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Early Nutrition and Physical Activity Interventions in Childhood Cancer Survivors

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Abstract

Purpose of review—Childhood cancer survivors experience excessive weight gain early in treatment. Lifestyle interventions need to be initiated early in cancer care to prevent the early onset of obesity and cardiovascular disease (CVD). We reviewed the existing literature on early lifestyle interventions in childhood cancer survivors and consider implications for clinical care.

Recent findings—Few lifestyle interventions focus on improving nutrition in childhood cancer survivors. A consistent effect on reducing obesity and CVD risk factors is not evident from the limited number of studies with heterogeneous intervention characteristics, although interventions with a longer duration and follow-up show more promising trends.

Summary—Future lifestyle interventions should be of a longer duration and include a nutrition component. Interventions with a longer duration and follow-up are needed to assess the timing and sustainability of the intervention effect. Lifestyle interventions introduced early in cancer care are both safe and feasible.

Keywords

nutrition; physical activity; weight management; interventions; obesity; childhood cancer survivors; cancer survivors

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Compliance with Ethics Guidelines

Conflict of Interest

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Introduction

Dramatic improvements in the diagnosis and treatment of cancer in childhood have led to a rapidly growing cohort of survivors, now estimated to exceed 450,000.¹ However, this success is accompanied by the recognition that childhood cancer survivors have substantially elevated risks of premature mortality and serious morbidity.^{2,3} Notably, young adult survivors of childhood cancer are seven times more likely to die from cardiovascular causes than the general population.^{3,4} Obesity is an established risk factor for cardiovascular diseases (CVDs). Our meta-analysis in 1,742 survivors of childhood acute lymphoblastic leukemia (ALL), the most common cancer diagnosed in children, identified a mean body mass index (BMI) z-score of 0.83, corresponding to the 80th BMI percentile.⁵ This indicates that young survivors, mostly preteenagers and adolescents, have a significantly higher BMI than their peers. Dietary intake and physical activity are modifiable risk factors for obesity and CVDs. Healthy eating and active living have demonstrated effects on reducing obesity and chronic disease burden in the general population.⁶ Promoting healthy lifestyles can be an effective intervention strategy to reduce obesity and obesity-associated cardiometabolic conditions in this high-risk population.

This paper will review the existing literature on lifestyle interventions in childhood cancer survivors and discuss implications of the findings for clinical care. In particular, we will focus on interventions that are initiated early in cancer care to prevent the early onset of obesity and CVD risk in childhood cancer survivors. Much of the research on the feasibility and effectiveness of lifestyle interventions in childhood cancer survivors focuses on pediatric ALL patients and survivors, as ALL is the by far the most common cancer in children.

Early Onset of Obesity in Childhood Cancer Survivors

Accumulating evidence suggests that childhood cancer survivors not only have significantly higher BMI than their peers⁵ but also experience unhealthy weight gain early in treatment.^{7–9} Increases in weight are maintained throughout treatment and beyond. In addition, childhood cancer survivors experience elevated risk of chronic health conditions at a young age. Data from the Childhood Cancer Survivor Study suggest that a 24-year-old childhood cancer survivor has the same risk of a developing severe, life threatening or fatal conditions as their 50-year-old sibling.¹⁰ In a retrospective cohort of 83 pediatric ALL patients diagnosed between 1985–2010, we examined weight patterns at several key time points during and after treatment: diagnosis, end of induction (the initial phase of chemotherapy), end of consolidation (the second phase immediately following induction), every 6 months during maintenance, and yearly for up to five years post-treatment. We found that the proportion of patients who were overweight or obese (BMI 85th percentile) increased from 20% at diagnosis to approximately 40% at the end of treatment (Figure 1).⁹ In particular, a rapid weight gain was observed during induction, and again, during the first 6 months of maintenance therapy. Similar findings were reported by others who also evaluated the trajectory of BMI changes at various phases of treatment. For example, Esbenshade et al. reported a rapid increase in BMI z-score during induction and the first 22 months of maintenance therapy in 183 pediatric ALL patients;⁷ and Withycombe et al. found a substantial weight gain during early maintenance cycles in 1,017 patients with high risk

