

## **Study Title:** Impact of Rurality on Healthcare Utilization, Health Behaviors, and Health Status of Childhood Cancer Survivors

### **Working Group and Investigators:**

CCSS Working Group: Cancer Control and Intervention (Primary), Epidemiology (Secondary)

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### **Background and Rationale:**

*Health of Childhood Cancer Survivors:* There are nearly 500,000 childhood cancer survivors the United States and this number is growing as survival rates improve with advances in treatment of pediatric cancer.<sup>1,2</sup> Survivors are at increased risk of early mortality, chronic health conditions, reduced quality of life, and higher symptom burden compared to their siblings and peers.<sup>2,3</sup> Decreased physical quality of life is associated with older age, lower educational attainment, and unmarried status.<sup>4</sup> Survivor programs that help screen for chronic health conditions are typically located in metropolitan areas and serve large catchment areas, including rural populations. Survivors experience more healthcare cost barriers compared to noncancer controls.<sup>5</sup>

*Disparities in Care Among Childhood Cancer Survivors:* There is evidence that subgroups of survivors experience disparities in survivorship care initiation and follow up.<sup>6</sup> Uninsured survivors are less likely to have a healthcare visit and more likely to experience healthcare cost barriers.<sup>5</sup> There is mixed evidence regarding the distance to cancer survivorship clinic as a factor leading to disparate care with some population-based studies reporting farther distance from survivor clinic as a risk factor for clinic non-attendance and others reporting farther distance from clinic as a protective factor.<sup>7-10</sup> Although longer distance to clinic has been studied as a barrier to survivor clinic attendance, rurality has not been as thoroughly explored as a variable leading to differences in survivor care.

*Rurality and Childhood Cancer Survivors:* A recent population-based cohort study in Oklahoma found that a higher percentage of survivors from large towns had sub-optimal survivor follow-up compared to urban and rural survivors.<sup>11</sup> Our preliminary data from a Southeastern United States pediatric institutional cohort show that rurality is a risk factor for non-initiation and non-continuation of survivor care.<sup>12</sup>

*Rural-Urban Disparities:* It is estimated that 19.3% of the United States population lives in a rural area.<sup>13</sup> All-cause mortality is higher in rural persons as compared to their urban counterparts.<sup>14</sup> Patterns of healthcare utilization and health behaviors differ between the general rural and urban populations. Rurality is associated with reduced access to healthcare providers and decreased engagement in preventative care.<sup>15</sup> Engagement in healthy behaviors among rural adults is suboptimal with older adults engaging in less physical activity<sup>16</sup> and smoking prevalence is higher in rural areas.<sup>17</sup> There is age and geographic variation in alcohol use patterns with higher alcohol use rates in rural adolescents compared to urban adolescents<sup>18</sup> and those living in the rural Midwest.<sup>19</sup>

*Conceptual Model:* The Vulnerable Populations Conceptual Model describes the relationships between resource availability, risk, and health status, and these concepts have been applied to rural populations (Figure 1).<sup>20,21</sup> Survivors of childhood cancer can be considered a vulnerable population (Figure 2). Adult survivors have lower incomes,<sup>22,23</sup> experience higher rates of unemployment,<sup>24,25</sup> experience barriers to health insurance coverage<sup>26</sup>, and have lower marriage rates<sup>27</sup> as compared to sibling and population controls. There is also lower educational achievement and an increased need for educational support in subgroups of survivors.<sup>25</sup> Adult survivors can have persistent psychological stress beyond their cancer diagnosis and treatment.<sup>28</sup> Survivors have lower rates of adequate physical activity compared to their siblings<sup>29</sup> and report more sleep difficulties.<sup>30</sup> These findings in the childhood cancer survivor population define survivors as a vulnerable population at risk for poor health outcomes.

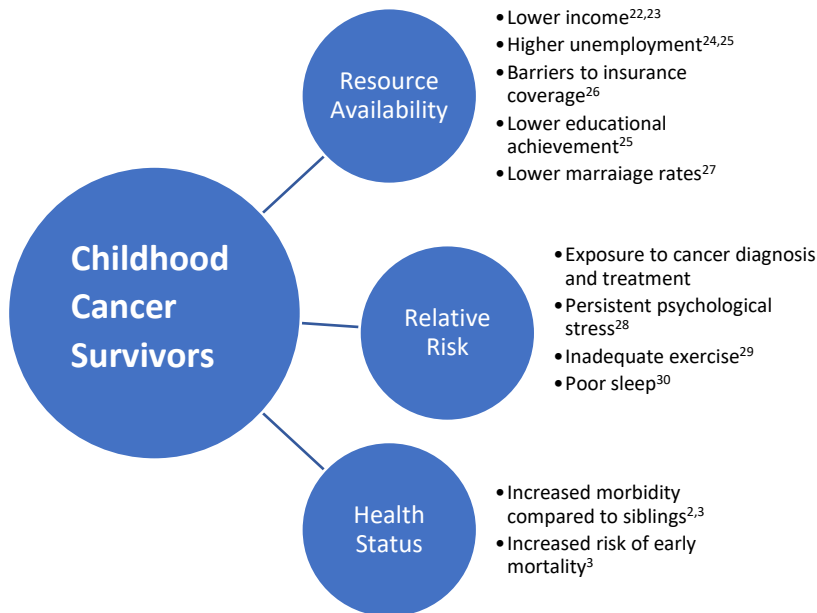
Rural survivors of childhood cancer are a uniquely vulnerable population at higher risk for poor health outcomes and likely to have poor healthcare utilization, increased incidence of poor health behaviors, and poor health status; however, this has not yet been studied utilizing a large cohort of survivors, This proposed project will

address this gap by leveraging the Childhood Cancer Survivor Study (CCSS) to identify the association between rurality and self-reported measures of healthcare utilization, health behaviors, and health status in long-term survivors of childhood cancer.

