

1. STUDY TITLE: Sociodemographic Factors Associated with Adherence to Colorectal Cancer Surveillance Among High-Risk Childhood Cancer Survivors

2. WORKING GROUPS AND INVESTIGATORS

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3. BACKGROUND AND RATIONALE

Due to advances in pediatric cancer treatment, there is a growing population of more than 500,000 childhood cancer survivors in the US.^{1,2} Surviving childhood cancer often brings the burden of late effects from curative therapies that may not appear decades later.³⁻⁸ Among all late effects, subsequent malignant neoplasms (SMNs) are the leading cause of premature death in survivors, second only to recurrence of primary cancer.⁹ A key goal of long-term survivorship care is to detect treatment-related toxicities early, prevent and manage late effects through education, surveillance, and reduce risky health behaviors.¹⁰

Radiation therapy (RT) significantly heightens the risk of SMNs among childhood cancer survivors, which often develop within the radiation field.^{3,11-14} Childhood cancer survivors who received abdominal or pelvic RT face a 4- to 11-fold greater risk of developing colorectal cancer compared with the general population.^{4,15-19} Notably, survivors who developed secondary colorectal cancer were diagnosed at substantially younger ages than in the general population.²⁰ Given these elevated risks, the Children's Oncology Group (COG) has developed surveillance guidelines for long-term follow-up care.²¹

Despite established guidelines, adherence to surveillance recommendations remains low. In a CCSS cohort analysis, the colorectal cancer screening adherence rate was only 37.0%.²² As the survivor population grows, their healthcare needs are becoming increasingly complex, posing significant challenges to long-term follow-up care. One major barrier is that late effects often do not become clinically apparent until 10 to 20 years after treatment.²³ Survivors and healthcare providers are often unaware of these risks, potentially limiting proactive care-seeking and timely surveillance.²⁴⁻²⁷ In response to persistently low surveillance adherence, the current CCSS study, the Activating Cancer Survivors and their Primary Care Provider to Increase Colorectal Cancer Screening (ASPIRES), is evaluating the effectiveness of a patient-activation mHealth intervention using interactive text messaging to increase colorectal cancer screening among high-risk childhood cancer survivors.²⁸

Sociodemographic characteristics, including education, employment, income, and healthcare access, may influence long-term outcomes of survivorship.²⁹ Childhood cancer

survivors often face adversity related to socioeconomic status, such as lower educational attainment,³⁰ unemployment or employment in lower-skilled jobs,³¹⁻³³ inadequate health insurance coverage,³⁴ and lower income.^{31,32} Notably, adult childhood cancer survivors living in the most disadvantaged census blocks were at a 5-fold to 8-fold increased risk of all-cause death compared to those living in the least disadvantaged census blocks.³⁵ Sociodemographic characteristics have been widely studied in the general population and have been found to influence colorectal cancer screening uptake significantly.³⁶ However, these factors are understudied among childhood cancer survivors who require earlier colorectal cancer screening due to treatment-related risk. It remains unclear which sociodemographic factors are associated with adherence to colorectal cancer screening among high-risk childhood cancer survivors, and whether these factors are positively or negatively associated with adherence. The parent ASPIRES study provides a unique opportunity to evaluate sociodemographic factors associated with colorectal cancer screening adherence among survivors at elevated colorectal cancer risk.

In the average-risk general population, sociodemographic characteristics were frequently reported to be associated with adherence to colorectal screening recommendations from the US Preventive Services Task Force (USPSTF).³⁶ Increasing age and higher education were significantly associated with screening adherence.³⁷⁻³⁹ Moreover, being married and employed were reported as positive factors in adherence in several studies.^{37,39-41} However, living in rural areas may decrease adherence to screening.^{37,39,41,42} In fact, the more convenient a screening location is and the shorter the distance to primary care facilities, the more likely patients are to get screened.^{43,44} These sociodemographic factors may influence survivors' ability to access, afford, and understand the importance of completing colorectal cancer surveillance. Identifying sociodemographic disparities in screening adherence may inform targeted interventions to improve the delivery of survivorship care.