ALL from the Children's Oncology Group (COG).⁸ Such findings are further supported by our meta-analysis in 1,514 childhood ALL patients from 16 studies: unhealthy weight gain occurs early in treatment and persists beyond treatment completion.¹¹ Furthermore, CVD risk factors such as insulin resistance and dyslipidemia also occur early in treatment for childhood ALL survivors. These findings provide strong support that treatment phase is a sensitive window for patients to develop obesity and obesity-related morbidities.

Why Are Childhood Cancer Survivors at Risk for Obesity?

Weight gain is usually the result of positive energy balance, i.e., levels of energy intake exceeding levels of energy expenditure. Existing studies provide consistent evidence that childhood cancer survivors are sedentary and have low levels of physical activity.^{12–20} However, the energy gap identified in childhood cancer survivors is quite large - the mean total energy expenditure was approximately 500 kcal/day lower than the estimated energy requirement.²¹ For a 7-year old boy who weighs 60 pounds, 60 minutes of moderate-to-vigorous physical activity daily, such as running and swimming, will expend about 250–400 kcal/day. Therefore, increasing physical activity alone is unlikely to fill this energy deficit in childhood cancer survivors. Lifestyle interventions need to incorporate both components - increasing physical activity and improving diet quality to reduce the overconsumption of calories - to achieve energy balance. In fact, recent studies found consistent evidence that childhood cancer survivors have poor adherence to dietary guidelines.^{22–27} Their intake patterns are particularly poor for whole grains, fiber, sodium, and empty calories - calories from solid fats and added sugars, which are well-established risk factors for obesity and CVD risk.

In addition to having poor diet quality and being sedentary, the treatments for childhood cancer may elevate risk for obesity. All regimens for treating ALL and pediatric non-Hodgkin lymphoma and most regimens for treating Hodgkin lymphoma include corticosteroids, which are known to be critically involved in regulating energy intake, storage, and mobilization. Prolonged use of corticosteroids has demonstrable effects on body composition, and is associated with increases in percentage of body fat and caloric intake in ALL survivors.^{28,29} Anthracyclines, used in low to moderate doses in some ALL treatment protocols, have been shown to cause left ventricular dysfunction and subsequent impairment in cardiovascular fitness. Vincristine, used in all phases of ALL treatment, is an established risk factor for neuropathy, which often results in reduced muscle strength, impaired balance, and other mobility limitations. Finally, some chemotherapeutic drugs such as L-asparaginase^{30–32} and prednisone³³ can directly impair β -cell function and lipid synthesis, causing hyperinsulinemia and dyslipidemia.

Psychosocial factors also can affect dietary intake and physical activity behaviors in childhood cancer survivors. Parents often report changes in parenting styles after their child is diagnosed with cancer. Parents often become more permissive, allowing the child to eat whatever he or she can or wants to eat and encouraging sedentary behavior.³⁴ Cancer diagnosis and treatment are also stressful and can negatively impact food choices and eating patterns of the child and the whole family. These changes were initially thought to be acute responses to cancer treatment. Recent evidence, however, indicates that these changes are

carried over to longer survivorship.^{33,35,36} Long-term survivors also have poor adherence to the current dietary^{22–25,27} and physical activity guidelines,^{15,18,37} and experience a high risk for CVD^{38–40} and associated risk factors such as hypertension,^{41,42} dyslipidemia,^{41,42} insulin resistance or diabetes,^{41–44} and obesity^{5,45}.

