Initial Exercise Guidance for Children and Adolescents during and beyond Cancer Treatment: ACSM Expert Consensus Statement

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ABSTRACT

FRIDH, M. K., S. KESTING, M. A. NEU, P. L. VALENZUELA, M. WOGKSCH, S. N. CULOS-REED, K. H. SCHMITZ, K. K. NESS, S. J. FLECK, C. FIUZA-LUCES, and A. LUCIA. Initial Exercise Guidance for Children and Adolescents during and beyond Cancer Treatment: ACSM Expert Consensus Statement. *Med. Sci. Sports Exerc.*, Vol. 58, No. 7, pp. 1615–1628, 2026. **Purpose:** In children (≤14 yr) and adolescents (15–19 yr), cancer is highly heterogeneous and essentially differs from adult malignancies. Given the numerous sequelae and fitness impairments associated with treatment, there is a growing number of randomized controlled trials assessing the effects of exercise interventions in affected children/adolescents. As such, the purpose of this American College of Sports Medicine Expert Consensus Statement was to develop the first set of exercise guidelines for children/adolescents with cancer. **Methods:** We identified a list of outcomes with clinical relevance for the target population on which exercise may theoretically induce an improvement and developed exercise recommendations for those outcomes where there is sufficient evidence supporting such effect during/beyond treatment in children/adolescents. **Results:** Exercise training can generally be performed safely for children/adolescents with cancer. There is moderate evidence that concurrent (aerobic and strength) exercise training can improve two common cancer/treatment-related health outcomes, muscle strength and physical function, but not physical activity levels. Moderate evidence also supports that aerobic exercise improves cardiorespiratory fitness after (but not during) treatment. The evidence is, however, insufficient for other important outcomes (e.g., cardiac function, bone health, and immune function), reflecting a gap in the current state of knowledge. **Conclusions:** The proposed recommendations should serve as an initial guide for healthcare and fitness professionals working with children/adolescents with cancer. Although current advances in the field are tantalizing, more research is needed to fill remaining gaps in knowledge to better serve this population and to improve clinical practice.

Key Words: CARDIORESPIRATORY FITNESS, EXERCISE RECOMMENDATIONS, MUSCLE STRENGTH, PEDIATRIC CANCER, PHYSICAL ACTIVITY

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INTRODUCTION

Main Characteristics of Childhood/Adolescent Cancer—Differences from Adult Cancer

Although age definitions often overlap, the American Cancer Society considers childhood (or "pediatric") cancers as those that affect children from birth through age 14 yr (1). On the other hand, there are varying age categorizations for "adolescence," the phase of life stretching between childhood and adulthood. According to the Surveillance, Epidemiology, and End Results program of the National Cancer Institute and the American Cancer Society, adolescents are those in the quintile of 15–19 yr of age (2,3).

Cancer is a leading cause of death in children and adolescents from North America and Western Europe (4,5). More than 380,000 individuals of age 0–19 yr worldwide (or 14,910 U.S. individuals of this age in 2024) are diagnosed with cancer yearly (5–7). Yet, the absolute risk of childhood/adolescent cancer (herein simply "childhood cancer") is relatively low, especially when compared with adult tumors—for example, 5-yr–adjusted incidence of 17 diagnoses per 100,000 U.S. children, versus 4497 per 100,000 adults of age ≥40 yr (8).

Childhood cancer is highly heterogeneous and essentially differs from adult malignancies in many aspects (tumor biology, clinical symptoms, treatment options, and outcomes) (9). Additionally, some tumors are not even found in adulthood. The most common malignancies are acute leukemias, malignant brain and other central nervous system tumors, lymphomas, neuroblastoma, kidney tumors, soft-tissue and bone tumors, malignant germ cell tumors, epithelial neoplasms, and melanomas (10). The tumor distribution changes throughout childhood and adolescence: acute leukemias (predominantly acute lymphoblastic leukemia [ALL]) show a pronounced peak in incidence between the age of 2 and 5 yr, whereas central nervous system tumors demonstrate a relatively stable incidence throughout childhood; the incidence of non–central nervous system embryonal tumors peaks in infancy and subsequently declines to near zero by age of 10 yr; and there is a peak in the incidence of bone and soft-tissue sarcomas in mid-adolescence, accompanied by an increasing incidence of lymphomas and other solid tumors that persists into adulthood (11). The treatment of childhood cancer requires a multidisciplinary approach that integrates different modalities, including chemotherapy, radiotherapy, surgery, immunotherapy, or hematopoietic stem cell transplantation. Typically, most patients in high- and middle-income countries are treated according to standardized protocols, which are often implemented within the framework of clinical trials or therapy optimization studies (12,13). In pediatric oncology, these studies represent the basis for standard therapy and guideline development rather than being regarded as purely experimental options. Compared with adult tumors, childhood cancers tend to respond better to certain therapeutic modalities. This may be attributed to the fact that most tumors exhibit a higher proliferative rate, rendering them more susceptible to chemotherapeutic agents that target rapidly-dividing cells (14). Additionally, children and adolescents typically present with fewer preexisting health complications than adults, which facilitates greater tolerability of aggressive treatments, as well as a faster recovery (15). However, the treatment of very young children requires special considerations because their organ systems are still growing and vulnerable, and thus more susceptible to treatment-related toxicities (16). Thus, the use of aggressive chemotherapy protocols in the inpatient may provide a suitable opportunity for a more effective treatment compared with adult patients, but at the expense of a higher incidence of associated toxicities.

Childhood cancer is rarely associated with environmental exposures and increasingly linked to specific genetic predispositions that differ from those associated with adult cancers (17). Hence, childhood cancer is typically associated with fewer somatic mutations but with a higher prevalence of germline alterations in cancer predisposition genes (18). However, screening has not yet been able to effectively detect or prevent pediatric tumors in general (18). Conversely, considerable advances in diagnostics, pharmacology, treatment modalities and combinations, and supportive care over the last 5 decades have led to major improvements in survival (19,20). In high-income countries, more than 80% of children and adolescents with cancer are now cured and survive 5 or more years (21). These figures for most tumor types have led to a growing population of childhood cancer survivors (19,22) and thus to an increased recognition of treatment toxicities in these individuals, often persisting long after treatment.

