CHILDHOOD CANCER SURVIVOR STUDY
Analysis Concept Proposal

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1. Title: Physical Activity and Psychological Functioning Among Teenage Survivors of Childhood Cancers

2. Working group and investigators

2.1 Working Group: Psychology (primary) and Cancer Control (secondary).

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3. Background and Rationale:

Survivors of childhood cancers are at risk for increased body mass index (BMI), decreased physical fitness, and physical inactivity.[1-7] Physical inactivity is a risk factor for health problems and can exacerbate late effects of treatment. A previous report on physical activity in adult survivors of childhood cancer from the CCSS cohort indicated that survivors were less likely to meet physical activity guidelines and more likely to be physically inactive.[8] In that report, several demographic, diagnostic, and treatment-related correlates of an inactive lifestyle were identified, including female gender, black race, older current age, lower educational attainment, underweight or obese status, smoking, depression, diagnosis of medulloblastoma or osteosarcoma, and treatment with cranial radiation or amputation. A longitudinal report examining adolescent behavioral predictors of adult obesity and inactivity found that social withdrawal and antidepressant use in adolescence was associated with subsequent physical inactivity in adulthood.[9] However, this report limited predictors to narrow classes of psychopathology, and did not include factors such as self-esteem, family involvement, or peer influences. Furthermore, the reports from the CCSS cohort have thus far been limited to self report by adult survivors or parent report of adolescent survivors. A manuscript by Mertens and colleagues (under review) used the Teen Survey to demonstrate child and treatment influences on lower self-reported satisfaction, increased risk from peer influences, and increased rates of functional disorders. The proposed project will examine associations between adolescent self-reported physical activity and comprehensive psychosocial functioning on the Teen Survey.

In the general population, several correlates of increased adolescent physical activity have been consistently identified, including male gender, white race, perceived competence, and support from parents.[10] The number of hours of television watched has demonstrated a small, negative association with physical activity[11,12] and has been associated with greater body fat and BMI.[13]

The purpose of this study is to examine concurrent associations between adolescent-reported physical activity and psychological functioning (self-esteem, emotional discomfort, psychosocial disorders), family involvement, home safety and health (diet and sedentary behavior), and demographic and treatment-related characteristics. The psychological functioning, family involvement, and home safety and health data collected at adolescence would then be used in a secondary aim to examine associations with future physical activity and BMI (2007 follow-up survey).

4. Specific aims and Hypotheses:

4.1 Primary Aim

4.1.1. To examine concurrent associations between adolescent-reported physical activity and psychological functioning (self-esteem, emotional discomfort, psychosocial disorders), family involvement, home safety and health (diet and sedentary behavior), while controlling for relevant treatment and demographic characteristics.

4.2 Primary Hypotheses

4.2.1 Physical activity will be positively associated with better psychological functioning (higher self-esteem, lower emotional discomfort, and lower psychosocial disorders).

4.2.2. Physical activity will be positively associated with healthy diet behaviors and family involvement, and negatively associated with unhealthy diet behaviors and sedentary time.

4.3 Secondary Aims

4.3.1. To examine predictors of future physical activity (2007 follow-up survey) from adolescent-reported functioning (i.e., psychological functioning, family involvement, diet, sedentary behavior, and limitations of activity), controlling for levels of physical activity as an adolescent.

4.3.2. To examine predictors of future BMI (2007 follow-up survey) from adolescent-reported functioning (i.e., psychological functioning, family involvement, diet, sedentary behavior, and limitations of activity).

4.4 Secondary Hypotheses

4.4.1 Higher levels of adolescent-reported self-esteem, family involvement, and healthy diet behaviors, and lower emotional discomfort, sedentary time, and limitations of activity will predict higher levels of future physical activity.

4.4.2. Higher levels of adolescent-reported self-esteem, family involvement, and healthy diet behaviors, and lower levels of emotional discomfort, sedentary time, unhealthy diet behaviors, and limitations of activity will predict lower future BMI.

5. Analysis Framework

5.1 Study population

CCSS participants who completed the Teen Survey (2001-2003) will be used to address Aim 1, while those who completed the Teen Survey and the 2007 follow-up questionnaire will be included in analyses for Aim 2. Given the focus on physical activity and BMI, we will exclude survivors who had lower limb amputations. Due to the timing of questionnaires and age requirements, survivors who responded to the Teen Survey were 0-3 years old at the time of diagnosis.

