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REVIEW ARTICLE

Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies

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Abstract

Purpose The number of pediatric cancer survivors has increased dramatically over recent decades. Prior studies involving pediatric cancer survivors have reported reduced physical activity and fitness levels. Thus, the aim of this meta-analysis was to synthesize previous findings on physical activity and fitness levels of pediatric cancer survivors, who had completed cancer treatment and are in complete remission compared with age-matched, non-athletic healthy controls with no history of cancer diagnosis.

Methods Three electronic databases (PubMed, Web of Science, and EBSCO) were searched using a combination of 24 terms. Observational studies examining the post-treatment physical activity and/or fitness levels of pediatric cancer survivors compared with that of non-cancer controls and published in peer-reviewed, English-language journals before August 22, 2018 were eligible. Random-effect models were used in Comprehensive Meta-Analysis software for effect-size estimations of eight studies for physical activity and eight for fitness.

Results The studies included a total sample of 2628; 1413 pediatric cancer survivors and 1215 non-cancer controls. Both physical activity and fitness were significantly lower in childhood cancer survivors than in non-cancer controls ($g = -0.889$; 95% confidence interval [CI] = − 1.648 − 0.130; $p = 0.022$) and ($g = -1.435$; 95% CI = − 2.615 − 0.225; $p = 0.017$), respectively, with high heterogeneity.

Conclusions Pediatric cancer sequelae and its treatment may limit participation in physical activity and fitness activities by survivors of pediatric cancer. Accentuating the need to incorporate physical activity and fitness into treatment protocols and post-treatment recommendations may improve pediatric cancer survivors' health and well-being.

Keywords Physical activity · Fitness · Pediatric cancer survivors

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Introduction

Overall survival rates for childhood cancers have improved significantly over past decades owing to new and advanced treatment protocols [1, 2]. In the USA, for example, the overall 5-year survival rate for all pediatric cancers combined rose from approximately 58% in the mid-1970s to 83.9% in 2017 [3, 4]. While cancer remission is celebrated, pediatric cancer survivors must still cope with cancer sequelae along with the rigors of treatments such as chemotherapy, surgery, and/or radiation, all of which can have deleterious side effects. Examples of such adverse effects include excess stress, depression, anxiety, pain, fatigue, fear of recurrence, and immune system impairment, many of which can adversely affect cognitive and physical functioning [5, 6].

Compared with their healthy peers with no history of cancer diagnosis (referred to as the non-cancer controls), pediatric cancer survivors are also at greater risk for other negative health conditions like obesity, diabetes, and cardiovascular disease [5, 7, 8]. In 2011, 66% of the estimated 338,501 pediatric cancer survivors (aged 5–19 years) in the USA experienced other chronic disease, with specific morbidities for pain and neurocognitive dysfunction estimated at 12% and 35%, respectively [6]. Importantly, the probability of developing metabolic syndrome is greater in pediatric cancer survivors of acute lymphoblastic leukemia and brain tumors who were treated with chemotherapy or radiotherapy because of an alteration in metabolic function caused by treatment protocols [9–11].

Engaging in life-long health-enhancing behaviors such as regular physical activity (PA), healthy eating, and avoidance of excess alcohol and any tobacco use is paramount to the health and well-being of cancer survivors. For PA in particular, most pediatric cancer survivors typically do not meet the Centers for Disease Control and Prevention's (CDC) weekly recommendations as compared to non-cancer peers [12, 13]. Generally, pediatric cancer survivors engage in low levels of PA and fitness activities [14–17], with factors such as minimal interest in exercise, pain, functional status, and beliefs about the importance of exercise influencing their decisions about PA engagement [18, 19]. However, a comprehensive meta-analysis of available observational studies on PA and fitness levels in pediatric cancer survivors, who had completed cancer treatment and are in complete remission, has yet to be performed. Previous meta-analyses of PA and fitness among pediatric cancer survivors focused on PA interventions or on the evaluation of intervention programs plus the underlying theoretical factors for PA among pediatric cancer survivors [13, 20, 21]. Therefore, it would be prudent to synthesize previous findings regarding PA levels in pediatric cancer survivors to inform future research related to devising additional strategies for motivating this population to engage in recommended PA levels. Thus, the purpose of the current meta-analysis was to systematically examine post-treatment PA and fitness levels of pediatric cancer survivors compared with non-cancer controls. The current study can contribute substantially to the medical literature evaluating the effects of cancer and its treatment on the physical health of pediatric cancer survivors.

Methods

Protocol

The authors agreed on inclusion criteria, outcome measures, and analysis methods and documented them in a pre-literature-search protocol. The study's PROSPERO registration number is CRD42016050345.

