculoskeletal, neurological, other hematologic, other infectious/immunologic, and second malignant neoplasms.^{23,38}
 - b. CCSS has categorized and coded individual late effects/CHCs at baseline and FUs according to the grade/severity of the CTCAE version 4.0: mild = grade 1 (G1), moderate = grade 2 (G2), severe/disabling = grade 3 (G3), life-threatening = grade 4 (G4), or fatal = grade 5 (G5). In this study, late effects/CHCs \geq G2 will be categorized as presence; otherwise, categorized as absence. The presence of highest grade of an individual late effect/CHC within a specific late effect/CHC group will be selected to represent the grade of a specific late effect/CHC group.
3. Measures of **total intensity** (or total burden) **across all late effects/CHCs**:
 - a. We will use different methods to quantify total intensity of different late effect/CHC groups, including Geenen et al³⁴ (Method 1), Charlson/Deyo et al^{35,36} (Method 2), and Mukherjee et al³⁷ (Method 3). The method created by Geenen et al is cancer-specific yet evidence-based (arbitrary), whereas the methods by Charlson/Deyo et al and by Mukherjee et al are evidence-based yet non-cancer-specific.
 - b. **Method 1:** Total intensity across all late effect/CHC groups for each participant will be assigned score = 1 to 4 per the Geenen's method.³⁴
 - Low intensity if ≥ 1 G1 late effect/CHC groups
 - Medium intensity if ≥ 1 G2 late effect/CHC groups and/or 1 G3 late effect/CHC groups
 - High intensity if ≥ 2 G3 late effect/CHC groups, or 1 G4 late effect/CHC groups and at most 1 G3 late effect/CHC groups

- Severe intensity if ≥ 2 G4 late effect/CHC groups
- c. **Method 2:** We will map a list of CCSS's individual late effects/CHCs to a list of Charlson/Deyo's CHCs.^{35,36} Subsequently, we will use the coding algorithms created by Quan et al³⁹ to assign a weight to each late effect/CHC, and create a Charlson Comorbidity Index (CCI) score (0, 1, 2 and 3 or more) for each survivor. We will classify the total intensity across all late effects/CHCs for each survivor into 1 of the 4 categories:
- Low intensity if CCI score = 0
 - Medium intensity if CCI score = 1
 - High intensity if CCI score = 2
 - Severe intensity if CCI score = 3 or more
- d. **Method 3:** Algorithms derived from Method 2 were based on mortality as the dependent variable. An alternative method to create total intensity of all late effect/CHC groups is using HRQOL as dependent variable. This alternative method is known as "HRQOL-Comorbidity Index" (HRQOL-CI),³⁷ and a modified version using health-utility metric (SF-6D) has been pilot tested by Huang and Bhakta through SJLIFE data. Using a similar method to create Charlson CCI, we will assign a weight to each late effect/CHC group, and create a HRQOL-CI score (0, 1, 2 and 3 or more) for each survivor. We will classify the total intensity of all late effect/CHC groups for each survivor into 1 of the 4 categories
- Low intensity if HRQOL-CI score = 0
 - Medium intensity if HRQOL-CI score = 1
 - High intensity if HRQOL-CI score = 2
 - Severe intensity if HRQOL-CI score = 3 or more
4. Definitions for the **progression** of late effects/CHCs:
- a. Progression of specific late effect/CHC groups:
- Onset: from none/G1 at baseline to $\geq G2$ at a recent FU
 - Worsening: from G2 at baseline to $\geq G3$ at a recent FU, or from G3 at baseline to G4 at a recent FU
 - Progression of a specific late effect/CHC group: a categorical variable indicating persistently no late effects/CHCs (=1), new onset (=2), and worsening (=3) over time
- b. Progression of total intensity across all late effects/CHCs:
- An ordinal variable indicating the progression of intensity scores from baseline to a recent FU with range -3 to +3 (i.e., the intensity score at a recent FU subtracts the intensity score at baseline)
- c. Time factor of new onset:
- Years between off-therapy and the first $\geq G2$ events occurred
 - Age (in years) when first $\geq G2$ events occurred

