Analysis Concept Proposal

1. **Study title:** Social Determinants of Health, Chronic Health Conditions, and Healthcare Utilization Among Childhood Cancer Survivors

2. **Working groups:** Cancer Control (primary); Chronic Disease (secondary)

3. **Investigators:**

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4. **Summary of key terms**

Social determinants of health (SDOH)	Neighborhood-level measures, including socioenvironmental vulnerability, persistent poverty, rurality, and contemporary redlining
Socioeconomic status (SES)	Individual-level measures (e.g., income, education, health insurance)
Global CHC burden	Based on CTCAE gradings and classified as no, low, medium, high, or very high burden as in Table A below.
Organ-specific CHC burden	Based on CTCAE gradings with each of 13 organ systems (hearing, vision, speech, endocrine, respiratory, cardiovascular, gastrointestinal, renal, musculoskeletal, neurological, other hematologic, other infectious/immunologic, and second malignant neoplasms) classified as none, mild, moderate, severe or disabling, life-threatening, or fatal

5. **Background and rationale**

It is well-established that childhood cancer survivors experience substantial disparities in health outcomes during young adulthood compared with the general population. Childhood cancer survivors have a 5-fold increased risk of developing a chronic health condition (CHC) compared to age-matched siblings.[1] It is therefore critical for these survivors to undergo routine health maintenance and recommended screening for late effects in the context of their prior diagnosis and treatment history. However, less than one-third of survivors report receiving guideline-recommended late-effects surveillance.[2] It is also increasingly recognized that social determinants of health (SDOH) are drivers of adverse health outcomes in both the general and childhood cancer survivor populations.[3,4] However, there remains a gap in understanding how different domains of SDOH relate to the development and progression of CHCs and to healthcare utilization patterns in childhood cancer survivors.

Beyond individual-level socioeconomic status (SES; e.g., income, education, insurance), a broader conceptualization of SDOH encompasses **neighborhood-level socioenvironmental conditions** (e.g., characteristics of the places where people live and work). Multiple measures of neighborhood-level SDOH based

on geographic residence have been associated with adverse health outcomes in both the general and oncology populations. Living in areas with higher social vulnerability is associated with elevated risks of cardiovascular comorbidities in the general population and non-relapse mortality following hematopoietic cell transplantation.[5,6] Similarly, individuals living in areas with **persistent poverty**, defined as ≥20% of the population having reported incomes below the federal poverty level for ≥30 years, have an increased risk of cancer-related mortality.[7,8] In the general population, **rurality** is strongly associated with rates of emergency room (ER) visits and hospitalizations,[9] and individuals living in rural areas are more likely to have cardiac-related hospitalizations.[10] Rural areas may also have fewer preventative service programs, reflecting limited healthcare infrastructure, workforce shortages, and reduced access to public health resources. For example, a recent study found that implementation of the Diabetes Prevention Program was less common in rural areas of the US.[11] In another study, rurality and living in a region with greater area deprivation were associated with lower rates of breast, cervical, and colorectal cancer screening in the general population.[12] **Contemporary redlining** is a structural dimension of SDOH reflecting ongoing patterns of disinvestment and restricted access to financial and community resources in historically marginalized neighborhoods. These conditions have been associated with poorer survival outcomes in adult breast and prostate cancer populations.[13,14] These differences may be related to worse environmental exposures (e.g., air quality) or barriers in access to care (e.g., distance to healthcare providers, transportation issues). However, there is a paucity of research that comprehensively evaluates these distinct measures in relation to CHCs and healthcare utilization practices among survivors of childhood cancer. Therefore, this study aims to examine the association between SDOH (both cross-sectionally and longitudinally), CHC burden and progression, and healthcare utilization among long-term survivors of childhood cancer.

6. Specific aims/objectives/research hypotheses

Aim 1: Evaluate the association between baseline neighborhood-level SDOH, including socioenvironmental vulnerability, persistent poverty, contemporary redlining, and urban/rural status, and the subsequent CHC burden, including assessing temporal patterns in the severity of both global and organ-specific CHC burden.
Aim 1a: Evaluate the association between SDOH at baseline and severity of global and organ-specific CHC burden (see Table A for classification of global CHC burden severity).

- ***Hypothesis 1a.1:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a higher global CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.
- ***Hypothesis 1a.2***: Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a higher organ-specific CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Aim 1b: Evaluate the association between baseline neighborhood-level SDOH and temporal patterns in the severity of global and organ-specific CHC burden (see the operational definitions in the Methods section).

- ***Hypothesis 1b.1:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a greater progression in the severity of global CHC burden compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.
- ***Hypothesis 1b.2:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a greater incidence and worsening of organ-specific CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Aim 2: Evaluate the association between baseline and most recent SDOH and healthcare utilization.
***Aim 2a*:** Evaluate the association between baseline SDOH and subsequent healthcare utilization (ER visits, hospitalizations, PCP engagement).

- ***Hypothesis 2a:*** Adjusting for global CHC burden as a covariate, survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas at baseline will have a higher number of ER visits, a higher number of hospitalizations, and lower likelihood of having seen a PCP (past 2 years) post-baseline (at individual FU and across all FUs) compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Aim 2b: Evaluate the association between the most recent SDOH and healthcare utilization (ER visits, hospitalizations, PCP engagement).

- ***Hypothesis 2b:*** Given the same level of global CHC burden, survivors currently living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will have a higher number of ER visits (past 12 months), higher number of hospitalizations (past 12 months), and lower likelihood of having seen a PCP (past 2 years) compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Aim 3: Evaluate the association between the most recent SDOH and the likelihood of having received indicated screening tests for late effects, including echocardiogram, colonoscopy, mammogram/breast MRI, cervical cancer screening, and skin exam.

- ***Hypothesis 3:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be less likely to have received indicated screening tests for late effects compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas, after accounting for global CHC burden and treatment modalities.

7. Analysis Framework

Participants:
All aims will include all CCSS participants who have completed a baseline and any FU questionnaire. Questionnaire responses will be stratified as 1) using only questionnaires completed before December 31, 2019 (this will be the primary result for reporting); and 2) using only questionnaires completed on or after January 1, 2020, to address potential bias on CHC burden and healthcare utilization due to the Covid-19 pandemic.

