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REVIEW

Physical Activity Interventions in Children with Juvenile Idiopathic Arthritis: A Systematic Review of Randomized Controlled Trials

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Introduction: Children with juvenile arthritis (JA) experience pain, stiffness, fatigue, and decreased motion leading to difficulties with daily activities and low physical activity (PA). PA is critical to improve health and function and mitigate JA-associated symptoms. This study evaluated the evidence for PA interventions in children with JA.

Materials and Methods: A systematic review of randomized controlled trials (RCTs) of PA interventions in children with JA was conducted. Ovid (Medline), Cochrane Library, EMBASE, and CINAHL databases were searched for papers published in English between 1/1/1946 and 9/1/2021. Studies which concurrently assessed medical interventions were excluded. Participant and intervention characteristics and outcomes were extracted. Study internal validity and intervention attributes were assessed.

Results: A total of 555 studies were identified, with 13 studies from 10 countries included. Data from 672 children diagnosed with juvenile idiopathic arthritis (JIA) (range of mean ages, 8.7 to 16.1 years) were analyzed. Fifty-two percent of intervention arms incorporated strengthening exercise alone or combined with other exercise, with 61.9% performed 3x/week. About 43.5% of sessions lasted >45 to ≤60 minutes and 65.2% of programs were ≥12 to <28 weeks. PA interventions improved function and symptoms without adverse events. Intervention details were missing especially regarding PA intensity, reasons for dropouts, and adherence. Only two studies incorporated strategies to promote adherence.

Discussion: RCTs of PA interventions in JA only include JIA. Available RCTs used mixed modes of interventions. Reporting of PA interventions lacks sufficient detail to discern the dose-response relationship. Strategies to motivate engagement in PA and to support families to promote PA are lacking, as are studies of long-term outcomes.

Conclusion: There are limited RCTs of PA interventions in JIA. Adherence was better with low intensity programs. PA interventions for JIA yield positive health benefits but better reporting of PA intervention details is needed to generate more high-quality evidence and inform clinical practice.

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Keywords: physical activity, juvenile idiopathic arthritis, exercise

Plain Language Summary

- Physical activity (PA) is an important component of juvenile idiopathic arthritis (JIA) management and may prevent long-term consequences of the disease.
- We reviewed studies which evaluated PA interventions for children with JIA to determine whether PA interventions provide positive health benefits.
- There is limited number of RCTs of PA in children with JIA and the majority of studies included children with polyarticular or oligoarthritis JIA subtypes.

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- Most studies incorporated strengthening exercises alone or in combination with other forms of exercise.
- Studies noted improved physical function and mental health and programs were well tolerated with no adverse events.
- Adherence was generally better with lower intensity exercise compared to high intensity. Identifying strategies to motivate children to adhere is needed.
- Better reporting of PA interventions may inform clinical practice and research.

Introduction

Juvenile idiopathic arthritis (JIA), the most prevalent rheumatic disease in children, has many subtypes including: oligoarthritis, polyarthritis, systemic, psoriatic arthritis, enthesitis-related or spondyloarthritis, and undifferentiated.[1] JIA-associated symptoms include joint pain, stiffness and movement restrictions, fatigue, fever and muscle weakness.[1] These symptoms and some forms of medical therapy used to manage JIA, place children at increased risk of sub-optimal bone mineralization and osteoporosis, undernutrition, muscle weakness, mobility impairments, and limitations in activities of daily living such as play.[1–5] JIA also leads to reduced quality of life and the potential for increased mortality in adulthood.[1] Physical activity (PA) and exercise are important components of a healthy lifestyle for all children including children with JIA.[6–10] Current PA recommendations for children include participation in 60 minutes of moderate to vigorous activity per day, with vigorous activity completed on at least 3 days per week.[11–13]

Studies of PA participation in children with JIA show these children are considerably less active than their peers.[6,14] Bos et al found children with JIA spent substantial time in sedentary behaviors and less time in moderate to vigorous activity compared to health controls, adjusting for age, gender, body mass index and season.[15] Children with JIA also demonstrate reduced aerobic and anaerobic exercise capacity.[6] These factors lead to a higher rate of disability, especially among adolescent girls with polyarticular rheumatoid factor-positive subtype.[16]

Earlier investigative studies of children with JIA suggest weight-bearing PA and muscle strengthening are positively associated with a number of health outcomes.[2,17] Farpour-Lambert et al reported weight-bearing and strengthening exercises can improve bone health.[2] Sandstedt et al found a 12-week exercise program of weight-bearing exercise plus standardized muscle strengthening exercises for children with JIA led to significant improvements in bone mineral density, bringing measurements for children with JIA within the reference range of healthy children.[3] Physical activity and exercise (both aerobic and low intensity resistance exercise) also increase exercise capacity, muscle strength and composition, enhance mood, and improve quality of life.[18] Studies indicate these benefits lead to reduced disability in adulthood.[19] Among children with JIA, the goal is to achieve recommended PA levels, accounting for baseline PA levels, disease status, and JIA-associated symptoms.[20] Treatment guidelines indicate a comprehensive approach to JIA management includes a combination of pharmacologic interventions plus moderate, consistent exercise and/or a more active lifestyle.[10]

Despite the evidence suggesting the positive impact of many forms of PA participation on health outcomes in children with JIA, parents and their children still fear exercise will exacerbate symptoms. This fear coupled with the vagueness of exercise prescriptions provided in clinical encounters leads to hesitancy and uncertainty regarding the best exercise and PA recommendations for children with JIA. This systematic review evaluated randomized controlled trials (RCTs) of PA interventions, including exercise, for children with JIA in terms of the breadth and quality of studies and synthesized these data to provide more detailed PA recommendations for children with JIA and their families.

Materials and Methods

Data and Data Sources

The research team conducted a systematic review of RCTs of PA and exercise in children with Juvenile Arthritis (JA) including JIA, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[21] and registered in the International Prospective Register of Systematic Reviews (PROSPERO)[22] prior to beginning the search. The Ovid (Medline), Cochrane Library, EMBASE and CINAHL databases were searched for articles published in English between 1/1/1946 to 9/1/2021. Two reference librarians (JP and SG) conducted the literature search using our pre-specified criteria and search terms, see Supplementary Materials (Figure S1–4).

Eligibility Criteria: Studies were included if they: (1) evaluated exercise or PA interventions, or evaluated PA interventions which combined exercise with a modality (inferential current, hot packs) or (2) employed an interactive digital intervention (eg via computers, handheld devices, web-based programs, wearable technology or applications (apps)) which aimed to measure and promote PA, as long as a PA was incorporated into the intervention. The constructs exercise and physical activity are related but different. Exercise is defined as planned, structured behavior and is a subset of physical activity. Thus, to be comprehensive, this review included studies of PA including exercise interventions.[23] This study includes only RCTs as non-randomized studies have an inherently greater risk of bias than RCTs and most observational cohorts studies use large databases which present data estimates than may appear to be more precise than they really are. Studies were excluded if they examined PA in adults with JA, were secondary analyses of a primary PA intervention in children with JA and were not published in English.

Study Selection: Two librarians (JP and SG) compiled all citations identified from the searches using Endnote bibliographic software (EndNote X9, Clarivate Analytics, Philadelphia, PA) and removed duplicate records. The team members (MDI and JvH) individually examined the title and abstract of each study applying a screening process used in prior publications[24,25] and eliminated studies that did not meet the inclusion criteria. The team was not masked to the name(s) of the study author(s), institution(s) or publication source. If study eligibility was unclear, they deliberated whether or not the study met inclusion/exclusion criteria and came to a consensus regarding inclusion. Next, the team excluded conference abstracts and individually reviewed the full text articles to determine whether the study met the inclusion criteria. The search results and process of study elimination are summarized in the PRISMA flow diagram portrayed in Figure 1. For a list of excluded full text manuscripts and the reason for exclusions, please see Supplementary Materials (Table S1).

