Study Title: **Temporal Changes in Unemployment of Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)**

Working Group: Primary: Psychology and Cancer Control
Secondary: Chronic Disease

Investigators:

Neel S. Bhatt	neel.bhatt@stjude.org
Daniel A. Mulrooney	daniel.mulrooney@stjude.org
Melissa Hudson	melissa.hudson@stjude.org
Anne Kirchhoff	anne.kirchhoff@hci.utah.edu
Wendy Leisenring	wleisenr@fredhutch.org
Rebecca M. Howell	rhowell@mdanderson.org
Paul Nathan	paul.nathan@sickkids.ca
Kevin Krull	kevin.krull@stjude.org
Kevin Oeffinger	kevin.oeffinger@duke.edu
Leslie L. Robison	les.robison@stjude.org
Gregory T. Armstrong	greg.armstrong@stjude.org

Background:

With advancement in childhood cancer therapies, 5-year survival rates now exceed 80%[1] and estimates suggest there will be over half a million survivors of childhood cancer in the United States by 2020[2]. As the number of survivors continues to increase, so does our understanding of the life-threatening and life-altering complications these survivors face after completing therapy. Almost 90% of survivors are projected to have a chronic health condition (CHC) by the fifth decade of life[3]. These conditions and prior treatment exposures not only put survivors at higher risk of mortality, but also affect the psychological (emotional distress, depression, anxiety, post-traumatic stress, cognitive dysfunction), social-environmental (return to work, adherence to treatment), physical (pain, fatigue, sleep disturbance, sexual dysfunction), and behavioral (risk-taking behaviors, unhealthy diet, physical inactivity) aspects of their lives. Employment status is an important indicator of survivors' health recovery and overall function and can impact social and economic well-being. As of 2011, 66% of living childhood cancer survivors were within the eligible ages of work force participation[3]. As more survivors continue to enter adulthood, it is important to study their employment status, and the causes and risk factors for unemployment in this vulnerable population.

Unemployment is a Significant Problem in Adult Survivors of Childhood Cancer

Prior studies focusing on adult survivors of childhood cancer have consistently reported higher unemployment rates among survivors compared to controls[4-7]. A meta-analysis using 24 publications between 1966 and 2006 showed that survivors were nearly two times more likely to be unemployed (odds ratio [OR]: 1.85, 95% confidence interval [CI]: 1.27-2.69)[4]. In 2010, Kirchhoff and colleagues published an analysis from the CCSS that demonstrated that the relative risk (RR) of self-reported health-related unemployment was significantly higher in survivors compared to their age-matched siblings (RR: 6.07, 95% CI: 4.32-8.53)[5]. Survivors were also more likely to be unemployed and looking for work than their siblings (RR: 1.90; 95% CI: 1.43–2.54). Younger age at cancer diagnosis, female sex, CNS tumors, and exposure to cranial radiation were noted to be significant risk factors for unemployment in this study focused

on survivors treated between 1970-1986[5,6]. Similar findings were noted in a recent population-based investigation from the British Childhood Cancer Survivor Study (BCCSS) which showed that survivors were five times more likely to be unemployed due to illness/disability compared to the general population of the United Kingdom[7]. While these studies have established the problem of unemployment in survivors, there are still several remaining gaps in the literature:

What is The Impact of Temporal Changes in Treatment on Unemployment Among Survivors?
Pediatric oncology treatment has evolved over time to a risk stratified approach that assigns therapy based on cancer biology/cytogenetics and therapy responses[8]. While therapies still rely heavily on conventional chemotherapeutic agents and radiation therapy, cumulative exposures have been lowered and radiation delivery methods adapted in an effort to reduce late effects. For example, contemporary treatment protocols have largely reduced or eliminated cranial radiation for the treatment of children with acute lymphoblastic leukemia[9] but have intensified intrathecal therapy and increased use of high dose methotrexate, dexamethasone, and asparaginase[8]. Reduction in anthracycline doses and radiation exposures have also been implemented in patients with Hodgkin lymphoma, Wilms' tumor, and astrocytoma[10]. Similarly, limb salvage surgery has been more commonly used since the 1980s over amputation for the local control of osteosarcoma and Ewing sarcoma[11]. With changes in treatment modalities, late mortality has significantly declined[10]. Since expanding the CCSS cohort to include survivors treated from 1987-1999, there have been several study proposals aiming to investigate temporal changes in the spectrum of late effects across the decades of treatment[12,13]. However, none have yet assessed changes in employment status over time.