Main Exposure: SDOH
We will include three neighborhood-level SDOH measures to comprehensively assess their associations with CHC burden and healthcare utilization, including (1) socioenvironmental vulnerabilities, (2) contemporary redlining and rurality, and (3) persistent poverty. These measures provide a multidimensional characterization of survivors' residential environments, reflecting both contemporary and historical inequities that shape exposure, opportunity, and health risk.

Social and Environmental Vulnerabilities
We will use established metrics to assess neighborhood-level socioenvironmental vulnerabilities. The CCSS study has geocoded participants' baseline residential addresses into 11-digit Federal Information Processing Standard (FIPS) codes that align with 2010 U.S. Census tracts. The CCSS study has geocoded residential addresses for survivors, including 19,463 at baseline, 17,458 at FU5/FU7, and 22,724 from either baseline or FU5/FU7. We will assess socioenvironmental vulnerabilities across the five domains of the Healthy People 2030 framework (economic stability, education access and quality, healthcare access and quality, neighborhood and built environment, social and community context). We will measure *social vulnerability* using the U.S. Centers for Disease Control and Prevention's Social Vulnerability Index (SVI), which includes 15 indicators across four domains: socioeconomic status, household composition/disability, minority status/language, and housing/transportation.[15] We will also measure *environmental vulnerability* using indicators from U.S. government agencies, covering two domains: healthcare accessibility (e.g., density of primary care physicians) and built environment (e.g., food accessibility). We will classify scores for each domain and indicator into national quartiles (Q1: best; Q4: worst).

Contemporary Redlining and Rurality
We will include redlining and rurality as structural, systematic risk factors that shape neighborhood conditions and access to resources. We will estimate contemporary redlining using a validated mortgage bias index derived from the Home Mortgage Disclosure Act (HMDA) dataset.[16] Census tracts with an index score greater than 2 will be classified as redlined. Because this measure applies only to urban neighborhoods, we will additionally incorporate rurality to ensure comprehensive coverage of all geographic contexts. Rural-Urban Commuting Area (RUCA) codes will be used to define rurality: tracts with a primary RUCA code ≤3 will be categorized as urban, and those with a code >3 as rural, reflecting commuting patterns and population density. We will then combine

these measures to create a three-level structural variable: non-redlined urban areas, redlined urban areas, and rural areas.

Persistent Poverty

Persistent poverty refers to sustained economic deprivation experienced by individuals or communities over an extended period, rather than at a single point in time. It is typically measured as the 20% of households living below the federal poverty threshold across a defined period, often 30 years or more. We will use this longitudinal measure to capture the chronic nature of economic hardship and its cumulative effects on health, social mobility, and overall well-being at the community level.

Outcome Measures:

Primary Outcomes: Chronic Health Conditions

We will use the following metrics to examine CHC burden comprehensively. These metrics have been investigated in previous CCSS and SJLIFE concepts:[17]

- Global CHC burden severity
- Organ-specific CHC burden severity
- Temporal patterns of global CHC burden severity
- Organ-specific temporal patterns of severity of CHCs

Self-reported CHCs collected from baseline and follow-up (FU) questionnaires will be analyzed. Severity of CHCs will be assessed per CCSS's adaptation of the Common Terminology Criteria for Adverse Events, consistent with prior CCSS reports.[18] **Each CHC** is graded as none, mild (grade 1), moderate (grade 2), severe or disabling (grade 3), life-threatening (grade 4), or fatal (grade 5). Individual CHCs are categorized into the following 13 **organ-specific condition groups**: hearing, vision, speech, endocrine, respiratory, cardiovascular, gastrointestinal, renal, musculoskeletal, neurological, other hematologic, other infectious/immunologic, and second malignant neoplasms.

Global CHC burden severity at the time of the CCSS baseline survey and each FU survey is assessed using the methods described by Geenen et al.[17] Low CHC burden is defined as one or more grade 1 CHCs; medium CHC burden as one or more grade 2 CHCs or one grade 3 CHC; high CHC burden as two or more grade 3 CHCs or one grade 4 CHC with no more than one grade 3 CHC; and very high CHC burden as two or more grade 4 CHCs or one grade 4 CHC with at least two greater than grade 3 CHCs (Table A). Since CHCs are self-reported in CCSS, and grade 1 CHCs may be inaccurate, we will also consider combining no-burden and low-severity CHC burdens in a sensitivity analysis. At each FU, all CHCs up until the time of the FU completion will be counted.

Table A. Severity grading for **global CHC burden** per Geenen et al, JAMA 2007

Severity	CTCAE Grade 4	CTCAE Grade 3	CTCAE Grade 2	CTCAE Grade 1
Very high burden	≥2	Any count	Any count	Any count
	1	≥2	Any count	Any count
High burden	1	1	Any count	Any count
	1	0	Any count	Any count
	0	≥2	Any count	Any count
Medium burden	0	1	Any count	Any count
	0	0	≥1	Any count
Low burden	0	0	0	≥1
No burden	0	0	0	0

Temporal pattern of global CHC burden severity

Based on this metric, we will classify the **temporal pattern** of global CHC burden severity by comparing *baseline* to *the most recent FU* by 1) persistent no/low burden, 2) persistent medium burden, 3) moderate burden increase (e.g., from no/low burden to medium burden or medium burden to high or very high burden), 4) substantial burden increase (e.g., from no/low burden to high or very high burden), and 5) persistent high or very high burden. In addition, we will define **progression status** as 1) present if there is escalation across categories (i.e., from

none/low to medium/high/very high, from medium to high/very high, or from high to very high), and 2) otherwise, it will be considered absent.

Temporal pattern of severity of organ-specific CHCs

We will apply a similar approach to that used for the global CHC burden to quantify temporal patterns of severity of **CHCs by organ system**, recognizing that healthcare utilization and SDOH may differentially impact CHC severity by the involved organ system.[19] CHCs will be categorized into **13 organ-specific groups** as described above.[18,20] For each organ system group, the highest grade among its CHCs will be recorded. To examine temporal patterns, survivors will be classified into incident (CHC newly reaching a clinically significant grade ≥2), worsening (increasing from grade 2 or 3 to a higher grade), persistent (remaining at grade ≥2 without worsening), or non-progressive status (remaining at grades 0-1) for each CHC group.