Figure 1: Table from Leight highlighting rural findings within the context of the Vulnerable Populations Conceptual Model<sup>21</sup>

Concept	Theoretical Structure	Empirical Indicators	Selected Rural Findings
Resource availability	Social resources	Income	17% living in poverty
	• Human capital	Jobs	Loss of manufacturing jobs
		Education	Fewer college degrees
	• Social connectedness	Housing	Rural homeless
	• Social skills	Patterns of family and community life	Loss of traditional family infrastructure
	Environmental resources	Health care	Distance to health care as a barrier
Relative risk	Increased risk factors	Quality of care	Inadequate health care resources
		Lifestyle behaviors and choices	Less than optimal nutrition, exercise, and sleep
		Health-promoting behaviors (screening, immunization)	Less likely to use seat belts, have pap smears, get immunizations, and have dental and physical examinations
	Exposure to stressful events	Increase in motor vehicle accidents and accidental work-related injuries	
Health status	Morbidity	Delayed diagnosis	Increased chronic illness and disability
	Mortality	Increased illness	
		Premature death	Higher infant mortality

Figure 2: The vulnerable populations conceptual model as applied to childhood cancer survivors.



**Specific aims:**

**Aim 1: To determine the association between rurality of survivor residence and healthcare utilization and type of medical care among adult survivors of childhood cancer.**

Hypothesis 1a: Rural survivors will report lower adherence to guideline-recommended late effects surveillance than their urban counterparts.

Hypothesis 1b: Rural survivors will be less likely to report completion of a primary care visit and less likely to report completion of a cancer specialist visit compared to their urban counterparts.

**Aim 2: To describe the association of rurality with health behaviors among childhood cancer survivors.**

Hypothesis: Rural survivors will have an increased incidence of risky health behaviors (e.g., tobacco and alcohol use) and a decreased incidence of protective health behaviors (e.g., adequate physical activity) as compared to their urban counterparts.

**Aim 3: To evaluate the association between rural residence and self-reported health status in childhood cancer survivors compared to urban/suburban residence.** Hypothesis: Rural survivors will have poorer self-reported health status as compared to their urban counterparts.

**Aim 4: To evaluate whether there are differences in urban/rural gaps in self-reported healthcare utilization, health behaviors, and health status between cancer survivors and their sibling controls.**

Hypothesis 4a: Compared with sibling controls, the urban/rural gap in the likelihood of reporting completion of a primary care visit is larger among cancer survivors.

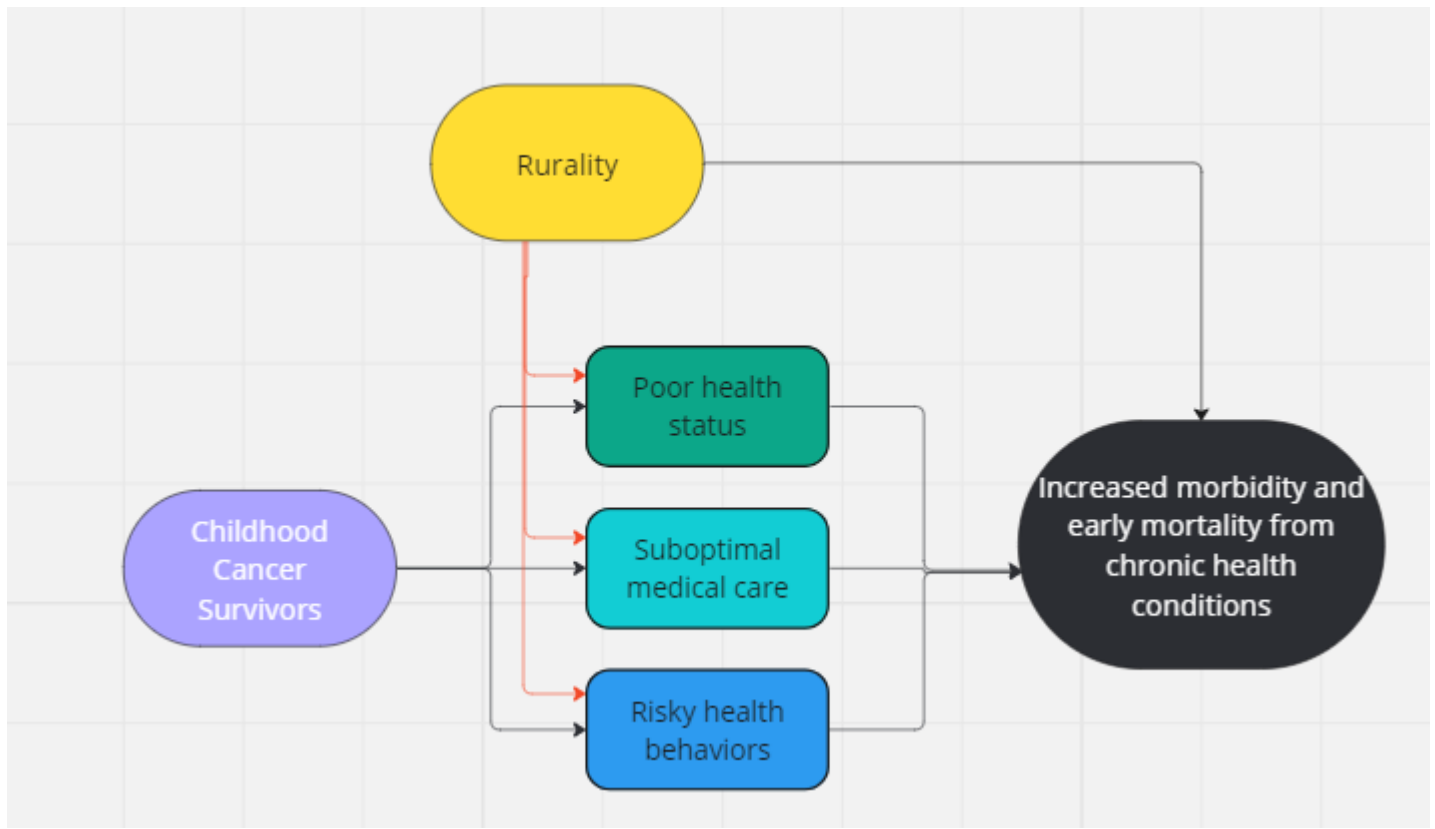
Hypothesis 4b: Compared with sibling controls, the urban/rural gaps in the incidence of risky health behaviors (e.g., tobacco and alcohol use) and the incidence of protective health behaviors (e.g., adequate physical activity) are larger among cancer survivors.

