

CHILDHOOD CANCER SURVIVOR STUDY Analysis Concept Proposal

1. **STUDY TITLE:** Adherence to surveillance guidelines in survivors of Hodgkin lymphoma: a report from the Childhood Cancer Survivor Study (CCSS)

2. **WORKING GROUP AND INVESTIGATORS:**

Primary CCSS Working Group: Cancer control

Secondary CCSS Working Groups: Chronic disease, Second neoplasms

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3. **BACKGROUND AND RATIONALE:**

Hodgkin lymphoma (HL) in children, adolescents, and young adults (AYA) is a highly curable disease with 5-year overall survival (OS) rates nearing 95%.¹ Indeed, current therapy and clinical trials aim to optimize disease control while minimizing the risk of late health complications.² Survivors of HL have amongst the highest risk for long-term complications of therapy including subsequent malignant neoplasms (SMN) and cardiovascular (CV) disease.² Complications of therapy are the leading cause of mortality for HL survivors and their incidence increases over the lifespan.^{3,4}

The Children's Oncology Group (COG) Long-Term Follow-Up (LTFU) Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancer recommends risk-based, exposure-related screening.^{4,5} Screening guidelines for survivors of HL depend on radiation exposure to target organs and treatment with specific chemotherapeutic agents. The COG LTFU Guidelines Version 4.0 (Table 1) recommended breast cancer screening for those women who were treated

with chest radiation ≥ 20 Gy potentially exposing the breast and screening is recommended to begin 8 years after radiation or at 25 years old (whichever occurs later). Colorectal cancer screening was recommended for those treated with abdomen and pelvis radiation ≥ 30 Gy potentially exposing the bowel to begin screening 10 years after radiation or at 35 years old (whichever occurs later). Skin cancer screening was recommended for those exposed to any radiation.⁶ Cardiac screening recommendations were based on age at first treatment, lifetime anthracycline dose, and radiation dose with impact to the heart (Table 2). The COG LTFU guidelines are updated periodically based on relevant medical literature.⁵ In October 2018, COG LTFU Guidelines Version 5.0 were released and included changes in breast, colorectal, and cardiac screening. These changes included removal of a minimum dose of radiation for breast and colorectal cancer screening and changes in chemo-radiation threshold doses and elimination of age at treatment parameters for cardiac screening.⁵

Studies have shown the benefit and cost-effectiveness of screening measures.^{4,7-11} However, less than half of survivors at high-risk for these morbidities adhere to recommended surveillance guidelines.¹² Across all childhood cancer survivors, sociodemographic factors impact adherence to guideline-recommended risk-based survivor focused care.¹²⁻¹⁵ This poses a significant threat for outcome disparities among survivors based on socioeconomic, geographic, and racial/ethnic differences.¹⁶ The Social Vulnerability Index (SoVI), is a validated measurement of neighborhood-level socioeconomic and demographic factors that has been shown to effect cancer outcomes in adults, however has not been examined in pediatric cancer patients undergoing therapy or in long-term childhood cancer survivors.^{17,18,19,20}

Encouragingly, a recent study from the Childhood Cancer Survivor Study (CCSS) showed improvements in adherence to the COG colorectal cancer and cardiac dysfunction screening guidelines from 2003 to 2016,¹² perhaps reflecting progress in educating providers and patients, disseminating screening guidelines, and expanding access to care. However, whether these improvements in adherence are equitably shared across different populations, remains unknown.

Screening for late effects of treatment is paramount for survivors of HL as it provides an opportunity for early detection and interventions to improve health outcomes. Previous studies have shown racial/ethnic and socioeconomic disparities in long-term survivors of HL,²¹⁻²⁵ however, no prior studies have examined the extent to which adherence to screening guidelines influences disparities in long-term morbidity. To enhance health equity and improve quality of life for all childhood cancer survivors, it is critical to understand the barriers to adherence to post-treatment recommended health surveillance.

