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## **Health Behavior Profiles in Young Survivors of Childhood Cancer: Findings from the St. Jude Lifetime Cohort Study (SJLIFE)**

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## **Abstract**

**Background:** There is limited understanding of associations between a combination of health behaviors (physical activity, sedentary/screen-time, diet) and cardiometabolic health risk factors, physical performance, and emotional health among young (<18) childhood cancer survivors (CCS). The aims of this research were to address this gap by: (1) deriving health behavior adherence profiles among CCS, and (2) examining associations among demographic, diagnosis/ treatment exposures , cardiometabolic, physical performance, and emotional functioning with health behavior profile membership.

**Methods:** Participants included 397 CCS ( $\frac{5 \text{ years}}{2}$  years post-diagnosis; aged 10-17) enrolled in the St. Jude Lifetime Cohort Study who completed physical health evaluations and questionnaires assessing health behaviors and psychological functioning. Latent profile analysis was used to derive profiles of health behavior adherence. Logistic regression and t-tests were used to examine mean-level differences and associations between profile membership with demographic, diagnosis, treatment exposures, cardiometabolic health, psychological functioning, and physical performance.

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**Author Contributions:** Drs. Webster, Gordon, and Ness conceptualized drafted, reviewed, and revised the manuscript. Ms. Partin and Dr. Lanctot designed data collection instruments/approach, supervised data collection, and reviewed/ revised manuscript. Mr. Dhaduk and Mr. Li conducted data analyses. Drs. Kunin-Batson, Brinkman, Willard, Allen, Alberts, and Ehrhardt edited the manuscript and reviewed scientific content. Drs. Hudson, Ness, and Robison conceptualized and designed the study, coordinated, and supervised study teams carrying out this research, and critically reviewed and edited the manuscript's scientific content.

**Results:** Two profiles emerged: inactive-unhealthy-diet ("IU") and active-sedentary-unhealthydiet ("ASU") to guidelines. More participants in IU demonstrated higher resting heart rate (*mean*  $[M]=76.54$ , standard deviation  $[SD] = 12.00$ ) and lower motor proficiency scores ( $M=34.73$ , SD =29.15) compared to ASU (resting heart rate,  $M=71.95$ ,  $SD=10.74$ ; motor proficiency,  $M=50.40$ ,  $SD = 31.02$ ).

**Conclusion:** CCS exhibited low adherence to multiple health behavior guidelines, with adherence patterns differentially associated with cardiometabolic health (i.e., resting heart rate) and physical performance. However, robust protection against all health variables was not observed. Findings suggest interventions designed to improve health outcomes should target multiple health behaviors simultaneously.

## **Plain Language Summary:**

Pediatric cancer survivors are at-risk for detrimental health outcomes associated with cancer and treatment. Engagement in healthy lifestyle behaviors serves to reduce health vulnerabilities among adult survivors, but less is known about associations with lifestyle behaviors on young survivors. This study documents patterns of lifestyle behaviors among survivors of pediatric cancer, factors that increase susceptibility to nonadherence, and associations among lifestyle behaviors and health indicators.

## **Precis:**

Young (<18 years of age) survivors of pediatric cancer exhibit poor adherence to diet and physical activity guidelines. Adherence associated with clinical health outcomes.

## **Keywords**

child and adolescent survivors; physical activity; diet; cardiometabolic risk; mobility

Childhood cancer survivors (CCS) are at increased risk of poor health outcomes secondary to treatment and disease-related factors, including poor cardiometabolic, physical, and emotional health.<sup>1</sup> Engagement in healthy lifestyle behaviors (HLB; i.e., exercise, healthful diet, limited sedentary/screen-time behavior) substantially reduces risk of adverse cancerrelated sequelae and improves health functioning in adult  $CCS$ <sup>2-4</sup> While many studies have examined links between HLBs and health outcomes in adult CCS, research devoted to this relationship in young CCS (i.e.,  $\langle 18 \rangle$  years of age) is sparse.<sup>5</sup>

Findings in younger CCS populations consistently indicate CCS are not meeting behavioral guidelines across multiple health domains,<sup>6</sup> but little is understand about the associations among HLBs and how patterns relate to cardiometabolic, physical, and emotional health. A recent review of HLB among youth without chronic illnesses found HLBs typically cluster into combinations of healthy and unhealthy behaviors (i.e., high physical activity and high sedentary behavior), and the combination of these behaviors differentially predicted health outcomes.<sup>7</sup> Thus, it is not sufficient to examine a single health behavior in isolation, as patterns of engagement may differentially predict health outcomes in young CCS.

