Cancer Epidemiology, Biomarkers & Prevention

Research Article

Decline in Physical Activity Level in the Childhood Cancer Survivor Study Cohort

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Abstract

Background: We aimed to identify demographic and health-related predictors of declining physical activity levels over a four-year period among participants in the Childhood Cancer Survivor Study.

Methods: Analyses included 7,287 $\geq$5-year childhood cancer survivors and 2,107 siblings who completed multiple follow-up questionnaires. Participants were classified as active if they met the Centers for Disease Control and Prevention guidelines for physical activity. Generalized linear models were used to compare participants whose physical activity levels declined from active to inactive over the study to those who remained active. In addition, selected chronic conditions (CTCAE v4.03 Grade 3 and 4) were evaluated as risk factors in an analysis limited to survivors only.

Results: The median age at last follow-up among survivors and siblings was 36 (range, 21–58) and 38 (range, 21–62) years, respectively. The rate of decline did not accelerate over time among survivors when compared with siblings. Factors that predicted declining activity included body mass index $\geq$30 kg/m^2 [RR = 1.32; 95% confidence interval (CI), 1.19–1.46, $P < 0.01$], not completing high school (RR = 1.31; 95% CI, 1.08–1.60, $P < 0.01$), and female sex (RR = 1.33; 95% CI, 1.22–1.44, $P < 0.01$). Declining physical activity levels were associated with the presence of chronic musculoskeletal conditions ($P = 0.034$), but not with the presence of cardiac ($P = 0.10$), respiratory ($P = 0.92$), or neurologic conditions ($P = 0.21$).

Conclusions: Interventions designed to maximize physical activity should target female, obese, and less educated survivors. Survivors with chronic musculoskeletal conditions should be monitored, counseled, and/or referred for physical therapy.

Impact: Clinicians should be aware of low activity levels among subpopulations of childhood cancer survivors, which may heighten their risk for chronic illness. *Cancer Epidemiol Biomarkers Prev; 23(8); 1619–27. ©2014 AACR.*

Introduction

Approximately 80% of individuals diagnosed with cancer during childhood are expected to survive for at least 5 years after diagnosis (1). Improved survival rates have been largely brought about by improvements in multimodal therapy and supportive care. However, increases in survival have not come without cost. Many survivors of childhood cancer are at risk of long-term adverse health conditions (2). It is estimated that by 45 years of age, approximately 80% of survivors of childhood cancer will develop at least one serious, disabling, or life-threatening chronic condition as a result of the therapy received in childhood (3). Late effects include, but are not limited to, endocrine dysfunction, osteoporosis, obesity, and cardiovascular disease (3–5).

In the general population, physical activity is an important contributor to maintaining a healthy weight, and is associated with decreased risk of developing many chronic conditions such as obesity, cardiovascular disease (6, 7), hypertension (8), noninsulin-dependent diabetes mellitus (9), osteoporosis (10), and some cancers (11). As physical activity is an important contributor to weight control and disease prevention in healthy populations, physical activity may be of particular significance to survivors of childhood cancer who are at increased risk of developing treatment-related chronic health conditions. Previous

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studies indicate that many survivors do not engage in regular exercise (12–14); some studies report that less than 50% of cancer survivors meet recommended guidelines for physical activity (15–17). Factors associated with inactivity include female sex (13, 18), Hispanic ethnicity (19), and prior therapy with cranial radiation (15). In addition, psychologic and somatic symptoms, including anxiety, fatigue, low stamina, and cancer-related pain, are also associated with reduced likelihood to participate in exercise (20). Although there is some evidence to suggest that childhood cancer survivors are less likely than peers to engage in recommended levels of activity as they age (13, 21), reports are contradictory (12, 22), and little longitudinal data exist examining how physical activity levels change over time among childhood cancer survivors (23).

The aim of this study was to identify demographic-, treatment-, and health-related predictors of decline in physical activity levels among participants in the Childhood Cancer Survivor Study (CCSS) cohort. Specifically, we hypothesized that greater decline in physical activity levels would be observed among survivors of childhood cancer when compared with their siblings. By evaluating potential associations between demographic- and health-related characteristics and declines in activity, we aimed to identify survivors who may most benefit from intervention and educational programs promoting regular physical activity.

