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REVIEW ARTICLE

Ottawa Panel Evidence-Based Clinical Practice Guidelines for Structured Physical Activity in the Management of Juvenile Idiopathic Arthritis

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Abstract

Objective: To create guidelines focused on the use of structured physical activity (PA) in the management of juvenile idiopathic arthritis (JIA).

Data Sources: A systematic literature search was conducted using the electronic databases Cochrane Central Register of Controlled Trials, MEDLINE (Ovid), EMBASE (Ovid), and Physiotherapy Evidence Database for all studies related to PA programs for JIA from January 1966 until December 2014, and was updated in May 2015.

Study Selection: Study selection was completed independently by 2 reviewers. Studies were included if they involved individuals aged ≤21 years diagnosed with JIA who were taking part in therapeutic exercise or other PA interventions for which effects of various disease-related outcomes were compared with a control group (eg, no PA program or activity of lower intensity).

Data Extraction: Two reviewers independently extracted information on interventions, comparators, outcomes, time period, and study design. The statistical analysis was reported using the Cochrane Collaboration methods. The quality of the included studies was assessed according to the Physiotherapy Evidence Database Scale.

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Data Synthesis: Five randomized controlled trials (RCTs) fit the selection criteria; of these, 4 were high-quality RCTs. The following recommendations were developed: (1) Pilates for improving quality of life, pain, functional ability, and range of motion (ROM) (grade A); (2) home exercise program for improving quality of life and functional ability (grade A); (3) aquatic aerobic fitness for decreasing the number of active joints (grade A); and (4) and cardio-karate aerobic exercise for improving ROM and number of active joints (grade C+).

Conclusions: The Ottawa Panel recommends the following structured exercises and physical activities for the management of JIA: Pilates, cardio-karate, home and aquatic exercises. Pilates showed improvement in a higher number of outcomes.

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Juvenile idiopathic arthritis (JIA) is a chronic childhood autoimmune disease that has significant implications on a child's physical health and psychosocial integration.[1] JIA is diagnosed if symptoms are experienced for a minimum of 6 consecutive weeks before 16 years of age and differential diagnoses have been excluded.[2] Common symptoms of JIA include pain, joint stiffness, joint swelling, fatigue, and decreased physical function.[3-5] JIA is the most common childhood rheumatic disease, with a worldwide prevalence ranging from 7 to 401 cases per 100,000 youth and an incidence ranging from 0.8 to 22.6 cases per 100,000 youth per year.[6] This tremendous variation in prevalence and incidence may be attributed to discrepancies in diagnostic criteria and quality of health care resources, as well as study design and sample size.[6-8] An American population-based study[9] showed that childhood chronic diseases, including JIA, were more prevalent in children (aged 10−17y) than both diabetes and epilepsy. Furthermore, childhood arthritis was shown to result in a greater financial burden than more prevalent childhood chronic conditions such as asthma.[9,10]

The management of JIA is complex and involves a multidisciplinary treatment approach, which typically includes care from medical, nursing, and rehabilitation professionals.[11] Medication is often prescribed together with an exercise or splinting regimen, or both. Current rehabilitation (occupational therapy and physiotherapy) programs for children with JIA focus on improving muscle strength and flexibility through the use of orthotics and exercise regimens. Although physical activity (PA) as tolerated is generally encouraged by rheumatologists and rehabilitation specialists,[12,13] structured PA programs beyond simple repetitive strengthening and stretching exercise regimens have yet to be incorporated into a comprehensive care plan.

PA is defined as "any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level."[14(pC-1)] According to the conceptual framework developed by Pettee Gabriel et al,[15] structured PA is best defined in this study as leisure-time PA, identified as therapeutic exercises (eg, aerobic, muscle strengthening, flexibility), sports, and mind-body exercises (eg, tai chi, yoga, Pilates).

Existing literature reviews[16,17] and evidence-based clinical practice guidelines (EBCPGs)[18,19] support the benefits of PA for improving certain disease-related symptoms in JIA. However, none of the published JIA EBCPGs have, to date, been exclusively developed to identify recommendations for PA or specifically structured PA.[18-20] These clinical practice guidelines have limitations that should be noted. They have not been developed using quantitative systematic methods; are broad and offer little to no detail on the featured PA interventions; are not exclusively based on high-rated randomized controlled trials (RCTs); and have used more subjective types of grading systems to assess the strength of the clinical recommendations.[18-20] High-quality EBCPGs based specifically on structured PA interventions in JIA are needed to inform health care professionals, and those living with JIA and their families on therapeutic exercises and PA (duration, intensity, frequency) that may be safe and effective in relieving disease-related symptoms.[20]

