Effect of exercise interventions on physical function, cardiorespiratory fitness, and health-related quality of life in patients with juvenile idiopathic arthritis: a protocol for a systematic review and meta-analysis of randomized controlled trials

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Abstract

Introduction: Juvenile idiopathic arthritis (JIA) frequently leads to reduced physical ability, diminished aerobic capacity, and impaired quality of life in children. Exercise has emerged as a promising adjunctive therapy, however its overall efficacy remains uncertain.

Methods and analysis: Randomized controlled clinical trials comparing the effects of exercise on physical function, cardiorespiratory fitness, and health-related quality of life in patients with juvenile idiopathic arthritis will be included. A detailed computer-aided search of the literature will be performed from inception to April 2025 in the following databases: MEDLINE, Embase, and the Cochrane Library. Two independent reviewers will screen articles for relevance and methodological validity. The Cochrane Risk of Bias tool will be used to evaluate the risk of bias of selected studies. Data from included studies will be extracted by two independent reviewers through a preset data extraction sheet. We plan to conduct meta-analysis to quantitatively synthesise the effects under study.

Ethics and dissemination: Ethical approval and informed consent will not be required since this is a protocol for a meta-analysis with no confidential personal data be collected. The results of this study will be submitted to a peer-reviewed journal for publication.

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Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood, with a global incidence estimated at 1.6 to 23 per 100,000 children and a prevalence ranging from 3.8 and 400 per 100,000.[1] It is characterized by persistent joint inflammation of unknown etiology with onset before the age of 16 and a duration of more than six weeks, encompassing a heterogeneous group of clinical subtypes.[2] Children with JIA frequently experience substantial physical impairments, including reduced mobility, decreased muscle strength, and diminished cardiorespiratory fitness. Sedentary behavior is also prevalent in this population, often aggravated by pain, fatigue, and limited joint range of motion, prolonged physical inactivity. This inactivity not only exacerbates existing impairments but also increases the risk of comorbidities such as obesity and cardiovascular disease. Together, these factors result in reduced functional capacity and marked impaired health-related quality of life (HRQoL).[3, 4]

Despite significant advancements in pharmacologic therapies, particularly biologic disease-modifying antirheumatic drugs (DMARDs), many patients continue to experience functional impairments, such as muscle weakness, reduced aerobic capacity, and compromised physical mobility.[5, 6] Additionally, chronic inflammation and prolonged corticosteroid use further elevate the risk of musculoskeletal deterioration and cardiovascular morbidity, thereby exacerbating physical inactivity and predisposing affected children to long-term disability.[7, 8]

Exercise interventions have emerged as a promising adjunctive therapy capable of mitigating these systemic and functional impairments.[9] Growing evidence indicates that appropriately structured exercise regimens, including resistance training, aerobic conditioning, aquatic exercises, and balance-focused interventions, may enhance muscle strength, cardiorespiratory endurance, and HRQoL in children with JIA.[10-12] However, existing randomized controlled trials (RCTs) are expected to yielded heterogeneous and sometimes conflicting results, possibly due to methodological variability in the type of exercise, intervention duration, delivery mode, and outcome measures employed. While several trials have reported improvements in physical function and selected cardiorespiratory outcomes following exercise interventions, others have found no significant effects, particularly with respect to quality of life or aerobic capacity.[13, 14] These mixed findings highlight the need for a comprehensive synthesis of the available evidence.

Given the growing body of randomized trials and the persistent clinical need for robust, evidence-based rehabilitation strategies, a systematic synthesis of the literature examining the effects of exercise interventions on physical function, cardiorespiratory fitness, and HRQoL is both timely and critical.

Objective

This study aims to conduct a systematic review and meta-analysis to assess the effects of exercise interventions on physical function, cardiorespiratory fitness, and health-related quality of life (HRQoL) in patients with juvenile idiopathic arthritis.

Methods and analysis

The reported items will be in accordance with the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P).[15] This protocol is registered on the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD420251048687. Any modification to this protocol will be described in the final review.

Eligibility criteria

Eligibility criteria will be designed according to the PICOS (Participant-Intervention-Comparator-Outcomes-Study design) framework.

1) Participant: Studies enrolling children or adolescents under 18 years of age with a clinical diagnosis of JIA will be considered eligible. The age criterion will be based on the age at intervention, and all participants will be required to meet the standard definition of JIA, with disease onset occurring before the age of 16..

2) Intervention: Structured exercise interventions, including but not limited to aerobic, resistance, balance-proprioceptive, core stability, and aquatic training programs.

3) Comparator: Control groups receiving usual care or non-exercise interventions.

4) Outcomes: Reporting at least one primary outcome related to physical function (e.g., child health assessment questionnaire [CHAQ], 6-minute walk test [6MWT]), cardiorespiratory fitness (e.g., peak oxygen consumption [VO_2peak], maximum heart rate [HRmax]), or HRQoL.