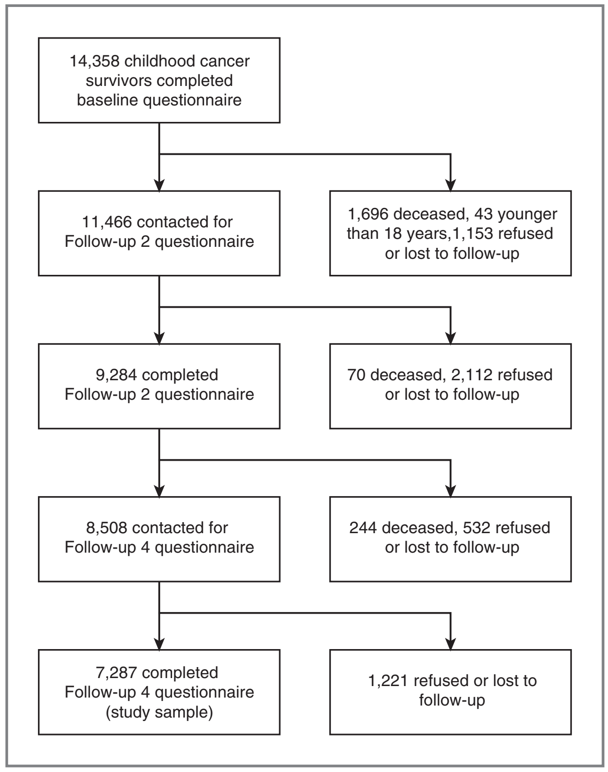

Figure 1. Consort diagram of study participation.

Materials and Methods

The CCSS is a multisite, retrospective cohort designed to study the late effects of childhood cancer therapy. Childhood cancer survivors were recruited from 26 participating institutions located in the United States and Canada. To be eligible, individuals had to be diagnosed and treated for childhood cancer between 1970 and 1986 and had to have survived $\geq$5 years from their initial diagnosis. Details about the CCSS study protocol and cohort characteristics have been previously published (24–26). All CCSS protocol and contact documents were reviewed and approved by the human subjects committees at participating institutions. Informed consent was obtained from all study participants.

There were 20,690 survivors potentially eligible for participation in the CCSS; 17,632 were successfully contacted and 14,358 completed the baseline questionnaire. CCSS participants who were of the age 18 years or older in 2003 and who completed the Follow-up 2 (initiated in 2003) and Follow-up 4 (initiated in 2007) questionnaires were included in the current study (N = 7,287: Fig. 1). Survivors of childhood cancer who completed baseline, but completed only one or none of the follow-up questionnaires, were considered nonparticipants for the current analysis. Survivors who died before Follow-up 4 were not eligible for this longitudinal analysis. A comparison group of 2,107 siblings who completed both follow-up questionnaires were also included in analyses.

Data on the primary outcome of interest were collected from survivors and siblings by asking questions, adapted from the Behavioral Risk Factor Surveillance Survey, about their levels of physical activity (27). Participants were classified as active if they met the Centers for Disease Control and Prevention (CDC) guidelines for physical activity (150 minutes of moderate intensity physical activity or 75 minutes of vigorous activity per week; ref. 28). We first evaluated predictors of inactivity at the end of the study period, where cases were defined as those who did not meet CDC guidelines at the Follow-up 4 questionnaire regardless of activity status at Follow-up 2 and noncases were defined as those active at the Follow-up 4 questionnaire regardless of activity status at Follow-up 2. We also evaluated predictors of declining physical activity, where participants whose activity level fell from meeting the CDC guidelines (active) to not meeting the CDC guidelines (inactive) over the study interval were defined as cases, and compared with participants who remained active across the study interval. Accordingly, only participants who were active at Follow-up 2 (study entry), and therefore, at risk of declining activity levels, were included in the second analysis.

