# Physical Activity in Childhood Cancer Survivors

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## Dedication

This work is dedicated to the two cancer survivors closest to my heart: my father, Larry, and my mother, Scarlett. Thank you for your unwavering and unconditional love and support over the years.

**Abstract**

Background: Childhood cancer survivors (CCS) are at high risk of developing treatment-related late effects, including cardiovascular disease and diabetes, which can be exacerbated by inadequate physical activity (PA). Relationships between PA, physical fitness, and cardiometabolic risk factors in CCS have not been well described. Furthermore, active transportation, a specific domain of PA, has not been previously studied in CCS. The primary aims of this dissertation were to examine associations between PA/fitness and cardiometabolic risk factors and to identify active transportation behaviors and barriers in CCS.

Methods: In Project 1, associations between PA and cardiometabolic risk factors were examined in 319 CCS and 208 sibling controls aged 9-18 years. In Project 2, associations between PA/fitness and cardiometabolic risk factors were examined in 119 adult CCS with a history of hematopoietic cell transplantation and 66 adult sibling controls. In Project 3, we recruited 158 adult CCS and 153 controls matched on age, sex, and location to complete a survey regarding active transportation behaviors and perceptions. Linear and logistic regression models accounting for correlation among siblings or matched participants were used to address research questions.

Results: Higher levels of PA in CCS aged 9-18 (Project 1) and higher levels of endurance in adult CCS (Project 2) were associated with a favorable cardiometabolic profile. In Project 3, adult CCS engaged in similar levels of active transportation as controls despite perceiving greater health-related barriers. Marital/relationship status, planning/psychosocial barriers, and perceived neighborhood walkability were the strongest correlates of active transportation among CCS, while objective neighborhood walkability was the strongest correlate among controls.

Conclusions: Findings suggest that efforts to increase PA and endurance in CCS may reduce the risk of future cardiovascular disease. Interventions might consider promoting active transportation as a moderate intensity PA option, since it appears to be as well accepted in CCS as in healthy adults. Such interventions will not be successful, however, without existing or improved pedestrian and bicycle infrastructure, safety, and access to local amenities. Additional research is needed to confirm results and explore the feasibility and efficacy of active transportation interventions in this population.

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## A. INTRODUCTION & SPECIFIC AIMS

Over the past several decades, significant advances in the treatment of childhood cancer have dramatically improved rates of survival. Currently, over 80% of pediatric cancer patients survive for five years or longer. As the number of long-term childhood cancer survivors (CCS) has continued to increase to more than 375,000 individuals in the United States, attention has naturally shifted towards the prevention of adverse late effects (i.e., side effects of cancer treatment that become apparent after treatment has ended). Survivors are at an increased risk for numerous chronic health conditions often related to their cancer treatment, including premature cardiovascular disease and type 2 diabetes (i.e., high cardiometabolic risk).

One strategy to potentially prevent and/or mitigate late effects is through increasing physical activity (PA). Evidence among the general population supports various benefits of PA, including improvements in insulin sensitivity and blood lipids and the reduction of fasting insulin, serum triglycerides, body fat, and blood pressure.

CCS are often found to be less physically active than controls. However, very little is known about how activity levels actually impact cardiometabolic risk factors in CCS. Recently, a home-based exercise program was able to increase physical fitness and reduce fasting insulin, insulin resistance, waist circumference, and percent body fat in a small group of young adult CCS, while an observational study of 117 adult CCS observed lower percent body fat among those with greater energy expenditure. These limited, yet promising findings highlight the need for additional work in this area. Another weakness of past research is the general lack of studies that consider mode of

PA. Active transportation (i.e., walking or biking to work, school, stores, etc.) is one mode that has not yet been examined in CCS. Among the general population, active transportation has been associated with reduced all-cause mortality, and previous intervention studies have suggested that encouraging active transportation may be an effective strategy for increasing total activity. The following three projects and related aims are included in this dissertation to address the aforementioned research needs:

1. *Physical Activity and Cardiometabolic Risk Factors in Childhood Cancer Survivors During Childhood*
    a. Aim 1: Examine associations between self-reported PA and objectively measured cardiometabolic risk factors among CCS and sibling controls during childhood.
    b. Aim 2: Assess whether the associations between PA and cardiometabolic risk factors differ between CCS and controls.
2. *Physical Activity and Cardiometabolic Risk Factors in Adult Survivors of Childhood Cancer with a History of Hematopoietic Cell Transplantation*
    a. Aim 1: Examine associations between both self-reported PA and objective measures of physical fitness and cardiometabolic risk factors among adult survivors of childhood cancer who underwent hematopoietic cell transplantation (HCT) and sibling controls.
    b. Aim 2: Assess whether the associations between PA/fitness and cardiometabolic risk factors differ between CCS and controls.

3. *Active Transportation in Adult Survivors of Childhood Cancer: Results from the Transportation-Related Activities of Childhood Cancer Survivors (TRACCS) Study*

    a. Aim 1: Identify active transportation behaviors, perceived barriers, and correlates among adult CCS and compare them to those of matched neighborhood controls.

    b. Aim 2: Examine associations between perceived and objective neighborhood walkability among adult CCS and compare them to those of matched neighborhood controls.

These projects will add new knowledge to the limited evidence base regarding the role of PA in reducing the risk of adverse late effects experienced by CCS. Also, by including the first known investigation of active transportation in CCS, this work may also serve to inform future PA interventions and help identify innovative strategies to increase PA via active transportation. This line of research could lead to significant improvements in the overall health and longevity of CCS in the future and might be translated to other similar populations.

## B. BACKGROUND

B.1. Childhood Cancer Survivorship

Approximately 13,500 children and adolescents (0-19 years of age) are diagnosed with cancer each year in the United States.[1] Due to marked improvements in treatment over the past 40 years, 5-year relative survival is currently 83%.[2] Before the 1970s, survival rates were less than 50%. The number of childhood cancer survivors (CCS) now exceeds 375,000 individuals in the United States and continues to rise.[2] As of 2010, one in every 250 individuals between the ages of 16 and 44 was projected to be a survivor of childhood cancer.[3] Survivors of acute lymphoblastic leukemia (ALL), the most common malignancy of childhood, comprise the largest diagnostic group and account for 16% of all CCS.[2]

B.2. Treatment-Related Adverse Late Effects

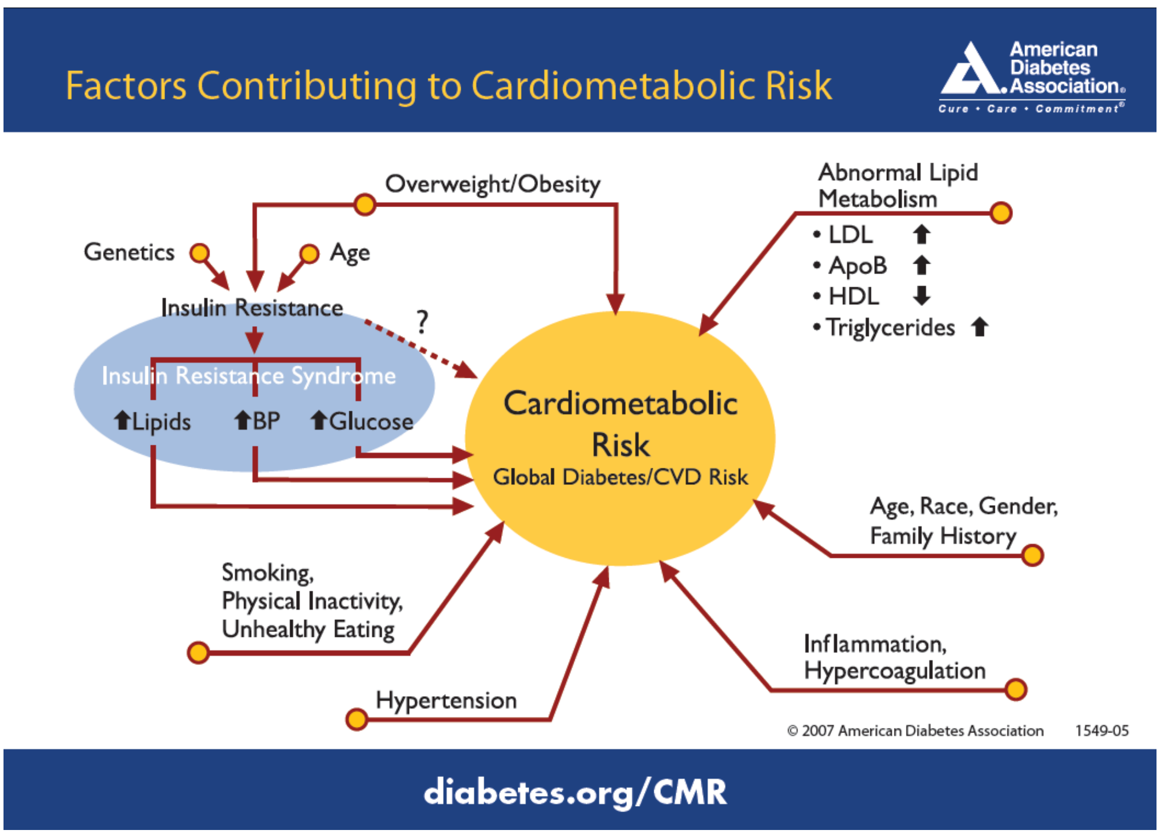
Despite advances in cancer treatment and survival, CCS face significantly increased risks of numerous adverse late effects, including premature mortality, due to treatment toxicities. For example, anthracyclines, a class of chemotherapy drugs used to treat up to 60% of childhood cancer patients and nearly all pediatric ALL cases, are notorious cardiotoxic agents.[4] Oxygen free radicals produced by anthracyclines damage cardiac myocytes, leading to myocardial necrosis and fibrosis and progressive cardiomyopathy. Depending on the cumulative dose of anthrycyclines received, up to 36% of cases go on to develop congestive heart failure. Late effects of radiation therapy often depend on the area of the body exposed and can include secondary malignancies, vascular damage, organ dysfunction, and impaired growth.[5] Cranial radiation, in particular, has been linked to neurocognitive and psychosocial problems, hearing loss, endocrine and metabolic disorders, reproductive problems, and secondary tumors.[6] Although intrathecal and systemic chemotherapy has largely replaced prophylactic cranial radiation as a component of the standard treatment protocol for leukemia in recent years, patients with persisting or recurrent central nervous system (CNS) disease still receive cranial radiation, as do children who have high-grade CNS tumors or who undergo total body irradiation prior to bone marrow transplantation. Surgeries, high-dose glucocorticoids, and other chemotherapy drugs also come with their own extensive lists of sequelae.

Approximately 75% of survivors who were treated before 2000 will develop at least one chronic disease by age 40, and more than 40% will develop a serious health problem.[7-9] These estimates may be low considering the subclinical nature of many outcomes. A recent cohort study of 1700 adult CCS who underwent systematic exposure-based medical assessments estimated that at age 45 the cumulative prevalence of any chronic health condition was 95.5%.[10] In addition to those previously mentioned, some of these chronic conditions include cardiovascular and pulmonary disease, type 2 diabetes, obesity, osteoporosis, and avascular necrosis. Survivors experience such conditions at nearly twice the frequency as their sibling controls and are five times as likely to consider their condition to be severe and/or life-threatening.[9] Notably, adult CCS experience higher than expected risks of obesity,[11-15] type 2 diabetes,[16,17] and cardiovascular disease,[9,18-21] and are seven times more likely to die from cardiovascular disease than similar aged individuals from the general population.[22]

*B.2.1. Cardiometabolic Risk*

Risk factors for cardiovascular disease and type 2 diabetes tend to cluster and thus fall under the construct of cardiometabolic risk. These aptly named cardiometabolic risk factors are depicted below in Figure 1.

**Figure 1.** Cardiometabolic Risk Factors




Most of these risk factors are considered modifiable, with the exception of genetics, age, race, gender, and family history. In addition to the higher risk of obesity already discussed, CCS have greater risks of insulin resistance, dyslipidemia, and hypertension according to some prior evidence.[4]

The process of atherosclerosis, the predominant underlying cause of cardiovascular disease, starts in childhood,[23,24] and the presence of cardiometabolic risk factors during both childhood and adulthood can accelerate this process and negatively impact vascular function.[25,26] Two of the earliest stages of atherosclerosis, vascular stiffness and endothelial dysfunction, can be detected non-invasively in asymptomatic children and adults[26] and have been associated with cardiometabolic risk factors such as insulin resistance, hypertension, dyslipidemia, and central obesity.[27-30] Vascular damage has been detected among both adolescent and adult CCS and is thought to be a subclinical sign of cardiovascular morbidity in CCS.[31,32]

### B.3. Prevention of Adverse Late Effects

In recent years, more attention has been placed on the prevention of adverse late effects among CCS via lifestyle factors such as diet, physical activity (PA), and smoking cessation. Physical *in*activity is thought to exacerbate several late effects such as early mortality,[33] obesity,[34] cardiovascular disease,[35] osteoporosis,[36] cognitive decline,[37] and physical performance limitations.[38] Adult CCS from the Childhood Cancer Survivor Study who reported engaging in no leisure-time PA in the previous month were more likely to be obese and to take medications for hypertension and diabetes or impaired glucose tolerance.[16] Similarly, in a small investigation of adult survivors of pediatric sarcoma, decreased self-reported activity levels were associated with an increased number of prevalent cardiometabolic risk factors (e.g., central obesity, dyslipidemia, hyperglycemia, and hypertension).[39]

Among the general population, the benefits of regular PA on overall health and chronic disease prevention have been well documented. For example, PA has been shown to reduce the risk of all-cause mortality, obesity, cardiovascular disease, stroke, hypertension, type 2 diabetes, osteoporosis, and cognitive impairment.[40] Increased levels of PA are also associated with clinically significant improvements in the following cardiometabolic risk factors: visceral adiposity, insulin resistance, high-density lipoprotein cholesterol (HDL-C), triglycerides, apolipoprotein-B, blood pressure, and inflammatory and thrombotic status.[41] Notably, these improvements tend to be greater in magnitude among individuals who have poorer baseline values. The same trend is seen with measures of vascular function, which are improved by PA in individuals with pre-existing cardiovascular risk factors and disease[26,42] but less consistently so in healthy individuals.[43] Although data on CCS are lacking in these areas, it is hypothesized that adequate amounts of regular PA could potentially prevent or mitigate many of the aforementioned adverse effects that these individuals face.[44]

### B.4. Physical Inactivity among CCS

Not surprisingly, PA levels of childhood cancer patients undergoing treatment are lower than those of healthy children;[45] however, there is evidence to suggest this inactivity persists well beyond the treatment period. A study examining PA across the pre-diagnosis, treatment, and post-treatment periods found that adolescents decreased their activity levels after diagnosis and many did not return to their pre-diagnostic activity levels after completing treatment.[46] According to a review by Stolley et al., most studies observe low levels of PA in CCS, especially among survivors who are now adults.[3] Survivors are less likely to be physically active compared to non-cancer controls; fewer than half engage in regular PA or meet guidelines for regular PA. In one study of childhood ALL, survivors reported levels of inactivity (defined as no leisure-time-PA in the past month) that were more than 74% higher than those of the general population.[47] Although the comparison group (participants in the 2003 Behavioral Risk Factor Surveillance System (BRFSS) survey) was limited to adults aged 18-45 years for this study, survivors were still younger on average, and were more likely to be nonsmokers, male, obese, White, non-Hispanic, and have a higher level of education and income. Thus, models were stratified by sex and adjusted for age, smoking status, body mass index (BMI), race/ethnicity, education, and income.

*B.4.1. Physical Activity Interventions*

There have been a limited number of PA interventions conducted that specifically target CCS post-treatment. Many have consisted of weekly or twice weekly aerobic training sessions with or without additional strength and flexibility training, and a 2010 review noted moderate success overall.[3] Three of the five studies reviewed observed modest increases in PA post-intervention; however, one of these studies reported lack of maintenance at a 3-month follow-up visit. Like many similar interventions, there have been problems with recruitment, attendance, retention, and maintenance. More recently, Jarvela et al., recruited 17 of 77 eligible long-term ALL survivors for a 16-week home-based exercise program.[48,49] Despite a nonsignificant increasing trend in PA, several measures of fitness and cardiometabolic risk improved significantly over the course of the program. Another recent intervention involving a 4-day integrated adventure-based training and health education program in 9 to 16-year-old Hong Kong Chinese CCS resulted in higher levels of PA, self-efficacy, and quality of life.[50]

*B.4.2. Barriers to Physical Activity*

Predictors/correlates of PA in CCS include certain demographic, disease, and treatment factors, along with self-reported health problems and fears, beliefs about their cognitive capabilities, and social influences such as family and peer support for PA.[51-54] Perceived barriers to PA in CCS have been described twice in the literature. Among both adolescent CCS and healthy adolescents, the most common perceived barriers included lack of energy, lack of self-discipline, and lack of time.[55] Among young adult CCS, being too tired or too busy, not belonging to a gym, or preferring to do other activities such as reading or watching television were the most frequently reported barriers.[56] These types of barriers are also typically reported by healthy young adults. Barriers that differed from those experienced by healthy young adults included physical limitations such as being wheelchair-bound or bedridden and suffering from pain or the side effects of illness. Importantly, some CCS display diminished exercise capacity (i.e., cardiorespiratory fitness), which may be an effect of cardiotoxic treatments, a result of a sedentary lifestyle, a barrier to PA, or likely all three.[57]

B.5. Active Transportation

Currently, the literature on PA among CCS is limited by the lack of studies that consider mode of activity (i.e., biking, swimming, walking, etc.).[3] Furthermore, studies have generally failed to distinguish between four common domains of PA: leisure-time/sport/recreation, occupation, household, and transportation. Active transportation can be defined as any "self-propelled" mode of transportation and includes walking, running, bicycling, in-line skating, skateboarding, etc. What distinguishes these activities from leisure-time activities is they are performed not solely for recreation but for the purpose of traveling to work, school, neighborhood amenities, or other local destinations. Active transportation is also commonly known as active travel, active transit, or when referring to trips made to/from work or school, active commuting.

*B.5.1. Active Transportation among Cancer Survivors*

To date, no studies have evaluated the use of active transportation by CCS, and only two known studies have investigated active transportation among survivors of adult cancer. Baseline data from a cohort study of 2321 early stage breast cancer survivors revealed a significant decrease in the median level of active transportation with age.[58] Bock et al.[59] assessed PA, including active transportation, before diagnosis, during therapy, and one year after surgery among 1067 postmenopausal breast cancer survivors in Germany. Unfortunately, walking for pleasure and walking for transportation were combined into one category while biking for transportation remained a separate category. The proportion of women who biked for transportation declined from 56.5% before diagnosis to 19.3% during therapy and then rebounded to 50% one year after surgery.

Translating these results to CCS in the United States is very difficult because biking for transportation is much more common in Germany (14.1% of Germans versus 1.8% of Americans)[60] and because PA levels in breast cancer survivors have been found to be equal to or greater than those of healthy women.[61]

*B.5.2. Health Benefits of Active Transportation*

Among the general population, a number of studies have detected relationships between active transportation and favorable health outcomes. In some cross-sectional studies of adults, all-cause mortality, obesity, diabetes, hypertension, low cardiorespiratory fitness, and incidence of myocardial infarction have been inversely associated with active transportation.[62-64] Among children and adolescents, active commuting to school has been correlated with a healthier body composition and higher levels of cardiorespiratory fitness.[65] In randomized/non-randomized controlled trials and cohort studies, reductions in risk of all-cause mortality, hypertension, and type 2 diabetes have been observed among groups who actively travel longer distances.[66] A 2013 systematic review found that the strength of evidence for associations with active transportation to work or school varied from weak (mental health and cancer), moderate (body weight), to strong (cardiovascular health).[67] CCS and other similar populations who may be less able to engage in more vigorous types of activity due to medical conditions, physical limitations, etc., could possibly incorporate the more moderate intensity option of active transportation into their daily lives, which may subsequently improve their health and quality of life.

B.6. Conclusion

Based primarily on research conducted in the general population or in other disease states, it is hypothesized that PA could help prevent and/or mitigate many of the adverse late effects-- including cardiometabolic risk-- experienced by a growing population of CCS. However, relationships between PA and cardiometabolic risk factors have not been well described among CCS. There is also no information regarding the use of active transportation as a potential source of moderate PA in this population. Through the completion of three projects, this dissertation seeks to fill these gaps in knowledge. In the first project, associations between PA and cardiometabolic risk factors among CCS and sibling controls during childhood will be examined. In the second project, associations between both PA and physical fitness and cardiometabolic risk factors among adult survivors of childhood cancer who underwent hematopoietic cell transplantation (HCT) and sibling controls will be assessed. In the third project, active transportation behaviors, perceptions, and correlates will be identified among adult survivors of childhood cancer and their matched controls.