Early Lifestyle Interventions in Childhood Cancer Survivors

With evidence that unhealthy weight gain and development of CVD risk factors occur early in treatment and persist beyond treatment completion, early intervention is appropriate and necessary. Early adaptive behaviors such as poor dietary intake and physical inactivity can be difficult to reverse when children become long-term survivors. Thus, the timing of introducing lifestyle modification can critically impact the effectiveness of interventions to prevent the early onset of obesity and CVD risk in childhood cancer survivors. To understand the feasibility of initiating lifestyle interventions early in cancer care, we conducted a mixed-methods study, including 4 focus groups with 20 health care providers (e.g., oncology dietitians, nurses, oncologists and social workers) and surveyed 46 parents of childhood ALL survivors (mean age = 6.5 years old, 61% on-treatment) to evaluate their perceptions of weight management in childhood ALL survivors.⁴⁶ About 76% of the parents indicated that they would like to help their child maintain a healthy weight and the most preferred time (47%) to participate in lifestyle interventions was within 3 months after starting maintenance chemotherapy. Health care providers also considered the maintenance phase an appropriate time to introduce lifestyle modification largely because the treatment is less intense and the patients' family has had time to adapt to the diagnosis of childhood cancer. These data support the feasibility of integrating lifestyle interventions early in cancer care to promote healthy lifestyles in childhood cancer survivors.

We reviewed early lifestyle interventions conducted in childhood cancer survivors with a focus on nutrition, physical activity, and weight management (Table 1). While nutrition and physical activity are both important modifiable risk factors for reducing obesity and CVD risk, few lifestyle interventions specifically targeted nutrition as a component. Among the six intervention studies that included a nutrition component, three aimed to increase calcium and vitamin D intake from supplements^{47,48} or from both food sources and supplements,⁴⁹ with the primary goal of improving bone health outcomes such as bone mineral density in survivors of pediatric ALL. The other three interventions had a broader nutrition focus. One provided health behavior training to adolescent survivors such as smoking cessation, sun protection, reducing dietary fat, exercising, and weight reduction through written curricula and oral guidance.⁵⁰ The survivors randomized to the intervention group significantly reduced junk food consumption one year post intervention, although it was unclear whether the reduction was greater in the intervention than the control group (i.e. standard care).⁵¹ A recent intervention in pediatric ALL survivors focused explicitly on weight management through calorie reduction (i.e., portion control, choosing low- over high-calorie foods, and choosing healthy foods when eating out) and physical activity, and was delivered remotely through a web-based curriculum, text messages and telephone counseling.⁵² The intervention resulted in less weight gain and greater increase in moderate-to-vigorous physical activity (MVPA) compared to the control group. These interventions, however, were not initiated early in cancer care. The trials enrolled pediatric ALL survivors who were

at least at least 8–11 years post diagnosis and at least two years post treatment completion. The only early intervention was conducted in pediatric ALL patients at the start of maintenance therapy (i.e., on-treatment), and consisted of providing general nutrition education materials that reflected standard recommendations to eat a well-balanced diet plus a daily multivitamin supplements.⁵³ This intervention did not result in significant improvement in patients' dietary intake or BMI, however.

Most of the lifestyle interventions in childhood cancer survivors have focused on increasing physical activity or improving physical functioning. A recent review by Raber et al⁵⁴ identified 25 interventions on physical activity of which half (n=13, 52%) were conducted in patients who were on-treatment at the time of intervention. Among these 13 early interventions^{53,55–58}, five^{53,55–58} were RCTs and eight^{59–66} had a quasi-experimental design (four employed a pre-/post design with no controls and the other four used external controls). These interventions measured a wide range of outcomes including anthropometrics (weight, height, BMI, BMI z-score, % body fat, lean body mass), cardiovascular endurance and fitness, functional mobility and motor performance, muscular strength, steps, physical activity, bone mineral density, and quality of life. They also varied in sample size (range: 6–51 participants) and length of the intervention (range: 6 weeks–2 years). Twelve focused exclusively on physical activity and one included both physical activity and nutrition.⁵³