Independent variables were selected on the basis of findings from cross-sectional studies that reported characteristics of childhood cancer survivors with reduced levels of physical activity or exercise (13, 15, 19). Factors with the potential for change over time utilized information up to or at the time of the Follow-up 2 questionnaire (study entry) for analyses. Candidate factors included sex, race/ethnicity, employment status, annual household income, and highest level of educational attainment, as well as smoking history, body mass index (BMI), and the presence of depression or pain. Smoking history was categorized as current, former, or never smoker. BMI was calculated as weight (kg) divided by height (m) squared with participants classified as either underweight (<18.5 kg/m^2), normal (20–24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese ($\geq$30 kg/m^2). Participants with T-scores of 63 or higher on the depression scale of the Brief Symptom Inventory-18 were defined as depressed (29, 30). Pain was classified as none, mild, moderate, or severe, based on pain reported by participants in the 4 weeks before completing the Follow-up 2 questionnaire. We also expanded our analyses to include the presence of chronic diseases, which were not considered in previous analyses of physical activity or exercise among CCSS participants (15). The National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03 (CTCAE) scoring rubric was used to grade the severity of chronic conditions affecting cardiovascular, respiratory, musculoskeletal, and neurological systems, with age of onset before Follow-up 2 survey (31). Participants reporting grade 3 (severe) or grade 4 (disabling or life threatening) conditions were compared with survivors reporting none, grade 1 (mild), or grade 2 (moderate) conditions.

Information related to original cancer diagnoses and treatment was abstracted from medical records. Radiotherapy exposure was grouped into four categories; cranial (no chest), chest, other, and none. Exposure to selected chemotherapeutic agents was categorized as binary variables and included: anthracycline cumulative dose (no anthracyclines or $\leq$150 mg/m^2 vs. >150 mg/m^2) and platinum agent cumulative dose (no platinum agent or $\leq$400 mg/m^2 vs. >400 mg/m^2). Surgical history involving an amputation of a lower limb (transtibial, transfemoral, or hemipelvectomy) was also considered in analyses.

Descriptive statistics were calculated for demographic characteristics, treatment information, and selected characteristics and compared between survivor participants and nonparticipants using χ^2 statistics. The demographic distributions from the Follow-up 2 questionnaire were compared between survivor and sibling participants using P values from a robust Wald test adjusted for intra-family correlation. Descriptive statistics indicated that the prevalence of low physical activity was relatively common among CCSS survivor participants (>10%). Therefore, RR and corresponding 95% confidence intervals (CI) for declining physical activity for each independent variable were calculated in multivariable generalized linear models with a log link function, a Poisson distribution, and robust error variances (32). The first models evaluated whether either rates of inactivity at Follow-up 4 or rates of declining physical activity across the study period differed between survivors and siblings, after adjusting for factors listed above (other than treatment information and chronic disease status). Interactions between survivor status and each covariate were evaluated. Separate analyses were performed using the full cohort (7,287 survivors and 2,107 siblings) for the inactivity status outcome at Follow-up 4, and using a subcohort (4,034 survivors and 1,261 siblings) for the declining activity outcome at from Follow-up 2 to Follow-up 4. The remaining models, restricted to survivors only, evaluated the influence of treatment modality or chronic disease on rates of declining physical activity with age. Because chronic disease is often treatment related, the impact of treatment and chronic disease on declining physical activity were assessed in separate models. Sex, race/ethnicity, and age at Follow-up 2 (study entry) were included as covariates of interest in all models. Interactions of each treatment/condition with sex, race/ethnicity, and age at Follow-up 2 were assessed. For the comparison between survivors and siblings, with 80% power, 5% type I error, and assuming sample sizes and prevalence rates in referent groups corresponding to our data, minimum detectable RRs were 1.09 and 1.15 for the inactive at Follow-up 4 and declining activity outcomes, respectively. Among survivors, RRs of 1.14 to 1.16 (inactive at Follow-up 4) and 1.28 to 1.30 (declining activity) were detectable for the comparison groups defined by cardiac, neurologic, and musculoskeletal conditions. For respiratory condition group comparisons, the detectable RRs were somewhat higher, at 1.35 (inactive at Follow-up 4) and 1.69 (declining activity). All calculations were performed using the statistical package SAS (v9.3).

