Physical Activity Among Adolescent Cancer Survivors: The PACCS Study

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abstract

OBJECTIVES: Physical activity (PA) may modify risks of late effects after cancer. We aimed to examine levels of PA and sedentary time (ST) in a large, international sample of adolescent childhood cancer survivors in relation to sociodemographic and cancer-related factors and compare levels of PA and ST to reference cohorts.

METHODS: Survivors from any cancer diagnosis who had completed cancer treatment ≥1 year ago, aged 9 to 16 years, were eligible for the multicenter Physical Activity in Childhood Cancer Survivors study. PA and ST were measured by ActiGraph GT3X+ accelerometers. We performed linear regression analyses to assess factors associated with moderate-to-vigorous PA (MVPA) and ST, and compared marginal means of total PA, MVPA, and ST in 432 survivors to sex- and age-stratified references (2-year intervals) using immediate t-tests for aggregated data.

RESULTS: Among survivors, 34% fulfilled the World Health Organization's PA recommendation of ≥60 min of daily MVPA on average and their ST was 8.7 hours per day. Being female, older, overweight, a survivor of central nervous system tumor, or having experienced relapse were associated with lower MVPA and/or higher ST. Generally, male survivors spent less time in MVPA compared with references, whereas female survivors had similar levels. Both male and female survivors had higher ST than references in nearly all age groups.

CONCLUSIONS: The low PA and high ST in this large sample of adolescent childhood cancer survivors is worrisome. Combined, our results call for targeted interventions addressing both PA and ST in follow-up care after childhood cancer.

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WHAT'S KNOWN ON THIS SUBJECT: Physical activity may modify risks of late effects after cancer. The existing knowledge of physical activity and sedentary time in childhood cancer survivors is limited by studies mainly in adult survivors, use of self-reported measures, or small and selected samples.

WHAT THIS STUDY ADDS: We found low levels of accelerometer-measured physical activity and high levels of sedentary time in adolescent childhood cancer survivors. Survivors of central nervous system tumors had lower physical activity and higher sedentary time compared with the other diagnostic groups.

To cite: Grydeland M, Bratteteig M, Rueegg CS, et al. Physical Activity Among Adolescent Cancer Survivors: The PACCS Study. *Pediatrics.* 2023;152(3):e2023061778

With the growing population of childhood cancer survivors (CCS) at greater risk of premature morbidity and mortality than the general population,[1,2] there is increasing need for preventing treatment-related late effects, such as secondary cancers, cardiovascular diseases, diabetes mellitus, musculoskeletal disorders, fatigue, and reduced quality of life.[3–6] Pediatric cancer is heterogeneous with more than 100 different entities treated in various ways. Previous research has mainly focused on survivors of acute lymphatic leukemia (ALL), representing about one third of cases. However, ALL-survivors have less late effects than other CCS and are not considered representative for the entire group.[3] Physical activity (PA) and sedentary time (ST) may be 2 key lifestyle factors influencing the risk of late effects in CCS.[7–9] PA is defined as any bodily movement produced by skeletal muscles that requires energy expenditure, whereas ST is defined as time spent sitting, reclining, or lying.[10] In adolescent CCS, observational studies have shown that higher PA and/or lower ST is associated with improved cardiorespiratory and muscular fitness,[11,12] bone health,[13] body composition,[14] and quality of life.[15,16] During and immediately after cancer treatment, children and adolescents often have significant impairments in motor performance, potentially affecting their ability to re-engage in PA.[17–19] Exercise training interventions in children with any type of cancer during treatment and/or shortly after treatment have shown to improve functional mobility without increasing the risk of mortality, recurrence, or associated adverse effects.[20] However, knowledge regarding levels of PA and ST in long-term adolescent CCS and whether they return to similar levels as peers after the early phase of survivorship is sparse.[21] Studies using device-measured PA and ST are lacking in large samples of adolescent CCS. Furthermore, levels have not been compared with population-based norms, and factors associated with low PA and high ST have not been investigated. The current cross-sectional study addresses the lack of knowledge regarding device-measured PA and ST in adolescent CCS and associated factors; basic knowledge that is needed to develop future targeted interventions to mitigate severity of late effects, and to identify those at greatest need of such interventions.

Using the to date largest multicenter European sample of adolescent CCS, the aims of the current study are therefore to:

1. Describe levels of device-measured total PA, moderate-to-vigorous PA (MVPA), and ST, stratified by sociodemographic and cancer-related factors
2. Examine sociodemographic and cancer-related factors associated with lower MVPA and higher ST
3. Compare levels of total PA, MVPA, and ST with age- and sex-stratified references

METHODS

Study Design

The Physical Activity in Childhood Cancer Survivors (PACCS) study is a multicenter, mixed methods study of CCS from 5 European countries (Norway, Germany, Denmark, Finland, and Switzerland). The PACCS study is thoroughly described by Lie et al.[22] Below we describe the methods relevant to this cross-sectional substudy.

Participants

CCS aged 9 to 16 years with any previous cancer diagnosis ≥1 year postcompletion of cancer treatment were eligible. Criteria for exclusion were language difficulties (questionnaires in main native language of each participating country) or limited cognitive function that made it impossible to complete the questionnaire or wear an accelerometer. Participants were recruited during scheduled visits at their follow-up hospital between October 2017 and December 2020. As part of public health services in the participating countries, CCS are scheduled for regular follow-up visits at least once per year, depending on time from diagnosis.

Physical Activity and Sedentary Time

PA and ST were assessed by accelerometers (ActiGraph GT3X+, ActiGraph LLC, Pensacola, FL), registering acceleration in the vertical axis translated into counts per minute. The participants received a programmed monitor and were instructed to wear it on the right hip for 7 consecutive days during all awake hours, except for swimming and showering. Participants returned the monitor to the study site by postal mail. The accelerometer data were downloaded by the ActiLife software (ActiGraph LLC, Pensacola, FL) at each study site and later uploaded to 1 common secure server at the Norwegian School of Sports Sciences for processing in the Kinesoft software (version 3.3.80, Loughborough, UK).