Treatment Sequelae—Impact on Fitness

Early sequelae. Childhood cancer treatment may affect numerous body tissues and functions. Early side effects are experienced during (or shortly after) treatment and include mostly immunosuppression and infection, thrombocytopenia, anemia, malnutrition, nausea and vomiting, mucositis, fatigue, pain, and the psychosocial aspects of the illness (23–25). In turn, impairments in cardiorespiratory fitness (CRF), muscle mass and strength, and physical function are evident within the first month after treatment initiation (26–28). In addition, chemotherapy-induced peripheral neuropathy is highly prevalent (90%) in patients (and survivors of) childhood cancer, which also affects physical capacity (29).

Hematopoietic stem cell transplantation, a treatment option for several pediatric tumors (e.g., leukemias and lymphomas, but also several solid tumors), can lead to important toxicities and both functional and fitness

impairments. Transplant recipients are indeed at high risk of health-related adverse effects leading to pathologies (especially cardiometabolic conditions and frailty (30)) and physical function decline (31,32). Besides impairing CRF, total body irradiation applied in the conditioning regimens preceding the transplant can negatively affect muscle mass (32). A severe condition potentially associated with hematopoietic stem cell transplantation, graft versus host disease—wherein white blood cells of the donor's immune system that remain within the donated tissue (the graft) recognize the recipient (the host) as foreign (nonself)—can reduce muscle mass and lung function, in addition to the catabolic effect of corticosteroids used to manage the disease (33).

For pediatric patients with sarcomas, the initial sequelae are primarily related to local tumor control through surgery and, when applicable, radiotherapy and multi-agent chemotherapy (34). Common sequelae include postoperative pain, wound complications, transient edema or stiffness, and short-term reductions in limb function. Early-onset neuro- and ototoxicity, most often related to vinca alkaloids and platinum compounds, can manifest as peripheral neuropathy, which in turn may affect balance and gait, as well as hearing loss (35–37). On the other hand, in pediatric patients with primary central nervous system tumors, early complications predominantly result from the acute and early delayed effects of central nervous system–directed therapy (35,36). Neurological symptoms are associated with cerebral edema, seizures, altered consciousness, and headaches. Functional impairments such as motor weakness, coordination and balance deficits, and steroid-induced myopathy are frequently observed (35,36). Neurosurgical interventions have been observed to exacerbate preexisting deficits, and cranial radiotherapy has been documented to frequently result in fatigue, nausea, and cognitive impairment (35–37).

Long-term sequelae. Childhood cancer survivors are at an increased risk of disease and treatment-related long-term sequelae and premature mortality. By age 50 yr, they will experience an average of ~17 chronic health conditions compared with ~9 among peers (38), with rates increasing over time and contributing to both all-cause and organ-specific mortality (39). Multiple studies have identified treatment-related risk for organ-specific morbidity and mortality, most notably the well-documented associations between cranial radiation and neuroendocrine (40) and neurocognitive (41) dysfunction and between anthracyclines and/or chest radiotherapy and cardiotoxicity (42). Survivors who were treated with mitoxantrone, cyclophosphamide, anthracyclines, or radiotherapy involving the heart are at a high risk for severe, life-threatening, or fatal heart failure at a young age (median age 27 yr) (43). At the cardiometabolic level, compared with age- and sex-matched controls, childhood cancer survivors show a decline in echocardiography-determined left ventricular function, lower high-density lipoprotein cholesterol levels, and a higher waist-to-hip ratio (44). Compared with siblings, survivors are more likely to report functional limitations during activities of daily living, such as personal care in the case of survivors of central nervous system tumors (45). In addition, some studies have reported impairments in the CRF or muscle strength of childhood cancer survivors (46–49), and there is meta-analytical evidence for an impaired overall physical fitness (as assessed through a combination of different indicators such as CRF, muscle strength, and physical function) (32,50).

Treatment-related chronic health conditions are prevalent across organ systems, with disease distribution and severity evolving over time. A report from the Childhood Cancer Survivor Study (CCSS) showed that, among 23,601 survivors treated during 1970–1999 in North America, the cumulative incidence of severe, disabling, life-threatening, and fatal chronic conditions decreased by ~3% for each increasing decade of diagnosis for most tumor types, thanks to advances in therapeutic approaches (51). Efforts to minimize toxicity have eliminated cranial radiation exposure for most children. As a result, ALL survivors treated before 1991 have endocrinopathies (including adrenal and growth hormone insufficiency and hypothyroidism), whereas those treated later present with metabolic disorders comprised primarily of obesity and impaired glucose metabolism (52). For instance, there is recent evidence for a higher prevalence of metabolic syndrome—a cluster of cardiovascular risk factors including hypertension, (pre)diabetes, overweight/obesity, and dyslipidemia—in ALL survivors (median age 14 yr and median age after diagnosis 7 yr) from Northern Europe (7.6%) compared with controls (3.8%), a result attributable to those patients undergoing total body irradiation (53). On the other hand, musculoskeletal late effects were uncommon among ALL survivors treated in earlier eras but are more prevalent among those treated with contemporary therapeutic protocols, likely because high-dose glucocorticoid exposure negatively impacts muscle and bone mass and asparaginase exposure precipitates osteonecrosis (52).

Epidemiology studies in survivors: the importance of physical activity exposure. Observational data indicate that previous treatment exposures do not explain all-of-the risk for morbidity and mortality: modifiable risk factors also contribute. One of these is low physical activity (PA) levels. A recent report from the CCSS indicated that after accounting for host demographics and treatment exposures, absence of diabetes and hypertension and engaging in a healthy lifestyle (with respect to PA, smoking, and alcohol habits, as well as body mass index) reduced the risk for health-related mortality by 20%–30% (54). These data are supported by

a report from the St. Jude Lifetime Cohort (a prospective database designed to track health outcomes in childhood cancer survivors), where risk for health-related mortality, after accounting for host demographics and treatment exposures, was 2.5-fold higher among survivors with a phenotype consistent with reduced physiologic reserve (i.e., low muscle mass, weakness, slow walking speed, self-reported exhaustion, or low energy expenditure) (55).