Nine of the 13 interventions enrolled pediatric ALL patients who were on maintenance therapy (n=7)^{53,55,57–59,64,65} or at pre-maintenance therapy (n=2)^{56,63}, and the remaining four were conducted in patients who had received a hematopoietic stem cell transplantation (HSCT) (n=2)^{61,62} during their inpatient stay or patients with malignant bone tumors (n=2)^{60,66}. Interventions were either home-based (n=4)^{53,55,58,59}, clinic-based (n=7),^{56,61,62,64–67} or a combination of the two (n=2).^{57,63} Compared to the RCTs that were primary home-based or a combination of home- and clinic-based (4 of 5), quasi-experimental studies were mostly clinic-based (6 of 8). Interventions conducted during the inpatient stay were generally shorter in duration compared to home-based interventions. The majority of the interventions included a comprehensive exercise program that combined stretching and strengthening activities and aerobic exercise.

With considerable heterogeneity in intervention design, duration, and outcome assessment, existing studies did not reveal a consistent effect of lifestyle interventions on weight, dietary intake, physical activity, physical functioning or quality of life outcomes. The two RCTs^{53,56} and two quasi-experiments^{59,62} that assessed anthropometrics at the end of the intervention did not report a significant effect on patients' BMI although increases in physical activity were observed in one. For physical functioning, positive effects were more consistently reported for muscular strength (2^{55,57} of 3 RCTs and 3^{59,64,65} of 4 quasi-experiments) and less for cardiovascular endurance or fitness (1⁵⁵ of 3 RCTs and 2^{59,64} of 2 quasi-experiments) and functional mobility or motor performance (1⁵⁵ of 3 RCTs and 2^{63,64} of 2 quasi-experiments). The existing interventions did not result in significant improvements in bone health or quality of life. It is important to note, however, many interventions were short in duration (< 6 months) and assessed outcomes at the end of the intervention only. The only RCT that followed participants for an additional year post treatment completion found that,

despite similar increases in BMI and body fat during treatment, the intervention group experienced a more rapid decline of BMI and body fat than the control group post treatment completion⁵⁶. This effect, however, was not evident at the end of the treatment but became apparent one year post treatment completion. Interventions^{55,59,63,64} that were of relatively longer duration (e.g., 3–6 months) also tended to observe more positive trends than those with a shorter duration (e.g., 3 weeks to < 3 months).^{58,60–62,66} These results suggest that the lack of consistent intervention effect could be due to the short intervention duration or the lack of long-term measurements.

Despite this heterogeneity, all of the studies reviewed demonstrate the safety of lifestyle interventions when healthy eating and active living were introduced to childhood cancer patients who were still receiving cancer treatments. No adverse outcomes directly resulting from the intervention were documented. The existing intervention studies also demonstrate the feasibility of early lifestyle interventions, with the percentage of the eligible patients who consented and participated in interventions ranging from 64 to 89% across studies. The completion rate was overall high, ranging from 71 to 100%. Although intervention adherence was defined differently across the studies, those that assessed adherence reported moderate to high adherence, ranging from 55 to 90%.

Future Directions

- *Enhance diet quality in childhood cancer survivors.* Few survivorship programs for childhood cancer have a specific focus on nutrition; or when nutrition is introduced, the priority is to satisfy caloric needs and prevent weight loss. Although malnutrition due to cancer-related anorexia and cachexia still represents an important concern in cancer care,⁶⁸ overconsumption of calories through poor eating habits^{22–25,69} is increasingly recognized as a concern in childhood ALL survivors.^{5,45} Lifestyle interventions need to respond to the growing need to prevent the early onset of obesity and moderate CVD risk in childhood ALL by enhancing diet quality, targeting excessive intakes of empty calories and sodium, and inadequate intakes of greens, beans, and whole grains in the survivors.^{22–25,69} Although these intake patterns are also commonly observed in children without a history of cancer, the far greater chronic disease burden in childhood cancer survivors makes improving diet quality a particularly important target for chronic disease prevention in this population.
- *Address barriers to healthy eating and active living.* Cancer treatment poses a number of issues that can impact survivors' ability to maintain long-term healthy eating habits and physical activity.^{70–72} Childhood cancer survivors report fatigue,^{73,74} and stress,⁷⁵ food craving,⁷⁶ and change in taste preference,⁷⁷ all of which can make healthy food choices and physical activity challenging. Lifestyle interventions need to be designed to address the specific barriers that childhood cancer survivors experience to effectively facilitate positive behavior change.
- *Empower parents with effective parenting skills and practices.* Family environment and parenting style play important roles in shaping children's dietary and activity behaviors,^{78–83} and can be particularly important for children