There is a critical need to identify young CCS at-risk for poor health habits and how the combination of HLBs impact cardiometabolic, physical, and emotional health. As such our aims for this investigation were: (1) to empirically derive health behavior profiles of young CCS (10-17 years of age), and (2) to determine which demographic, cancer-related medical factors (i.e., diagnosis, treatment exposures), cardiometabolic risk (i.e., blood pressure, body mass index, body fat percentage), emotional functioning (i.e., depression, anxiety, pain interference),and physical performance (i.e., motor proficiency, physiological cost, physical activity exertion, average respiration) factors were associated with health behavior (i.e., physical activity, strength training, sedentary behavior, screen time, diet) profile membership. Based on prior research, we hypothesize demographic and medical characteristics such as female sex, lower socioeconomic status, and history of cranial radiation will be associated with profiles characterized by decreased physical activity.<sup>6,8,9</sup> Younger age at diagnosis, lower socioeconomic status, and abdominal radiation will be associated with profiles characterized by poor dietary behaviors.<sup>6,10</sup> Mental health difficulties<sup>8,11</sup> and experiences of pain<sup>12</sup> will be associated with profiles characterized by poor diet and low physical activity levels.

## **Methods**

#### **Study Population and Procedures.**

Participants included members of the St. Jude Lifetime Cohort Study (SJLIFE), a retrospective cohort with longitudinal follow-up and ongoing enrollment, which was designed to examine health outcomes among CCS. Surveys and self-reported data were collected by trained study coordinators. Cardiometabolic and physiological data were collected by trained study staff including exercise physiologists and physical therapists. Comprehensive details related to study methodology and characteristics have been described elsewhere.13 Participants included in these analyses were between 10-17.99 years of age with a history of pediatric cancer and >5 years post diagnosis at the time of the assessment. Details pertaining to demographic, diagnosis, and treatment exposures are presented in Table 1. Legal guardians provided consent and patients provided assent for participation. All procedures were approved by the institutional IRB.

### **Measures**

**Demographic and Medical History.—**Participants' medical diagnosis, birth date, and diagnosis date, and treatment exposures were collected through medical records. Caregivers self-reported income and race/ethnicity. Chronic health conditions were categorized as present (CTCAE grades 2-4) or not present (no diagnosed chronic health condition or CTCAE grade  $1$ )<sup>14</sup>

**Health Behaviors.—**Physical activity, screen time, and sedentary behaviors were assessed using items from the National Health and Nutrition Examination Survey<sup>15</sup> via adolescent self-report. Items included physical activity (i.e., number of days physically active for 60 or minutes within a week, number of days strength training or toning muscles), sedentary time (i.e., number of hours of sedentary time per day), screen time (i.e., number of hours viewing television, number of hours of playing video games per day). Higher scores indicate

more time spent within that behavior. Dietary behaviors were measured using the wellestablished Block Kids Food Frequency Questionnaire via adolescent self-report.16-18An overall Healthy Eating Index (HEI) score, which is a summary indicator of participant conformance to the Dietary Guidelines for Americans, was assigned. The HEI ranges from 0 to 100 with higher scores indicating better diet quality. The average score for the United States population of 59.<sup>19</sup>

#### **Cardiometabolic Health Risk Indicators.—***Resting heart rate (HR) and blood*

*pressure* were assessed following a 5-minute resting period, in which participants were in a seated position with feet flat on the floor. Readings were manually measured in duplicate, with five minutes between readings and the lowest value was recorded. Blood pressure levels were considered elevated when all three readings for systolic blood pressure (SBP)  $120$ and all three readings of diastolic blood pressure (DBP)  $\,80$  were elevated.<sup>20</sup>

*Body mass index* **(BMI)** was calculated as weight in kilograms divided by height in meters squared. Sex and age-adjusted standardized BMI scores were calculated using the 2000 Centers for Disease Control (CDC) growth chart.<sup>21</sup>

*Body fat percentage* was assessed via skinfolds following established guidelines.<sup>22</sup> The average of two skinfolds were measured at the triceps and subscapular skinfolds for both males and females, and the sum of the two averaged skinfolds were imputed to the appropriate prediction equation based on sex, race, and maturation.<sup>23</sup> Sex and age-specific thresholds were used to create cut scores for elevated body fat.<sup>24</sup>

**Physical Performance Indicators.—R***espiration rate* was assessed following a 5 minute resting period, while participants were seated. Readings were manually measured in duplicate, with five minutes between readings and the lowest value was recorded.