We applied 2 versions of processing the accelerometer data (Supplemental Table 4): (1) the predefined "PACCS criteria" that were chosen to best capture the PA behavior of children and adolescents; and (2) the "reference criteria" that reflected the same processing as described for the reference material. We used the PACCS criteria for analyses in CCS only (aims 1 and 2) and reference criteria when comparing CCS to the references (aim 3). For the PACCS criteria, the accelerometer measured raw signals at 30 Hz summarized in 10-second intervals (epochs) to capture short bouts of PA typically in children.[23] We set nonwear criteria to ≥20 consecutive minutes of 0 counts with no interruptions as this is a commonly used nonwear criterion in children.[24] For the reference criteria, we reintegrated accelerometer data into 60-second epochs, and nonwear time was defined as ≥60 consecutive minutes of 0 counts, allowing 2 minutes of interruptions.

For both criteria, a valid day was defined as ≥480 minutes per day of wear time. In CCS, we compared total PA (counts per minute per day) by the number of valid days, adjusted for multiple comparisons (Bonferroni correction), and found no significant differences in total PA by the number of valid days (Supplemental Fig 4). Thus, participants with ≥1 valid day of accelerometer registration were included in our analyses.

We described total PA as the number of counts per minute and categorized the activity counts into intensities based on metabolic energy equivalents as ST (<101 cpm), light (101 <2296 cpm), moderate (2296 <4012 cpm), and vigorous (≥4012 cpm) PA based on the cut-off points proposed by Evenson et al.[25] We calculated the average number of minutes spent per day in each of these intensities. Average minutes per day in MVPA were calculated by summing the time spent in moderate and vigorous PA. Participants were categorized as meeting the World Health Organization's recommendation for PA[26] if they engaged in ≥60 minutes of MVPA per day on average.

Demographic and Medical Data

We extracted information on sex, date of birth, height, weight, diagnosis, date of diagnosis, cancer treatment modality (yes or no for chemotherapy, radiation, surgery, hematopoietic stem cell treatment, dosages and intensity were not available for neither modalities, nor chemotherapeutic agents), date of treatment completion, and potential cancer relapse from the participants' medical records. Based on this information, we calculated age at study participation, BMI (BMI, kg/m^2), age at diagnosis, time since diagnosis, and time since treatment completion. Values of BMI were converted into iso-BMI categories (age- and sex-adjusted values of child BMI equivalent to adult BMI categories) according to the International Obesity Task Force cut-offs.[27] Diagnoses were based on the International Classification of Childhood Cancer, third edition and grouped into leukemias, lymphomas, central nervous system (CNS) tumors, sarcomas, and other tumors (neuroblastoma, renal tumor, liver tumor, retinoblastoma, germ cell tumor, carcinoma, and "other").[28] Leukemia (acute lymphatic leukemia, acute myeloid leukemia, juvenile myelomonocytic leukemia or myelodysplastic syndrome), lymphoma (Hodgkin's lymphoma and non-Hodgkin's lymphoma), and sarcoma (soft tissue sarcoma, bone tumors), were further divided into subgroups to describe potential differences within these diagnostic groups.

Parents provided information on parental education in an electronic questionnaire.

Reference Material

The reference material consists of pooled and harmonized accelerometer data representing 47 497 individuals (2–18 years) from 18 European countries.[29] We did not have the raw material available and thus stratified our sample of CCS in accordance to the reference material as sex- and age-stratified (2-year intervals) numbers, marginal means, and SD of the 8 to 9 through 16 to 17-year-olds by contacting the first author to compare total PA, MVPA, and ST to the PACCS data. In the harmonized data, values of total PA were adjusted for country, season, study year, and ActiGraph models. Values of MVPA and ST were additionally adjusted for wear time.

Statistical Analyses

Characteristics of CCS are presented as mean values ± SDs or frequencies with proportions. For 234 of 294 nonparticipants, we had basic demographic and cancer-related information that we compared with corresponding participants information using *t* test for unequal variances.

For aim 1, we described total PA (counts per minute), MVPA and ST (minutes per day), and proportion meeting the PA recommendation by sociodemographic variables (country, sex, age, iso-BMI, parental education), and cancer-related factors (diagnosis, age at diagnosis, time since diagnosis, relapse). Continuous variables are presented as marginal means ± SDs (calculated from $SE^{*}\sqrt{n}$) adjusted for season and country, and MVPA and ST were additionally adjusted for wear time.

For aim 2, we performed univariable and multivariable linear regression models to examine sociodemographic and cancer-related factors associated with MVPA and ST. MVPA was chosen as the PA outcome in the models, as opposed to total PA, as higher intensity PA is shown to have more consistent and robust relationships with health indicators than PA of lower intensity.[30] Multivariable models included all variables of interest (sex, age, iso-BMI, parental education, diagnostic group, age at diagnosis, relapse). All univariable and multivariable models were adjusted for country, season, and wear time. We defined missing information on parental education as its own category to avoid losing participants in the analyses. Global *P* values for categorical variables were calculated using likelihood-ratio tests. As MVPA and ST have shown to differ by sex and age groups,[29] we tested each association in the multivariable model for interaction with sex and age category (9–11 vs 12–16 years).

For aim 3, we compared marginal means of total PA, MVPA, and ST between CCS and references, stratified by sex and age group (2-year interval) using immediate *t* tests for unequal variances, ie, a *t* test that tests the difference of a variable of interest between 2 groups based on information of sample size, mean, and SD, if no individual-level data are available.

Statistical analyses were performed in Stata 17 (StataCorp LP, College Station, TX, USA).