The aim of this study is to evaluate the influence of individual-level characteristics (age, sex, race-ethnicity, household income, education level, insurance status, employment, marital status), area-level variables (region of residence, SoVI score of residence), disease specific parameters (age at diagnosis, time from diagnosis), medical care (recent survivor focused care, care by generalist versus specialist, possession of survivor care plan), number and severity of chronic health conditions on adherence to risk-based screening recommendations in adult survivors of childhood and AYA HL using the Childhood Cancer Survivor Study (CCSS) cohort. Recently, Yan et. al. described overall adherence to screening guidelines and found an alarmingly high percentage of survivors did not receive the recommended screening.¹² Here we will investigate how granular socioeconomic characteristics influence adherence to screening guidelines. The ultimate goal of this study is to help develop targeted strategies to reduce

disparities in the frequency and severity of adverse long-term outcomes in a particularly high-risk group of survivors.

Here, we will assess adherence to COG LTFU screening guidelines for the main treatment-related morbidities experienced by HL survivors for which there are specific screening guidelines, including, cardiomyopathy, breast cancer, colorectal cancer, and skin cancer.³ Notably, these are not comprehensive of all complications experienced by HL survivors. Other long-term toxicities including thyroid disease, gonadal dysfunction, and pulmonary toxicity are also common.³ However, adherence to screening recommendations for these complications is not captured by the CCSS questionnaires.

Given that Version 5.0 guidelines were introduced after the most recent questionnaire from childhood cancer survivors, we will use the previous Version 4.0 as the reference for adherence in this study. The primary aim is to improve our understanding of screening practices in order to address barriers to preventative care and reduce inequalities from long-term morbidity. Additionally, we will address how screening practices have changed over time as well as changes in the target population as a result of changes in screening guidelines.

Table 1a COG LTFU Version 4.0 Recommended Screening for HL Survivors based on Treatment Exposures⁶

Potential Late Effect	High-Risk Population	Periodic Evaluation	Frequency
Skin Cancer	Received any radiation	Dermatologic exam of irradiated fields	Annually
Breast Cancer	Females who received ≥ 20 Gy of radiation potentially exposing the breast	Mammogram and breast MRI	Annually beginning 8 years after radiation or at 25 years old, whichever occurs later
Colorectal Cancer	Received ≥ 30 Gy of radiation potentially exposing the colon	Colonoscopy	Every 5 years beginning 10 years after radiation or at 35 years old, whichever occurs later
Cardiomyopathy	Received radiation with potentially exposing the heart and/or anthracyclines	Echocardiogram or MUGA scan	Dependent on age of treatment, radiation dose and cumulative anthracycline dose (see Table 2a)

Table 2a COG LTFU Version 4.0 Recommended Frequency of Echocardiogram or Comparable Cardiac Imaging⁶ (*these guidelines are consistent with COG LTFU Version 1.0 guidelines*)

Age at Treatment [†]	Radiation Dose ^{††}	Anthracycline Dose ^{†††}	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	<200 mg/m ²	Every 2 years
		≥ 200 mg/m ²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m ²	Every 5 years
		≥ 100 to <300 mg/m ²	Every 2 years
		≥ 300 mg/m ²	Every year
≥ 5 years old	Yes	<300 mg/m ²	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
† Age at first cardiotoxic therapy			
†† Based on radiation dose with potential impact to heart (chest, abdomen, spine, TBI)			
††† Based on Doxorubicin isotoxic equivalent dose			

Table 3a COG LTFU Version 4.0 Anthracycline Isotoxic Equivalents

Anthracycline	Doxorubicin isotoxic equivalents
Doxorubicin	x 1
Daunorubicin	x 1
Epirubicin	x 0.67
Idarubicin	x 5
Mitoxantrone	x 4

4. SPECIFIC AIMS / OBJECTIVES / RESEARCH HYPOTHESES:

The specific aims and objectives of this proposal are to:

- I. Determine the proportion of Hodgkin lymphoma survivors who require routine surveillance for breast cancer, colorectal cancer, skin cancer, and cardiovascular disease based on COG LTFU Version 4.0 guidelines
- II. Determine the proportion of HL survivors who adhere to required COG LTFU Version 4.0 screening guidelines based on the follow up 2017 questionnaire.
- III. Determine whether individual-level characteristics (age, sex, race-ethnicity, household income, education level, insurance status, employment, marital status), area-level variables (region of residence, SoVI score* of residence), disease specific parameters (age at diagnosis, time from diagnosis), medical care (recent survivor focused care, care by generalist versus specialist, possession of survivor care plan), and presence of chronic health conditions (number and severity) affect adherence with screening and surveillance guidelines.