*Motor proficiency* was assessed using the Bruininks-Oseretsky Test of Motor Proficiency Short Form 2nd Edition (BOT-2).25 An overall mobility score was derived: fine motor precision, fine motor integration, manual dexteriy, bilateral coordination, balance, running speed and agility, upper-limb coordination, and strength. Raw scores were converted into a standard score based on sex, age, and the type of push-up performed in the strength section (knee or full push-up).<sup>26</sup> The standard score has a mean of 50 and a standard deviation of 10, and participants were classified as well-above average (standard score  $\pi$ 70), above average (standard score 60-69), average (standard score 41-59), below average (standard score 31-40), or well-below average (standard score  $30$ ).<sup>26</sup>

*Physiological cost index (PCI)* was assessed using the six minute walk test (6MW). PCI is a valid and reliable method to measure the energy cost of walking in healthy and diseased populations.<sup>27-30</sup> A resting heart rate (HR) and Borg rating of perceived exertion (RPE)<sup>31</sup> were documented after participants rested for 5 minutes prior to the start of the 6MW. Participants were instructed to walk as quickly as possible, without running, for the entire 6 minutes on a predetermined 40 meter course. HR and RPE were documented at the 2, 4, and 6 minute time points.32 PCI was calculated as maximal working HR minus resting HR

divided by walking speed (total distance walked in meters per minute), and a lower score indicates better energy efficiency.

**Emotional Functioning Indicators.—***Pain* was assessed using the 8-item Patient-Reported Outcomes Measures Information System (PROMIS) Pain Interference-Short Form v 2.0 was used to evaluate self-reported consequences of pain. *Anxiety* was assessed using the PROMIS 8-item Pediatric Anxiety-Short Form version 2.0. *Depression* was assessed using the PROMIS 8-item Pediatric Depressive Symptoms-Short Form version 2.0. Each measure included response items on a 5-point scale ranging from "never" to "almost always". Total scores are converted to T scores with a mean of 50 and standard deviation of 10. Higher scores indicate worse functioning. Each measures has excellent psychometric properties.33,34

#### **Statistical Analyses.**

Latent profiles analysis was conducted to empirically derive health behavior profiles of young CCS using physical activity, sedentary behavior, and dietary intake. The Bayesian information criterion  $(BIC)^{35}$  was used to determine model fit for each number of classes estimated, with lower BIC values indicating better model fit.36 The Vuong-Lo-Mendell-Rubin  $(VLRM)^{37,38}$  was used to compare model improvement between neighboring classes solutions (e.g., 2 class solution vs. 3 class solution, 3 vs. 4). A significant  $p$ -value (<.05) derived from these tests indicates statistically significant improvement in fit by the addition of a class.<sup>36</sup> Entropy values were used to assess model classification, with values above 0.75 considered ideal.<sup>39</sup> To compare mean-level differences in cardiometabolic risk, physical performance, and emotional functioning across latent profiles, a series of ttests were performed. To determine associations between demographic, diagnosis/treatment exposures, cardiometabolic risk, physical performance, and emotional functioning logistic regressions were performed. Regressions were performed separately for diagnosis and treatment exposures. All analyses were performed using SAS/STAT version 9.4 software of the SAS System for Windows (Cary, NC, USA).

## **Results**

#### **Participants.**

Of 635 eligible, consented participants, 445 (70%) completed an on-site comprehensive health evaluation (Supplemental Figure 1). The majority of participants were female (52%) and non-Hispanic White (69%), with a history of hematologic, neurologic, and solid tumor diagnoses, and ranged in age from 0-10 years at cancer diagnosis (Table 1). Participants and non-participants (i.e., those who did not yet complete onsite visits) did not differ by sex (X<sup>2</sup> [df=1]=2.18,  $p=14$ ), race/ethnicity (X<sup>2</sup> [df=3]=3.87,  $p=28$ ), age at assessment  $t(431) = 0.82, p = 0.41$ , or family income  $(X^2 \text{ [df=5]} = 4.44, p = 0.60)$ . Non-participants varied in diagnostic category ( $p=0.03$ ) and were slightly older at age of diagnosis (Mean [M]=4.48, SD =2.56) as compared to participants (M=3.34, SD =2.40; t(479) =2.72,  $p<0$ .