diagnosed with cancer at a young age. It is reasonable to expect that parents practice permissive parenting that is often associated with unhealthy eating and sedentary behavior while the child is going through active cancer treatment. Following treatment completion, as reported in qualitative research, parents find it difficult to reverse the unhealthy eating habits and sedentary lifestyle that have been established during cancer treatment.³⁴ It is important that parents be empowered with effective parenting skills and practices to facilitate healthy lifestyle changes.

- *Identify and evaluate effective delivery method.* Childhood cancer survivors are typically geographically dispersed.⁸⁴ Consequently, they may experience difficulty attending intervention programs delivered at a central location. The intensive time commitment to cancer-related care represents an additional barrier for families to participate in interventions scheduled at fixed times.⁸⁵ Interventions delivered remotely through phone, web- and mobile-based applications, or other social media platforms (e.g. Facebook or Twitter) represent flexible and inexpensive alternatives to survivors and families. Nonetheless, cancer survivors ranked health care providers the most trustable source for seeking health information,^{86,87} Oncology care providers need to play a larger role in promoting healthy lifestyles in cancer care. Remotely delivered programs, combined with individualized support provided by health care providers, may serve a cost-effective strategy for integrating lifestyle interventions into cancer care for childhood cancer survivors.

Conclusions

Although treatment exposure, alone or in combination, contributes to elevated risk of obesity and CVD risk in childhood cancer survivors, the attributable fraction was less than 50%, ranging from 9.3% for hypertension, to 15.5% for dyslipidemia, 41.7% for diabetes, and 42.1% for obesity.² This leaves ample opportunity to reduce chronic disease burden through lifestyle interventions. Strong evidence supports the notion that unhealthy weight gain and development of CVD risk factors occur early in cancer treatment and persist beyond treatment completion. Thus, healthy lifestyles need to be promoted early in cancer care to capture a sensitive window of excessive weight gain and negative behavioral change. Existing studies have demonstrated safety and feasibility of introducing lifestyle interventions while patients are receiving cancer treatment. Although the consistent effect on reducing obesity and preventing CVD risk is not evident from a limited number of heterogeneous studies, interventions with a longer duration and longer follow-up show more promising trends. Future lifestyle interventions need to be designed with sufficient durations and follow-up periods to assess the timing and sustainability of the intervention effect. Both nutrition and physical activity are central to reducing the early onset of obesity and chronic diseases in childhood cancer survivors. Future interventions should include a nutrition component to improve dietary intake and address the specific barriers that survivors are facing in attaining a healthy lifestyle. Increasing physical activity is unlikely to fully offset the energy surplus from increased caloric intake in childhood cancer survivors. Parental involvement is important, as is the oncology care team, in promoting healthy lifestyles for

children in cancer care. Future lifestyle interventions developed in partnership with cancer survivors, caregivers, and health care providers will help ensure that the interventions address the needs of childhood cancer survivors and have the greatest potential impact.

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Figure 1.

Change in Prevalence of Overweight and Obesity During and After Treatment in Childhood ALL Survivors. Values are prevalence (%), n=83. *Consol*: consolidation; *Induct*: induction. Reproduced from Zhang FF, Rodday AM, Kelly MJ, et al. Predictors of being overweight or obese in survivors of pediatric acute lymphoblastic leukemia (ALL). *Pediatr Blood Cancer* 2014;61:1263–9, with kind permission from John Wiley and Sons.