Ethics

We collected approvals from the Regional Ethical Committees for Medical and Health Research at all sites and the project owner institution before implementing the project. Children <16 years provided oral assent, whereas adolescents ≥16 years and guardians provided written consent.

RESULTS

Participants

Of 726 invited CCS, 526 (72%) participated in the study, of which 432 (60%) contributed valid data to the analyses (Fig 1). At study, participants' mean age was 12.2 years (SD = 2.2), 48% (n = 206) were female, and 64% (n = 276) were categorized as normal weight (Table 1). Comparison of participants and nonparticipants (Supplemental Table 5) showed no differences in basic characteristics, except that participants were slightly younger at study compared with nonparticipants (12.2 vs 12.6 years, P = .02).

Physical Activity and Sedentary Time in Childhood Cancer Survivors

On average, participants wore their accelerometer 12.9 hours per day (SD = 1.3) for 6.1 days (SD = 1.4). Overall, marginal mean of total PA was 486 cpm, and minutes per day spent in MVPA and ST were 54 and 523, respectively (Table 2). In total, 34% of participants met the PA recommendation.

Descriptive analyses showed that compared with 9 to 11-year-olds, the 12 to 16-year-olds had a lower level of total PA (437 vs 544 cpm), spent less time in MVPA (51 vs 58 min), were more sedentary (549 vs 491 min), and a lower proportion (28 vs 42%) met the PA recommendation (Table 2). Compared with the other diagnostic groups, survivors of CNS tumor had the lowest level of total PA (424 ± 175 cpm per day) and MVPA (46 ± 23 min per day), the highest level of ST (542 ± 58 min per day), and the lowest proportion (17%) meeting the PA recommendation (Table 2, Fig 2).

Factors Associated With Lower MVPA and Higher ST in Childhood Cancer Survivors

Female sex, being overweight, a survivor of CNS tumor, and having experienced relapse were associated with lower MVPA (Table 3). Factors associated with higher ST were female sex, older age, overweight, and being a survivor of CNS tumor (Table 3).

We found no significant interaction of sex or age category on the association between sociodemographic (sex, age, iso-BMI, parental education) or cancer-related factors (diagnostic group, age at diagnosis, relapse) and MVPA

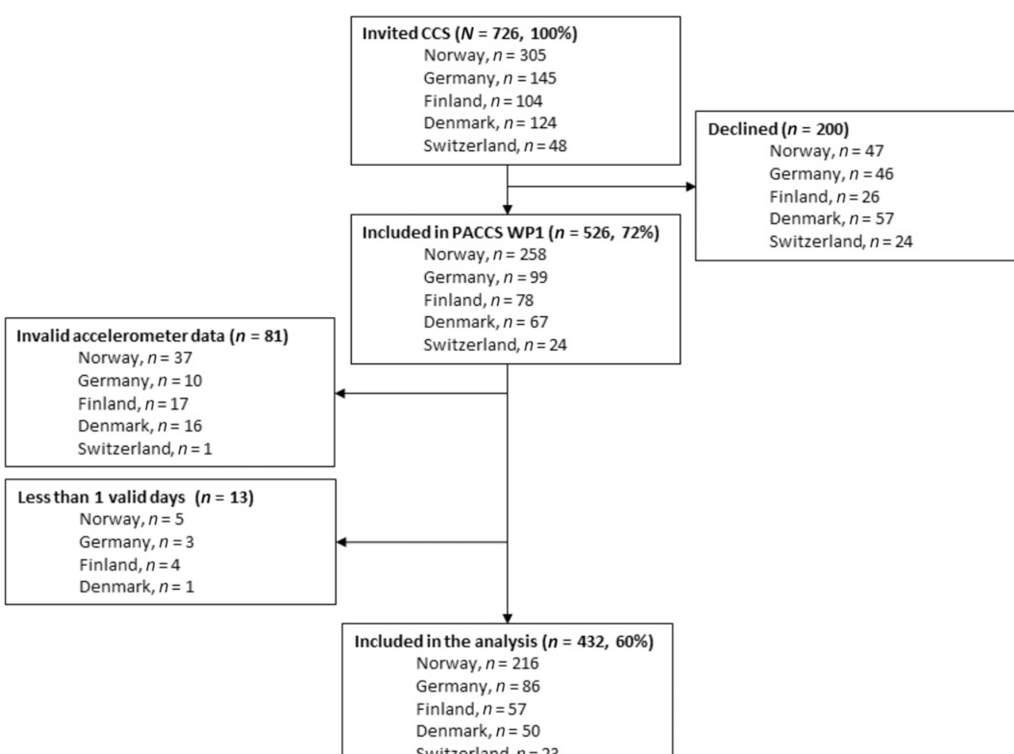

FIGURE 1
Flowchart of the inclusion process in PACCS. WP, work package.

TABLE 1 Characteristics of Adolescent Childhood Cancer Survivors in PACCS (n = 432)

Socio-demographic Characteristics	*N* (%) or Mean ± SD
Country	
Norway	216 (50)
Germany	86 (20)
Finland	57 (13)
Denmark	50 (12)
Switzerland	23 (5)
Sex	
Male	226 (52)
Female	206 (48)
Age at study (years)[a]	12.2 ± 2.2
9–11	196 (45)
12–16	236 (55)
Height (cm)	153 ± 14
Wt (kg)	47.4 ± 14.3
Iso-BMI category	
Underweight	35 (8)
Normal wt	276 (64)
Overweight	99 (23)
Obese	22 (5)
Parental education, (years)[b]	
9–10	41 (12)
11–13	138 (40)
>13	169 (48)
Cancer-related characteristics	
ICCC-3 diagnostic group	
I. Leukemia	203 (47)
II. Lymphomas	47 (11)
III. CNS tumor	69 (16)
VIII–IX. Sarcomas[c]	36 (8)
IV–VII, X–XI. Other[d]	77 (18)
Age at diagnosis (years)	5.1 ± 3.3
0–4	233 (54)
5–10	172 (40)
11–15	27 (6)
Time since diagnosis (years)	7.0 ± 3.3
1–4	135 (31)
5–10	239 (55)
11–15	58 (13)
Treatment	
Chemotherapy	393 (91)
Surgery	159 (37)
Radiotherapy	97 (23)
HSCT	50 (12)
Autologous	18 (4)
Allogeneic	32 (7)
Relapse	
No	390 (90)
Yes	42 (10)