Hypothesis 4c: Compared with sibling controls, the urban/rural gap in the self-reported health status is larger among cancer survivors.

#### **Analysis framework:**

Conceptual Framework: Using the vulnerable populations model as applied to survivors and rurality, we propose that the dual vulnerability of rural survivors places them at higher risk for suboptimal medical care, risky health behaviors, and poor health status compared to their urban counterparts (Figure 3) which would ultimately lead to increased morbidity and early mortality. A previously submitted concept proposal by Drs. Winestone and Howell is investigating rurality as a small-area measure and its association with mortality and presence of chronic health conditions. This concept proposal will build on that work by investigating rurality and its relationship with contributors (i.e. poor health status, suboptimal medical care, and risky health behaviors) to morbidity and mortality (Figure 3).

Figure 3: Conceptual framework describing the proposed relationship between rurality, health status, medical care, and risky health behaviors in survivors



Concept map created using Miro Mind-Map Maker (<https://miro.com/mind-map/>).

**Subject Population:** For Aim 1-3, we will include survivors in the CCSS cohort who completed Follow-up 5 survey, Follow-up 6 Long survey, and/or Follow-up 7 survey and have addresses available for analysis.. For Aim 4, we will include both survivors and sibling controls in the CCSS cohort who participated in the Follow-up 5, 6, and/or 7 surveys and addresses available.

**Key Independent Variable:** Rurality is the key independent variable in this analysis. Census tract from each survey will be linked to Rural-Urban Commuting Area (RUCA) Codes to determine rurality. RUCA Codes will be obtained from the 2020 dataset published by the United States Department of Agriculture.<sup>31</sup> Primary RUCA codes range from 1-10 with 1 being “Metropolitan area core” and 10 being “Rural areas”. Primary RUCA codes will be categorized as rural or urban according to the University of Washington Rural Health Center Categorization C schema in which <10% of the commuting flow is to an urbanized center.<sup>32</sup> Other classification schemas will be considered based on the distribution (i.e. metropolitan, micropolitan, small town and rural). Since there are varying classifications of rurality which can over- or under-report disparities, we will conduct sensitivity analyses with different measures of rurality such as urban influence codes, rural continuum codes, and the CDC rural classification scheme.<sup>33</sup>

**Correlative Factors:** Correlative factors will include: insurance, marriage, education, employment, chronic conditions (CTCAE v.5.0; Total number Grade 1-4, Total number of Grade 3-4, by organ system), attained age at survey, race/ethnicity, sex, primary cancer diagnosis, and cancer treatment (chemotherapy type and cumulative dose, radiation therapy field and dose, surgery, and stem cell transplantation). If there is a determination that rurality is associated with our chosen outcomes, a future concept proposal will be generated to explore other small-area measures such as area deprivation index (ADI), Health Professional Shortage Areas (HPSAs) and Medically Underserved Areas (MUAs) as mediators of the relationship between rurality and healthcare utilization, health behaviors, and health status.

## Outcomes of Interest:

### Self-Reported Healthcare Utilization:

Responses to the following questions on the CCSS questionnaires will be analyzed. If there are multiple surveys per survivor, we will use responses from the most recent survey:

#### 1. Medical Care: Questions to determine primary care provider and cancer specialist visits

a. During the PAST 2 YEARS, how many times did you see or talk to the following healthcare providers for medical care? (Choices: None, 1-2, 3-4, 5-10, 11-20, or >20 times) Provider categories include:

- A) Primary care doctor in the community
- B) Clinician at a cancer center

Related items include: FU5 B2, FU6 Long B2, and FU7 B1 a-b. In FU5 and FU6 Long, survivors were asked “how many times did you see a doctor” and “how many times of the visits to the doctor were related to cancer”; In FU7, survivors were asked about the number of visits in the past 2 years at each type of location.

b. When was the LAST TIME you saw a healthcare provider in each of the following locations where the provider asked you questions or examined you to see whether you had any health problems from your cancer or your cancer treatment? (Choices: <1 year ago, 1-2 years ago, >2 but <5 years ago, ≥5 years ago, or Never) Location categories include:

- A) At a cancer survivor clinic
- B) At a cancer center, but not in a cancer survivor clinic
- C) At my primary care doctor's office

Related items include: FU5 B4; FU6 Long B4 and FU7 B2. In FU7, survivors provided the last time of visit at each type of location.

c. Do you currently have a cancer survivorship care plan and/or a summary of treatment for your cancer (records from your cancer doctor that have details about your cancer treatment and medical tests you should have to check for future health problems)?