* The Social Vulnerability Index (SoVI), initially developed by the Hazards and Vulnerability Research Institute (HVRI) at the University of South Carolina and now available through the Center for Disease Control (CDC), is a measure of neighborhood-level socioeconomic and demographic factors that impact the resilience of communities.^{17,18} SoVI scores are continuous from negative to positive infinity but are stratified by the CDC into four quartiles.¹⁷⁻¹⁹ A greater score represents a community that is more vulnerable.¹⁷⁻¹⁹ Neighborhood SoVI scores has been shown to effect cancer outcomes in adults, however have not been examined in pediatric oncology.^{19,20}

- IV. Assess whether changes in screening adherence over time have occurred differently for different sociodemographic groups using current (2017) and past (2003) questionnaires. We will define adherence in 2003 by the original COG LTFU guidelines (released in 2003) with adherence in 2017 based on the COG LTFU V4.0 guidelines.

The hypotheses of this proposed study are:

- I. The majority of survivors of HL will require screening of at least one organ system based on the COG LTFU guidelines.
- II. The proportion of HL survivors who adhere to all recommended multisystem surveillance guidelines will be low, approximating that of other childhood cancer survivors (12.6%-41.4%)¹²
- III. Racial and ethnic minorities, those of lower socioeconomic status, those of lower education levels, those who are unemployed, uninsured, or unmarried, and those residing in a high SoVI score area will be less adherent to recommended screening guidelines. Those who were diagnosed at a younger age and are further from cancer diagnosis will be less adherent. Those who have less frequent physician visits, those who have general rather than survivor-focused care, and those without a survivorship care plan (SCP) will be less adherent to screening guidelines. Those who have a greater number of chronic health conditions and more severe chronic health conditions will be less adherent to screening guidelines.
- IV. Improvements in adherence over time will be inequitably distributed across sociodemographic groups.

5. ANALYSIS FRAMEWORK:

Subject Population:

The study sample will consist of all survivors of HL (N=3107) enrolled in the CCSS cohort who responded to the 6th long-term follow-up questionnaire (2017). For *Aim 4*, the analysis will be performed in a subset of the original study sample who responded to both the 2003 and the 2017 questionnaires. Survivors will be excluded if they participated in the ECHOS, ASK, or EMPOWER studies.²⁶⁻²⁸ Survivors who have developed one of the target events (grade 3 or 4 cardiac toxicity, breast cancer, colorectal cancer, or skin cancer) will be excluded from the analysis for screening of that event. However, they will not be excluded from analysis for screening of other potential late effects.

Survivors will be defined as at risk of developing a specific malignancy if they meet the following criteria (per COG LTFU Version 4.0 guidelines):

- A. Skin Cancer:
 - Received any radiation
- B. Colorectal Cancer:

- Received ≥ 30 Gy of radiation to the abdomen, pelvis, spinal, or TBI, which had the potential to impact the colon/rectum and are at least 10 years after radiation or at 35 years old, whichever occurs later

C. Breast Cancer:

Received ≥ 20 Gy of chest radiation with potential impact to the breast and are at least 8 years after radiation or at 25 years old, whichever occurs later

Survivors will be defined as high-risk of developing cardiac dysfunction if they meet either/both the following criteria:

A. Anthracycline exposure:

- Received any anthracycline agent (frequency dependent on age of treatment, radiation dose and cumulative anthracycline dose [see Table 2])

B. Radiation exposure:

- Any radiation exposure to a field that potentially exposes the heart agent (frequency dependent on age of treatment, radiation dose and cumulative anthracycline dose [see Table 2])