Information sources

Three databases were comprehensively searched—Medline (PubMed), Web of Science, and EBSCO—through August 2018 to retrieve all studies meeting inclusion criteria. Additionally, we manually examined the content pages of two relevant journals and the reference lists of the studies included in the meta-analysis to identify additional studies. We also solicited input from an expert in the field. A systematic search using a combination of 24 terms was executed: [("cancer survivors," "cancer patients," cancer, leukemia, "acute leukemia," lymphoma, "acute lymphoblastic leukemia," "acute myelogenous leukemia," "bone cancer," "central nervous system tumors," adolescent*, child*, pediatric, teen*, "physical activity," exercise, fitness, "resistance training," strength, "physical endurance," "physical functioning," "physical performance," "fine motor deficits," and exertion)]. Boolean operators "OR" and "AND" were used to combined these search terms. The initial search was limited to studies published in English only.

Study selection

Inclusion was determined via three-stage screening: title, abstract, and full text. Two authors independently evaluated the full texts of articles appearing to meet the criteria for inclusion after title and abstract screening. Disagreements were resolved via consensus.

Eligibility criteria

Observational studies examining the post-treatment PA or fitness of pediatric and adolescent cancer survivors compared with that of non-cancer controls and published in peer-reviewed, English-language journals before August 22, 2018, were eligible. Unpublished dissertations and abstracts were excluded. Pediatric cancer survivors (aged 18 years or younger) who had completed cancer treatment and were in complete remission were eligible for this meta-analysis. However, age ranges in two retained studies were somewhat extended (Brussel et al. [17], [8–23 years] and Batra et al. [22], [5–21 years]). Individual study participants varied relative to cancer type. Of the 16 included studies, six focused solely on pediatric cancer survivors of acute lymphoblastic leukemia (ALL), while the remaining 10 studies included pediatric cancer survivors of different cancers, including non-Hodgkin lymphoma, Hodgkin lymphoma, central nervous system tumors, neuroblastoma, leukemia, acute myelogenous leukemia, Ewing's sarcoma, retinoblastoma, acute lymphoblastic leukemia, solid tumors, and acute nonlymphoblastic leukemia. Survivors in all included studies had completed cancer treatment and were in complete remission. Treatment protocols involved chemotherapy and/or radiotherapy and/or surgery. Pediatric cancer survivors in one study were treated via stem cell transplantation with a minimum time since transplantation of 12 months. For each included study, the authors obtained the consent and approval of the primary physicians before recruiting pediatric cancer survivors. Thus, pediatric survivors were excluded from a study if they were still undergoing active cancer-related treatment and/or were hospitalized for other conditions.

Data collection process

Based on the Cochrane guidelines for reporting systematic reviews (Cochrane Consumers and Communication Review Group, 2015) [23], a study-specific data extraction sheet was developed. Two authors independently completed sheets for all studies meeting the inclusion criteria. Discrepancies were resolved via consensus and the involvement of a third author. The extraction sheet captured relevant data including author(s) name(s) and study date, study design, participant age range, sample size, measurement type, and variables measured. The methods and analysis sections of all eligible studies were independently reviewed by two authors using the Cochrane Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (attached as supplementary file) to assess methodological quality and outcome measures and ensure each was bias free.

Statistical analysis

Comprehensive Meta-Analysis Software Version-3 (2014) was used. On the basis of known statistics, study means obtained without variance estimates (standard deviation or standard error) were inputted. Mean difference in each eligible study was estimated along with standard error, standard deviation, confidence interval, and p value for effect-size calculation. The bias-corrected standardized mean difference was calculated (Hedges' g) [24]. Using sample size, relative weights were assigned to studies and the heterogeneity test was performed using Q and I^2 [24]. High-resolution forest plots, with random effects, were separately created.

Using the inverse of each study's standard error, effects were plotted to assess any negative or small effect size versus sample size correlations [25]. Regarding unpublished studies with negative or nonsignificant results, funnel plots of mean differences in PA or fitness were evaluated for asymmetry to identify publication bias. Study heterogeneity and differences in methodological quality could have affected this test [25].

Results

Study selection

The study flow diagram is shown in Fig. 1. Of 6709 articles retrieved following an initial 24-term search, 56 were retained for full-text screening following title and abstract screening. Detailed, full-text examination of the 56 remaining studies revealed 40 that failed to meet the inclusion criteria. Reasons for excluding 40 studies after the full-text examination included lack of control groups, participants still receiving active treatments or maintenance therapy for cancer, and studies providing frequencies only for PA or fitness levels in the general population without sample size and other important statistics (including standard deviation, mean, and range) needed for effect-size calculations. For instance, Götte et al. [19] and Ross et al. [26] were dropped from the final analysis because there were no control groups and standard deviation was not provided.