Other dependent variables/covariates

** Longitudinal classification for variables over 2 time points: specific risk factors of interest that potentially modify the association of late effects/CHCs with financial hardship*

A. Socio-demographics

1. Age at the time of survey completion (in years):
 - a. Baseline, a recent FU prior to FU6, and FU6

2. Sex:
 - a. Male; female
3. Race/ethnicity:
 - a. Baseline
 - b. Classification
 - White, non-Hispanic; black, non-Hispanic; Hispanic; other
4. Educational attainment:
 - a. Baseline, a recent FU prior to FU6, and FU6
 - b. Classification
 - Did not complete high school (HS); HS graduate/GED/training after HS or some college; college graduate or postgraduate level
5. Marital status:
 - a. Baseline, a recent FU prior to FU6, and FU6
 - b. Classification
 - Married/living with partner; widowed/divorced/separated; single (never married)
6. Annual family income:
 - a. Baseline, a recent FU prior to FU6, and FU6
 - b. Consider number of household members in the analysis
 - c. Classification Method 1
 - Cross-sectional: <\$20,000 (low); \$20,000-\$79,999 (moderate); ≥\$80,000 (high) with CPI inflation adjustment
 - Longitudinal (baseline vs. a recent FU prior to FU6)*: consistently low; inconsistently change; consistently high family income
 - d. Classification Method 2
 - Cross-sectional: below vs. above federal poverty line (FPL) in a particular year that accounts for household income and number of family members
 - Longitudinal (baseline vs. a recent FU prior to FU6)*: consistently below FPL; inconsistently change; consistently above FPL
7. Personal health insurance coverage:
 - a. Baseline, a recent FU prior to FU6, and FU6
 - b. Classification:
 - Cross-sectional: no insurance coverage vs. insurance coverage
 - Longitudinal (baseline vs. a recent FU prior to FU6)*: consistent no insurance coverage; inconsistent coverage; consistent insurance coverage
- B. Cancer diagnosis
8. Primary cancer:
 - a. Leukemia; CNS tumor; Hodgkin lymphoma; non-Hodgkin lymphoma; Wilms tumor; neuroblastoma; soft tissue sarcoma; bone tumor; other
9. Secondary cancer or recurrence
- C. Cancer treatment

10. Chemotherapy:
- a. Corticosteroids; mercaptopurine/thioguanine; methotrexate; Erwinia-/L-/Peg-asparaginase; cisplatin/carboplatin/oxaliplatin; anthracycline; alkylating agents; vincristine; other chemotherapy; any chemotherapy (yes or no for each)
11. Radiation therapy:
- a. Brain irradiation; chest irradiation; abdominal irradiation; pelvic irradiation; other radiation therapy; any radiation therapy (yes or no for each)
12. Surgery:
- a. Splenectomy; nephrectomy; amputation; other major surgery (yes or no for each)

D. Time interval

13. Years since cancer diagnosis:
- a. Interval between age at cancer diagnosis and age at FU6 (in years)
14. Years since CCSS participation:
- a. Interval between age at baseline and age at FU6 (in years)