Results

There were 7,287 survivors of childhood cancer and 2,107 siblings who completed both follow-up questionnaires. The median age at last follow-up among survivors and siblings was 36.1 (range, 21–58) and 38.0 (range, 21–62) years, respectively. The median time between questionnaire completion was 4.6 years (interquartile range = 0.7 years) for survivors and 4.2 years (interquartile range = 0.5 years) for siblings. Compared with siblings, a higher proportion of survivors were never smokers (70.7% vs. 60.1%), unable to work (6.4% vs. 1.1%), or resided in a household with income <$20,000 per annum (10.3% vs. 5.9%; Table 1). When compared with nonparticipant survivors, participants were more likely to be female (51.0% vs. 41.7%; P < 0.001), older age at diagnosis (ages $\geq$15 years; 17.8% vs. 13.1%), and of White, non-Hispanic descent (90.4% vs. 80.6%; Supplementary Table S1).

Approximately 47.5% of survivors and 41.5% of siblings did not meet CDC guidelines for physical activity at the end of the study interval. Among these, 19.0% of survivors and 17.6% of siblings reported declining activity levels from Follow-up 2 to Follow-up 4.

In multivariate analyses, survivors were 1.14 times more likely to report inactivity at the end of the study interval when compared with siblings (95% CI, 1.08–1.21; Table 2). Factors significantly associated with inactivity at the end of follow-up included female sex, older age at follow-up (>40 years vs. 18–29 years of age), Black

Table 1. Demographic characteristics of the cancer survivor population and their siblings

	Survivors (N = 7,287), (%)	Siblings (N = 2,107), (%)	P^b
Gender			
Male	3,568 (49.0)	960 (45.6)	0.006
Female	3,719 (51.0)	1,147 (54.4)	
Race/ethnicity			
Black	205 (2.8)	45 (2.1)	<0.001
Hispanic	287 (3.9)	51 (2.4)	
White	6,586 (90.4)	1,887 (89.6)	
Other/unknown	209 (2.8)	124 (5.9)	
Educational attainment[a]			
< High school	286 (3.9)	37 (1.8)	<0.001
High school graduate	3,609 (49.5)	962 (45.7)	
College graduate	3,316 (45.5)	1,104 (52.4)	
Unknown	76 (1.0)	4 (0.2)	
Employment[a]			
Working/caring for home	5,973 (82.0)	1,935 (91.8)	<0.001
Student	388 (5.3)	87 (4.1)	
Unemployed	305 (4.2)	43 (2.0)	
Unable to work	465 (6.4)	24 (1.1)	
Unknown	156 (2.1)	18 (0.9)	
Annual household income[a]			
<$20,000	754 (10.3)	124 (5.9)	<0.001
≥$20,000	5,582 (76.6)	1,798 (85.3)	
Unknown	951 (13.1)	185 (8.8)	
BMI[a]			
Underweight	282 (3.9)	50 (2.4)	0.002
Normal weight	3,210 (44.1)	930 (44.1)	
Overweight	2,135 (29.3)	643 (30.5)	
Obese	1,397 (19.1)	421 (20.0)	
Unknown	263 (3.6)	63 (3.0)	
Smoking status[a]			
Current	1,011 (13.9)	366 (17.4)	<0.001
Former	975 (13.4)	420 (19.9)	
Never	5,154 (70.7)	1,267 (60.1)	
Unknown	147 (2.0)	54 (2.6)	
Antidepressant medication use[a]			
Yes	945 (13.0)	241 (11.4)	0.052
No	6,342 (87.0)	1,866 (88.6)	
Anxiolytics/sedative/hypnotic medication use[a]			
Yes	253 (3.5)	40 (1.9)	<0.001
No	7,034 (96.5)	2,067 (98.1)	
Active at Follow-up 2			
Yes	4,034 (55.4)	1,261 (59.8)	0.001
No	3,064 (42.0)	812 (38.5)	
Unknown	189 (2.6)	34 (1.6)	
Active at Follow-up 4			
Yes	3,654 (50.1)	1,201 (57.0)	<0.001
No	3,463 (47.5)	875 (41.5)	
Unknown	170 (2.3)	31 (1.5)	

[a]Characteristics of survivors and siblings at Follow-up 2.
[b]P value calculated using robust Wald statistic among nonmissing values.