How Do Survivors' Chronic Health Conditions (CHC) Affect Longitudinal Changes in Employment Status?
In addition to treatment-related factors, CHCs may also impact employment outcomes of survivors. According to Bhakta et al., on an average a survivor experienced 17 CHCs by the age of 50, with 27% of them being severe/ disabling, life-threatening, or fatal[14]. While no prior study has directly studied the relationship between CHCs and employment outcomes, a report from the St. Jude Lifetime Cohort (SJLIFE) evaluated the association of CHC with survivors' financial hardship[15]. CHCs affecting the cardiovascular (myocardial infarction), neurologic (peripheral neuropathy, seizure, stroke), gastrointestinal (upper gastrointestinal disorders), and reproductive (reproductive disorders) systems, as well as subsequent neoplasms and amputations, were significantly associated with greater material hardship. Results of this study underscore the importance of understanding the association of CHCs with other psychosocial morbidities including unemployment. As these chronic conditions continue to develop in the aging population of childhood cancer survivors, it is also important to longitudinally assess the impact of CHCs on survivors' employment outcomes.

What are the Insurance Consequences of Unemployment Among Survivors?
As a majority of the US population receive health insurance benefits through their employment[16], unemployment can lead to lack of insurance coverage and subsequently negatively impact health care access and utilization. Employment-related difficulties (such as frequent job/position changes, lack of health insurance) can also lead to increasing medical and non-medical financial burdens in survivors, affect quality of life and well-being[17], lead to unhealthy lifestyles (abnormal dietary habits, smoking and alcohol use), and poor adherence to medical management[18].

Summary
The goal of this study is to evaluate the employment outcomes of adult survivors of childhood cancer compared to siblings and determine how these outcomes have evolved over time, both according to the era of treatment and longitudinally after completion of therapy. Through this study, for the first time we will show the employment changes in survivors at two separate time-points more than 10 years apart. This study will also evaluate the patient-, disease-, and treatment-related predictors of unemployment and the relationship between CHCs and employment outcomes longitudinally. We will also conduct analyses to look at the insurance and financial concerns among survivors according to their employment status. Ultimately, we aim to identify childhood cancer survivors to whom vocational guidance and resources could be directed earlier in their treatment or survivorship courses, to avoid long-term employment-related difficulties.

Specific Aims:

Aim 1: Cross-sectional assessment:

Aim 1a: To evaluate the employment outcomes of survivors according to the era of treatment (i.e. 1970-79, 1980-89, 1990-1999) and compare with their siblings.

Hypothesis: Survivors in all treatment eras will be more likely to be unemployed (due to illness/ disability and looking for work) than the sibling comparison group within each decade; however, differences between survivors and siblings will be smaller for survivors diagnosed in more recent decades (1980-89; 1990-99) compared to 1970-79 (Table 2). Even after adjusting for the age, sex, and, race, survivors will be at higher risk of unemployment compared to siblings (Table 3).

Aim 1b: To determine patient-, disease-, and treatment-related factors associated with unemployment due to illness/ disability, and looking for work among survivors

Hypothesis: Factors associated with higher risk of unemployment (due to illness/ disability and looking for work) will be: female sex, younger age at treatment, survivors of CNS tumors, exposure to cranial radiation in higher dose (≥25 Gy), hematopoietic cell transplant (HCT) as a treatment modality, and earlier treatment era (i.e. 1970-79, 1980-89) (Table 4, 5). The impact of treatment era will diminish when adjusted for the treatment modalities.

Aim 1c: To examine associations between unemployment (due to illness/ disability, and looking for work) and CHC among survivors

Hypothesis: Survivors who report a higher number of and/or more severe CHCs (>1 condition and/ or grades 3 or 4) will be more likely to report unemployment compared to survivors with none or fewer severe conditions (≤1 condition and/ or grades 1-2) (Table 6). Additionally, disease recurrence and subsequent neoplasms will also predict unemployment due to illness/ disability and looking for work.

Aim 2: Longitudinal assessment:

Aim 2a: To assess if survivors have higher unemployment due to illness/ disability and looking for work compared to siblings at each time point from FU2 to FU5 (original cohort only).

Hypothesis: Compared to siblings, survivors will have higher unemployment rates (due to illness/ disability and looking for work) at each of the three time-points (FU2, FU4, and FU5) (Table 9). We anticipate the differences in unemployment rates between survivors and siblings to vary by their age groups and sex.

Aim 2b: To examine changes in unemployment (persistent unemployment and from full-time to either part-time work, unemployment due to disability or illness, unemployed and looking for work, or not being part of the labor force) from FU2 to FU5 among survivors and its relationship with chronic health conditions (CHCs)

Hypothesis: Survivors with more and/or severe CHCs at the time of FU2 questionnaire will be more likely to report persistent unemployment (either due to illness/ disability or looking for work) at the time of FU5 questionnaire compared to those with no or mild conditions at FU2 (Table 11).

Hypothesis: Survivors who develop more and/or severe CHCs from FU2 to FU5 will be more likely to have a change in employment from full-time to part-time, unemployed (due to illness/ disability and looking for work), or not being part of the labor force compared to those with no or mild conditions (Table 12).

Exploratory aim: To evaluate the financial concerns among survivors of childhood cancer with regards to their current employment status (using the FU5 questionnaire) and sociodemographic factors at the time of FU5 questionnaire

Hypothesis: Compared to employed survivors, unemployed survivors will be more likely to be concerned about their ability to get health insurance and life insurance, and to cover expenses for health care and/or prescribed medicine (Table 13).