## C. PROJECT 1: PHYSICAL ACTIVITY AND CARDIOMETABOLIC RISK FACTORS IN SURVIVORS OF CHILDHOOD CANCER DURING CHILDHOOD

### C.1. Background

As has been discussed, a growing number of CCS are at high risk of developing treatment-related adverse late effects, including cardiovascular disease and type 2 diabetes. Late effects can be exasperated by the low levels of physical activity (PA) commonly observed among CCS. Although some effects may not manifest themselves until later in adulthood,[68] the extent of early subclinical atherosclerosis and vascular dysfunction that is present in childhood has been associated with many of the cardiometabolic risk factors in Figure 1.[69-72] Likewise, obesity and its associated risk factors frequently track from childhood to adulthood.[73-76] Early implementation of potential prevention and intervention strategies may therefore be important to consider among CCS. The relationships between PA and cardiometabolic risk factors among children who survived childhood cancer have not been well established. To address this gap in knowledge, we examined the cross-sectional association of self-reported PA with directly measured cardiometabolic risk factors among CCS and sibling control children. Cardiometabolic risk factors have been reported for this study population in prior publications;[77,78] this analysis extends that work.

## C.2. Methods

### C.2.1. Study Design

The study was approved by the Institutional Review Board Human Subjects Committees at the University of Minnesota Medical Center and Children's Hospitals and Clinics of Minnesota. All parents and pediatric participants provided written informed consent and assent, respectively. CCS were selected from Pediatric Oncology databases and were eligible to participate if they were treated for cancer at the University of Minnesota/Fairview-University Medical Center or the Children's Hospitals and Clinics of Minneapolis and St. Paul, were 9-18 years old, were in remission, and had survived ≥5 years after diagnosis. Hematopoietic cell transplant recipients were excluded from the study because an identical companion study was being performed simultaneously in a population of hematopoietic cell transplant survivors. Sibling controls were eligible to participate if they were 9-18 years of age at the time of examination and had never had cancer.

Of the 723 eligible CCS identified, 66 could not be located. The remaining 657 were contacted, and consent for participation was obtained from 322 (49%). Three CCS were determined ineligible after consent, leaving a final study population of 319 CCS. There were no significant differences in age, sex, race, diagnosis, age at diagnosis, or length of follow-up (time from diagnosis to study evaluation) between the 319 CCS participants and the 338 CCS non-participants. Based on similarities in therapeutic exposures, CCS were grouped into three major diagnostic groups: leukemia (n=110), central nervous system tumors (n=82), and solid tumors (n=127).

Siblings were informed of the study by parents, and if they agreed to participate they were evaluated at the same time as the CCS. From the 322 families enrolled (including the 3 later determined to be ineligible), 164 had no eligible or consenting siblings, 124 had one sibling who participated, and 33 had more than one sibling participate (n=72). (The number of potentially eligible siblings from each family was not collected, nor was demographic information about non-participants). Twelve additional siblings from the companion study of hematopoietic cell transplant survivors who met the same sibling eligibility criteria were also included in the final control group (n=208).

C.2.2. Data Collection

All participants underwent a two-day examination at the University of Minnesota Clinical Research Center/Clinical and Translational Science Institute (CTSI). Height, weight, waist circumference, Tanner stage, and blood pressure were assessed according to standard protocols, as previously described.[78] Fat mass and lean body mass were measured using dual-energy X-ray absorptiometry (DXA, Lunar Prodigy scanner, software version 9.3; General Electric Medical Systems, Madison, WI). Measurements of abdominal visceral and subcutaneous adipose tissue were also obtained by computed tomography using a Siemens Sensation 16 (Siemens Medical Solutions, Malvern, PA, USA) with two separate 10 mm slices obtained at the L4-L5 interspace. The two images were subdivided into five mm slices and the 1$^{st}$ and 3$^{rd}$ five mm slices were combined and analyzed for visceral adipose tissue. The upper limit of adipose tissue density was -30 Hounsfield units (HU) and the lower limit was -190 HU. Image slices were individually analyzed by a trained technician using Fat Scan version 3.0 software (N2 System, Osaka, Japan).

After a 10- to 12-hour overnight fast, the hyperinsulinemic euglycemic clamp method was used to assess insulin sensitivity, as described previously.[78,79] Insulin infusion was started at time 0 at a rate of 1 mU/kg/min for 3 hours. An infusion of 20% glucose was given and adjusted to maintain euglycemia (serum glucose level of 100 mg/dL [5.6 mmol/L]) with plasma glucose determined every 10 minutes. Insulin sensitivity (M) was determined by the amount of glucose required to maintain euglycemia in the final 40 minutes of the clamp study and expressed as mg/kg/min of glucose with adjustment for lean body mass ($M_{lbm}$). Lower $M_{lbm}$ values are indicative of lower insulin sensitivity (i.e., greater insulin resistance).

Fasting blood samples obtained at the start of the insulin clamp were analyzed for serum lipid levels (low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides), serum insulin, and plasma glucose using a Vitros 5600 (Ortho-Clinical Diagnostics, Inc., Rochester, NY), a chemoluminescence immunoassay (Immulite Insulin DPC, Los Angeles, CA), and a Beckman Glucose Analyzer II (Beckman Instruments, Fullerton, CA), respectively. LDL-C was calculated by the Friedewald equation. Homeostasis model assessment insulin resistance (HOMA-IR) was calculated with fasting insulin and glucose values using the equation HOMA-IR = [(fasting glucose units of mmol/L * insulin units in $\mu$U/mL)/22.5].[80]

Following 15 minutes of quiet rest in the supine position, vascular images were obtained of the left common carotid artery using a conventional ultrasound scanner

(Acuson, Sequoia 512, Siemens Medical Solutions USA, Inc., Mountain View, CA, USA) with a 15-8 MHz linear array probe. Systolic and diastolic blood pressures were recorded with an automated blood pressure sphygmomanometer during the 10-sec carotid measurements. To measure carotid elasticity properties, electronic wall-tracking software was used for analysis of carotid cross-sectional compliance (cCSC) and distensibility (cCSD) (Vascular Research Tools 5, Medical Imaging Application, LLC, Iowa City, IA, USA).

To assess PA, participants completed the Modifiable Activity Questionnaire for Adolescents (MAQ-A), which was self-administered with parental supervision, as needed. See Appendix 1 for a copy of the MAQ-A. For this study, we focused on past year leisure-time PA. Participants reported activities in which they had participated at least ten times during the past year in their leisure time, along with the number of months over the year, the average number of days per week, and the average minutes per day that each activity was performed. The MAQ-A has been shown to provide valid and reproducible estimates of past year leisure-time PA.[81,82]

C.2.3. Statistical Analysis

All analyses were conducted with SAS version 9.2 (SAS Institute, Inc., Cary, NC). Participants who met the U.S. federal recommendation of ≥60 minutes per day of moderate-to-vigorous PA in children[83,84] were categorized as high PA while those reporting less than 60 minutes per day were categorized as low PA. Descriptive statistics are expressed as frequencies and percents or mean ± standard error (SE), as appropriate.

All analyses including data from sibling controls were implemented in SAS's GENMOD procedure using generalized estimating equations (GEE) to account for intra-family correlation, with the exchangeable working correlation and robust variance estimates. All adjusted comparisons used multivariable linear regression models with adjustments for age, sex, race/ethnicity, and Tanner stage. As indicated, models were further adjusted for percent fat mass, height, and/or diagnosis when appropriate. Adjusted means were evaluated at the mean levels of covariates included in the models. A two-sided *P*-value <0.05 was considered to be statistically significant, although because of the large number of statistical tests carried out, those between 0.01 and 0.05 should be viewed with caution.

## C.3. Results

Table 1 presents demographic characteristics of the study population; Table 2 describes measures of body composition and physical activity. CCS were on average one year older than controls, but Tanner stage was similar between the two groups. CCS were shorter, had greater waist circumference and percent fat mass and lower lean body mass than controls, but there were no significant differences in weight, body mass index (BMI), abdominal subcutaneous fat, and abdominal visceral fat. After adjustment for percent fat mass, CCS had higher LDL-C (88.0 ± 1.7 vs 84.1 ± 2.1 mg/dL, *P* = .03) and lower insulin sensitivity ($M_{lbm}$) (12.2 ± 0.3 vs 13.3 ± 0.4 mg/kg/min, *P* = .002) and cCSD (30.7 ± 0.5 vs 32.7 ± 0.6 %, *P* = .002) than controls. As shown in Table 2, CCS were less physically active in their leisure time compared to controls.

**Table 1.** Characteristics of CCS and Sibling Controls

| | CCS (N=319) | | Controls (N=208) | | |
|---|---|---|---|---|---|
| | N (%) | Mean ± SE | N (%) | Mean ± SE | *P* |
| **Age** (years) | | 14.6 ± 0.1 | | 13.6 ± 0.2 | <.0001 |
| **Sex** | | | | | |
| Male | 171 (53.6) | | 112 (53.9) | | .93 |
| Female | 148 (46.4) | | 96 (46.2) | | |
| **Race/ethnicity**[a] | | | | | |
| White Non-Hispanic | 274 (85.9) | | 194 (93.3) | | .0008 |
| Others | 45 (14.1) | | 14 (6.7) | | |
| White Hispanic | 4 (1.3) | | 4 (1.9) | | |
| Black | 14 (4.4) | | 2 (1.0) | | |
| Other | 27 (8.5) | | 8 (3.8) | | |
| **Tanner Stage** | | 3.6 ± 0.1 | | 3.3 ± 0.1 | .07 |
| 1 | 33 (10.3) | | 34 (16.5) | | |
| 2 | 54 (16.9) | | 31 (15.1) | | |
| 3 | 39 (12.2) | | 36 (17.5) | | |
| 4 | 88 (27.6) | | 45 (21.8) | | |
| 5 | 105 (32.9) | | 60 (29.1) | | |
| **Diagnosis** | | | | | |
| Leukemia (ALL, AML) | 110 (34.5) | | NA | | |
| Central nervous system | 82 (25.7) | | | | |
| Solid tumors | 127 (39.8) | | | | |
| **Time from diagnosis to study** (years) | | 10.1 ± 0.2 | | NA | |
| **Cranial Radiation Therapy** | | | | | |
| Yes | 37 (11.6) | | NA | | |
| No | 282 (88.4) | | | | |
| **Corticosteroid Therapy** | | | | | |
| ≥90 days | 94 (29.5) | | NA | | |
| <90 days | 225 (70.5) | | | | |
| **Vincristine Chemotherapy** | | | | | |
| Yes | 212 (66.5) | | NA | | |
| No | 107 (33.5) | | | | |

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CCS, childhood cancer survivors; NA, not applicable; SE, standard error.
[a] White Hispanic, black, and other categories were collapsed for the comparison between CCS and controls.

**Table 2.** Body Composition and Physical Activity in CCS and Sibling Controls

| | CCS (N=319) | Controls (N=208) | |
|---|---|---|---|
| | Mean ± SE | Mean ± SE | *P* |
| **Height** (cm) | 158.2 ± 0.6 | 159.9 ± 0.7 | .01 |
| **Weight** (kg) | 57.2 ± 1.1 | 57.0 ± 1.2 | .85 |
| **Body Mass Index** ($kg/m^2$) | 22.4 ± 0.3 | 21.8 ± 0.4 | .08 |
| **Waist Circumference** (cm) | 73.1 ± 0.9 | 71.1 ± 1.0 | .02 |
| **Percent Fat Mass** (%) | 28.1 ± 0.8 | 25.9 ± 0.9 | .007 |
| **Abdominal Subcutaneous Fat** ($cm^3$) | 85.2 ± 4.5 | 77.0 ± 4.9 | .07 |
| **Abdominal Visceral Fat** ($cm^3$) | 22.3 ± 1.1 | 21.0 ± 1.2 | .17 |
| **Lean Body Mass** (kg) | 38.4 ± 0.5 | 39.9 ± 0.6 | .01 |
| **Leisure-time Physical Activity** (min/day) | 46.6 ± 3.2 | 55.8 ± 4.0 | .01 |

Abbreviations: CCS, childhood cancer survivors; SE, standard error.
All means and *P*-values are adjusted for age, sex, race/ethnicity, and Tanner stage.

Table 3 shows associations of cardiometabolic risk factors with PA level in CCS and controls, with PA either dichotomized at 60 minutes/day ("High vs low PA") or as a continuous measure ("Continuous PA" minutes/day). Among CCS, the high PA group had lower percent fat mass, abdominal subcutaneous fat, and abdominal visceral fat, greater lean body mass, and marginally greater ($P$ = .07) insulin sensitivity ($M_{lbm}$) compared to the low PA group. Among controls, the high PA group had greater lean body mass and marginally lower ($P$ = .05) percent fat mass but no difference in abdominal fat and insulin sensitivity compared to the low PA group. Among both CCS and controls, there were no significant differences between the low and high PA groups for the following risk factors: waist circumference, triglycerides, HDL-C, LDL-C, systolic and diastolic blood pressure, HOMA-IR, cCSC, cCSD, and cIMT. Analyses treating PA as a continuous measure gave similar results overall, with these exceptions: among CCS, cCSD (i.e., carotid elasticity) was positively associated with PA (beta =

0.03; $P = .02$), whereas among controls, percent fat mass (beta = -0.06; $P = .0008$) and abdominal subcutaneous fat (beta = -0.21; $P = .03$) were negatively associated with PA.

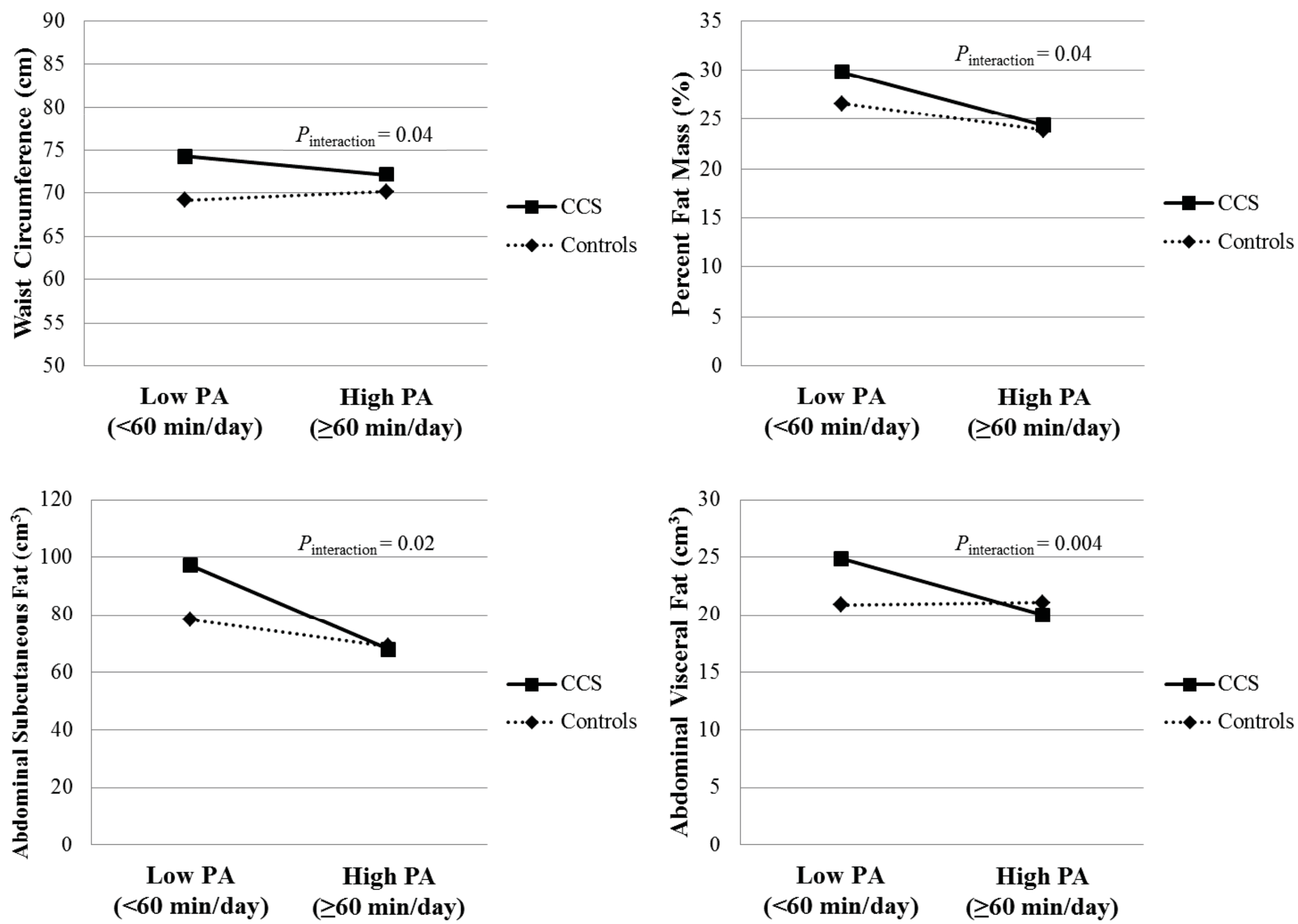
To assess whether the PA effect differed between CCS and controls, we tested the interaction between CCS/control status and PA level (high vs low) for each cardiometabolic risk factor. As depicted by the interaction plots in Figure 2, the associations between PA and waist circumference, percent fat mass, abdominal subcutaneous fat, and abdominal visceral fat appeared to be stronger in CCS than controls (all $P_{interaction} < .05$). In general, CCS had sharper reductions in these risk factors at the higher PA level compared to controls. There was no such evidence of effect modification by CCS/control status for the other risk factors examined in Table 3 (all $P_{interaction} > .05$). When PA was treated as a continuous measure, the interaction terms for waist circumference ($P_{interaction} = .06$) and percent fat mass ($P_{interaction} = .18$) did not remain statistically significant.

**Table 3.** Cardiometabolic Risk Factors by Physical Activity Level in CCS and Sibling Controls

| | CCS[a] | | | | Controls | | | | Interaction Models | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Low PA** <60 min/day (N=202) | **High PA** ≥60 min/day (N=84) | High *vs* Low PA | Contin -uous PA[b] | **Low PA** <60 min/day (N=112) | **High PA** ≥60 min/day (N=80) | High *vs* Low PA | Contin -uous PA[b] | CCS/ control x PA group | CCS/ control x contin- uous PA[b] |
| | Mean ± SE | Mean ± SE | *P* | *P* | Mean ± SE | Mean ± SE | *P* | *P* | $P_{interaction}$ | $P_{interaction}$ |
| **Waist Circumference** (cm) | 74.3 ± 1.1 | 72.2 ± 1.5 | .16 | .10 | 69.2 ± 1.2 | 70.2 ± 1.4 | .56 | .52 | .04 | .06 |
| **Percent Fat Mass** (%) | 29.8 ± 0.9 | 24.4 ± 1.3 | <.0001 | <.0001 | 26.6 ± 1.1 | 23.9 ± 1.3 | .05 | .0008 | .04 | .18 |
| **Abdominal Subcutaneous Fat** ($cm^3$)[c] | 97.3 ± 5.7 | 67.9 ± 8.0 | .0004 | <.0001 | 78.3 ± 6.6 | 69.1 ± 7.5 | .30 | .03 | .02 | .04 |
| **Abdominal Visceral Fat** ($cm^3$)[c] | 24.9 ± 1.3 | 20.0 ± 1.8 | .007 | .0007 | 20.9 ± 1.5 | 21.1 ± 1.8 | .93 | .07 | .004 | .02 |
| **Lean Body Mass** (kg)[c] | 39.5 ± 0.5 | 41.3 ± 0.7 | .009 | .01 | 39.7 ± 0.6 | 41.1 ± 0.6 | .02 | .04 | .99 | .78 |
| **Triglycerides** (mg/dL)[d] | 94.5 ± 5.0 | 92.8 ± 7.1 | .82 | .50 | 81.0 ± 5.2 | 74.0 ± 5.3 | .24 | .56 | .81 | .44 |
| **HDL-C** (mg/dL)[d] | 48.0 ± 1.0 | 48.6 ± 1.4 | .68 | .45 | 47.7 ± 1.3 | 48.7 ± 1.4 | .53 | .43 | .53 | .13 |
| **LDL-C** (mg/dL)[d] | 90.5 ± 2.3 | 88.5 ± 3.3 | .55 | .39 | 79.9 ± 3.5 | 78.7 ± 3.7 | .71 | .83 | .63 | .21 |
| **Systolic Blood Pressure** (mmHg)[c,d] | 110.7 ± 1.0 | 112.4 ± 1.4 | .26 | .47 | 109.1 ± 1.3 | 109.6 ± 1.4 | .70 | .89 | .81 | .97 |
| **Diastolic Blood Pressure** (mmHg)[c,d] | 58.1 ± 0.7 | 58.6 ± 1.0 | .57 | .39 | 57.1 ± 1.0 | 56.3 ± 1.0 | .42 | .49 | .40 | .37 |
| **Insulin Sensitivity** (mg glucose/kg lean body mass/min)[d] | 11.9 ± 0.4 | 13.0 ± 0.6 | .07 | .10 | 12.4 ± 0.5 | 12.7 ± 0.6 | .63 | .79 | .38 | .37 |
| **HOMA-IR**[d] | 2.16 ± 0.18 | 2.21 ± 0.25 | .84 | .73 | 2.01 ± 0.21 | 2.20 ± 0.25 | .42 | .31 | .39 | .44 |
| **cCSC** ($mm^2$/mmHg)[d] | 0.16 ± 0.004 | 0.16 ± 0.006 | .54 | .70 | 0.18 ± 0.01 | 0.18 ± 0.01 | .85 | .44 | .70 | .44 |
| **cCSD** (%)[d] | 29.9 ± 0.7 | 30.9 ± 0.9 | .28 | .02 | 34.3 ± 1.0 | 34.0 ± 1.1 | .82 | .26 | .61 | .06 |
| **cIMT** (mm)[d] | 0.44 ± 0.004 | 0.45 ± 0.006 | .77 | .61 | 0.44 ± 0.007 | 0.44 ± 0.006 | .89 | .87 | .38 | .19 |

All means and P-values are adjusted for age, sex, race/ethnicity, and Tanner stage.
[a] Additional adjustment for diagnosis in all models of CCS.
[b] *P*-values from models using PA treated as a continuous measure (minutes per day) instead of dichotomized PA.
[c] Additional adjustment for height.
[d] Additional adjustment for percent fat mass.