Therefore, the development of an Ottawa Panel EBCPG highlighting effective interventions based on structured PA will serve to supplement current information on PA interventions in JIA and facilitate informed decision-making among clinicians (eg, pediatricians, rheumatologists, exercise physiologists, physiotherapists, occupational therapists) and patients with JIA and their families, as well as optimize health outcomes in JIA. Structured PA programs may be more easily reproduced compared with unstructured and spontaneous activities, possibly facilitating integration in clinical care. The objectives motivating the development of this Ottawa Panel EBCPG are to (1) identify comparative controlled studies assessing the efficacy of structured PA interventions in JIA; (2) assess the strength of the existing evidence-based research on structured PA in JIA; and (3) highlight the most effective structured PA interventions in JIA. This work will provide knowledge users with current and highly rated clinical recommendations focusing on structured PA in the disease management of JIA.

List of abbreviations:

EBCPG	**evidence-based clinical practice guidelines**
JIA	**juvenile idiopathic arthritis**
OMG	**Ottawa Methods Group**
PA	**physical activity**
PGrip-JIA	**People Getting a Grip on Arthritis for juvenile idiopathic arthritis**
RCT	**randomized controlled trial**
ROM	**range of motion**

Methods

This EBCPG was developed in a similar fashion to those previously created by the Ottawa Panel,[21-32] as well as those created by the Philadelphia Panel.[33] The methodology for the systematic review met the criteria enumerated in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[34] Procedures previously used for calculating the clinical improvement of interventions and for grading studies mirror those adopted in the creation of a previous Ottawa Panel EBCPG.[21-32] This EBCPG was drafted following the Cochrane Collaboration methodology[35] and methods of a previous study[25] by the Ottawa Panel.

Development of Ottawa Panel EBCPG

The Ottawa Panel consists of 2 groups: (1) the Ottawa Methods Group (OMG) and (2) the external Expert Panel. The OMG is composed of 14 experienced methodologists (S.C., L.B., K.T.-A., G.A.W., C.A.S., A.G.P., J.S., R.T., S.A., C.M.D., P.R.,

Table 1 Selection criteria

Inclusion	Exclusion
Population	Population
• Age groups 0 to ≤21 years old	• Cardiac conditions
• Diagnosed with JIA* at least 1 affected joint in the extremities	• Decompensated organ failure
• Stable disease state not requiring treatment modifications	• Metabolic disorder
	• Moderate to severe hip pain while walking
	• Neurologic conditions
	• Pulmonary conditions
Interventions related to PA†	Interventions
• Therapeutic exercises (eg, aerobic, muscle strengthening, flexibility)	• Only pharmacologic interventions
• PAs	• Only psychological interventions
• Sports (eg, aquatic, land based, weight-bearing, individual, team)	• Only surgical interventions
• Mind-body exercises (eg, tai chi, yoga, Pilates)	
Comparisons	Comparisons
• Routine conventional therapies (eg, educational pamphlets)	• Healthy participants in comparison group
• Comparison/control group is lower-intensity PA compared with the intervention group with an active or higher-intensity PA (eg, nonaerobic control vs aerobic intervention)	• Head-to-head comparison of 2 active therapeutic interventions (eg, aerobic vs strengthening)
• Waiting list	• No control group
	• Within-subject comparisons
Outcomes‡	Outcomes
• Costs	• No. of affected joints
• Disease activity	• Pain
• Flexibility	• Physical endurance
• Functional assessment/status	• Physical fitness (eg, $\dot{V}_{O_2}$max)
• Grip strength	• Quality of life
• Inflammation	• Range of motion
• Joint imaging	• Treadmill time
• Mobility	• Walking distance
• Muscle force and power	• Walking speed
• No. of acute-phase reactants (eg, erythrocyte sedimentation rate)	• Assessment of posture
	• Biochemical markers
	• Compliance to pharmacologic treatment
	• Nonvalidated outcomes
	• Psychological measures
	• Serum markers
Study designs	Study designs
Comparative control studies:	• Case series or case report
• RCT§	• Dropout rate >20%
• CCT	• Sample size <5 participants in intervention group
• Cohort study	• Studies without a mean and SD for outcome measures
• Case-control study	

Abbreviations: CCT, clinical controlled trial; $\dot{V}_{O_2}$max, maximum oxygen consumption.

* All JIA subtypes defined by the International League of Associations for Rheumatology[2] are considered.

† Intervention types based on the conceptual framework of Pettee Gabriel.[15]

‡ See key recommendations for specific outcome measures in included studies.

§ Pilot RCTs can be considered if >5 participants in intervention group.