#### **Latent Profiles.**

Complete data were available for 397 participants. Those with missing data were excluded from latent profile analyses. Latent profile analyses indicated a 4-class solution provided the best BIC value (Supplemental Table 1); however, this solution provided a non-significant VLMR and a class size too small (5%) to be considered meaningful. The 2 and 3-class solution provided the next optimal BIC values. Based on model fit indices, the 2-class solution was chosen over the 3-class solution as the BIC value change was not robust, and the entropy for the 3-class model was low. Finally, we explored if the 4-class and 2-class models were qualitatively different. Based on mean differences across the profiles, the addition of 2 profiles did not meaningfully change the characterization of the population. Thus, we chose the more parsimonious model (see Supplemental Table 2).

The majority of participants (75%) were characterized as "inactive-unhealthy-diet" group ("IU") with an average of  $\sim$ 3 days of 60 minutes of physical activity,  $\lt$ 1 day of strength training per week, >7 daily hours of sitting time, > 6 daily hours of screen time, and an overall HEI score of 53.59 (Table 2). The remaining participants comprised a group characterized as "active-sedentary-unhealthy-diet" to health guidelines ("ASU"). This group exhibited a combination of higher physical activity, as they self-reported an average of 5 days of 60 minutes of physical activity and ~5 days of strength training per week. However, participants in the ASU group also exhibited high sedentary behaviors including 6.5 daily hours of sitting time and > 6 daily hours of screen time. In addition overall HEI dietary scores were 53.59, falling below recommended guidelines (Table 2).

## **Mean Differences in Cardiometabolic Risk Factors, Physical Performance, and Psychological Health.**

More participants had elevated body fat (26%) in the IU group compared to the ASU group (19%), though overall mean-level differences in body fat percentage were not statistically significant across profiles. The IU group also demonstrated significantly higher resting heart rate values than the ASU and lower motor proficiency scores (Table 3).

#### **Multiple Variable Models.**

Across the two multiple variable models examining demographic, diagnosis or treatment exposure-related variables, cardiometabolic risk indicators, physical performance indicators, and emotional health indicators, only motor proficiency emerged as a significant indicator of profile membership with higher motor proficiency scores increasing the odds of belonging to the ASU as compared to the IU profile (OR=1.01, CI: 1.00-1.02, p=.02; Supplemental Tables 3 and 4). Given non-significant associations with demographic, diagnosis, and treatment variables, a third model was performed with those variables removed. In this model (Table 4), average resting rate (OR=0.97, CI: 0.95-1.00, p=.05) and physical activity exertion (OR=0.91, CI: 0.84-0.99,  $p=.04$ ) decreased the odds of belonging to the ASU as compared to the IU profile, whereas motor proficiency  $(OR=1.01, CI: 1.00-1.02, p=.01)$ increased the odds of belonging to the ASU profile.

## **Discussion**

To reduce morbidity and mortality associated with cancer and cancer treatment, CCS are encouraged to exercise regularly, eat a healthful diet, and limit sedentary behavior. Though previous research has documented limited uptake of HLBs among young  $CCS$ ,  $8$  these behaviors were often considered in isolation with limited understanding of the impact of poor HLB engagement on health comorbidities. The present research examined patterns of multiple HLBs and the implications of HLBs among young CCS.

Consistent with prior literature, that documented a combination of healthful and unhealthful behaviors in non-cancer youth, $40,41$  our findings highlight a significant proportion of young CCS exhibit a combination of healthful and unhealthful behavior patterns. That is, for a subset of adolescents engaging in higher than average physical activity behaviors, they also reported elevated sedentary behavior and unhealthy dietary behaviors. Though one profile (ASU) emerged as on-average more active, no profile pattern emerged that demonstrated adherence to any health behavior guideline. These findings suggest all young CCS would benefit from regular and routine guidance to optimize lifestyle behaviors, and that screenings and interventions should be designed to target multiple HLBs.

Research among adult CCS found associations between poor health behavior uptake and risks for long-term health outcomes. Indeed, findings from this research indicate that decreased physical activity, poor dietary habits, and high sedentary behavior were associated with higher resting heart rate and worse physical performance. Thus, focusing on HLBs in early survivorship through increasing physical activity, reducing sedentary behavior/screen time, and improving healthful dietary uptake is critical for mitigating, concurrent difficulties with cardiometabolic and physical performance health and the risks to long-term health outcomes.