Related items include: FU5 B7; FU6 Long B7 and FU7 B5.

#### 2. Medical Tests: Questions to determine adherence to risk-based and general health surveillance

a. When was the last time you had (Choices: Never, <1 year ago, 1-2 years ago, >2 but <5 years ago, ≥5 years ago, I had one, but don't recall when, or I don't know if I ever had one for medical screening test):

- A) an echocardiogram, B) a MRI of your heart, E) a home blood stool test to determine whether your stool contains blood, F) sigmoidoscopy or colonoscopy to view the colon for signs of cancer or other problems, I) a skin exam for skin cancer by a healthcare provider, J) a mammogram, K) a breast ultrasound, L) a breast MRI, M) a pap smear, N) A PSA or blood test to detect prostate cancer

Related items include: FU5 a-n, FU6 Long C1 a-n, and FU7 C1 a-n.

Prior definitions will be used to describe healthcare utilization.<sup>34,35</sup>

### Self-Reported Health Behaviors:

Responses from the following questions on the CCSS questionnaires will be analyzed:

#### 3. Health Habits:

##### a. Alcohol

- i. During the last 12 months, A) how many alcoholic drinks did you have on a typical day when you drank alcohol?, C) how often did you usually have any kind of drink containing alcohol?, D) how often did you have 5 or more (males) or 4 or more (females) drinks containing any kind of alcohol in a single day?

Related items: FU5 N3 – N6; FU7 M3-M6.

##### b. Smoking

- i. How old were you when you started smoking?
- ii. Do you smoke cigarettes now?
- iii. On average, how many cigarettes a day do/did you smoke?

Related items: FU5 N8-N10; FU7 M8-M10.

##### c. Physical Activity

- i. During the past month, did you participate in any physical activities or exercises?
- ii. Now thinking about the vigorous physical activities you do in a usual week, do you do vigorous activities for at least 10 minutes at a time?
- iii. How many days per week do you do these vigorous activities for at least 10 minutes at a time?
- iv. On days when you do vigorous activities for at least 10 minutes at a time, how much total time per day do you spend doing these activities?
- v. The last three questions are repeated for moderate and light activities.

Related items: FU5 N15-N24; FU6 Long D1-D10; FU7 M15-M24.

Prior definitions will be used to describe alcohol consumption and tobacco usage.<sup>38,39</sup> Current drinking will be defined as any answer >0 to question ii.A. Descriptive statistics will be used to calculate number, frequency, and type of substance usage and Prior definitions will be used to describe physical activity.<sup>29</sup> We will compare both percentage of those meeting physical activity standards and those reporting no physical activity between rural and urban survivors. Physical activity standards will be defined using CDC guidelines for adults with at least 150 minutes (2 hours and 30 minutes) or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity.<sup>40</sup> Survivors who answered “no” to participation in any physical activity or exercise in the last month will be considered as having an inactive lifestyle.

### Self-Reported Health Status:

The following questions will be analyzed to determine health status measures:

#### 4. Health Status

- i. General Health: In general, would you say your health is: Excellent, Very good, Good, Fair, Poor
- ii. Mental Health: 18-item Brief Symptom Inventory
- iii. Activity Limitations: Over the last 2 years how long... has your health limited you in each of the following activities: B. moderate activities, C. walking uphill, E. walking one block (Choices: Limited >3 months, Limited ≤3 months, not limited)
- iv. Functional Impairment: Because of any impairment or health problems, do you need help... with A. personal care needs, B. handling routine needs, or C. does it keep you from holding a job or attending school? (Choices: No, Yes)

- v. Cancer-related Pain: Do you currently have pain as a result of your cancer or similar illness, or its treatment? (Choices: No, small amount, medium amount, a lot, very bad, excruciating pain)
- vi. Cancer-related Anxiety: Do you currently have anxieties/fears as a result of your cancer... or its treatment? (Choices: No, small amount, medium amount, a lot, very many, extreme anxiety/fears)

Related items: FU 5 O1, N29, N25-N27, L1-L18, L20, L19; FU6 Long E1, E3 (no questions related to BSI 18, functional impairment, cancer-related pain or cancer-related anxiety); FU7 N1, M29, M25-M27, L1-1L8 L22, L21.

Prior definitions will be used to describe health status in survivors.<sup>41</sup> Survivors with adverse general health will be considered those who answer “poor” for question 4.i. The 18-item Brief Symptom Inventory (BSI-18), a self-report measure of psychological symptoms, will be used for the mental health domain and responses will be scored according to the published manual with each survivor receiving a sex-specific T-score (mean = 50, SD = 10) on the Global Severity Index or one of three symptom scales.<sup>42</sup> T-scores 63 or higher represent the upper 10th percentile of scores reported in a community sample and will be considered to be significantly elevated. Using this cutoff, scores will be classified as elevated vs. not elevated. Activity limitation will be defined as any response to 4.iii in which the survivor answers “limited.” Functional impairment will be defined as survivors answering “no” to any questions listed in 4.iv. Survivors with significant cancer-related pain will be defined as those answering “very bad” or “excruciating pain” to question 4.v and survivors with significant cancer-related anxiety will be defined as those answering “very many” and “extreme anxiety/fears” to question 4.vi.

