PHYSICAL ACTIVITY, EXERCISE AND CANCER

REVIEW ARTICLE

Effects of physical activity in pediatric acute lymphoblastic leukemia after oncologic treatment: A systematic review

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ABSTRACT

Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy. Although survival rates have improved, children and survivors frequently experience long-term impairments in aerobic capacity, muscle strength, functional mobility, and health-related quality of life (HRQoL). Objective: To systematically synthesize evidence regarding the effects of structured physical activity and exercise programs in paediatric patients with ALL after oncologic treatment or during late phases of therapy. A systematic review was conducted following PRISMA 2020 and the PICO framework. PubMed, PEDro, and SciELO were searched (September–December 2025). Randomized controlled trials (RCTs), non-randomized trials, and pre–post studies in participants <15 years with ALL were included if the intervention was described and outcomes included physical function, biological markers, and/or HRQoL. Methodological quality was assessed using the McMaster tool. Six studies met eligibility criteria. Most interventions were multicomponent (aerobic + resistance ± flexibility), lasting 12–16 weeks, 2–5 sessions/week. Exercise improved aerobic capacity (VO_2 outcomes), functional mobility (TUG, TUDS, 9-min walk), and selected strength outcomes. HRQoL results were inconsistent and often non-significant. Biological outcomes were heterogeneous, including stable oxygen pressure, no clear effects on bone mineral density, and improvements in haematological parameters in one study. Structured exercise appears feasible and may improve physical fitness outcomes in paediatric ALL, but evidence remains limited by heterogeneity in interventions and outcomes. Larger standardized trials are required.

Keywords: Acute lymphoblastic leukaemia, Paediatric oncology, Exercise, Physical activity, Functional capacity, Quality of life.

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INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a hematologic malignancy characterized by the clonal expansion of immature lymphoid progenitors in the bone marrow, resulting in disruption of normal hematopoiesis and impaired immune function (Abd El Baky & Adel Elhakk, 2017). Clinically, this pathophysiology translates into anemia, thrombocytopenia, and leukocyte dysfunction, which may manifest as fatigue, bleeding tendencies, recurrent infections, fever, and musculoskeletal pain (Castañeda-Huerta, 2009; Lassaletta Atienza, 2016). Although ALL is relatively uncommon in the general population, it represents the most frequent pediatric cancer diagnosis and accounts for a substantial proportion of malignancies in children younger than 15 years (Tanir & Kuguoglu, 2013; White et al., 2005).

Over the past decades, improvements in risk-adapted chemotherapy protocols, supportive care, and stratified treatment intensification have markedly increased survival rates, transforming pediatric ALL into a paradigmatic success story of modern oncology (Raetz, 2014). As a consequence, the clinical focus has progressively expanded beyond survival toward the prevention and management of treatment-related toxicities and long-term morbidity (Järvelä et al., 2010). This shift is particularly relevant because children and adolescents treated for ALL are vulnerable to persistent deficits in physical function, including reduced cardiorespiratory fitness, muscle weakness, limitations in functional mobility, and impaired participation in age-appropriate activities (Järvelä et al., 2010; Tanir & Kuguoglu, 2013). Notably, long-term survivors may exhibit significantly lower peak oxygen uptake (VO_{2peak}) than healthy peers, suggesting clinically meaningful impairment in aerobic capacity that may persist years after therapy completion (Järvelä et al., 2010).

The mechanisms underlying functional decline in pediatric ALL are multifactorial. Treatment-related neurotoxicity, corticosteroid exposure, reduced habitual activity, prolonged hospitalization, and cancer-related fatigue contribute to deconditioning and neuromuscular impairment (Tanir & Kuguoglu, 2013). Additionally, musculoskeletal limitations—such as ankle range-of-motion restriction—have been reported among survivors, potentially compromising gait efficiency and functional independence (Wright et al., 1999). These sequelae are not merely transient inconveniences; rather, they can influence long-term health trajectories by promoting sedentary behaviors and reducing physical reserve, which may ultimately increase vulnerability to cardiometabolic complications across survivorship (Järvelä et al., 2010).

Physical activity (PA), defined by the World Health Organization as any bodily movement produced by skeletal muscles that requires energy expenditure, is associated with wide-ranging benefits including improved physical health, mental well-being, and quality of life (Bull et al., 2020). In pediatric oncology, PA and structured exercise training have gained increasing recognition as supportive care interventions aimed at counteracting deconditioning and improving functional outcomes (White et al., 2005). Exercise may provide clinically meaningful benefits by enhancing aerobic fitness, neuromuscular performance, and functional mobility, while potentially attenuating cancer-related fatigue and supporting psychosocial recovery (Abd El Baky & Adel Elhakk, 2017).