Scanning the reference lists of the remaining 16 studies and manually searching the content pages of two journals added no further studies. No duplicates of the 16 eligible studies [17, 22, 27–40] were found. Eight studies measured PA levels in pediatric cancer survivors and non-cancer controls, and the remaining eight measured fitness levels. Study sample sizes ranged from 13 [17] to 527 [39], yielding a total sample size of 2628; 1413 pediatric cancer survivors and 1215 non-cancer controls, who were predominantly aged 18 years or younger.

Outcomes

PA and/or fitness levels in pediatric cancer survivors and non-cancer controls were primary outcomes, measured with standard measures such as pedometers, the GT1M ACTi Graph accelerometer, the Actical accelerometer (Bio-Lynx), and the 6-min walk test along with self-reported PA frequency. For studies using identical measurement instruments, differences in scale did not influence effect size as calculated on the basis of the standardized mean difference. Table 1 provides the mean PA and fitness scores of cancer survivors and children with no history of cancer. Figures 2 and 3 present estimated effect-size (Hedges' g) and confidence intervals for PA and fitness, respectively, for all included studies, as well as the Z value, statistical significance, and assigned random weight for each.

Results of meta-analysis of physical activity and fitness levels

Pooled analysis of eight observational studies using random effects to compare PA in pediatric cancer survivors and non-cancer controls demonstrated significantly lower levels of PA in pediatric cancer survivors than in non-cancer controls ($g =$