Table 2. Relative risk of not meeting national recommendations for physical activity in survivors compared with siblings

	Inactive at Follow-up 4 (survivors $N = 7{,}287$; siblings $N = 2{,}107$)			Declining activity levels across study interval[a] (survivors $N = 4{,}034$; siblings $N = 1{,}261$)		
	RR[b]	95% CI	*P*	RR[b]	95% CI	*P*
Siblings	1.0			1.0		
Survivors	1.14	1.08–1.21	<0.001	1.18	1.07–1.30	<0.001
Age at Follow-up 2, y						
18–29	1.0					
30–39	1.13	1.08–1.19	<0.001	1.16	1.06–1.27	<0.001
≥40	1.09	1.03–1.17	0.007	1.05	0.94–1.18	0.370
Gender						
Male	1.0					
Female	1.24	1.18–1.30	<0.001	1.33	1.22–1.44	<0.001
Race/ethnicity						
Black	1.24	1.11–1.39	<0.001	1.22	0.95–1.55	0.11
Hispanic	0.94	0.82–1.07	0.35	0.90	0.72–1.13	0.36
White	1.0					
Other	1.09	0.95–1.26	0.21	1.10	0.85–1.42	0.47
Educational attainment						
<High school	1.28	1.15–1.43	<0.001	1.31	1.08–1.60	0.007
High school graduate	1.10	1.05–1.16	<0.001	1.13	1.04–1.23	0.004
College graduate	1.0					
BMI						
Underweight	1.14	1.02–1.28	0.021	1.09	0.88–1.36	0.42
Normal weight	1.0					
Overweight	1.10	1.04–1.17	<0.001	1.18	1.08–1.30	<0.001
Obese	1.24	1.17–1.31	<0.001	1.32	1.19–1.46	<0.001
Smoking status						
Current	0.98	0.91–1.04	0.48	1.12	1.01–1.25	0.032
Former	0.94	0.88–1.00	0.06	1.02	0.91–1.14	0.71
Never	1.0			1.0		
Antidepressant medication use						
Yes	1.0			1.0		
No	1.11	1.04–1.18	0.001	1.04	0.93–1.17	0.48
Anxiolytic/sedative/hypnotics medication use						
Yes	1.0			1.0		
No	1.11	1.00–1.24	0.056	1.12	0.92–1.37	0.27

[a]This analysis excluded 3,253 cancer survivors and 846 siblings whose activity levels were low at Follow-up 2.
[b]Risk ratios from multivariate analyses are reported.

race, and lower educational attainment (<high school education vs. college graduate), as well as being underweight, overweight, or obese. With the exception of Black race and being underweight, similar factors were associated with an increased risk of declining physical activity levels in survivors when compared with siblings (Table 2).

Figure 2A depicts the proportion of survivors and siblings whose physical activity levels declined, by age at study entry, after removing those who were inactive at Follow-up 2. Although the proportion of individuals who did not meet the CDC guidelines for physical activity was greater among survivors than siblings in the 18 to 29 years age group, the overall percent decline in physical activity levels was comparable between survivors and siblings among the older age groups. As seen in Fig. 2B, declining levels of physical activity were highest among survivors of central nervous system (CNS) and kidney tumors.

In models limited to survivors only, the risk of being inactive at the end of the study period was higher among survivors who reported the presence of severe/disabling or life threatening neurologic (RR = 1.26; 95% CI, 1.16–1.36, $P < 0.001$), cardiac (RR = 1.10; 95% CI, 1.00–1.20, $P = 0.047$), or musculoskeletal conditions (RR = 1.22; 95% CI, 1.12–1.34, $P < 0.001$) than for those survivors who did not