Number of survivors at each time point

	Teen Survey	Teen & 2007 Follow-Up	% at both times
Leukemia	95	73	76.8%
CNS tumor	40	35	87.5%
Hodgkins disease	0	0	
NHL	4	3	75.0%
Wilms tumor	56	46	82.1%

Neuroblastoma	90	72	80.0%
Soft tissue sarcoma	19	17	89.5%
Bone tumor	3	2	66.7%
Total	307	248	80.8%

5.2 Outcomes of interest:

The primary outcome of interest is adolescent-reported physical activity as measured by the physical activity subdomain on the CHIP-AE (Teen Survey questions D1 through D5). We will analyze the subdomain score as a continuous variable. Each subdomain of the CHIP-AE has a standard score of 20 and a standard deviation of 5. There are also cut-points for poor (<17), average (17-23), and excellent (>23) health, which are approximately 0.6 standard deviations from the mean of 20. We will explore the distribution of scores along these cut-points to determine if we could create a clinically meaningful dichotomous or categorical variable for physical activity instead of using it as a continuous variable.

Secondary outcomes include physical activity and BMI as measured in the 2007 Follow-up Questionnaire (questions A1, A2, N15 through N21). For the secondary outcomes, we will analyze physical activity as a dichotomous variable based on whether survivor-reported weekly minutes of moderate and vigorous activity met the Centers for Disease Control (CDC) established standards. BMI will be calculated from questions A1 and A2 and classified as normal weight = BMI < 25 or overweight = BMI $\geq$ 25. Secondary analyses will predict overweight BMI at the 2007 follow-up. Unfortunately, BMI was not collected on the Teen Survey so it cannot be included in the model.

5.3 Primary Predictors

- CHIP-AE Self-Esteem subdomain score (calculated from B5, B7-B9, B11)
- CHIP-AE Emotional Discomfort subdomain score (calculated from C19, C22-28, C45, C31, C33-34, C43-44)
- CHIP-AE Psychosocial Disorders subdomain score (calculated from F30-F32, F12)
- CHIP-AE Family Involvement subdomain score (calculated from G1-G5, G27-28)
- CHIP-AE Home Safety & Health index items
  a. Item E7 (sedentary TV hours)
  b. Healthy Foods in Diet ("GDFD"): average of items E52 through E55
  c. Unhealthy Foods in Diet ("BDFD"): average of items E56 through E58
- CHIP-AE Limitations of Activity subdomain score (calculated from C35 to C41).

5. 4 Covariates

- Age at Teen Survey completion (Question A2)
- Current age at 2007 Follow-Up Survey (for secondary aims)
- Parental education as proxy for SES (Questions A10, A12)
- Sex (Male/Female)
- Date of cancer diagnosis/Time since Cancer Diagnosis
- Race/ethnicity
- Chemotherapy (yes/no)
- Radiation Variables
  - Cranial (yes/no)
  - Other bodily (yes/no)
  - None

5.5 Statistical analyses

5.5.1 Frequency distributions will be used to categorize relevant outcome variables, predictors, and covariates according to reasonable groupings and consistent with previous CCSS manuscripts.

5.5.2. Descriptive statistics (means, standard deviations, percents) will be calculated to describe survivor characteristics, including diagnosis and treatment (Table 1). Descriptive statistics including means, standard deviations, medians, ranges, frequencies, and percents will be calculated for the primary outcome of interest (adolescent physical activity) as well as for the primary predictors and secondary outcomes (Table 2). Since the population of subjects who completed all the teen survey and the 2007 questionnaire may differ from those who completed only the teen survey, we will examine differences in predictors and outcomes for survivors who responded to both surveys compared with those who responded to only the teen survey (Table 3).

5.5.3 To address the first aim, associations between adolescent-reported physical activity and psychological functioning (self-esteem, emotional discomfort, psychosocial disorders), family involvement, home and health safety (diet and sedentary behavior), and limitations of activity will be evaluated in a hierarchical multivariable linear regression model, with demographic and treatment-related covariates entered at the first step and psychosocial variables entered at the second step (Table 4). This will allow us to determine the contribution of psychosocial variables beyond demographic and treatment-related factors. We will also examine the model including psychosocial variables without treatment variables.

5.5.4 To address the secondary aim, the association of adolescent-reported functioning (i.e., psychological functioning, family involvement, diet, sedentary behavior, and limitations of activity) and future physical activity (binary meets recommendation variable from 2007 follow-up survey) will be examined using a logistic regression model. A multivariable model adjusted for adolescent physical activity and demographic and treatment-related characteristics will be fitted and Odds Ratios with 95% confidence intervals will be reported for the comparison between groups of survivors (Table 5). We will also examine intercorrelations among predictors and the covariate to explore if any are confounded or collinear. The association of adolescent-reported functioning (i.e., psychological functioning, family involvement, diet, sedentary behavior, and limitations of activity) and future BMI (overweight category from 2007 follow-up survey) will be examined using a logistic regression model. Odds Ratio and 95% confidence interval will be reported for the comparison between groups of survivors (Table 6).