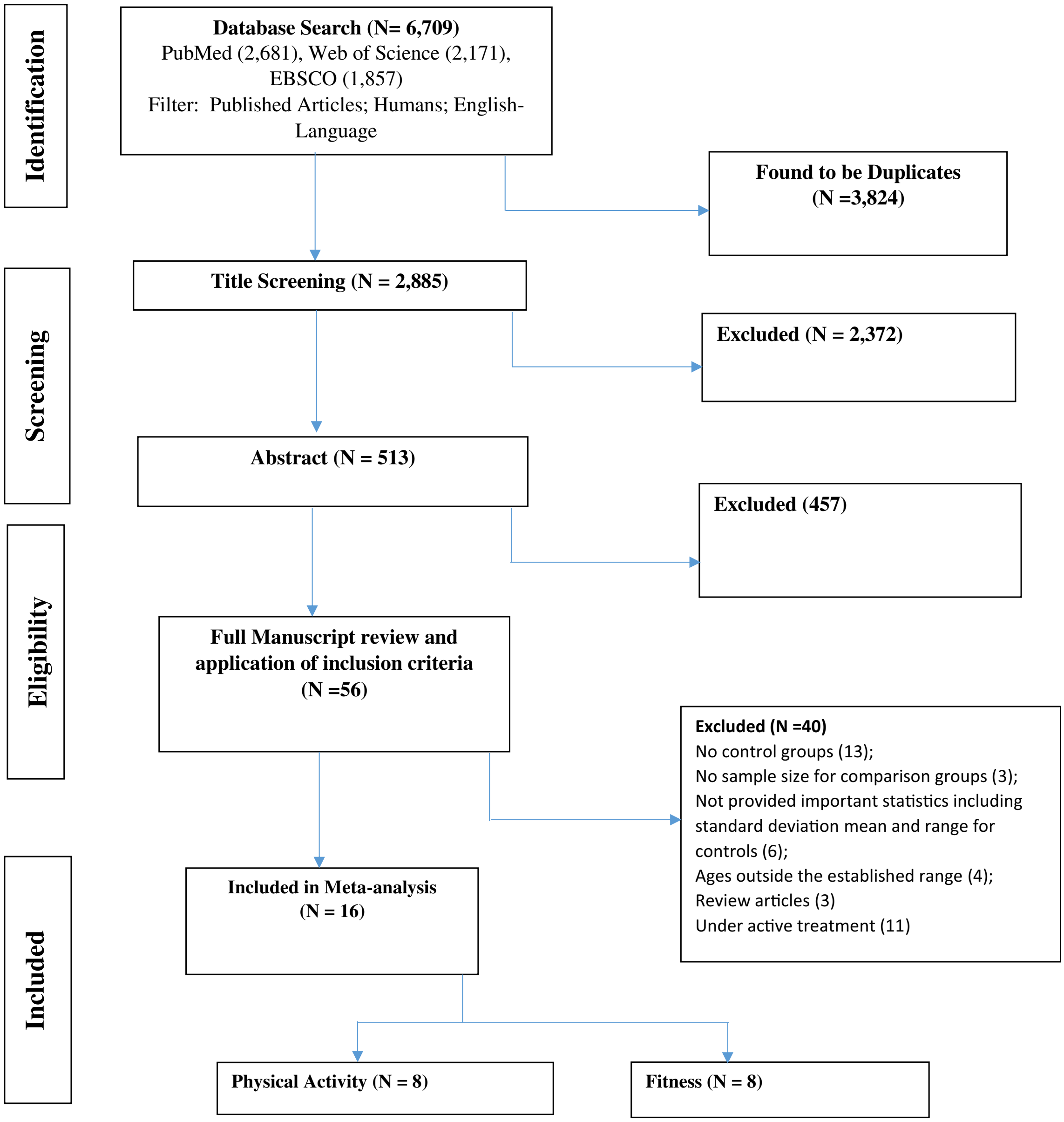

Fig. 1 Study flow diagram

− 0.889; 95% CI = − 1.648, − 0.130; $p = 0.022$; Fig. 2). However, heterogeneity was high (Q = 328.637; $p < 0.001$; $I^2 = 97.870$).

Similarly, the analysis demonstrated significantly lower levels of fitness in pediatric cancer survivors than in non-cancer controls ($g = -1.435$; 95% CI = − 2.615, − 0.255; $p = 0.017$) (Fig. 3). High heterogeneity was observed ($Q = 307.483$; $p < 0.001$; $I^2 = 97.723$).

Risk of bias across studies

Meta-analysis revealed a high level of heterogeneity across studies on both PA and fitness levels. Two funnel plots examined whether heterogeneity was related to publication bias. In the funnel plot demonstrating effects of cancer survival on PA, five studies fell to the right of the mean effect, of which three fell outside of the triangular region. This suggested evidence of publication bias [41], suggesting one missing study to the left of the mean effect in the funnel plot (i.e., overestimation of difference). Additionally, Duval and Tweedie's trim-and-fill method changed the point estimate of the random effects model (from − 0.889 to − 1.013). Similarly, in the funnel plot demonstrating fitness levels, seven studies fell outside the triangular region to the right, indicating a higher likelihood of publication bias [41]. The trim-and-fill method changed the point estimate of the random effects model (from − 1.435 to − 2.170), suggesting three missing studies to the left side of the mean effect in the funnel plot (i.e., overestimation of difference).

Table 1 Individual study characteristics of the 16 studies included in the meta-analysis