#### Statistical Analysis:

Demographic, cancer treatment and other correlative factors will be analyzed using descriptive statistics (median and ranges for continuous variables, percentages for categorical variables) and compared between rural and urban survivors and siblings using two-sample Wilcoxon’s rank sum test for continuous variables and Fisher’s exact test for categorical variables (Table 1).

**Aim 1:** Descriptive statistics will be used to compare medical visits to a primary care provider (percentage reporting “yes”) and cancer specialists (percentage reporting “yes”) between rural and urban survivors. Additionally, survivor-focused care including cancer center visits (frequency), cancer-related visits (frequency), and presence of a cancer survivor care plan or summary of treatment (percentage reporting “yes”) will be compared between rural and urban survivors using similar methods (Table 2a). Percentage of at-risk survivors receiving surveillance for subsequent malignant neoplasms (SMN) and cardiomyopathy, as well as percentage of survivors adherent to the secondary cancer screening guidelines will be compared between rural and urban (Table 2b). Eligibility for this analysis will be determined for each survey timepoint using the appropriate Children’s Oncology Group (COG) Long-Term Follow-Up (LTFU) guidelines (Table 3). Adherence will be defined using the most recent COG guideline at the time of the survey.

Multivariable logistic regression models will be used to determine the odds ratio of rurality on having a recent visit to healthcare providers, having a cancer survivorship care plan and/or summary of cancer treatment, and

adherence to general health surveillance for colorectal, skin, breast (among women), cervical, and cardiac screening (separately for each category). Analysis of cancer screening will only be restricted to applicable survivors as described in Table 3. We will adjust for age, sex, insurance status, presence of chronic conditions, education, and race/ethnicity. Additional covariates with a univariable significance level of  $<0.1$  will be included in multivariable models. For cancer screening, we will also adjust for the risk status.

**Aim 2:** Descriptive statistics will be used to calculate the number and proportion of inactive survivors and those who do not meet physical activity guidelines. These will be compared between urban and rural survivors using multivariate regression (Table 5) adjusting for age, gender, race/ethnicity, and presence of chronic conditions as well as additional covariates with a univariable significance level of  $<0.1$ . Comparison between urban and rural survivors using multivariate logistic regression (Table 4). For smoking and drinking behaviors, we will adjust for age, sex, race/ethnicity, education, and age of at first use. Additional covariates with a univariable significance level of  $<0.1$  will be included in multivariable models.

**Aim 3:** Multiple logistic regression models with each health status domain serving as the dependent variable will be used to compare the percentage of survivors reporting adverse status in each domain between rural and urban survivors, adjusting for age, sex, and race/ethnicity (Table 5). Analytic samples may differ between health status domains due to differences in survey items between FU5, FU6 long, and FU7.

**Aim 4:** Outcomes from Aims 1-3 will be assessed among controls using the same regression models except for adherence to late-effects screening and cancer specialist visits as these do not apply to siblings, including survivor/control status and its interaction term with rural/urban status. In each applicable analysis, the obtained aOR will be compared with the aOR in cancer survivors. The multiplicative difference in the aOR, their standard errors and 95% CIs will be computed using Delta method. Comparison of aOR in each domain between survivor and control will also be visualized using forest plots.



Table 1: Demographics of cancer survivors and sibling controls completing FU5, FU6 Long and/or FU7.

	Cancer survivors			Sibling controls		
	Rural (n=***)	Urban (n=***)	P- value	Rural (n=***)	Urban (n=***)	P- value
<b>Sex</b>						
% Male						
% Female						
<b>Age at Cancer Diagnosis</b>						
Median						
Interquartile Range						
<b>Age at Survey</b>						
Median						
Interquartile Range						
<b>Age Category</b>						
Young Adult (18-39.99 years old)						
Middle-Aged Adult (40-64.99 years old)						
Older Adult (65+ years old)						
<b>Race/Ethnicity</b>						
White non-Hispanic						
Black non-Hispanic						
Hispanic						
Other <sup>1</sup>						
<b>Insurance Status</b>						
Insured/Canadian						
Uninsured						
<b>Education</b>						
Less than high school						
Some college						
College or higher						
<b>Marriage</b>						
Ever Married						
Never Married						
<b>Employment</b>						
Employed						
Unemployed						
<b>Chronic Conditions<sup>2</sup></b>						
Total Number Grade 1-4						
Total Number Grade 3-4						
<b>Diagnosis</b>				/		
Leukemia						
Lymphoma						
Central Nervous System Tumors						
Solid Tumors						
Bone and Soft-Tissue Sarcomas						
Neuroblastoma						
Kidney and Liver Tumors						
Other						
<b>Cancer Treatment</b>				/		
Treatment Modality						
Chemotherapy-Only						
Treatment Included Radiation						

Treatment Included HSCT				
Chemotherapy Exposure				
Anthracycline Equivalent Dose, mg/m <sup>2</sup> (mean±SD)				
Cyclophosphamide Equivalent Dose, mg/m <sup>2</sup> (mean±SD)				
Radiation Field				
Head				
Chest				
Abdomen/Pelvis				
Extremities				
<p>HSCT: Hematopoietic Stem Cell Transplant, bolded values significant at a level of p&lt;0.05  SD: standard deviation  <sup>1</sup>Other category includes Asian/Pacific Islander, Native American, and multi-racial  <sup>2</sup>Grade defined per CTCAE (Common Terminology Criteria for Adverse Events) v.5.0</p>				