I.C.À.-G., L.L., G.D.A.) who are well versed in the development of EBCPGs. To help draft the EBCPG, the OMG reviewed findings from the literature review, created summary tables, and recommended specific structured PA interventions. The Expert Panel (D.E.F., A.M., I.J.G., D.M., M.-E.M., G.P.K., S.T., K.W.-M., S.B., K.L., C.L.), composed of 11 experts (6 physiotherapists, 1 occupational therapist, 1 kinesiologist, and 1 exercise physiologist, as well as a patient with JIA [K.L.] and the parent of K.L. [C.L.]), then reviewed the recommendations made by the OMG. The parent of the child with JIA was asked to read through the draft EBCPG, while the research assistant explained the content in age-appropriate lay terms to the child with JIA. The Expert Panel assessed the feasibility and clinical usefulness of the structured PA interventions included in the EBCPG drafted by the OMG.

The development of this EBCPG involved the following steps: (1) systematic literature review; (2) selection of articles based on a priori inclusion and exclusion criteria; (3) data extraction and assessment of study quality; (4) data synthesis and grading; (5) expert review and endorsement of the drafted EBCPGs; and (6) systematic evaluation of the EBCPGs (appendix 1). These steps are described in the next sections.

Eligibility criteria

A list of inclusion and exclusion criteria for the systematic literature review was developed by the OMG using the population, intervention, comparator, outcomes, and study design process. The full list of selection criteria is found in table 1. Although reviewed for pertinent information and potential references, review articles,

Table 2 Grading system

Grade	Clinical Importance	Statistical Significance	Study Design (Strength of Evidence)
A	>30%	$P<.05$	RCT (single or meta-analysis)
B	>30%	$P<.05$	CCT or observational (single or meta-analysis)
C+	>30%	Not significant	RCT or CCT or observational (single or meta-analysis)
C	<30%	Unimportant	Any study design
D+	>30% (favors control)	Not significant	RCT or CCT or observational (single or meta-analysis)
D	<30% (favors control)	Unimportant	Any study design
D−	>30% (favors control)	$P<.05$ (favors control)	Well-designed RCT with >100 patients (if <100 patients becomes a grade D)

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Abbreviation: CCT, clinical controlled trial.

commentaries or letters to the editor, study protocols, work group or conference proceedings, and studies aimed at validating measures were not retained for the systematic review.

Studies were included if participants had a diagnosis of JIA and ranged in age from 0 to ≤21 years. All 7 diagnostic subtypes provided by the International League of Associations for Rheumatology were accepted.[2] Joints affected by arthritis had to be localized in at least 1 of the extremities. Studies were excluded if the participants had active disease that required adjustments to medication.

Information sources

A library scientist systematically searched the literature using the following electronic databases: Cochrane Central Register of Controlled Trials, MEDLINE (Ovid) (appendix 2: full search strategy for MEDLINE), EMBASE (Ovid), and Physiotherapy Evidence Database for all studies related to PA programs for JIA from January 1966 until December 2014. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow sheet is presented in appendix 3. The library scientist performed the search using a strategy proposed by the Cochrane Collaboration[36-38] focusing on methodology and study design. The library scientist searched for systematic reviews, meta-analyses, comparative controlled studies, and case-control, cohort, and randomized studies. Reference lists of included studies were also hand searched to find relevant studies. To ensure that all relevant articles meeting our selection criteria (see table 1) were identified, the search was updated in May 2015 as part of a larger systematic literature search focused on identifying pharmacologic and nonpharmacologic interventions in JIA. No additional articles relevant to structured PA interventions in JIA were found to include in this EBCPG. Time and translation costs were limited; therefore, only English and French studies were selected.

Study selection

Two reviewers (L.B., A.G.P.) independently screened titles, abstracts, and keywords for pertinent articles according to the selection criteria (see table 1). After initial screening, the retained full articles were assessed to ensure that they met inclusion criteria, and a list of relevant articles was compiled. Reviewers independently selected articles for the systematic review and reported reasons for exclusion. If consensus between reviewers could not be reached, a third reviewer (C.A.S.) was brought in to resolve potential disagreements.

Data extraction

Two trained research staff members independently abstracted data from the final list of retained articles using an extraction table. Specifically, information on participant characteristics, interventions, comparative results, allocation and concealment, duration of the study, and study design was recorded.

Methodologic quality of included studies

The Physiotherapy Evidence Database Scale is a reliable and valid tool and is commonly used to assess the methodologic quality of RCTs and clinical controlled trials investigating rehabilitation interventions.[39-45] The quality of the studies are scored out of a possible 10 points based on the following items: random allocation, concealed allocation, baseline comparability, blinding of subjects, blinding of therapists, blinding of assessors, adequate follow-up, intention-to-treat analysis, between-group comparisons, point estimates, and variability. A cutoff of 6 (ie, high-quality study has a score of ≥6) was used to assess included PA studies.[46]

Strength of recommendations

Recommendations were graded according to the strength of the published evidence (eg, level I for RCTs, level II for clinical controlled trials), clinical importance (minimal clinically important difference ≥30%), and statistical significance ($P<.05$). The Ottawa Panel assessed the strength of the evidence according to a hierarchical alphabetic system (ie, A, B, C+, C, D+, D, D−).[25] Table 2 describes the meaning of each grade. This grading system follows the Appraisal of Guidelines Research and Evaluation criteria (www.agreetrust.org).