E. Risk factors for the association of late effects/CHCs and financial hardship

15. Emotional distress:
- a. Baseline and a recent FU prior to FU6
 - b. Brief Symptom Inventory-18 (BSI-18) by three domains (anxiety, depression, somatization) and global severity index (GSI)
 - c. Classification
 - Cross-sectional: distress (sex-adjusted GSI ≥ 63) and non-distress (sex-adjusted GSI < 63)
 - Longitudinal*: consistently distress (distress over two timepoints), inconsistently distress/non-distress, and consistently non-distress (non-distress over two timepoints)
16. Self-reported cigarette smoking:
- a. Baseline and a recent FU survey prior to FU6
 - b. Classification for impairment
 - Cross-sectional/longitudinal*: never, past, and current cigarette smokers based on CDC guideline
17. Self-reported physical activity:
- a. Baseline and a recent FU prior to FU6
 - b. Physically active and inactive based on CDC guideline
 - c. Classification
 - Cross-sectional: active and inactive
 - Longitudinal*: consistently active (active over two timepoints), inconsistently active/inactive, and consistently inactive (inactive over two timepoints)
18. Area SES deprivation and rural-urban status:
- a. Area SES deprivation
 - Measure: area deprivation index (ADI) consisting of 17 neighborhood-based SES measures including income, employment, education, and housing collected in the 2009–2013 American Community Survey.^{40,41}

- Procedure: geocode full home addresses of each participant and calculate the percentile of ADI (per ranking of all U.S. census blocks)
- Category: high (>75th percentile), moderate (40th to 70th); low (<40th percentile) area deprivation.
- b. Rural-urban status
 - Measure: rural-urban commuting area (RUCA) codes classify U.S. census tracts based on population density, urbanization, and daily commuting.
 - Procedure: geocode full home addresses of each participant and categorize rural-urban status
 - Classification (will use the secondary codes): urban [1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, 10.1]; large rural town [4.0, 4.2, 5.0, 5.2, 6.0, 6.1]; small rural town [7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2, 10.0, 10.2, 10.3, 10.4, 10.5, 10.6]

Analytic approach

Summary Statistics

Chi-square/t-tests will be performed to compare differences in individual characteristics between those who completed baseline and FU6 surveys (Table 1) and between CCSS participants who were included and excluded in this study (Table S1).

Descriptive analyses (%) will be performed to report prevalence of financial hardship, including individual hardship domains (i.e., material, psychological, and coping/behavioral), overall hardship across 3 domains (i.e., total number of problematic domains and total intensity), and other financial hardship-related items (financial sacrifices, job/position change, home ownership/mortgage status, and other debts) (Table 2). Chi-square/t-tests will be performed to compare associations of baseline participant characteristics (including specific late effect/CHC groups and total intensity across all late effects/CHCs at CCSS baseline) with financial hardship (Table S2).

Descriptive analyses (%) will be performed to report the frequency of progression of specific late effect/CHC groups from baseline to FU6, including no change, new onset, and worsening (Table 3A). In addition, descriptive analyses (%) will be performed to report the total intensity progression across all late effects/CHCs (Table 3B). Three methods will calculate total intensity of all late effects/CHCs, including Geenen's approach, Modified Charlson/Deyo's approach, and HRQOL-Comorbidity-based approach (see header "Measures of total intensity of late effects/CHCs"). Each method will classify total intensity as low intensity (=0), medium intensity (=1), high intensity (=2) and severe intensity (=3). The progression of total intensity over time ranges from -3 to +3.

Aim 1: Identify late effects/CHCs that are associated with cross-sectional assessment of financial hardship domains

Financial hardship outcome 1: total number of hardship domains

Multivariable multinomial logistic regression models will be performed to test associations of onset/worsening late effect/CHC groups with the total number of financial hardship domains (the 2nd and 3rd columns in Table 4A). Each late effect/CHC group will be included in an individual regression model and the change status will be classified as new onset, worsening, and no change (as the reference group). Total number of financial hardship domains will be classified as none (as the reference group), 1, and 2 or 3. The

following covariates will be adjusted in each analytic model: age (in years) when first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity.

Multivariable multinomial logistic regression models will be performed to test associations of the total intensity progression across all late effects/CHCs with the total number of financial hardship domains (the 2nd and 3rd columns in Table 4B). Total intensity progression will be estimated by three methods: Geenen's approach (Method 1), Modified Charlson/Deyo's approach (Method 2), and HRQOL-Comorbidity-based approach (Method 3). Each method will be included in an individual regression model and the change status will be classified by 7 categories (-3 to +3, using 0 as the reference group). Total number of financial hardship domains will be classified as none (as the reference group), 1, and 2 or 3. The following covariates will be adjusted in each analytic model: age (in years) when first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity.