Epidemiological evidence indicates that inactivity is independently associated with morbidity and mortality in childhood cancer survivors. A study (median follow-up, 11.9 yr) in 1187 five-year survivors of Hodgkin lymphoma (median age, 31.2 yr) reported that engaging in vigorous PA (≥9 metabolic equivalent of task [MET]-h·wk^{-1}) was linked to a lower risk for developing major cardiovascular events by 51% (56). Another report applied a similar PA rubric to the entire 15,450 members of the original CCSS cohort diagnosed between 1970 and 1986, documenting an inverse, dose–response association between PA and mortality over 15 yr and a 40% lower all-cause mortality over 8 yr among survivors who engaged in ≥7.9 MET-h·wk^{-1} (57). Others have documented associations between reduced PA and modifiable cardiovascular risk factors (high body mass index, obesity, hypertension, and dyslipidemia) in adolescent or adult survivors of childhood cancer (58–60).

Scientific Rationale

Given the toxicities and functional impairments associated with treatment protocols and the association of inactivity/low physiological reserve with the often-persisting sequelae found in childhood cancer survivors, there is a rationale for introducing exercise interventions earlier in life—that is, in affected children and adolescents. Especially when considering that youth inactivity "tracks into adulthood" and ~80% of children/adolescents (age 11–17 yr) in Western societies are inactive (61).

It is thus conceivable that exercise intervention in children and adolescents with cancer could have the potential to attenuate, at least partly, some treatment-associated sequelae, thereby helping these individuals to enter adulthood in the best possible health and functioning conditions. Besides, many of the abovementioned outcomes affected by treatment, such as CRF or muscle strength, among others, are known to be highly responsive to the appropriate exercise stimuli. Our purpose was therefore to develop initial exercise guidance for children and adolescents with cancer.

EVIDENCE REVIEW

Overview

In 2024, the American College of Sports Medicine (ACSM) convened a roundtable meeting composed of clinical and research experts from North America and Europe to develop the first set of exercise guidelines for children and adolescents with cancer. The first (online) meeting took place on March 20, 2024. Five *a priori* decisions were made by consensus at that meeting. The first was to follow the structure of the *Exercise Guidelines for* (Adult) *Cancer Survivors: Consensus statement from International Multidisciplinary Roundtable* (62). The second was to identify a list of outcomes of clinical relevance for children and adolescents with cancer on which exercise may have a potential positive effect during or after treatment. The third was to focus the review of evidence on interventions during or beyond treatment for children and adolescents (age ≤ 19 yr) and including "traditional" exercise modalities (i.e., aerobic, strength, or concurrent [aerobic and strength] training). The fourth was to develop exercise recommendations only for those outcomes for which there was sufficient evidence—see further below—supporting positive effects of exercise intervention. The fifth was to provide recommendations for future research and identify gaps in the available literature.

Methodology for Evidence Review

A search was conducted (from January 2024 to April 2024) of randomized controlled trials (RCTs), systematic reviews, and meta-analyses for childhood cancer-related health outcomes published (Box 1) using Medline/PubMed, EMBASE, CINAHL, The Physical Therapy Evidence Database (PEDro), and Web of Science. The search was done for articles published before February 22, 2024, using standardized search terms for childhood cancer and exercise (Supplemental File 1, Supplemental Digital Content, https://links.lww.com/MSS/D370).

Weekly online meetings for discussion were held from May 2024 to June 2024. At least two reviewers independently screened all titles and abstracts of identified

BOX 1. List of identified common acute and long-term fitness- and health-related outcomes for review of evidence for therapeutic efficacy.

- Physical function
- Anxiety
- Body composition
- Bone health
- Cardiorespiratory fitness
- Cardiotoxicity
- Cognitive function
- Depression symptoms
- Cancer-related fatigue (asthenia[a])
- Immune function
- Health-related quality of life
- Metabolism (glucose and lipid profile in blood)
- Muscle strength
- Physical activity
- Sleep
- Chemotherapy-induced peripheral neuropathy

[a]Asthenia refers to a feeling of generalized physical weakness and/or a lack of energy and strength.

studies (n = 12,281). Further, teams of two reviewers independently assessed the studies included for full text (n = 310). Disagreements between reviewers in any of these processes were solved by discussion or by consulting a third reviewer. For each outcome, two authors reviewed the included studies to identify the most recent, relevant, and high-quality publications that could facilitate evaluation of the state of science concerning exercise effects on a particular outcome.

A decision framework adapted from ACSM exercise guidelines for adult cancer (62) was applied to determine whether there was sufficient evidence to conclude that exercise intervention improves specific outcomes and warrants evidence-based exercise recommendations (Fig. 1). Of note, because the rarity of childhood cancer represents a major limiting factor in terms of achievable sample sizes in clinical trials, less stringent criteria were used concerning sample sizes with respect to the previously published adult guidelines (62). Thus, evidence for a given outcome was judged to be sufficient and strong when (i) there was a substantial number of RCTs (≥3), (ii) the aggregate sample size (children and adolescents during and/or after treatment) was large ($n \geq 100$), and (iii) the same type of effect (improvement, no change, or decrease) of exercise intervention compared with the control group was observed consistently across studies. For those outcomes with result heterogeneity, where the majority of studies suggested the same type of effect, the evidence was classified as sufficient but moderate. For outcomes where the relevant studies showed heterogeneity and conflicting evidence (i.e., no clear majority supported one direction), no recommendation was made, and further research was deemed necessary. For outcomes with <3 RCTs, small aggregate sample size (n < 100), or when there were conflicting results across studies, the evidence was classified as insufficient.

For those outcomes with sufficient—whether strong or moderate—evidence for a positive effect of exercise training based on the literature, two reviewers independently extracted data concerning Frequency, Intensity, Time, and Type (FITT) and related effects from all studies addressing a specific outcome. Disagreements between reviewers in any of these processes were solved by discussion or by consulting a third reviewer. Following the data extraction, the two reviewers compared FITT information between the respective studies, while taking general exercise recommendations into account, and developed specific recommendations targeting these outcomes based on the FITT principle. These recommendations were presented to all members of the roundtable and discussed. Following the discussion, the recommendations were finalized.