Table 2A: Summary Statistics of Medical Care and Screening (descriptive) / logistic regression, cutoff decide later  
 There is a guideline for medical tests

Medical test: compliant to guideline or not --- separate analyses for each category

	Rural N (%)	Urban N (%)	p-value	
<b>Medical Care</b>				
<i>Primary Care Visit in the past two years</i>				
<b>Survivor-Focused Care</b>				
<i>Last time of having a cancer-related visit or examination</i>				
<i>&lt; 1 year ago</i>				
<i>1-2 year ago</i>				
<i>&gt;2 and &lt;5 years ago</i>				
<i>&gt;= 5 years ago</i>				
<i>Never</i>				
<b>Cancer Survivor Care Plan/Treatment Summary</b>				
<b>SMN surveillance (Presence of Screening Test)</b>				
<b>Colonoscopy or Stool Blood Test</b>				
General population at risk, N=***				
<i>&lt; 1 year ago</i>				
<i>&gt;=1 and &lt;2 years ago</i>				
<i>&gt;2 and &lt;5 years ago</i>				
<i>&gt;= 5 years ago</i>				
<i>Do not recall</i>				
<i>Don't know if ever had one</i>				
Those at increased risk due to treatment exposure, N=***				
<i>&lt; 1 year ago</i>				
<i>&gt;=1 and &lt;2 years ago</i>				
<i>&gt;2 and &lt;5 years ago</i>				
<i>&gt;= 5 years ago</i>				
<i>Do not recall</i>				
<i>Don't know if ever had one</i>				
Mammogram or other breast imaging, N = *** at risk				
General population at risk, N= ***				
<i>&lt; 1 year ago</i>				
<i>&gt;=1 and &lt;2 years ago</i>				
<i>&gt;2 and &lt;5 years ago</i>				
<i>&gt;= 5 years ago</i>				
<i>Do not recall</i>				
<i>Don't know if ever had one</i>				
Those at increased risk due to treatment exposure, N=***				
<i>&lt; 1 year ago</i>				
<i>&gt;=1 and &lt;2 years ago</i>				
<i>&gt;2 and &lt;5 years ago</i>				
<i>&gt;= 5 years ago</i>				
<i>Do not recall</i>				
<i>Don't know if ever had one</i>				
Pap Smear, N = *** at risk				
<i>&lt; 1 year ago</i>				
<i>&gt;=1 and &lt;2 years ago</i>				

<p>&gt;2 and &lt;5 years ago          &gt;= 5 years ago          Do not recall          Don't know if ever had one</p>				
<p>Dermatologic Exam, N = *** at risk          &lt; 1 year ago          &gt;=1 and &lt;2 years ago          &gt;2 and &lt;5 years ago          &gt;= 5 years ago          Do not recall          Don't know if ever had one</p>				
<p>Late Effects Screening (Presence of Screening Test)</p>				
<p>Cardiac Screening, N = *** at risk          &lt; 1 year ago          1-2 years ago          &gt;2 and &lt;5 years ago          &gt;= 5 years ago          Do not recall          Don't know if ever had one</p>				
<p>p-values are obtained from Fisher's exact test</p>				

Table 2B: Association between Rurality and Medical Care / Screening					
	Cancer survivors		Sibling controls		Multiplicative difference in aORs (95% CI)
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	
Medical Care					
Having a recent primary care visit					
Survivor-Focused Care					
Cancer Center Visit			/	/	/
Having a recent cancer center or cancer-related visit			/	/	/
Having a Cancer Survivor Care Plan/Treatment Summary			/	/	/
Compliance to screening guidelines					
Colorectal					
Breast					
Cervical					
Skin			/	/	/
aOR: adjusted odds ratio, CI: confidence interval, values considered significant at a p-value <0.05 Adjusted for age, sex, insurance status, presence of chronic conditions, risk status and race/ethnicity					