Analysis framework:

Study Population: This study will include the survivors and siblings enrolled in the entire CCSS cohort and will focus on two samples. Below we describe the two samples.

Sample 1 (Cross-sectional assessment, aim 1a-c): We will study the employment outcomes in adult survivors of childhood cancer and siblings ≥25 years of age at questionnaire assessment. Considering the unequal duration of follow-up of original and expansion cohorts, and since employment status often differs by age, we will study the employment outcomes at a unique time-point (described below) for each cohort. This method will allow us to compare survivors and siblings at the time of the questionnaire among similar age groups and have a similar length of follow-up time among survivors between the two cohorts.
We will examine employment status at the time-point of:

- Original cohort: 2003 follow-up questionnaire (FU2)
- Expansion cohort: 2014 follow-up questionnaire (FU5)

Sample 2 (Longitudinal assessment, aim 2a-b): We will study the changes in employment outcomes in adult (≥25 years) survivors of childhood cancer and siblings included in the original cohort at three time-points: 2003 (FU2), 2007 (FU4), and 2014 (FU5) questionnaires. For aim 2a, we will include all participants (survivors and siblings) in the original cohort regardless of whether they responded to all three questionnaires (FU2, FU4, FU5). For aim 2b, we will include participants who responded to both FU2 and FU5 questionnaires. Due to limited longitudinal follow-up available for the expansion cohort, we will limit the sample to original cohort only. Here we will also examine changes in employment status defined as:

- Persistent unemployment: Persistence of any type of unemployment (due to illness/ disability or looking for work) from FU2 to FU5 questionnaire
- Full-time to part-time or unemployed: Change in employment status from full-time (defined as more than or equal to 30 hours per week) at the time of FU2 to part-time (defined as less than 30 hours per week), unemployed (due to disability or illness or looking for work) or not part of the labor force at the time of FU5 questionnaire

Exploratory aim: We will include survivors from both original and expansion cohort who filled out FU5 questionnaire.

Outcomes of Interest: Employment status will be derived from response to the CCSS questionnaire question "What is your current employment status?" (FU2- Question#4, FU4- Question#A4, FU5- Question#A5).

Primary outcomes:

- Unemployed due to illness/ disability
- Unemployed and looking for work

Secondary outcomes:

- Changes in employment status (persistent unemployment, full-time to part-time, unemployed or not part of the labor force) between FU2 and FU5
- Not part of the labor force (caring for home or family, retired, students)

Exploratory aim:

- Concern regarding ability to get health insurance
- Concern regarding ability to get life insurance
- Concern regarding ability to cover health care expenses
- Concern regarding ability to cover prescribed medicine expenses

Outcomes and independent variables of interest are described by the aims in the table below.

Independent Variables:

Variable	Aim 1	Aim 2	Exploratory aim
	Questionnaire/ Question	**Questionnaire/ Question**	**Questionnaire/ Question**
Outcomes:			
Employment status (Working full-time (30 or more hours per week, Working part-time (less than 30 hours per week), Caring for home or family (not seeking paid work), Unemployed and looking for work, Unable to work due to illness or disability, Retired, Student, Other	FU2/ 4 FU5/ A5	FU2/ 4 FU4/ A4 FU5/ A5	FU5/ A5
Concern regarding ability to get health insurance (Very concerned**,** Somewhat concerned**,** Concerned**,** Not very concerned**,** Not at all concerned)			FU5/ R4
Concern regarding ability to get life insurance (Very concerned**,** Somewhat concerned**,** Concerned**,** Not very concerned**,** Not at all concerned)			FU5/ R5
Concern regarding ability to cover health care expenses (Very concerned**,** Somewhat concerned**,** Concerned**,** Not very concerned**,** Not at all concerned)			FU5/ R6
Concern regarding ability to cover prescribed medicine expenses (Very concerned**,** Somewhat concerned**,** Concerned**,** Not very concerned**,** Not at all concerned)			FU5/ R7
Predictors			
Age at questionnaire, years (25-34, 35-44, ≥ 45)	Medical records	Medical records	
Sex (Male, Female)	Medical records	Medical records	
Race/ ethnicity (Non-Hispanic white, Non-Hispanic black, Hispanic, Asian, Others)	Medical records	Medical records	
Age at diagnosis, years (0-4, 5-9, 10-14, ≥15)	Medical records	Medical records	
Time from diagnosis, years (0-4, 5-14, 15-24, 25-34, ≥35)	Medical records		
Primary cancer diagnosis (leukemia, Hodgkin lymphoma, Non-Hodgkin lymphoma, neuroblastoma, CNS tumors, bone cancer, soft tissue sarcoma, kidney tumors)	Medical records		
Era of treatment (1970-79, 1980-89, 1990-99)	Medical records	Medical records	