HSCT, hematopoietic stem cell transplantation; ICCC-3, International Classification of Childhood Cancer, third edition.
[a] In the age category 9 < 12 y, 2 8-y-olds are included. In the age category 13 to 16 y, 4 17-y-olds are included.
[b] Missing information on parental education in 84 participants.
[c] Sarcomas include sarcomas in soft tissue (n = 22), bone tumors (n = 12), eye (n = 1), and kidney (n = 1).
[d] Other diagnoses include neuroblastoma (n = 18), renal tumor (n = 30), liver tumor (n = 4), retinoblastoma (n = 14), germ cell tumor (n = 2), carcinoma (n = 3), and "other" (n = 6).

(all $P_{\text{interaction}} > 0.05$; Table 3). For ST, there were no significant interactions between sex and associated factors, but there was a stronger association between cancer diagnosis and ST in younger survivors (9–11 years) compared with older survivors (12–16 years); Table 3 and Supplemental Fig 5.

Physical Activity and Sedentary Time in Childhood Cancer Survivors Compared With References

On average, references wore their accelerometer for 5 days (SD = 1.7) with 12.9 hours of daily wear time (SD = 1.7). Using reference processing criteria, male survivors had lower total PA than references in 3 of 5 age groups; 8–9 years (523 vs 633 cpm, P = .003), 12–13 years (490 vs 559 cpm, P = .005), and 14–15 years (432 vs 483 cpm, P = .03) (Fig 3A). Also, male survivors spent less time in MVPA at all ages (8–9-year-olds: 42 vs 61 min, P < .001; 10–11-year-olds: 54 vs 61 min, P = .05; 12–13-year-olds: 48 vs 56 min, P = .02; 14–15-year-olds: 44 vs 50 min, P = .04), except for 16–17-year-olds (Fig 3C). Both total PA and MVPA were similar between female survivors and references in all age groups (Fig 3 B and D). Both male and female survivors accumulated more ST than references reaching statistical significance for some of the age groups; in male 8 to 9-year-olds (402 vs 356 min, P = .002), 12 to 13-year-olds (443 vs 416 min, P = .005), and 14 to 15-year-olds (489 vs 471 min, P = .04), and in female 8 to 9-year-olds (396 vs 367 min, P = .02), 10 to 11-year-olds (416 vs 400 min, P = .03) and 16 to 17-year-olds (533 vs 492 min, P = .009); Fig 3, E–F.

In Supplemental Fig 6, A–F, we display the results in survivors also using the PACCS criteria. The different processing criteria had little influence on total PA, however the PACCS criteria yielded ~10 minutes more in MVPA and ~60 to 90 minutes more in ST compared with the reference criteria.

DISCUSSION

Main Findings

Within this international sample of adolescent CCS, we found that only a third of the participants reached the World Health Organization's PA recommendation and that CCS spent most of their day sedentary. Factors associated with both less MVPA and/or more ST were being female, older, overweight, having had a diagnosis of CNS tumor, or a relapse. Comparing CCS to references, we found that male survivors were less physically active (both total PA and MVPA), whereas female survivors had equally low levels of PA. Importantly, male and female survivors in all age groups registered more ST than references. As "every minute counts,"[10] these differences in PA and ST may be considered clinically meaningful.

TABLE 2 Physical Activity and Sedentary Time in Adolescent Childhood Cancer Survivors, Stratified by Socio-Demographic and Clinical Variables.

	N	Total PA (cpm per day) Mean ± SD	MVPA (min per day) Mean ± SD	ST (min per day) Mean ± SD	Meets PA Rec,[10] *N* (%)
Total	432	486 ± 183	54 ± 23	523 ± 58	149 (34)
Country					
Norway	216	501 ± 184	56 ± 23	516 ± 58	79 (37)
Germany	86	433 ± 186	49 ± 23	540 ± 59	22 (26)
Finland	57	522 ± 186	56 ± 23	512 ± 59	21 (37)
Denmark	50	480 ± 183	55 ± 23	529 ± 58	19 (38)
Switzerland	23	463 ± 185	49 ± 24	532 ± 61	8 (35)
Sex					
Male	226	508 ± 182	58 ± 23	515 ± 57	97 (43)
Female	206	462 ± 182	50 ± 23	531 ± 57	52 (25)
Age category at study (years)					
9–11	198	544 ± 176	58 ± 23	491 ± 50	84 (42)
12–16	234	437 ± 176	51 ± 23	549 ± 50	65 (28)
Iso-BMI category					
Underweight	35	474 ± 184	53 ± 23	536 ± 58	12 (34)
Normal wt	276	508 ± 182	57 ± 22	518 ± 57	107 (39)
Overweight	99	442 ± 185	48 ± 23	529 ± 59	25 (25)
Obesity	22	433 ± 183	48 ± 23	526 ± 58	5 (23)
Parental education (years)[a]					
9–10 y	41	450 ± 198	51 ± 24	537 ± 62	11 (27)
11–13 y	138	483 ± 187	54 ± 24	524 ± 59	52 (38)
>13 y	169	485 ± 190	54 ± 24	529 ± 60	59 (35)
Diagnostic group					
I. Leukemia	203	482 ± 180	54 ± 22	524 ± 57	75 (37)
ALL	183	486 ± 181	54 ± 23	521 ± 57	67 (37)
AML	19	447 ± 183	50 ± 23	544 ± 57	8 (42)
JMML and MDS	1	409 ± 180	41 ± 22	528 ± 56	0 (0)
II. Lymphoma	47	509 ± 180	58 ± 23	513 ± 57	17 (36)
Hodgkin	14	448 ± 181	52 ± 23	542 ± 57	4 (29)
Non-Hodgkin	33	534 ± 181	61 ± 22	501 ± 57	13 (39)
III. CNS tumor	69	424 ± 175	46 ± 23	542 ± 58	12 (17)
VIII–IX. Sarcomas	36	466 ± 180	53 ± 22	524 ± 57	11 (31)
Bone tumors	12	446 ± 183	47 ± 23	535 ± 58	3 (25)
Soft tissue[b]	24	477 ± 184	56 ± 23	519 ± 58	8 (33)
IV–VII, X–XI. Other cancer[c]	77	547 ± 183	60 ± 23	508 ± 58	34 (44)
Age at diagnosis category (years)					
0–3	233	510 ± 182	56 ± 23	514 ± 57	94 (40)
4–7	172	461 ± 183	51 ± 23	528 ± 57	49 (28)
8–15	27	440 ± 182	53 ± 23	560 ± 57	6 (22)
Time since diagnosis category (years)					
1–4	135	466 ± 183	52 ± 23	526 ± 56	38 (28)
5–10	239	509 ± 182	56 ± 23	512 ± 56	93 (39)
11–16	58	438 ± 183	52 ± 23	558 ± 56	18 (31)
Relapse					
No	390	491 ± 183	55 ± 23	521 ± 58	141 (36)
Yes	42	437 ± 184	48 ± 23	532 ± 58	8 (19)