Secondary Outcomes (For Aims 2 and 3): Healthcare Utilization

Self-reported data on healthcare utilization will be captured from FU questionnaires. We will use healthcare utilization information from all FU questionnaires since baseline. We will examine:

- ER visits over the past 12 months (FU5 B6, FU6 Long B6, FU7 T1-T2)
- Average number of ER visits across follow-up questionnaires.
- Hospitalizations over the past 12 months[21] (FU5 U1-U2, FU6 Long I1-I2, FU7 U1-U2)
- Average number of hospitalizations across follow-up questionnaires
- Yes/No: Visit with a PCP over the past 2 years as indicated on the most recent FU questionnaire (FU5 B1, FU6 B1, FU7 B1)
- The above numbers of ER visits, hospitalizations, or PCP visits, will be dichotomized or categorized based on their distribution in the study sample.
- Receipt of indicated screening tests as indicated on each participant's most recent FU questionnaire:
    - We will use two different sets of definitions for the high-risk population and compliance with COG LTFU Guidelines. The *primary analysis* will follow the approach as in Yan et al[22] (**Table B**).
    - A sensitivity analysis will be performed using the definitions of high-risk population and compliance in Snyder et al.'s ongoing analysis (**Table C**). As screening guidelines have evolved over time, adherence to the COG LTFU Guidelines was determined by the version in effect immediately preceding each FU questionnaire, consistent with the approach used by Yan et al.[22] For example, screening adherence for responses to FU 5 and 6 will be as per COG LTFU Guidelines V4.0, whereas adherence for responses to FU 7 will be as per COG LTFU Guidelines V5.0. The analysis will be performed among individuals at high risk for each outcome and those at standard risk, as screening guidance for both groups was included in the COG LTFU Guidelines V4.0 and V5.0.

Table B: Definition of meeting COG LTFU screening guideline in CCSS*

FU5, 6 (COG LTFU Guidelines V4.0)				
	Definition of high-risk population	**Adherence in the high-risk population**	**Definition of the standard risk population**	**Adherence in the standard risk population**
Colorectal cancer screening	(Abdominal RT + TBI ≥ 30 Gy OR Pelvis RT + TBI ≥30 Gy) AND 11 years after cancer diagnosis AND At least 36 years old	Colonoscopy in the last 5 years (FU5 C1f, FU6 Long C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago	Age ≥ 51	Fecal occult blood in the last year (Use home blood stool test, FU5 C1e, FU6 C1e) • Less than 1 year ago OR Flexible sigmoidoscopy in the last 5 years (FU5 C1f, FU6 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago OR

				Double contrast barium enema (No information from CCSS) OR Colonoscopy in the last 5 years (FU5 C1f, FU6 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago
Breast cancer screening	Chest radiation + TBI ≥ 20 Gy AND 9 years after primary cancer diagnosis AND Over 26 years old	Mammogram in the last year (FU5 C1j, FU6 Long C1j) • Less than 1 year ago OR Breast MRI in the last two years (FU5 C1j, FU6 Long C1j) • Less than 1 year ago	Age ≥ 41	Mammogram in the last year (FU5 C1j, FU6 Long C1j) • Less than 1 year ago
Cervical cancer screening	Age ≥ 21	21-29 yo: PAP in the last 3 years 30-65 yo: both HPV and PAP in the last 5 years or PAP in the last 3 years (*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU5 C1m, FU6 Long C1m) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago •	Age ≥ 21	21-29 yo: PAP in the last 3 years 30-65 yo: both HPV and PAP in the last 5 years or PAP in the last 3 years (*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU5 C1m, FU6 Long C1m) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago
Skin cancer screening	Any radiation	Dermatology exam in the last year (FU5 C1i, FU6 Long C1i) • Less than 1 year ago	NA	No screening recommended
Cardiac screening	Chest radiation or TBI or Anthracyclines**	**RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)** [1] Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 80], whichever was given first) [2] See Section 80 [3] Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, "Info Link (Dose Conversion)"] (FU5 C1a, C1b; FU6 C1a, C1b)	NA	No screening recommended

Age at Treatment[1]	Radiation with Potential Impact to the Heart[2]	Anthracycline Dose[3]	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	< 200 mg/m²	Every 2 years
		≥ 200 mg/m²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m²	Every 5 years
		≥100 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
≥5 years old	Yes	<300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
	No	<200 mg/m²	Every 5 years
		≥200 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
Any age with decrease in serial function			Every year

FU7 (COG LTFU Guidelines V5.0)				
	Definition of high risk population	Adherence in the high risk population	Definition of the standard risk population	Adherence in the standard risk population
Colorectal cancer screening	Radiation to the pelvis, abdomen, or TBI AND	Colonoscopy in the last 5 years (FU7 C1f) • Less than 1 year ago • 1-2 years ago	Age ≥ 45	Fecal occult blood in the last year (Use home stool blood test FU7 C1e) • Less than 1 year ago

<table>
<tr><td></td><td>5 years after cancer diagnosis

AND

age ≥ 30</td><td>More than 2 years but less than 5 years ago</td><td></td><td>OR

Flexible sigmoidoscopy in the last 5 years (FU7 C1f)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago
OR

Colonoscopy in the last 10 years (FU7 C1f)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago
5 or more years ago</td></tr>
<tr><td>Breast cancer screening</td><td>Radiation to the chest or TBI

AND

8 years after primary cancer diagnosis

AND

Over 25 years old, whichever occurs later</td><td>Mammogram in the last year (FU7 C1j)
Less than 1 year ago
OR