Strong Evidence

None of the intervention effects met the criteria for strong evidence, underlining that pediatric exercise oncology is still an emerging research field.

Moderate Evidence

Muscle strength. Based on 14 RCTs (total n = 741 enrolled), we concluded that concurrent (strength and aerobic) exercise improves muscle strength in childhood (59,63–75) (Supplemental Table 1, Supplemental Digital Content, https://links.lww.com/MSS/D370). The evidence primarily derives from studies including a mix of tumor diagnoses during (67,68,70–72,74) and after (59,64,70,74) treatment. Eight of the 14 RCTs (n = 510)

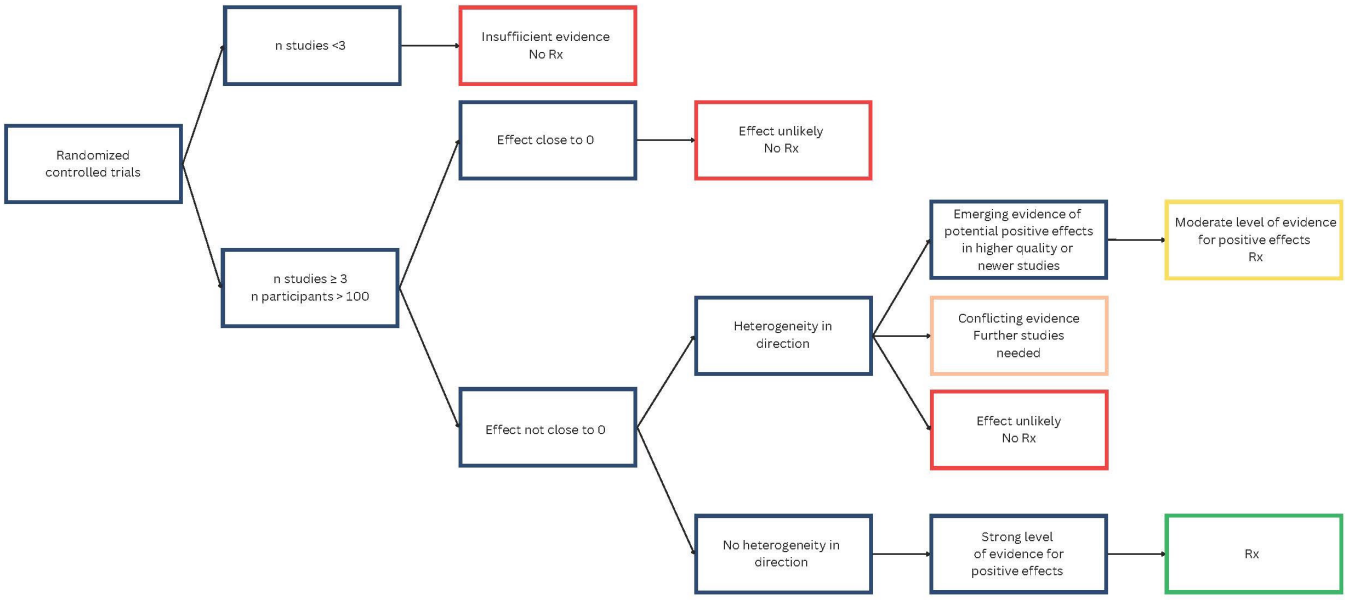

FIGURE 1—Decision framework for evidence-based exercise recommendations in children and adolescents during/beyond cancer treatment (adapted version based on Figure 1 in Campbell et al. (62)). Rx, exercise recommendations.

showed significant intervention-induced increases in one or more strength assessments (59,64,67,68,70–72,74). In the hematopoietic stem cell transplantation setting, all RCTs showed improvements in strength following 6–8 wk of exercise (67,73).

On the other hand, no study examined the effects of strength training alone on muscle strength in children/adolescents with cancer.

Cardiorespiratory fitness. Based on seven RCTs (n = 323) (66,67,71,74,76–78), we concluded that exercise does not improve CRF during active treatment, as four RCTs (n = 211) found no significant increase (or maintenance) in the response of this variable with concurrent (aerobic and strength) exercise intervention compared with the control group (67,71,74,76). However, there is evidence that aerobic exercise interventions can improve CRF in ALL survivors off treatment (i.e., based on all three RCTs studying this population, total n = 122) (66,77,78).

On the other hand, there is insufficient evidence (i.e., no studies) to conclude that concurrent or strength training alone can improve CRF in children/adolescents with cancer.

Physical function. Based on 12 RCTs (n = 655) (66,67,69–73,77,79–82), we concluded that concurrent (strength and aerobic) exercise improves physical function (e.g., performance in the Timed-up-and-Go or Timed-Up-and-Down-Stairs test, and in other physical function test batteries), with the evidence primarily derived from studies including a mix of cancer diagnoses during (67,70,72,73,83) or after (66,70,77) treatment. Seven studies (n = 360) found a significant improvement in the exercise intervention compared with the control group (66,67,70,72,73,77,81), whereas five showed no change (69,71,79,80,82).

On the other hand, there is insufficient evidence to suggest that aerobic or strength exercise alone improves physical function (i.e., no studies).

Physical activity. Based on 10 RCTs (n = 592), we concluded that exercise or PA behavior interventions do not change the habitual PA levels in this population (59,66,68,69,71,74,79,84–86). Of note, none of the studies assessing PA objectively (i.e., with accelerometers) reported improvements in PA levels (59,69,71).

Insufficient Evidence

Sleep. To date, there are too few high-quality studies to draw any conclusion regarding the effects of exercise on sleep quality in children/adolescents with cancer. Three RCTs (n = 151) have been conducted (79,87,88). Only one assessed sleep through specific methods (i.e., using both the Children's Sleep Habit Questionnaire and polysomnography) (88), whereas the remaining two used a subitem of a self-reported fatigue questionnaire (i.e., the sleep–rest fatigue subscale of the Pediatric Quality of Life Inventory). Of the three RCTs, two reported positive effects (79,88) and one found no change (87).