In children with ALL, growing evidence supports the feasibility and potential efficacy of structured exercise programs. A randomized clinical trial of a home-based multicomponent intervention in childhood ALL survivors demonstrated significant improvements in VO_{2peak} and functional performance tests, supporting exercise as a strategy to restore physical fitness after treatment (Manchola-González et al., 2020). Likewise, a randomized controlled trial (RCT) reported that systematic exercise training improved functional mobility (Timed Up and Go, stair performance) and exercise capacity compared with usual care in children in remission (Tanir & Kuguoglu, 2013). Aerobic exercise interventions have also been associated with

improvements in physical fitness and reductions in fatigue, reinforcing the role of PA in symptom management and functional recovery (Abd El Baky & Adel Elhakk, 2017).

Nevertheless, the current literature remains heterogeneous regarding intervention timing, training dose, supervision, and clinical endpoints. Importantly, not all trials report consistent benefits, particularly when interventions are initiated during intensive treatment. In a long-duration randomized trial beginning shortly after diagnosis, a physical therapy and motivational program did not significantly modify bone mineral density, physical function, or health-related quality of life (HRQoL), suggesting that achieving sufficient training intensity and adherence during early treatment phases may be challenging (Cox et al., 2017). This inconsistency highlights the need to clarify which exercise prescriptions are most effective, at what stage of the therapeutic pathway they should be implemented, and which outcomes are most responsive to change in pediatric ALL.

Given the increasing population of pediatric ALL survivors and the clinical relevance of persistent physical impairments, a rigorous synthesis of the evidence is warranted to inform exercise prescription and supportive care strategies. Therefore, the aim of this systematic review was to critically evaluate the effects of PA and structured exercise interventions on physical fitness, functional performance, fatigue, and HRQoL in children and adolescents with ALL after oncologic treatment or during late phases of therapy.

MATERIALS AND METHODS

Study design and reporting framework

This systematic review was conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA 2020) statement (Page et al., 2021) and was structured using the PICO framework to define eligibility criteria and the research question (Santos et al., 2007).

The PICO components were defined as follows: P (Population): pediatric patients diagnosed with ALL; I (Intervention): implementation of structured PA or exercise programs; C (Comparison): usual care, placebo/sham intervention, no intervention, or within-group pre–post comparisons; O (Outcomes): changes in physical function, biological markers, and/or HRQoL; S (Study design): RCTs, non-randomized clinical trials, and pre–post test studies.

Information sources and search strategy

A structured literature search was performed in the following electronic databases: Medline (PubMed), PEDro, and SciELO, covering the period from September 2025 to December 2025. The search included studies, published in English or Spanish in the last 25 years (January 2000 to May 2025).

Search terms were developed using a combination of Medical Subject Headings (MeSH) and free-text keywords related to ALL and exercise/PA. The main concepts included *acute lymphoblastic leukemia*, *exercise*, *physical exercise*, *physical function*, and *aerobic exercise*, combined using the Boolean operator AND and OR. Additional records were retrieved through manual reference list screening of eligible studies.

Study selection process

Two reviewers independently screened titles, abstracts, and full texts to identify potentially eligible studies. Eligibility criteria were applied independently by both reviewers, and disagreements were resolved through discussion and arbitration by a third reviewer.

Eligibility criteria

Studies were included if they met all of the following criteria:

1. Population: participants diagnosed with ALL who had received oncologic treatment.
2. Study type: human studies only (animal and in vitro studies were excluded).
3. Design: randomized or non-randomized clinical trials and pre–post intervention studies (reviews, notes, and non-original research were excluded).
4. Intervention reporting: studies describing the exercise program in sufficient detail, including type, duration, frequency, and intensity.
5. Outcomes: studies reporting outcomes related to physical function, biological markers, and/or HRQoL.
6. Age: pediatric participants aged <15 years.
7. Methodological quality threshold: studies with a score of ≥8 points using the McMaster Critical Review Form for Quantitative Studies (Law et al., 2018).

Records that did not meet the inclusion criteria were excluded from the final synthesis.

Methodological quality assessment

Methodological quality of the included studies was assessed using the *McMaster Critical Review Form for Quantitative Studies*, developed by the Evidence-Based Practice Research Group at McMaster University (Law et al., 2018). This tool evaluates methodological rigor across domains such as study purpose, design, sampling, outcomes, intervention integrity, analysis, and clinical relevance.

Data extraction

Data from the included studies were extracted independently by two reviewers and summarized in a standardized table. Extracted variables included: first author, year of publication, country, study design, sample size, sex and age of participants, intervention duration, intervention characteristics, and primary outcomes. Disagreements were resolved through consensus and, when necessary, consultation with a third reviewer.

RESULTS

Study selection

The electronic search identified 59 records across PubMed, PEDro, and SciELO. After removing 36 duplicates, 23 records were screened by title and abstract. Of these, 15 articles were excluded because they did not meet the eligibility criteria (e.g., descriptive studies without a structured intervention, interventions performed exclusively during intensive treatment, or studies without an exercise component). Two additional records were excluded because they were not aligned with the objective of this review. After full-text assessment, 2 studies were excluded due to non-eligible outcomes. In addition, two studies were identified through snowball sampling, which were incorporated into the PRISMA flow diagram. Finally, 6 studies fulfilled the inclusion criteria and were included in the qualitative synthesis (Figure 1).