First author, year of publication	Age range	Sample size	Physical activity or fitness score	Pediatric cancer survivors	Non-cancer controls
Batra et al. 2016	60–248 months (5–21 years)	172	Outcome measurement, mean ± SD	($n = 122$)	($n = 50$)
			Physical health	79.2 ± 9	81.4 ± 10.1
			Walking	80.5 ± 12.7	84.5 ± 18.8
			Running	80.7 ± 14.3	80.5 ± 19.9
			Household work	82.2 ± 14.5	84.5 ± 17.4
			Sports activity	79.1 ± 15.2	76.5 ± 19.8
			Self-care	81.9 ± 14.8	82 ± 20
			Lifting heavy objects	77.7 ± 17.2	80 ± 17.5
			Pain	84.22 ± 14.4	84 ± 20
			Low energy levels	66.8 ± 21.4	79.5 ± 18
Bansal et al. 2013	5–18 years	120	Outcome measurement, mean ± SD [*n*]	($n = 40$)	($n = 80$)
			Walking	74.38 ± 23.24 [40]	Sibling, 98.75 ± 5.51 [40] Healthy, 98.75 ± 5.51 [40]
			Running	76.88 ± 26.52 [39]	Sibling, 98.75 ± 5.51 [40] Healthy, 95.63 ± 11.16 [40]
			Exercise	91.88 ± 19.10 [40]	Sibling, 97.50 ± 9.47 [40] Healthy, 98.13 ± 8.47 [40]
			Weight lifting	75.00 ± 20.48 [40]	Sibling, 97.50 ± 9.47 [40] Healthy, 96.88 ± 10.10 [40]
			Household work	95.63 ± 15.90 [40]	Sibling, 98.13 ± 8.74 [40]
				($n = 13$)	($n = 13$)
Beulertz et al. 2016	4–17 years	26	Outcome measurement	Mean ± SD	Reference data
			Physical well-being	70.45 ± 13.72	77.10
			Overall motor performance	22.36 ± 22.24	50.00
Bianco et al. 2014	7.55 ± 2.43 years	58	Outcome measurement, mean ± SD	($n = 18$)	($n = 40$)
			Standing broad jump (cm)	99.78 ± 22.38	121.5 ± 28.44
			4 × 10 m shuttle run (s)	16.04 ± 2.20	14.28 ± 1.50
			Sit-up test (reps)	21.33 ± 16.48	24.58 ± 13.01
			Hand grip test DX (kg)	9.23 ± 2.96	12.55 ± 4.26
			Hand grip test SX (kg)	9.43 ± 3.06	12.21 ± 4.49
Brussel et al. 2006	8.6–23.7 years	13	Outcome measurement, mean ± SD (range)	($n = 13$)	(Referenced data)
			Grip strength	117.4 ± 75.20 (36.0–290.0)	120.5 ± 57.0 (57.4–192.0)
			Shoulder abductor	161.8 ± 64.17 (75.0–298.0)	144.7 ± 46.2 (93.7–226.3)
			Knee extensor	252.1 ± 81.13 (129.0–350.0)	299.7 ± 98.9 (116.0–396.0)
			Foot dorsal flexor	206.6 ± 81.77 (78.0–346.0)	185.7 ± 50.9 (127.5–248.9)
			Wrist extensor	142.3 ± 68.46 (64.0–280.0)	153.2 ± 66.0 (75.0–237.0)
			Hip flexor	212.0 ± 78.31 (112.0–336.0)	206.6 ± 65.6 (129.4–291.4)
Caro et al. 2006	< 21 years	163	Outcome measurement, mean (SD)	($n = 84$)	($n = 69$)
			VO_2 max, oxygen consumption at peak exercise	36.5 (7.7)	38.2 (8.2)
			VO_2 AT, oxygen consumption at anaerobic threshold	24.4 (5.6)	24.4 (6.9)
			VE, minute ventilation at peak exercise	67.9 (23.3)	64.5 (21.8)
			RER, respiratory exchange ratio at peak exercise	1.1 (0.1)	1.1 (0.1)
			BP, blood pressure at peak exercise	147 (23)	148 (25)

Table 1 (continued)

First author, year of publication	Age range	Sample size	Physical activity or fitness score	Pediatric cancer survivors	Non-cancer controls
			Outcome measurement	($n = 183$)	($n = 147$)
Hoffman et al. 2013	< 18 years	330	Overall, mean (SD)	89.0 (89.2)	94.0 (63.9)
			6-min test (m)+, mean (SE)	567.8 (7.0)	594.1 (8.3)
			Time-up-and-Go (s), mean (SE)	4.7 (0.1)	4.4 (0.1)
			Grip strength (kg), mean (SE)	19.1 (0.7)	18.7 (0.5)
Jenny et al. 1995	14.6 (13.3–15.9) years	200	Outcome measurement, mean (range)	($n = 61$)	($n = 139$)
			W MAX	91.4 (86.6–96.2)	99.7 (96.9–102.5)
			HR MAX	98.8 (96.8–100.9)	100 (98.8–101.2)
			VO, MAX	89.3 (96.8–100.9)	99.9 (97.0–102.8)
			VENT MAX	91.2 (84.6–97.7)	99.7 (96.1–103.3)
			HR500	107.4 (102.6–1 12.3)	100 (98.3–102.0)
			HR750	107.8 (103.9–1 11.6)	100 (98.3–101.7)
			HRIOOO	107.1 (103.7–111.6)	100.1 (98.3–101.8)
			VENTIO00	104.1 (100.0–108.2)	100 (97.4–102.5)
			VT30	98.2 (93–103.2)	100.1 (96.8–103.0)
			VO, 170	87.7 (82.6–92.7)	100.1 (97.1–103.0)
					Matched controls *n* (8) siblings
Kobayashi et al. 2017	8–18 years	90	Outcome measurement, mean ± SD [*n*]		
			Physical functioning	($n = 35$)	($n = 55$)
			Consolidation phase	65.96 ± 23.17 [8]	Matched controls, 88.80 ± 13.28 [8] Siblings, 83.60 ± 26.93 [4]
			Maintenance phase	71.42 ± 21.11 [21]	Matched controls, 86.13 ± 12.75 [21] Siblings, 11 93.47 ± 7.71 [9]
			Off-treatment	83.33 ± 17.53 [6]	Matched controls, 94.83 ± 8.30 [6] Siblings, 96.25 ± 5.59 [5]
Norris et al. 2010	13.7 (2.3)	27	Physical activity levels, mean ± SD (range)	($n = 17$)	($n = 10$)
			Mild		
			Metabolic equivalent (MET) hours/week	11.32 ± 13.62 (0–42)	10.55 ± 8.90 (0–30)
			Frequency	3.29 ± 2.23 (1–17)	3.17 ± 2.12 (0–7)
			Duration	60.59 ± 64.00 (20–450)	66.05 ± 54.37 (0–180)
			Moderate		
			MET hours/week	17.18 ± 21.04 (0–70)	7.62 ± 5.96 (0–20)
			Frequency	3.29 ± 2.37 (0–7)	2.63 ± 1.44 (0–5)
			Duration	45.59 ± 41.60 (0–120)	7.62 ± 5.96 (0–20)
			Strenuous		
			MET hours/week	29.86 ± 36.95 (0–126)	37.28 ± 35.72 (5–126)
			Frequency	3.21 ± 2.48 (0–7)	3.60 ± 2.12 (1–7)
			Duration	43.09 ± 42.20 (0–120)	69.50 ± 41.26 (15–120)
			Total		
			MET hours/week	58.36 ± 55.43 (1.5–208)	55.44 ± 37.44 (20.2–135.8)
			Frequency	9.79 ± 4.69 (1–17)	9.40 ± 2.84 (5–13)
			Duration	149.26 ± 115.29 (20–450)	170.05 ± 91.04 (40–360)
				($n = 35$)	($n = 65$)
Nuss and Wilson 2007	2–18 years	100	Physical functioning, mean ± SD	77 ± 23.5	84.41 ± 17.26
				($n = 319$)	($n = 208$)
Polgreen et al. 2012	younger than 18 years	527	Physical activity score, MET minutes/week, mean ± SD [*n*]	58.6 ± 3.8 [319]	65.9 ± 4.9 [208]
				($n = 51$)	($n = 51$)