Outcomes of Interest:

- Cardiac screening (FU 2017- C1a, C1b; FU 2003 – B1)
- Colorectal screening (FU 2017- C1e, C1f; FU 2003 – B2)
- Dermatologic screening (FU 2017- C1i; FU 2003 – C12)
- Breast screening (FU 2017- C1j, C1k, C1l; FU 2003 – B4)

Exploratory Variables:

A. Individual-level Variables:

- Age (BL, FU 2017 & birth date)
- Sex (BL- A2)
- Race/ ethnicity (BL- A4)
- Highest grade or level of schooling (FU 2014- A4)
- Current employment status (FU 2014- A5)
- Household income (FU 2-14- A7)
- Insurance coverage (FU 2014- A10)
- Marital status (FU 2014- M2)

B. Area-level Variables

- Region of residence (i.e. Northeast, Midwest, South, West) (FU 2017- ZIP)
- Social Vulnerability Index (FU 2017- ZIP in conjunction with publicly available SoVI score when available)

C. Disease / Treatment Variables:

- Cancer diagnosis

- Age at diagnosis
- Time from diagnosis
- Treatment Variables: *We will use two separate classifications of treatment for our analysis. First, we will classify treatment based on Oeffinger et.al recent schema of treatment group. Secondly, we will classify treatment based on anthracycline equivalent dose (based on version 4.0 guidelines) and radiation site. This will allow us to evaluate screening according to a newly developed framework while also preventing exclusion of subjects who did not fall into one of the treatment groups in this schema.*
- #1 Treatment Group (per Oeffinger et. al)
 - Contemporary therapy (defined as doxorubicin < 250 mg/m², cyclophosphamide 2000-3900 mg/m², any vincristine, and prednisone, with or without involved field radiation <26 Gy)
 - Chemotherapy without chest RT (any anthracycline dose plus any alkylator dose and no chest radiation)
 - Salvage therapy (treatment for relapse with or without an autologous or allogeneic hematopoietic cell transplant within 5 years of cancer diagnosis)
 - Chest RT ≥35 Gy (With or without chemotherapy. Not mutually exclusive with salvage therapy group)
- #2 Treatment Classification
- If “yes” to chemotherapy, then
 - Doxorubicin-equivalent dose (using Doxorubicin equivalents for the survey time-period)
 - <100 mg/m²
 - ≥100 to <200 mg/m²
 - ≥200 to <300 mg/m²
 - ≥300 mg/m²
- If “yes” to radiation, then
 - Did they receive chest/thorax radiation with potential impact to the breast?
 - Did they receive abdomen/pelvis radiation?
 - Did they receive TBI?
 - Did they receive radiation with potential impact to the heart?

D. Medical Care

- Medical care within the prior 2 years (FU 2017- B1)
- Survivor focused care within the prior 2 years (FU 2017 – B3)
- Care at survivorship clinic/cancer center vs general (FU 2017 – B4a)
- Survivorship care plan (SCP) by patient and/or physician (FU 2017 – B7-8)

E. Chronic health conditions²

- ≥2 chronic health conditions (grade 1-4) (FU 2014- D1 through K15)
- Any high-grade (grade 3-4) chronic health condition (FU 2014- D1 through K15)

Data Analysis Plan:

Aim 1: Determine the proportion and 95% confidence interval of all HL survivors who require routine surveillance based on COG guidelines Version 4.0 guidelines. We will assess each outcome separately:

- Determine the proportion of survivors who require breast-cancer surveillance (mammography and MRI)
- Determine the proportion of survivors who require colorectal-cancer surveillance (colonoscopy)
- Determine the proportion of survivors who require skin-cancer surveillance (complete skin exam)
- Determine the proportion of survivors who require echocardiography

Aim 2: Determine the proportion and 95% confidence interval of HL survivors who require screening that adhere to required routine surveillance guidelines based on COG LTFU Version 4.0 guidelines. We will assess each outcome separately using the relevant denominator for that screening requirement.