**Figure 2.** CCS/Control Status x Physical Activity Level (low versus high PA) Interaction Plots for Waist Circumference, Percent Fat Mass, Abdominal Subcutaneous Fat, and Abdominal Visceral Fat



## C.4. Discussion

This study found that CCS who reported higher levels of PA had lower percent fat mass and abdominal subcutaneous and visceral fat, greater lean body mass, and slightly greater insulin sensitivity and carotid artery distensibility compared to CCS who reported lower levels of PA. However, controls who reported higher PA had only greater lean body mass and slightly lower percent fat mass and abdominal subcutaneous fat compared to controls who reported lower PA. This result may be explained by the fact that CCS have greater potential for change than controls simply because they start with poorer levels of certain cardiometabolic risk factors that have finite "normal" or "healthy" ranges. In other words, while an already healthy cardiometabolic profile could be improved slightly (perhaps to the top of the normal range) with PA alone, a sub-optimal or abnormal cardiometabolic profile could be improved more dramatically to reach normal or even optimal levels with the same amount of PA.

Prior knowledge is very limited regarding these relationships in CCS; this study complements the literature by supporting associations previously observed between PA and adiposity in adult CCS and extends the findings to children. In a recent study of 117 adult survivors of childhood acute lymphoblastic leukemia (ALL), greater PA energy expenditure was associated with lower percent body fat but was not associated with waist circumference, HOMA-IR, or metabolic syndrome.[85] A 16-week home-based exercise intervention in a small group of 16- to 30-year-old survivors of childhood ALL resulted in significant improvements in measures of adiposity and HOMA-IR, while cIMT, lipids, and fasting plasma glucose remained unchanged; the effect on blood pressure was variable.[48,49] The current study is the first to examine the associations between PA and directly measured subcutaneous fat, visceral fat, insulin sensitivity ($M_{lbm}$), and arterial compliance and distensibility in CCS in general and specifically during childhood. Hoffman et al. reported that CCS aged <18 years performed more poorly on measures of physical function despite reporting similar levels and types of PA as their sibling controls.[86] However, measures of physical function (strength, mobility) are not equivalent to measures of cardiometabolic risk or PA.

Results of the current study indicate that PA may be a useful tool for limiting excess fat mass while preserving lean mass and possibly improving insulin sensitivity and arterial health in CCS children. Previously, increased fat mass[87] and decreased lean mass[88] have been independently associated with greater insulin resistance, highlighting the importance of reducing excess fat mass while simultaneously maintaining or increasing lean mass. In fact, sarcopenia, a condition of reduced lean skeletal muscle mass, and obesity have been shown to have an additive effect on insulin resistance.[89] Previous studies have also found that healthy children who are more physically active are leaner and have greater insulin sensitivity (independent of adiposity) than their less active peers, especially when engaged in vigorous PA.[90-94] After dichotomizing by high/low PA groups we documented statistically significant associations of PA with measures of adiposity but not with measures of insulin sensitivity; this may be due to low power in each of the groups, the use of a relatively crude measure of PA, and the fact that we evaluated a young population (children) in whom the elevations of cardiometabolic risk factor levels are less pronounced than in the previously reported adult studies.

Unfavorable vascular endothelial thickness and function are important early markers of subclinical atherosclerosis and increased cardiovascular disease risk. Among adults, regular PA has been shown to delay, slow, or even prevent the age-associated decline in early measures of atherosclerosis such as vascular compliance and distensibility.[95] We have previously shown in this cohort that survivors of leukemia had lower carotid artery distensibility and compliance, indicating increased arterial stiffness, when compared to controls.[77] In the current study, when the analyses were dichotomized by high/low PA, the effect of PA on vascular health was not obvious, however, when PA was treated as a continuous measure, carotid distensibility (cCSD) was associated with higher levels of PA in CCS. The relatively small effect of PA on the vascular markers may be due to the fact that the current study was focused on children, who have not yet developed clinically significant vascular abnormalities, and may suggest that as children progress into adulthood these findings will become more prominent and established cardiovascular risk factors. It is well known in pediatric populations that cardiometabolic risk is a continuum and that threshold levels and dichotomized classifications are less useful in establishing risk levels than in adults.[96]

This study's cross-sectional design and retrospective measure of PA restricted the ability to make causal inferences. Prospective longitudinal cohorts or randomized controlled trials will be needed to verify such inferences. Another limitation was the inability to completely control for differences in treatment. Diagnostic group served as a proxy for treatment regimen in this analysis. In post-hoc analyses, controlling for cranial radiation, corticosteroid therapy, or vincristine chemotherapy instead of diagnosis did not substantially alter the results. We also considered possible implications of lower extremity surgical procedures such as amputation, femur resection, and/or limb salvage, but too few CCS were affected (one amputation, two femur resections, and one limb salvage) to permit an analysis.

The pattern of adverse body composition and lower carotid elasticity in CCS suggests that as these children progress into adulthood, these levels will likely become overtly abnormal. The finding that PA was associated with cardiometabolic risk factors in CCS suggests that greater levels of PA could serve as a tangible target in mitigating the already high cardiometabolic risk of CCS.

## D. PROJECT 2: PHYSICAL ACTIVITY AND CARDIOMETABOLIC RISK FACTORS IN ADULT SURVIVORS OF CHILDHOOD CANCER WITH A HISTORY OF HEMATOPOIETIC CELL TRANSPLANTATION

### D.1. Background

Nearly 45 years since the first successful allogeneic bone marrow transplant was conducted,[97] hematopoietic cell transplantation (HCT) has become a standard treatment for a number of malignant and non-malignant conditions in children. As the number of transplants being performed has increased, survival after HCT has also been increasing, resulting in a growing population of long-term survivors.[98] Unfortunately, along with other childhood cancer survivors (CCS), HCT survivors are at high risk for numerous adverse late effects and exhibit more cardiometabolic risk factors than healthy controls.[99] Although the etiology of these late effects is multifactorial and not well understood, exposure to total body irradiation and other forms of prolonged immunosuppressive treatment during the HCT process and post-transplant endocrine dysfunction and/or leptin resistance have been suggested to play a role.[100-102]

As previously discussed, higher levels of physical activity are hypothesized to help prevent and/or mitigate several adverse late effects. In addition, greater cardiorespiratory fitness and muscle strength have been inversely associated with several cardiometabolic risk factors in healthy populations.[103-108] Reduced cardiorespiratory fitness, mobility, and muscle strength have been reported among adult CCS; such deficits might result from and/or contribute to low PA levels.[109,110] Relationships between physical activity/fitness and cardiometabolic risk factors among CCS with a history of

HCT remain to be characterized. Therefore, we examined cross-sectional associations of PA/fitness measures with cardiometabolic risk factors among CCS who underwent HCT and their sibling controls.

## D.2. Methods

### D.2.1. Study Design and Participants

The study was approved by the Institutional Review Board Human Subjects Committees at the University of Minnesota and the Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance (FHCRC/SCCA). All participants provided written informed consent. CCS were selected from transplant databases at each institution and were eligible to participate if they were diagnosed with a primary hematologic malignancy at age 21 years or younger, received HCT, were treated at either Fairview-University Medical Center or the FHCRC/SCCA, were ≥9 years of age at the time of study participation, survived a minimum of two years post-transplant, and were currently in remission. Sibling controls were eligible to participate if they were ≥9 years of age at the time of examination and had never had cancer. Controls were frequency matched to CCS by age and sex. Pregnant women were excluded until three or more months after the end of their pregnancy. Of the 339 potentially eligible survivors identified, 60 refused participation, and we were unable to establish contact (passive refusal) with an additional 125 subjects. The remaining 154 (45%) provided informed written consent to participate along with 92 of their siblings. Three CCS were found to be ineligible at the time of study due to previously undiagnosed diabetes (n=1), severe hypertension (n=1), and multiple medical issues (n=1) that all required immediate medical attention. This left the final study population of 151 subjects. For the purposes of this analysis we excluded the 32 CCS and 26 controls who were less than 18 years of age, leaving a total of 119 CCS and 66 controls.

D.2.2. Data Collection

All participants underwent a two-day examination at the University of Minnesota Clinical Research Center/Clinical and Translational Science Institute or the Clinical Research Center at FHCRC/SCCA. Height, weight, waist circumference, and blood pressure were assessed according to a standard protocol, as previously described.[78] Fat mass and lean body mass were measured using dual-energy X-ray absorptiometry (DXA, Lunar Prodigy scanner, software version 9.3; General Electric Medical Systems, Madison, WI).

After a 10- to 12-hour overnight fast, the hyperinsulinemic euglycemic clamp method was used to assess insulin sensitivity, as described previously.[78,79] Insulin infusion was started at time 0 at a rate of 1 mU/kg/min for 3 hours. An infusion of 20% glucose was given and adjusted to maintain euglycemia (serum glucose level of 100 mg/dL [5.6 mmol/L]) with plasma glucose determined every 10 minutes. Insulin sensitivity (M) was determined by the amount of glucose required to maintain euglycemia in the final 40 minutes of the clamp study and expressed as mg/kg/min of glucose with adjustment for lean body mass ($M_{lbm}$). Lower $M_{lbm}$ values are indicative of lower insulin sensitivity (i.e., greater insulin resistance).

Fasting blood samples obtained at the start of the insulin clamp were analyzed for serum lipid levels (low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides), serum insulin, and plasma glucose using a Vitros 5600 (Ortho-Clinical Diagnostics, Inc., Rochester, NY), a chemoluminescence immunoassay (Immulite Insulin DPC, Los Angeles, CA), and a Beckman Glucose Analyzer II (Beckman Instruments, Fullerton, CA), respectively. LDL-C was calculated by the Friedewald equation. Homeostasis model assessment insulin resistance (HOMA-IR) was calculated with fasting insulin and glucose values using the equation HOMA-IR = [(fasting glucose units of mmol/L * insulin units in $\mu$U/mL)/22.5].[80]

To assess PA, participants completed the Modifiable Activity Questionnaire (MAQ). See Appendix 2 for a copy of the MAQ. Participants reported activities in which they had participated at least ten times during the past year in their leisure time, along with the number of months over the year, the average number of times per month, and the average minutes per time that each activity was performed. In addition, participants reported average minutes per day spent walking or bicycling to/from work along with the number of days per week and months per year they attended their job(s). The MAQ-A has been shown to provide valid and reproducible estimates of past year leisure-time PA in adult populations.[111,112]

A subset of participants (82 CCS, 33 controls) completed physical functioning assessments to objectively measure mobility, endurance, and strength. Functional mobility was evaluated by the “Timed Up and Go” measure, which is the time in seconds taken by an individual to stand up from a 46 cm height arm chair, walk three meters, turn, walk back to the chair and sit down again. Endurance was measured by a six-minute walking test (a modified Cooper test) in which the total distance (in meters) traveled in six minutes is recorded by a pedometer. Handgrip strength was measured in both hands using a mechanical hand- held dynamometer.

D.2.3. Statistical Analysis

All analyses were conducted with SAS version 9.2 (SAS Institute, Inc., Cary, NC). Hours per week spent walking/biking to work and engaging in leisure-time PA were summed to obtain total hours per week of PA. Participants who met the U.S. federal recommendation of at least 2.5 hours per week of moderate-intensity PA in adults[84] were categorized as high PA while those reporting less than 2.5 hours per week were categorized as low PA. Participants were categorized into low and high groups for mobility, endurance, and handgrip strength based upon location either below or at/above the median (median mobility = 4.66 seconds, median endurance = 588.9 meters, median handgrip strength = 27.5 kg).

Descriptive statistics are expressed as frequencies and percents or mean ± standard error (SE), as appropriate. CCS were grouped into three treatment groups based on their HCT preparative regimen: total body irradiation and central nervous system irradiation (TBI+CNS), TBI but no CNS irradiation (TBI not CNS), and no TBI nor CNS irradiation (chemotherapy only). Analysis of covariance models adjusted for multiple pairwise comparisons by the post hoc Tukey-Kramer test were used to detect differences in PA, fitness, and cardiometabolic risk factors between the three treatment groups. All analyses including data from sibling controls were implemented in SAS's GENMOD procedure using generalized estimating equations (GEE) to account for intra-family correlation, with the default working correlation (independence) and robust variance estimates. All adjusted comparisons used multivariable linear regression models with adjustments for age, sex, and race/ethnicity. As indicated, models were further adjusted for percent fat mass, height, weight, and/or treatment when appropriate. Adjusted means were evaluated at the mean levels of covariates included in the models. A two-sided *P*-value $<0.05$ was considered to be statistically significant, although because of the high number of statistical tests carried out, those between 0.01 and 0.05 should be viewed with caution.

## D.3. Results

Characteristics of the study population are presented in Table 4. On average, CCS were older and shorter and weighed less than sibling controls, but BMI was similar between the two groups. Table 5 includes average levels of PA, fitness, and cardiometabolic risk factors for controls, all CCS, and CCS by treatment group. Controls and CCS as a whole had similar levels of PA, mobility, endurance, and strength, as well as waist circumference, HDL-C, and systolic and diastolic blood pressure. CCS had greater percent fat mass, triglycerides, LDL-C, and HOMA-IR and lower lean body mass and insulin sensitivity than controls after adjusting for covariates. These patterns differed somewhat across the three treatment groups. Pairwise analysis revealed that the TBI+CNS group had lower mobility, strength, lean body mass, HDL-C, and higher

**Table 4.** Characteristics of Adult CCS and Sibling Controls

| | CCS (n=119) | | Controls (n=66) | | |
|---|---|---|---|---|---|
| | **N (%)** | **Mean ± SE** | **N (%)** | **Mean ± SE** | ***P*** |
| **Age at Study** (years) | | 27.4 ± 0.7 | | 25.0 ± 1.0 | .02 |
| **Sex** | | | | | |
| Male | 67 (56.3) | | 36 (54.6) | | .80 |
| Female | 52 (43.7) | | 30 (45.5) | | |
| **Race/ethnicity**[a] | | | | | |
| White Non-Hispanic | 109 (91.6) | | 61 (92.4) | | .83 |
| Other | 10 (8.4) | | 5 (7.6) | | |
| **Diagnosis** | | | | | |
| ALL | 32 (26.9) | | | | |
| AML | 39 (32.8) | | NA | | |
| CML | 15 (12.6) | | | | |
| HOD | 10 (8.4) | | | | |
| MDS | 11 (9.2) | | | | |
| Others | 12 (10.1) | | | | |
| **HCT Preparative Regimen** | | | | | |
| TBI+CNS | 24 (20.2) | | NA | | |
| TBI not CNS | 62 (52.1) | | | | |
| Chemotherapy only[b] | 33 (27.7) | | | | |
| **HCT Type** | | | | | |
| Allogeneic | 87 (73.1) | | NA | | |
| Autologous | 32 (26.9) | | | | |
| **Age at Most Recent HCT** (years) | | 12.7 ± 0.6 | | NA | |
| **Graft Versus Host Disease** | | | | | |
| Chronic or chronic + acute | 34 (28.6) | | | | |
| Acute grades II-III | 11 (9.2) | | NA | | |
| None or acute grade I | 42 (35.3) | | | | |
| Missing | 32 (26.9) | | | | |
| **Height** (cm) | | 166.1 ± 1.0 | | 173.7 ± 1.2 | <.0001 |
| **Weight** (kg) | | 68.6 ± 1.8 | | 73.8 ± 2.0 | .04 |
| **Body Mass Index** ($kg/m^2$) | | 24.6 ± 0.5 | | 24.3 ± 0.5 | .71 |

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CCS, childhood cancer survivors; CML, chronic myeloid leukemia; CNS, central nervous system; HCT, hematopoietic cell transplantation; HOD, Hodgkin's lymphoma; MDS, myelodysplastic syndrome; NA, not applicable; NHL, non-Hodgkin lymphoma; SE, standard error; TBI, total body irradiation.

[a] White Hispanic, black, and other categories were collapsed for the comparison between CCS and controls.

[b] Some received other radiation prior to or after HCT: Mantle/mediastinal (n=10 for HD), arm, orbit (n=2 for chloromas), temple (n=1 with history of sarcoma and HCT for secondary AML), abdominal (n=1 for NHL).