Metabolism. No RCT was identified assessing the effects of exercise on metabolism (i.e., indicators of glucose homeostasis or lipid profile) within our search. There is thus no evidence to recommend the implementation of exercise to alter metabolic outcomes, revealing a clear gap in knowledge of the positive effects of exercise.

Cardiotoxicity. No RCT has specifically assessed the effects of exercise on echocardiography-determined cardiac function. There is thus no evidence to recommend exercise to attenuate cardiotoxicity, also revealing a clear gap in the field. However, it is worth noting that CRF partly reflects (and is determined by) cardiac function.

Bone health. Three RCTs (n = 219) have studied exercise intervention effects on bone health (69,80,83). One reported that a 12-month multicomponent supervised exercise program (1–2 sessions·wk^{-1}) induced improvements in total body and spine bone mineral density in children with acute leukemias receiving maintenance phase of chemotherapy (83). However, the two other RCTs found no changes in bone mineral density (69,80). Given the heterogeneity between studies in the applied intervention and the findings, there is insufficient evidence to recommend the implementation of exercise intervention for improving bone health in children/adolescents with cancer.

Body composition. Based on five RCTs (n = 248), there is conflicting evidence on the effects of exercise intervention on body composition (70,71,74,80,83). The fact that four of these studies found no changes (70,71,74,80) and the heterogeneity between the applied interventions makes it difficult to provide meaningful exercise recommendations regarding body composition.

Health-related quality of life. The evidence is conflicting based on the results of eight RCTs (n = 493) (64,68–72,74,82). Five studies found no effect of exercise intervention on health-related quality of life (64,69,71,74,82), whereas three showed significant improvements in subscales of health-related quality of life questionnaires (68,70,72). Given the heterogeneity between studies in the intervention and the findings, there is insufficient evidence to recommend exercise interventions for improving health-related quality of life in children/adolescents with cancer.

Cancer-related fatigue. Seven RCTs (n = 356) have been conducted, with fatigue assessed through self- and/or parent-reported questionnaires (68,72,74,78,79,85,89). Four RCTs found a significant improvement in the intervention group compared with controls (68,72,78,79), whereas three reported no effect (74,85,89). Thus, research is still needed to determine whether children/adolescents with cancer can obtain the positive effects of exercise to reduce fatigue.

Cognitive function. Only two RCTs (n = 167) have been conducted (59,65). Thus, although both studies showed a positive effect of exercise on cognitive function, no recommendation with respect to the impact of exercise intervention on cognitive outcome can be made at present.

Depression and anxiety. One RCT (n = 68) investigated the effects of 12-wk concurrent strength and aerobic training and found no difference in depression symptoms between the intervention and control group (87). On the other hand, no RCT has specifically investigated the effects of exercise on anxiety (as primary outcome) in children/adolescents with cancer. As such, no recommendation with respect to the impact of exercise intervention on depression or anxiety can be made at present.

Immune function. Three RCTs (n = 96) assessed the effects of exercise on immune-related outcomes, including immune cell subpopulations (67,75,90) and cytotoxic activity of natural killer (NK) cells (67,75,90). Although one study with a very limited sample size (total n = 6) found improvements in NK-cell cytotoxicity with exercise intervention in children undergoing hematopoietic stem cell transplantation (75), the two other reports found essentially no changes in immune subsets (67,75,90) or in NK-cell cytotoxicity (67,90). No recommendation with respect to the impact of exercise intervention on immune function can be made at present.

Chemotherapy-induced peripheral neuropathy. No RCT was identified assessing the effects of exercise on chemotherapy-induced peripheral neuropathy within our search. There is thus no evidence to recommend the implementation of exercise to alter this outcome, revealing a clear gap in knowledge of the potential effects of exercise.

SPECIFIC RECOMMENDATIONS

See also Table 1 and Figure 2.

Muscle Strength

Based on the literature, the following FITT recommendations can be made for improving muscle strength with concurrent (strength and aerobic) exercise training during or after treatment: *Frequency*, 2–3 sessions·wk^{-1} during ≥8 wk; *Intensity*, moderate-to-vigorous, that is, score of 5–8 ("somewhat hard to hard") in the 0–10 OMNI-resistance exercise scale rate of perceived exertion (91) for strength exercises and ~60%–80% of peak heart rate, with the latter preferably estimated with the Tanaka equation (208 − 0.7*age [in yr]) if direct (derived from cardiopulmonary exercise testing) assessment is not possible (92) for aerobic exercises; *Time*, 30–45 min per session; *Type*, aerobic (running, cycling, ball games) and strength/power exercises (free weight, strength machines, plyometrics involving major muscle groups (two to three sets of 8–15 repetitions per set with 1- to 2-min rest periods between consecutive sets).

Cardiorespiratory Fitness

The following FITT recommendations can be made for aerobic exercise training to improve CRF off treatment in ALL survivors: *Frequency*, 2–3 sessions·wk^{-1} for ≥12 wk; *Intensity*, moderate-to-vigorous (same as for aerobic exercise in the section above [Muscle Strength]); *Time*, 15–40 min per session; *Type*, aerobic exercise (running, cycling, and ball games).

Physical Function

The FITT recommendations previously described in the section on Muscle Strength can also be made for concurrent (strength and aerobic) exercise training to improve physical function on or off treatment. In the hematopoietic stem cell transplantation setting, ≥6 wk of these recommendations seems sufficient to induce improvements (67,73,81). This is also supported by a recent meta-analysis (93).

LIMITATIONS

The exercise recommendations provided for various outcomes are intended to serve as an initial guide for healthcare and exercise professionals working in the childhood cancer context. However, these recommendations come with limitations that should be considered when managing individual patients, as explained below.