- Determine the proportion of HL survivors who are adherent to the COG guidelines based on their treatment exposures
 - Determine the proportion of survivors who adhere to breast-cancer surveillance (mammography and MRI)
 - Determine the proportion of survivors who adhere to colorectal-cancer surveillance (colonoscopy)
 - Determine the proportion of survivors who adhere to skin-cancer surveillance (complete skin exam)
 - Determine the proportion of survivors who adhere to echocardiography
- For each screening test, survivors will be classified as (i) completing the test within the recommended period; (ii) completing the test, but not within the recommended period; or (iii) never having completed the test. The percentage of people in each of these three groups will be calculated. However, only those survivors who completed the test within the recommended period will be considered to be “adherent” to the guidelines for multivariable analysis and comparison of changes over time.

Aim 3: Determine whether individual-level factors, area-level variables, disease-related characteristics, or medical care predict risk of adherence with screening

- Compare adherence by individual-level characteristics (age, sex, race-ethnicity, household income, education level, insurance status, employment, marital status), area-level variables (region of residence, SoVI score residence), disease specific parameters (cancer diagnosis, age at diagnosis, time from diagnosis), medical (recent survivor focused care, care by generalist versus specialist, possession of survivor care plan), and presence of chronic health conditions (number and severity)

- For each screening outcome, the relevant risk factors will be evaluated using separate generalized multivariate linear regression models with either a logit or log-link function, as appropriate, to directly estimate relative risks
- The impact of potential predictors of compliance with each of the recommended screening guidelines will be examined in multivariable regression models as described above.

Aim 4: Assess whether changes in adherence to screening over time differs based on sociodemographic groups using current and past questionnaires.

- This analysis will be performed in a subset of people who answered both 2003 and 2017 follow up questionnaires
- An initial examination on how this group differs from original study group (those who answered the 2017 but not the 2003 questionnaire) will be carried out and thought will be given to what potential biases exist in this subset
- There will be 4 groups of people in this analysis:
 1. Those who remained adherent in 2003 and in 2017
 2. Those who remained nonadherent in 2003 and in 2017
 3. Those who were adherent in 2003 but were nonadherent in 2017
 4. Those who were nonadherent in 2003 but were adherent in 2017
- Compare differences in these 4 groups by covariates previously described. Results will be reported as odds ratios or relative risks with 95% confidence intervals.

Table 1. Cohort Demographics and Treatment Characteristics		
Characteristic	N	%
Race/Ethnicity		
White (non-Hispanic)		
Black (non-Hispanic)		
Hispanic		
Other		
Current Age		
<18		
18-24 years		
25-35 years		
25+ years		
Sex		
Male		
Female		
Marital Status		
Married		
Single		
Divorced or separated		
Unknown		

Education		
< High School		
High School Graduate		
College Graduate		
Postgraduate		
Other		
Employment		
Working (full/part-time)		
Unemployed and looking for work		
Unable to work due to illness or disability		
Student		
Other		
Household income		
<\$20,000		
\$20,000-<\$40,000		
\$40,000-<\$60,000		
\$60,000+		
Unknown		
Insurance Status		
Canadian		
American Public		
American Private		
American None		
Currently have Children		
No children		
Children		
Region of Residence		
Northeast		
Midwest		
South		
West		
SoVI Score		
Canadian		
Highest		
2 nd highest		
3 rd highest		
Lowest		
Age at Diagnosis		
0 to 5-years-old		
6 to 10-years-old		
11 to 14-years-old		
15 to 20-years-old		
Time from Diagnosis		
>30 years		
21-30 years		

Other								
Current Age								
<18								
18-24 years								
25-35 years								
25+ years								
Gender								
Male								
Female								
Marital Status								
Married								
Single								
Divorced or separated								
Unknown								
Education								
< High School								
High School Graduate								
College Graduate								
Postgraduate								
Other								
Employment								
Working (full/part-time)								
Unemployed and looking for work								
Unable to work due to illness or disability								
Student								
Other								
Household income								
<\$20,000								
\$20,000-<\$40,000								
\$40,000-<\$60,000								
\$60,000+								
Unknown								
Insurance Status								
Canadian								
American Public								
American Private								
American None								
Currently have Children								
No children								
Children								
Region of Residence								
Northeast								
Midwest								