Methodological quality

Methodological quality was assessed using the McMaster Critical Review Form for Quantitative Studies (Law et al., 2018). Four studies were classified as excellent quality (Manchola-González et al., 2019; Tanir et al., 2012; Abd El Baky et al., 2017; Perondi et al., 2012), whereas two studies were rated as very good quality (Cox et al., 2017; Järvelä et al., 2010). No study was excluded for failing to meet the minimum methodological quality threshold (Table 1).

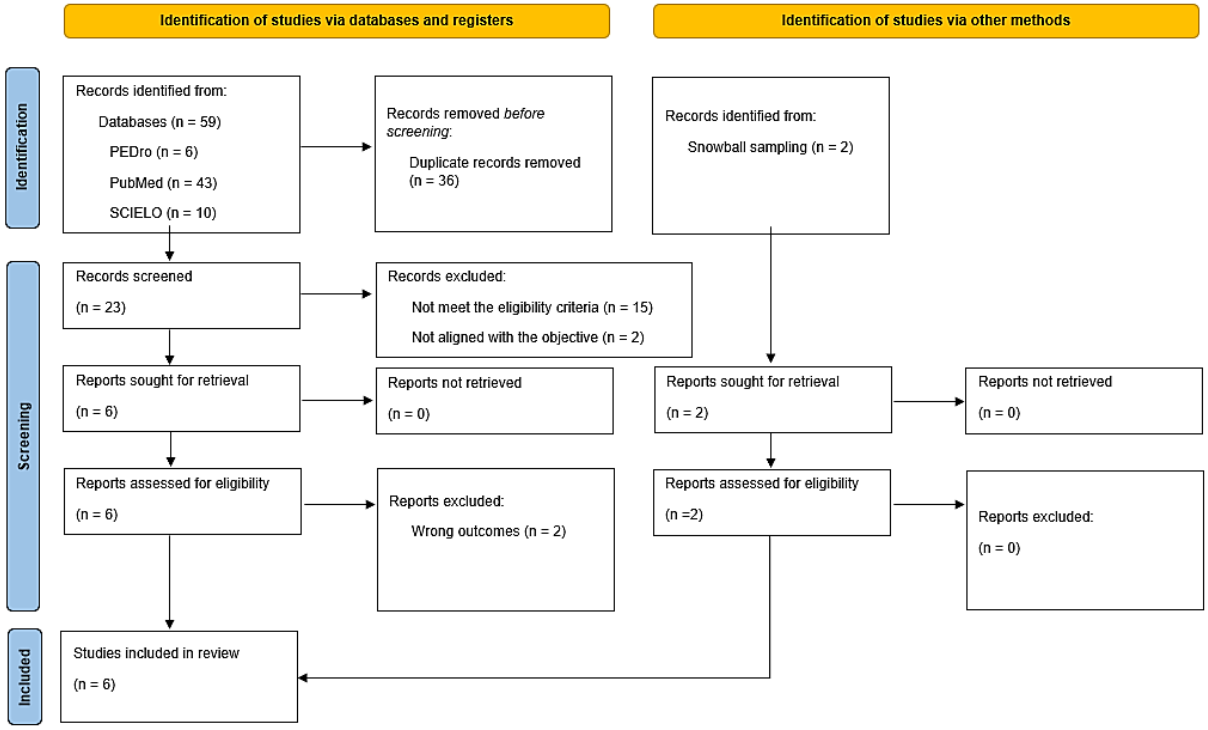

Figure 1. Flowchart represents the processes of identifying and selecting relevant studies according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Table 1. Methodological quality assessment of included studies using the McMaster Critical Review Form for Quantitative Studies (Law et al., 2018).

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total	%	Quality
Manchola-González et al. (2019)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	16	100.0	E
Cox et al. (2017)	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	14	87.5	VG
Tanir et al. (2012)	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	15	93.8	E
Järvelä et al. (2010)	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	14	87.5	VG
Abd El Baky et al. (2017)	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	15	93.8	E
Perondi et al. (2012)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	16	100.0	E

Note. (1) criterion met; (0) criterion not met; Total: Total number of criteria met; %: percentage of criteria met; G: Good, 11-12 points; VG: Very good, 13-14 points; E: Excellent, ≥15 points. The modified form consists of criteria concerning the following: item 1 -Study purpose; item 2 - Literature review; item 3 - Study design; item - 4 Blinding; item 5 - Sample description; item 6 - Sample size; item 7 - Ethics and consent; item 8 - Validity of outcomes; item 9 - Reliability of outcomes; item 10 - Intervention description; item 11 - Statistical significance; item 12 - Statistical analysis; item 13 - Clinical importance; item 14 - Conclusions; item 15 - Clinical implications; and item 16 - Study limitations.