**Table 3: Screening Guidelines**

**Secondary Cancer Screening**

	<b>Surveys 5&amp;6 (2014 and 2017) using COG LTFU Guidelines v 4.0 (October 2013)<sup>36</sup></b>	<b>Survey 7 (2019) using COG LTFU Guidelines v 5.0 (October 2018)<sup>37</sup></b>																						
	<b>High Risk Due to Treatment</b>	<b>Standard Risk (ACS Recommendations)</b>	<b>High Risk Due to Treatment</b>	<b>Standard Risk (ACS Recommendations)</b>																				
Colorectal	Radiation to specified fields at ≥ 30 Gy or radiation to specified field + relevant spinal radiation and/or TBI with total sum ≥30Gy: Colonoscopy every 5 years beginning 10 years after radiation or 35 years old (whichever occurs last)	<ol style="list-style-type: none"> <li>1. Fecal occult blood yearly starting at age 50 OR</li> <li>2. Flexible sigmoidoscopy every 5 years starting at age 50 OR</li> <li>3. Double contrast barium enema every 5 years starting at age 50 OR</li> <li>4. Colonoscopy every 10 years beginning at age 50</li> </ol>	Radiation to abdomen, pelvis, spine, or TBI: multitarget stool DNA test every 3 years or colonoscopy every 5 years beginning 5 years after radiation or age 30 (whichever occurs last)	Beginning Age 45: <table border="1"> <thead> <tr> <th colspan="3">Colorectal Cancer Screening Options</th> </tr> <tr> <th>Type</th> <th>Test</th> <th>Frequency</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Stool-Based Tests</td> <td>Fecal immunochemical test*</td> <td>Yearly</td> </tr> <tr> <td>High-sensitivity, guaiac-based fecal occult blood test*</td> <td>Yearly</td> </tr> <tr> <td>Multitarget stool DNA test*</td> <td>Every 3 years</td> </tr> <tr> <td rowspan="3">Structural Examinations</td> <td>Colonoscopy</td> <td>Every 10 years</td> </tr> <tr> <td>CT colonography*</td> <td>Every 5 years</td> </tr> <tr> <td>Flexible sigmoidoscopy*</td> <td>Every 5 years</td> </tr> </tbody> </table> <p><small>*All positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy.</small></p>	Colorectal Cancer Screening Options			Type	Test	Frequency	Stool-Based Tests	Fecal immunochemical test*	Yearly	High-sensitivity, guaiac-based fecal occult blood test*	Yearly	Multitarget stool DNA test*	Every 3 years	Structural Examinations	Colonoscopy	Every 10 years	CT colonography*	Every 5 years	Flexible sigmoidoscopy*	Every 5 years
Colorectal Cancer Screening Options																								
Type	Test	Frequency																						
Stool-Based Tests	Fecal immunochemical test*	Yearly																						
	High-sensitivity, guaiac-based fecal occult blood test*	Yearly																						
	Multitarget stool DNA test*	Every 3 years																						
Structural Examinations	Colonoscopy	Every 10 years																						
	CT colonography*	Every 5 years																						
	Flexible sigmoidoscopy*	Every 5 years																						
Breast	Radiation to specified fields or combination at ≥ 20Gy : yearly mammogram beginning 8 years after radiation or at age 25, whichever occurs last	Mammogram yearly beginning at age 40	Radiation to chest, axilla, or TBI: yearly mammogram beginning 8 years after radiation or at age 25, whichever occurs last	Mammogram: 45-54 years old: yearly ≥55 years: biennial or yearly																				
Cervical	No additional screening based on treatment exposure	Cervical PAP Smear starting age 21 years: 21-29 yo: PAP every 3 years 30-65 yo: HPV and PAP every 5 years or PAP alone every 3 years	No additional screening based on treatment exposure	Cervical PAP Smear starting at age 21 years: 21-29 yo: PAP every 3 years 30-65 yo: HPV and PAP every 5 years or PAP alone every 3 years																				
Skin	Any radiation including TBI: yearly dermatologic exam to irradiated fields	<i>No screening for standard risk patients</i>	Any radiation including TBI: yearly dermatologic exam to irradiated fields	<i>No screening for standard risk patients</i>																				

**Late Effects Screening**

	<b>Surveys 5&amp;6 (2014 and 2017) using COG LTFU Guidelines v 4.0 (October 2013)<sup>29</sup></b>	<b>Survey 7 (2019) using COG LTFU Guidelines v 5.0 (October 2018)<sup>30</sup></b>																																																														
Cardiac Screening (Echocardiogram or comparable cardiac imaging)	<table border="1"> <thead> <tr> <th colspan="4">RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)</th> </tr> <tr> <th>Age at Treatment<sup>a</sup></th> <th>Radiation with Potential Impact to the Heart<sup>b</sup></th> <th>Anthracycline Dose<sup>c</sup></th> <th>Recommended Frequency</th> </tr> </thead> <tbody> <tr> <td rowspan="2">&lt;1 year old</td> <td>Yes</td> <td>Any</td> <td>Every year</td> </tr> <tr> <td>No</td> <td>&lt; 200 mg/m<sup>2</sup> ≥ 200 mg/m<sup>2</sup></td> <td>Every 2 years Every year</td> </tr> <tr> <td rowspan="4">1-4 years old</td> <td>Yes</td> <td>Any</td> <td>Every year</td> </tr> <tr> <td rowspan="3">No</td> <td>&lt;100 mg/m<sup>2</sup></td> <td>Every 5 years</td> </tr> <tr> <td>≥100 to &lt;300 mg/m<sup>2</sup></td> <td>Every 2 years</td> </tr> <tr> <td>≥300 mg/m<sup>2</sup></td> <td>Every year</td> </tr> <tr> <td rowspan="4">≥5 years old</td> <td>Yes</td> <td>&lt;300 mg/m<sup>2</sup> ≥300 mg/m<sup>2</sup></td> <td>Every 2 years Every year</td> </tr> <tr> <td rowspan="3">No</td> <td>&lt;200 mg/m<sup>2</sup></td> <td>Every 5 years</td> </tr> <tr> <td>≥200 to &lt;300 mg/m<sup>2</sup></td> <td>Every 2 years</td> </tr> <tr> <td>≥300 mg/m<sup>2</sup></td> <td>Every year</td> </tr> <tr> <td colspan="4">Any age with decrease in serial function</td> </tr> </tbody> </table> <p><small><sup>a</sup>Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 80], whichever was given first) <sup>b</sup>See Section 80 <sup>c</sup>Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, "Info Link (Dose Conversion)"]</small></p>	RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)				Age at Treatment <sup>a</sup>	Radiation with Potential Impact to the Heart <sup>b</sup>	Anthracycline Dose <sup>c</sup>	Recommended Frequency	<1 year old	Yes	Any	Every year	No	< 200 mg/m <sup>2</sup> ≥ 200 mg/m <sup>2</sup>	Every 2 years Every year	1-4 years old	Yes	Any	Every year	No	<100 mg/m <sup>2</sup>	Every 5 years	≥100 to <300 mg/m <sup>2</sup>	Every 2 years	≥300 mg/m <sup>2</sup>	Every year	≥5 years old	Yes	<300 mg/m <sup>2</sup> ≥300 mg/m <sup>2</sup>	Every 2 years Every year	No	<200 mg/m <sup>2</sup>	Every 5 years	≥200 to <300 mg/m <sup>2</sup>	Every 2 years	≥300 mg/m <sup>2</sup>	Every year	Any age with decrease in serial function				<table border="1"> <thead> <tr> <th colspan="3">Recommended Frequency of Echocardiogram</th> </tr> <tr> <th>Anthracycline Dose<sup>a</sup></th> <th>Radiation Dose<sup>bb</sup></th> <th>Recommended Frequency</th> </tr> </thead> <tbody> <tr> <td rowspan="3">None</td> <td>&lt; 15 Gy or none</td> <td>No screening</td> </tr> <tr> <td>≥ 15 - &lt; 35 Gy</td> <td>Every 5 years</td> </tr> <tr> <td>≥ 35 Gy</td> <td>Every 2 years</td> </tr> <tr> <td rowspan="2">&lt; 250 mg/m<sup>2</sup></td> <td>&lt; 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/m<sup>2</sup></td> <td>Any or none</td> <td>Every 2 years</td> </tr> </tbody> </table> <p><small><sup>a</sup>Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33. <sup>bb</sup>Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.</small></p>	Recommended Frequency of Echocardiogram			Anthracycline Dose <sup>a</sup>	Radiation Dose <sup>bb</sup>	Recommended Frequency	None	< 15 Gy or none	No screening	≥ 15 - < 35 Gy	Every 5 years	≥ 35 Gy	Every 2 years	< 250 mg/m <sup>2</sup>	< 15 Gy or none	Every 5 years	≥ 15 Gy	Every 2 years	≥ 250 mg/m <sup>2</sup>	Any or none	Every 2 years
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COG LTFU: Children's Oncology Group Long-Term Follow-Up, ACS: American Cancer Society, TBI total body irradiation, HSCT: hematopoietic stem cell transplant