Data Extraction and Risk of Bias

After identifying all studies that met the inclusion criteria, data were extracted using a standardized form. Specific data elements included: author; year of publication; source of funding; country where study was conducted; total number of participants in PA arms and comparison/control arms; participant demographics and clinical characteristics (eg diagnosis, subtype, age, sex); program attributes such as setting, program length in weeks; type of intervention, frequency, duration, intensity, and the amount and type of supervision; whether there was a clear statement of adverse events (AEs) and drop outs (DOs) and the severity of AEs related to the intervention. The aim was to classify AEs as severe (fracture, permanent damage, disability, or death) or non-serious (muscle strain, soreness, or a fall not related to the exercise program).[26]

The team (JvH, MDI) used the Physiotherapy Evidence Database (PEDro) scoring method to independently assess the risk of bias in the included studies.[27] The PEDro scale consists of 11 items to rate the internal validity and sufficiency of statistical information provided in the RCTs to inform clinical decisions. Allocation of points for each item are as follows: one or no points for the presence or absence of random allocation, concealed allocation, baseline comparability, participant blinded to allocation, therapist blinded to allocation, assessor blinded to allocation, measures of key outcomes, intention to treat analysis, comparison of study arm results, and reporting of point estimates of variability. Reporting subject eligibility criteria is acquired but not included in the total score. Points across the items are summarized to create a single score for each study ranging from 0 to 10. PEDro scores traditionally are reported as a range versus a mean or median. If the researchers disagreed on the PEDro score of a study, a normative group process was used to reach a consensus.

Sources of Funding for Included Studies

Following the recommendations of the critical appraisal tool "A MeaSurement Tool to Assess Systematic Reviews" (AMSTAR 2), the researchers examined all included studies to determine the source of funding for the project and recorded the source of funding. If no source of funding was mentioned, this fact was recorded as well.[28] Recording of funding is recommended as bias may be present with commercial funding.

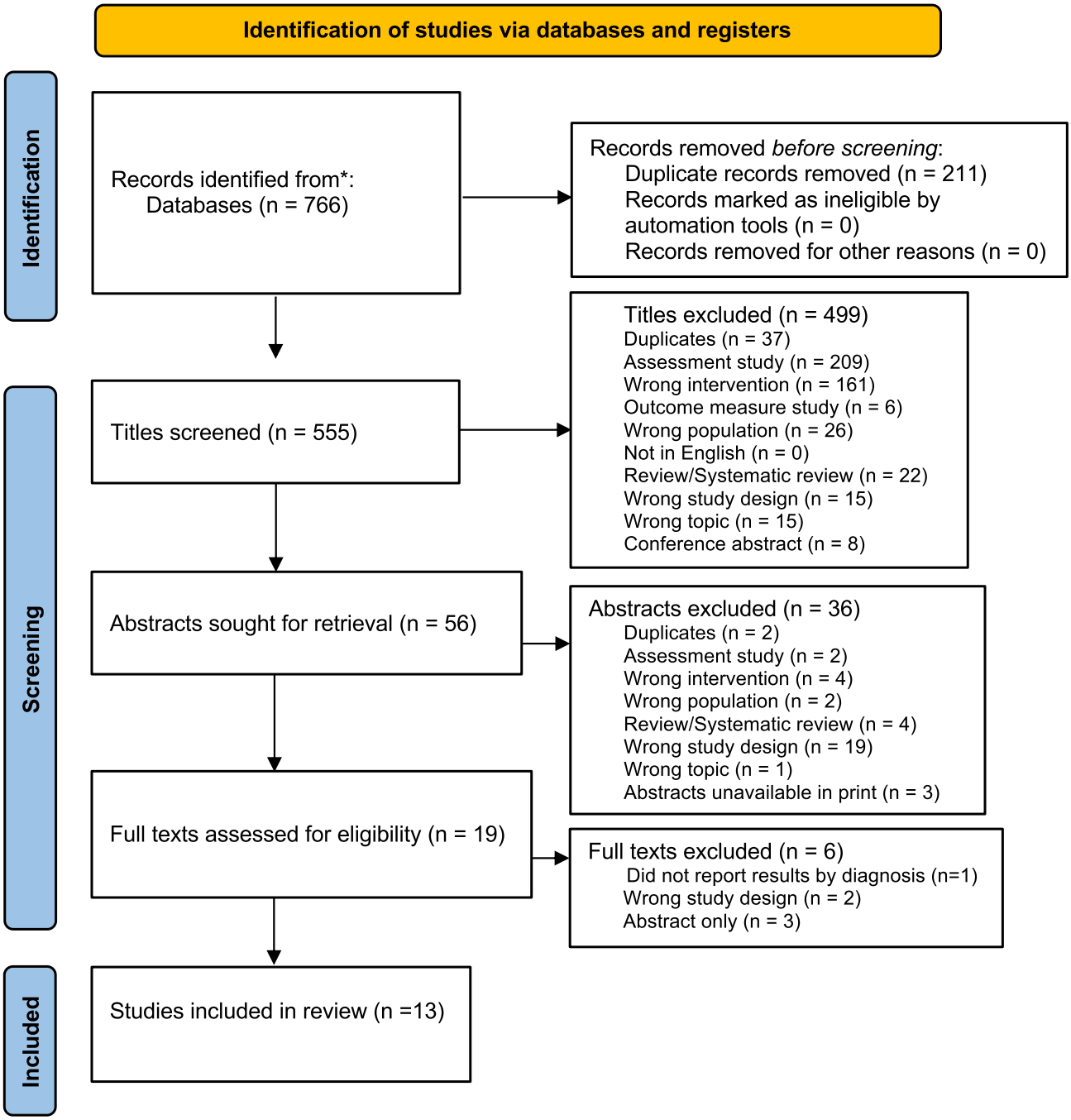

Figure 1 PRISMA flow diagram of randomized studies of PA and exercise in children with Juvenile Arthritis.
Notes: Adapted From: Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. I. 2021;372:n71. doi: 10.1136/bmj.n71. This paper was published under Open Access, Creative Commons. For more information, visit: http://www.prisma-statement.org/.

Quality of PA Intervention Reporting

The team used the Consensus for Exercise Reporting Template (CERT) checklist to assess the quality of the PA interventions. This checklist provides a best practice for reporting and replicating interventions in research to address deficiencies noted in PA studies. The checklist includes 16 items within seven domains such as: what (materials, exercises), who (provider), how (delivery including supervision), where (location), when, how much (dosage), tailoring

of exercise (what, how), and how well the program was implemented (compliance/planned and actual), with a maximal attainable score of 19.[29]

Outcome Measures

The primary outcome measures typically used were PA level, physical function, or exercise capacity assessed from baseline to the end of the intervention. Assessment of PA level, physical function, or exercise capacity could be conducted using physical examination measures (such as Metabolic equivalent of task (METS), maximal aerobic capacity (VO_2 Max), device-acquired data such as pedometer step counts, accelerometry measures of PA levels, time spent in various activities, level of achievement of PA guideline recommendations, and/or self-reported PA levels via a validated questionnaire or diary.[30] Examples of secondary outcomes included health-related quality of life (HRQoL) pain, fatigue, joint stiffness, range-of-motion (ROM), muscle integrity (eg strength, mass etc), and mental health using validated generic or disease-specific outcome measures. Intervention timeframe was documented for each study.

Data Synthesis and Analysis

The team conducted a narrative synthesis of the included studies such as subject characteristics, the country where the study was conducted, PA or exercise intervention attributes (eg frequency of PA (days/week), program intensity, duration of individual sessions (minutes), total program duration (weeks), PA modes, and level of supervision (partial or complete). Modes of PA interventions were categorized as follows: strengthening alone; strengthening plus flexibility, a combination of strengthening, balance, flexibility and/or range of motion (ROM) or Pilates; aerobic exercise alone, conventional physical therapy alone or with an emphasis on a specific mode of PA, Qi Gong, or aquatic exercise. In cases where a range of time, frequency or intensity was reported for any PA intervention, the team calculated the average or rounded up the number to the next category. The team also identified whether the authors included a statement of AEs or DOs. The outcomes were then synthesized (eg function, pain, adherence etc), along with the number and type of AEs and DOs and reported across study arms. Data heterogeneity with respect to modes to intervention, duration and patient demographics and disease type, duration and activity level coupled with lack of information on intervention intensity, prohibited the use of meta-analysis. The results were presented in a descriptive analysis, and all data were analyzed using IBM SPSS Statistics version 26 (SPSS Inc., Chicago, USA).

Results

Study Characteristics

The initial literature search yielded 555 studies. Of these, 13 studies met the inclusion criteria (Figure 1).[17,31–42] These studies were conducted in 10 countries, with 4 studies[31–33,42] (31%) conducted in Turkey. All studies included children with JIA. There were 672 participants randomized. Of these, 579 were analyzed; 494 participants in the PA intervention arms and 85 in non-physical activity groups. The participant demographic and clinical characteristics are similar to a typical population of children with JIA. For example, the mean age across studies ranged from 8.7 to 16.1 years, with a higher prevalence of oligoarthritis and polyarticular arthritis diagnoses and a higher prevalence of female patients (Table 1).