Therapy (Surgery, Radiation (RT) only, Chemotherapy, Chemotherapy and RT, Chemotherapy, RT, and surgery, RT and surgery, Chemotherapy and surgery)	Medical records		
Hematopoietic cell transplant (No, Yes)	Medical records		
Total body irradiation (No, Yes)	Medical records		
CNS radiation therapy (No, stray (low), stray (high), <18 Gy, 18-24 Gy, ≥25 Gy)	Medical records		
History of amputation (No, Yes)	Medical records		
History of limb salvage surgery (No, Yes)	Medical records		
History of CNS tumor resection (No, Yes)	Medical records		
Tumor recurrence (No, Yes)	Medical records		
Subsequent neoplasm (No, Yes)	Medical records		
Educational level (less than high school or GED, high school graduate, some college or higher)	FU2/ 1 FU5/ A4	FU2/ 1 FU4/ A3 FU5/ A4	FU5/ A4
Annual household income (<$20,000, $20,000-39,999, $40,000-59,999, $60,000-79,999, ≥$80,000)	FU2/ S1 FU5/ A7	FU2/ S1 FU4/ A6 FU5/ A7	FU5/ A7
Number of individuals supported by the income (1, 2, 3, ≥4)	FU2/ S2 FU5/ A8	FU2/ S2 FU4/ A7 FU5/ A8	FU5/ A8
Annual personal income (<$20,000, $20,000-39,999, $40,000-59,999, $60,000-79,999, ≥$80,000)	FU2/ S3 FU5/ A9	FU2/ S3 FU4/ A8 FU5/ A9	FU5/ A9
Insurance status (No, Yes, Canadian resident)	FU2/ M1 FU5/ A10	FU2/ M1 FU4/ B9 FU5/ A10	FU5/ A10
Marital status (Single, never married, Married/ living with a partner, Divorced/ Widowed/ Separated)	FU2/ 2 FU5/ M1	FU2/ 2 FU4/ M1 FU5/ M1	
Current living arrangement (With spouse/ partner, with parent(s)/ sibling(s)/ relative(s), with roommates, Alone)	FU2/ 3 FU5/ M2	FU2/ 3 FU4/ M2 FU5/ M2	

Chronic conditions per CTCAE (v4.03) (vision, hearing, cardiovascular, pulmonary, renal, endocrine/ metabolic, GI/ hepatic, neurologic, musculoskeletal)	FU2 FU5	FU2 FU4 FU5	

Statistical Analyses:
Due to the anticipated differences in employment status by sex, we will examine all analyses stratified by sex. Due to the small number of non-White survivors and siblings, we may not be able to stratify analyses by race/ ethnicity, although multivariable analyses will be adjusted for race/ethnicity. Survivors and siblings who report not being part of the labor force (defined by the answer choices of "Caring for home or family (not seeking paid work)", "Student", or "Retired" on FU2- Question#4, FU4- Question#A4, FU5- Question#A5) will be described but excluded from the analyses examining employment in Aim 1. This is in accordance with the Bureau of Labor Statistics that defines "not in the labor force" as persons neither employed nor unemployed – that is, retired persons, students, those taking care of children or other family members, and others who are neither working nor seeking work. Additionally, survivors and siblings who report being unemployed and looking for work will be excluded from the reference group when studying the predictors of unemployment due to illness/ disability, and vice versa.

First, we will describe characteristics of survivors (demographics and treatment) stratified by the treatment era (i.e. 1970-79, 1980-89, 1990-99) and siblings (demographics), using means (SD) and medians (range) for continuous variables and frequencies (percentages) for categorical variables (Table 1).

Sample 1 (Cross-sectional assessment): A sensitivity analysis will be performed to assess the variations in employment trends between the original and expansion cohorts prior to merging both cohorts for this analysis.

Aim 1a: To evaluate the employment outcomes of survivors according to the era of treatment (i.e. 1970-79, 1980-89, 1990-99) and compare with their siblings

Prevalence of employment status for survivors and siblings at the time of FU2 (original cohort) and FU5 (expansion cohort) questionnaires will be compared using univariable logistic regressions (or similar log binomial models) with robust sandwich variances to account for intra-family correlation (Table 2) by treatment era. Multivariable logistic regression analysis will be conducted to examine an adjusted comparison between survivors and siblings of risk of unemployment due to illness/disability, adjusting for age, sex, race, and era of treatment (Table 3). A backward selection approach will be used and the type of participant (sibling vs. survivor) predictor will be forced in the model. Factors that modify the survivor vs. sibling association meaningfully will be retained in the model. We will also assess interactions between retained factors and survivor/sibling to determine whether the relationship differs by subgroups. Robust variance estimates will be utilized to account for intra-family correlations. Additionally, we will also explore the role of education and CHCs in mediating the differences in unemployment (due to disability/ illness and looking for work) between survivors and siblings.