Most of the available research has focused on the most common tumors (mainly ALL) in children/adolescents or a mix of diagnoses, making it challenging to generalize findings with respect to specific cancers, risk stratifications, or advanced stages. Further research is therefore needed to enhance the specificity of the literature in the field to address a wider variety of cancer types, risk stratifications, and disease stages. Additionally, published studies have not consistently reported compliance with the prescribed exercise programs for specific groups of patients, likely due to the challenges associated with tracking and quantifying adherence. It is therefore possible that some children/adolescents may struggle to tolerate the recommended exercise programs. Most studies indicate that exercise programs are tailored to the patient's daily well-being, often involving dose modifications. Consequently, healthcare and exercise professionals should closely monitor early signs of exercise intolerance and adjust the exercise dosage as needed, even if this requires reducing training volumes and intensity below the recommended levels. Furthermore, many studies lack detailed information about the FITT principles. Thus, the development of the recommendations was supplemented with the experience of the authors, as well as information from exercise recommendations for

TABLE 1. Different aspects to be considered in individualized exercise prescriptions for aerobic and strength training in children and adolescents during/beyond cancer treatment.

Aspects	Aerobic Exercises	Strength Exercises
Practical factors	Ensure that training equipment is appropriately sized to fit the child's body, allowing for proper aerobic (i.e., use child-appropriate ergometers for children below the size of 1.40 m) and resistance (i.e., allowing for proper exercise technique and a full range of motion) training. Use equipment that permits small incremental changes in workload/resistance.	
Instructor qualifications	Aerobic and strength training should be supervised by qualified instructors who are ideally certified in pediatric exercise and have a strong understanding of the complexities of cancer treatment.[a]	
Feedback and safety	Screen participants for infections and other medical risks before each session; suspend or adapt training in the presence of fever, systemic infection, or other conditions outlined in Box 2. No matter the exercise choice or child's age, the child must be able to follow instructions to perform the exercise safely and correctly. If the child cannot follow instructions for a given exercise, it should not be included in the exercise prescription. Careful observation is essential; monitor objective (e.g., sweating and increased respiration) and subjective (scale for rating of perceived exertion and ability to speak) signs of exercise intensity, to minimize risk of overexertion while maximizing training benefits. Reduce workload and intensity and adjust with the pediatrician's recommendation during acute infection, fever, very low blood counts, or severe cardiopulmonary limitations.	
	• Provide guidance on revolutions or steps per minute (e.g., on an ergometer or stepper) to encourage continuous movement and to ensure correct techniques and performance. • Gradually increase workload and intensity; include a warm-up and a cooldown and pause sessions as needed.	• Provide real-time feedback on exercise techniques to minimize injury risk and maximize training benefits. • Begin with little or no resistance to ensure mastery of proper technique. • Gradually increase resistance while maintaining correct exercise form.
Exercise selection	• Incorporate partial- or full-body aerobic activities, depending on individual limitations, to stimulate the cardiovascular system. • Consider preferences, variation, and motivation. • For young and smaller children, use a playful approach and enjoyable activities and reduce stationary equipment.	• Include exercises targeting all major muscle groups, such as the upper body, lower body, and core. • Incorporate multi-joint exercises (e.g., bench press, leg press, push-ups, and body weight squats) and single-joint exercises where appropriate. • Prioritize exercises for larger muscle groups and multi-joint movements before progressing to smaller muscle groups and single-joint movements.
Progression and adaptation	• As endurance improves, gradually increase intensity, duration, and/or frequency in small increments. • Allow for a temporary reduction in duration or pace when intensity is increased to maintain proper form and avoid overexertion.	• As strength improves and consistency in technique is demonstrated, increase resistance by 5%–10% in small increments. • Allow for a temporary decrease in repetitions when resistance is increased to maintain proper exercise form. • The desired resistance for a certain number of repetitions per set can be found by trial and error during training. • "Somewhat hard" to "hard" (or 5–8 on the 10-point OMNI scale) can be used to adjust the resistance for an exercise or strength activity.
Training frequency and volume	Follow the standard training frequencies, volumes, and intensities recommended for healthy children and adolescents, adapting them to the individual's health and physical capacity.	
Bodyweight movements	–	• Strength training is not limited to weight lifting but also includes a range of bodyweight exercises suitable for young ages, such as push-ups, planks, and bodyweight squats, to develop foundational strength. • Many forms of play, such as running, jumping and climbing, are forms of strength training and can be included as part of the training prescription especially for very young children.

The abovementioned exercise prescriptions follow the guidelines recommended for healthy children and adolescents (105,106) and include specific aspects to consider in exercise interventions in the context of childhood/adolescent cancer.

[a]Exercise instructors should have at least a BSc degree in exercise science/physiology, ideally experience in working with children/adolescents with cancer, and ideally certified in pediatric exercise and with a strong understanding of the complexities of cancer treatment. Concerning the latter, there are yet no specific courses for exercise in the context of pediatric cancer other than a German initiative, in the frame of the Network ActiveOncoKids in close collaboration with the German Childhood Cancer Society (Website in German: https://www.activeoncokids.org/einladung-bop-schulung); nevertheless, the American College of Sports Medicine offers *Youth Fitness Specialist Certificate Course and Cancer* (in general) *Exercise Trainer*, and the National Strength and Conditioning Association's *Certified Special Populations Specialist* includes children and cancer (in general).

healthy children and adolescents (94,95). Further studies are needed to differentiate between various exercise doses. Another limitation of these initial guidelines is the omission of specific therapy-modalities (i.e., occupational therapy, play therapy, physiotherapy). These modalities may improve the selected outcomes of clinical relevance. Therefore, specific guidelines for these types of intervention are needed.

The lack of evidence for a particular outcome does not necessarily imply that children/adolescents with cancer will not benefit from exercise intervention in other ways, nor does it suggest they should avoid exercise. Instead, it highlights that current research has not yet demonstrated positive effects of exercise for these specific outcomes, reflecting a gap in knowledge that the research community needs to address. On the other hand, as opposed to adult malignancies, specific training and certifications are essentially lacking for those interested in the field of exercise in childhood cancer. Finally, before developing the guidelines, we decided to conduct a systematic literature search to ensure comprehensive identification of relevant studies and to follow the structure of the ACSM exercise guidelines for adult cancer (62). While we did not assess risk of bias or quality of evidence, nor perform statistical analyses of effect sizes, this approach enabled the inclusion of