**Table 5.** Physical Activity, Fitness, and Cardiometabolic Risk Factors in Adult CCS and Sibling Controls

| | All CCS (n=119) | | TBI + CNS (n=24) | | TBI not CNS (n=62) | | Chemotherapy only (n=33) | | Controls (n=66) |
|---|---|---|---|---|---|---|---|---|---|
| | **Mean ± SE** | ***P*[a]** | **Mean ± SE** | ***P*[a]** | **Mean ± SE** | ***P*[a]** | **Mean ± SE** | ***P*[a]** | **Mean ± SE** |
| **Physical Activity/Fitness** | | | | | | | | | |
| Physical Activity (hours/week) | 7.25 ± 1.29 | .62 | 6.16 ± 1.73 | .73 | 7.71 ± 0.95 | .61 | 8.04 ± 1.73 | .97 | 6.70 ± 1.47 |
| Mobility (seconds) | 5.38 ± 0.26 | .07 | **5.71 ± 0.24A** | .002 | **5.07 ± 0.32B** | .29 | **5.28 ± 0.43B** | .48 | 4.98 ± 0.29 |
| Endurance (meters) | 583.1 ± 29.8 | .69 | 608.2 ± 36.9 | .11 | 585.7 ± 72.9 | .78 | 627.2 ± 36.6 | .77 | 591.9 ± 39.1 |
| Handgrip Strength (kg) | 30.5 ± 2.1 | .21 | **31.6 ± 3.2A** | .17 | **24.9 ± 1.2A** | .02 | **34.4 ± 2.8B** | .05 | 32.8 ± 2.4 |
| **Cardiometabolic Risk Factors** | | | | | | | | | |
| Waist Circumference (cm) | 83.0 ± 2.5 | .62 | 82.3 ± 3.9 | .82 | 81.9 ± 4.7 | .79 | 86.1 ± 3.6 | .13 | 82.1 ± 3.3 |
| Percent Fat Mass (%) | 36.0 ± 1.2 | <.0001 | 36.7 ± 2.1 | .002 | 34.2 ± 2.1 | .0007 | 36.5 ± 1.7 | .004 | 30.2 ± 1.5 |
| Lean Body Mass (kg)[b] | 42.7 ± 0.7 | <.0001 | **39.3 ± 1.1A** | <.0001 | **42.0 ± 0.9AB** | <.0001 | **46.9 ± 1.0B** | .04 | 48.8 ± 0.4 |
| Triglycerides (mg/dL)[c] | 181.3 ± 19.4 | .0001 | **268.1 ± 46.4A** | .002 | **179.3 ± 27.0AB** | .002 | **136.0 ± 21.7B** | .13 | 98.2 ± 14.0 |
| HDL-C (mg/dL)[c] | 43.1 ± 1.7 | .12 | **37.5 ± 2.2A** | .004 | **44.0 ± 2.3B** | .29 | **44.7 ± 2.6AB** | .74 | 45.9 ± 1.8 |
| LDL-C (mg/dL)[c] | 106.8 ± 4.4 | .007 | 115.4 ± 6.3 | .001 | 102.2 ± 5.9 | .07 | 109.5 ± 6.8 | .03 | 93.5 ± 3.9 |
| Systolic Blood Pressure (mmHg)[c] | 114.2 ± 2.0 | .25 | 119.6 ± 3.7 | .32 | 115.7 ± 2.9 | .19 | 110.6 ± 2.2 | .13 | 116.4 ± 2.3 |
| Diastolic Blood Pressure (mmHg)[c] | 68.7 ± 1.6 | .47 | 69.9 ± 3.5 | .27 | 68.3 ± 1.9 | .63 | 66.1 ± 1.5 | .75 | 67.7 ± 1.6 |
| HOMA-IR[c] | 2.95 ± 0.31 | .0007 | 4.28 ± 0.61 | .0006 | 3.37 ± 0.52 | .02 | 2.15 ± 0.35 | .16 | 1.57 ± 0.38 |
| Insulin Sensitivity (mg/kg/min)[c] | 9.98 ± 0.62 | .03 | 7.76 ± 1.03 | .003 | 9.61 ± 0.91 | .08 | 11.3 ± 0.8 | .51 | 11.9 ± 0.7 |

Abbreviations: CCS, childhood cancer survivors; CNS, central nervous system; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL-C, low-density lipoprotein cholesterol; SE, standard error; TBI, total body irradiation.
All models adjusted for age, sex, and race/ethnicity.
For comparisons between TBI+CNS, TBI not CNS, and chemotherapy only groups, means within bolded rows that do not share the same letter are significantly different from each other (Tukey-Kramer test, $P < .05$). There were no significant differences within non-bolded rows.
[a] P value for comparison between CCS (or subgroup) and controls, on the basis of adjusted linear regression models.
[b] Additional adjustment for height and weight.
[c] Additional adjustment for percent fat mass.

triglycerides compared to one or both of the other treatment groups, particularly the chemotherapy only group.

Cardiometabolic risk factors by levels of PA, mobility, endurance, and handgrip strength are displayed in Tables 6, 7, 8, and 9, respectively. Among CCS, the high PA had lower waist circumference than the low PA group (see Table 6). Among controls, the high PA group had lower diastolic blood pressure than the low PA group. As seen in Tables 7 and 9, there were no statistically significant differences between the low and high mobility groups or between the low and high handgrip strength groups within CCS or controls. However, there seemed to be a pattern of leanness among CCS in the high mobility group, as they had marginally lower waist circumference ($P$ = .07) and percent fat mass ($P$ = .09) and greater lean body mass ($P$ = .10) than the low mobility group (see Table 7). Similarly, there was a trend toward lower insulin resistance among controls in the high mobility group, as they had marginally lower HOMA-IR ($P$ = .05) and greater insulin sensitivity ($P$ = .07) than the low mobility group. Among CCS, the high endurance group (see Table 8) had lower waist circumference and percent fat mass, and greater insulin sensitivity than the low endurance group. Among controls, only marginally ($P$ = .05) lower HOMA-IR was observed in the high endurance group compared to the low endurance group.

We tested the significance of the interaction between CCS/control status and PA/fitness level for each cardiometabolic risk factor. As depicted by the interaction plots in Figure 3 and as displayed in the rightmost column of Tables 6 and 7, differences in waist circumference between low and high PA and differences in triglycerides between

**Table 6.** Cardiometabolic Risk Factors by Physical Activity Level in Adult CCS and Sibling Controls

| | CCS[a] | | | Controls | | | Interaction Model |
|---|---|---|---|---|---|---|---|
| | **Low PA** (<2.5hr/wk) (N=33) | **High PA** (≥2.5hr/wk) (N=72) | | **Low PA** (<2.5hr/wk) (N=13) | **High PA** (≥2.5hr/wk) (N=31) | | CCS/control x PA group |
| | Mean ± SE | Mean ± SE | *P* | Mean ± SE | Mean ± SE | *P* | $P_{interaction}$ |
| **Waist Circumference** (cm) | 88.6 ± 3.1 | 81.9 ± 2.5 | .009 | 72.7 ± 3.3 | 75.7 ± 3.0 | .21 | .008 |
| **Percent Fat Mass** (%) | 38.8 ± 2.0 | 35.8 ± 1.6 | .07 | 24.3 ± 3.3 | 25.5 ± 2.6 | .63 | .28 |
| **Lean Body Mass** (kg)[b] | 42.2 ± 1.2 | 42.6 ± 0.9 | .63 | 49.3 ± 1.2 | 50.1 ± 0.6 | .55 | .55 |
| **Triglycerides** (mg/dL)[c] | 221.2 ± 51.3 | 192.2 ± 41.0 | .48 | 108.8 ± 12.5 | 97.5 ± 6.6 | .38 | .67 |
| **HDL Cholesterol** (mg/dL)[c] | 41.0 ± 2.8 | 42.4 ± 2.2 | .54 | 40.8 ± 3.4 | 44.8 ± 2.7 | .19 | .71 |
| **LDL Cholesterol** (mg/dL)[c] | 116.8 ± 9.3 | 114.1 ± 7.3 | .71 | 94.8 ± 6.5 | 90.6 ± 3.2 | .63 | .68 |
| **Systolic Blood Pressure** (mmHg)[c] | 118.0 ± 3.6 | 114.3 ± 2.9 | .21 | 113.3 ± 3.0 | 111.2 ± 2.1 | .44 | .24 |
| **Diastolic Blood Pressure** (mmHg)[c] | 71.8 ± 2.7 | 71.1 ± 2.2 | .77 | 66.6 ± 1.3 | 61.6 ± 0.8 | .02 | .30 |
| **HOMA-IR**[c] | 2.82 ± 1.69 | 3.19 ± 1.33 | .79 | 2.38 ± 0.61 | 1.51 ± 0.23 | .11 | .48 |
| **Insulin Sensitivity** (mg/kg/min)[c] | 8.19 ± 1.37 | 9.46 ± 1.07 | .26 | 10.3 ± 1.4 | 12.2 ± 0.9 | .18 | .70 |

Abbreviations: CCS, childhood cancer survivors; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL-C, low-density lipoprotein cholesterol; PA, physical activity; SE, standard error.
All models adjusted for age, sex, and race/ethnicity.
[a] Additional adjustment for treatment (HCT preparative regimen) in all models of CCS.
[b] Additional adjustment for height and weight.
[c] Additional adjustment for percent fat mass.

**Table 7.** Cardiometabolic Risk Factors by Mobility Level in Adult CCS and Sibling Controls

| | CCS[a] | | | Controls | | | Interaction Model |
|---|---|---|---|---|---|---|---|
| | **Low Mobility** (N=43) | **High Mobility** (N=39) | | **Low Mobility** (N=14) | **High Mobility** (N=19) | | CCS/control x mobility group |
| | Mean ± SE | Mean ± SE | *P* | Mean ± SE | Mean ± SE | *P* | $P_{interaction}$ |
| **Waist Circumference** (cm) | 85.2 ± 2.6 | 79.9 ± 3.0 | .07 | 80.8 ± 3.0 | 77.9 ± 1.0 | .27 | .38 |
| **Percent Fat Mass** (%) | 37.9 ± 1.7 | 34.7 ± 2.0 | .09 | 31.4 ± 2.6 | 28.6 ± 1.4 | .42 | .80 |
| **Lean Body Mass** (kg)[b] | 40.6 ± 1.5 | 42.4 ± 1.8 | .09 | 47.0 ± 1.4 | 49.1 ± 1.1 | .30 | .67 |
| **Triglycerides** (mg/dL)[c] | 213.2 ± 42.9 | 147.5 ± 47.7 | .16 | 101.2 ± 8.3 | 106.3 ± 8.4 | .72 | .02 |
| **HDL Cholesterol** (mg/dL)[c] | 43.0 ± 2.1 | 45.7 ± 2.3 | .22 | 37.9 ± 2.6 | 42.8 ± 1.4 | .15 | .86 |
| **LDL Cholesterol** (mg/dL)[c] | 110.0 ± 8.5 | 122.0 ± 8.5 | .15 | 88.1 ± 5.9 | 92.0 ± 3.2 | .56 | .67 |
| **Systolic Blood Pressure** (mmHg)[c] | 118.2 ± 3.1 | 115.9 ± 3.4 | .48 | 110.7 ± 2.4 | 114.0 ± 1.2 | .34 | .17 |
| **Diastolic Blood Pressure** (mmHg)[c] | 71.7 ± 2.4 | 70.9 ± 2.7 | .77 | 63.4 ± 1.8 | 62.2 ± 1.1 | .60 | .99 |
| **HOMA-IR**[c] | 2.74 ± 1.67 | 2.21 ± 1.75 | .76 | 2.05 ± 0.19 | 1.52 ± 0.11 | .05 | .50 |
| **Insulin Sensitivity** (mg/kg/min)[c] | 10.2 ± 1.12 | 8.87 ± 1.18 | .26 | 15.4 ± 1.2 | 12.9 ± 0.6 | .07 | .33 |

Abbreviations: CCS, childhood cancer survivors; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL-C, low-density lipoprotein cholesterol; SE, standard error.
All models adjusted for age, sex, and race/ethnicity.
[a] Additional adjustment for treatment (HCT preparative regimen) in all models of CCS.
[b] Additional adjustment for height and weight.
[c] Additional adjustment for percent fat mass.

**Table 8.** Cardiometabolic Risk Factors by Endurance Level in Adult CCS and Sibling Controls

| | CCS[a] | | | Controls | | | Interaction Model |
|---|---|---|---|---|---|---|---|
| | **Low Endurance** (N=40) | **High Endurance** (N=42) | | **Low Endurance** (N=17) | **High Endurance** (N=16) | | CCS/control x endurance group |
| | Mean ± SE | Mean ± SE | *P* | Mean ± SE | Mean ± SE | *P* | $P_{interaction}$ |
| **Waist Circumference** (cm) | 87.8 ± 2.5 | 77.8 ± 2.6 | .0001 | 76.7 ± 2.3 | 79.3 ± 1.5 | .30 | .001 |
| **Percent Fat Mass** (%) | 39.4 ± 1.7 | 33.6 ± 1.8 | .0008 | 30.1 ± 3.0 | 29.3 ± 1.1 | .79 | .17 |
| **Lean Body Mass** (kg)[b] | 40.4 ± 1.1 | 41.7 ± 1.0 | .25 | 46.2 ± 1.8 | 49.0 ± 0.9 | .20 | .77 |
| **Triglycerides** (mg/dL)[c] | 217.0 ± 45.6 | 160.1 ± 44.4 | .21 | 91.9 ± 9.4 | 107.9 ± 7.0 | .26 | .10 |
| **HDL Cholesterol** (mg/dL)[c] | 43.0 ± 2.2 | 45.0 ± 2.1 | .37 | 39.5 ± 3.0 | 41.8 ± 1.3 | .47 | .88 |
| **LDL Cholesterol** (mg/dL)[c] | 112.8 ± 9.0 | 118.0 ± 8.2 | .52 | 91.2 ± 6.0 | 90.8 ± 3.3 | .95 | .90 |
| **Systolic Blood Pressure** (mmHg)[c] | 120.3 ± 3.2 | 114.6 ± 3.1 | .08 | 109.9 ± 2.1 | 113.7 ± 0.9 | .15 | .02 |
| **Diastolic Blood Pressure** (mmHg)[c] | 71.5 ± 2.6 | 71.2 ± 2.5 | .92 | 62.9 ± 1.7 | 62.5 ± 1.0 | .83 | .80 |
| **HOMA-IR**[c] | 3.63 ± 1.79 | 1.80 ± 1.60 | .27 | 2.05 ± 0.19 | 1.59 ± 0.10 | .05 | .24 |
| **Insulin Sensitivity** (mg/kg/min)[c] | 7.42 ± 1.14 | 10.9 ± 1.0 | .001 | 14.4 ± 1.3 | 13.5 ± 0.6 | .49 | .02 |

Abbreviations: CCS, childhood cancer survivors; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL-C, low-density lipoprotein cholesterol; SE, standard error.
All models adjusted for age, sex, and race/ethnicity.
[a] Additional adjustment for treatment (HCT preparative regimen) in all models of CCS.
[b] Additional adjustment for height and weight.
[c] Additional adjustment for percent fat mass.

**Table 9.** Cardiometabolic Risk Factors by Handgrip Strength Level in Adult CCS and Sibling Controls

| | CCS[a] | | | Controls | | | **Interaction Model** |
|---|---|---|---|---|---|---|---|
| | **Low Strength** (N=38) | **High Strength** (N=39) | | **Low Strength** (N=16) | **High Strength** (N=16) | | CCS/control x strength group |
| | Mean ± SE | Mean ± SE | *P* | Mean ± SE | Mean ± SE | *P* | $P_{interaction}$ |
| **Waist Circumference** (cm) | 80.5 ± 3.0 | 85.0 ± 3.0 | .20 | 82.6 ± 1.6 | 74.8 ± 1.8 | .29 | .20 |
| **Percent Fat Mass** (%) | 35.7 ± 2.0 | 37.6 ± 2.0 | .42 | 35.5 ± 0.9 | 23.1 ± 2.3 | .29 | .88 |
| **Lean Body Mass** (kg)[b] | 40.8 ± 1.2 | 41.4 ± 1.1 | .63 | 45.4 ± 0.7 | 52.1 ± 2.1 | .31 | .15 |
| **Triglycerides** (mg/dL)[c] | 200.5 ± 49.3 | 180.7 ± 49.5 | .73 | 96.6 ± 11.6 | 111.9 ± 17.2 | .61 | .85 |
| **HDL Cholesterol** (mg/dL)[c] | 43.2 ± 2.3 | 44.8 ± 2.3 | .57 | 35.1 ± 1.8 | 48.0 ± 2.1 | .26 | .26 |
| **LDL Cholesterol** (mg/dL)[c] | 120.6 ± 9.1 | 112.0 ± 9.0 | .38 | 82.9 ± 6.1 | 97.5 ± 7.6 | .40 | .31 |
| **Systolic Blood Pressure** (mmHg)[c] | 114.7 ± 3.1 | 118.2 ± 3.1 | .34 | 108.3 ± 1.9 | 117.7 ± 2.4 | .29 | .23 |
| **Diastolic Blood Pressure** (mmHg)[c] | 68.7 ± 2.6 | 73.8 ± 2.7 | .10 | 61.6 ± 1.2 | 63.6 ± 2.1 | .55 | .46 |
| **HOMA-IR**[c] | 2.48 ± 1.82 | 2.47 ± 1.87 | .99 | 1.71 ± 0.20 | 1.65 ± 0.28 | .89 | .73 |
| **Insulin Sensitivity** (mg/kg/min)[c] | 8.71 ± 1.16 | 10.5 ± 1.2 | .18 | 14.9 ± 0.7 | 12.4 ± 0.9 | .31 | .24 |

Abbreviations: CCS, childhood cancer survivors; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL-C, low-density lipoprotein cholesterol; SE, standard error.
All models adjusted for age, sex, and race/ethnicity.
[a] Additional adjustment for treatment (HCT preparative regimen) in all models of CCS.
[b] Additional adjustment for height and weight.
[c] Additional adjustment for percent fat mass.

**Figure 3**. CCS/Control Status x Physical Activity Level (low versus high PA) Interaction Plot for Waist Circumference and CCS/Control Status x Mobility Level (low versus high mobility) Interaction Plot for Triglycerides

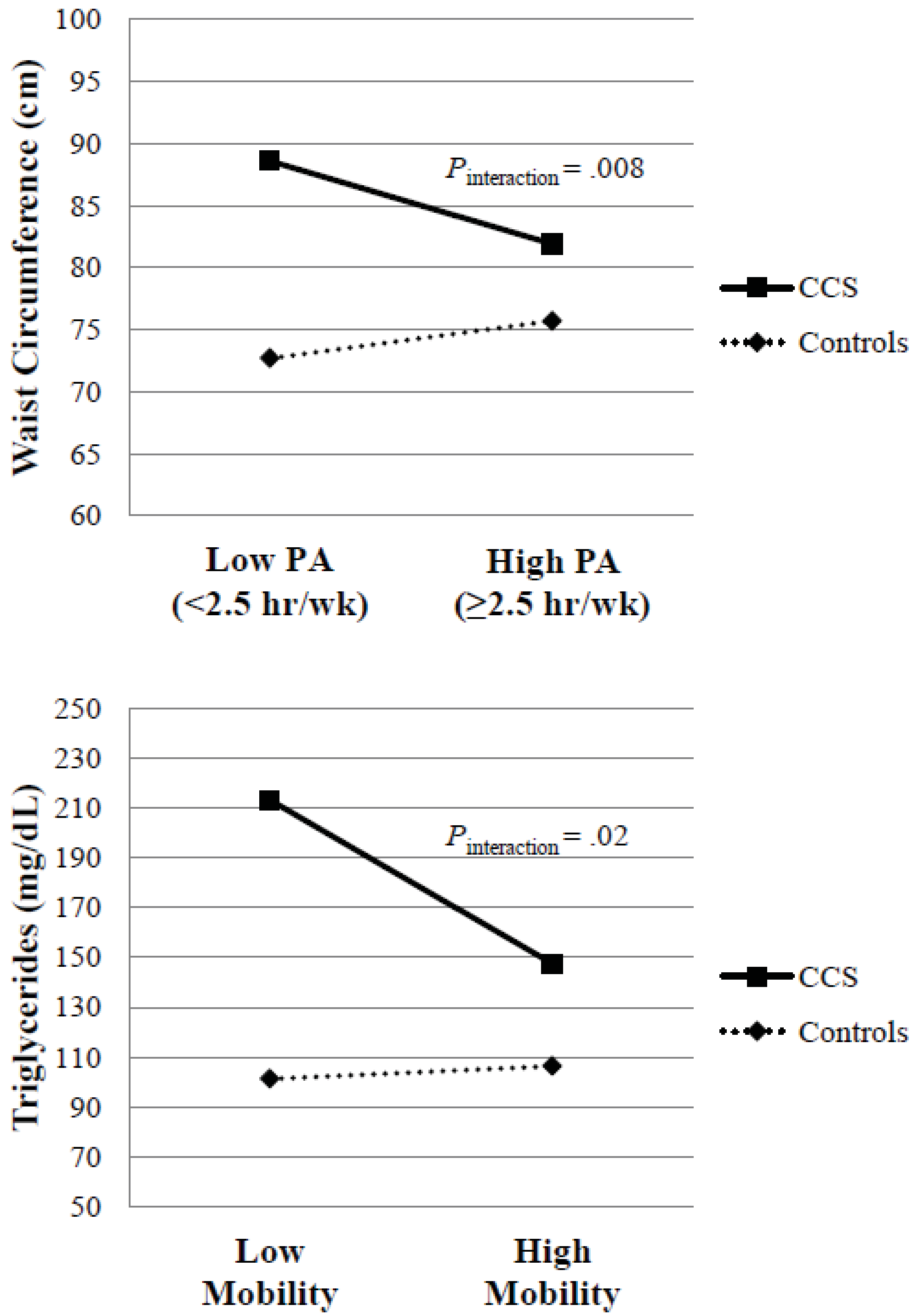
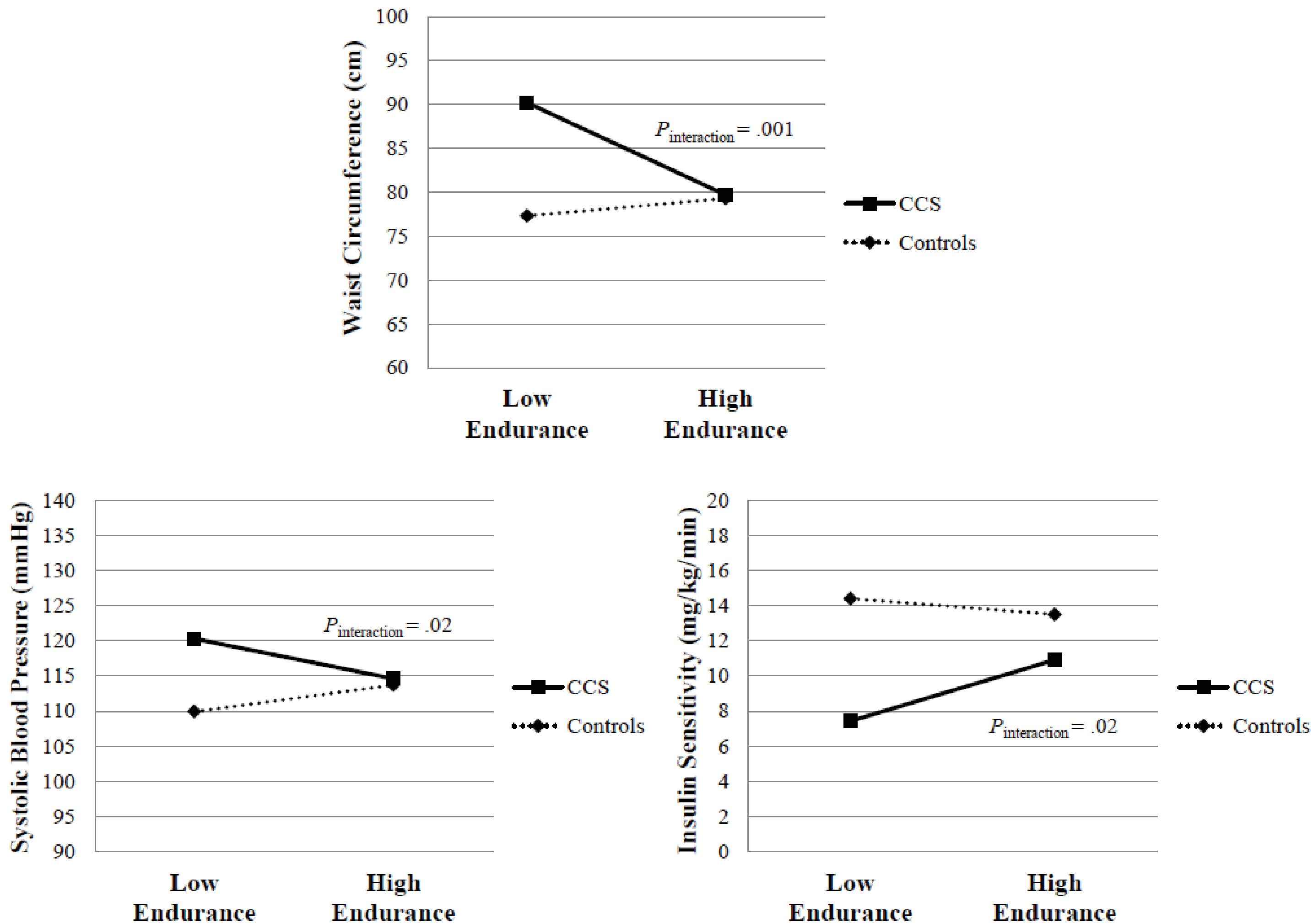