Table 1 (continued)

First author, year of publication	Age range	Sample size	Physical activity or fitness score	Pediatric cancer survivors	Non-cancer controls
Schulte et al. 2016	6–18 years	102	Physical functioning, mean ± SD	83.97 ± 15.60 ($n = 319$)	Sibling, 86.62 ± 13.05 Published norm, 87.53 ± 13.50 ($n = 208$)
Slater et al. 2015	9–18 years	527	Leisure-time physical activity (min/day), mean ± SD [*n*]	46.6 ± 3.3 [319]	55.8 ± 4.0 [208]
Warner 1998	7.2–18.4 years	87	Outcome measurement, median (range) Standing HR (beats/min) Walking 2 km/h (beats/min) Sitting HR (beats/min)	($n = 55$) 112 (84–136) 119 (91–148) 99 (74–118) (n = 48)	($n = 32$) 108 (83–132) 107 (79–140) 93 (65–118) ($n = 48$)
Wright et al. 2013	13–18 years	96	Godin-Leisure-Time Exercise Questionnaire, mean ± SD [*n*]	60.0 ± 32.8 [48]	65.5 ± 32.4 [48]

Discussion

In this meta-analysis of observational studies, our findings indicated that levels of both PA and fitness were significantly lower in pediatric cancer survivors than in non-cancer controls. Potential physical limitations or medical comorbidities of pediatric cancer survivors are important considerations relative to the significantly lower PA and fitness levels found in this study. Those pediatric cancer survivors who experience significant toxicities or require major surgeries, including amputation or resections, may have impaired ability to participate in PA. The range of physical impairment or organ dysfunction is typically related to the type of cancer, the chemotherapy agents given, and the inclusion of radiation or surgical resection. For example, pediatric cancer survivors who received chest radiation or certain chemotherapy (i.e., bleomycin or alkylating agents) experience higher rates of pulmonary toxicity, which can affect daily activities of living or the ability to tolerate cardiovascular exercise [42, 43]. Moreover, a 2015 review of the effects of cancer-treatment-related organ toxicities on physical performance and functioning among pediatric found an association between cranial radiation and obesity, low bone mineral density, and neuro-motor impairments in young children [44].

Similarly, pediatric cancer patients who received anthracyclines or chest radiation have an increased risk of a full range of cardiac complications, ranging from asymptomatic left ventricular dysfunction and accelerated atherosclerosis to congestive heart failure [45–48]. A prior study concluded that "higher cumulative doses ≥ 300 mg/m^2 in patients younger than 18 years of age at the time of treatment are associated with higher risk of developing clinically significant cardiomyopathy" [8]. Moreover, pediatric cancer patients with extremity tumors are likely to experience a wide range of complications including sensory impairment [49], skeletal dysplasia or asymmetry [50, 52], muscular hypoplasia/atrophy [53, 54], and limited joint range of motion [53, 55]. Lastly, patients who undergo limb-sparing surgeries often require additional surgical intervention over the course of their lifetime [56], which could limit their engagement in PA.