Study characteristics

Study characteristics and intervention prescriptions are summarized in Table 2. Participants included pediatric patients with ALL across different clinical phases, including early after diagnosis, maintenance therapy, remission, and survivorship. Most included studies were RCTs evaluating structured exercise programs compared with usual care or control conditions (Manchola-González et al., 2020; Cox et al., 2017; Tanir & Kuguoglu, 2013; Abd El Baky & Adel Elhakk, 2017). In addition, one study employed a pretest–posttest design without a control group (Perondi et al., 2012), and one controlled observational study compared long-term ALL survivors with healthy controls to characterize PA and fitness profiles (Järvelä et al., 2010).

Interventions were heterogeneous in terms of exercise modality and dose, ranging from supervised aerobic training (Abd El Baky & Adel Elhakk, 2017) to multicomponent home-based programs combining aerobic, resistance, and flexibility exercises (Manchola-González et al., 2020), as well as mixed interventions incorporating mobility, strengthening, and aerobic components (Tanir & Kuguoglu, 2013). Cox et al. (2017) implemented a physiotherapy-based intervention with motivational support targeting strength, range of motion, endurance, and gross motor function early after diagnosis.

Table 2. Characteristics of included studies and exercise prescription.

Study	Country	Design	Participants	Clinical phase	Intervention	Dose	Comparator	Primary outcomes
Manchola-González et al. (2020)	Spain	RCT	Paediatric ALL survivors	≥1 year remission	Home-based multicomponent (aerobic + resistance + flexibility)	16 weeks; 3 sessions/week	Usual care	VO_{2peak}, TUG, TUDS, strength, flexibility
Cox et al. (2017)	USA	RCT	Children with newly diagnosed ALL	≤10 days post-diagnosis	PT + motivational intervention (strength, ROM, endurance, gross motor)	Long duration; frequent sessions	Usual care	BMD, physical function, HRQoL
Tanir & Kuguoglu (2013)	Turkey	RCT	Children with ALL	≥1 year remission	ROM + strengthening + aerobic training	12 weeks; 3 sessions/week (+ daily ROM)	Usual care	9-min walk, TUG, stairs, strength, HRQoL, haematology
Järvelä et al. (2010)	Finland	Controlled study	Adolescents/young adults	Long-term survivors	Physical activity exposure	Not specified	Healthy controls	VO_{2peak}, strength, fitness
Abd El Baky & Adel Elhakk (2017)	Egypt	RCT	Children with ALL	Remission	Aerobic training	16 weeks; 3 sessions/week	Usual care	Fitness outcomes, fatigue
Perondi et al. (2012)	Brazil	Pre–post	Young ALL patients	Maintenance therapy	Combined aerobic + resistance training	12 weeks; 2 sessions/week	None	Strength, fatigue, HRQoL

Note. ALL: acute lymphoblastic leukemia; BMD: bone mineral density; HRQoL: health-related quality of life; PT: physiotherapy; RCT: ramdomized controlled trial; ROM: range of movement; TUDs: timed up and down stairs test; TUG: timed up and go test; VO_{2peak}: peak oxygen uptake.

Synthesis of outcomes

A qualitative synthesis by outcome domain is presented in Table 3, while quantitative results reported across studies (including pre–post changes and between-group effects when available) are summarized in Table 4.

Physical function and physical fitness

Overall, structured PA interventions were consistently associated with improvements in aerobic capacity and functional performance. Manchola-González et al. (2020) reported that a 16-week home-based exercise program significantly improved VO_{2peak} compared with controls, with favorable trends in functional mobility (Timed Up and Go [TUG]) and stair performance (Timed Up and Down Stairs [TUDs]). In a pediatric RCT conducted in remission, Tanir and Kuguoglu (2013) observed significant improvements in exercise capacity (9-minute walk), functional mobility (TUG), stair-climbing performance, and lower-limb strength compared with controls. In long-term survivors, Järvelä et al. (2010) identified lower VO_{2peak} and differences in physical fitness compared with healthy controls, supporting the presence of persistent aerobic impairment after treatment and reinforcing the clinical rationale for exercise interventions.

Quality of life and fatigue

Quality-of-life outcomes were more heterogeneous. In Cox et al. (2017), long-duration physical therapy and a motivational intervention initiated soon after diagnosis did not produce significant improvements in HRQoL compared with controls. In contrast, Perondi et al. (2012) reported improvements in parent-reported quality-of-life and fatigue measures following combined aerobic and resistance training, alongside marked gains in strength outcomes. However, HRQoL and fatigue outcomes were not consistently reported with complete numerical data across studies, limiting quantitative comparability (Table 4).

Biological outcomes

Table 3. Qualitative synthesis of effects by outcome domain.