In this proposed student project, we will use data from individuals who completed the CCSS Follow-Up 7 questionnaire. The parent ASPIRES study identified 1,422 potentially eligible CCSS survivors who had received radiation to the abdomen, pelvis, spine, or whole body and met other inclusion criteria, including age > 30 years old, no history of colorectal cancer, no family history of colorectal cancer, and had not had a colonoscopy in the past 5 years or multitarget stool DNA test in the last 3 years. Among the 1,422 survivors, 187 were determined to be ineligible during initial screening because they reported recent colorectal cancer screening. An additional 491 survivors completed an eligibility assessment survey, of whom 142 were subsequently found to be ineligible because they reported recent colorectal cancer screening. Ultimately, 300 survivors who were not up to date with colorectal cancer screening met all eligibility criteria and enrolled in the ASPIRES study. The remaining 793 potentially eligible survivors did not enroll in the study for various reasons, including refusal, nonresponse, death, or a history of colorectal cancer.

The proposed project will include 629 survivors: 329 (187+142) who reported completing colorectal cancer screening within the intervals listed in the ASPIRES study during the initial screening and eligibility assessment, and 300 who enrolled in the ASPIRES study. These two groups represent survivors who have adhered to screening and those who have not (nonadherence), respectively. The primary objective of this analysis is to compare sociodemographic characteristics associated with colorectal cancer screening adherence among high-risk childhood cancer survivors. Figure 1 presents the CONSORT diagram of the ASPIRES study, with the red boxes highlighting the survivors who will be included in the proposed student project. This project is intended as a focused ancillary analysis rather than a stand-alone manuscript.

Figure 1. CONSORT Diagram for the SPIRES Study



4. SPECIFIC AIMS

Understanding sociodemographic disparities in colorectal cancer screening adherence may help identify survivor subgroups that could benefit from targeted survivorship interventions and tailored screening outreach efforts. This project has two aims:

4.1. Aim 1: Compare sociodemographic characteristics by colorectal cancer screening adherence status among high-risk childhood cancer survivors.

4.2. Aim 2: Examine sociodemographic factors associated with colorectal cancer screening adherence among high-risk childhood cancer survivors.

5. ANALYSIS FRAMEWORK

5.1. Study Population:

The analytic cohort, consisting of 629 survivors, will be derived from survivors identified through the CCSS Follow-Up 7 questionnaire and subsequently evaluated for participation in ASPIRES. Sociodemographic characteristics will be obtained from the CCSS Follow-Up 7 questionnaire. Colorectal cancer screening adherence status will be determined using information collected during the ASPIRES eligibility screening. Survivors who were up to date with colorectal cancer screening at initial and eligibility assessment will be classified as adherent, whereas survivors who remained eligible and enrolled in ASPIRES because they were not up to date with screening will be classified as nonadherent.

5.1.1. Adherent survivors (n = 329)

Self-reported completion of a colonoscopy within the previous 5 years or a multitarget DNA stool test within the previous 3 years during the ASPIRES screening and eligibility assessment process.

5.1.2. Nonadherent survivors (n = 300)

Did not report completion of colorectal cancer screening within the recommended interval and subsequently enrolled in the ASPIRES study.

5.2. Independent Variables

Sociodemographic characteristics from the CCSS Follow-Up 7 questionnaire

- Attained age
- Sex
- Race/ethnicity
- Marital status
- Annual household income
- Educational attainment
- Employment status
- Health insurance coverage
- Geographic location (rural, suburban, urban)

5.3. Dependent Variable

Self-reported colorectal cancer screening adherence during the ASPIRES study screening and eligibility assessment process was defined as reporting a colonoscopy within the previous 5 years or a multitarget stool DNA test within the previous 3 years.