Financial hardship outcome 2: weighted intensity scores over 3 financial hardship domains

Multivariable multinomial logistic regression models will be performed to test associations of onset/worsening late effect/CHC groups with the weighted intensity over three financial hardship domains (the 3rd and 4th columns in Table 4A). Each individual late effect/CHC group will be included in an individual regression model and the change status will be classified as new onset/ worsening and no change (as the reference group). The weighted intensity of financial hardship domains will be classified by low (as the reference group), moderate, and high. The following covariates will be adjusted in each analytic model: age (in years) when first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity.

Multivariable multinomial logistic regression models will be performed to test the association of the total intensity progression across all late effects/CHCs with the weighted intensity over three financial hardship domains (the 4th and 5th columns in Table 4B). Total intensity progression will be estimated by three methods: Geenen's approach (Method 1), Modified Charlson/Deyo's approach (Method 2), and HRQOL-Comorbidity-based approach (Method 3). Each method will be included in an individual regression model and the change status will be classified by 7 categories (-3 to +3, using 0 as the reference group). The weighted intensity over three financial hardship domains will be classified by low (as the reference group), moderate, and high. The following covariates will be adjusted in each analytic model: age (in years) when first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity.

Aim 2: Identify risk factors that influence the impact of late effects/CHCs on cross-sectional assessment of financial hardship

Aim 2 will evaluate whether the impact of late effects/CHCs progression on financial hardship depends upon the levels of SES/psychological/behavior risk factors. These factors include educational attainment, annual family income change, health insurance coverage change, psychological distress change, smoking status, physical activity change, and area SES deprivation. We consider these risk factors as "modifiers" for the association of late effects/CHCs and financial hardship. These modifiers will be tested by adding interaction terms between late effect/CHC progression and risk factors to the models created in Aim 1. For testing specific modification effects, see Table 5 (race/ethnicity), Table 6 (household income), Table 7 (insurance coverage), Table 8 (psychological distress), Table 9 (smoking status), Table 10 (physical activity status), and Table 11 (area SES deprivation).

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8. TABLES/FIGURES

Table 1: Participant characteristics at baseline and FU6

Characteristics	Baseline	FU6
	Mean (SD/range) or N (%)	Mean (SD/range) or N (%)
Socio-demographic factors		
Age (in years)		
18 – 24		
25 – 29		
30 – 34		
35 – 39		
40 – 44		
45 – 49		
50 – 54		
55 – 59		
≥ 60		
Sex		
Male		
Female		
Race/ethnicity		
White, non-Hispanic		
Black, non-Hispanic		
Hispanic		
Other		
Educational attainment		
Not complete high school (HS)		
HS graduate/GED		
Training after HS/some college		
College graduate/postgraduate level		
Marital status		
Married/living with partner		
Widowed/divorced/separated		
Single/never married		
Annual household income [†]		
<\$20,000		
\$20,000-\$79,999		
≥\$80,000		
Health insurance coverage		
Public insurance		
Private insurance		
No insurance		
Cancer diagnosis		
Leukemia		
CNS tumor		
Hodgkin lymphoma		
Non-Hodgkin lymphoma		
Wilms tumor		