Domain	Outcomes	Main findings	Studies
Aerobic capacity	VO_{2peak}/VO_{2max}, walking tests	Improvements observed in most interventions, especially in post-treatment/remission settings	Manchola-González et al., 2020; Tanir & Kuguoglu, 2013; Järvelä et al., 2010
Functional mobility	TUG, TUDS, stairs	Functional mobility improved mainly in multicomponent programs	Manchola-González et al., 2020; Tanir & Kuguoglu, 2013
Strength	Dynamometry, 10-RM	Strength improved in remission and maintenance interventions	Tanir & Kuguoglu, 2013; Perondi et al., 2012
HRQoL & fatigue	PedsQL, fatigue scales	Mixed results; improvements more evident in maintenance/pre–post designs	Cox et al., 2017; Perondi et al., 2012; Abd El Baky & Adel Elhakk, 2017
Biological outcomes	BMD, haematology	No effect on BMD during early treatment; haematology improved in one remission trial	Cox et al., 2017; Tanir & Kuguoglu, 2013

Note. BMD: bone mineral density; HRQoL: health-related quality of life; PedsQL: Pediatric Quality of Life Inventory; RM: Maximum repetition; TUDs: timed up and down stairs test; TUG: timed up and go test; VO_{2peak}: peak oxygen uptake; VO_{2max}: maximum oxygen uptake.

Table 4. Quantitative results.

Study	Outcome	Intervention (PRE → POST)	Control (PRE → POST)	Main effect / Between-group result	*p*-value (between-group / main effect)	*p*-value (within IG)
Manchola-González et al., 2020	VO_{2peak} (ml/kg/min)	NR	NR	Group×time: +6.7 (95% CI 0.6–12.8)	.035	NR
Manchola-González et al., 2020	TUG (s)	6.4 ± 1.5 → NR	6.5 ± 1.8 → NR	Δ between: −0.5 (95% CI −1.1 to 0.4)	.068	NR
Manchola-González et al., 2020	TUDS (s)	11.1 ± 1.5 → NR	10.8 ± 2.0 → NR	Δ between: −0.5 (95% CI −1.3 to 0.3)	.217	NR
Tanir & Kuguoglu, 2013	9-min walk (cycles)	27.05 ± 6.59 → 35.89 ± 8.46	26.27 ± 9.28 → 26.76 ± 10.57	Post-test IG vs CG significant	.005	NR
Tanir & Kuguoglu, 2013	TUG (s)	8.31 ± 1.60 → 6.57 ± 1.34	8.77 ± 1.60 → 8.33 ± 1.62	Post-test IG vs CG significant	.001	NR
Tanir & Kuguoglu, 2013	Leg strength (dynamometer)	50.52 ± 27.38 → 75.52 ± 30.22	39.09 ± 13.85 → 40.71 ± 17.19	Post-test IG vs CG significant	.001	NR
Tanir & Kuguoglu, 2013	Haemoglobin (g/dL)	12.40 ± 1.13 → 12.94 ± 0.69	12.36 ± 0.77 → 12.60 ± 0.63	Post-test IG vs CG not significant	.126	.002
Tanir & Kuguoglu, 2013	Haematocrit (%)	37.58 ± 3.14 → 39.22 ± 2.16	38.94 ± 2.61 → 39.80 ± 2.11	Post-test IG vs CG not significant	.411	.002
Cox et al., 2017	BMD (Z-score)	−0.21 → −0.55	−0.62 → −0.78	Rates of decline did not differ	.56	NR
Perondi et al., 2012	10-RM leg press (kg)	29.5 ± 13.7 → 51.2 ± 12.9	NR	Pre–post improvement	NR	<.001

Note. BMD: bone mineral density; CI: confidence interval; dL: decilitres; g: grams; Kg: kilograms; min: minute; ml: millilitre; NR: not reported; RM: Maximum repetition; s: seconds; TUDs: timed up and down stairs test; TUG: timed up and go test; VO_{2peak}: peak oxygen uptake.

Biological outcomes varied across trials. Cox et al. (2017) found no significant between-group differences in bone mineral density trajectories, suggesting limited osteoprotective effects of the intervention during early

treatment. Conversely, Tanir and Kuguoglu (2013) reported improvements in hematological parameters (hemoglobin and hematocrit) in the intervention group, although these outcomes were not consistently available for quantitative comparison across studies (Table 4).

Quantitative synthesis (post-intervention values)

In the present review, quantitative synthesis was limited by the small number of trials reporting comparable outcomes with complete post-intervention dispersion data. Nevertheless, single-study effect estimates suggested clinically meaningful improvements in functional mobility and aerobic capacity following structured exercise interventions. Quantitative synthesis was performed using post-intervention values to estimate between-group effects for outcomes reported with sufficient statistical detail. Given the heterogeneity in intervention content, clinical phase, and outcome assessment across studies, pooled meta-analysis was not feasible for most endpoints. Therefore, single-study effect estimates are presented as mean differences (MD) with 95% confidence intervals (95% CI), complemented by standardized mean differences (Hedges g) to facilitate interpretation of effect magnitude (Table 5).

Table 5. Quantitative synthesis (post-intervention values).