Risk of Bias

The PEDro scores of included studies ranged from 4 to 8, out of a possible 10 points. Only one study (7.7%) did not use concealed allocation.[40] In most studies, subjects and interventionists were not blinded to the intervention due to the nature of the interventions provided. In two studies (15.3%), assessors were also not blinded (84.6%).[34,40] Regarding measurement of key outcomes, five studies[31–33,38,40] (38.4%) had less than the required 85% threshold for measurement of key outcomes and four studies (30.7%) used an intention-to-treat analysis[36,38,39,41] (Table 2). No studies were funded by a commercial source (Table 1).

Table 1 Characteristics of Study Participants, Physical Activity Interventions, Adverse Events, and Dropouts in Randomized Controlled Trials of Physical Activity Interventions in Children with Juvenile Idiopathic Arthritis

Author, Year and Source of Funding	Country	Inclusion Criteria	Sample Size of Allocated (Analyzed) Subjects and Diagnoses*	Mean Age (SD or Min-Max)*	Female, n (%)*	Intervention Description and Setting	Adverse Events statement (Yes/No)	Number of Adverse Events	Drop Out Statement	Number of Drop Outs
Arman et al, 2019[31] Academic funding	Turkey	Clinical diagnosis of JIA based on ILAR criteria Symptoms for at least 6 months, age 6–18 years	31 (25) 13 Oligoarthritis 12 Polyarticular	13.16 (3.35)	21 (84.0)	**Group 1**: Canadian occupational performance measures were used to identify the tasks the individual would practice for the Task Oriented Activity Training (TOAT). TOAT was individually progressed using real materials from daily life, supervised for 60 minutes, 3 times per week over 8 weeks. Intensity unspecified.	Yes	0	Yes	6
			31 (25) 9 Oligoarthritis 16 Polyarticular	12.36 (2.98)	21 (84.0)	**Group 2**: Canadian occupational performance measures were used to identify the tasks the individual would practice. Video game based (Xbox 360 Kinect), TOAT activities supervised for 60 minutes sessions, 3 times per/week over 8 weeks. Intensity unspecified.		0		6
Baydogan et al, 2015[32] No documentation of funding	Turkey	Clinical diagnosis of JIA based on ILAR criteria, age 6–18 years	18 (15) 5 Oligoarthritis 9 Polyarticular 1 Psoriatic Arthritis	9.27 (1.43)	11 (73.3)	**Group 1**: Lower extremity strengthening and stretching exercises, supervised sessions of 45 minutes, 3 times per week over 12 weeks. Intensity unspecified.	No	N/A	Yes	3
			18 (15) 7 Oligoarthritis 6 Polyarticular 2 Psoriatic Arthritis	10.00 (3.66)	10 (66.7)	**Group 2**: Proprioceptive and balance exercises (including same strengthening and stretching as group 1) supervised sessions of 45 minutes duration, 3 times per week over 12 weeks. Intensity unspecified.		N/A		3

Calik et al, 2020[33] No funding was received	Turkey	Clinical diagnosis of JIA based on ILAR criteria, age 6–16 years	10 (6) 4 Oligoarthritis 1 Entheses 1 Systemic	12.5 (4.03)	6 (100)	**Group 1**: Clinical Pilates progressive exercise supervised by an experienced physical therapist trained in Pilates performed for 60 minutes, 3 times per week over 6 weeks. Intensity unspecified.	Yes	0	Yes	4
			10 (9) 7 Oligoarthritis 2 Enthesitis	11.66 (3.12)	4 (44.4)	**Group 2**: Home progressive exercises including a total of 12 exercises (whole body stretching and strengthening exercises). Supervised over phone. Performed for 40 minutes, 3 times per week for 6 weeks. Intensity unspecified.		0		1
Elnaggar and Elshafey, 2016[34] No funding was received	Egypt	Clinical diagnosis of JIA based on ILAR criteria, age range not provided	15 (15) 15 Polyarticular	9.7 (1.5)	Not provided	**Group 1**: Supervised nonprogressive resistive aquatic exercises for a total of 30 minutes (20 of resistive exercise plus warm up and cool down) and 15 minutes of interferential therapy, performed 3 times per week for 12 weeks. Intensity unspecified.	No	N/A	Yes	0
			15 (15) 15 Polyarticular	10.1 (1.2)	Not provided	**Group 2**: Traditional nonprogressive physical therapy (hot packs, quad exercises, range-of-motion (ROM), isometric, hold-relax technique, weight-bearing exercise, flexibility, fitness (bike, treadmill) for 45 minutes per session, 3 times per week for 12 weeks. Intensity unspecified.		N/A		0
Elnaggar et al, 2021[35] No documentation of funding	Saudi Arabia	Clinical diagnosis of JIA based on ILAR criteria, age 10–14 years	18 (17) 17 Polyarticular	12.11 (1.65)	12 (70.6)	**Group 1**: Supervised core stability exercises plus conventional physical therapy 45 minutes per session, 3 times per week for 12 weeks. Intensity unspecified.	No	N/A	Yes	1

(*Continued*)

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Table 1 (Continued).

Author, Year and Source of Funding	Country	Inclusion Criteria	Sample Size of Allocated (Analyzed) Subjects and Diagnoses*	Mean Age (SD or Min-Max)*	Female, n (%)*	Intervention Description and Setting	Adverse Events statement (Yes/No)	Number of Adverse Events	Drop Out Statement	Number of Drop Outs
			18 (16) 16 Polyarticular	11.31 (1.35)	13 (81.3)	**Group 2**: Conventional physical therapy consisting of ROM, strengthening, flexibility, and aerobic exercises performed 30 minutes per session, 3 times per week over 12 weeks. Intensity unspecified.		N/A		2
Epps et al, 2005[36] No documentation of funding	UK	Patients diagnosed more than 3 months with idiopathic arthritis, onset before 16 years of age, stable on medication with at least one active joint, aged 4–19 years	39 (36) 15 Polyarticular 3 Oligoarthritis 8 Extended oligoarticular 8 Enthesitis-related arthritis 5 Systemic	11 (4–19)	24 (66.7)	**Group 1**: Land physical therapy for 16 hourly sessions at one of the trial centers over 2 weeks. Following this block of intensive treatment, supervised land physical therapy once per week or fortnight for 2 months on an outpatient basis. Community physical therapists used their clinical judgement to decide whether a patient's treatment should continue or stop, but were asked to exclude hydrotherapy until a 6-month follow-up assessment was completed. Swimming was not excluded from patient's usual activities at any time during the trial. Intensity unspecified.	No	N/A	Yes	3
			39 (36) 18 Polyarticular 4 Oligoarthritis 7 Extended oligoarticular 4 Enthesitis-related arthritis 1 Psoriatic arthritis with psoriasis 5 Systemic	12 (6–19)	19 (52.8)	**Group 2**: Hydrotherapy plus land physical therapy; 8 hourly sessions of hydrotherapy and 8 hourly supervised sessions of land physical therapy over 2 weeks. Following this block of intensive treatment, hydrotherapy only, once per week or fortnight for 2 months on an outpatient basis. Intensity unspecified.	No	N/A		3

Mendonca et al, 2013[37] No documentation of funding	Brazil	Clinical diagnosis of JIA based on ILAR criteria, age 8–18 years	25 (25) 10 Oligoarthritis 8 Polyarticular 7 Systemic	11.0 (8–18)	16 (64.0)	**Group 1**: Conventional exercise adapted to each patient including a warm-up, a workout, and a cooling-down period. Exercises were supervised and performed with a series of 6 to 10 repetitions in the supine, prone, and seated positions. Stretching exercise positions were maintained for 30 seconds. Exercises were performed for 50 minutes, 2 times per week for 6 months. Intensity unspecified	Yes	0	Yes	0
			25 (25) 14 Oligoarthritis 4 Polyarticular 7 Systemic	11.8 (3.4)	16 (64.0)	**Group 2**: Pilates exercises included floor exercises and exercises with the reformer, stability chair, Cadillac, and ladder barrel. These exercises were adapted to the patient's physical and cognitive specifications. Exercises were introduced in order of increasing difficulty and were performed with 5 repetitions of each exercise for the first 3 classes, 8 repetitions for the next 3 classes, and 10 repetitions in subsequent classes. Sessions lasted 50 minutes, 2 times per week for 6 months.		0		0
Perez Ramirez et al, 2019[38] Foundation funding	Chile	Clinical diagnosis of JIA, age 8–18 years	24 (16) 5 Oligoarthritis 7 Polyarticular 6 Entesitis 2 Systemic 4 Undifferentiated	13.17 (3.02)	15 (62.5)	**Group 1**: Watsu therapy (passive movement sequences, stretches, and massages), 45 minutes per supervised session, 1 time per week for 10 weeks. Intensity unspecified.	Yes	0	Yes	8
			22 (14) 4 Oligoarthritis 5 Polyarticular 2 Enthesitis 2 Systemic 8 Undifferentiated 1 Psoriatic	12.68 (3.00)	20 (90.9)	**Group 2**: Supervised hydrotherapy (stretching, strengthening exercises, and swimming) for 45 minutes, 1 time per week for 10 weeks. Intensity unspecified.		0		8

(*Continued*)

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Table 1 (Continued).