Neuroblastoma		
Soft tissue sarcoma		
Bone tumor		
Other		
Cancer treatment		
Methotrexate		
Corticosteroid		
Anthracyclines		
Alkylating agents		
Other chemotherapy		
Brain irradiation		
Chest irradiation		
Abdominal irradiation		
Pelvic irradiation		
Other radiation therapy		
Any chemotherapy		
Any radiation therapy		
Major surgery		
Psycho-behavior factors		
Psychological distress		
Anxiety		
Depression		
Somatization		
Global		
Cigarette smoking		
Never smoker		
Past smoker		
Current smoker		
Physical activity		
Physically active		
Physically inactive		
Specific late effect/CHC groups		
Hearing		
Vision		
Speech		
Endocrine		
Respiratory		
Cardiac		
Gastrointestinal		
Renal		
Musculoskeletal		
Neurological		
Other hematologic		
Other infectious/immunologic		
Second malignant neoplasms		
Total intensity across all late effects/CHCs[‡]		
Low		
Medium		

High		
Severe		
Time interval		
Years since cancer diagnosis		
Years since CCSS participation		

† CPI inflation adjustment (https://www.bls.gov/data/inflation_calculator.htm)

‡ Separate analyses Method 1: Geenen's approach; Method 2: Modified Charlson/Deyo's approach; Method 3: HRQOL-Comorbidity-based approach

Table 2: Prevalence of financial hardship at FU6

Type of financial hardship	N (%)
Financial hardship domain	
Material (Y/N)	
Psychological (Y/N)	
Coping/Behavioral (Y/N)	
Overall financial hardship	
Total number of three hardship domains	
0	
1	
2 or 3	
Total intensity	
Low	
Moderate	
High	
Other financial hardship-related measures at the item level	
Financial sacrifices (Y/N)	
Job or position change (Y/N)	
Home ownership/mortgage (Y/N)	
Other debts (Y/N)	

Table 3A: Progression of specific late effect/CHC groups: from baseline to a recent FU prior to FU6

Specific late effect/CHC groups	No change	New onset	Worsening
	N (%)	N (%)	N (%)
Hearing			
Vision			
Speech			
Endocrine			
Respiratory			
Cardiac			
Gastrointestinal			
Renal			
Musculoskeletal			
Neurological			
Other hematologic			
Other infectious/immunologic			
Second malignant neoplasms			

Table 3B: Total intensity progression across all late effects/CHCs: from baseline to a recent FU prior to FU6

Methods to classify total intensity across all late effect/CHC groups	Total intensity progression across all late effects/CHCs [†]						
	-3	-2	-1	0	1	2	3
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Method 1: Geenen's approach							
Method 2: Modified Charlson/Deyo's approach							
Method 3: HRQOL-Comorbidity-based approach							

[†] Each method will classify total intensity as low intensity (=0), medium intensity (=1), high intensity (=2) and severe intensity (=3). The progression of total intensity ranges from -3 to +3.

Table 4A: Association of onset/worsening late effect/CHC groups and overall financial hardship: multivariable multinomial logistic regression analysis^{&,\$}

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Vision				
Onset				
Worsening				
Speech				
Onset				
Worsening				
Endocrine				
Onset				
Worsening				
Respiratory				
Onset				
Worsening				
Cardiac				
Onset				
Worsening				
Gastrointestinal				
Onset				
Worsening				
Renal				
Onset				
Worsening				
Musculoskeletal				
Onset				
Worsening				
Neurological				
Onset				
Worsening				
Other hematologic				
Onset				
Worsening				
Other infectious/immunologic				
Onset				
Worsening				
Second malignant neoplasms				
Onset				
Worsening				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity
No late effects/CHCs at both baseline and a recent FU as the reference group
† 0 as the reference group
‡ Low as the reference group

Table 4B: Association of the total intensity progression across all late effects/CHCs with overall financial hardship: multivariable multinomial logistic regression analysis^{&,\$}

Total intensity progression across all late effects/CHCs	Total number over three hardship domains		Intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Method 1: Geenen's approach				
-3				
-2				
-1				
0 [#]				
+1				
+2				
+3				
Method 2: Modified Charlson/Deyo's approach				
-3				
-2				
-1				
0 [#]				
+1				
+2				
+3				
Method 3: HRQOL-Comorbidity-based approach				
-3				
-2				
-1				
0 [#]				
+1				
+2				
+3				