Table 4A: Summary statistics of health behaviors						
	Survivors			Controls		
	Rural (N = *)	Urban (N = *)	p-value	Rural (N = *)	Urban (N = *)	p-value
Alcohol Use in the Last 12 months <sup>1</sup>						
Current Drinker, N(%)						
Number of Alcoholic Drinks Per Day, Median (IQR)						
Frequency of Alcohol Use, Median(IQR)						
Frequency of Risky Drinking <sup>2</sup> , Median(IQR)						
Smoking <sup>3</sup>						
Current Smoking Status, N(%)						
Number of cigarettes per day, Median(IQR)						

OR: odds ratio, aOR: adjusted odds ratio, CI: confidence interval, values considered significant at p-value <0.05

<sup>1</sup>Adjusted odds ratios for drinking behaviors between rural and urban survivors, controlling for well known risk factors for heavy drinking including age, gender, race/ethnicity, education, and age of first drinking.

<sup>2</sup>Risky drinking defined as 5 or more drinks containing any kind of alcohol in a single day for males and 4 or more drinks containing any kind of alcohol in a single day for females.

<sup>3</sup>Adjusted odds ratios for smoking behaviors between rural and urban survivors, controlling for age, gender, race/ethnicity, education, and age of first smoking.

<sup>4</sup> Adjusted for age, gender, race/ethnicity, education, presence of chronic conditions.

	Survivors			Controls		
	Rural (N = *)	Urban (N = *)	p-value	Rural (N = *)	Urban (N = *)	p-value
Physical Activity <sup>4</sup>						
Inadequate Physical Activity <sup>5</sup> , N(%)						
Inactive Lifestyle, N(%)						

<sup>5</sup> Defined as those not meeting CDC guidelines of at least 150 minutes (2 hours and 30 minutes) or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity.  
p-values were obtained using Fisher's exact test

Table 4B: Association between Rurality and Medical Care / Screening

	Cancer survivors		Sibling controls		Multiplicative difference in aORs (95% CI)
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	
Alcohol Use in the Last 12 months <sup>1</sup>					
Current Drinker					
Risky Drinking <sup>2</sup>					
Smoking <sup>3</sup>					
Current Smoker					
Heavy smoker					
Physical Activity <sup>4</sup>					
Inadequate Physical Activity <sup>5</sup>					
Inactive Lifestyle					

OR: odds ratio, aOR: adjusted odds ratio, CI: confidence interval, values considered significant at p-value <0.05

<sup>1</sup>Adjusted odds ratios for drinking behaviors between rural and urban survivors, controlling for well known risk factors for heavy drinking including age, gender, race/ethnicity, education, and age of first drinking.

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<sup>4</sup> Adjusted for age, gender, race/ethnicity, education, presence of chronic conditions.

<sup>5</sup> Defined as those not meeting CDC guidelines of at least 150 minutes (2 hours and 30 minutes) or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity.



Table 5: Percent of Rural and Urban Survivors Reporting Adverse Health Status

Domain	Survivors				Siblings				Multiplicative difference in aORs (95% CI)
	Rural	Urban	OR, 95% CI	aOR, 95% CI	Rural	Urban	OR, 95% CI	aOR, 95% CI	
General Health									
Mental Health									
Activity Limitation									
Functional Impairment									
Cancer-Related Pain									
Cancer-Related Anxiety									
OR: Odds ratio, aOR: adjusted odds ratio, CI: confidence interval Adjusted for age, sex, race/ethnicity									

**Figure: Forest plot of adjusted OR comparing rural and urban participants in each domain, stratified by survivor / control status.**

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