Author, Year and Source of Funding	Country	Inclusion Criteria	Sample Size of Allocated (Analyzed) Subjects and Diagnoses*	Mean Age (SD or Min-Max)*	Female, n (%)*	Intervention Description and Setting	Adverse Events statement (Yes/No)	Number of Adverse Events	Drop Out Statement	Number of Drop Outs
Sandstedt et al, 2013[17] Foundation and Academic Funding	Sweden	Clinical diagnosis of JIA, age 9–21 years	33 (28) 20 Polyarticular 7 Oligoarthritis 1 Psoriatic arthritis	13.3 (8.8–19.9)	25 (76)	**Group 1**: Exercises consisted of rope skipping, muscle strength, core exercises and exercises with free weights for arms (10 repetitions per set for 3 sets), duration not specified, unsupervised, performed 3 times per week for 12 weeks. Intensity unspecified.	No	N/A	Yes	5
			21 (20) 9 Polyarticular 8 Oligoarthritis 3 Psoriatic arthritis	14.9 (8.8–20.6)	17 (81)	**Group 2**: Control group (no intervention)		N/A		1
Singh-Grewal et al, 2007[39] Foundation and Canadian Institutes of Health Research	Canada	Clinical diagnosis of JIA, age 8–16 years	41 (35) 19 Polyarticular 11 Oligoarthritis 1 Systemic 7 Enthesitis 2 Psoriatic arthritis 1 Other	11.7 (2.5)	35 (85.4)	**Group 1**: High intensity aerobic exercise for 50 minutes (10-minute warm-up with flexibility exercises and 10 minutes cool down. 30 minutes of aerobic exercises consisted of dance and martial arts (cardio-karate). Intensity was increased from low to moderate/high as tolerated. Heart rate (HR) measured either as a manual 15-second count at the carotid artery or by HR monitor (Polar 650i, Polar Instruments, Kempele, Finland). Target HR range was 75% of the maximal HR (MHR) determined from VO_2peak testing conducted at enrollment and rating of perceived exertion (RPE). Exercises performed for 50 minutes, 3 per times week, 1 session supervised the rest unsupervised for 12 weeks.	Yes	0	Yes	6

			39 (34) 15 Polyarticular 7 Oligoarthritis 6 Systemic 4 Enthesitis 6 Psoriatic 1 Other	11.5 (2.4)	29 (74.4)	**Group 2**: Qigong exercise, a gentle relaxation program similar to tai chi performed for 50 minutes, 3 times per week (1 session supervised the rest unsupervised (videotape instruction)/ for 12 weeks. Intensity unspecified.		0		5
Sule and Fontaine, 2019[40] National Institutes of health	USA	Clinical diagnosis of JIA, age 10–18 years	17 (9) 9 Polyarticular	14.0 (3.3)	6 (66.7)	**Group 1**: Slow speed resistance exercises individualized by a certified trainer. Exercises included the leg press, chest press and compound row using machines manufactured by RenEx (Beachwood, OH, USA). Resistance was gradually increased when the individual could perform 5 repetitions before reaching momentary muscular fatigue (ie, until they could not perform another repetition in good form). Supervised sessions, duration unspecified, were performed 1–2 times per week for 12 weeks.	Yes	0	Yes	8
			16 (8) 8 Polyarticular	16.1 (2.8)	5 (62.5)	**Group 2**: Attention control program consisted of aerobic exercise (unsupervised), such as walking, for 30 minutes per day, 3 times per week for 12 weeks. Intensity unspecified.		0		8
Takken et al, 2003[41] No documentation of funding	The Netherlands	Clinical diagnosis of JIA based on ILAR criteria, age 5–13 years	27 (27) 11 Oligoarthritis 15 Polyarticular 1 Systemic	8.66 (2.29)	16 (59)	**Group 1**: Aquatic exercises, supervised and performed in small groups (2–4 children/group) for 60 minutes duration approximately 20 sessions over 6 months. Intensity assessed with heart rate monitors.	No	N/A	Yes	1**

(*Continued*)

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Table 1 (Continued).

Author, Year and Source of Funding	Country	Inclusion Criteria	Sample Size of Allocated (Analyzed) Subjects and Diagnoses*	Mean Age (SD or Min-Max)*	Female, n (%)*	Intervention Description and Setting	Adverse Events statement (Yes/No)	Number of Adverse Events	Drop Out Statement	Number of Drop Outs
			27 (27) 12 Oligoarthritis 14 Polyarticular 1 Systemic	8.88 (1.86)	24 (89)	**Group 2**: Control group (no intervention)		N/A		0
Tarakci et al, 2012[42] No documentation of funding	Turkey	Clinical diagnosis of JIA based on ILAR criteria, age 5–17 years	47 (43) 27 Polyarticular 14 Oligoarthritis 1 Systemic 1 Psoriatic	10.02 (3.44)	25 (58)	**Group 1**: Individualized progressive exercises including ROM, strengthening, stretching, and posture exercises, 20–45 minutes 4 x/week (1 time a week, supervised at the hospital by a physical therapist and performed 3 times per week at home supervised by parents) for 12 weeks. Intensity unspecified.	No	N/A	Yes	4
			46 (38) 19 Polyarticular 16 Oligoarthritis 3 Systemic	10.82 (4.00)	19 (50)	**Group 2**: Wait list control group		N/A		8

Notes: *As reported in the study, some studies reported these variables for the allocated participants and some studies reported for analyzed participants. **Dropout included in analysis as the subject met the 75% threshold for adherence.

Abbreviations: ILAR, International League of Associations for Rheumatology; JIA, juvenile idiopathic arthritis.

Table 2 Risk of Bias Assessment of Included Randomized Trials Using the PEDro Scoring Format; Measures of at Least One Key Outcome Were Obtained from More Than 85% of the Subjects Initially Allocated to Groups

Author, Year	Random Allocation	Concealed Allocation	Baseline Comparability	Subjects Blinded	Therapists Blinded	Assessor Blinded	Measures of Key Outcome (>85% Allocated)	Intention to Treat	Results Comparisons	Point Estimate Variability
Arman et al, 2011[31]	1	1	1	0	0	1	0	0	1	1
Baydogan et al, 2015[32]	1	1	1	0	0	1	0	0	1	1
Calik et al, 2020[33]	1	1	1	0	0	1	0	0	1	1
Elnaggar and Elshafey, 2016[34]	1	1	1	0	0	0	1	0	1	1
Elnaggar et al, 2021[35]	1	1	1	0	0	1	1	0	1	1
Epps et al, 2005[36]	1	1	1	0	0	1	1	1	1	1
Mendonca et al, 2013[37]	1	1	1	0	0	1	1	0	1	1
Perez Ramirez et al, 2019[38]	1	1	1	0	0	1	0	1	1	1
Sandstedt et al, 2013[17]	1	1	1	0	0	1	1	0	1	1
Singh-Grewal et al, 2007[39]	1	1	1	0	0	1	1	1	1	1
Sule and Fontaine, 2019[40]	1	0	1	0	0	0	0	0	1	1
Takken et al, 2003[41]	1	1	1	0	0	1	1	1	1	1
Tarakci et al, 2012[42]	1	1	1	0	0	1	1	0	1	1

Notes: The PEDro score contains 11 components; the eligibility score is not calculated in the total score, and therefore not shown in the table.