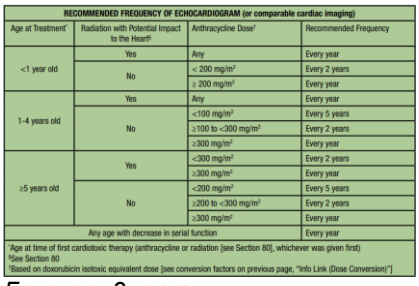
Breast MRI in the last two years (FU7 C1l)
Less than 1 year ago</td><td>Age ≥ 45</td><td>Mammogram in the last year (FU7 C1j)
Less than 1 year ago</td></tr>
<tr><td>Cervical cancer screening</td><td>Age ≥ 21 and <66</td><td>21-29 yo: PAP in the last 3 years
30-65 yo: both HPV and PAP in the last 5 years or PAP alone in the last 3 years
(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU7 C1j)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago</td><td>Age ≥ 21 and <66</td><td>21-29 yo: PAP in the last 3 years
30-65 yo: both HPV and PAP in the last 5 years or PAP alone in the last 3 years
(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU7 C1j)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago</td></tr>
<tr><td>Skin cancer screening</td><td>Any radiation</td><td>Dermatology exam in the year (FU7 C1i)
Less than 1 year ago</td><td>NA</td><td>No screening recommended</td></tr>
<tr><td>Cardiac screening</td><td>Chest radiation or TBI or Anthracyclines**</td><td><table><tr><th colspan="3">Recommended Frequency of Echocardiogram</th></tr><tr><th>Anthracycline Dose*</th><th>Radiation Dose**</th><th>Recommended Frequency</th></tr><tr><td rowspan="3">None</td><td>< 15 Gy or none</td><td>No screening</td></tr><tr><td>≥ 15 - < 35 Gy</td><td>Every 5 years</td></tr><tr><td>≥ 35 Gy</td><td>Every 2 years</td></tr><tr><td rowspan="2">< 250 mg/m²</td><td>< 15 Gy or none</td><td>Every 5 years</td></tr><tr><td>≥ 15 Gy</td><td>Every 2 years</td></tr><tr><td>≥ 250 mg/m²</td><td>Any or none</td><td>Every 2 years</td></tr><tr><td colspan="3">*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.</td></tr></table>(FU7 C1a, C1b)</td><td>NA</td><td>No screening recommended</td></tr>
</table>

*Standard risk screening is based on American Cancer Society recommendations as reproduced in the COG LTFU Guidelines v4.0 and v5.0, respectively

**Doxorubicin isotoxic equivalent dose = doxorubicin * 1 + daunorubicin * 0.5 + epirubicin * 0.67 + idarubicin * 5 + mitoxantrone * 4

Table C: Alternative definition of meeting COG LTFU screening guideline in CCSS*

FU5, 6 (COG LTFU Guidelines V4.0)				
	Definition of high-risk population	**Compliance in the high-risk population**	**Definition of the standard risk population**	**Compliance in the standard risk population**
Colorectal cancer screening	(Abdominal RT + TBI ≥ 30 Gy OR Pelvis RT + TBI ≥30 Gy) AND 11 years after cancer diagnosis AND At least 36 years old	Colonoscopy (FU5 C1f, FU6 Long C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago	Age ≥ 51	Fecal occult blood in the last two years (Use home blood stool test, FU5 C1e, FU6 C1e) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago OR Flexible sigmoidoscopy (FU5 C1f, FU6 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago OR Double contrast barium enema (No information from CCSS) OR Colonoscopy (FU5 C1f, FU6 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago
Breast cancer screening	Chest radiation + TBI ≥ 20 Gy AND 9 years after primary cancer diagnosis AND Age ≥ 26	Mammogram in the last two years (FU5 C1j, FU6 Long C1j) • Less than 1 year ago • 1-2 years ago OR Breast MRI in the last two years (FU7 C1l) • Less than 1 year ago • 1-2 years ago	Age ≥ 41	Mammogram in the last two years (FU5 C1j, FU6 Long C1j) • Less than 1 year ago • 1-2 years ago
Cervical cancer screening	Age ≥ 22	21-29 yo: PAP in the last 3 years 30-65 yo: both HPV and PAP in the last 5 years or PAP in the last 3 years	Age ≥ 22	21-29 yo: PAP in the last 3 years 30-65 yo: both HPV and PAP in the last 5 years or PAP in the last 3 years

		(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU5 C1m, FU6 Long C1m) Less than 1 year ago 1-2 years ago More than 2 years but less than 5 years ago 5 or more years ago		(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU5 C1m, FU6 Long C1m) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago
Skin cancer screening	Any radiation	Dermatology exam in the last two years (FU5 C1i, FU6 Long C1i) • Less than 1 year ago • 1-2 years ago	NA	No screening recommended
Cardiac screening	Chest radiation or TBI or Anthracyclines**	 *For every 2 years* • Less than 1 year ago • 1-2 years ago *For every 5 years* • Less than 1 year ago • 1-2 years ago • More than 2 but less than 5 years • 5 or more years ago • (FU5 C1a, C1b; FU6 C1a, C1b)	NA	No screening recommended

FU7 (COG LTFU Guidelines V5.0)				
	Definition of high risk population	**Compliance in the high risk population**	**Definition of the standard risk population**	**Compliance in the standard risk population**
Colorectal cancer screening	Radiation to the pelvis, abdomen, or TBI AND 6 years after cancer diagnosis AND age ≥ 31	Colonoscopy (FU7 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago	Age ≥ 51	Fecal occult blood in the last two years (Use home stool blood test FU7 C1e) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago OR Flexible sigmoidoscopy (FU7 C1f) • Less than 1 year ago • 1-2 years ago • More than 2 years but less than 5 years ago • 5 or more years ago OR Colonoscopy (FU7 C1f) • Less than 1 year ago • 1-2 years ago

<table>
<tr><td></td><td></td><td></td><td></td><td>More than 2 years but less than 5 years ago
5 or more years ago</td></tr>
<tr><td>Breast cancer screening</td><td>Radiation to the chest or TBI

AND

9 years after primary cancer diagnosis

AND

Over 26 years old, whichever occurs later</td><td>Mammogram in the last two years (FU7 C1j)
Less than 1 year ago
1-2 years ago
OR