Characteristics of Early Lifestyle Interventions in Childhood Cancer Survivors

Table 1

Author, Year, Country	Age, years mean/median (age range for inclusion)	N	Cancer Diagnosis	Treatment Status	Intervention Component	Intervention Design	Duration	Completion /Adherence N (%)	Outcome Measured and Results
Nutrition Intervention									
RCT									
Moyer- Mileur et al 2009	6.5 (4–10)	14	ALL	On maintenance therapy	Nutrition education material (standard recommendations to eat a well-balanced diet) + multivitamin supplement, reviewed monthly in clinic or over the phone	RCT	12 months	Completion: 13/14 (93%) Adherence: N/A	<ul style="list-style-type: none">Dietary intake: nullAnthropometry (weight, height, and BMI): null
Physical Activity Intervention									
RCT									
Tanir et al. 2013 Turkey	10 (8–12)	41	ALL	On maintenance therapy	Home-based stretching, and strengthening (5 d/wk, 3x/day) and aerobic (3d/wk, 30 min/session) exercise + 1 clinic-based introduction + 2 home visits, follow-up calls (two in 1 st month and monthly thereafter)	RCT	3 months	Completion: 19/20 (95%) Adherence: N/A	<ul style="list-style-type: none">Cardiovascular endurance (9-minute walk test): ↑Functional mobility (TUDS, TUGT): ↑Muscular strength (dynamometer): ↑QOL (PedsQL): null
Yeh et al, 2011 China	11.5 (<18)	24	ALL	On maintenance therapy	Home-based aerobic exercise (3 d/wk, 30 min/session)	RCT	6 weeks	Completion: N/A Adherence: 75%	Fatigue (PedsQL): null
Moyer- Mileur et al 2009 United States	6.5 (4–10)	14	ALL	On maintenance therapy	Home-based stretching, strengthening and aerobic exercise (15–20 min MVPA/ session, 3 sessions /week), reviewed monthly in clinic or over the phone	RCT	12 months	Completion: 13/14 (93%) Adherence: N/A	<ul style="list-style-type: none">Cardiovascular fitness (PACER): nullSteps (pedometer): ↑PA (self-report): nullAnthropometry (weight/height/BMI z-score): null
Hartman et al 2009 The Netherlands	5 (1–18)	51	ALL	On treatment (intervention initiated at the time of diagnosis)	Clinic-based stretching, strengthening and jumping exercise (1 introduction + every 6 weeks)	RCT	2 years	Completion: 20/25 (80%) Adherence: N/A	<ul style="list-style-type: none">Motor performance (BSID-II): nullMuscular strength (DAROM): nullBMD: nullAnthropometry (height, weight, BMI, % body fat, lean body mass): null at treatment cessation