South								
West								
Age at Diagnosis								
0 to 5-years-old								
6 to 10-years-old								
11 to 14-years-old								
15 to 20-years-old								
SoVI Score								
Canadian								
Highest								
2 nd highest								
3 rd highest								
Lowest								
Age at Diagnosis								
0 to 5-years-old								
6 to 10-years-old								
11 to 14-years-old								
15 to 20-years-old								
Time from Diagnosis								
>30 years								
21-30 years								
≤20 years								
# Chronic Health Condition								
<2 chronic health conditions								
≥2 chronic health conditions								
Highest Grade Chronic Health Condition								
<1 Grade 3-4								
≥1 Grade 3-4								
Most recent routine check-up								
>2 years								
≤2 years								
Last visit at cancer center or survivorship clinic								
>2 years								
≤2 years								
Possession of SCP by self or physician								
Yes								
No								

Table 4a. Multivariable Regression of the Relative Risk in Adherence in 2017 and in 2003 for HL survivors at risk				
	Cardiomyopathy RR (95% CI), p-value	Breast Cancer RR (95% CI), p-value	Skin Cancer RR (95% CI), p-value	Colorectal Cancer RR (95% CI), p-value

Total				
Race/Ethnicity				
White (non-Hispanic)				
Black (non-Hispanic)				
Hispanic				
Other				
Current Age				
<18				
18-24 years				
25-35 years				
25+ years				
Gender				
Male				
Female				
Marital Status				
Married				
Unmarried				
Unknown				
Education				
< High School				
High School Graduate				
College Graduate				
Postgraduate				
Other				
Employment				
Working (full/part-time)				
Unemployed and looking for work				
Unable to work due to illness or disability				
Student				
Other				
Household income				
<\$20,000				
\$20,000-<\$40,000				
\$40,000-<\$60,000				
\$60,000+				
Unknown				
Insurance Status				
Canadian				
American Public				
American Private				
American None				
Region of Residence				
Northeast				

Midwest				
South				
West				
Age at Diagnosis				
0 to 5-years-old				
6 to 10-years-old				
11 to 14-years-old				
15 to 20-years-old				
SoVI Score				
Canadian				
Highest				
2 nd highest				
3 rd highest				
Lowest				
Time from Diagnosis				
>30 years				
21-30 years				
≤20 years				
Highest Grade Chronic Health Condition				
≥2 chronic health conditions				
Any Grade 3-4				
Most recent routine check-up				
>2 years				
≤2 years				
Last visit at cancer center or survivorship clinic				
>2 years				
≤2 years				
Possession of SCP by self or physician				
Yes				
No				
Table 4b. Multivariable Regression of the Relative Risk in Nonadherence in 2017 and in 2003 for HL survivors at risk				
	Cardiomyopathy RR (95% CI), p-value	Breast Cancer RR (95% CI), p-value	Skin Cancer RR (95% CI), p-value	Colorectal Cancer RR (95% CI), p-value
Total				
Race/Ethnicity				
White (non-Hispanic)				
Black (non-Hispanic)				
Hispanic				
Other				

Current Age				
<18				
18-24 years				
25-35 years				
25+ years				
Gender				
Male				
Female				
Marital Status				
Married				
Unmarried				
Unknown				
Education				
< High School				
High School Graduate				
College Graduate				
Postgraduate				
Other				
Employment				
Working (full/part-time)				
Unemployed and looking for work				
Unable to work due to illness or disability				
Student				
Other				
Household income				
<\$20,000				
\$20,000-<\$40,000				
\$40,000-<\$60,000				
\$60,000+				
Unknown				
Insurance Status				
Canadian				
American Public				
American Private				
American None				
Region of Residence				
Northeast				
Midwest				
South				
West				
Age at Diagnosis				
0 to 5-years-old				
6 to 10-years-old				