Table 1: Characteristics of survivors

	Survivors N (%) or *M(SD)*
Sex	
Female	
Male	
Current age	
M(SD)	
Range	
Race	
White	
Black	
Hispanic	
Other race	
Diagnosis	
Leukemia	
CNS tumor	
Hodgkins disease	
NHL	
Wilms tumor	
Neuroblastoma	
Soft tissue sarcoma	
Bone tumor	
Age at diagnosis	
0-1	
2-3	
Time Since Diagnosis	*M(SD)*
Chemotherapy (y/n)	
Radiation	
Cranial (y/n)	
Other bodily (y/n)	
None	

Table 2. Descriptive statistics for primary predictors and outcomes.

	Survivors N (%) or *M(SD)*
Psychosocial Functioning	
Self-Esteem	
Emotional Discomfort	
Psychosocial Disorder	
Family Involvement	
Sedentary Behavior (TV hours)	
Healthy Foods in Diet	
Unhealthy Foods in Diet	
Limitations of Activity	
Physical Activity	
Adolescent *M(SD)*	
Young Adult Meets Recommendation	
BMI (Young Adult)	
Normal <25	
Overweight ≥25	

Table 3. Primary Predictors and Physical Activity Scores for Survivors at Teen Survey and 2007 Follow-Up

	Teen Survey Only (n=)	Teen Survey and 2007 Follow-Up (n=)	Group Difference
	M(SD)	*M(SD)* or n (%)	*p*
Psychosocial Functioning			
Self-Esteem			
Emotional Discomfort			
Psychosocial Disorder			
Family Involvement			
Sedentary Behavior (TV hours)			
Healthy Foods in Diet			
Unhealthy Foods in Diet			
Limitations of Activity			
Physical Activity			
Adolescent Physical Activity			
Adult Physical Activity Meets CDC Guidelines			--
Yes	N/A		
No			

Note. There are no questions on the Teen Survey that provide data to determine if respondents met CDC physical activity guidelines; therefore, we can only report the number of respondents who met CDC physical activity guidelines among those who completed the 2007 Follow-Up. For the Teen Survey, we report on the physical activity subdomain of the CHIP-AE.

Table 4. Multivariable regression model of current physical activity

	B	*SE B*	*B* [95% CI]	*p*-value
Step 1				
Sex (Female = 0; Male =1)				
Age				
Race (Nonwhite = 0; White = 1)				
Parental Education				
Cranial Radiation (No = 0; Yes = 1)				
Step 2				
Sex (Female = 0; Male =1)				
Age				
Race (Nonwhite = 0; White = 1)				
Parental Education				
Cranial Radiation (No = 0; Yes = 1)				
Self-Esteem				
Emotional Discomfort				
Psychosocial Disorder				
Family Involvement				
Sedentary Behavior (TV hours)				
Healthy Foods in Diet				
Unhealthy Foods in Diet				
Limitations of Activity				

Note. R^2 = ?, p = ? for Step 1; ΔR^2 = ?, p = ? for Step 2.

Table 5. Multivariable model to predict likelihood of meeting CDC physical activity guidelines as an adult

	OR	95% CI	*p*-value
Sex			
Female			
Male			
Current Age			
Race			
White			
Nonwhite			
Cranial Radiation			
Adolescent Physical Activity			
Adolescent Psychosocial Variables			
Self-Esteem			
Emotional Discomfort			
Psychosocial Disorder			
Family Involvement			
Sedentary Behavior (TV hours)			
Healthy Foods in Diet			
Unhealthy Foods in Diet			
Limitations of Activity			

Table 6. Multivariable model to predict the likelihood of being overweight/obese as an adult

	OR	95% CI	*p*-value
Sex			
Female			
Male			
Age			
Race			
White			
Nonwhite			
Cranial Radiation			
Adolescent Physical Activity			
Adolescent Psychosocial Variables			
Self-Esteem			
Emotional Discomfort			
Psychosocial disorder			
Family Involvement			
Sedentary Behavior (TV hours)			
Healthy Foods in Diet			
Unhealthy Foods in Diet			
Limitations of Activity			

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