Results on counts per minute are adjusted for season and country, results on MVPA and ST are additionally adjusted for wear time. AML, acute myeloid leukemia; JMML, juvenile myelomonocytic leukemia; MDS, myelodysplastic syndrome; Rec, Recommendations >60 min MVPA per day.

[a] Missing information on parental education in 84 participants.

[b] Including 1 kidney sarcoma and 1 eye sarcoma.

[c] Other diagnoses include neuroblastoma ($n = 18$), renal tumor ($n = 30$), liver tumor ($n = 4$), retinoblastoma ($n = 14$), germ cell tumor ($n = 2$), carcinoma ($n = 3$), and "other" ($n = 6$).

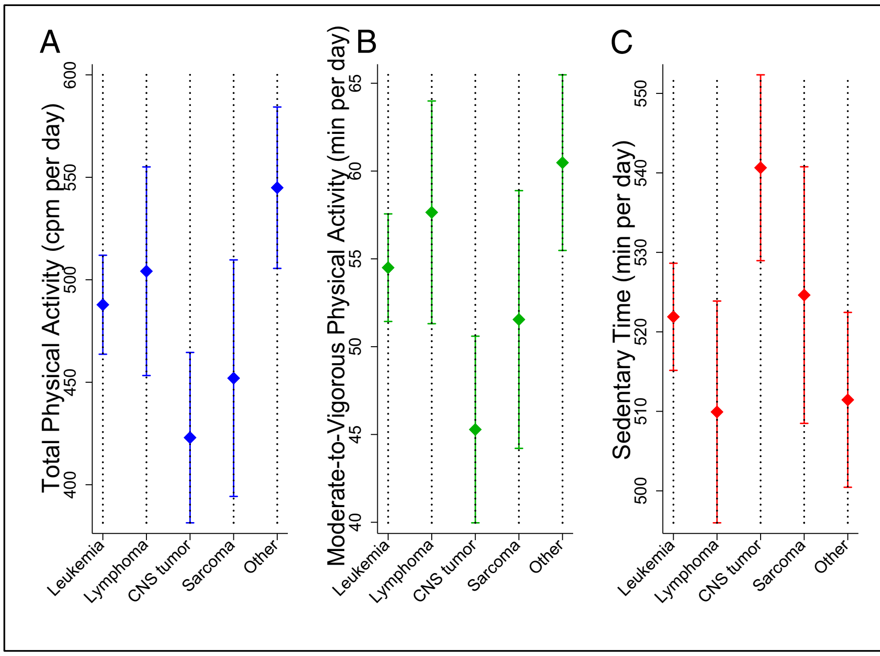

FIGURE 2

Marginal means (diamonds) with 95% confidence intervals (whiskers) for (A). Total physical activity. (B) Moderate-to-vigorous physical activity. (C) Sedentary time in adolescent childhood cancer survivors, stratified by diagnostic group ($n = 432$). Analyses on MVPA and ST are additionally adjusted for wear time. Other, other cancer diagnoses (includes neuroblastoma [$n = 18$], renal tumor [$n = 30$], liver tumor [$n = 4$], retinoblastoma [$n = 14$], germ cell tumor [$n = 2$], carcinoma [$n = 3$], and "other" [$n = 6$]). The models are adjusted for age, sex, country, and season.

Physical Activity and Sedentary Time in Childhood Cancer Survivors

The expected lower levels of total PA and MVPA, and higher ST in female compared with male survivors are in line with previous findings.[31,32] Differences in PA levels between sexes have been discussed by Caru and Curnier (2020), highlighting that parents less often encourage female than male survivors to be physically active and accept a sedentary lifestyle more often in female compared with male survivors.[33] Cultural and socio-demographic factors were found to influence MVPA levels in adult CCS,[34] and substantial country and region-specific differences in MVPA and ST were found in European youth.[29] These issues may be even more pronounced in some cultural groups.