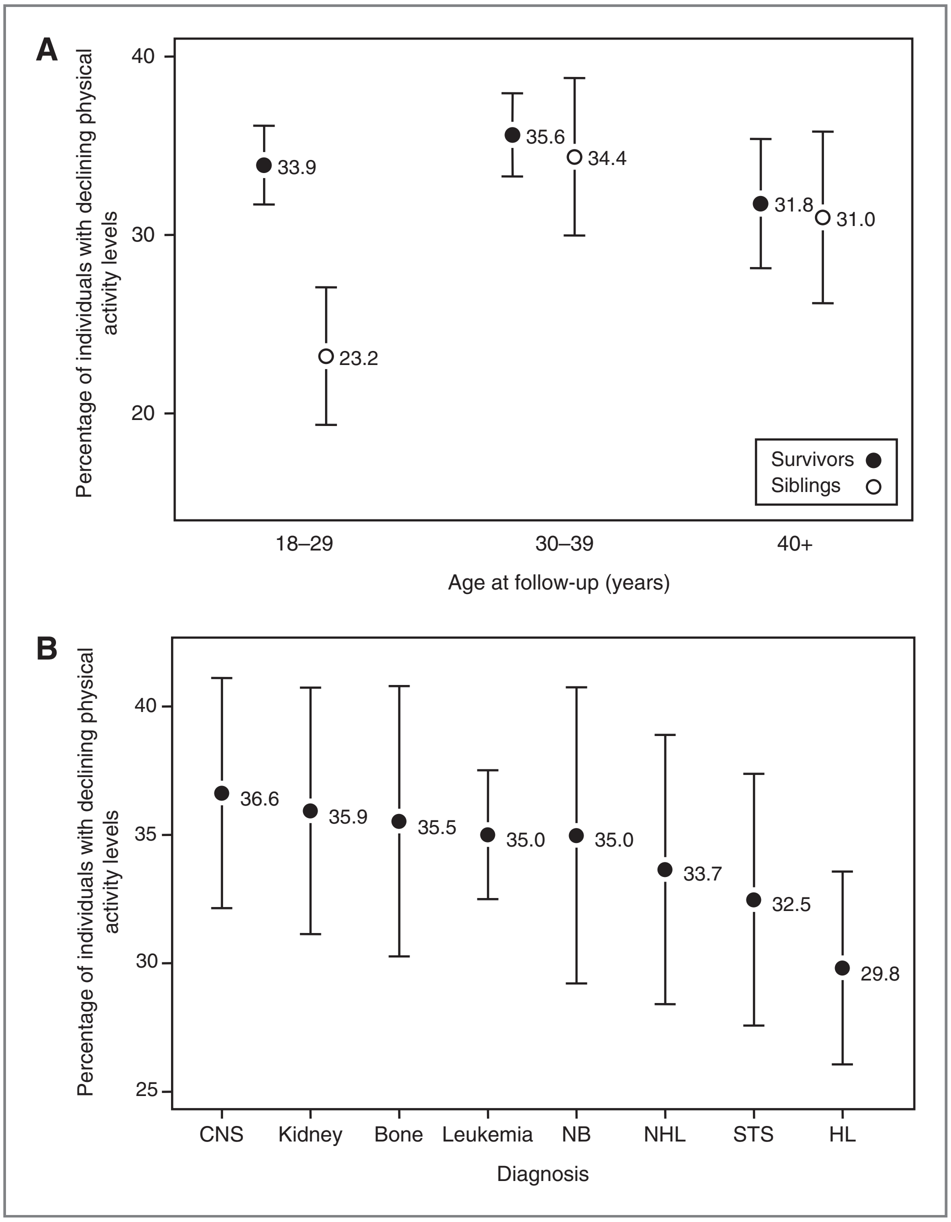

Figure 2. A, the proportion of survivors and sibling controls (with 95% CI) who reported declines in physical activity by age at study entry (Follow-up 2). This figure includes 4,034 cancer survivors and 1,261 siblings who met the CDC guidelines for physical activity at Follow-up 2 and excludes those survivors and siblings who were inactive at Follow-up 2. B, the proportion of survivors (with 95% CI) reporting declines in physical activity by diagnosis. Only those survivors who met the CDC guidelines for physical activity at Follow-up 2 were included in this analysis. Accordingly, there were 445 survivors of CNS tumors, 384 kidney tumor survivors, 318 bone tumor survivors, 1,391 leukemia survivors, 263 neuroblastoma (NB) survivors, 312 non-Hodgkin lymphoma (NHL) survivors, 351 soft tissue sarcoma (STS) survivors, and 570 Hodgkin lymphoma survivors included in this analysis.