Author, Year, Country	Age, years mean/median (age range for inclusion)	N	Cancer Diagnosis	Treatment Status	Intervention Component	Intervention Design	Duration	Completion /Adherence N (%)	Outcome Measured and Results
Marchese et al, 2004 United States	7.7 (4–18)	28	ALL	On maintenance therapy	Clinic- (5 in-person sessions, 20–60 minutes/session) and home-based (5 d/week) stretching, strengthening, and aerobic exercise	RCT	4 months	Completion: 28/29 (97%) Adherence: N/A	<ul style="list-style-type: none">• BMI: ↓ 1-year post- treatment completion• % body fat: ↓ 1-year post- treatment completion• Cardiovascular endurance (9-minute run-walk): null• Functional mobility (TUDS): null• Muscular strength (DAROM, KE): ↑• QOL(PedsQL): null
Quasi-Experiment									
Esbenshade et al, 2014 United States	7.4 (5–10)	17	ALL	On maintenance therapy	Home-based flexibility, strengthening and balance exercise (30–45 min/d, 3d/week) + general fitness activities (3d/week) follow-up calls weekly	No control (pre-/post)	6 months	Completion: 12/17 (71%) Adherence: 75%	<ul style="list-style-type: none">• Cardiovascular endurance (6-minute walk test): ↑• Muscular strength (KE, DS): ↑• BMI: ↓
Muller et al, 2014, Germany	14 (8–18)	10	Malignant bone tumor	On treatment	Clinic-based stretching, resistance and aerobic exercise during inpatient stay (15–45 min/session, every other day)	External patient control	Approximately 2.5 months	Completion: N/A Adherence: 78%	<ul style="list-style-type: none">• PA (accelerometer): ↑ at 12-month follow-up• BMC: null
Winter et al, 2013 Germany	14 (8–18)	16	Malignant bone tumor	On treatment	Clinic-based stretching, resistance and aerobic exercise during inpatient stay (15–45 min/session, every other day)	External patient control	Approximately 2.5 months	Completion: 16/16 (100%) Adherence: 55%	<ul style="list-style-type: none">• PA (accelerometer): null
Perondi et al, 2012 Brazil	10.3 (5–16)	6	ALL	On maintenance therapy	Clinic-based strengthening, stretching and aerobic exercise (2 sessions/week; 60 min/session)	No control (Pre-/Post)	3 months	Completion: 6/6 (100%) Adherence: N/A	<ul style="list-style-type: none">• Muscular strength (10- RM): ↑• QOL (PedsQL): mixed
Rosenhagen et al, 2011 Germany	15.3 (N/A)	13	HSCT	On treatment	Clinic-based endurance and strengthening exercise during inpatient stay (3x/week)	External patient control	Approximately 1 month)	Completion: 10/13 (77%) Adherence: 75%	<ul style="list-style-type: none">• Muscular strength: null• Fatigue (PedsQL): null
Gohar et al, 2011 United States	4 (2–14)	9	ALL	Pre- maintenance	Home-based (5 d/week) stretching, strengthening and aerobic exercise + clinic-based (3 times/week) physical therapy sessions during inpatient stay	No control (Pre-/Post)	6–7 months	Completion: 9/9 (100%) Adherence: N/A	<ul style="list-style-type: none">• Gross motor function (GMFEM): ↑• QOL (PedsQL): ↑

Author, Year, Country	Age, years mean/median (age range for inclusion)	N	Cancer Diagnosis	Treatment Status	Intervention Component	Intervention Design	Duration	Completion /Adherence N (%)	Outcome Measured and Results
Chamorro- Vina et al, 2010, United States	8 (4–16)	7	HSCT	On treatment	Clinic-based aerobic and resistance exercise during inpatient stay (5 session/ week, 50 min/session)	Matched historical patient control	3 weeks	Completion: 7/7 (100%) Adherence: >90%	<ul style="list-style-type: none">• Anthropometry (BMI, % body fat, lean mass): null
San Juan et al, 2007 Spain	5.1 (4–7)	7	ALL	On maintenance therapy	Clinic-based strengthening, stretching, and aerobic exercise (3 session/week, 30–40 min/session)	No control (Pre-/Post)	4 months	Completion: 7/7 (100%) Adherence: 85%	<ul style="list-style-type: none">• Cardiovascular fitness (VO_{2peak}): ↑• Functioning mobility (TUDS, TUG 3 m, TUG 10 m): ↑• Muscle strength (seated bench press, row, and leg press): ↑• QOL (CHIP-CE/CRF): ↑

10-RM test: 10-repetition-maximum test; BMC: bone mineral content; BSID: Bayley Scales of Infant Development; CHIP-CE/CRF: Child’s Health and Illness Profile-Child Edition; DAROM: dorsiflexion active range of motion; DS: ankle dorsiflexion strength; HSCT: hematopoietic stem cell transplantation; KE: knee extension strength; Movement-ABC: Movement Assessment Battery for Children; QOL: quality of life; TUDS: timed up and down stairs; TUG: timed up and go; VO_{2peak}: peak oxygen uptake