Breast MRI in the last two years (FU7 C1l)
Less than 1 year ago
1-2 years ago</td><td>Age ≥ 46</td><td>Mammogram in the last two years (FU7 C1j)
Less than 1 year ago
1-2 years ago</td></tr>
<tr><td>Cervical cancer screening</td><td>Age ≥ 22 and <66</td><td>21-29 yo: PAP in the last 3 years
30-65 yo: both HPV and PAP in the last 5 years or PAP alone in the last 3 years
(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU7 C1m)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago
5 or more years ago</td><td>Age ≥ 22 and <66</td><td>21-29 yo: PAP in the last 3 years
30-65 yo: both HPV and PAP in the last 5 years or PAP alone in the last 3 years
(*Since HPV information was not available in CCSS, compliance will be defined as PAP in the last 5 years; FU7 C1m)
Less than 1 year ago
1-2 years ago
More than 2 years but less than 5 years ago
5 or more years ago</td></tr>
<tr><td>Skin cancer screening</td><td>Any radiation</td><td>Dermatology exam in the last two years (FU7 C1i)
Less than 1 year ago
1-2 years ago</td><td>NA</td><td>No screening recommended</td></tr>
<tr><td>Cardiac screening</td><td>Chest radiation or TBI or Anthracyclines**</td><td><table><tr><th colspan="3">Recommended Frequency of Echocardiogram</th></tr><tr><th>Anthracycline Dose*</th><th>Radiation Dose**</th><th>Recommended Frequency</th></tr><tr><td rowspan="3">None</td><td>< 15 Gy or none</td><td>No screening</td></tr><tr><td>≥ 15 - < 35 Gy</td><td>Every 5 years</td></tr><tr><td>≥ 35 Gy</td><td>Every 2 years</td></tr><tr><td rowspan="2">< 250 mg/m²</td><td>< 15 Gy or none</td><td>Every 5 years</td></tr><tr><td>≥ 15 Gy</td><td>Every 2 years</td></tr><tr><td>≥ 250 mg/m²</td><td>Any or none</td><td>Every 2 years</td></tr><tr><td colspan="3">*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.</td></tr></table>For every 2 years
Less than 1 year ago
1-2 years ago
For every 5 years
Less than 1 year ago
1-2 years ago
More than 2 but less than 5 years
5 or more years ago (FU7 C1a, or C1b)</td><td>NA</td><td>No screening recommended</td></tr>
</table>

*Standard risk screening is based on American Cancer Society recommendations as reproduced in the COG LTFU Guidelines v4.0 and v5.0, respectively

**Doxorubicin isotoxic equivalent dose = doxorubicin * 1 + daunorubicin * 0.5 + epirubicin * 0.67 + idarubicin * 5 + mitoxantrone * 4

Independent Variables:

1. Sociodemographic/SES
   - Age at diagnosis
   - Age at questionnaires (baseline and FU)
   - Sex
   - Race/Ethnicity
   - Education
   - Employment
   - Personal income
   - Insurance status
   - Marital status

2. Socioenvironmental SDOH
   - Social Vulnerability Index (SVI) score
   - Persistent poverty (yes/no)
   - Contemporary redlining (yes/no)
   - Urban/rural status

3. Primary cancer diagnosis

4. Treatment-related
   - Chemotherapy exposures (yes/no, lifetime cumulative dose)
     - Alkylating agents
     - Anthracyclines
     - Epipodophyllotoxins
     - Platinum agents
     - Radiation (field, dose)
       - Any site (yes/no)
       - Cranial
       - Neck
       - Chest
       - Abdomen
       - Pelvis
       - Arm
       - Leg
       - TBI
   - Hematopoietic cell transplantation (yes/no)

5. Behavioral
   - Smoking
     - Number of years smoked
     - Never smoker
     - Former smoker
     - Current smoker
   - Alcohol consumption[23]
     - Never-drinker
     - Low risk
     - High-risk
   - Physical activity[24]
     - Sedentary
     - Non-sedentary

6. Cancer-related medical care & records
   - Has a survivorship care plan (FU5 B7, FU6-long B7, FU7 B5)
   - Had a cancer-related follow-up care visit in the past 2 years (FU5 B4, FU6-long B4, FU7 B2a + B2b + B2c + B2d)

Analytic Approach:

Table 1 will include descriptive statistics of the sociodemographic, diagnosis, and treatment characteristics of all CCSS participants, stratified by the number of questionnaires completed (completing baseline and at least one FU questionnaire, or only completing the baseline). **Table 2** will include descriptive statistics of the SDOH-related characteristics of CCSS participants, stratified by the same groups.
Sampling weights due to the under-sampling of ALL survivors will be adjusted in all regression analyses below.

Aim 1: Evaluate the association between baseline neighborhood-level SDOH, including socioenvironmental vulnerability, persistent poverty, contemporary redlining, and urban/rural status, and the subsequent CHC burden, including assessing temporal patterns in the severity of both global and organ-specific CHC burden.

- ***Hypothesis 1a.1:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a higher global CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.
- ***Hypothesis 1a.2***: Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a higher organ-specific CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Unadjusted and adjusted multiple logistic regression models will be used to study the association between global CHC burden severity and SDOH variables at baseline. The adjusted model will additionally include sociodemographic variables, cancer treatment exposures, and lifestyle factors as covariates. A preliminary variable selection will be performed for the adjusted model using 10-fold elastic net logistic regression using deviance as the selection criterion, with age at baseline survey and sex always included in the model. In the primary analysis, the global CHC burden will be categorized into 5 groups: no burden, low burden, medium burden, high burden, and very high burden; sensitivity analyses will be performed for all analyses involving CHC, where survivors with no burden or low burden will be combined into a single group. Collinearity of the SDOH variables will be evaluated. For correlated SDOH variables, separate regression analyses will be performed. Since the personal sociodemographic variables may mediate the effects of SDOH variables, separate regression models will be performed without adjusting personal SDOH variables, including education, employment, income, marital status, and insurance status.

Analyses will be repeated using organ-specific CHC burden as the outcome

Aim 1b: Evaluate the association between baseline neighborhood-level SDOH and temporal patterns in the severity of global and organ-specific CHC burden.