Age was negatively associated with MVPA but not after adjusting for other factors. In contrast, age remained positively associated with ST when adjusting for other factors. In adolescent CCS, the existing knowledge concerning the relationship between age and MVPA and ST is limited, but our results align with results from the general population; namely that levels of total PA and MVPA decrease during adolescence, whereas ST increases.[29,35,36] Reasons for these changes are not clear but factors like less facilities perceived suitable or accessible, lack of time, increasing autonomy, and less social support from family and peers have been suggested as reasons in noncancer youth samples.[35,37]

Being overweight was associated with lower MVPA and higher ST. This is in line with evidence from the general population linking device-measured MVPA to adiposity in children and adolescents.[26,38] The current literature on ST and adiposity in the general population is more limited,[39] but sedentary behaviors, especially screen time, have been linked to unfavorable measures of adiposity.[26,39] Our results contrast Schindera et al who found no association between iso-BMI and meeting PA or screen time recommendations in childhood and adolescent CCS.[40] However, their dichotomization of PA and screen time may have led to loss of power in finding an association between iso-BMI and PA to screen time. Importantly, weight status was the only factor that we examined that is modifiable. If we assume a directional association between iso-BMI and MVPA to ST, helping overweight CCS to do more MVPA may also counterbalance ST and yield synergic improvements to their health, which is important in this population at high long-term risk of cardiovascular disease.[41,42]

Methodologically robust descriptions of MVPA and ST in adolescent survivors of CNS tumor are sparse, which emphasizes the significance of our findings. We found lower levels of MVPA and higher ST in this vulnerable diagnostic group compared with the other diagnostic groups. Moreover, cancer relapse was associated with lower MVPA. This is in line with Schindera et al who found that self-reported PA (of any intensity) was lower in survivors with relapse.[40]

TABLE 3 Factors Associated with (A) Moderate-to-Vigorous Physical Activity (min per day) and (B) Sedentary Time (min per day) in Adolescent Childhood Cancer Survivors ($n = 432$)

	Univariable Regression[a]			Multivariable Regression[b]				
A. Moderate-to-Vigorous Physical Activity	β-coeff	95% CI	P[c]	β-coeff	95% CI	P[c]	$P_{interaction}$ With Sex	$P_{interaction}$ With Age
Sex			.001			<.001	NA	0.512
Male	Ref	−11.5 to −2.9		Ref	−13.1 to −4.6			
Female	−7.2			−8.9				
Age (years)	−1.2	−2.1 to −0.2	.022	−1.0	−2.0 to 0.1	.066	0.352	NA
Iso-BMI category			.004			<.001	0.226	0.966
Underweight	−4.1	−12.2 to 3.9		−4.0	−11.7 to 3.8			
Normal wt	Ref			Ref				
Overweight	−9.1	−14.5 to −3.8		−10.5	−15.6 to −5.3			
Obese	−9.2	−19.1 to 0.7		−9.6	−19.3 to 0.1			
Parental education[d]			.882			.986	0.473	0.333
Low	Ref			Ref				
Middle	2.5	−5.8 to 10.9		−0.2	−8.2 to 7.8			
High	2.7	−5.7 to 11.1		−0.2	−8.3 to 7.9			
Missing	3.7	−5.4 to 12.8		0.8	−8.0 to 9.6			
Diagnostic group		−2.5 to 11.8	.003			<.001	0.946	0.154
I. Leukemia	Ref	−14.0 to −1.4		Ref				
II. Lymphoma	4.7	−8.9 to 7.3		4.9	−2.5 to 12.2			
III. CNS tumor	−7.7	0.4 to 12.4		−8.9	−15.1 to −2.7			
VIII–IX. Sarcomas	−0.8			0.3	−7.6 to 8.1			
IV–VII, X–XI. Other	6.4			5.9	0.1 to 11.5			
Age at diagnosis (years)	−0.7	−1.4 to −0.1	.030	−0.5	−1.2 to 0.2	.178	0.944	NA
Relapse						.021	0.421	0.930
No	Ref			Ref				
Yes	−6.5	−13.9 to 0.8	.080	−8.3	−15.4 to −1.2			
B. Sedentary Time								
Sex			.003			<.001	NA	0.455
Male	Ref			Ref				
Female	16.6	5.7 to 27.5		19.5	10.2 to 28.9			
Age (years)	13.4	11.3 to 15.6	<.001	13.0	10.8 to 15.3	.001	0.476	NA
Iso-BMI category			.173			.004	0.128	0.946
Underweight	17.9	−2.6 to 38.4		13.1	−4.1 to 30.2			
Normal wt	Ref			Ref				
Overweight	11.2	−2.4 to 24.7		19.5	8.1 to 30.9			
Obese	7.7	−17.7 to 33.1		14.4	−6.9 to 35.8			
Parental education[d]			.104			.641	0.473	0.142
Low	Ref			Ref				
Middle	−10.9	−31.8 to 10.1		−1.4	−19.0 to 16.2			
High	−5.4	−26.5 to 15.8		3.8	−14.0 to 21.7			
Missing	−22.5	−45.3 to 0.4		−3.7	−23.2 to 15.7			
Diagnostic group			.007			.001	0.946	0.017
I. Leukemia	Ref			Ref				
II. Lymphoma	−10.4	−28.5 to 7.8		−15.9	−32.1 to 0.3			
III. CNS tumor	18.1	2.1 to 34.0		17.6	3.9 to 31.2			
VIII–IX. Sarcomas	0.9	−19.6 to 21.3		−1.4	−18.8 to 16.0			
IV–VII, X–XI. Other	−16.0	−31.3 to −0.8		−10.5	−23.4 to 2.4			
Age 9–11 y								
Leukemia				Ref		<.001		
Lymphoma				−31.7	−55.7 to −7.6			
CNS tumor				34.7	13.1 to 56.3			
Sarcomas				−4.4	−31.9 to 23.2			
Other				3.2	−13.8 to 20.2			