6. ANALYTIC APPROACH

The analytic cohort will consist of 629 childhood cancer survivors identified through the CCSS Follow-Up 7 questionnaire who underwent screening and eligibility assessment for participation in the ASPIRES study. Survivors will be classified according to colorectal cancer screening adherence status:

- Adherent survivors (n = 329): survivors who reported being up to date with colorectal cancer screening during either the initial ASPIRES screening process or the subsequent eligibility assessment and were therefore ineligible for ASPIRES study enrollment.
- Nonadherent survivors (n = 300): survivors who were not up to date with colorectal cancer screening, remained eligible, and subsequently enrolled in the ASPIRES study.

Aim 1: Compare sociodemographic characteristics by colorectal cancer screening adherence status among high-risk childhood cancer survivors.

Descriptive analyses will summarize survivors' sociodemographic characteristics overall and by colorectal cancer screening adherence status. Frequencies and percentages will be reported for categorical variables, while means and standard deviations will be reported for continuous variables, as appropriate. Group differences by screening adherence status will be assessed using the chi-square test. Fisher's exact tests will be used when expected cell counts are five or fewer. Independent samples t-tests will be used for continuous variables. Statistical significance will be assessed using two-sided tests with $\alpha = 0.05$.

Aim 2: Examine sociodemographic factors associated with colorectal cancer screening adherence among high-risk childhood cancer survivors.

Univariate logistic regression analyses will be conducted to examine associations between individual sociodemographic variables and colorectal cancer screening adherence. Multivariable logistic regression will then be used to identify independent sociodemographic factors associated with adherence. In the logistic regression model, colorectal cancer screening adherence (adherence vs. nonadherence) will serve as the binary outcome, with adherent survivors coded as the event of interest. All prespecified sociodemographic variables will be included in the multivariable logistic regression model based on clinical relevance and prior literature. Multicollinearity among independent variables will be assessed using variance inflation factors. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) will be reported. Model fit and discrimination will be evaluated using the Hosmer-Lemeshow goodness-of-fit test and the c-statistic. Statistical significance will be assessed using two-sided tests with $\alpha = 0.05$.

Missing data will be evaluated for all study variables. Analyses will be conducted using complete-case data. The extent of missingness for each variable will be reported.

Table 1. Sociodemographic by colorectal cancer surveillance status.

Sociodemographic Characteristics	Overall N= n (%)	Adherence n= n (%)	Non-Adherence n= n (%)
Age at assessment (mean, SD)			
Sex Female Male			
Race White Other			
Ethnicity Hispanic Non-Hispanic			
Household Annual Income Less than \$20,000 \$20,000-39,999 \$40,000-59,999 \$60,000-79,999 \$80,000-99,999 \$100,000 or more Don't know Prefer not to answer Unknown			
Health Insurance Coverage Individual insurance Employer-sponsored insurance Medicare Medicaid Indian Health Service Military Health Care Don't know Other			
Marital Status Single, never married Married Living with a partner Widowed Divorced Separated			
Educational Attainment 1 – 8 years 9 – 12 years Completed high school/GED Training after high school Some college College graduate Postgraduate level Other			

Employment Status			
Full-time			
Part-time			
Caring for home or family			
Unemployment & looking for work			
Unable to work			
Retired			
Student			
other			

Table 2. Univariate tests of sociodemographic factors associated with colorectal cancer surveillance status.

Factor	Adherence n =		
	n(%)	OR (95%CI)	p-value
Sex			
Female (Ref)			
Male			
Race			
White (Ref)			
Other			
Ethnicity			
Hispanic (Ref)			
Non-Hispanic			
Household Annual Income			
Less than \$39,999			
\$40,000-99,999			
\$100,000 or more (Ref)			
Health Insurance Coverage			
Private insurance (Ref)			
Non-private insurance (e.g., Medicaid)			
Marital Status			
Married or living with a partner (Ref)			
Single, widowed, divorced, separated			
Educational Attainment			
≤12 years (Ref)			
>12 years			
Employment Status			
Employed full-time or part-time (Ref)			
Unemployed (include student, retired, disabled)			

Table 3. Sociodemographic predictors for adherence to colorectal surveillance in a multivariable logistic regression model.

Sociodemographic Factor	OR (95%CI)	<i>p</i> -value

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