- ***Hypothesis 1b.1:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a greater progression in the severity of global CHC burden compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.
- ***Hypothesis 1b.2:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be more likely to have a greater incidence and worsening of organ-specific CHC burden severity compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

For survivors who responded to the baseline survey and at least one follow-up questionnaire, unadjusted and adjusted multiple logistic regression models will be used to examine the association between SDOH variables at baseline and burden at the end of follow-up (last questionnaire). The adjusted model will additionally include age at the baseline survey, follow-up duration, sociodemographic variables, cancer treatment exposures, and

lifestyle factors as covariates. A preliminary variable selection will be performed for the adjusted model using 10-fold elastic net logistic regression, with age at baseline survey, follow-up duration, and sex always included in the model. In models where we define progression outcomes as present/absent, we will remove the survivors with very high burden at baseline and also adjust for the burden at baseline. As in Aim 1a, separate regression models will be performed without adjusting for the personal sociodemographic variables.

Analyses will be repeated using organ-specific CHC burden (or its progression) as the outcome.

Aim 2: Evaluate the association between baseline and most recent SDOH and healthcare utilization.
***Aim 2a*:** Evaluate the association between baseline SDOH and subsequent healthcare utilization (ER visits, hospitalizations, PCP engagement).

- ***Hypothesis 2a:*** Adjusting for global CHC burden as a covariate, survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas at baseline will have a higher number of ER visits, a higher number of hospitalizations, and lower likelihood of having seen a PCP (past 2 years) post-baseline (at individual FU and across all FUs) compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Distribution of ER visits at each FU questionnaire as well as the average numbers of ER visits will be summarized among survivors and categorized as none, low, or high, or dichotomized, as appropriate, for individual FU and across all FUs. Unadjusted and adjusted multiple logistic regression models with individual-specific random intercepts will be used to study the association between baseline SDOH and the average number of ER visits since baseline. Modified Poisson regression will also be considered unless the distribution of the average numbers of ER visits is highly skewed to 0 and 1. The adjusted model will additionally include age at baseline questionnaire completion, sex, cumulative CHC burden, sociodemographic variables, cancer treatment exposures, and lifestyle factors as covariates. A preliminary variable selection will be performed for the adjusted model using 10-fold elastic net logistic regression, with age at baseline survey completion and sex always included in the model. Separate regression models will be performed without adjusting for the sociodemographic variables. Analyses will also be replicated with number of hospitalizations and binary outcome of having seen a PCP (past 2 years) as outcomes.

Aim 2b: Evaluate the association between the most recent SDOH and healthcare utilization (ER visits, hospitalizations, PCP engagement).

- ***Hypothesis 2b:*** Given the same level of global CHC burden, survivors currently living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will have a higher number of ER visits (past 12 months), higher number of hospitalizations (past 12 months), and lower likelihood of having seen a PCP (past 2 years) compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas.

Unadjusted and adjusted mixed-effects multiple logistic regression model with individual-specific random intercepts will be used to study the association between each individual participant's most recently available SDOH and the healthcare utilization data (i.e. number of ER visits in the last 12 months, number of hospitalizations in the last 12 months, yes/no PCP visit in the last 2 years) from that corresponding FU survey number. The adjusted model will additionally include age at questionnaire completion, cumulative CHC burden, and other covariates in the regression model of Aim 2a.

Aim 3: Evaluate the association between the most recent SDOH and the likelihood of having received indicated screening tests for late effects, including echocardiogram, colonoscopy, mammogram/breast MRI, cervical cancer screening, and skin exam.

- ***Hypothesis 3:*** Survivors living in higher social vulnerability, persistent poverty, or redlined urban or rural areas will be less likely to have received indicated screening tests for late effects compared to those living in lower social vulnerability, non-persistent poverty, or non-redlined urban areas, after accounting for global CHC burden and treatment modalities.

As in prior published screening outcome analyses (Yan et al) and approved concept proposals (Shoag et al), CCSS participants who enrolled in the ECHOS, ASK, or EMPOWER clinical trials will be excluded from screening outcomes for echocardiograms, skin exams, or mammograms/breast MRIs, respectively. Participants who developed cardiac toxicity (grade 3 or higher), colorectal cancer, breast cancer, cervical cancer, or skin cancer will be excluded from screening for that outcome but included in the other screening outcomes.

Unadjusted and adjusted mixed-effects multiple logistic regression model with individual-specific random intercepts will be used to study the association between most recent SDOH and the binary outcome of having had the indicated screening test within the recommended time period, stratified by high risk and standard risk status. For each regression analysis, only the survivors with a corresponding screening recommendation will be included. Multivariable models will include age at survey completion, global CHC burden, sociodemographic variables, cancer treatment exposures, and lifestyle factors as covariates. A preliminary variable selection will be performed for the adjusted model using 10-fold elastic net logistic regression, with age at survey completion and sex always included in the model (note that sex will not be included in sex-specific screening models, e.g. breast and cervical cancer). Separate regression models will be performed without adjusting for the sociodemographic variables. Table B will be used to define the high-risk and standard risk populations and to determine compliance with the screening guidelines. A sensitivity analysis will be performed using Table C instead.

Given that a prior analysis (Yan et al, JCO 2020) has demonstrated that late effects screening for breast cancer, skin cancer, and cardiac dysfunction was positively associated with recent cancer-related follow-up care and having a survivorship care plan (SCP), we will also evaluate these variables in the multivariable analysis for Aim 3. To investigate whether the association between SDOH and late effect screening can be explained by SCP possession and recent cancer-related follow-up care, sensitivity analyses will be performed in the above regression models for late effect screening by including SCP possession and cancer-related follow-up care as additional covariates.