report these conditions (Table 3). Survivors with severe/disabling or life-threatening musculoskeletal conditions also had a higher risk of declining activity levels (RR = 1.21; 95% CI, 1.01–1.45, $P = 0.034$). However, the risk of declining activity over the study interval was not associated with the presence of a severe/disabling or life-threatening respiratory, cardiac, or neurologic chronic condition (Table 3). The most common severe/disabling or life-threatening cardiac conditions reported by participants included cerebrovascular accident (28%), congestive heart failure (23%), and myocardial infarction requiring surgical intervention (15%). Amputation (73%) and joint replacement (27%) were the most frequently reported musculoskeletal conditions, while the most frequently reported neurologic condition was paralysis (53%).

After adjusting for sex, race/ethnicity, age at diagnosis, and age at Follow-up 2, cancer survivors who had undergone a lower limb amputation (RR = 1.27; 95% CI, 1.13–1.43, $P < 0.001$), or who were treated with >400 mg/m^2 platinum-based chemotherapy (RR = 1.19; 95% CI, 1.02–1.38, $P = 0.026$) had an increased risk of being inactive at Follow-up 4 when compared with survivors who had not received these treatments. Previous exposure to cranial radiation was also observed to increase the risk of inactivity among survivors (RR = 1.22; 95% CI, 1.14–1.31, $P < 0.001$). Exposure to anthracyclines in excess of 150 mg/m^2 was not associated with an increased risk of inactivity ($P = 0.77$). Although exposure to cranial radiation was also associated with an increased risk of declining activity levels (RR = 1.24; 95% CI, 1.10–1.39, $P < 0.001$), lower

Table 3. Relative risk describing associations between chronic health conditions and not meeting national recommendations for physical activity in survivors

	Inactive at Follow-up 4 ($N = 7,287$)			Declining activity levels across study interval[a] ($N = 4,034$)		
Treatment	**RR[b]**	**95% CI**	***P***	**RR[b]**	**95% CI**	***P***
Cardiac condition						
None/mild/moderate	1.0					
Severe/disabling	1.10	1.00–1.20	0.047	1.16	0.97–1.40	0.10
Neurologic condition						
None/mild/moderate	1.0					
Severe/disabling	1.26	1.16–1.36	<0.001	1.11	0.94–1.32	0.21
Musculoskeletal condition						
None/mild/moderate	1.0					
Severe/disabling	1.22	1.12–1.34	<0.001	1.21	1.01–1.45	0.034
Respiratory condition						
None/mild/moderate	1.0					
Severe/disabling	1.01	0.82–1.25	0.93	1.02	0.67–1.56	0.92

NOTE: Risk ratios were adjusted for sex, race, age at diagnosis, age at Follow-up 2 (study entry), and use of antidepressant, anxiolytic, sedative, or hypnotic medications.
[a]This analysis excluded 3,253 cancer survivors whose activity levels were low at Follow-up 2.

limb amputation and prior therapy with platinum-based agents were not associated with declining activity levels ($P > 0.05$).

Discussion

Although previous studies carried out among CCSS participants have identified factors associated with low physical activity in cross-sectional analyses (13, 15, 18, 19), this study is among the first to evaluate factors that predict declining levels of physical activity among survivors of childhood cancer as they age. In this study, approximately 19% of survivors and 18% of siblings reported declining activity levels over a 4-year period, such that by the end of the study interval, 48% of survivors and 42% of siblings did not meet CDC guidelines for physical activity. However, when analyses were limited to consider those participants at risk of declines in physical activity at the beginning of the study period, we observed that the trajectory of decline in activity levels among childhood cancer survivors was not greater than that among siblings. Characteristics associated with declining activity levels among both survivors and siblings included female sex, being obese, and a lower level of education. In models limited to survivors only, the presence of severe or disabling chronic conditions was associated with low activity levels at the end of the study period. However, only the presence of severe or disabling musculoskeletal conditions was associated with declining physical activity over time.