**Figure 4.** CCS/Control Status x Endurance Level (low versus high endurance) Interaction Plots for Waist Circumference, Systolic Blood Pressure, and Insulin Sensitivity



low and high mobility depended on CCS/control status (all $P_{interaction} < .05$). As depicted in Figure 4 and as displayed in the rightmost column of Table 8, differences in waist circumference, systolic blood pressure, and insulin sensitivity between low and high endurance depended on CCS/control status (all $P_{interaction} < .05$). In general, CCS had sharper reductions in waist circumference, triglycerides, and systolic blood pressure and a sharper increase in insulin sensitivity at the higher PA/fitness levels compared to controls. There was no such evidence of effect modification by CCS/control status for the other risk factors examined in Tables 6-9 (all $P_{interaction} > .05$).

**D.4. Discussion**

This study found that endurance, to a greater degree than mobility, strength, or self-reported PA, was associated with certain cardiometabolic risk factors in CCS with a history of HCT. Specifically, high endurance was associated with lower waist circumference and percent fat mass and greater insulin sensitivity among CCS. Similar patterns of leanness emerged among CCS with high mobility, although these differences did not reach statistical significance. Significantly lower waist circumference and marginally lower percent fat mass was also observed among CCS with high self-reported PA compared to low PA. Among controls, the only statistically significant association occurred between self-reported PA and diastolic blood pressure. However, a trend toward lower insulin resistance appeared among controls with high mobility and high endurance. Handgrip strength did not appear to be associated with any of the cardiometabolic risk factors in either CCS or controls.

In support of our findings, prior studies of healthy individuals have indicated that associations with obesity[113-115] and insulin sensitivity[114,116] are often stronger for measures of cardiorespiratory fitness than for measures of PA or muscle strength. Similar comparisons between PA and fitness measures have not been previously made in CCS. However, a recent 16-week home-based exercise intervention involving seventeen 16- to 30-year-old survivors of childhood acute lymphoblastic leukemia (ALL) without HCT resulted in significant improvements in waist circumference, waist-to-hip ratio, percent body fat, fasting plasma insulin, and HOMA-IR, while simultaneously improving $VO_2$ max, maximal work load, and muscle strength.[48] Weight, BMI, triglycerides, total cholesterol, LDL-C, HDL-C, and fasting plasma glucose remained unchanged and the effect on blood pressure was variable. Results were also mixed in a larger study of adult survivors of childhood ALL (6 of 117 had underwent HCT); greater PA energy expenditure was associated with lower percent body fat but not with BMI, waist circumference, HOMA-IR, or metabolic syndrome.[85]

Results from our interaction tests implied that PA, especially that which increases endurance, might work more effectively to decrease and/or maintain waist circumference in CCS than in controls. The interaction models also suggested that increases in endurance may lead to more effective improvement or maintenance of systolic blood pressure and insulin sensitivity, while increases in mobility may lead to more effective improvement or maintenance of triglyceride levels in CCS compared to controls. No known prior studies have made similar types of comparisons. These new findings support the use of PA interventions in CCS after HCT and highlight the importance of focusing on activities that improve endurance.

In general agreement with the literature,[110,117-119] CCS who had CNS irradiation as a part of their HCT preparative regimen had lower mobility, strength, and lean body mass and appeared to be at higher risk of dyslipidemia (low HDL-C and high triglycerides and/or LDL-C) when compared to one or more of the groups who did not receive CNS irradiation. These associations with CNS irradiation are thought to be partially explained by growth hormone deficiency, which results from damage to the hypothalamic-pituitary axis.[117,120] We also considered possible effects of HCT type (allogeneic versus autologous) and graft versus host disease (3 categories: chronic only or chronic plus acute, acute grades II-III, none or acute grade I). There were no statistically significant differences in PA, fitness, or cardiometabolic risk factors between HCT types or between categories of graft versus host disease severity.

To our knowledge, the current study is the first to examine associations between PA or fitness and cardiometabolic risk factors exclusively in HCT survivors. It is possible we lacked power to detect statistically significant differences for some of the risk factors examined; and conversely, some of the findings could have been due to chance. Further research in this population is needed to confirm our results. Using objective measures of PA/fitness, such as the fitness tests utilized in this study, is recommended over the use of less reliable self-report measures. Lastly, direct measures of abdominal subcutaneous and visceral fat mass (via computed tomography), vascular health (i.e., endothelial-dependent dilation, intima-media thickness, carotid artery cross-sectional compliance and distensibility), and knee extension strength were not available for a majority of participants in this study, but will be important to consider in future investigations.

This study serves to fill important gaps in knowledge regarding associations between PA/fitness and cardiometabolic risk factors among CCS with a history of HCT. Although it is not new to find an association between PA/fitness and cardiometbolic risk factors in healthy populations, results suggesting that these relationships are stronger in CCS than in controls are of importance, since they imply that PA could serve as a tangible target in mitigating the already high cardiometabolic risks of CCS. Sustainable PA programs focused on improving endurance and tailored to CCS are worth exploring as a means of reducing early morbidity and mortality.

## E. PROJECT 3: ACTIVE TRANSPORTATION IN ADULT SURVIVORS OF CHILDHOOD CANCER: RESULTS FROM THE TRANSPORTATION-RELATED ACTIVITIES OF CHILDHOOD CANCER SURVIVORS (TRACCS) STUDY

### E.1. Background

Rates of active transportation in the United States declined throughout the 1980s and 90s and continue to remain much lower than rates of motorized travel.[121] Data from the two most recent National Household Travel Surveys (NHTS) indicated small overall per capita increases in active transportation between 2001 and 2009.[122] The U.S. Census Bureau's 2008-2012 American Community Survey reported a 60% increase in the number of people traveling to work by bicycle since 2000 (0.6%, up from 0.4%), while the number of people walking to work remained stable at 2.8%.[121] Active transportation is correlated with higher levels of leisure-time and total PA in both children[123-125] and adults;[126,127] therefore, we might expect that CCS engage in active transportation less frequently than the general population since CCS are often less physically active overall.[3]

Common perceived barriers to using active transportation include personal (e.g., time availability, convenience, health), social (e.g., family and peer support) and environmental factors (e.g., availability and safety of sidewalks, bike paths and crosswalks).[128,129] In general, individuals who are more sedentary tend to underestimate the walkability of their own neighborhoods.[130,131] Thus, we would expect CCS to report experiencing a greater number of barriers and to perceive their environment as less walkable compared to controls.

The use of behavioral interventions has been one strategy used to combat low rates of active transportation and a few of the associated barriers identified by healthy adults. Promotional media campaigns, educational programs, bike-share programs, “bikepooling”, and active transportation challenges based in workplaces, schools, and communities are some of the intervention methods that have been utilized. Although previous interventions have been methodologically heterogeneous, many have demonstrated at least some improvement in the use of active transportation.[63,132,133] Despite promising findings, most of these studies have suffered from various methodological problems, including selection bias, low power, lack of valid/reliable measures of active transportation, and lack of assessment of long-term outcomes and sustainability. No known active transportation interventions have specifically targeted cancer survivors.

As discussed previously, CCS may benefit from interventions designed to increase PA, which might help prevent or mitigate various treatment-related late effects. Previous interventions relying on more traditional methodologies have been only moderately successful and might be improved by incorporating innovative strategies to increase PA. There is currently an absence of knowledge about the use of active transportation among CCS. We conducted the Transportation-Related Activities of Childhood Cancer Survivors (TRACCS) study to examine this topic for the first time.

## E.2. Methods

E.2.1. Study Design and Participants

The TRACCS study was a cross-sectional survey of adult CCS and matched neighborhood controls. It was approved by the Institutional Review Board Human Subjects Committee at the University of Minnesota. CCS were identified through patient databases from the University of Minnesota Long-term Follow-up and Hematology/Oncology clinics; all patients had provided written informed consent to be listed in clinic databases and contacted about future non-therapeutic studies. CCS aged 18 to 45 years who were diagnosed at least three years prior to the study with any form of pediatric (0-21 years of age) cancer, were not currently undergoing intravenous chemotherapy or radiation treatment, had a mailing address in the United States, and were able to complete a questionnaire in English were eligible to participate.

Controls were identified using lists of randomly selected names and addresses generated from infoUSA services from Infogroup (available at: http://www.infousa.com) and were matched to CCS (1:m matching) on sex, age (within five years), and location (within a one mile radius unless closest eligible control lived more than one mile away). For CCS living in a rural area without a matched control within one mile, we used an expanded radius of up to four miles. Eligible control participants were 18 to 45 years of age, had no history of cancer as a child or adult, and were able to complete a questionnaire in English.

Of the 531 eligible CCS identified, 74 could not be located. The remaining 457 were contacted by mail, and completed questionnaires were obtained from 161 (35%). Of the 1364 potentially eligible controls identified, 180 could not be located. The remaining 1184 were contacted by mail, and completed questionnaires were obtained from 215 (18%). Three CCS (currently undergoing chemotherapy and/or radiation treatment) and 62 controls (incorrect age or address, and/or had a history of cancer) were determined ineligible after completing the questionnaire, leaving a final study population of 158 CCS and 153 controls. Of the 130 CCS with at least one matched control, 112 (86%) were located within a one mile radius of their control(s). CCS participants were more likely to be female (54.4% vs 38.3%, $P = .001$), non-Hispanic white (94.9% vs 87.6%, $P = .02$), and a leukemia survivor (35.4% vs 23.7%, $P = .01$) compared to non-participants. Control participants were more likely to be female (62.7% vs 49.5%, $P = .0002$) and aged 35 years or older (29.4% vs 19.8%, $P = .02$) compared to non-participants.

E.2.3. Data Collection

Self-reported active transportation behaviors and perceptions as well as demographics and other covariates were ascertained via mailed paper questionnaire or over the phone with a trained interviewer (one participant). There were two versions of the TRACCS questionnaire, one for CCS and one for controls. See Appendix 3 and 4 for a copy of each version. The bulk of the questionnaire consisted of modified versions of the 7-item International Physical Activity Questionnaire (IPAQ – short, self-administered version),[134] the 6-item transportation portion (Part 2) of an adapted IPAQ (long, self-administered version),[135] the 18-item sections E., F., and V. from the Active Where?

Study adolescent survey,[136] and the unmodified 23-item section B. from the Neighborhood Environment Walkability Scale (NEWS).[137]

We modified the IPAQ to obtain usual transportation-related activity levels and other activity levels (occupational, household, and leisure-time domains combined) in summer, winter, and fall/spring to account for the seasonal variability in behavior typical of Minnesota and other Midwest states.[138] Activity levels were averaged over the four seasons to obtain usual hours per week of active transportation and other PA over the past year. Intraclass correlation (ICC) reliability coefficients for the original IPAQ range from 0.78 to 0.94.[139] Correlations between accelerometer-measured and IPAQ-measured physical activity are low (<0.4) but are reportedly a sign of fair criterion validity.[139]

Sections E., F., and V. of the Active Where? adolescent survey inquire about barriers to walking and biking to stores/restaurants, parks, and school, respectively. We modified the text slightly for age-appropriateness (i.e., included gyms/workout facilities in addition to parks and work in addition to school). Also, one additional subscale containing two health-related items (feeling too tired/fatigued and being limited by a physical or medical condition) was added to assess whether survivors disproportionately experience barriers potentially related to their disease and/or treatment. Individual items were grouped into four subscale scores (means of individual items) for analysis: environmental, planning/psychosocial, safety, and health. Participants can agree or disagree according to a four-point Likert scale (1=strongly disagree, 2=somewhat disagree, 3=somewhat agree, 4=strongly agree) as to whether a particular barrier makes it difficult to actively travel to a certain type of destination, thus a higher subscale score indicates a greater barrier to walking or cycling. ICC values for test-retest reliability range from 0.40 to 0.80 for individual items and from 0.56 to 0.81 for the original environmental, planning/psychosocial, and safety subscales.[140] Subscales have also demonstrated acceptable internal consistency (Cronbach's alphas 0.70-0.86) and good validity (t-tests showed those who walked/cycled reported significantly lower scores than those who did not walk/cycle).

The NEWS was designed to measure perceived neighborhood walkability; in other words, residents' perceptions of the environmental attributes of their neighborhood that are hypothesized to be related to active transportation.[141] The proximity to stores and facilities subscale (section B.) was included in the TRACCS questionnaire. Subscale scores can range from 1 to 5, with higher scores indicating greater perceived walkability. The test-retest ICC for this subscale was 0.78, and construct validity has been demonstrated through statistically significant differences between responses from residents of objectively defined high-walkability versus low-walkability neighborhoods.[137]

An objectively measured neighborhood walkability score, called Walk Score, was obtained on a publicly available website (available at: http://www.walkscore.com). Walk Score uses a geography-based algorithm to calculate walkability based on distance to 13 categories of amenities (e.g., grocery stores, coffee shops, restaurants, bars, movie theaters, schools, parks, libraries, bookstores, fitness centers, drugstores, hardware stores, clothing/music stores).[142] Each category is weighted equally and points are summed and normalized to yield a score from 0 to 100, with higher scores indicating greater walkability. Walk Score has been found to be valid and reliable for estimating access to nearby walkable amenities.[143,144] Walk Scores were obtained for all participants and non-participants, and participants' scores were compared to perceived walkability (i.e., NEWS proximity subscale). Walk Scores did not differ between participants and non-participants.

E.2.5. Statistical Analysis

All analyses were conducted with SAS version 9.2 (SAS Institute, Inc., Cary, NC). Descriptive statistics are expressed as frequencies and percents or mean ± standard error (SE), as appropriate. Correlations between perceived and objective walkability were examined using partial Pearson correlations adjusted for sex and age. All analyses that included matched controls, except Pearson correlations, were implemented in SAS's GENMOD procedure using generalized estimating equations (GEE) with robust variance estimates to account for clustering between matched participants. The exchangeable working correlation was used for all models with continuous and binary outcomes, while the default working correlation (independence) was used for those with multinomial outcomes due to SAS constraints.

Multivariable linear regression models with adjustments for BMI, income, and current smoking were used to compare measures of active transportation, non-transportation PA, barriers to active transportation, and neighborhood walkability (including interaction model for perceived versus objective walkability) between CCS and controls. Adjusted means were evaluated at the mean levels of covariates included in the models. Each independent variable was also entered into bivariate logistic regression models estimating the odds of engaging in active transportation (versus no active transportation). Variables with statistically significant odds ratios in bivariate analyses were included in a multivariable logistic regression model. All logistic regression analyses were performed separately for CCS and controls. A two-sided *P*-value <0.05 was considered to be statistically significant.

**E.3. Results**

Characteristics of CCS and controls are shown in Table 10. Controls were older, had higher household incomes, and were more likely to be female and a current smoker compared to CCS. BMI was marginally greater (26.5 *v* 25.2 kg/m$^2$, *P* = .06) in controls. There were no notable differences between CCS and controls in terms of race/ethnicity, education, the ratio of automobiles to drivers in the household, or the number of days required to go outside of the home for work, school, or volunteering.

Table 11 presents levels of active transportation and non-transportation PA, perceived barriers to active transportation, and perceived and objective neighborhood walkability scores. CCS and controls reported similar levels of active transportation and non-transportation PA (leisure, work, and household) and had comparable perceptions of environmental, planning/psychosocial, and safety barriers to active transportation. CCS scored significantly higher on the health barriers subscale (1.88 *v* 1.65, *P* = .01), meaning they were more likely to indicate that their health (i.e., feeling too tired/fatigued and/or

**Table 10.** Characteristics of CCS and Neighborhood Controls

| | CCS (N=158) | | Controls (N=153) | | |
|---|---|---|---|---|---|
| | N (%) | Mean ± SE | N (%) | Mean ± SE | *P* |
| **Sex** | | | | | |
| Male | 72 (45.6) | | 57 (37.3) | | .002 |
| Female | 86 (54.4) | | 96 (62.7) | | |
| **Age (years)** | | 29.0 ± 0.6 | | 30.9 ± 0.6 | .0001 |
| **Body Mass Index (kg/m$^2$)** | | 25.2 ± 0.5 | | 26.5 ± 0.5 | .06 |
| **Race/Ethnicity** | | | | | |
| White Non-Hispanic | 150 (94.9) | | 139 (90.9) | | .54 |
| Others | 8 (5.1) | | 10 (6.5) | | |
| Missing | -- | | 4 (2.6) | | |
| **Married or living with a partner** | | | | | |
| No | 92 (58.2) | | 64 (41.8) | | .001 |
| Yes | 64 (40.5) | | 85 (55.6) | | |
| Missing | 2 (1.3) | | 4 (2.6) | | |
| **Education** | | | | | |
| ≤ High school graduate or GED | 26 (16.5) | | 19 (12.4) | | .70 |
| Some college | 43 (27.2) | | 46 (30.1) | | |
| College graduate or more | 87 (55.1) | | 84 (54.9) | | |
| Missing | 2 (1.3) | | 4 (2.6) | | |
| **Household Income** | | | | | |
| ≤$20,000 | 28 (17.7) | | 17 (11.1) | | .001 |
| >$20,000-$40,000 | 24 (15.2) | | 16 (10.5) | | |
| >$40,000-$60,000 | 32 (20.3) | | 21 (13.7) | | |
| >$60,000-$100,000 | 34 (21.5) | | 52 (34.0) | | |
| >$100,000 | 28 (17.7) | | 41 (26.8) | | |
| Missing | 12 (7.6) | | 6 (3.9) | | |
| **Household Motor Vehicles (vehicles/driver)** | | | | | |
| <1 vehicle per driver | 23 (14.6) | | 15 (9.8) | | .18 |
| ≥1 vehicle per driver | 133 (84.2) | | 138 (90.2) | | |
| Missing | 2 (1.3) | | -- | | |
| **Days Required to Go Outside Home for Work/School/ Volunteering** | | | | | |
| 0-2 days per week | 24 (15.2) | | 15 (9.8) | | .88 |
| 3-4 days per week | 22 (13.9) | | 19 (12.4) | | |
| 5 days per week | 64 (40.5) | | 84 (54.9) | | |
| 6-7 days per week | 46 (29.1) | | 31 (20.3) | | |
| Missing | 2 (1.3) | | 4 (2.6) | | |
| **Current Smoker** | | | | | |
| No | 147 (93.0) | | 131 (85.6) | | .03 |
| Yes | 11 (7.0) | | 22 (14.4) | | |
| **Diagnosis** | | | | | |
| Leukemia (ALL, AML) | 56 (35.4) | | | | |
| Lymphoma (HOD, NHL) | 31 (19.6) | | NA | | |
| Osteosarcoma | 19 (12.0) | | | | |
| Central nervous system | 16 (10.1) | | | | |
| Others | 36 (22.8) | | | | |
| **Years since Diagnosis** | | 18.4 ± 0.7 | | NA | |

Abbreviations: CCS, childhood cancer survivors; NA, not applicable; SE, standard error.