TABLE 3 Continued

B. Sedentary Time	Univariable Regression[a]			Multivariable Regression[b]				
	β-coeff	95% CI	P^c	β-coeff	95% CI	P^c	$P_{interaction}$ With Sex	$P_{interaction}$ With Age
Age 12–16 y								
Leukemia				Ref		.059		
Lymphoma				−9.3	−32.3 to 13.6			
CNS tumor				−3.1	−22.1 to 15.8			
Sarcomas				−5.5	−29.2 to 18.1			
Other				−29.4	−49.9 to −8.9			
Age at diagnosis (years)	3.6	2.0 to 5.2	<.001	0.9	−0.7 to 2.4	.290	0.958	NA
Relapse			.267			.078	0.623	0.800
No	Ref			Ref				
Yes	10.5	−8.1 to 29.1		14.0	−1.6 to 29.7			

β-coeff, β coefficient; CI, confidence interval.
[a] Univariate regression models are adjusted for season, wear time and country.
[b] The multivariable regression model includes all variables of interest listed in the table, the model is additionally adjusted for season, wear time and country.
[c] Global P value from likelihood ratio test.
[d] Missing info on parental education in 84 participants.

In sum, our results suggest that sociodemographic variables (age, sex, iso-BMI) seem equally important as the cancer-related variables for MVPA and ST. However, as the sociodemographic risk factors are similar to those of the general population,[29] clinicians should pay particular attention to the need for PA interventions in CCS of CNS tumor. It has been hypothesized that increments in MVPA is accompanied by increments in ST (PA compensation hypothesis),[43] implicating that ST is not necessarily targeted by increasing MVPA. However, a recent systematic review showed that only 6 of 22 studies in general youth populations reported evidence of PA compensation, suggesting that one may also reduce ST by focusing on increasing PA.[44] Whether this applies to CCS, who often struggle with late effects from cancer treatment (ie, fatigue[6]), has not been studied.

Physical Activity and Sedentary Time in Childhood Cancer Survivors Compared With References

Previously published comparisons of device-measured PA between adolescent CCS and controls are few.[45] Using self-reported data, previous studies have shown that adolescent and young adult CCS are less physically active than their siblings or peers.[32,46] Our results support these findings, albeit in male survivors only. The visual impression when comparing male survivors to references might be interpreted as male survivors' progress into late adolescence (16 to 17 years), their levels of total PA, MVPA, and ST align to that of peers. However, the low numbers of male survivors in this age group (n = 11) requires careful interpretation. We found similar levels of total PA and MVPA between female survivors and references. Still, female survivors should be targeted to improve PA levels as they were less physically active compared with male survivors. Moreover, as CCS have higher disease risk than the general population, it is important that CCS are at least as physically active as the general population. A recent publication examining barriers and facilitators of PA within a subset of the current population who had various levels of PA (n = 63, mean age 14 years) reported that perceived reduced bodily function, together with fatigue, were barriers to PA, leading to fewer opportunities or less motivation to participate in PA. Moreover, the CCS perceived an ability gap between themselves and their peers that reduced motivation to participate.[47] In contrast, important facilitators were environmental factors, such as support from family, peers, and school, and personal factors, such as acceptance, motivation, and goal setting. These are important elements to consider when planning for and designing future PA interventions for CCS.

The addition of the PACCS criteria in Supplemental Figs 6, A–F demonstrates that comparing MVPA and ST across studies using different accelerometry processing criteria can lead to biased results and wrong conclusions. The reference data were pooled from several studies with different accelerometer settings, and thus the authors analyzed the gathered data based on longer epochs and nonwear time to avoid losing data, however with lower precision. As the nature of PA in children is characterized to be in short sporadic bouts, short epochs (such as 10 sec) are recommended to detect short bursts of high-intensity PA.[23] Until long-awaited consensus on common accelerometer settings in children and adolescents is reached, reporting detailed information about settings used in research studies is crucial.

Strengths and Limitations

A major strength of this study is the relatively large, international sample of adolescent CCS representing different diagnostic groups. Because of extensive public health services in the participating countries, we consider the recruitment strategy successful for reaching eligible participants.