Previous studies have demonstrated that survivors of childhood cancer are at an increased risk of chronic illness, and that in many instances, these chronic illnesses emerge decades earlier than expected (3–5). As the presence of chronic illness may limit the capacity of childhood cancer survivors to participate in physical activity, it is reasonable to hypothesize that activity levels may decline more rapidly in survivors as they age. Although we observed an increased risk of inactivity with increasing age in both survivors and their siblings in the current study, the rate of decline was not higher among survivors when compared with siblings. Furthermore, in analyses restricted to survivors, the risk of activity levels declining over time was not significantly elevated among those survivors with severe/disabling or life-threatening respiratory, neurologic and cardiac illnesses, perhaps driven by the fact that survivors with these severe/disabling conditions were already inactive at the first evaluation time point. This suggests that for many survivors with chronic illnesses, the inability to participate in organized sports and recreational activities at the levels recommended by the CDC occurs early in survivorship. This is important because studies among noncancer populations have shown that physical activity and exercise can be beneficial for chronically ill individuals. Multiple studies in patients with chronic heart failure, or who have experienced a cerebrovascular accident or myocardial infarction, have shown that specialized physical training programs can improve various indices of cardiovascular health (33–35), reduce fatigue (33), and improve physical function and quality-of-life (36, 37). Survivors with musculoskeletal late effects can benefit from working with specialists who have experience with prosthetics and movement retraining to facilitate physical function and improve body image (38). Thus, physical training programs may have important health benefits for survivors who develop chronic illnesses following cancer therapy. Tailoring physical activity and exercise interventions to accommodate health-specific limitations common among certain subgroups of childhood cancer survivors will be an essential element in the successful implementation of future programs.

In the current study, we found that female sex, having a lower level of education, and being obese, predicted declining levels of physical activity. Our findings are consistent with previous reports that have examined potential risk factors associated with inactivity using cross-sectional study designs (12, 13, 15, 18, 19, 39). Although we observed an association between the use of antidepressant and antianxiety medications with low levels of physical activity at the end of the study (Follow-up 4), we did not observe an association between medication use and declining levels of physical activity. Our lack of an association between medication use and declining activity may be, in part, due to the alleviation of depressive symptoms over time, due to effective pharmacotherapy, psychotherapy, and lifestyle strategies, including physical activity, which have been shown to improve mood (40, 41). We also observed that the reported frequency of survivors and siblings not meeting the CDC guidelines for physical activity in the Follow-up 2 questionnaire, 42.1% and 38.5%, respectively, was lower than that previously reported for the CCSS cohort in a study by Ness and colleagues (2009) for survivors (52.0%) and their siblings (46.7%; ref. 15). However, these differences were largely due to a change in the CDC guidelines for vigorous physical activity between the previous and current analyses, that is, three 20-minute sessions versus 75 minutes of aerobic activity every week (28, 42).

A strength of this study was the longitudinal design, which allowed for the temporal order between exposure and outcome to be observed. This is particularly pertinent for a risk factor such as obesity, where studies in noncancer survivor populations exist that demonstrate either an increased risk of obesity among those who are less physically active (43, 44), or that obese individuals are less likely to be physically active because they are obese (45, 46). This study had several limitations. First, the use of self-report questionnaires to collect information on physical activity among childhood cancer survivors and their siblings may have affected the accuracy of estimates. Second, the potential contribution of psychosocial factors on declining levels of physical activity among childhood cancer survivors, such as self-motivation, self-efficacy, social support, and perception of disability, was not measured. Third, we compared characteristics between participants and nonparticipants and found that participants were less likely to be male, non-Hispanic Caucasian, and younger age at diagnosis, which may negatively affect the generalizability of study findings to individuals with these characteristics.

As the number of individuals successfully treated for childhood cancer continues to grow, recognition of the need to promote positive lifestyle and health behaviors that may help prevent, or delay, the onset of late chronic illness among survivors is becoming increasingly important. Identification of the specific factors associated with both low levels of physical activity and declining physical activity with age is one such step toward this goal. Although the trajectory of age-related decline in physical activity among childhood cancer survivors does not differ from siblings, childhood cancer survivors are consistently less active. Ultimately, the success of future interventions to promote physical activity among all cancer survivors will be dependent on the ability of researchers and health practitioners to tailor programs to address the specific barriers that may exist for certain subpopulations of cancer survivors.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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