& One multivariable model for one late effect/CHC

\$ Each model adjusts for age (in years) when the first ≥G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

No CTCAE grade change in a specific late effects/CHC group as the reference group

† 0 as the reference group

‡ Low hardship as the reference group

Table 5: Effect of educational attainment on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis ^{&,\$}

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Educational attainment				
HS graduate/GED/training after HS or some college ^{&}				
Below HS ^{&}				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Vision				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Speech				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				

Worsening * HS graduate/ GED/training after HS or some college				
Worsening * below HS				
Endocrine				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/ GED/training after HS or some college				
Worsening * below HS				
Respiratory				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/ GED/training after HS or some college				
Worsening * below HS				
Cardiac				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/ GED/training after HS or some college				
Worsening * below HS				

Gastrointestinal				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Renal				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Musculoskeletal				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Neurological				
Onset				
Worsening				
Educational attainment				

HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Other hematologic				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Other infectious/immunologic				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				
Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/GED/training after HS or some college				
Worsening * below HS				
Second malignant neoplasms				
Onset				
Worsening				
Educational attainment				
HS graduate/GED/training after HS or some college				
Below HS				
Interaction				

Onset * HS graduate/GED/training after HS or some college				
Onset * below HS				
Worsening * HS graduate/ GED/training after HS or some college				
Worsening * below HS				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& College graduate or postgraduate as the reference group

Table 6: Effect of family income on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis &,\$,@

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Change of family income				
Inconsistently change over time ^{&}				
Consistently low over time ^{&}				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Vision				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Speech				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Endocrine				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				

Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Respiratory				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Cardiac				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Gastrointestinal				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Renal				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Musculoskeletal				
Onset				

Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Neurological				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Other hematologic				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Other infectious/immunologic				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				
Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				
Second malignant neoplasms				
Onset				
Worsening				
Change of family income				
Inconsistently change over time				
Consistently low over time				
Interaction				

Onset * inconsistently change				
Onset * consistently low				
Worsening * inconsistently change				
Worsening * consistently low				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

@ This table focuses on Method 1. A similar table will focus on Method 2: Federal Poverty Line (see Section 6. Annual family income).

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Consistently high family income over time as the reference group

Table 7: Effect of insurance coverage on associations onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis &,\$

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Change of insurance coverage				
Inconsistent coverage over time ^{&}				
Consistent no coverage over time ^{&}				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Vision				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Speech				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Endocrine				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				

Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Respiratory				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Cardiac				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Gastrointestinal				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Renal				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Musculoskeletal				
Onset				

Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Neurological				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Other hematologic				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Other infectious/immunologic				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				
Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				
Second malignant neoplasms				
Onset				
Worsening				
Change of insurance coverage				
Inconsistent coverage over time				
Consistent no coverage over time				
Interaction				

Onset * inconsistent coverage				
Onset * consistent no coverage				
Worsening * inconsistent coverage				
Worsening * consistent no coverage				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Consistently consistent insurance coverage over time as the reference group

Table 8: Effect of psychological distress on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis ^{&,\$}

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Change of psychological distress				
Inconsistently distress over time ^{&}				
Consistently distress over time ^{&}				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Vision				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Speech				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Endocrine				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				

Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Respiratory				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Cardiac				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Gastrointestinal				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Renal				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Musculoskeletal				
Onset				

Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Neurological				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Other hematologic				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Other infectious/immunologic				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				
Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				
Second malignant neoplasms				
Onset				
Worsening				
Change of psychological distress				
Inconsistently distress over time				
Consistently distress over time				
Interaction				

Onset * inconsistently distress				
Onset * consistently distress				
Worsening * inconsistently distress				
Worsening * consistently distress				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Consistently non-distress over time as the reference group

Table 9: Effect of smoking behavior on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis &,\$