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Attributes of Therapeutic Exercise and Physical Activity Interventions

Studies included a mix of PA interventions such as strengthening exercises, task-based activities, aquatic or hydrotherapy, Watsu, Pilates, Qigong or a combination of modes of exercise. The most common form of PA intervention was strengthening exercise plus some combination of other exercise modes. Among the 23 intervention arms, five arms (21.7%) included physical therapy.[33–36] The mean number of participants per intervention arm and comparison arms was 21.5 (range 6 to 43) and 28.3 (range 20–38), respectively Three studies included a true control or wait list arm (Table 3).[17,41,42]

The duration of most interventions (65.2%) lasted more than 12 weeks and up to 28 weeks and interventions were often scheduled three times per week (60.9%). Intervention sessions typically lasted more than 45 minutes, up to and including 60 minutes (43.5%). Intervention arms typically incorporated in-person supervision (78.2%) or partial supervision (13.1%) to ensure proper performance of PA intervention. Program intensity was not specified in 15 intervention arms (65.2%). In six intervention arms,[31,33,37,40,42] the authors stated a trained person was individualizing and progressing the PA, but details regarding how the intervention was tailored and progressed were not provided. In two

Table 3 Summary of Physical Activity Intervention Durations, Frequencies, Intensities, Modes, and Levels of Supervision Among the Exercise Arms (n = 23) Included in the 13 Studies

Category	Number (%)		Reference Number
Total program duration			
≤ 6 weeks	2	(8.7)	[33]
> 6 weeks and < 12 weeks	6	(26.1)	[31,36,38]
≥ 12 weeks to < 28 weeks	15	(65.2)	[17,32,34,35,37,39–42]
Frequency per week			
Unspecified	1	(4.3)	[36]
< 3 days/week	6	(26.1)	[37,38,40,41]
3 days/week	14	(60.9)	[31–35,39,40]
> 3 to 7 days/week	2	(8.7)	[42]
Duration of individual exercise sessions			
Unspecified	2	(8.7)	[17,40]
≤ 30 minutes	3	(13.0)	[34,40]
>30 minutes to ≤ 45 minutes	8	(34.8)	[32–35,38,42]
> 45 minutes to ≤ 60 minutes	10	(43.5)	[31,33,36,37,39,41]
Intensity of exercise*			
Unspecified	15	(65.2)	[17,32,34–40,42]
Progressive statement, unspecified	6	(26.1)	[31,33,37,40]
Perceived exertion scale or % heart rate reserve or maximal heart rate	2	(8.7)	[39,41]
Modes of exercise			
Strengthening alone (progressive or not)	1	(4.3)	[40]
Strengthening + flexibility	6	(26.1)	[17,32,33,37]
Strengthening, balance, flexibility, ROM or Pilates	5	(21.7)	[31,32,39,42]
Aerobic alone	1	(4.3)	[40]
Conventional PT alone with additional mode	5	(21.7)	[34–36]
Watsu or Qigong	2	(8.7)	[38,39]
Aquatic	3	(13.0)	[34,38,41]
Supervised sessions			
No	2	(8.7)	[17,40]
Partial	3	(13.1)	[33,39,42]
Yes	18	(78.2)	[31–41]

Note: *Intensity is reported per mode to reflect therapeutic exercise interventions with >1 mode.

intervention arms,[39,41] heart rate monitors or heart rate monitors plus perceived exertion scales were used to assess PA intensity.

The CERT scoring method was used to evaluate the quality of the reporting of PA interventions.[29] The CERT scores ranged from 5 to 17, out of a possible 19 points. Only one study[31] used motivational strategies to promote intervention adherence. Other areas where studies lacked information and did not receive CERT points pertained to the threshold at which PA was initiated, details regarding PA progression, and the measurement and reporting of adherence. Table 4 shows CERT scores and details for all interventions.

Reporting of Adverse Events (AEs) and Dropouts (DOs)

Table 1 summarizes the information on the number of AEs and DOs reported. No studies included an a priori definition for AEs, nor information on the threshold for reporting AEs or methods for collecting AEs (ie patient-report log and online survey at the end of the intervention). Only six studies (46.1%) included a statement of AEs and no AEs were reported in any study.[31,33,37–40]

All 13 studies included a clear statement regarding DOs. Two studies[34,37] reported no DOs during the study. One study[41] reported a single DO but the researchers included the subject in the analysis, as the subject met their threshold for program adherence. In total, there were 94 (16.3%) DOs across the 23 intervention arms and 9 DOs (1.5%) across the 3 control arms.[17,41,42] Fifty-eight DOs were non-exercise related, with 45 dropouts (77.6%) recorded as providing no reason for stopping the study, providing an unspecified personal reason or were lost to follow up. The remainder of the DOs were recorded as either ineligible or having family issues. Among the 36 exercise-related DOs, 34 (94.4%) dropped out due to lack of time or scheduling issues.

Outcomes of Study

Within the 13 RCTs of PA interventions, all studies used a generic or disease-specific functional outcome measure. Eleven studies[17,31–35,37–40,42] (84.6%) included a measure of pain, seven studies[17,32,34–36,39,41,42] (53.8%) incorporated measures of aerobic capacity, fitness or functional performance, 8 studies[17,32,36–41] (61.5%) measured ROM and 7 studies[17,33,36–38,40–42] (53.8%) assessed quality of life. Only one study assessed fatigue[40] and one study measured balance[32] (Table 5).

In all studies, health outcomes improved across a variety of domains. In the study by Arman et al,[31] data indicated that a video-based task-oriented training program resulted in similar health benefits to a traditional task-oriented training program, but the video games appeared to have a greater motivating effect on patient behavior. The use of Pilates[33,37] and Watsu[38] and Qigong[39] exercises appeared to be effective, and in the case of Qigong,[39] this PA format was better tolerated than high intensity PA. Additionally, the use of conventional physical therapy with focused attention on core stability exercises appeared to yield additional benefits than conventional physical therapy.[35]

Intervention Adherence: Four studies (30.7%) made no mention of assessing adherence.[31,33–35] The remaining studies measured adherence as either a percent of sessions attended, via a questionnaire, or defined adherence as the number of completed repetitions of all exercises performed in the program. In five studies,[17,39–42] an a priori threshold for adherence was defined (ranging from 70% to greater than 75% adherence) and two studies[32,37] reported the mean number of sessions attended out of all possible sessions.

Discussion

This systematic review aimed to evaluate the literature regarding PA interventions for children with JIA. The review focused on the breadth of the studies (PA intervention attributes such as the mode(s), frequency, intensity, duration etc) and study quality, in order to ascertain detailed recommendations and perspectives on PA interventions for children with JIA and their families. This issue is important as PA guidelines are most often nonspecific. Current recommendations published by the US Centers for Disease Control recommend school-aged children should participate in ≥ 60 minutes of moderate to vigorous PA daily, noting that activities be enjoyable, variable (eg aerobic, muscle and bone strengthening exercises), and developmentally appropriate.[12] Similar recommendations are published across other countries.[11,13]

Table 4 Key Items of Exercise Interventions of Included Randomized Trials Using the Consensus on Exercise Reporting Template (CERT) Scoring Format

Section/ Topic	Item#	Checklist Item Description	Author, Year												
			Arman et al, 2011[31]	Baydogan et al, 2015[32]	Calik et al, 2020[33]	Elnaggar and Elshafey, 2016[34]	Elnaggar et al, 2021[35]	Epps et al, 2005[36]	Mendonca et al, 2013[37]	Perez Ramirez et al, 2019[38]	Sandstedt et al, 2013[17]	Singh-Grewal et al, 2007[39]	Sule & Fontain, 2019[40]	Takken et al, 2003[41]	Tarakci et al, 2012[42]
WHAT: materials	1	Detailed description of type of exercise equipment (eg weights, exercise equipment/ machines, treadmill, bicycle ergometer)	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **No**	Group 1: Yes Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
WHO: provider	2	Detailed description of qualifications, teaching/ supervising expertise, and/or training undertaken by exercise instructor	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**:
HOW: delivery	3	Describe whether exercises are performed individually or in a group	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**:

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	4	Describe whether exercises are supervised or unsupervised and how they are delivered	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **N/A#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
	5	Detailed description of how adherence to exercise is measured and reported	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
	6	Detailed description of motivation strategies	Group 1: **No** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **No** Group 2: **NA#**
	7a	Detailed description of the decision rule(s) for determining exercise progression	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
	7b	Detailed description of how the exercise program was progressed	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**

(*Continued*)

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Table 4 (Continued).