Across all models, motor proficiency was higher within the ASU group as compared to the IU group, whose mean score fell within the low average range. Given the cross-sectional design of this research, it is impossible to determine the directionality of this finding. Certainly, increasing physical activity can improve motor proficiency;42 however decreased motor proficiency after treatment may be associated with decreased physical activity.<sup>43</sup> In either scenario, regular, ongoing assessment of motor proficiency and rehabilitative interventions are necessary for the significant subset of young CCS with poor motor proficiency.

A number of cardiometabolic risk (i.e., blood pressure, body mass index, body fat), physical performance (i.e., activity exertion, physiological cost, average respirations), and emotional health (i.e., depression, pain, anxiety) indicators did not differentiate between profiles as hypothesized. There may be several contributing factors. First, it is possible these factors are not associated with adherence to HLB guidelines. Given the robust literature documenting otherwise,  $6.8-12$  this is an unlikely explanation. An alternative possibility is that physical activity alone, without adherence to sedentary and dietary guidelines, was insufficient for protecting against certain cardiometabolic, physical performance, and emotional health indicators. Indeed, research supports links between sedentary and dietary behaviors with

cardiometabolic risk, physical performance, and emotional functioning.<sup>6,44,45</sup> Finally, some variables were elevated across both profiles and that may be more likely due to the cancer experience than adherence to HLBs alone. For example, though pain interference scores (IU, T=43.692; ASU, T=45.17), were slightly elevated as compared to normative levels (i.e.,  $T=36$ ,  $46$  pain was not associated with profile membership in the present study. Restricted variability due to elevated pain scores across the current samples compared to national norms suggests may explain why adherence to guidelines is low across the entire sample. This is consistent with prior research.<sup>12</sup>

Prior research has indicated medical diagnoses and comorbidities associated with treatment exposures (e.g., radiation) were linked to engagement in healthful lifestyle behaviors;<sup>6,9</sup> however these factors were not associated in this study. In addition, prior research has documented marginalized youth from lower income families were more susceptible to poor health behavior engagement,  $6,10$  but again, this did not appear to drive associations within this study. Though these findings were not consistent with our hypotheses, research exploring HLBs among CCS in early survivorship have documented similar findings.<sup>47</sup> Non-significant findings may be related to younger age of this sample, and indicate other factors not included in the present study (e.g., parenting behaviors) may explain HLB adherence within this unique population. Alternatively, given poor adherence across both profiles, limited variability may have concealed these associations.

Though these findings are novel, and a major strength of this research includes objective assessments of physical performance and cardiometabolic risk indicators, findings should be considered in-light of several limitations. First, the cross-sectional, correlational design limits implications that can be drawn from this research. Examining these associations over time and within randomized clinical trials will be important for future research. Second, HLBs were only assessed via child/adolescent self-report, who historically underreport poor dietary intake48 and moderate congruency with physical activity.49 However, even with potential for inflation of self-reported engagement in HLBs, adolescents across both profiles, on average, failed to meet guidelines. Third, physical activity assessments did not consider the intensity (i.e., moderate-vigorous) of physical activity adolescents were engaging in, so it is possible findings indicate greater nonadherence than was found in the present study. Fourth, caregivers are critical to the uptake of adolescent HLBs,<sup>50</sup> but caregiver factors were not considered in this study. This will be imperative in future research, particularly for intervention development. Finally, the majority of the sample identified as non-Hispanic White and non-Hispanic Black, and it isunclear how these findings might translate to other populations in the US, and therefore should be interpreted with caution.

Our findings highlight that young CCS fall short of established health behavior guidelines in multiple domains. Even among survivors who were more physically active, physical activity alone was not sufficient to offset the risk of poor dietary behaviors and elevated sedentary behaviors. Taken together, all young CCS should receive routine assessment of HLBs across multiple health behavior domains. Interventions designed to improve health behavior uptake among young CCS should target multiple HLBs as adherence to one health behavior may not offer robust protection against multiple indicators of health.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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### **Table 1.**

Descriptive statistics of demographic, medical, cardiometabolic, physical performance, and emotional functioning variables





## **Table 2.**

## Descriptive statistics for the model indicators across profiles for best fitting model



Note. SD=standard deviation

#### **Table 3.**

Mean differences in cardiometabolic risk, physical performance, and psychological functioning across latent classes



Note. SD=standard deviation

#### **Table 4.**

Chronic health conditions, cardiometabolic, physical performance, and emotional health factors associated with health behavior profiles



Note. IU=Inactive-unhealthy-diet class