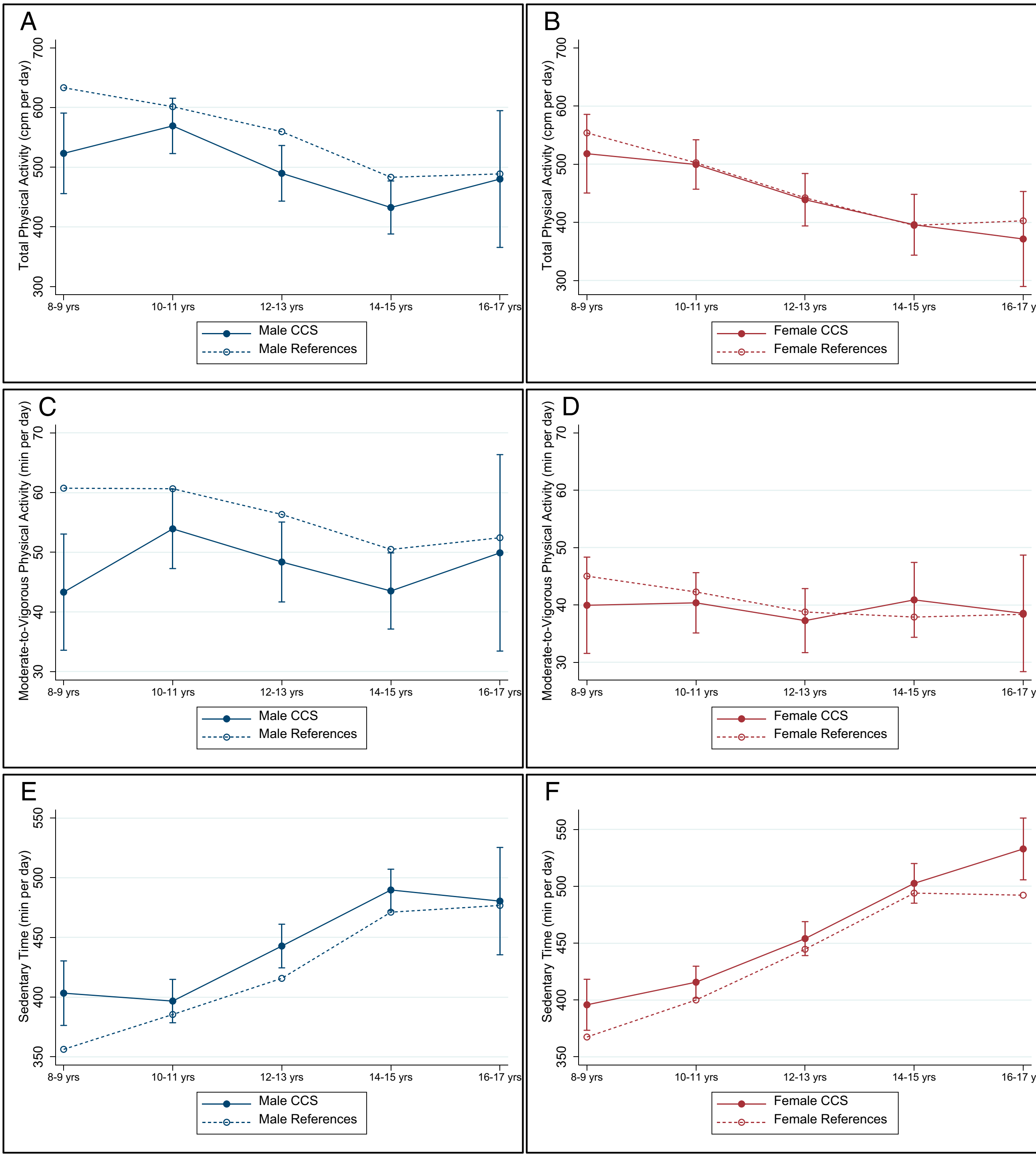

FIGURE 3
(A and B) Total physical activity (count per minute). (C and D) Moderate-to-vigorous physical activity. (E and F) Sedentary time in adolescent childhood cancer survivors (solid lines, $n = 432$) and references[29] (dashed lines), stratified by sex and age category.* Dots represent marginal means and whiskers represent 95% confidence intervals. Graphs represent cross-sectional data (connective lines for visual purposes only). Analyses are adjusted for country and season. Analyses on moderate-to-vigorous physical activity and sedentary time are additionally adjusted for wear time. *In the age category 8 to 9 years, only 2, 8-year-old CCS are included. In the age category 16 to 17 years, only 4, 17-year-old CCS are included. Female CCS, $n = 206$; Male CCS, $n = 226$.

The use of accelerometers to assess PA and ST has clear advantages over self-report, which are subject to both recall- and social desirability bias.[48] However, accelerometers have some limitations: they lack ability to detect water-based activities (eg, swimming) because of poor water resistance; activities with little vertical acceleration (eg, cycling); and stationary activities with high load (eg, resistance training). Also, wearing an activity monitor could change PA behavior. The PACCS criteria for nonwear classification may have underestimated the CCS' time spent sedentary. Aadland et al compared 10 accelerometer nonwear time criteria, together with logs of nonwear time, in 891 10-year-olds, and reported a 4% and 5% reduction in ST when nonwear criteria were set to 20 minutes versus 45 and 60 minutes of consecutive 0s, respectively.[49] However, this has little impact on association analyses. The study response rate was overall high. Except a slightly older age, there were no differences between participants and nonparticipants regarding diagnosis, age at diagnosis, or time since diagnosis, supporting the generalizability of our results. However, generalizability is limited to CCS without cognitive impairment and within the same range of age and weight-status. Moreover, the numbers of participants from the respective countries were disproportional because of different start-up dates. Norway started ahead of the other countries as funding and approvals were earlier available. Inclusion was stopped when the required number for participants according to power calculations were met.[22] Unfortunately, we lacked detailed treatment information (ie, specific location or doses of the different treatment modalities) to investigate the impact of treatment burden on MVPA and ST. The cross-sectional study design hinders conclusions on causal relationships of the results, but the data form an important basis for future much-needed prospective and tailored intervention studies in this population.

CONCLUSIONS

As CCS are already at greater risk of premature morbidity and mortality than the general population, adding the negative health impacts of low PA and high ST may further exacerbate the risk of premature morbidity and mortality in CCS. Clinicians and healthcare personnel should have the demonstrated low levels of PA and high ST in mind when addressing follow-up care for CCS, especially in survivors of CNS tumors.

As adolescence is a crucial period with respect to establishing lifestyle habits, we call for tailored interventions to increase PA and reduce ST in adolescent CCS.

ACKNOWLEDGMENT

We are grateful to the children and their parents and guardians for giving of their time and effort. It is through their generosity that we were able to complete the study. The authors thank all members of the PACCS study group not listed as coauthors of this paper.

ABBREVIATIONS

CCS: childhood cancer survivors
CNS: central nervous system tumors
MVPA: moderate-to-vigorous physical activity
PA: physical activity
ST: sedentary time

Fridh, Lähteenmäki, and Kriemler coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content; Drs Rueegg, Lie, Thorsen, Anderssen, and Ruud conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2023-061778

Accepted for publication Jun 22, 2023

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FUNDING: The study is funded by the Norwegian Research Council (ID number: 273500), The Norwegian Cancer Society (202062), Dagmar Marshall Foundation (Denmark) (500020), and The Norwegian Childhood Cancer Society (220004). The funding bodies had no role in the design, conduct and publication of the study.

CONFLICT OF INTEREST DISCLOSURES: The authors have indicated they have no conflicts of interest relevant to this article to disclose.

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