Section/ Topic	Item[#]	Checklist Item Description	Author, Year												
	8	Detailed description of each exercise to enable replication (eg photos, illustrations, video etc)	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA[#]**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA[#]**	Group 1: **Yes** Group 2: **NA[#]**
	9	Detailed description of any home program component (eg other exercises, stretching)	Group 1: **N/A** Group 2: **N/A**	Group 1: **Yes** Group 2: **Yes**	Group 1: **NA** Group 2: **NA**	Group 1: **NA** Group 2: **NA**	Group 1: **NA** Group 2: **NA**	Group 1: **Yes** Group 2: **Yes**	Group 1: **NA** Group 2: **NA**	Group 1: **NA*** Group 2: **NA***	Group 1: **NA*** Group 2: **NA[#]**	Group 1: **Yes** Group 2: **Yes**	Group 1: **NA** Group 2: **NA**	Group 1: **NA** Group 2: **NA[#]**	Group 1: **Yes** Group 2: **NA[#]**
	10	Described whether there are any non-exercise components (eg education, cognitive behavioral therapy, massage etc)	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA[#]**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **Yes**	Group 1: **No** Group 2: **NA[#]**	Group 1: **Yes** Group 2: **NA[#]**
	11	Described the type and number of adverse events that occurred during exercise	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **Yes, 0** Group 2: **Yes, 0**	Group 1: **No, NA** Group 2: **No, NA**	Group 1: **No, NA** Group 2: **No, NA**

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WHERE: location	12	Described setting in which the exercises are performed	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
WHEN, HOW MUCH: dosage	13	Detailed description of exercise including, but not limited to, # of exercise reps / sets/sessions, session duration, intervention /program duration etc	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
TAILORING: what, how	14a	Described whether the exercises are generic (one size fits all) or tailored whether individually tailored	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
	14b	Detailed description of how exercises are tailored to the individual	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**

(*Continued*)

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Table 4 (Continued).

Section/ Topic	Item#	Checklist Item Description	Author, Year												
	15	Described decision rule for determining the starting level at which people begin exercise program (eg beginner, intermed., advanced etc)	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
HOW WELL: planned, actual	16a	Describe how adherence or fidelity to the exercise intervention is assessed/ measured	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA**	Group 1: **Yes** Group 2: **NA#**
	16b	Describe the extent to which the intervention was delivered as planned	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **No** Group 2: **No**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2:**Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **Yes**	Group 1: **Yes** Group 2: **NA#**	Group 1: **Yes** Group 2: **NA#**
Total CERT Score		Summary of Yes scores, Yes = 1 point; possible total = 19	Group 1: **11** Group 2: **13**	Group 1: **10** Group 2: **10**	Group 1: 13 Group 2: 7	Group 1: 8 Group 2: 7	Group 1: 7 Group 2: 5	Group 1: 14 Group 2: 14	Group 1: 16 Group 2: 16	Group 1: 10 Group 2: 10	Group 1: 7 Group 2: **NA#**	Group 1: 14 Group 2: 12	Group 1: 11 Group 2: 10	Group 1: 10 Group 2: **NA#**	Group 1: 17 Group 2: **NA#**

Notes: * did not offer a home exercise program in addition to intervention. #Study included a control group which received no intervention therefore items are not applicable (NA).

Table 5 Summary of Study Outcome Measures and Results Among Included Randomized Controlled Trials of Physical Activity in Children with Juvenile Idiopathic Arthritis

Author, Year	Outcomes	Summary of Results and Conclusion
Arman et al, 2011[31]	Function (Child Health Assessment Questionnaire (C-HAQ), Derousse Hand Index (DHI), Canadian Occupational Performance Measures (COPM), Pain (NRS), Grip and muscle strength	Children in both the task-oriented activity training and the video game-based task-oriented activity training groups improved in all primary and secondary outcomes. However, between groups, video gamers demonstrated significantly greater improvements in DHI [mean of 19.32 vs 12.56; p=0.04] and COPM satisfaction [7.74 v 5.61; p<0.05]. Palmer pinch strength improved compared to video gamers. Both programs yielded improvements in key outcomes. **Video game–based task-oriented activity training provides a feasible treatment to improve health outcomes for children and adolescents with JIA. This new method has a motivating effect on behavior and may have widespread applicability.**
Baydogan et al, 2015[32]	Pain (VAS), Passive ROM, Knee muscle strength, Balance (Functional Reach test), Postural balance (Flamingo test), function (C-HAQ, 10-m walk test, 10-stair climbing test)	All outcomes were significantly improved for children in the lower extremity strength/ flexibility exercise group and lower extremity strength/flexibility exercise plus balance-proprioceptive exercises group, except for hip and ankle strength in the strengthening group. When comparing the two groups, the balance-proprioceptive group demonstrated greater improvements in all outcomes except pain, C-HAQ, passive ROM, hip extension, and knee flexion strength. **Exercise significantly improves musculoskeletal symptoms in children with JIA. Balance-proprioceptive exercises in addition to strengthening/flexibility exercises appeared to yield greater benefits than strengthening/flexibility exercises alone for improving lower extremity function.**
Calik et al, 2020[33]	JIA disease activity (JADAS), Pain (FACES) Motor skills (Bruininks-Oseretsky Test of Motor Proficiency 2nd Ed. Short Form (BOT-2SF), Juvenile Arthritis Biopsychosocial Scale (JAB-Q), Pediatric quality of life (PedsQL)	The Pilates group demonstrated significant improvements in JADAS, manual dexterity, running speed and agility subtests of BOT-2 SF, total score of BOT-2 SF, daily activity, and PedsQL child form subtests. The home exercise program group demonstrated statistically significant improvements in manual dexterity, running speed and agility, UE coordination subtests of BOT-2, and parent form of JAB-Q. However, greater improvements were found for the Pilates group compared to the home exercise group in UE coordination, subtest of BOT-2 SF, and PedsQL child daily activities. **Pilates is safe and effective and provides superior benefits in many health outcomes compared to a home exercise program.**

(*Continued*)

Table 5 (Continued).

Author, Year	Outcomes	Summary of Results and Conclusion
Elnaggar & Elshafey, 2016[34]	Peak torque of quadriceps and hamstrings (degrees/sec), Pain (VAS)	At 3 months, greater improvements in peak torque were found for the resistive aquatic exercise plus interferential therapy group compared to traditional physical therapy (PT) [aquatic mean=38.4 vs PT (right leg) mean=26.8; p=0.001] and aquatic (left leg) [mean=35.6 vs PT mean=25.9; p=0.001]. Greater improvements in pain were found for the aquatic group compared to traditional PT [aquatic mean=3.5 vs PT mean=6.7; p=0.001]. **Improvements in key outcomes were greater in the resistive aquatic exercise group combined with inferential therapy compared to conventional physical therapy. This combination treatment may be a valuable treatment for patients with JIA.**
Elnaggar et al, 2021[35]	Bone Densitometry, Functional Capacity (6MWT)	The core stability exercise plus traditional PT group demonstrated significant improvements in bone mineralization of lumbar spine and femoral neck compared to conventional PT, except for volumetric bone mineral density of lumbar spine. Functional capacity (6MWT) was significantly improved for the core stability exercise plus traditional PT group compared with the traditional PT group [mean=531.71 meters vs control mean=509.31 meters; (p<0.05)]. **Core stability exercises are an effective adjunctive therapy to conventional physical therapy to enhance bone health status and improve functional capacity in children with polyarticular JIA.**
Epps et al, 2005[36]	Function (C-HAQ), Physicians' global assessment of disease activity, Parents' global assessment of overall well-being, Number of joints with limited ROM, Number of active joints and erythrocyte sedimentation rate. Function (C-HAQ), Quality of Life (CHQ-PF50), Isometric strength, Pain (VAS), Cardiovascular fitness, Health-related QoL (EQ-5D), Quality-adjusted life- years (QALYs)	Two months after the intervention, 47% of patients allocated to the land-based PT plus hydrotherapy group and 61% allocated to land-based PT program improved in disease activity with little change in pain. At 6 months, disease improvements were found in 48% of patients allocated to the land-based PT plus hydrotherapy group and 68% of patients allocated land-based PT. The land-based PT plus hydrotherapy group had mean improvements in hip abductor strength at 6 months. Knee extensor strength, fitness and endurance were greater in land-based PT plus hydrotherapy group than the land-based PT group at both time points. Physical function (C-HAQ) scores improved at 2 months, with further improvements at 6 months in the land-based PT plus hydrotherapy group. The land-based PT improved in physical function but it was not maintained at 6 months. **Both treatments provided health benefits, with greater improvements in some areas with the land-based physical therapy plus hydrotherapy group.**

(*Continued*)

Table 5 (Continued).