Unemployment rates in survivors and siblings will be compared with the US general population unemployment rates available on the Bureau of Labor Statistics website (https://www.bls.gov/data/) to determine whether the siblings are representative of the US general population. We will attempt to match these rates as closely as possible by the age, sex, race of the cohorts, and calendar year of the reported unemployment.

Aim 1b: To determine patient-, disease-, and treatment-related factors associated with unemployment due to illness/ disability, and looking for work within survivors

Multivariable logistic regression analysis will be performed to study the predictors of unemployment due to illness/ disability and unemployed and looking for work among survivors using the primary diagnosis (Table 4). Models will be created to study the impact of disease diagnoses across treatment era both unadjusted for and adjusted for specific treatment-related exposures within each primary cancer diagnosis groups per earlier CCSS analyses[10,12] (Table 5). Survivors of HCT will be identified based on their history of total body irradiation (TBI) exposure and/ or through self-report. However, we are aware of the limitation of using HCT in the CCSS dataset; while HCT survivors are more easily identifiable in the expansion cohort we will be sure to discuss this with the study team.

Aim 1c: To examine associations between unemployment (due to illness/ disability, and looking for work) and CHC within survivors

Multivariable logistic regression models will be used to study the association between CHC and unemployment due to illness/ disability and unemployed and looking for work. The model will aim to study the association between more (>1) and/or severe (≥ grade 3) conditions, disease recurrence, and subsequent neoplasms, all occurring prior to the relevant questionnaire assessing employment and unemployment (Table 6). In case of sufficient numbers, we will consider exploring the association of specific CHCs (vision, hearing, etc.) with unemployment. The model will be run with and without adjusting for the treatment era. We will also test for interaction between CHC, era of treatment, and unemployment (Table 7).

Sample 2 (Longitudinal assessment): Analyses of sample 2 will be limited to the original cohort due to the limited longitudinal follow-up available for the expansion cohort.

Aim 2a: To assess if survivors have higher unemployment due to illness/ disability and looking for work compared to siblings at each time point from FU2 to FU5

For this aim, survivors aged ≥25 years who returned either of FU2, FU4, and FU5 questionnaires will be studied. Characteristics of survivors and siblings will be provided and compared at each time-point (Table 8). Employment status at each time-point will be studied in survivors and siblings using a logistic regression framework with age, questionnaire time point and sex as categorical factors. Tests for trend across questionnaire time and age and by sex will be evaluated (Table 9). In addition, we will consider performing this analysis using the time since diagnosis instead of questionnaire time-points to assess the longitudinal changes in unemployment for survivors and siblings.

Aim 2b: To determine the factors predicting changes in employment (persistent unemployment and from full-time to either part-time work, unemployment due to disability or illness, unemployed and looking for work, or not being part of the labor force) from FU2 to FU5 within survivors

For this aim, only survivors who returned both FU2 and FU5 questionnaires and were ≥25 years of age at both time-points will be studied. Change in employment categories for male and female survivors will be described (Table 10). Generalized linear models with a logit link and binomial family will be used to study predictors of changes in employment in survivors for two groups of outcomes, clustering to account for intragroup correlation. The models will aim to study the association of employment changes with more (>1) and/or severe (≥ grade 3) conditions. If we have sufficient numbers, we will consider exploring the association of specific CHCs with unemployment.

1) persistent unemployment at both time-points due to illness/ disability or looking for work (Table 11) using the CHCs at the time of FU2 questionnaire as the predictors. Survivors who reported to be unemployed (due to disability/ illness or looking for work) at FU2 will be included to study their predictors of persistent unemployment (due to disability/ illness or looking for work) at FU5.

2) change from full-time to either part-time work, unemployment (due to disability/ illness or looking for work), or not being part of the labor force from FU2 to FU5 using the interval development of any CHC and CHCs at the time of FU5 questionnaire as the predictors. Survivors who reported to be working full-time at FU2 will be included to study their predictors of change in employment to following categories at FU5: a) remained in full-time work, b) changed to part-time work, c) changed to unemployed due to disability/ illness, d) changed to unemployed and looking for work, and d) changed to not being part of the labor force (Table 12). A multinomial regression model will be used to study these changes and OR (95% CI) will be provided using the persistent full-time work as the reference group. Depending on the numbers, predicted probabilities of change in the employment categories may be provided instead of odds ratios.

Models will be stratified by sex to take the underlying employment differences into account.

Exploratory aim: To evaluate the financial concerns among survivors of childhood cancer with regards to their employment status and sociodemographic factors at the time of FU5 questionnaire. The analysis is limited to FU5 questionnaire since these questions were not asked in previous questionnaires.

A logistic regression model will be created to study the predictors of survivors' concerns regarding their ability to get health insurance, life insurance, cover health care expenses, and prescribed medicine expenses using survivors' employment status and sociodemographic factors. For convenience, the financial concern questions will be converted from 5-point likert scale to binary choices such as No (not concerned at all) and Yes (very concerned, concerned, somewhat concerned, not very concerned) (Table 13).