Although the aforementioned physical limitations and comorbidities [42–56] represent barriers for pediatric cancer survivors to participate in PA and fitness activities, future research could be focused on creating and implementing modified exercise programs personalized to the needs of individual survivors. Prior studies have revealed potential benefits of post-diagnosis PA and fitness on health and well-being of cancer survivors [57–59], including a strong protective effect on all-cause mortality [60]. A review of clinical benefits of PA on cancer survivorship found that increased levels of PA and fitness reduced mortality risk by 20 to 35% [60]. Additionally, a 2006 systematic review and meta-analysis examining the impact of exercise on breast cancer survivorship determined

Study name	Hedges's g	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	P-Value
	Statistics for each study						
Bansal et al 2013.	-1.429	0.249	0.062	-1.916	-0.942	-5.748	0.000
Batra et al 2016	-0.271	0.168	0.028	-0.599	0.058	-1.612	0.107
Hoffman et al 2013	-0.063	0.111	0.012	-0.280	0.153	-0.572	0.568
Norris et al 2010	-0.188	0.387	0.150	-0.947	0.571	-0.486	0.627
Polgreen et al 2012	-1.708	0.103	0.011	-1.911	-1.505	-16.522	0.000
Slater et al 2015	-2.557	0.119	0.014	-2.790	-2.324	-21.518	0.000
Warner et al 1998	-0.639	0.248	0.061	-1.125	-0.153	-2.576	0.010
Wright et al 2013	-0.167	0.203	0.041	-0.565	0.230	-0.825	0.409
	-0.889	0.387	0.150	-1.648	-0.130	-2.295	0.022

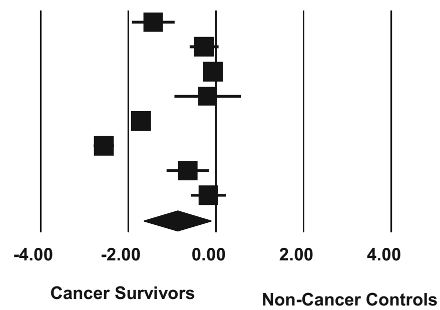

Fig. 2 Meta-analysis of physical activity levels

a significantly positive correlation between exercise and physical functioning, fitness, reduced fatigue, and overall quality of life [57]. Furthermore, improved levels of PA and fitness could reduce the rate of cardiovascular comorbidities and mortality plus the probability of developing diabetes and could help to maintain a healthy body weight. For example, Slater et al. [37], found improved cardiovascular health conditions, such as lower percentage fat mass and abdominal subcutaneous and visceral fat, greater lean body mass, and slightly greater insulin sensitivity in pediatric cancer survivors having high PA levels compared with lower PA levels.

Finally, PA and fitness are highly correlated with improved well-being and overall quality of life in the pediatric cancer survivor subpopulation [61–64]. In pediatric interventions (13 studies), we found strong evidence for a benefit to muscle strength and cardiorespiratory fitness was found, especially when training was conducted in the hospital setting [61].

Implications for practice and future research

Prior studies have identified physician-based exercise counseling as an effective strategy for improving PA levels in patients [65, 66]. A meta-analysis of primary care-based PA promotion determined a small to medium improvement in self-reported PA among sedentary adults after a 12-month follow-up period [66], thus highlighting the need to incorporate PA counseling into treatment protocols and post-treatment efforts to improve the health and well-being of pediatric cancer survivors. Pediatric oncologists must be trained in effective PA counseling to motivate cancer survivors' engagement in regular PA. Pediatric cancer survivors may have unique physical conditions and PA preferences; thus, oncologists must work with pediatric cancer survivors and their parents/guardians to design specific strategies, set goals, and track progress.

Furthermore, PA interventions should be tailored at improving PA self-efficacy among pediatric cancer survivors. Prior studies demonstrated significant positive correlations between social support, self-efficacy, and PA engagement among cancer survivors [67, 68]. Moreover, PA resources and information such as the "Physical Activity Tips for Survivors" by the American Society of Clinical Oncology (ASCO) must be made easily accessible. PA interventions tailored toward pediatric cancer survivors must also enhance