Outcome	Study	n (Int)	Mean (SD) Int	n (Ctrl)	Mean (SD) Ctrl	MD	95% CI	Direction
TUG (s)	Tanir & Kuguoglu (2013)	15	6.57 (1.34)	15	8.33 (1.62)	−1.76	[−2.82, −0.70]	Favours intervention
VO_{2max} (ml/kg/min)	Abd El Baky & Adel Elhakk (2017)	15	33.50 (3.72)	15	26.30 (4.70)	7.20	[4.17, 10.23]	Favours intervention

Abbreviation: CI: confidence interval; Ctrl: control group; Int: intervention group; MD: mean difference (Intervention − Control); SD: standard deviation; TUG: timed up and go; VO_{2max}: maximum oxygen uptake. Negative MD values indicate improvement for TUG (lower time), whereas positive MD values indicate improvement for VO_{2max} (higher aerobic capacity).

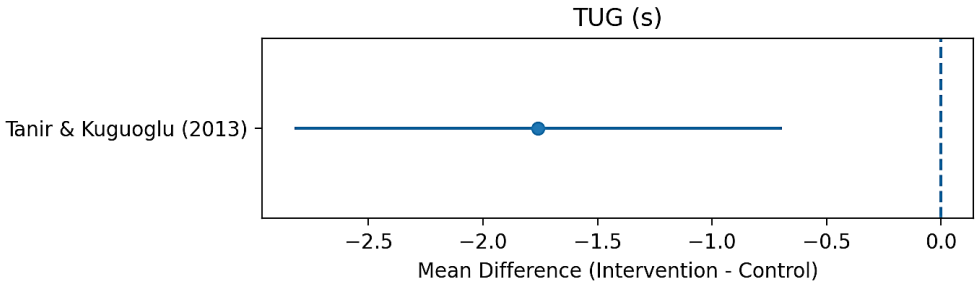

Figure 2. Forest plot for TUG (post-intervention values).

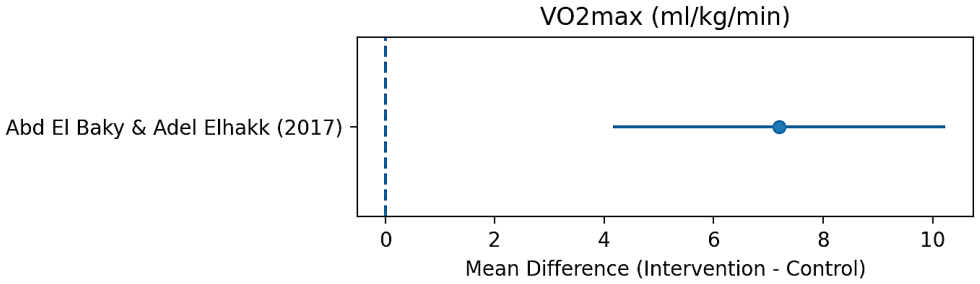

Figure 3. Forest plot for VO_{2max} (post-intervention values).

TUG (s): Tanir & Kuguoglu (2013) reported a lower post-intervention TUG time in the exercise group compared with controls (MD = −1.76 s; 95% CI −2.82 to −0.70; Hedges g = −1.15; 95% CI −1.93 to −0.38) (Figure 2 and Table 5).

VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$): Abd El Baky & Adel Elhakk (2017) reported higher post-intervention VO_{2max} in the exercise group compared with controls (MD = 7.20; 95% CI 4.17 to 10.23; Hedges g = 1.65; 95% CI 0.82 to 2.49) (Figure 3 and Table 5).

These findings support exercise as a promising supportive strategy in pediatric ALL; however, conclusions remain preliminary and should be confirmed in adequately powered randomized trials with standardized outcome reporting.

DISCUSSION

The aim of this systematic review was to critically evaluate the potential effects of structured PA and exercise programs in paediatric patients with ALL after oncologic treatment. Six studies met the pre-specified eligibility criteria and were included in the qualitative synthesis (Manchola-González et al., 2020; Cox et al., 2017; Tanir & Kuguoglu, 2013; Järvelä et al., 2010; Abd El Baky & Adel Elhakk, 2017; Perondi et al., 2012). Overall, improvements were reported in key domains of physical fitness, particularly aerobic capacity (VO_2-related outcomes) and muscle strength. However, evidence regarding HRQoL was inconsistent, with several studies failing to demonstrate statistically significant between-group differences. In addition, selected biological outcomes showed variable responses to exercise, depending on the biomarker assessed and the clinical context of the intervention. Given the heterogeneity of outcomes and measurement methods across studies, findings are discussed below by domain to facilitate interpretation.

Exercise programs: characteristics and training prescription

Most interventions included in this review applied multicomponent exercise, combining aerobic exercise with flexibility/stretching and resistance training (Manchola-González et al., 2020; Tanir & Kuguoglu, 2013; Abd El Baky & Adel Elhakk, 2017; Perondi et al., 2012). In contrast, one study did not implement a structured protocol but examined associations between habitual PA and health-related parameters in long-term survivors (Järvelä et al., 2010).