Table 1: Characteristics of the study population by the era of treatment and siblings overall

Variable	All survivors	Era of treatment			Siblings
		1970-79	1980-89	1990-99	
	N=	N=	N=	N=	N=
Age at questionnaire (years)*, n (%)					
Median (range)					
25-34					
35-44					
≥ 45					
Sex, n (%)					
Female					
Male					
Race/ ethnicity, n (%)					
Non-Hispanic white					
Non-Hispanic black					
Hispanic					
Asian					
Other/ unknown					
Age at diagnosis (years), n (%)					N/A
Median (range)					
0-4					
5-9					
10-14					
≥15					
Time from diagnosis (years)					N/A
Median (range)					
Diagnosis, n (%)					N/A
Leukemia					
Hodgkin lymphoma					
Non-Hodgkin lymphoma					
CNS tumor					
Kidney tumors					
Neuroblastoma					
Soft tissue sarcoma					
Bone cancer					
Therapy, n (%)					N/A
Surgery					
Radiation (RT) only					
Chemotherapy					
Chemotherapy and RT					
Chemotherapy, RT, and surgery					
RT and surgery					
Chemotherapy and surgery					
Hematopoietic cell transplant, n (%)					N/A
Total body irradiation, n (%)					N/A
CNS radiation therapy, n (%)					N/A
No					

Stray (low) Stray (high) <18 Gy 18-24 Gy ≥25 Gy					
History of amputation, n (%)					N/A
History of limb salvage surgery, n (%)					N/A
History of CNS tumor resection, n (%)					N/A
Tumor recurrence, n (%)					N/A
Subsequent neoplasm, n (%)					N/A
Education, n (%) Less than high school or GED High school graduate Some college or higher					
Annual household income, n (%) <$20,000 $20,000-39,999 $40,000-59,999 $60,000-79,999 >$80,000					
Personal annual income, n (%) <$20,000 $20,000-39,999 $40,000-59,999 $60,000-79,999 >$80,000					
Number of people supported on household income, n (%) 1 2 3 ≥4					
Marital status, n (%) Single, never married Married/ living with a partner Divorced/ Widowed/ Separated					
Current living arrangement, n (%) With spouse/ partner With parent(s)/ sibling(s)/ relative(s) With roommates Alone					
Insurance status, n (%) Yes					

No Canadian resident					

*Questionnaires: FU2 for the original cohort, FU5 for the expansion cohort

Table 2: Employment outcomes of survivors and siblings according to survivors' era of treatment

Variable	Survivors			Sibling			*P*-value[3]		
	1970-79 N=	1980-89 N=	1990-99 N=	1970-79 N=	1980-89 N=	1990-99 N=	*P1*	*P2*	*P3*
Unemployed due to illness/ disability, n (%)									
Unemployed and looking for work, n (%)									
Employed full-time, n (%)[1]									
Employed part-time, n (%)[2]									
Not being part of the labor force, n (%)[4]									

[1]Full-time: defined as working 30 or more hours per week
[2]Part-time: defined as working less than 30 hours per week
[3]p-values compares the survivors and siblings by each treatment era
[4]Survivors and siblings who report not being part of the labor force (defined by the answer choices of "Caring for home or family (not seeking paid work)", "Student", or "Retired" on FU2- Question#4, FU4- Question#A4, FU5- Question#A5)

Table 3: Comparison of unemployment due to illness/ disability and looking for work using demographics and era of treatment between survivors and siblings

Variables	Unemployed due to illness/ disability		Unemployed and looking for work	
	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value
Participant				
Sibling				
Survivor				
Era of treatment				
1970-79				
1980-89				
1990-99				
Age at questionnaire*				
25-34				
35-44				
≥ 45				
Sex				
Female				
Male				
Race/ ethnicity				
Non-Hispanic white				
Non-Hispanic black				
Hispanic				
Asian				
Other/ unknown				

*Questionnaires: FU2 (2003) for the original cohort, FU5 (2014) for the expansion cohort

Table 4: Odds ratio and 95% CI of demographic and primary cancer diagnosis predictors of unemployment in survivors

Variables	Unemployed due to illness/ disability		Unemployed and looking for work	
	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value
Era of treatment				
1970-79				
1980-89				
1990-99				
Age at questionnaire*				
25-34				
35-44				
≥ 45				
Sex				
Female				
Male				
Race/ ethnicity				
Non-Hispanic white				
Non-Hispanic black				
Hispanic				
Asian				
Other/ unknown				
Diagnosis				
Acute lymphoblastic leukemia				
Acute myeloid leukemia				
Astrocytoma				
Hodgkin lymphoma				
Non-Hodgkin lymphoma				
Other CNS tumors				
Wilms tumor				
Neuroblastoma				
Soft tissue sarcoma				
Ewing sarcoma				
Osteosarcoma				
Year since diagnosis				
10-19 years				