**Table 11.** Self-Reported Active Transportation and Non-transportation Physical Activity, Perceived Barriers to Active Transportation, and Perceived and Objective Neighborhood Walkability in CCS and Controls

| | CCS (N=158) | | Controls (N=153) | | |
|---|---|---|---|---|---|
| | Mean ± SE[a] | N (%) | Mean ± SE[a] | N (%) | $P^{a}$ |
| **Active Transportation (hours/week)** | 2.72 ± 0.49 | | 2.32 ± 0.50 | | .40 |
| No Active Transportation | | 56 (35.4) | | 53 (34.6) | .39 |
| Some Active Transportation | | 98 (62.0) | | 98 (64.1) | |
| Missing | | 4 (2.5) | | 2 (1.3) | |
| **Non-transportation PA (hours/week)** | 18.2 ± 1.6 | | 17.2 ± 1.7 | | .52 |
| **Barriers to Active Transportation[b]** | | | | | |
| Environment | 2.04 ± 0.07 | | 2.07 ± 0.07 | | .70 |
| Planning/Psychosocial | 1.96 ± 0.07 | | 2.02 ± 0.06 | | .42 |
| Safety | 1.41 ± 0.06 | | 1.41 ± 0.07 | | .90 |
| Health | 1.88 ± 0.08 | | 1.65 ± 0.07 | | .01 |
| **Neighborhood Walkability** | | | | | |
| Perceived[c] | 2.13 ± 0.10 | | 2.24 ± 0.11 | | .21 |
| Objective (Walk Score)[d] | 29.3 ± 2.5 | | 30.4 ± 2.6 | | .39 |
| Car-Dependent (0-49) | | 123 (77.9) | | 118 (77.1) | |
| Somewhat Walkable (50-70) | | 25 (15.8) | | 23 (15.0) | |
| Very Walkable (70-100) | | 10 (6.3) | | 12 (7.8) | |
| | Partial Pearson Correlation[e] | *P* | Partial Pearson Correlation[e] | *P* | $P_{interaction}^{a}$ |
| **Perceived Walkability versus Objective Walkability** | 0.62 | <.0001 | 0.65 | <.0001 | .42 |

Abbreviations: CCS, childhood cancer survivors; PA, physical activity; SE, standard error.
[a] Adjusted for body mass index, income, smoking, and clustering of matched participants (matched on sex, age, and location).
[b] Measured on four-point Likert scales, where 1=strongly disagree, 2=somewhat disagree, 3=somewhat agree, and 4=strongly agree that a particular barrier makes it difficult to actively travel.
[c] Scores range from 1 to 5, with higher scores indicating greater perceived walkability.
[d] Walk Scores range from 0 to 100, with higher scores indicating greater walkability.
[e] Adjusted for sex and age.

**Table 12.** Odds of Engaging in Active Transportation among CCS and Controls

| | CCS (N=158) | | Controls (N=153) | |
|---|---|---|---|---|
| | Unadjusted OR (95% CI) | Adjusted[a] OR (95% CI) | Unadjusted[b] OR (95% CI) | Adjusted[a,b] OR (95% CI) |
| **Sex (ref = male)** | 0.62 (0.31-1.21) | -- | 0.70 (0.34-1.46) | -- |
| **Age (years)** | **0.91 (0.86-0.95)** | 0.96 (0.86-1.07) | 0.96 (0.91-1.01) | -- |
| **Body Mass Index (kg/m$^2$)** | **0.94 (0.88-0.99)** | 0.94 (0.86-1.03) | 0.99 (0.95-1.04) | -- |
| **White Non-Hispanic (ref = others)** | 0.09 (0.01-1.98) | -- | 3.25 (0.76-13.8) | -- |
| **Education** | | | | |
| ≤ High school graduate or GED (ref) | 1.00 | -- | 1.00 | -- |
| Some college | 1.85 (0.67-5.09) | -- | 0.65 (0.16-2.62) | -- |
| College graduate or more | 1.69 (0.69-4.17) | -- | 0.97 (0.26-3.60) | -- |
| **Household Income** | | | | |
| ≤$20,000 (ref) | 1.00 | -- | 1.00 | 1.00 |
| >$20,000-$40,000 | 0.69 (0.20-2.46) | -- | 1.65 (0.49-5.60) | 2.20 (0.56-8.60) |
| >$40,000-$60,000 | 0.33 (0.10-1.04) | -- | 1.43 (0.38-5.41) | 1.29 (0.31-5.39) |
| >$60,000-$100,000 | 0.39 (0.12-1.21) | -- | **3.60 (1.21-10.7)** | 3.25 (0.98-10.8) |
| >$100,000 | 0.33 (0.10-1.07) | -- | 1.04 (0.38-2.84) | 1.13 (0.35-3.68) |
| **Married or living with a partner (ref = no)** | **0.27 (0.13-0.53)** | **0.28 (0.10-0.75)** | 0.60 (0.32-1.13) | -- |
| **Vehicles per driver** | **0.13 (0.04-0.48)** | 0.14 (0.01-1.33) | 0.33 (0.11-1.01) | -- |
| **Days Required to Go Outside Home for Work/School/Volunteering** | | | | |
| 0-2 days per week (ref) | 1.00 | -- | 1.00 | -- |
| 3-4 days per week | 1.05 (0.32-3.48) | -- | 0.57 (0.16-2.05) | -- |
| 5 days per week | 0.78 (0.30-2.05) | -- | 0.92 (0.29-2.89) | -- |
| 6-7 days per week | 1.60 (0.55-4.62) | -- | 0.75 (0.21-2.67) | -- |
| **Current Smoker (ref = no)** | 0.30 (0.08-1.07) | -- | 1.70 (0.62-4.62) | -- |
| **Diagnosis** | | | NA | NA |
| Leukemia (ALL, AML) (ref) | 1.00 | -- | | |
| Lymphoma (HOD, NHL) | 0.67 (0.27-1.68) | -- | | |
| Osteosarcoma | 0.93 (0.31-2.76) | -- | | |
| Central nervous system | 0.54 (0.18-1.68) | -- | | |
| Others | 1.63 (0.64-4.16) | -- | | |

| | | | | |
|---|---|---|---|---|
| **Years since Diagnosis** | **0.93 (0.90-0.97)** | 0.99 (0.92-1.07) | NA | NA |
| **Leisure/work/household PA (hours/week)** | 1.01 (0.99-1.04) | -- | 1.02 (0.99-1.04) | -- |
| **Environmental Barriers[c]** | **0.36 (0.20-0.65)** | 1.52 (0.55-4.19) | 1.27 (0.71-2.29) | -- |
| **Planning/Psychosocial Barriers[c]** | **0.27 (0.14-0.53)** | **0.15 (0.04-0.53)** | 1.22 (0.73-2.06) | -- |
| **Safety Barriers[c]** | 0.67 (0.34-1.34) | -- | 2.01 (0.80-5.07) | -- |
| **Health Barriers[c]** | **0.64 (0.43-0.95)** | 1.19 (0.64-2.22) | 1.05 (0.70-1.58) | -- |
| **Perceived Walkability[d]** | **2.91 (1.76-4.83)** | **2.38 (1.05-5.40)** | **1.73 (1.08-2.77)** | 0.97 (0.51-1.86) |
| **Objective Walkability[e]** | **1.02 (1.01-1.04)** | 1.01 (0.99-1.04) | **1.03 (1.01-1.05)** | **1.03 (1.01-1.05)** |

Abbreviations: CCS, childhood cancer survivors; CI, confidence interval; NA, not applicable; OR, odds ratio.
Bolded ORs and 95% CIs indicate statistical significance (*P* < .05).
[a] Adjusted for variables that were significantly related to the dependent variable in unadjusted analyses.
[b] Adjusted for clustering of matched controls (matched on sex, age, and location).
[c] Measured on four-point Likert scales, where 1=strongly disagree, 2=somewhat disagree, 3=somewhat agree, and 4=strongly agree that a particular barrier makes it difficult to actively travel.
[d] Scores range from 1 to 5, with higher scores indicating greater perceived walkability.
[e] Walk Scores range from 0 to 100, with higher scores indicating greater walkability.

being limited by a physical or medical condition) makes it difficult to walk or bike for transportation. Perceived and objective neighborhood walkability did not differ between CCS and controls. Furthermore, the correlation between perceived and objective walkability was similar for CCS and controls ($P_{\text{interaction}}$ = .42).

Table 12 includes unadjusted and adjusted odds ratios for potential correlates of active transportation. In bivariate (unadjusted) models, CCS who were older, had a higher BMI, were married or living with a partner, had access to more vehicles, had been diagnosed less recently, and perceived greater environmental, planning/psychosocial, and health barriers were less likely to engage in active transportation. CCS who lived in a more walkable neighborhood and perceived their neighborhood as more walkable (i.e., greater objective and perceived walkability) were more likely to engage in active transportation. After combining all statistically significant correlates into one adjusted model, marital/relationship status, planning/psychosocial barriers, and perceived walkability remained significant correlates of active transportation in CCS. Among controls, those with a higher household income and greater perceived and objective walkability were more likely to engage in active transportation in unadjusted models. Objective walkability remained the only statistically significant correlate in the adjusted model.

## E.4. Discussion

Results from the TRACCS study suggest that adult CCS engage in similar levels of active transportation as controls despite facing greater health-related barriers. CCS and controls also had comparable perceptions of neighborhood walkability and reported experiencing similar environmental, planning/psychosocial, and safety-related barriers to active transportation. Given the high prevalence of chronic health conditions in CCS, we expected health to be a greater barrier to active transportation in CCS than in controls. Although the difference in the health subscale between CCS and controls was statistically significant, it may be too small (0.23 on a 4-point Likert scale) to translate into appreciable differences in behavior. Moreover, CCS likely encounter other factors that influence their transportation choices to a greater degree than their health. As the adjusted logistic regression model suggested, marital/relationship status, planning/psychosocial barriers, and perceived neighborhood walkability may have more influence on active transportation behaviors than health barriers among CCS. Among controls, living in a more walkable neighborhood appeared to be the predominant indicator of active transportation behavior.

Although no prior studies have examined active transportation in CCS nor compared active transportation between cancer survivors and controls, we are able to compare some of our findings with those from studies of adults from the general population. TRACCS participants and adults from previous studies that used the long, past seven days version of the IPAQ reported comparable levels of active transportation. In TRACCS, 62% of CCS and 64% of controls engaged in active transportation, with averages of 2.7 and 2.3 hours per week, respectively. Van Dyck et al. found approximately 68% of study participants from the Seattle and Baltimore regions engaged in any transport-related walking, with an average of 2.6 to 2.9 hours per week of combined walking and cycling for transportation.[145] Hearst et al. also noted an average of 2.6 hours per week of active transportation among participants from the Minneapolis/St Paul metropolitan area.[146]

Levels of active transportation in the U.S. have been shown to generally decrease with age, income, and vehicle access/availability and are lower among females.[121] Those with a graduate or professional degree and those who did not graduate from high school typically have the highest levels of active transportation. Non-Hispanic Whites tend to have the lowest levels of walking, while Blacks tend to have the lowest levels of bicycling.[121] There is limited or mixed evidence across studies for associations between active transportation and body weight, other physical activity, marital/relationship status, and smoking.[64,147-149] Although no other known studies have examined the actual number of days required to travel outside the home, there is evidence to suggest that individuals who work less than full time are more likely to use active transportation.[64,150] We saw comparable, albeit mostly non-significant, trends for age, vehicle access/availability, and sex in this study, along with similarly mixed results for BMI, other physical activity, marital/relationship status, and smoking.

Individuals who perceive greater barriers to active transportation (i.e., have low perceived behavioral control) typically engage in less active transportation, as do those who live in less walkable neighborhoods (lower objective walkability).[151,152] Greater access (perceived and objective) to destinations has been the most consistent individual environmental correlate of active transportation despite a fair amount of discordance between objective and perceived walkability.[130,142,151,153,154] Other environmental correlates such as street connectivity, aesthetics, and the presence of sidewalks have shown mixed results, along with measures of social support and safety.[151] No known studies have directly examined health-related barriers to active transportation, but some have shown that perceived health status, physical wellbeing, and/or reported number of chronic diseases are associated with active commuting to work.[150,155-157] Overall, there were mixed results for environmental, planning/psychosocial, safety, and health barriers in this study.

Notably, higher Walk Scores have been associated with lower odds of not walking for transportation and with more minutes per week of walking for transportation.[158] Our results were consistent with this evidence, as higher Walk Scores were associated with active transportation in unadjusted models among CCS and controls and in fully adjusted models among controls. Self-selection, or personal preferences for residential neighborhoods based on travel preferences, may play a role in these observations, however. Evidence from studies that have attempted to account for the effects of self-selection suggests the built environment remains a significant predictor of active transportation behavior after controlling for the partial explanation provided by self-selection.[151] Unfortunately, a measure of self-selection was not available in this study.

We would have also liked to examine the presence of children in the household, since having children has been associated with lower levels of active transportation,[121] but lacked a proper measure. Although the TRACCS survey ascertained the number of adults and children in the household, an unknown number of participants still lived at home with their parent(s) and/or sibling(s); thus we were unable to determine whether the children listed were underage siblings, dependents, or other relatives/non-relatives. Relying on self-reported cross-sectional data created other limitations in this study, including possible misclassification due to inaccurate recall of activities, non-responder bias, and the inability to accurately assess changes in behaviors and perceptions over time. It would particularly be of interest to know how survivors' behaviors and perceptions have changed from before diagnosis to during and after treatment. Longitudinal studies may be warranted to explore potential changes and patterns. If feasible, objective measures of active transportation such as pedometers, bike odometers, or GPS tracking, could be used in combination with self-report measures to improve accuracy.

The TRACCS study had some important strengths in addition to being the first to investigate active transportation among CCS. The use of matched neighborhood controls allowed for more efficient control of both known and unknown (i.e., neighborhood-level) covariates in the analysis and permitted us to check for spatial correlation in the data, of which there was none. Unlike most studies, ours was able to account for seasonal variations in behavior by asking participants to recall their usual patterns of travel during a typical week in the summer, winter, and fall/spring seasons. Lastly, using Walk Score, which uses the Google application programming interface to regularly update geographic data, helped avoid temporal problems that afflict GIS data sets.[142]

According to our findings, CCS and matched neighborhood controls have generally similar active transportation behaviors and perceptions. Although CCS consider their health to be a greater barrier to active transportation compared to controls, other factors appear to influence their behavior to a greater degree than their health. This evidence supports exploring the use of active transportation interventions in CCS to incorporate more moderate-intensity PA into their daily lives. Such interventions are more likely to be effective if participants live in highly walkable/bikeable communities. Additional research is needed to confirm these results and investigate the feasibility and efficacy of active transportation interventions in this population.

## F. CONCLUSIONS

The findings of this dissertation suggest that efforts to increase PA and endurance in CCS may reduce the risk of future cardiovascular disease by improving certain cardiometabolic risk factors. Abdominal obesity, as measured by abdominal subcutaneous and visceral fat in Project 1 and by waist circumference in Project 2, was the most consistent correlate of PA and endurance. Comparing results from Projects 1 and 2 also revealed that small PA-related differences in insulin sensitivity (independent of percent fat mass) during childhood may become more apparent during adulthood. Early implementation of strategies to increase PA in this population is therefore an important consideration.

Interventions targeting CCS might also consider promoting active transportation as a potentially more moderate and sustainable PA option, since results indicated it is as well accepted in CCS as in healthy adults. These types of interventions will not be widely successful, however, without existing or improved pedestrian and bicycle infrastructure, safety, and access to local amenities in all communities. Further research is needed to confirm our findings, explore potential mechanisms underlying observed associations, and examine the feasibility and efficacy of active transportation interventions in this population.

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## H. APPENDICES

### H.1. Appendix 1

**Modifiable Activity Questionnaire for Adolescents**

1. How many times in the past 14 days have you done at least 20 minutes of exercise **hard** enough to make you breathe heavily and make your heart beat fast? (Hard exercise includes, for example, playing basketball, jogging, or fast bicycling; include time in physical education class)

- ☐ None
- ☐ 1 to 2 days
- ☐ 3 to 5 days
- ☐ 6 to 8 days
- ☐ 9 or more days

2. How many times in the past 14 days have you done at least 20 minutes of **light** exercise that was **not hard** enough to make you breathe heavily and make your heart beat fast? (Light exercise includes playing basketball, walking or slow bicycling; include time in physical education class)

- ☐ None
- ☐ 1 to 2 days
- ☐ 3 to 5 days
- ☐ 6 to 8 days
- ☐ 9 or more days

3. During a normal week, how many **hours a day** do you watch television and videos, or play computer games before or after school or work?

- ☐ None
- ☐ 1 hour or less
- ☐ 2 to 3 hours
- ☐ 4 to 5 hours
- ☐ 6 or more hours

Continue to next page.

4. During the past 12 months, how many team or individual **sports** or activities did you participate in on a **competitive** level, such as varsity or junior varsity sports, intramurals, or out of school programs?

- ☐ None
- ☐ 1 activity
- ☐ 2 activities
- ☐ 3 activities
- ☐ 4 or more activities

What activities did you compete in?

________________________________________

________________________________________

________________________________________

________________________________________

________________________________________

Continue to next page.