Author, Year	Outcomes	Summary of Results and Conclusion
Mendonca et al, 2013[37]	Health-related Quality of life (PedsQL 4.0), Joint pain (VAS), Functional (C-HAQ), Joint Status (Pediatric Escola Paulista de Medicina ROM Scale), Total PedsQL 4.0 score, ROM, Adherence, Adverse events	Both the Pilates group and conventional exercise (strengthening and flexibility) group demonstrated mean improvements in the PedsQoL physical and psychosocial scales. The Pilates group showed greater gains in physical function [mean $_{diff}$=37.4; p<0.000] and greater reductions psychosocial score than convention exercise group at 6 months [mean $_{diff}$=36.5 p<0.001). Improvement in the VAS-joint pain score reached the Minimal Clinically Important Difference (MCID) for 7 Pilates participants and 18 conventional exercise participants [RR=2.57; p=0.002]. Pilates group showed greater improvements in functional ability (C-HAQ) compared to conventional group [mean $_{diff=}$0.83; p<0.0001] with C-HAQ score reaching the MCID for 8 Pilates participants and 23 conventional exercisers [RR=2.88; p<0.0001]. Pilates group showed greater improvements in ROM than conventional exercisers [mean $_{diff=}$10.20; p=0.002]. Adherence was similar across groups and no adverse events were reported. **The Pilates group reported more positive physical and psychosocial improvements [HRQOL] in children and adolescents with JIA compared with the conventional exercise group. Pilates exercises should be considered as part of a rehabilitation program for patients with JIA.**
Perez Ramirez et al, 2019[38]	Health-related Quality of Life (HRQoL), Function, Pain, Disability (C-HAQ), 10-joints Global ROM Scale (GROMS)	The Watsu group significantly improved in the psychosocial health sub-dimension scale between baseline evaluation and follow-up. Hydrotherapy group showed no significant improvements in sub-dimensions or overall QoL scores. Watsu group showed greater improvements in HRQoL, disability C-HAQ, discomfort, health status index, and total C-HAQ scores, and functional health status compared to hydrotherapy. In the GROMS evaluation, there were no statistically significant differences between the Watsu and hydrotherapy groups pre- and post-intervention. **Watsu therapy improves HRQoL in the short-term related to physical functioning, pain, disability, and functional health status compared to hydrotherapy in patients with JIA**.
Sandstedt et al, 2013[17]	ROM, Balance, Muscle strength, Physical fitness, Quality of life (QoL), Pain	Hip and knee muscle strength increased after the 12-week exercise program and was maintained in knee extensors at follow-up. No significant improvements were found in ROM, grip strength, heart rate or perceived exertion after training. There was no increase in pain. There were only small changes in QoL and well-being. **The exercise program was well tolerated and improved hip and knee muscle strength. Compliance was good at 70% and pain was not exacerbated.**

(*Continued*)

Table 5 (Continued).

Author, Year	Outcomes	Summary of Results and Conclusion
Singh-Grewal et al, 2007[39]	VO_2submax, Ventilatory equivalent ratio for oxygen (VE/VO_2), Carbon dioxide (VE/VCO_2), Respiratory exchange ratio (RER), Heart rate (HR), VO_2 peak, C-HAQ, Habitual Activity Estimation Scale (HAES), HRQoL, QoL, Joint Status (Pediatric Escola Paulista de Medicina Range of Motion scale), Pain, Function (C-HAQ), Adherence	No differences in improvements were seen in VO_2 submax and other exercise testing measures between the high intensity aerobic group and the Qi Gong group. Physical function (C-HAQ) improved in both groups but there was no statistically significant difference between groups. Adherence was higher in the control (Qi Gong) than the experimental group. There was no change in disease activity (worsening of active joint count), function or quality of life in either group. **Both exercise programs were well tolerated. PA interventions with or without aerobic training are safe and may lead to improvements in physical function. Lower intensity programs such as Qi Gong may be easier for children to comply with and seem to provide equivalent benefits.**
Sule & Fontaine, 2019[40]	Body Mass Index (BMI), Muscle mass, Joint count, Pain (FACES), ROM, Function (C-HAQ), Fatigue, Quality of Life (QoL)	Adherence was low in the slow speed resistance exercise group with 53% completing any exercise training and in the aerobic exercise group, where adherence was 50%. Post intervention there were no significant differences in VO_2 max, BMI, fatigue severity scores, and pain. In the aerobic exercise group, there were no significant differences in any outcome measure. Comparing the two groups post intervention, there were no significant differences in BMI, percent of fat or muscle mass, arm or knee flexion and extension, VO_2 max, C-HAQ, FACES, or fatigue severity scores. There were no significant adverse events and no worsening of JIA symptoms. **The exercise was well-tolerated with no serious adverse events. While individual subjects reported improvements in fatigue and energy, there was no statistical differences in BMI or QoL. Adherence was low and there is a need to identify strategies to improve exercise adherence.**
Takken et al, 2003[41]	Function (C-HAQ and JAFAS), Health-related quality of life (JAQQ and CHQ-50), Joint status (ROM, swollen and tender joint count), Physical fitness (VO_{2max} and VO_{2peak}, 6MWT)	The aquatic group improved 27% compared to the control (5%) but this difference was not statistically significant. The control group showed a slight decline in health-related QoL (JAQQ score=−15%), whereas the QoL scores for the aquatic group remained stable throughout the intervention; these differences were not statistically significant. Compared to the control group, the aquatic group showed small improvements in physical and psychological CHQ summary scores (8.4 and 7%, respectively), while the control group scores decreased or remained stable The aquatic group showed slight improvements in the 6MWT (3%) compared to control (0%), though these differences were not statistically significant. VO_{2peak} remained stable during the training period for both groups. **Small, non-significant improvements were found for aquatic fitness in children with JIA and the program was well tolerated.**

(*Continued*)

Table 5 (Continued).

Author, Year	Outcomes	Summary of Results and Conclusion
Tarakci et al, 2012[42]	Physical function (6MWT and C-HAQ), Pain (VAS), Quality of life (PedsQoL, PedsQL)	Statistically significant improvements were found in all outcome measures (mean $_{diff}$ 6MWT=30.79; C-HAQ mean $_{diff=-0}$.43; VA mean $_{diff=-9}$.41; mean $_{diff}$ PedsQL=21.99; p<0.001) in the ROM, strengthening, stretching and posture exercise group after 12 weeks. Improvements in physical function and quality of life were greater in the ROM, strengthening, stretching and posture exercise group compared to the wait list control group. **A 12-week land-based home exercise program may improve physical function and quality of life in patients with JIA**.

Organizations that represent healthcare providers who work with children diagnosed with JIA suggest these recommendations be tailored to address health-specific changes associated with JIA disease.[8–10]

Our search found 555 published studies of PA interventions for children with JA. However, the number of RCTs of PA interventions was considerably low, at 13 studies. These studies included only children with JIA and then limited to certain subtypes of JIA. Included studies provided a mix of interventions (eg strengthening, aerobic) which is reflective of current recommendations and clinical practice.[11,12] Using a mix of PA interventions helps to address the various manifestations of JIA-associated symptoms and has the added benefit providing a variety PA interventions which may be more appealing to children.

To provide the best interventions, clinicians and families need detailed information such as how, when, and why to engage in PA and what interventions are most effective. The CERT checklist provides a guideline to help researchers describe in detail the attributes of the interventions they have tested so that the results can be readily transferrable to clinical practice and to enable other researchers to replicate their findings.[29] Using the CERT, we found a number of deficiencies in the reporting of the interventions employed in these studies. Most notable, was the lack of detail regarding the starting point for PA programs (eg amount of resistance within the activity, speed etc). Most studies did not indicate that the program was tailored to the patient's health status and a number of studies did not provide specific details on how to the intervention was progressed. Whereas, Taracki et al, engaged physical therapists with expertise in JIA to design the PA program.[42] These physical therapists established the baseline components of the PA program, progressed the repetitions of exercise per patient tolerance, and provided a detailed list of activities for patients and families. The study incorporated patient diaries and supervision help to patients understand the PA progression.