20-29 years ≥30 years				

*Questionnaires: FU2 for the original cohort, FU5 for the expansion cohort

Table 5: Odds ratios and 95% CI for association between unemployment and treatment era and the impact of specific treatment exposures after adjusting for age at diagnosis and sex

Diagnosis		Unemployed due to illness/ disability		Unemployed and looking for work	
		Model without treatment variables	Model with treatment variables	Model without treatment variables	Model with treatment variables
		Odds Ratio (95% CI)		Odds Ratio (95% CI)	
Acute lymphoblastic leukemia					
Treatment era	Per 10 years				
Cranial radiation	Dosing groups				
Anthracyclines	Dosing groups				
HCT	No/ Yes				
Total body irradiation	No/ Yes				
.					
.					
Etc.					
Acute myeloid leukemia					
Treatment era	Per 10 years				
Anthracyclines	Dosing groups				
HCT	No/ Yes				
.					
.					
Etc.					
Hodgkin lymphoma					
Treatment era	Per 10 years				
Specific treatment					
.					
.					
Non-Hodgkin lymphoma					
Treatment era	Per 10 years				
Specific treatment					
.					
.					
CNS tumor					
Treatment era	Per 10 years				

Tumor resection . .	No/Yes				
Wilms tumor **Treatment era** .	Per 10 years				
Ewing sarcoma **Treatment era** **Amputation** **Limb salvage therapy** . .	Per 10 years No/Yes No/Yes				
Osteosarcoma **Treatment era** **Amputation** **Limb salvage therapy** . .	Per 10 years No/Yes No/Yes				
Soft tissue sarcoma **Treatment era** .	Per 10 years				

Table 6: Assessing the predictors of unemployment due to illness/ disability and unemployed and looking for work by the chronic conditions among survivors

Variable	Unemployment due to illness/ disability		Unemployment looking for work	
	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value
Sex				
Female				
Male				
Age at questionnaire*				
25-34				
35-44				
≥ 45				
Race/ ethnicity				
Non-Hispanic white				
Non-Hispanic black				
Hispanic				
Asian				
Other/ unknown				
Era of treatment				
1970-79				
1980-89				
1990-99				
Any CHC				
< Grade 3				
≥ Grade 3				
Any grade CHC				
≤1 condition				
>1 condition				
Number of severe CHC (grade 3-4)				
≤1 condition				
>1 condition				
Subsequent neoplasm				
No				
Yes				

Tumor recurrence No Yes				
Onset of CHC				
Year since diagnosis 10-19 years 20-29 years ≥30 years				

*Questionnaires: FU2 for the original cohort, FU5 for the expansion cohort

Table 7: Odds ratios and 95% CI of unemployment by chronic health conditions and treatment era after adjusting for age at diagnosis, sex, and race

Diagnosis	Treatment era	Unemployed due to illness/ disability	Unemployed and looking for work
		Odds Ratio (95% CI)	Odds Ratio (95% CI)
Any, grade 1-4	1970-79 1980-89 1990-99		
Any, grade 3-4	1970-79 1980-89 1990-99		
Vision	1970-79 1980-89 1990-99		
Hearing	1970-79 1980-89 1990-99		
Cardiac	1970-79 1980-89 1990-99		
Pulmonary	1970-79 1980-89 1990-99		
Renal	1970-79 1980-89 1990-99		
Endocrine/ Metabolic	1970-79 1980-89 1990-99		
GI/ Hepatic	1970-79 1980-89 1990-99		
Neurologic	1970-79 1980-89 1990-99		
Musculoskeletal	1970-79 1980-89		

	1990-99		
>1 condition	1970-79 1980-89 1990-99		

Table 8: Characteristics of survivors and siblings at each time-point

Variable	Survivors				Siblings			
	FU2	FU4	FU5	*P*-value	FU2	FU4	FU5	*P*-value
Age at questionnaire (years), n (%)								
Median (range)								
25-34								
35-44								
≥ 45								
Sex, n (%)								
Female								
Male								
Race/ ethnicity, n (%)								
Non-Hispanic white								
Non-Hispanic black								
Hispanic								
Asian								
Other/ unknown								
Education, n (%)								
Less than high school or GED								
High school graduate								
Some college or higher								
Annual household income, n (%)								
<$20,000								
$20,000-39,999								
$40,000-59,999								
$60,000-79,999								
>$80,000								
Personal annual income, n (%)								
<$20,000								
$20,000-39,999								
$40,000-59,999								
$60,000-79,999								
>$80,000								

Number of people supported on income, n (%) 1 2 3 ≥4								
Marital status, n (%) Single, never married Married/ living with a partner Divorced/ Widowed/ Separated								
Current living arrangement, n (%) With spouse/ partner With parent(s)/ sibling(s)/ relative(s) With roommates Alone								
Insurance status, n (%) Yes No Canadian resident								
Working full-time, n (%)								
Working part-time n (%)								
Unemployed due to illness/ disability n (%)								
Unemployed and looking for work n (%)								
Not part of labor force (student, caring for home or family, retired) n (%)								
Chronic health conditions								
Vision								
Hearing								
Cardiovascular								
Pulmonary								