Past Year Leisure-Time Physical Activity

Circle all activities that you did **at least 10 times** in the **past year.** Do not include time spent in physical education classes. Make sure you include all sport teams that you participated in during the **past year**.

| | | |
|---|---|---|
| Aerobics | Gymnastics | Swimming (laps) |
| Band/Drill Team | Hiking | Tennis |
| Baseball | Ice Skating | Volleyball |
| Basketball | Roller Skating | Water Skiing |
| Bicycling | Running for exercise | Weight Training (competitive) |
| Bowling | Skateboarding | Wrestling |
| Cheerleading | Snow Skiing | Others: |
| Dance Class | Soccer | ____________________ |
| Football | Softball | ____________________ |
| Garden/Yard Work | Street Hockey | ____________________ |

List each activity that you checked above in the “Activity” box below.
Check the months of the year that you did each activity and then estimate the amount of time spent in each activity.

| Activity | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Months per Year | Days per Week | Minutes per Day |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| EXAMPLE: Jogging | | | | X | X | X | X | X | X | | | | 6 | 4 | 30 |
| | | | | | | | | | | | | | | | |
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## H.2. Appendix 2

# Modifiable Activity Questionnaire

1. Please circle all activities listed below that you have done more than 10 times in the past year

| | | |
|---|---|---|
| Jogging (outdoor, treadmill) …. 1 | Football/Soccer …..……..….. 14 | Stair Master …………..…............... 27 |
| Swimming (laps, snorkeling) .... 2 | Racquetball/Handball/Squash 15 | Fencing …………………................ 28 |
| Bicycling (indoor, outdoor) ….. 3 | Horseback riding …..............… 16 | Hiking ………………….................. 29 |
| Softball/Baseball ………..……. 4 | Hunting ……………………..….. 17 | Tennis ………………...……..…...… 30 |
| Volleyball ……………………. 5 | Fishing ……………………….... 18 | Golf ……………………………….. 31 |
| Bowling ……………………… 6 | Aerobic Dance/Step Aerobic 19 | Canoeing/Rowing/Kayaking ……… 32 |
| Basketball ……………………. 7 | Water Aerobics …………..…. 20 | Water skiing ………………………. 33 |
| Skating (roller, ice, blading) … 8 | Dance (square, line, ballrm) 21 | Jumping rope ……………...………. 34 |
| Martial Arts (Karate, Judo) ...... 9 | Gardening or Yardwork ….... .22 | Snow skiing (X-country/Nordic trk) 35 |
| Tai Chi …………………….... 10 | Badminton ………………….. 23 | (downhill) ….......………... 36 |
| Calisthenics/Toning exercises 11 | Strength/Weight training …... 24 | Snow shoeing ……………………... 37 |
| Wood chopping ………….... 12 | Rock climbing ……………… 25 | Yoga ………………………………. 38 |
| Water/Coal hauling ……….. 13 | Scuba diving ……………….. 26 | Other ……………………………… 39 |

Walking for exercise (outdoor, indoor at mall or fitness center, treadmill) ……………………………..................…. 40

List each activity that you circled in the "Activity" box below, check the months that you did each activity over the past year (12 months) and then estimate the average amount of time spent in that activity.

| Activity | JAN | FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC | Average # of times per month | Average # of minutes each time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | |
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2. In general, how many HOURS per DAY do you usually spend watching television? ________ hrs

3. Over this past year, have you spent more than one week confined to a bed or a chair as a result of an injury, illness or surgery? Yes________ No________
   If yes, how many weeks over this past year were you confined to a bed or a chair? ______weeks

4. Do you have difficulty doing any of the following activities?
   a. getting in or out of a bed or chair? Yes________ No________
   b. walking across a small room without resting? Yes________ No________
   c. walking for 10 minutes without resting? Yes________ No________

5. Did you ever compete in an individual or team sport (not including any time spent in sports performed during school physical education classes)? Yes________ No________

If yes, how many total years did you participate in competitive sports? ________ yrs

6. Have you had a job for more than one month over the past year? Yes________ No________

List all JOBS that you held over the past year for more than one month. Account for all 12 months of the past year. If unemployed/disabled/retired/homemaker/student during all or part of the past year, list as such.

| Job Name | Job Code | Walk or bicycle to/from work | AVERAGE JOB SCHEDULE | | | Out of the total # of "Hrs/Day" you reported working at a job, how much of this time was usually spent sitting? Enter this # in "Hrs Sitting" column, then place a check in the category which best describes your job activities when you were not sitting. | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Hrs spent sitting at work | Check the category that best describes job activities when not sitting | | |
| | | Min/Day | Mos/Yr | Day/Wk | Hrs/Day | Hrs Sitting | A | B | C |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

**Category A**

(includes all sitting activities)

Sitting

Standing still w/o heavy lifting
Light cleaning - ironing, cooking, washing, dusting
Driving a bus, taxi, tractor
Jewelry making/weaving

General office work
Occasional/short distance walking

**Category B**

(includes most indoor activities)

Carrying light loads

Continuous walking
Heavy cleaning - mopping, sweeping, scrubbing, vacuuming
Gardening - planting, weeding
Painting/plastering

Plumbing/welding
Electrical work
Sheep herding

**Category C**

(heavy industrial work, outdoor construction, farming)

Carrying moderate to heavy loads
Heavy construction
Farming - mowing, digging - mowing, raking
Digging ditches, shoveling
Chopping (ax), sawing wood
Tree/pole climbing
Water/coal/wood hauling

**JOB CODES**

Not employed outside of the home:

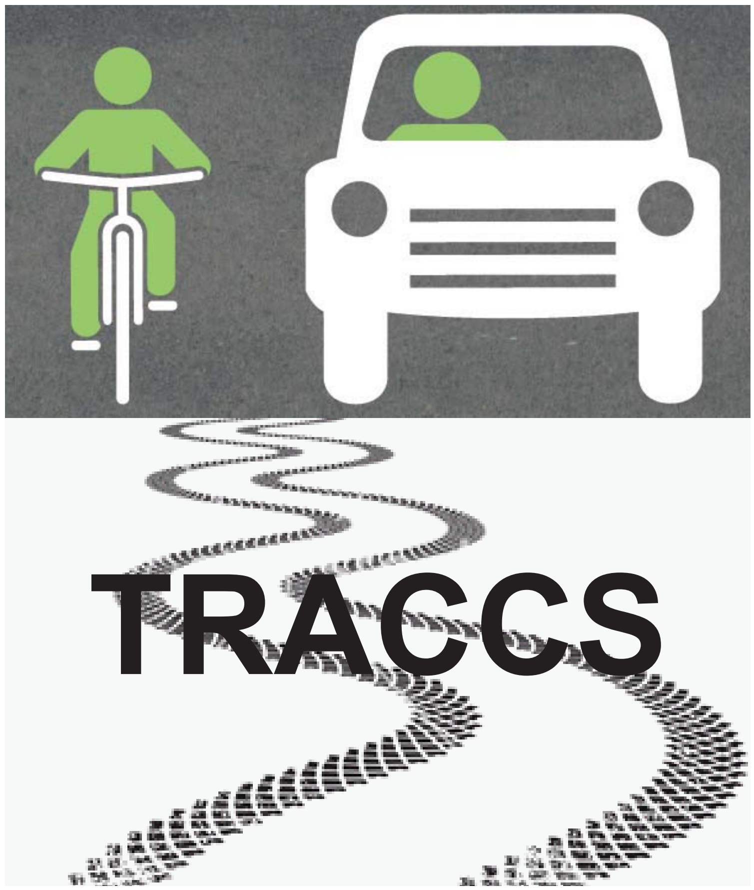
1. Student
2. Home Maker
3. Retired
4. Disabled
5. Unemployed

Employed (or volunteer):

6. Armed Services
7. Office worker
8. Non-office worker

**H.3. Appendix 3: TRACCS Questionnaire for Survivors**

UNIVERSITY OF MINNESOTA




# Transportation-Related Activities of Childhood Cancer Survivors (TRACCS) Study Questionnaire

**University of Minnesota**
**Department of Pediatrics**
**2013**

# How to fill out this survey

Please take about 30 minutes to fill out this survey. It asks for information about your walking and biking activities, other exercise and health habits, current medical issues, and your neighborhood environment. Please answer every question as best you can. If you do not know the answer to a question, please provide your best guess.

For some questions, you will **PUT AN X OR ✓ IN THE BOX** that goes with your answer, like this:

1. Are you? 1 ☒ Male 2 ☐ Female **OR** 1 ☑ Male 2 ☐ Female

You will sometimes be told to skip over some questions in this survey. When this happens, you will see an arrow with a note that tells you what questions to answer next, like this:

☐ Yes ⟶ ***Go to page 6 question 13.***

For some questions, you will enter letters or numbers in boxes or on lines, like this:

| A | B | 2 | 8 | **OR** AB28

For some questions, you will circle your answer, like this:

| | 1<br>strongly<br>disagree | 2<br>somewhat<br>disagree | 3<br>somewhat<br>agree | 4<br>strongly<br>agree |
|---|---|---|---|---|
| 2. The route is boring | 1 | (2) | 3 | 4 |

## Transportation activities

Today's Date: ☐☐ / ☐☐ / ☐☐☐☐
month day year

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spend being physically active in a **usual week during the summer, winter, and spring/fall**. Please consider only your usual activities **during the past year**. Please answer each question even if you do not consider yourself to be an active person.

The first 6 questions are about how you **travel** from place to place, including places like work, stores, movies, and so on.

**1.** During a **usual week**, on how many days do you **travel in a motor vehicle** like a train, bus, car, or tram?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No traveling in a motor vehicle ⟶ ***Go to page 4 question 3.***

**2.** How much time do you **usually** spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

Now think only about the **bicycling** and **walking** you do to travel to and from work, to do errands, or to go from place to place.

**3.** During a **usual week**, on how many days do you **bicycle** to go **from place to place**?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No bicycling from place to place ⟶ ***Go to question 5 below.***

**4.** How much time do you usually spend on one of those days to **bicycle** from place to place?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**5.** During a **usual week**, on how many days do you **walk** to go **from place to place**?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No walking from place to place ⟶ ***Go to page 5 question 7.***

**6.** How much time do you usually spend on one of those days **walking** from place to place?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

## Work, home, and leisure-time physical activity

Please think about the usual activities you have done **during the past year** at work, as part of your house and yard work, and in your spare time for recreation, exercise, or sport. The questions will ask about the following types of activities in four separate sections: A) vigorous activities, B) moderate activities, C) walking activities, and D) sitting activities. Please **do not include any transportation-related activities** you have already mentioned.

**A)** Think about all the **vigorous** activities that you do in a **usual week during the summer, winter, and spring/fall. Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

**7.** During a **usual week**, on how many days do you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No vigorous physical activities ⟶ ***Go to page 6 question 9.***

**8.** How much time do you usually spend doing **vigorous** physical activities on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**B)** Think about all the **moderate** activities that you do in a **usual week during the summer, winter, and spring/fall** at work, as part of your house and yard work, and in your spare time for recreation, exercise, or sport. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those activities that you did for at least 10 minutes at a time.

**9.** During a **usual week**, on how many days do you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Please **<u>do not include</u>** walking.

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No moderate physical activities ⟶ ***Go to page 7 question 11.***

**10.** How much time do you usually spend doing **moderate** physical activities on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**C)** Think about the time you spend **walking** in a **usual week during the summer, winter, and spring/fall.** This includes at work and at home and any other walking that you might do solely for recreation, sport, exercise, or leisure. Please **do not include** any transportation-related walking you have already mentioned.

**11.** During a **usual week**, on how many days do you **walk** at least 10 minutes at a time?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No walking ⟶ ***Go to question 13 below.***

**12.** How much time do you usually spend **walking** on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**D)** This question is about the time you spend **sitting** on weekdays during a **usual week during the summer, winter, and spring/fall**. Include time spent at work, at home, while doing schoolwork, and during leisure time.

**13.** During a **usual week**, how much time do you spend **sitting** on a **week day**?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

## Barriers to walking and biking to local parks/gyms/recreational facilities

Please circle the answer that best applies to you.

| | | |
|---|---|---|
| **1a.** Are there parks, gyms, and/or recreational facilities within a 15-minute walk or bike from your home? | Yes | No |
| **1b.** If yes, do you walk or bike to get there (alone or with someone)? | Yes | No |

Do you agree or disagree with the following statements:

It is difficult to walk or bike to local parks/gyms/recreational facilities (alone or with someone) because…

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):________________________ | 1 | 2 | 3 | 4 |

## Barriers to walking and biking to shops and restaurants

Please circle the answer that best applies to you.

| | | |
|---|---|---|
| **1a.** Are there shops, restaurants, or food stores within a 15-minute walk or bike from your home? | Yes | No |
| **1b.** If yes, do you walk or bike to get there (alone or with someone)? | Yes | No |

Do you agree or disagree with the following statements:

It is difficult to walk or bike to the local stores and restuarants (alone or with someone) because…

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):________________________ | 1 | 2 | 3 | 4 |

## Barriers to walking and biking to work or school

Please circle the answer that best applies to you.

| | | | |
|---|---|---|---|
| **1a.** Is your work or school within a 30-minute walk or bike from your home? | Yes | No | N/A |
| **1b.** Do you walk or bike to work or school at least once per week? | Yes | No | N/A |

***If you do not attend school or work outside your home, please skip to page 11***

Do you agree or disagree with the following statements:
It is difficult to walk or bike to work or school (alone or with someone) because...

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):________________________ | 1 | 2 | 3 | 4 |

## Stores, facilities, and other things in your neighborhood

About how long would it take to get from your home to the nearest businesses or facilities listed below if you walked to them? Please circle only one option for each business or facility.

| | 1-5 min | 6-10 min | 11-20 min | 20-30 min | 30+ min | don't know |
|---|---|---|---|---|---|---|
| **Example:** gas station | 1 | 2 | (3) | 4 | 5 | 6 |
| **1.** convenience/small grocery store | 1 | 2 | 3 | 4 | 5 | 6 |
| **2.** supermarket | 1 | 2 | 3 | 4 | 5 | 6 |
| **3.** hardware store | 1 | 2 | 3 | 4 | 5 | 6 |
| **4.** fruit/vegetable market | 1 | 2 | 3 | 4 | 5 | 6 |
| **5.** laundry/dry cleaners | 1 | 2 | 3 | 4 | 5 | 6 |
| **6.** clothing store | 1 | 2 | 3 | 4 | 5 | 6 |
| **7.** post office | 1 | 2 | 3 | 4 | 5 | 6 |
| **8.** library | 1 | 2 | 3 | 4 | 5 | 6 |
| **9.** elementary school | 1 | 2 | 3 | 4 | 5 | 6 |
| **10.** other schools | 1 | 2 | 3 | 4 | 5 | 6 |
| **11.** book store | 1 | 2 | 3 | 4 | 5 | 6 |
| **12.** fast food restaurant | 1 | 2 | 3 | 4 | 5 | 6 |
| **13.** coffee place | 1 | 2 | 3 | 4 | 5 | 6 |
| **14.** bank/credit union | 1 | 2 | 3 | 4 | 5 | 6 |
| **15.** non-fast food restaurant | 1 | 2 | 3 | 4 | 5 | 6 |
| **16.** video store | 1 | 2 | 3 | 4 | 5 | 6 |
| **17.** pharmacy/drug store | 1 | 2 | 3 | 4 | 5 | 6 |
| **18.** salon/barber shop | 1 | 2 | 3 | 4 | 5 | 6 |
| **19.** your job or school [check here__if not applicable] | 1 | 2 | 3 | 4 | 5 | 6 |
| **20.** bus or train stop | 1 | 2 | 3 | 4 | 5 | 6 |
| **21.** park | 1 | 2 | 3 | 4 | 5 | 6 |
| **22.** recreation center | 1 | 2 | 3 | 4 | 5 | 6 |
| **23.** gym or fitness facility | 1 | 2 | 3 | 4 | 5 | 6 |

## Cancer treatment information

**1.** Which of the following did you receive as part of your treatment for cancer? (*Mark all that apply*)

1 ☐ Radiation
2 ☐ Chemotherapy (intravenous (IV) or oral)
3 ☐ Bone marrow or stem cell transplant
4 ☐ Surgery
5 ☐ Other treatment(s), *please specify:*______________________________

**2.** When was the last time you received any of the above treatments for cancer?

☐☐ / ☐☐☐☐
month year

**3.** Are you **<u>currently</u>** experiencing any side effects or symptoms related to your treatment or your cancer?

0 ☐ No
1 ☐ Yes ↓

**4.** If so, please list any current side effects or symptoms that affect your daily activities:

________________________________________________________

________________________________________________________

**5.** Where do you receive your healthcare? (*Mark all that apply*)

1 ☐ Doctor's office
2 ☐ Oncology (cancer) center or clinic
3 ☐ Hospital
4 ☐ Emergency Room or Urgent Care Center
5 ☐ Long-Term Follow-Up Clinic for survivors of childhood cancer
6 ☐ Other, *please specify:*________________________________________

**6.** Considering your healthcare needs as a childhood cancer survivor, which of the following would you prefer? (*Mark all that apply*)

1 ☐ Visits only to a primary care provider
2 ☐ A one-time visit to a long-term follow-up clinic for survivors of childhood cancer
3 ☐ Yearly visits to a long-term follow-up clinic for survivors of childhood cancer
4 ☐ Other, *please specify:*____________________________________________

**7.** Would you have felt uncomfortable receiving your long-term follow-up care in a pediatric setting or children's hospital as a young adult over the age of 18 years?

0 ☐ No
1 ☐ Yes

**8.** Do you currently have health insurance coverage?

0 ☐ No
1 ☐ Yes

**9.** Have you ever had difficulty obtaining health insurance because of your health history?

0 ☐ No
1 ☐ Yes
↓
**10.** If so, how old were you when you had difficulty obtaining health insurance? ________

**11.** Has there ever been a period when you did not have health insurance coverage?

0 ☐ No
1 ☐ Yes
↓
**12.** If so, how old were you when you did not have health insurance coverage? ________

## Health and background information

**1.** Please indicate below which chronic condition(s) you currently have: (*Mark all that apply*)

1 ☐ Depression or anxiety
2 ☐ Asthma
3 ☐ Emphysema or COPD
4 ☐ Other lung disease, *Type of lung disease:*___________________________
5 ☐ Heart disease, *Type of heart disease:* ______________________________
6 ☐ Arthritis or other rheumatic disease, *Specify type:*___________________
7 ☐ Other chronic condition(s), *Specify:*________________________________
8 ☐ I do not have a chronic condition

**2.** (Females only) Are you currently or have you been pregnant in the past year?

0 ☐ No
1 ☐ Yes, *I was/have been pregnant for____ total weeks during the past year*

**3.** Have you experienced any significant changes in your exercise habits in the past year due to medical problems or other issues?

0 ☐ No
1 ☐ Yes, *please describe:*____________________________________________

**4.** Please list all prescription or over-the-counter medications (not vitamins) you take on a regular basis, or check here if none [ ]

______________________________________________________________________

______________________________________________________________________

**5.** Do you currently use any of the following mobility aids? *(Mark all that apply)*

1 ☐ Manual wheelchair
2 ☐ Power wheelchair/Power scooter
3 ☐ Walker
4 ☐ Cane
5 ☐ Other mobility aid, *please specify:*_______________________________
6 ☐ I do not use a mobility aid

**6.** How tall are you (without shoes on)? *(Round up to the nearest inch)*

☐ feet ☐☐ inches

**7.** How much do you currently weigh? ☐☐☐ pounds

**8.** Have you smoked at least 100 cigarettes in your entire life? (5 packs=100 cigarettes)

0 ☐ No ⟶ ***Go to page 16 question 14.***
1 ☐ Yes

↓

**9.** If yes, at what age did you start smoking cigarettes?

☐☐ years old

**10.** Do you currently smoke cigarettes?

0 ☐ No → (go to 12)
1 ☐ Yes ↓

**11.** If yes, how many cigarettes do you usually smoke per day?

☐☐ cigarettes per day

**12.** Before stopping, how many cigarettes did you usually smoke per day?
(1 pack=20 cigarettes)

☐☐☐ cigarettes per day

**13.** How old were you when you stopped smoking cigarettes?

☐☐ years old

**14.** How often do you usually have an alcoholic drink of any kind? (This includes wine, beer, and spirits)

1 ☐ Every day
2 ☐ 5-6 days per week
3 ☐ 3-4 days per week
4 ☐ 1-2 days per week
5 ☐ 1-3 days per **month**
6 ☐ Less than 1 day per **month**
7 ☐ Never → ***Go to page 17 question 16.***

**15.** On a day that you have alcoholic drinks, how many drinks do you usually have?

1 ☐ 1-2 drinks
2 ☐ 3-4 drinks
3 ☐ 5-6 drinks
4 ☐ 7-8 drinks
5 ☐ 9-12 drinks
6 ☐ 13 drinks or more

**16.** How long have you lived at your current residence?

☐☐ months **OR** ☐☐ years

↓

**17.** If less than 1 year, was your previous residence more than one mile away from your current residence?

0 ☐ No
1 ☐ Yes

**18.** How many children and adults, including yourself, live in your household? *(Do not include roommates unless you share an income or the regular use of a motor vehicle)*

☐☐ children ☐☐ adults, including yourself

**19.** How many motor vehicles are available for regular use by the people in your household? *(Do not include motorcycles, mopeds, or scooters)*

☐☐ motor vehicles

**20.** How many people in your household, including yourself, have a valid driver's license?

☐☐ drivers

**21.** What is your current employment status? *(Mark all that apply)*

1 ☐ Working or volunteering full time
2 ☐ Working or volunteering part time
3 ☐ Full-time homemaker or family caregiver
4 ☐ Retired
5 ☐ Unemployed
6 ☐ Full-time student
7 ☐ Part-time student
8 ☐ Other, *please specify:*___________________________________________

**22.** During a usual week, how many days are you required to go somewhere outside of your home for school or work (either paid or unpaid work)?