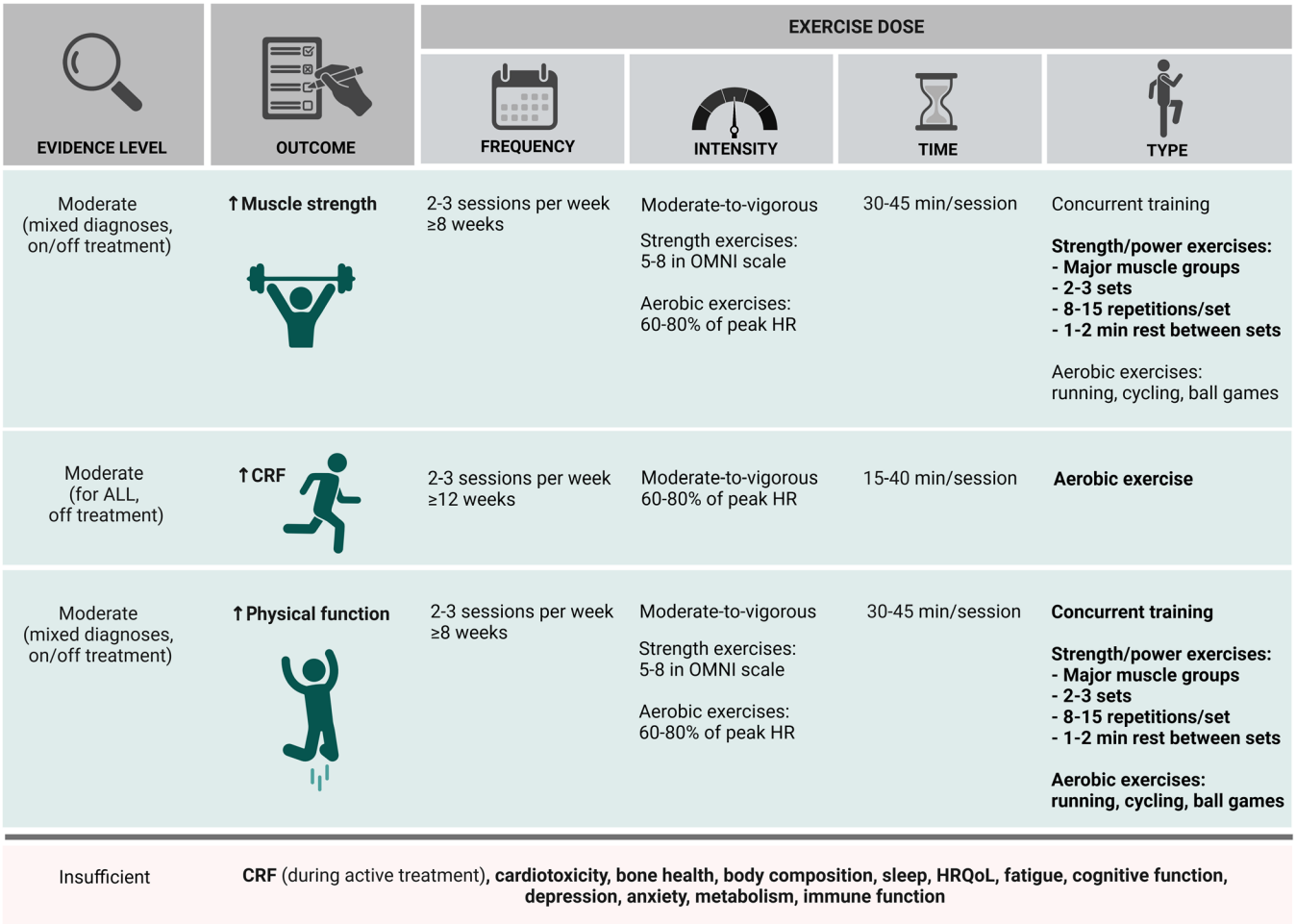

FIGURE 2—Recommended exercise dosage in children and adolescents during and beyond cancer treatment for improving muscle strength or physical function. CRF, cardiorespiratory fitness; HR, heart rate; HRQoL, health-related quality of life. The exercise types that are likely to account essentially for the improvement in the relevant outcome are marked in bold. Of note, although no study in our search assessed the effects of strength/power exercises alone (i.e., outside a concurrent exercise program), it is obviously conceivable that these types of exercises *per se* largely account for the gains in muscle strength induced by concurrent training. As such, if time limitations or other circumstances do not allow completing the aerobic component, performing "only" the strength component of the program is also highly recommended to achieve gains in muscle strength. Similarly, the lack of evidence for a particular outcome does not necessarily imply lack of benefit, and certainly does not suggest patients should avoid exercise.

expert clinical insight where evidence was limited or heterogeneous.

ADVERSE EVENTS

To effectively assess exercise tolerance and design a safe, effective exercise program, exercise professionals must understand the type and stage of the patient's cancer. Additionally, they need to be knowledgeable about common childhood cancer treatments and their potential side effects, and how these factors impact exercise capacity across different age groups.

Based on the literature, exercise can be performed safely with no acute exercise-related adverse events (66–68,70–72,74,85,96–98). Additionally, studies in the hematopoietic stem cell transplantation setting show that exercise has no harmful effects on the immune system (a crucial clinical safety aspect of transplants) (67,75,90,96,99). It should be recognized that most of the available evidence on the safety of exercise is derived from RCTs of supervised and home-based exercise. Hence, the studies took diagnosis-specific precautions. Furthermore, the participants enrolled in the studies commonly met prespecified eligibility criteria for comorbidities or baseline fitness levels, were from high-income western countries, and were willing to participate in research. This can lead to a sample that is healthier, fitter, and/or more motivated to engage in exercise than the broader population of children/adolescents with cancer. Nevertheless, the effects of exercise on important clinical safety aspects have been investigated to various degrees.

Adverse events are usually poorly audited and thus potentially underreported in clinical exercise trials (100). Similarly, no RCT of exercise has investigated overall adverse events throughout the entire childhood cancer

treatment trajectory. Future studies should therefore include overall and specific adverse events during exercise to strengthen the evidence on the potential harm related to exercise in the context of childhood cancer.

MEDICAL CLEARANCE AND PRECAUTIONS

Given the diversity of tumor types and toxicities of the different treatments, the question of whether affected children/adolescents require medical clearance (i.e., approval from a medical professional to engage in exercise or exercise testing) before starting an exercise program is always relevant.