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Cigarette smoking status				
Past smokers ^{&}				
Current smokers ^{&}				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Vision				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Speech				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Endocrine				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				

Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Respiratory				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Cardiac				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Gastrointestinal				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Renal				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Musculoskeletal				
Onset				

Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Neurological				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Other hematologic				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Other infectious/immunologic				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				
Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				
Second malignant neoplasms				
Onset				
Worsening				
Cigarette smoking status				
Past smokers				
Current smokers				
Interaction				

Onset * past smokers				
Onset * current smokers				
Worsening * past smokers				
Worsening * current smokers				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Never smokers as the reference group

Table 10: Effect of physical activity on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis &,\$

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Physical activity status				
Inconsistently active over time &				
Consistently inactive over time&				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Vision				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Speech				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Endocrine				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				

Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Respiratory				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Cardiac				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Gastrointestinal				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Renal				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Musculoskeletal				
Onset				

Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Neurological				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Other hematologic				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Other infectious/immunologic				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				
Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				
Second malignant neoplasms				
Onset				
Worsening				
Physical activity status				
Inconsistently active over time				
Consistently inactive over time				
Interaction				

Onset * inconsistently active				
Onset * consistently active				
Worsening * inconsistently active				
Worsening * consistently active				

& One multivariable model for one late effect/CHC

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Consistently physically active as the reference group

Table 11: Effect of area SES deprivation on associations of onset/worsening late effect/CHC groups with financial hardship: multivariable multinomial logistic regression analysis &,\$,@

Specific late effect/CHC groups	Total number over three hardship domains		Weighted intensity over three hardship domains	
	1 [†]	2 or 3 [†]	Moderate [‡]	High [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Hearing				
Onset [#]				
Worsening [#]				
Area SES deprivation				
Moderate area deprivation ^{&}				
High area deprivation ^{&}				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Vision				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Speech				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Endocrine				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				

Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Respiratory				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Cardiac				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Gastrointestinal				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Renal				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Musculoskeletal				
Onset				

Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Neurological				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Other hematologic				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Other infectious/immunologic				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				
Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				
Second malignant neoplasms				
Onset				
Worsening				
Area SES deprivation				
Moderate area deprivation				
High area deprivation				
Interaction				

Onset * moderate area deprivation				
Onset * high area deprivation				
Worsening * moderate area deprivation				
Worsening * high area deprivation				

& One multivariable model for one late effect/CHC group

\$ Each model adjusts for age (in years) when the first \geq G2 events were reported, age (in years) at FU6, sex, and race/ethnicity

@ This table focuses on the metric of area SES derivation (ADI). A similar table will focus on another metric RUCA codes (see Section E, 18: Area SES deprivation and rural-urban status).

† No hardship as the reference group

‡ Low hardship as the reference group

No CTCAE grade change in a specific late effects/CHC group as the reference group

& Low area deprivation as the reference group

9. Supplemental Materials

Figure 1: Diagram of inclusion/exclusion of study participants

Table S1: Comparisons between study participants and non-participants at CCSS baseline: bivariate analyses using chi-square test for categorical variables or t-test for continuous variable

Characteristics at CCSS baseline	Participants Mean (SD/range) or N (%)	Non-participants Mean (SD/range) or N (%)
Socio-demographic factors		
Age (in years)		
18 – 24		
25 – 29		
30 – 34		
35 – 39		
40 – 44		
45 – 49		
50 – 54		
55 – 59		
≥ 60		
Sex		
Male		
Female		
Race/ethnicity		
White, non-Hispanic		
Black, non-Hispanic		
Hispanic		
Other		
Educational attainment		
Not complete high school (HS)		
HS graduate/GED		
Training after HS/some college		
College graduate/postgraduate level		
Marital status		
Married/living with partner		
Widowed/divorced/separated		
Single/never married		
Annual household income		
<\$20,000		
\$20,000-\$79,999		
≥\$80,000		
Health insurance coverage		
Public insurance		
Private insurance		
No insurance		
Cancer diagnosis		
Leukemia		
CNS tumor		
Hodgkin lymphoma		
Non-Hodgkin lymphoma		
Wilms tumor		
Neuroblastoma		