Since the ability to determine dose-response effects of PA interventions on health outcomes is contingent upon detailed reporting of interventions in PA studies, further attention to these factors and use of the CERT when reporting results of PA interventions is necessary. For children and parents of children with JIA who may be fearful of PA, it is difficult to initiate and maintain engagement in a PA program without the requisite information to properly perform the activities. Fear avoidance is a cognitive construct that can have lifelong implications and is important to address in young children. Children's fear of movement coupled with parental protectiveness can lead to a sedentary lifestyle and disability in adulthood. Fear-avoidance beliefs mediate the association between parental protectiveness and PA limitations and are important to address when designing PA interventions for children with chronic pain.[43]

These 13 RCTs measured different aspects of JIA symptoms and outcomes of PA. For example, typical symptoms of JIA include joint pain, stiffness, loss of range-of-motion, muscle weakness, physical function, fatigue and reduced aerobic capacity. The most common outcomes assessed were pain, aerobic capacity, general function, and range-of-motion. However, fatigue was only measured in one study.[40] There was substantial heterogeneity in the outcome measures used which suggests the need for a standardized core set of outcomes measures for studies of PA interventions in this population.

The interventions in this systematic review were generally of a low to moderate intensity. One program compared higher intensity aerobic PA to a lower intensity Qi Gong program, and found children were more adherent to the lower intensity program.[39] This study included children with a mix of JIA subtypes ages 8 to 16 years. This sample reflects the heterogeneity of subtypes of JIA. It is important to note that these 13 studies did not measure or report the PA behaviors of children prior to their diagnosis of JIA or inclusion in the study. Thus, we do not know whether children who are very physically active prior to diagnosis may tolerate higher levels of PA.

None of the studies in the systematic review reported any AEs from the short-term PA interventions examined. This result is similar to the data from a 2008 Cochrane Review which included three RCTs.[44] However, information on dropouts was lacking in the included studies, so it may be difficult to state that individuals who dropped out did not experience an intervention-related adverse event.

Program adherence was not formally addressed in all studies. Adherence to PA interventions is a complex and multifaceted behavior. Personal factors such as past experience with PA, physical factors such as pain and fatigue and psychosocial factors (eg isolation, motivation) influence PA behaviors and PA programs may be burdensome (eg too much time commitment) and can make increasing PA challenging. Identifying barriers and facilitators to PA adherence is essential for positive health outcomes.[45] Favier et al identified barriers and facilitators to PA in children with JIA and reported that forgetting to attend therapy, pain, and the belief that therapy is not necessary were the main barriers to adherence.[46] These authors recommended assessing barriers to adherence and actions that facilitate adherence as essential to helping children with JIA achieve a better quality of life. Similarly, Risum et al examined barriers and facilitators to PA in Norwegian children with JIA compared to healthy age and sex matched controls. They found children with JIA reported pain and disease activity as barriers to PA and that fun was the most important facilitator for PA engagement for all children, followed by being with friends.[47] Sims-Gould et al in a study of parents and children with JIA reported potential health benefits, fun, and parental support as significant facilitators of PA engagement in these children. Whereas, time pressures and physical symptoms were barriers.[48] These data combined with clinical experience indicate the importance of incorporating strategies to motivate children to engage in PA. Potential strategies include the use of fun and engaging smartphone apps, modifying activities at school to enable these children to participate in activities with peers, and strategies to support parents to promote PA with their children. Select smartphone apps and interactive digital interventions combine health education and gaming can be used to promote behavior change. In certain apps, these data can be shared with health care providers.[49,50] For example, Wokamon © a commercial application, gamifies walking; the more you walk, the more food the creature eats and the more it grows.[51] Such interventions may provide a fun and efficient means of supporting PA behavior in children.

Study quality is an important aspect of research, as lower quality studies are at greater risk of bias. In studies of PA interventions, some mechanisms to reduce bias (blinding the interventionist or subject bias) cannot be addressed in the study design due to the inherent active engagement required of the subject and interventionist. Whereas, other design elements (eg using intention-to-treat analysis, imputing values for missing data, or blinding of the assessor) can be incorporated, regardless of the intervention, to control bias. We found two studies in which the assessor was not blinded,[34,40] five studies[31–33,38,40] that had less than the required 85% threshold for measurement of key outcomes and only four studies[36,38,39,41] that used an intention-to-treat analysis. These data suggest more attention to design elements and reporting of study quality may be warranted in RCTs examining PA interventions for children with JIA.

Limitations and Strengths

There are some limitations to this study. First, there are few published RCTs of PA interventions in children with JIA, this is an area that needs further investigation. This review was restricted to studies published in English, so studies published in other languages are not included. Finally, data heterogeneity prohibited the conduct of a meta-analysis. This study also has a number of strengths. Two research librarians conducted the literature search and the project was submitted to PROSPERO[22] for review prior to initiating the search. The team who reviewed the titles, abstracts and full text articles are experienced in systematic reviews and followed the PRIMSA[21] guidelines for the conduct of systematic reviews. The study includes both PA and exercise interventions to allow for a greater depth of information. Two validated and accepted

measures of study quality were used, the CERT to assess the quality of the PA intervention reporting and PEDro to assess the quality of the study design.[27,29]

Conclusions

There is a lack of RCTs of PA in children with JA other than in children with JIA. Even among studies of PA in JIA the number of RCTs is relatively small. Additionally, among the studies included in this review, most children with JIA were diagnosed with polyarthritis and oligoarthritis, so there is little data on PA interventions for children with other subtypes of JIA. These studies of PA interventions lacked sufficient details regarding the starting threshold for PA, the tailoring of PA to child-specific needs and PA progression. Several studies examined PA interventions in the short-term and did not evaluate the long-term impact of PA. Thus, there is little evidence for long-term benefits of PA among these children. There was insufficient attention to reporting of adverse events and dropouts, which limits the ability to determine the safety and efficacy of PA interventions in children with JIA. Additionally, the value of individualized PA training, nuanced and dosed by a physical therapist with expertise in the field in JIA cannot be overlooked. Including detailed description of PA evaluated in studies is warranted to determine the best design of PA interventions.

Most programs did not incorporate strategies to address motivation and adherence and relied on family support to ensure the program was followed. There needs to be greater attention to the resources and supports for families to facilitate PA adherence in children with JIA. Developing healthy behaviors early in a child's life and addressing fear-avoidance behaviors in children with JIA can improve musculoskeletal and cardiovascular health. Given advances in treatments for children with JIA, disease activity can be better controlled with less symptoms and affecting the ability to engage in PA. Children with JIA should be encouraged to participate in habitual PA and age appropriate play and sports to promote overall health.

Future RCTs of PA in children with JIA should: include children with various subtypes of JIA to provide evidence of best practices and benefits and potential harms, if any of PA for these children. We recommend future studies examine the impact of high and low intensity PA programs and include a core set of outcomes measures, along with detailed descriptions of dropouts and adverse events from PA. We also recommend study interventions vary the elements of the PA intervention to target different outcomes (strength, bone health etc) and incorporate strategies to address fear avoidance behaviors and motivate children to encourage active engagement in PA. Finally, more studies which evaluate the benefits of long-term PA engagement are needed.

Abbreviations

JIA, Juvenile idiopathic arthritis; PA, physical activity; RCT, randomized controlled trials; JA, juvenile arthritis; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International prospective register for systematic reviews; AEs, adverse events; DOs, drop outs; PEDro, Physiotherapy Evidence Database; AMSTRAM 2, A MeaSurement Tool to Assess systematic Reviews; CERT, Consensus on Exercise Reporting Template; METs, metabolic equivalent of task; VO2 Max, maximal aerobic capacity; HRQoL, health-related quality of life; ROM, range-of-motion.

Data Sharing Statement

The data extracted from these 13 studies are available from the corresponding author on reasonable request.

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Author Contributions

M.D. Iversen and J. von Heideken contributed to the conception of the study, study design, study execution, data collection and synthesis, data interpretation, and all drafts and revisions of the manuscript. M. Andre contributed to data synthesis, clinical relevance of the data and its interpretation, the analysis of results, and writing of the manuscript. All

authors reviewed the final draft of the manuscript, agreed on the version to submit to this journal and agreed to take responsibility and be accountable for the contents of the article.

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