Based on the available literature and consensus of the authors' group, we recommend that patients with some conditions avoid moderate/high-intensity exercise and that those at high risk of fractures avoid high-impact exercises (80), among other considerations (more details in Box 2).

EXERCISE PRESCRIPTION AND PRACTICAL STRUCTURE OF THE SESSIONS

Children/adolescents with cancer have several barriers toward engaging in exercise, including physical weakness, treatment-related side effects, fatigue, mood disturbance, and limited possibilities to engage in physical tasks (101–103). Furthermore, as opposed to adults, health benefits are seldom a motivating factor for these patients (104). Thus, creating a motivating environment for them is crucial. Exercise of any variety should therefore be fun for the participants, and this can be aided by including games as part of the exercise program.

Planning each exercise session after a similar structure can also help the patients' motivation as the structure can ensure familiarity, a sense of competence, appropriate challenge, and enjoyment (104). Starting all sessions with the same activity creates familiarity and lets the patient know that the exercise session has begun. This activity can be a dynamic warm-up for older children or adolescents or a "greeting song" for the younger children (starting activity) (104,105). The warm-up activity should be followed by an activity/exercise that the child knows and is competent with (known activity). The difficulty or intensity should be set at a level the child can master. The difficulty and intensity of the following exercises/activities can be subsequently increased to challenge the childhood cancer context. This is where the main content of the exercise session is performed (main exercises/activities). The main content is then followed by a known activity to finish the session with success and enjoyment (known activity). This can be a game, friendly competition, or activity that the child enjoys. All sessions should ideally end with the same activity, creating familiarity and letting the child know that the session is over. For older children and adolescents, this can be a cooldown exercise, such as stretching/relaxation and a "goodbye song" for the younger children (ending activity).

The most prevalent malignancies in children, acute leukemias, are more frequent during early infancy (≤5 yr), a period of life when muscle-strengthening training is not usually implemented in the general population. In this effect, resistance exercise prescription should follow the guidelines recommended for healthy children and adolescents (106), together with the medical precautions mentioned above. In addition to the FITT choice, other practical factors when training children/adolescents with cancer should be considered (Table 1).

SUMMARY AND FUTURE DIRECTIONS

A growing number of RCTs in recent years have reported the effects of exercise intervention in children and adolescents with cancer. Exercise training can generally be performed safely for this population, who should avoid bed rest and lack of movement, starting from the inpatient phase. There is moderate evidence for positive effects of concurrent aerobic and strength exercise training on muscle strength and physical function (but not on PA levels) during active treatment. In follow-up care, there is moderate evidence that aerobic exercise can improve CRF. There is therefore a need to verify these results in future studies. Yet the evidence is still insufficient in terms of delineating FITT-based recommendations as well as for other important outcomes, thereby reflecting additional gaps in the current state of knowledge. Although childhood cancer is

BOX 2. Medical clearance and precaution recommendations.

Patients should avoid moderate-to-vigorous exercise if they have low platelet count (<10,000 per μL)[a] or hemoglobin (<5 g·dL^{-1}),[b] temperature ≥38°C, severe muscle pain, severe infections, cardiovascular disorders, or persistent hypoxemia (peripheral oxygen saturation levels <90%).

Patients at a high risk of fractures (i.e., those with bone tumors or receiving high doses of corticosteroids) must avoid high-impact exercises.

Patients with CNS tumors are at higher risk of falling and seizures, which should be considered in the exercise selection.

If patients have undergone surgery, have platelet count between 10,000 and 20,000 per μL,[a] or hemoglobin between 5 and 8 g·dL^{-1},[b] exercise should be individually adjusted accordingly.

Specific health conditions might require individual adjustments—typically, lowering the intensity or changing the focus of the exercise session.

Real-time feedback and supervision should be provided by qualified exercise instructors[c] to minimize risk and maximize exercise training adaptations.

[a]Platelets: very low levels result in high bleeding risk; in nonhospital settings, this may be suspected if the child shows easy bruising, frequent nosebleeds, or small red skin spots.
[b]Hemoglobin: very low levels result in severe anemia; in nonhospital settings, this may be suspected if the child looks pale, fatigues quickly, is dizzy, or short of breath at rest.
[c]See Table 1 for more details.
CNS, central nervous system.

a rare disease and thus exercise studies do not necessarily have to match the sample size of those conducted in adult participants to build evidence, more powered RCTs are needed, ideally in the frame of multicenter efforts. More research is also needed addressing the sustainability of exercise interventions over time, especially when considering that most survivors have many decades of life ahead of them. Childhood cancer differs from adult malignancies in many aspects, and thus some special populations or challenging scenarios deserve special consideration and should be considered in future exercise interventional research; these include the younger children (age <4 yr) as well as adolescents (who must face the difficult transition from childhood to adulthood while suffering from cancer), the isolation phase of hematopoietic stem cell transplantation (a unique window of opportunity for exercise implementation but at the same time a challenging scenario due to isolation in the ward for at least 1 month), or eventual development of graft versus host disease.

This article is being published as an official pronouncement of the American College of Sports Medicine. This pronouncement was reviewed for the American College of Sports Medicine by members-at-large and the Pronouncements Committee. Care has been taken to confirm the accuracy of the information presented and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from the application of the information in this publication and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. The application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations. Research by C. F. -L. on childhood/adolescent cancer is funded by the Spanish Ministry of Science and Innovation (Fondo de Investigaciones Sanitarias [FIS]) and Fondos FEDER (grant numbers PI23/00396 and FORT23/00023) and by the Ministerio de Ciencia e Innovación (grant number #144144). Research by A. L. and C. F. –L. is funded by the Wereld Kanker Onderzoek Fonds (WKOF), as part of the World Cancer Research Fund International grant program (grant # IIG_FULL_2021_007). Research by A.L. in pediatric cancer is also funded by Fundación Aladina (Spain). Research by M. A. N. was supported by the European Union's Horizon 2020 research and innovation program under grant agreement No. 945153. M. K. F. is funded by Børnecancerfonden (2023-001075). The remaining authors declare that they have no conflicts of interest.

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