Aerobic exercise is widely regarded as a cornerstone of healthy recovery following chemotherapy and may contribute to improved cardiorespiratory capacity and functional performance in paediatric cancer survivors (Herrera de León Potente, 2019). In the included studies, aerobic exercise was delivered through accessible modalities such as walking, jogging, or cycling, and intensity was commonly individualized according to patient tolerance and baseline capacity (Manchola-González et al., 2020; Tanir & Kuguoglu, 2013; Abd El Baky & Adel Elhakk, 2017; Perondi et al., 2012). Conversely, Cox et al. (2017) implemented a long-duration physical therapy and motivational intervention early after diagnosis, reflecting a different clinical scenario where intensive training may be limited by treatment burden and symptom fluctuations.

Resistance training was also incorporated in several protocols, aiming to counteract treatment-related muscle loss and restore functional independence. Three studies included strengthening exercises targeting the lower limbs, upper limbs, and core musculature (Manchola-González et al., 2020; Abd El Baky & Adel Elhakk, 2017; Perondi et al., 2012). Notably, Tanir and Kuguoglu (2013) focused primarily on lower-limb strengthening, consistent with the importance of lower extremity function for mobility tasks such as walking and stair climbing. Cox et al. (2017) evaluated ankle strength outcomes, which is clinically relevant given that

ankle range-of-motion and function may be impaired in ALL survivors (Wright et al., 1999). Flexibility and mobility exercises were included in several programs, often targeting both upper and lower extremities (Manchola-González et al., 2020; Abd El Baky & Adel Elhakk, 2017; Perondi et al., 2012), whereas other trials did not clearly describe stretching components (Cox et al., 2017; Järvelä et al., 2010).

Across protocols, duration ranged from 12 to 16 weeks in most studies, with training frequencies typically between 2 and 5 sessions per week. Importantly, interventions generally emphasized gradual progression and individualization, and most were delivered with professional supervision or structured guidance. These characteristics are consistent with paediatric oncology recommendations highlighting safety, feasibility, and adaptation to treatment-related variability (White et al., 2005).

Effects on physical function and physical capacity

Early initiation of PA during the oncologic pathway may be clinically meaningful to attenuate rapid deconditioning, even when exercise intensity and volume must be reduced (Cox et al., 2017). Across included trials, exercise interventions were associated with improvements in aerobic capacity, mobility, and strength outcomes, supporting the hypothesis that structured PA can mitigate functional decline in paediatric ALL.

Aerobic capacity, typically measured using VO_2 outcomes or functional walking tests, improved in several interventions, particularly in remission or survivorship settings. Improvements in VO_{2peak} were observed following a home-based program in ALL survivors (Manchola-González et al., 2020) and following aerobic training protocols (Abd El Baky & Adel Elhakk, 2017). In contrast, long-term survivors still displayed reduced aerobic fitness compared with controls in Järvelä et al. (2010), highlighting the persistence of cardiopulmonary impairment and the need for long-term supportive care strategies. Regarding cardiovascular parameters, no significant differences in maximal heart rate were reported between groups in Järvelä et al. (2010), suggesting that functional capacity differences may be related to peripheral limitations, deconditioning, or reduced habitual activity rather than central cardiac impairment alone.

Strength outcomes were generally favourable but varied by muscle group and assessment method. Cox et al. (2017) reported improvements in ankle strength in both intervention and control groups, while Perondi et al. (2012) found significant strength gains in multiple resistance exercises (leg press, bench press, leg extension, and chest pull). In addition, Tanir and Kuguoglu (2013) and Manchola-González et al. (2020) demonstrated improvements in functional performance tests (e.g., walking capacity, stair performance), although handgrip strength did not consistently improve, potentially reflecting differences in training specificity or measurement sensitivity.

Unexpectedly, flexibility improvements were reported in the control group in Manchola-González et al. (2020), despite flexibility training being included in the intervention protocol. This finding may reflect measurement variability, spontaneous recovery over time, or unmeasured PA exposure in controls.

Effects on quality of life and fatigue

Beyond physical limitations, children with ALL may experience social isolation, loss of independence, anxiety, and depressive symptoms, which can negatively affect HRQoL in both patients and caregivers (Tanir & Kuguoglu, 2013). HRQoL was assessed primarily through standardized questionnaires administered pre- and post-intervention, but instruments varied across studies (Cox et al., 2017; Tanir & Kuguoglu, 2013; Perondi et al., 2012).

Overall, HRQoL findings were mixed. Cox et al. (2017) did not observe significant between-group differences in HRQoL outcomes, possibly due to intervention timing near diagnosis, high treatment burden, or insufficient training dose to induce psychosocial changes. Tanir and Kuguoglu (2013) reported domain-specific improvements (e.g., pain and cognitive problems) in the intervention group, whereas anxiety-related outcomes improved in controls, suggesting complex psychosocial trajectories that may not be solely driven by exercise exposure. In Perondi et al. (2012), parent-reported fatigue improved significantly, and HRQoL showed a positive trend without reaching statistical significance, which may be explained by limited sample size and the challenges of detecting change in multidimensional psychosocial constructs.

These findings suggest that while exercise may contribute to improved fatigue and perceived well-being, HRQoL outcomes in paediatric oncology likely require broader supportive interventions and longer follow-up to capture clinically meaningful changes.