Renal								
Endocrine/ Metabolic								
GI/ Hepatic								
Neurologic								
Musculoskeletal								
Any grade 1-4 condition								
Any grade 3-4 condition								
>1 condition vs ≤1 condition								

Table 9: Employment outcomes across questionnaire time-points in survivors and siblings

Age			Working full-time			Working part-time			Unemployed due to illness/ disability			Unemployed and looking for work			Not part of labor force (student, caring for home or family, retired		
			FU2	FU4	FU5	FU2	FU4	FU5	FU2	FU4	FU5	FU2	FU4	FU5	FU2	FU4	FU5
M	25-34 to 35-49	Survivor															
		Sibling															
		OR (95% CI)															
	35-44 to 45-59	Survivor															
		Sibling															
		OR (95% CI)															
	≥ 45	Survivor															
		Sibling															
		OR (95% CI)															
F	25-34 to 35-49	Survivor															
		Sibling															
		OR (95% CI)															
	35-44 to 45-59	Survivor															
		Sibling															
		OR (95% CI)															
	≥ 45	Survivor															
		Sibling															
		OR (95% CI)															

*P-value to be calculated for each employment category

Table 10: Longitudinal changes in employment status of survivors and siblings who returned both FU2 and FU5 questionnaires

Employment at FU2		Employment at FU5				
		Working full-time, n (%)	Working part-time n (%)	Unemployed due to illness/ disability n (%)	Unemployed and looking for work n (%)	Not part of labor force (student, caring for home or family, retired) n (%)
Working full-time, n (%)	Survivor					
	Sibling					
Working part-time n (%)	Survivor					
	Sibling					
Unemployed due to illness/ disability n (%)	Survivor					
	Sibling					
Unemployed and looking for work n (%)	Survivor					
	Sibling					
Not part of labor force (student, caring for home or family, retired) n (%)	Survivor					
	Sibling					

*Analysis to be stratified by sex

Table 11: Predictors of persistent unemployment due to illness/ disability or looking for work from FU2 to FU5 among survivors according to their sex

Variable	Male		Female	
	% Reporting persistent unemployment due to illness/ disability or looking of work from FU2 to FU5		% Reporting persistent unemployment due to illness/ disability or looking for work from FU2 to FU5	
	Relative risk (95% CI)	*P*-value	Relative risk (95% CI)	*P*-value
Current age				
25-34				
35-44				
≥ 45				
Race/ ethnicity				
Non-Hispanic, white				
Non-Hispanic, black				
Hispanic				
Asian				
Other				
Age at diagnosis				
0-4				
5-9				
10-14				
≥15				
CHC at the time of FU2 questionnaire				
Any CHC				
< Grade 3				
≥ Grade 3				
Any grade CHC				
≤1 condition				
>1 condition				
Number of severe CHC (grade 3-4)				
≤1 condition				
>1 condition				

Table 12: Change in employment status from full-time from FU2 to FU5 for survivors by interval development of chronic health condition between FU2 and FU5*

Variable	% Remaining in full-time work		% Transition from full-time to part-time employment		% Transition from full-time to unemployed due to illness/ disability		% Transition from full-time to unemployed and looking for work		% Transition from full-time to not part of the labor force	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Current age										
25-34										
35-44										
≥ 45										
Race/ ethnicity										
Non-Hispanic, white										
Non-Hispanic, black										
Hispanic										
Asian										
Other										
Age at diagnosis										
0-4										
5-9										
10-14										
≥15										
Change in chronic health condition from FU2 to FU5										
No change										
Onset of 1 new chronic disease										
Onset of >1 new chronic disease										
CHC at the time of FU5 questionnaire										
Any CHC										

< Grade 3 ≥ Grade 3										
Any grade CHC ≤1 condition >1 condition										
Number of severe CHC (grade 3-4) ≤1 condition >1 condition										

*****Analysis to be stratified by sex

Table 13: Predictors of the ability to cover expenses among survivors according to their employment status and sociodemographic factors

Variable	Concern regarding ability to get health insurance		Concern regarding ability to get life insurance		Concern regarding ability to cover health care expenses		Concern regarding ability to cover prescribed medicine expenses	
	OR	***P***	**OR**	***P***	**OR**	***P***	**OR**	***P***
Employment status Employed (full-time or part-time) Unemployed (due to illness/ disability or looking for work)								
Education, n (%) Less than high school or GED High school graduate Some college or higher								
Annual household income, n (%) <$20,000 $20,000-39,999 $40,000-59,999 $60,000-79,999 >$80,000								
Personal annual income, n (%) <$20,000 $20,000-39,999 $40,000-59,999 $60,000-79,999 >$80,000								
Number of people supported on income, n (%) 1 2 3 ≥4								

[1]Concerned (very concerned, somewhat concerned, concerned, not very concerned) vs. Not at all concerned
[2]No vs. Yes