Study name	Hedges's g	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	P-Value
	Statistics for each study						
Beulertz et al 2016	-0.778	0.395	0.156	-1.552	-0.004	-1.970	0.049
Bianco et al 2014.	-0.801	0.290	0.084	-1.369	-0.233	-2.765	0.006
Brussel et al 2006	-0.612	0.286	0.082	-1.172	-0.052	-2.141	0.032
Caro et al 2006	-0.213	0.162	0.026	-0.531	0.104	-1.316	0.188
Jenny et al 1995	-7.907	0.424	0.180	-8.737	-7.076	-18.652	0.000
Kobayashi et al 2017	-0.774	0.556	0.309	-1.863	0.315	-1.392	0.164
Nuss & Wilson, 2007	-0.424	0.183	0.033	-0.781	-0.066	-2.320	0.020
Schulte et al 2016	-0.183	0.197	0.039	-0.569	0.203	-0.929	0.353
	-1.435	0.602	0.362	-2.615	-0.255	-2.384	0.017

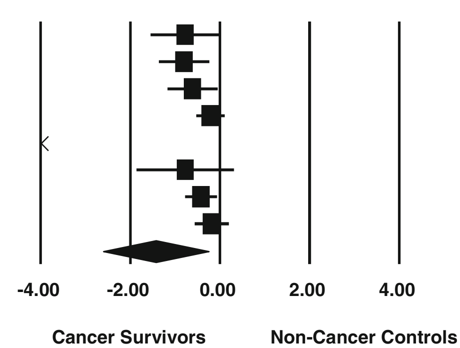

Fig. 3 Meta-analysis of fitness levels

social support from parents, siblings, and close friends, a significant predictor of PA engagement [69, 70]. To motivate regular engagement in PA by pediatric cancer survivors, policy makers and intervention designers must ensure that recreational facilities and spaces are safe and child-friendly [40].

Several approaches to future research are suggested, beginning with a clinically related approach intended to determine the efficacy of PA for improving the health and longevity of pediatric cancer survivors. Such research would utilize large, longitudinal, prospective cohort studies to examine the impact of cancer and/or cancer treatments on the PA and fitness levels of pediatric cancer survivors. Future research can investigate the effects of group-based PA among pediatric cancer survivors who successfully completed cancer treatments. Large, prospective cohort studies are also needed to evaluate the effects of treatment types on PA and fitness levels and to examine changes between pre-cancer, post-diagnosis, and post-treatment periods. To reduce measurement bias and improve the reliability and validity of results, future studies should employ standardized outcome measures such as accelerometers, VO_2 max, and pedometers to capture consistent, accurate, daily PA, and fitness levels. Finally, to examine the specific effects of cancer and its treatment on PA and fitness levels, future studies should involve individuals with other chronic conditions who have undergone other clinical, non-cancer treatment as control groups.

Limitations

Interpretation of the findings from the current meta-analysis must consider its several limitations. First, the small sample sizes of some included studies (e.g., the sample sizes for Brussel et al. and Norris et al. were 13 and 27 respectively) might have reduced the validity of the results, and the exclusion of theses, conference abstracts, and non-English studies could have affected the findings. Significant study heterogeneity may be due to different cancer types, severity of condition, measurement procedures, and the health conditions of the survivors during treatment or after cancer treatment. The high heterogeneity in both PA and fitness studies could reduce the validity of these findings. Additionally, not all studies used a standard measurement of PA or fitness, making comparisons between studies challenging. Moreover, interpretation of results must take into account that non-cancer controls in all included studies were healthy individuals with no chronic illness, making it difficult to conclude that cancer and its treatment, rather than any other life-threatening diseases, had the potential to negatively impact PA and fitness levels. Moreover, the significant time variation between the included studies could have influenced the results due to changing and improved cancer treatment protocols over time. Finally, all included studies had cross-sectional designs, thus limiting the ability to draw causal inferences. Despite these limitations, the current meta-analysis could substantially contribute to both clinical practice and research related to pediatric cancer survivorship. First, findings demonstrates the need for long-term follow-up PA/fitness intervention for pediatric survivors who have completed cancer treatment and are in full remission. In addition, ensuring regular PA participation among these survivors can help reduce their risk of developing other negative outcomes including overweight/obesity and cardiovascular disease as well as help improve their overall physical functioning. The comprehensive search strategy used in the current study accentuates its quality.

Conclusions

The current meta-analysis compared the PA and fitness levels of pediatric cancer survivors and non-cancer controls. A comprehensive literature search yielded 16 studies meeting the inclusion criteria. Pooled analysis of the included studies demonstrated significantly lower levels of both PA and fitness among pediatric cancer survivors than in non-cancer controls, with high heterogeneity across the included studies. The findings suggest that pediatric cancer survivors may have unique physical limitations and PA preferences; thus, future studies must explore innovative strategies for encouraging pediatric cancer survivors to engage in PA at the recommended levels.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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