1 ☐ 0 days per week
2 ☐ 1-2 days per week
3 ☐ 3-4 days per week
4 ☐ 5 days per week
5 ☐ 6-7 days per week

**23.** What is your race/ethnicity? (*Mark all that apply*)

1 ☐ American Indian or Alaskan Native
2 ☐ Asian or Pacific Islander
3 ☐ Black - not Hispanic
4 ☐ Latino/Hispanic
5 ☐ White - not Hispanic (includes Middle Eastern)
6 ☐ Other, *please specify:*___________________________________________

**24.** What is your marital status?

1 ☐ Married
2 ☐ Living with a partner
3 ☐ Widowed
4 ☐ Divorced
5 ☐ Separated
6 ☐ Never married
7 ☐ Other, *please specify:*________________________________________

**25.** What is the **highest** level of schooling you have completed?

1 ☐ 8th grade or less
2 ☐ Some high school
3 ☐ High school graduate or GED (high school equivalency)
4 ☐ One or more years vocational education beyond high school
5 ☐ Some college
6 ☐ College graduate
7 ☐ One or more years of graduate or professional school
8 ☐ Graduate or professional degree
9 ☐ Other, *please specify:*________________________________________

**26.** Which of the following best describes your **total** household income, before taxes?

1 ☐ Up to $10,000
2 ☐ More than $10,000 up to $20,000
3 ☐ More than $20,000 up to $40,000
4 ☐ More than $40,000 up to $60,000
5 ☐ More than $60,000 up to $80,000
6 ☐ More than $80,000 up to $100,000
7 ☐ More than $100,000

**Comments:**

Please provide any comments or additional information below.

Please turn to the next page.

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***To maintain your confidentiality, this page will be stored separately from your responses to the survey.***

**1.** What is your date of birth? ☐☐ / ☐☐ / ☐☐☐☐
month day year

**2.** To thank you for filling out this survey, we would like to send you a $5 gift card. Please select your favorite:

1 ☐ Target
2 ☐ Amazon.com
3 ☐ Dairy Queen

Please record your name and contact information:

Name ______________________________

Current street address ______________________________

City, State, Zip ______________________________

Permanent address (if different) ______________________________

City, State, Zip ______________________________

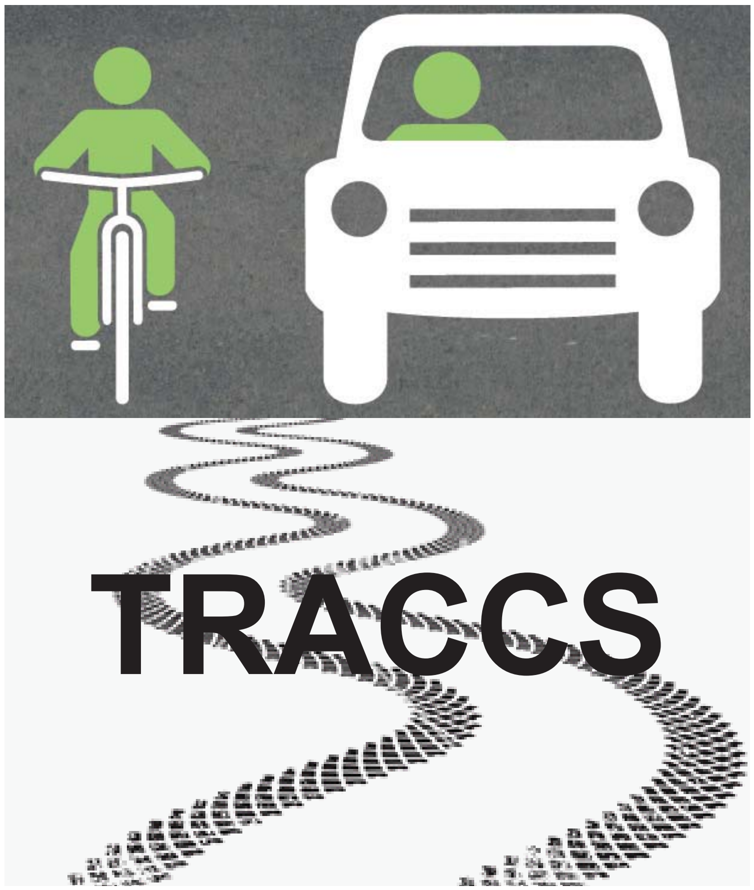
Phone ( _ _ _ ) _ _ _ - _ _ _ _

Email ______________________________

**Thank you for your time!**

**H.4. Appendix 4: TRACCS Questionnaire for Controls**

UNIVERSITY OF MINNESOTA




# Transportation-Related Activities of Childhood Cancer Survivors (TRACCS) Study Questionnaire

**University of Minnesota**
**Department of Pediatrics**
**2013**

# How to fill out this survey

Please take about 30 minutes to fill out this survey. It asks for information about your walking and biking activities, other exercise and health habits, current medical issues, and your neighborhood environment. Please answer every question as best you can. If you do not know the answer to a question, please provide your best guess.

For some questions, you will **PUT AN X OR ✓ IN THE BOX** that goes with your answer, like this:

1. Are you? 1 ☒ Male 2 ☐ Female **OR** 1 ☑ Male 2 ☐ Female

You will sometimes be told to skip over some questions in this survey. When this happens, you will see an arrow with a note that tells you what questions to answer next, like this:

☐ Yes ⟶ ***Go to page 6 question 13.***

For some questions, you will enter letters or numbers in boxes or on lines, like this:

| A | B | 2 | 8 | **OR** AB28 |
|---|---|---|---|---|

For some questions, you will circle your answer, like this:

| | 1 strongly disagree | 2 somewhat disagree | 3 somewhat agree | 4 strongly agree |
|---|---|---|---|---|
| 2. The route is boring | 1 | (2) | 3 | 4 |

## Transportation activities

Today's Date: ☐☐ / ☐☐ / ☐☐☐☐
month day year

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spend being physically active in a **usual week during the summer, winter, and spring/ fall**. Please consider only your usual activities **during the past year**. Please answer each question even if you do not consider yourself to be an active person.

The first 6 questions are about how you **travel** from place to place, including places like work, stores, movies, and so on.

**1.** During a **usual week**, on how many days do you **travel in a motor vehicle** like a train, bus, car, or tram?

**In summer:** _____ days per week

**In winter:** _____ days per week

**In spring/fall:** _____ days per week

☐ No traveling in a motor vehicle ⟶ ***Go to page 4 question 3.***

**2.** How much time do you **usually** spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

Now think only about the **bicycling** and **walking** you do to travel to and from work, to do errands, or to go from place to place.

**3.** During a **usual week**, on how many days do you **bicycle** to go **from place to place**?

**In summer:** _____ days per week

**In winter:** _____ days per week

**In spring/fall:** _____ days per week

☐ No bicycling from place to place ⟶ ***Go to question 5 below.***

**4.** How much time do you usually spend on one of those days to **bicycle** from place to place?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**5.** During a **usual week**, on how many days do you **walk** to go **from place to place**?

**In summer:** _____ days per week

**In winter:** _____ days per week

**In spring/fall:** _____ days per week

☐ No walking from place to place ⟶ ***Go to page 5 question 7.***

**6.** How much time do you usually spend on one of those days **walking** from place to place?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

## Work, home, and leisure-time physical activity

Please think about the usual activities you have done **during the past year** at work, as part of your house and yard work, and in your spare time for recreation, exercise, or sport. The questions will ask about the following types of activities in four separate sections: A) vigorous activities, B) moderate activities, C) walking activities, and D) sitting activities. Please **do not include any transportation-related activities** you have already mentioned.

**A)** Think about all the **vigorous** activities that you do in a **usual week during the summer, winter, and spring/fall. Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

**7.** During a **usual week**, on how many days do you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No vigorous physical activities ⟶ ***Go to page 6 question 9.***

**8.** How much time do you usually spend doing **vigorous** physical activities on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**B)** Think about all the **moderate** activities that you do in a **usual week during the summer, winter, and spring/fall** at work, as part of your house and yard work, and in your spare time for recreation, exercise, or sport. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those activities that you did for at least 10 minutes at a time.

**9.** During a **usual week**, on how many days do you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Please **do not include** walking.

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No moderate physical activities ⟶ ***Go to page 7 question 11.***

**10.** How much time do you usually spend doing **moderate** physical activities on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**C)** Think about the time you spend **walking** in a **usual week during the summer, winter, and spring/fall.** This includes at work and at home and any other walking that you might do solely for recreation, sport, exercise, or leisure. Please **do not include** any transportation-related walking you have already mentioned.

**11.** During a **usual week**, on how many days do you **walk** at least 10 minutes at a time?

| **In summer:** | **In winter:** | **In spring/fall:** |
|---|---|---|
| _____ days per week | _____ days per week | _____ days per week |

☐ No walking ⟶ ***Go to question 13 below.***

**12.** How much time do you usually spend **walking** on one of those days?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

**D)** This question is about the time you spend **sitting** on weekdays during a **usual week during the summer, winter, and spring/fall**. Include time spent at work, at home, while doing schoolwork, and during leisure time.

**13.** During a **usual week**, how much time do you spend **sitting** on a **week day**?

**In summer:** _____ hours and _____ minutes per day

**In winter:** _____ hours and _____ minutes per day

**In spring/fall:** _____ hours and _____ minutes per day

## Barriers to walking and biking to local parks/gyms/recreational facilities

Please circle the answer that best applies to you.

| | | |
|---|---|---|
| **1a.** Are there parks, gyms, and/or recreational facilities within a 15-minute walk or bike from your home? | Yes | No |
| **1b.** If yes, do you walk or bike to get there (alone or with someone)? | Yes | No |

Do you agree or disagree with the following statements:

It is difficult to walk or bike to local parks/gyms/recreational facilities (alone or with someone) because…

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):________________________ | 1 | 2 | 3 | 4 |

## Barriers to walking and biking to shops and restaurants

Please circle the answer that best applies to you.

| | | |
|---|---|---|
| **1a.** Are there shops, restaurants, or food stores within a 15-minute walk or bike from your home? | Yes | No |
| **1b.** If yes, do you walk or bike to get there (alone or with someone)? | Yes | No |

Do you agree or disagree with the following statements:

It is difficult to walk or bike to the local stores and restuarants (alone or with someone) because…

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):________________________ | 1 | 2 | 3 | 4 |

## Barriers to walking and biking to work or school

Please circle the answer that best applies to you.

| | | | |
|---|---|---|---|
| **1a.** Is your work or school within a 30-minute walk or bike from your home? | Yes | No | N/A |
| **1b.** Do you walk or bike to work or school at least once per week? | Yes | No | N/A |

***<u>If you do not attend school or work outside your home, please skip to page 11</u>***

Do you agree or disagree with the following statements:
It is difficult to walk or bike to work or school (alone or with someone) because…

| | 1<br>strongly disagree | 2<br>somewhat disagree | 3<br>somewhat agree | 4<br>strongly agree |
|---|---|---|---|---|
| **2.** There are too many hills along the way | 1 | 2 | 3 | 4 |
| **3.** There are no sidewalks or bike lanes | 1 | 2 | 3 | 4 |
| **4.** The route is boring | 1 | 2 | 3 | 4 |
| **5.** The route does not have good lighting | 1 | 2 | 3 | 4 |
| **6.** There is too much traffic along the route | 1 | 2 | 3 | 4 |
| **7.** There is one or more dangerous crossings | 1 | 2 | 3 | 4 |
| **8.** I get too hot and sweaty | 1 | 2 | 3 | 4 |
| **9.** Others do not walk or bike to these places | 1 | 2 | 3 | 4 |
| **10.** It is not considered socially acceptable to walk or bike | 1 | 2 | 3 | 4 |
| **11.** I have too much stuff to carry | 1 | 2 | 3 | 4 |
| **12.** It is easier for me or someone else to drive me there | 1 | 2 | 3 | 4 |
| **13.** It involves too much planning ahead | 1 | 2 | 3 | 4 |
| **14.** It is unsafe because of crime | 1 | 2 | 3 | 4 |
| **15.** I get harassed | 1 | 2 | 3 | 4 |
| **16.** There is nowhere to leave a bike safely | 1 | 2 | 3 | 4 |
| **17.** There are stray dogs | 1 | 2 | 3 | 4 |
| **18.** It is too far | 1 | 2 | 3 | 4 |
| **19.** I feel too tired/fatigued | 1 | 2 | 3 | 4 |
| **20.** I am limited by a physical or medical condition | 1 | 2 | 3 | 4 |
| **21.** Other (*specify*):____________________ | 1 | 2 | 3 | 4 |

## Stores, facilities, and other things in your neighborhood

About how long would it take to get from your home to the nearest businesses or facilities listed below if you walked to them? Please circle only one option for each business or facility.

| | 1-5 min | 6-10 min | 11-20 min | 20-30 min | 30+ min | don't know |
|---|---|---|---|---|---|---|
| **Example:** gas station | 1 | 2 | (3) | 4 | 5 | 6 |
| **1.** convenience/small grocery store | 1 | 2 | 3 | 4 | 5 | 6 |
| **2.** supermarket | 1 | 2 | 3 | 4 | 5 | 6 |
| **3.** hardware store | 1 | 2 | 3 | 4 | 5 | 6 |
| **4.** fruit/vegetable market | 1 | 2 | 3 | 4 | 5 | 6 |
| **5.** laundry/dry cleaners | 1 | 2 | 3 | 4 | 5 | 6 |
| **6.** clothing store | 1 | 2 | 3 | 4 | 5 | 6 |
| **7.** post office | 1 | 2 | 3 | 4 | 5 | 6 |
| **8.** library | 1 | 2 | 3 | 4 | 5 | 6 |
| **9.** elementary school | 1 | 2 | 3 | 4 | 5 | 6 |
| **10.** other schools | 1 | 2 | 3 | 4 | 5 | 6 |
| **11.** book store | 1 | 2 | 3 | 4 | 5 | 6 |
| **12.** fast food restaurant | 1 | 2 | 3 | 4 | 5 | 6 |
| **13.** coffee place | 1 | 2 | 3 | 4 | 5 | 6 |
| **14.** bank/credit union | 1 | 2 | 3 | 4 | 5 | 6 |
| **15.** non-fast food restaurant | 1 | 2 | 3 | 4 | 5 | 6 |
| **16.** video store | 1 | 2 | 3 | 4 | 5 | 6 |
| **17.** pharmacy/drug store | 1 | 2 | 3 | 4 | 5 | 6 |
| **18.** salon/barber shop | 1 | 2 | 3 | 4 | 5 | 6 |
| **19.** your job or school [check here__if not applicable] | 1 | 2 | 3 | 4 | 5 | 6 |
| **20.** bus or train stop | 1 | 2 | 3 | 4 | 5 | 6 |
| **21.** park | 1 | 2 | 3 | 4 | 5 | 6 |
| **22.** recreation center | 1 | 2 | 3 | 4 | 5 | 6 |
| **23.** gym or fitness facility | 1 | 2 | 3 | 4 | 5 | 6 |

## Health and background information

**1.** Please indicate below which chronic condition(s) you currently have: (*Mark all that apply*)

1 ☐ Depression or anxiety
2 ☐ Asthma
3 ☐ Emphysema or COPD
4 ☐ Other lung disease, *Type of lung disease:*___________________________
5 ☐ Heart disease, *Type of heart disease:* ______________________________
6 ☐ Arthritis or other rheumatic disease, *Specify type:*___________________
7 ☐ Other chronic condition(s), *Specify:*_______________________________
8 ☐ I do not have a chronic condition

**2.** Have you ever been diagnosed with cancer?

0 ☐ No
1 ☐ Yes *Type of cancer:*___________________________________________
↓
**3.** If yes, how old were you at the time of your cancer diagnosis? _______

**4.** (Females only) Are you currently or have you been pregnant in the past year?

0 ☐ No
1 ☐ Yes, *I was/have been pregnant for____ total weeks during the past year*

**5.** Have you experienced any significant changes in your exercise habits in the past year due to medical problems or other issues?

0 ☐ No
1 ☐ Yes, *please describe:*___________________________________________

**6.** Do you currently use any of the following mobility aids? *(Mark all that apply)*

1 ☐ Manual wheelchair
2 ☐ Power wheelchair/Power scooter
3 ☐ Walker
4 ☐ Cane
5 ☐ Other mobility aid, *please specify:*________________________________
6 ☐ I do not use a mobility aid

**7.** Please list all prescription or over-the-counter medications (not vitamins) you take on a regular basis, or check here if none [ ]

______________________________________________________________________

**8.** How tall are you (without shoes on)? *(Round up to the nearest inch)*

☐ feet ☐☐ inches

**9.** How much do you currently weigh? ☐☐☐ pounds

**10.** Have you smoked at least 100 cigarettes in your entire life? (5 packs=100 cigarettes)

0 ☐ No ⟶ ***Go to page 14 question 16.***
1 ☐ Yes
↓

**11.** If yes, at what age did you start smoking cigarettes?

☐☐ years old

**12.** Do you currently smoke cigarettes?

0 ☐ No → (go to 14)
1 ☐ Yes ↓

**13.** If yes, how many cigarettes do you usually smoke per day?

☐☐ cigarettes per day

**14.** Before stopping, how many cigarettes did you usually smoke per day? (1 pack=20 cigarettes)

☐☐☐ cigarettes per day

**15.** How old were you when you stopped smoking cigarettes?

☐☐ years old

**16.** How often do you usually have an alcoholic drink of any kind? (This includes wine, beer, and spirits)

1 ☐ Every day
2 ☐ 5-6 days per week
3 ☐ 3-4 days per week
4 ☐ 1-2 days per week
5 ☐ 1-3 days per **month**
6 ☐ Less than 1 day per **month**
7 ☐ Never → ***Go to page 15 question 18.***

**17.** On a day that you have alcoholic drinks, how many drinks do you usually have?

1 ☐ 1-2 drinks
2 ☐ 3-4 drinks
3 ☐ 5-6 drinks
4 ☐ 7-8 drinks
5 ☐ 9-12 drinks
6 ☐ 13 drinks or more

**18.** How long have you lived at your current residence?

☐☐ months **OR** ☐☐ years

↓

**19.** If less than 1 year, was your previous residence more than one mile away from your current residence?

0 ☐ No
1 ☐ Yes

**20.** How many children and adults, including yourself, live in your household? *(Do not include roommates unless you share an income or the regular use of a motor vehicle)*

☐☐ children ☐☐ adults, including yourself

**21.** How many motor vehicles are available for regular use by the people in your household? *(Do not include motorcycles, mopeds, or scooters)*

☐☐ motor vehicles

**22.** How many people in your household, including yourself, have a valid driver's license?

☐☐ drivers

**23.** What is your current employment status? *(Mark all that apply)*

1 ☐ Working or volunteering full time
2 ☐ Working or volunteering part time
3 ☐ Full-time homemaker or family caregiver
4 ☐ Retired
5 ☐ Unemployed
6 ☐ Full-time student
7 ☐ Part-time student
8 ☐ Other, *please specify:*________________________________________

**24.** During a usual week, how many days are you required to go somewhere outside of your home for school or work (either paid or unpaid work)?

1 ☐ 0 days per week
2 ☐ 1-2 days per week
3 ☐ 3-4 days per week
4 ☐ 5 days per week
5 ☐ 6-7 days per week

**25.** What is your race/ethnicity? (*Mark all that apply*)

1 ☐ American Indian or Alaskan Native
2 ☐ Asian or Pacific Islander
3 ☐ Black - not Hispanic
4 ☐ Latino/Hispanic
5 ☐ White - not Hispanic (includes Middle Eastern)
6 ☐ Other, *please specify:*________________________________________

**26.** What is your marital status?

1 ☐ Married
2 ☐ Living with a partner
3 ☐ Widowed
4 ☐ Divorced
5 ☐ Separated
6 ☐ Never married
7 ☐ Other, *please specify:*________________________________________

**27.** What is the **highest** level of schooling you have completed?

1 ☐ 8th grade or less
2 ☐ Some high school
3 ☐ High school graduate or GED (high school equivalency)
4 ☐ One or more years vocational education beyond high school
5 ☐ Some college
6 ☐ College graduate
7 ☐ One or more years of graduate or professional school
8 ☐ Graduate or professional degree
9 ☐ Other, *please specify:*________________________________________

**28.** Which of the following best describes your **total** household income, before taxes?

1 ☐ Up to $10,000
2 ☐ More than $10,000 up to $20,000
3 ☐ More than $20,000 up to $40,000
4 ☐ More than $40,000 up to $60,000
5 ☐ More than $60,000 up to $80,000
6 ☐ More than $80,000 up to $100,000
7 ☐ More than $100,000

**Comments:**

Please provide any comments or additional information below.

Please turn to the next page.

***To maintain your confidentiality, this page will be stored separately from your responses to the survey.***

**1.** What is your date of birth? ☐☐ / ☐☐ / ☐☐☐☐
month / day / year

**2.** To thank you for filling out this survey, we would like to send you a $5 gift card. Please select your favorite:

1 ☐ Target
2 ☐ Amazon.com
3 ☐ Dairy Queen

Please record your name and contact information:

Name ____________________

Current street address ____________________

City, State, Zip ____________________

Permanent address (if different) ____________________

City, State, Zip ____________________

Phone ( _ _ _ ) _ _ _ - _ _ _ _

Email ____________________

**Thank you for your time!**