11 to 14-years-old				
15 to 20-years-old				
SoVI Score				
Canadian				
Highest				
2 nd highest				
3 rd highest				
Lowest				
Time from Diagnosis				
>30 years				
21-30 years				
≤20 years				
Highest Grade Chronic Health Condition				
≥2 chronic health conditions				
Any Grade 3-4				
Most recent routine check-up				
>2 years				
≤2 years				
Last visit at cancer center or survivorship clinic				
>2 years				
≤2 years				
Possession of SCP by self or physician				
Yes				
No				

Table 4c. Multivariable Regression of the Relative Risk in Adherence in 2017 in those who were Nonadherent in 2003 for HL survivors at risk				
	Cardiomyopathy RR (95% CI), p-value	Breast Cancer RR (95% CI), p-value	Skin Cancer RR (95% CI), p-value	Colorectal Cancer RR (95% CI), p-value
Total				
Race/Ethnicity				
White (non-Hispanic)				
Black (non-Hispanic)				
Hispanic				
Other				
Current Age				
<18				
18-24 years				

25-35 years				
25+ years				
Gender				
Male				
Female				
Marital Status				
Married				
Unmarried				
Unknown				
Education				
< High School				
High School Graduate				
College Graduate				
Postgraduate				
Other				
Employment				
Working (full/part-time)				
Unemployed and looking for work				
Unable to work due to illness or disability				
Student				
Other				
Household income				
<\$20,000				
\$20,000-<\$40,000				
\$40,000-<\$60,000				
\$60,000+				
Unknown				
Insurance Status				
Canadian				
American Public				
American Private				
American None				
Region of Residence				
Northeast				
Midwest				
South				
West				
Age at Diagnosis				
0 to 5-years-old				
6 to 10-years-old				
11 to 14-years-old				
15 to 20-years-old				
SoVI Score				

Canadian				
Highest				
2 nd highest				
3 rd highest				
Lowest				
Time from Diagnosis				
>30 years				
21-30 years				
≤20 years				
Highest Grade Chronic Health Condition				
≥2 chronic health conditions				
Any Grade 3-4				
Most recent routine check-up				
>2 years				
≤2 years				
Last visit at cancer center or survivorship clinic				
>2 years				
≤2 years				
Possession of SCP by self or physician				
Yes				
No				

Table 4d. Multivariable Regression of the Relative Risk in Nonadherence in 2017 in those who were Adherent in 2003 for HL survivors at risk				
	Cardiomyopathy RR (95% CI), p-value	Breast Cancer RR (95% CI), p-value	Skin Cancer RR (95% CI), p-value	Colorectal Cancer RR (95% CI), p-value
Total				
Race/Ethnicity				
White (non-Hispanic)				
Black (non-Hispanic)				
Hispanic				
Other				
Current Age				
<18				
18-24 years				
25-35 years				
25+ years				
Gender				

Male				
Female				
Marital Status				
Married				
Unmarried				
Unknown				
Education				
< High School				
High School Graduate				
College Graduate				
Postgraduate				
Other				
Employment				
Working (full/part-time)				
Unemployed and looking for work				
Unable to work due to illness or disability				
Student				
Other				
Household income				
<\$20,000				
\$20,000-<\$40,000				
\$40,000-<\$60,000				
\$60,000+				
Unknown				
Insurance Status				
Canadian				
American Public				
American Private				
American None				
Region of Residence				
Northeast				
Midwest				
South				
West				
Age at Diagnosis				
0 to 5-years-old				
6 to 10-years-old				
11 to 14-years-old				
15 to 20-years-old				
SoVI Score				
Canadian				
Highest				
2 nd highest				

3 rd highest				
Lowest				
Time from Diagnosis				
>30 years				
21-30 years				
≤20 years				
Highest Grade Chronic Health Condition				
≥2 chronic health conditions				
Any Grade 3-4				
Most recent routine check-up				
>2 years				
≤2 years				
Last visit at cancer center or survivorship clinic				
>2 years				
≤2 years				
Possession of SCP by self or physician				
Yes				
No				

6. SPECIAL CONSIDERATIONS:

No special considerations exist for this proposal.

References:

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