Effects on biological markers

Biological markers are measurable indicators present in body fluids or tissues that reflect physiological or pathological processes and may be used to monitor disease status and treatment response (Iranzo, 2015). Biological outcomes in the included studies were heterogeneous and included oxygen-related parameters, bone mineral density, haematological indices, and cardiovascular variables.

In Manchola-González et al. (2020), oxygen pressure (mL/beat) remained stable in both intervention and control groups. Cox et al. (2017) found no significant effects of the intervention on bone mineral density, suggesting that the applied exercise dose may not be sufficient to counteract treatment-associated skeletal decline, particularly when initiated during intensive therapy. In contrast, Tanir and Kuguoglu (2013) reported significant improvements in haemoglobin and haematocrit in the intervention group, indicating that exercise may support physiological recovery in remission contexts. Finally, Järvelä et al. (2010) observed no significant between-group differences in systolic or diastolic blood pressure, which may reflect the relatively young age of participants and limited cardiovascular impairment detectable through resting hemodynamic measures.

Strengths and limitations

This review has several strengths. It was conducted following PRISMA 2020 guidelines (Page et al., 2021), used a structured search strategy across three electronic databases, and applied a standardized methodological quality assessment tool (Law et al., 2018). Additionally, the review focused on outcomes commonly evaluated in paediatric exercise oncology, including functional capacity, fitness markers, HRQoL, and selected biological parameters.

However, important limitations should be acknowledged. First, the number of eligible studies was limited, restricting the generalizability of conclusions. Second, there was substantial heterogeneity in intervention content, supervision, dose, clinical phase, and outcome measures, which prevented meta-analysis and requires caution in interpreting pooled conclusions. Third, some studies included participants early after diagnosis or during maintenance therapy, which may not strictly align with "*post-treatment*" definitions and complicates clinical extrapolation. Finally, sample sizes were generally small and follow-up periods were short, limiting the ability to evaluate long-term sustainability and safety.

Clinical and practical applications

Structured PA and exercise may be considered as supportive care interventions in paediatric ALL, with careful tailoring to clinical status and treatment phase. Based on the evidence synthesized in this review, the following practical recommendations can be proposed:

1. Exercise mode: Multicomponent programs combining aerobic training with resistance and flexibility exercises appear most suitable to address the broad functional deficits observed in paediatric ALL (Manchola-González et al., 2020; Tanir & Kuguoglu, 2013; Perondi et al., 2012).
2. Training dose: Interventions lasting 12–16 weeks, performed 2–3 sessions/week, with gradual progression, are feasible and may yield improvements in aerobic capacity and functional mobility.
3. Individualization and supervision: Exercise intensity should be individualized and adapted to fatigue, neuromuscular symptoms, and medical status. Professional supervision or structured guidance improves safety and adherence (White et al., 2005).
4. Key outcomes to monitor: Clinically relevant outcomes include VO_2-related measures or walking tests, TUG/TUDS, lower-limb strength, and fatigue scales.
5. Timing considerations: Exercise initiated during early intensive treatment may have limited impact on outcomes such as bone mineral density and HRQoL, potentially requiring longer or more targeted interventions (Cox et al., 2017).
6. Family-centred approach: Given the psychosocial burden of ALL, interventions may benefit from including family education and strategies to facilitate safe activity participation at home and school.

Figure 4. Clinical and practical applications of structured exercise in paediatric acute lymphoblastic leukaemia.

To facilitate clinical translation of the evidence, Figure 4 summarizes key practical recommendations for implementing structured PA as supportive care in paediatric ALL.

Overall, these recommendations highlight the importance of individualized, multicomponent exercise prescriptions with appropriate supervision and family involvement to optimize functional recovery and long-term health outcomes in this population.

CONCLUSIONS

Structured PA and exercise interventions appear feasible in paediatric ALL and are generally associated with improvements in aerobic capacity, functional mobility, and selected strength outcomes, particularly in remission and survivorship settings. Evidence regarding HRQoL remains inconsistent, and biological outcomes show heterogeneous responses across studies. Future research should prioritize adequately powered randomized trials with standardized exercise prescription, consistent outcome reporting, and long-term follow-up to establish optimal exercise protocols and clarify their role in improving survivorship health trajectories.

AUTHOR CONTRIBUTIONS

Conceptualization: D.F.-L., A.M.C.S.M., and C.D.O.; methodology: D.F.-L. and C.D.O.; software: N.H.-B. and G.S.; validation, A.M.C.S.M., N.H.-B. and G.S.; formal analysis, D.F.-L., A.M.C.S.M. and C.D.O.; investigation, N.H.-B. and G.S.; resources, D.F.-L., N.H.-B. and G.S.; data curation, D.F.-L.; writing—original draft preparation, D.F.-L. And C.D.O.; writing—review and editing, A.M.C.S.M., N.H.-B. and G.S.; visualization, A.M.C.S.M., N.H.-B. and G.S.; supervision, D.F.-L.; project administration, D.F.-L.; funding acquisition, D.F.-L.

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