Soft tissue sarcoma		
Bone tumor		
Other		
Cancer treatment		
Methotrexate		
Corticosteroid		
Anthracyclines		
Alkylating agents		
Other chemotherapy		
Brain irradiation		
Chest irradiation		
Abdominal irradiation		
Pelvic irradiation		
Other radiation therapy		
Any chemotherapy		
Any radiation therapy		
Major surgery		
Psycho-behavior factors		
Psychological distress		
Anxiety		
Depression		
Somatization		
Global		
Cigarette smoking		
Never smoker		
Past smoker		
Current smoker		
Physical activity		
Physically active		
Physically inactive		
Specific late effect/CHC groups		
Hearing		
Vision		
Speech		
Endocrine		
Respiratory		
Cardiac		
Gastrointestinal		
Renal		
Musculoskeletal		
Neurological		
Other hematologic		
Other infectious/immunologic		
Second malignant neoplasms		
Total intensity across all late effects/CHCs[†]		
Low		
Medium		

High		
Severe		
Time interval		
Years since cancer diagnosis		
Years since CCSS participation		

† Separate analyses for Method 1: Geenen's approach; Method 2: Modified Charlson/Deyo's approach; Method 3: HRQOL-Comorbidity-based approach

Table S2: Baseline participant characteristics associated with overall financial hardship: bivariate analyses using chi-square test for categorical variables or t-test for continuous variable

Characteristics at CCSS baseline	Total number over three hardship domains			Intensity over three hardship domains		
	0	1	2 or 3	Low	Moderate	High
Socio-demographic factors						
Age (in years)						
18 – 24						
25 – 29						
30 – 34						
35 – 39						
40 – 44						
45 – 49						
50 – 54						
55 – 59						
≥ 60						
Sex						
Male						
Female						
Race/ethnicity						
White, non-Hispanic						
Black, non-Hispanic						
Hispanic						
Other						
Educational attainment						
Not complete HS						
HS graduate/GED						
Training after HS/some college						
College graduate/postgraduate level						
Marital status						
Married/living with partner						
Widowed/divorced/separated						
Single/never married						
Annual household income						
<\$20,000						
\$20,000-\$79,999						
≥\$80,000						
Health insurance coverage						
Public insurance						
Private insurance						
No insurance						
Cancer diagnosis						
Leukemia						
CNS tumor						

Hodgkin lymphoma						
Non-Hodgkin lymphoma						
Wilms tumor						
Neuroblastoma						
Soft tissue sarcoma						
Bone tumor						
Other						
Cancer treatment						
Methotrexate						
Corticosteroid						
Anthracyclines						
Alkylating agents						
Other chemotherapy						
Brain irradiation						
Chest irradiation						
Abdominal irradiation						
Pelvic irradiation						
Other radiation therapy						
Any chemotherapy						
Any radiation therapy						
Major surgery						
Psycho-behavior factors						
Psychological distress						
Anxiety						
Depression						
Somatization						
Global						
Cigarette smoking						
Never smoker						
Past smoker						
Current smoker						
Physical activity						
Physically active						
Physically inactive						
Specific late effect/CHC groups						
Hearing						
Vision						
Speech						
Endocrine						
Respiratory						
Cardiac						
Gastrointestinal						
Renal						
Musculoskeletal						
Neurological						

Other hematologic						
Other infectious/immunologic						
Second malignant neoplasms						
Total intensity across all late effects/CHCs[†]						
Low						
Medium						
High						
Severe						
Time interval						
Years since diagnosis						
Years since CCSS participation						

† Separate analyses for Method 1: Geenen's approach; Method 2: Modified Charlson/Deyo's approach; Method 3: HRQOL-Comorbidity-based approach