SAMPLE TABLES

Table 1. Demographic and cancer treatment-related characteristics of the cohort

	All participants		Completed baseline only		Completed baseline + FU	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**
Age at diagnosis						
0-4						
5-9						
10-14						
15-19						
Age at questionnaire						
[categories]						
Sex						
Female						
Male						
Race/Ethnicity						
Non-Hispanic white						
Non-Hispanic Black						
Hispanic						
Other						
Education						
< High school						
High school graduate						
Some college						
College graduate						
Unknown						
Employment						
Employed or caring for home						
Looking for work or unable to work						
Household Income						
<$20,000						
$20,000-59,000						
$60,000-99,000						
≥$100,000						
Unknown						
Insurance Coverage						
Private						
Public						
Canadian						
None						
Marital Status						
Married						
Single						
Divorced or separated						
Unknown						
Primary cancer diagnosis						
ALL						
AML						
CNS tumor						
Hodgkin lymphoma						
Non-Hodgkin lymphoma						

Osteosarcoma						
Ewing sarcoma						
Wilms tumor						
Neuroblastoma						
Cancer Treatment						
Chemotherapy						
Any (yes/no)						
Alkylating agents (yes/no and cumulative dose)						
Anthracyclines (yes/no and cumulative dose)						
Epipodophyllotoxins (yes/no and cumulative dose)						
Platinum agents (yes/no and cumulative dose)						
Radiation						
Any (yes/no)						
Cranial (yes/no and cumulative dose)						
Chest (yes/no and cumulative dose)						
Abdomen/Pelvis (yes/no and cumulative dose)						
Total body irradiation (yes/no and cumulative dose)						
Hematopoietic stem cell transplantation						
Yes						
Autologous						
Allogeneic						
No						
Has a survivorship care plan						
Yes						
No						
Unknown						
Has had cancer-related follow-up care within past 2 years						
Yes						
No						
Unknown						
Smoking						
Never smoker						
Former smoker						
Current smoker						
Alcohol consumption						
Never-drinker						
Low risk						
High risk						
Physical activity						
Sedentary						
Non-sedentary						

Table 2. Socioenvironmental social determinants of health (SDOH) characteristics of the cohort

	All participants		Completed baseline only		Completed baseline + FU	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)						
[categories]						
Contemporary redlining and rurality						
Non-redlined urban areas						
Redlined urban areas						
Rural areas						
Persistent poverty area						
Yes						
No						

Table X (Aim 1). Baseline social determinants of health (SDOH) and current global CHC burden

	No Burden (N=)		Low burden (N=)		Medium Burden (N=)		High Burden (N=)		Very High Burden (N=)	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)										
[categories]										
Contemporary redlining and rurality										
Non-redlined urban areas										
Redlined urban areas										
Rural areas										
Persistent poverty area										
Yes										
No										

Table X (Aim 1). Baseline social determinants of health (SDOH) and temporal progression of global CHC burden

	Persistent No/Low burden (N=)		Persistent Medium Burden (N=)		Moderate Burden Increase (N=)		Substantial Burden Increase (N=)		Persistent High or Very High Burden (N=)	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)										
[categories]										
Contemporary redlining and rurality										
Non-redlined urban areas										
Redlined urban areas										
Rural areas										
Persistent poverty area										
Yes										
No										

Table X (Aim 1). Baseline social determinants of health (SDOH) and severity of organ-specific CHC burden (sample table, would repeat for each organ system)

	None		Grade 1		Grade 2		Grade 3		Grade 4		Grade 5	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)												
[categories]												
Contemporary redlining and rurality												
Non-redlined urban areas												
Redlined urban areas												
Rural areas												
Persistent poverty area												
Yes												
No												

Table X (Aim 1). Baseline social determinants of health (SDOH) and temporal patterns in severity of organ-specific CHC burden (sample table, would repeat for each organ system)

	Incident		Worsening		Persistent		Non-progressive	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)								
[categories]								
Contemporary redlining and rurality								
Non-redlined urban areas								
Redlined urban areas								
Rural areas								
Persistent poverty area								
Yes								
No								

Table X (Aim 1). Multivariable analysis of predictors of global and organ-specific CHC burden severity

	Global burden very high vs no		Hearing grade 3+ vs none/1		Repeat for each organ-specific category	
Risk Factor	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**

Table X (Aim 1). (Sensitivity Analysis) Multivariable analysis of predictors of global and organ-specific CHC burden severity

	Global burden very high vs no/low		Hearing grade 3+ vs none/1		Repeat for each organ-specific category	
Risk Factor	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**

Table X (Aim 1). Multivariable analysis of predictors of temporal progression of global CHC burden severity

	Persistent no/low burden		Persistent medium burden		Moderate burden increase		Substantial burden increase		Persistent high or very high burden	
Risk Factor	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**

Table X (Aim 1). Multivariable analysis of predictors of temporal progression of organ-specific CHC burden severity (sample table, would repeat for each organ system)

	Incident		Worsening		Persistent		Non-progressive	
Risk Factor	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**

Table. X (Aim 2) Descriptive table of baseline SDOH and ER visits; will also want to see overall histogram

	FU 5: ER visits in last 12 months Subcohort N=XX (mean, median, IQR)	FU 6: ER visits in last 12 months Subcohort N=XX (mean, median, IQR)	FU 7: ER visits in last 12 months Subcohort N=XX (mean, median, IQR)	Average number of ER visits in last 12 months across all available surveys N=XX (mean, median, IQR)
Overall				
Social Vulnerability Index (SVI)				
[categories]				
Contemporary redlining and rurality				
Non-redlined urban areas				
Redlined urban areas				
Rural areas				
Persistent poverty area				
Yes				
No				

After operationalizing categories:

	FU 5: ER visits in last 12 months Subcohort N=XX (N, %)			FU 6: ER visits in last 12 months Subcohort N=XX (N, %)			FU 7: ER visits in last 12 months Subcohort N=XX (N, %)			Average number of ER visits in last 12 months across all available surveys N=XX (N, %)		
	None	Low	High	None	Low	High	None	Low	High	None	Low	High
Overall												
Social Vulnerability Index (SVI)												
[categories]												
Contemporary redlining and rurality												
Non-redlined urban areas												
Redlined urban areas												
Rural areas												
Persistent poverty area												
Yes												
No												

Table X (Aim 2). Descriptive table of baseline SDOH and Hospitalizations, will also want to see overall histogram

	FU 5: Hospitalizations in last 12 months Subcohort N=XX (mean, median, IQR)	FU 6: Hospitalizations in last 12 months Subcohort N=XX (mean, median, IQR)	FU 7: Hospitalizations in last 12 months Subcohort N=XX (mean, median, IQR)	Average number of hospitalizations in last 12 months across all available surveys N=XX (mean, median, IQR)
Overall				
Social Vulnerability Index (SVI)				
[categories]				
Contemporary redlining and rurality				
Non-redlined urban areas				
Redlined urban areas				
Rural areas				
Persistent poverty area				
Yes				
No				

After operationalizing categories:

	FU 5: Hospitalizations in last 12 months Subcohort N=XX (N, %)			FU 6: Hospitalizations in last 12 months Subcohort N=XX (N, %)			FU 7: Hospitalizations in last 12 months Subcohort N=XX (N, %)			Average number of hospitalizations in last 12 months across all available surveys N=XX (N, %)		
	None	Low	High	None	Low	High	None	Low	High	None	Low	High
Overall												
Social Vulnerability Index (SVI)												
[categories]												
Contemporary redlining and rurality												
Non-redlined urban areas												
Redlined urban areas												
Rural areas												
Persistent poverty area												
Yes												
No												

Table X (Aim 2). Descriptive table of baseline SDOH and PCP engagement

	FU 5: Has engaged with PCP in last 2 years Subcohort N=XX (N, %)	FU 6: Has engaged with PCP in last 2 years Subcohort N=XX (N, %)	FU 7: Has engaged with PCP in last 2 years Subcohort N=XX (N, %)	Across all surveys, leveraging only most recently available survey for each participant N=XX (N, %)
Overall				
Social Vulnerability Index (SVI)				
[categories]				
Contemporary redlining and rurality				
Non-redlined urban areas				
Redlined urban areas				
Rural areas				
Persistent poverty area				
Yes				
No				

Table X (Aim 2). Associations between baseline SDOH and healthcare utilization

	Risk of high ER utilization (as measured by operationalized categories from average number across all available follow-up surveys)		Risk of high hospitalization utilization (as measured by operationalized categories from average number across all available follow-up surveys)		Risk of PCP non-engagement	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Social Vulnerability Index (SVI)						
[categories]						
Contemporary redlining and rurality						
Non-redlined urban areas						
Redlined urban areas						
Rural areas						
Persistent poverty area						
Yes						
No						

*Models adjusted for age at baseline questionnaire completion, sex, cumulative CHC burden, sociodemographic variables, cancer treatment exposures, and lifestyle factors as covariates. A preliminary variable selection will be performed for the adjusted model using 10-fold elastic net logistic regression, with age at baseline survey completion and sex always included in the model. Separate regression models will be performed without adjusting for the sociodemographic variables.

Above table would be repeated with most recent SDOH for Aim 2B

Table X (Aim 3). Late effects risk classification and recommended screening tests for participants

	All participants	
Late effects screening[a]	**N**	**%**
Breast cancer		
High risk, mammogram & MRI recommended		
Standard risk, mammogram recommended		
Not at risk		
Excluded[b]		
Colorectal cancer		
High risk, colonoscopy or multitarget stool DNA test recommended		
Standard risk, screening recommended		
Not at risk		
Excluded[a]		
Skin cancer		
High risk, full body skin exam recommended		
Not at risk		
Excluded[a]		
Cardiac dysfunction		
High risk, echocardiogram recommended every 1-2 years		
Moderate risk, echocardiogram recommended every 5 years		
Not at risk		
Excluded[a]		
Cervical cancer		
Standard risk, screening recommended		
Not at risk		
Excluded[a]		

a. Recommendations for screening are based on the applicable COG LTFU guidelines version that was in use at the time the survey was completed (e.g., v4.0 for FU5 or FU6; v5.0 for FU7); note that the COG LTFU guidelines v4.0 and v5.0 also included screening guidelines for standard risk participants based on American Cancer Society recommendations; Screening adherence is based on each participant's most recently completed follow-up survey that included this information

b. Excluded due to participation in clinical trial to increase screening (EMPOWER, ASK, ECHOS) or due to having developed the condition

Table X (Aim 3). Socioenvironmental social determinants of health (SDOH) and adherence to recommended late effects screening tests among survivors at risk (adherence is based on Table B as in Yan et al JCO 2020)

	Breast cancer, high risk (N=)		**Breast cancer, standard risk (N=)**		**Colorectal cancer, high risk (N=)**		**Colorectal cancer, standard risk (N=)**		**Skin cancer (N=)**		**Cardiac dysfunction(N=)**		**Cervical cancer (N=)**	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)														
[categories]														
Contemporary redlining and rurality														
Non-redlined urban areas														
Redlined urban areas														
Rural areas														
Persistent poverty area														
Yes														
No														

*This table shows the N and % of survivors who received recommended screening tests. The N for each column is based on the N's shown in Table X1 that correspond to the individuals at high and standard risk (or high and moderate risk for cardiac screening) for whom screening is recommended

Table X (Aim 3). Socioenvironmental social determinants of health (SDOH) and adherence to recommended late effects screening tests among survivors at risk (sensitivity analysis: adherence is based on Table C as in Snyder's ongoing analysis)

	Breast cancer, high risk (N=)		**Breast cancer, standard risk (N=)**		**Colorectal cancer, high risk (N=)**		**Colorectal cancer, standard risk (N=)**		**Skin cancer (N=)**		**Cardiac dysfunction (N=)**		**Cervical cancer (N=)**	
SDOH Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Social Vulnerability Index (SVI)														
[categories]														
Contemporary redlining and rurality														
Non-redlined urban areas														
Redlined urban areas														
Rural areas														
Persistent poverty area														
Yes														
No														

*This table shows the N and % of survivors who received recommended screening tests. The N for each column is based on the N's shown in Table X1 that corresponds to the individuals at high and standard risk (or high and moderate risk for cardiac screening) for whom screening is recommended

Table X (Aim 3). Multivariable analysis of predictors of adherence to recommended late effects screening tests among survivors at risk

	Breast cancer, high risk (n of N adherent)		Breast cancer, standard risk (n of N adherent)		Colorectal cancer, high risk (n of N adherent)		Colorectal cancer, standard risk (n of N adherent)		Skin cancer (n of N adherent)		Cardiac dysfunction (n of N adherent)		Cervical cancer (n of N adherent)	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Characteristic														

*All models are adjusted for age at survey completion. All models except those for breast and cervical cancer screening are also adjusted for biologic sex.

8. Special considerations

This project comprehensively evaluates the association between SDOH, health outcomes, and healthcare utilization. It is anticipated to result in a minimum of 3 individual publications, each led by a different early career investigator within the CCSS Cancer Control Working Group (Rusha Bhandari, Daniel Zheng, and Stephanie Smith).

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