5) Study Design: randomized controlled trials.

Exclusion criteria

1) Studies that do not report outcomes relevant to physical function, cardiorespiratory fitness, or HRQoL.

2) Non-randomized trials, observational studies, case series, or case reports.

Database and search strategy

Eligible studies will be identified through a systematic search of MEDLINE, Cochrane Library, and Embase from database inception up to April 2025 with no language and date restrictions. An experienced specialist in medical information will help to design search strategies for each database. The search strategy will be conducted using Medical Subject Headings (MeSH)/Emtree headings, combined with free text words. The following MeSH/Emtree/free text terms will be included: "physical function," "juvenile idiopathic arthritis," "exercise," "cardiorespiratory fitness," and "randomized controlled trial". The search strategies for other databases will be adapted accordingly. The reference lists of included studies and relevant review articles or meta-analyses will be hand-searched to identify all potential eligible studies.

Study selection

Literature search records will be imported into Endnote software (V.X7.7, Thomson Reuters, USA) for management. Study selection will be performed in two stages. After removing the duplicate records, two authors will screen the titles and abstracts independently to remove irrelevant studies according to eligibility criteria. Studies passing through this initial screening stage will then be subject to full-text examination. The two authors will independently confirm the eligibility of these potentially relevant articles after reviewing the full texts. Disagreements between two authors will be resolved through consensus or adjudication by a third author. Exclusion reasons for ineligible studies will be documented and reported. The study selection process will be documented in a PRISMA-compliant flow diagram.[16]

Data extraction

The following information will be extracted by two independent authors using a standardized extraction form, which will include authors, year of publication, participant characteristics (age, male/female ratio, JIA subtype), exercise intervention details (exercise modality, frequency, duration), control intervention and outcome measures (physical function, cardiorespiratory fitness, HRQoL). Discrepancies will be resolved through discussion and consensus, with involvement of a third author if needed. The final dataset will be reviewed for consistency and completeness prior to analysis.

Assessment of risk of bias

The Cochrane Risk of Bias Tool for RCTs will be applied to assess the quality of included studies.[17] The following aspects will be assessed: allocation sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias. Each aspect will be categorized as "low risk of bias", "high risk of bias", or "unclear risk of bias". Assessments will be performed by two authors independently, disagreements will be recorded and resolved through consensus or adjudication by a senior reviewer.

Statistical analysis

Meta-analysis will be conducted using Stata version 16.0 (College Station, Texas, USA). For continuous outcomes measured on the same scale, the weighted mean difference (WMD) with 95% confidence intervals (CIs) will be calculated. Standardized mean differences (SMDs) with 95% CIs will be computed for outcomes measured on different scales. Statistical heterogeneity among studies will be assessed using the I^2 statistic.[18] A random-effects model will be applied if significant heterogeneity is present ($I^2 \geqslant 50\%$), otherwise, a fixed-effect model will be utilized ($I^2 < 50\%$).[19] To complement statistical significance with estimates of clinical relevance, we will calculate effect sizes (Cohen's d) for each continuous outcome. For outcomes reported as SMD, the SMD will be considered equivalent to Cohen's d. For outcomes reported as WMD, we will estimate effect sizes using pooled standard deviations derived from the included studies where available. Thresholds for interpretation will follow Cohen's conventional criteria: small (d = 0.20), medium (d = 0.50), and large (d = 0.80).[20]

Presentation and reporting of results

The findings of the present systematic review and meta-analysis will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. We will illustrate the process of study selection using a flow diagram. A table with the main characteristics of each study will also be provided.

Patient and public involvement

There will be no direct patient or public involvement in this study, as it is a secondary study based on other studies.

Ethics and dissemination

Ethical approval will not be required for this review. The study's findings will be presented at scientific meetings and published in peer-reviewed journals. All study-

related publications and presentations will be authorized and reviewed by the study investigators.

Limitation

First, substantial heterogeneity is expected across the included studies, both in the clinical characteristics of participants and in the design of the exercise interventions. Although we will extract information on JIA subtypes, their uneven distribution and inconsistent reporting may preclude subtype-specific analyses and limit our ability to evaluate differential intervention effects across JIA phenotypes. Exercise intensity, a critical determinant of training response, is likely to be underreported or described using non-standardized metrics, which may hinder formal analysis of its impact. This overall heterogeneity is anticipated to contribute to variability in effect sizes and reduce comparability across studies. Second, many studies are likely to lack blinding of participants and/or outcome assessors, which may introduce bias in outcome measurement and reporting, potentially inflating observed effects. Third, although reduced muscle strength is a hallmark of JIA, few eligible RCTs are expected to assess this outcome using standardized and reliable methods. Consequently, it is unlikely to be included in our meta-analysis, limiting the comprehensiveness of our synthesis.

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