Endorsement of recommendations

The members of the Expert Panel were asked to complete an electronic Delphi questionnaire sent via e-mail.[47] They provided feedback on the content of the draft EBCPG, specifically the level of detail provided in the text (part 1) and whether or not they endorsed the recommendations made by the Ottawa Panel (part 2).

The first part of the Delphi questionnaire (appendix 4) included 6 questions scored using a 5-point Likert scale, where 1 represented either "not clear" or "strongly disagree" and 5 was either "very clear" or "strongly agree." In the second part of this questionnaire, the panelists were asked, for each of the 5 interventions,

Table 3 AGREE II appraisal of Ottawa Panel EBCPG for JIA

Domain 1: Scope and purpose	
Overall objective	The objectives of this EBCPG are to identify (1) comparative controlled studies on efficacy of PA interventions for JIA; (2) the strength of evidence from these studies; and (3) the most effective PA interventions from comparative controlled studies in order to formulate strong recommendations for the appropriate use of PA to manage JIA.
Domain 2: Stakeholder involvement	
Stakeholder involvement	The Expert Panel consisted of physiotherapists, occupational therapists, an exercise physiologist, and a parent and patient with JIA.
Patient preference	Patient preference was obtained through application of recommendations and feedback on the experience, viewing instructional videos that were available, and e-mail correspondence. Consensus was attained for the Expert Panel using the Delphi method and an electronic Delphi questionnaire.
Target users	Various health care professionals and users 0—21 years old with diagnosed JIA.
Domain 3: Rigor of development	
Evidence search strategy	Systematic search: inception to 2014; databases: Cochrane Library, EMBASE, PEDro. Full search strategy in appendix 3 (PRISMA flow diagram).
Quality assessment and summary	To avoid bias, an extraction form was used to record information about the study design, study population, interventions, allocation concealment, and outcomes. The PEDro score was used to assess the internal validity of RCTs and CCTs and whether the results were interpretable.
Strengths and limitations of the body of evidence	The study design, the PEDro score, and the outcomes are written in the key recommendations and in appendix 7. The harms and side effects for each of the interventions are mentioned in the discussion.
Recommendation development process	First the recommendations were graded based on quantitative data from the evidence. The OMG then sent a draft of the EBCPG to the external Expert Panel to be reviewed for feasibility and to come to a consensus to endorse the recommendations.
Methods for consensus on recommendations	Propositions of the recommendations based on the evidence were made by the OMG; a Delphi method was followed using electronic questionnaires to consult the Expert Panel.
Guideline update	This EBCPG is intended to be updated every 5 years based on new evidence on the management of JIA with PA. The draft recommendations based on the evidence review will again be presented to the Expert Panel for approval.
Domain 4: Clarity of presentation	
Recommendations	The key recommendations are found in the main text, and a summary of the recommendations can be found in the executive summary.
Domain 5: Applicability	
Implementation tool	People Getting a Grip on Arthritis (PGrip) for JIA
Domain 6: Editorial independence	
The funding body	This article was funded by the University of Ottawa Research Chair and the Knowledge Translation (KT) Canada Student Research Project Stipend.
Competing interest	None to declare.

Abbreviations: AGREE, Appraisal of Guidelines Research and Evaluation; CCT, clinical controlled trial; PEDro, Physiotherapy Evidence Database; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

to answer yes-or-no questions and comment on the clarity of the recommendations, their level of agreement with the recommendations, and how well they understood the recommendations. Descriptive statistics (ie, central tendency [mode for nominal data; mode and median for ordinal data], frequency of responses per respondent, and within-group consensus level) were calculated using Microsoft Excel.[a] A second Delphi round involved circulating the same questionnaire to the respondents, along with the corrected EBCPG based on respondents' comments, the executive summary, and the coded results of each expert's responses. Once consensus was reached (ie, all respondents report a score of 4 or 5 out of 5 in part 1 and 80% of respondents reporting a "yes" for the questions in part 2), no further Delphi rounds were required and the EBCPG is approved.[48,49]

Guidelines for reporting in the EBCPG

The OMG used the Ottawa Panel grading system for recommendations, reported statistics on the weighted mean difference, and followed the Appraisal of Guidelines for Research and Evaluation II criteria for the development of high-quality EBCPGs (table 3).[50,51] Appendix 1 illustrates the Ottawa Panel guideline development process.

Statistical analysis

The Review Manager software[b] (version 5.3) was used to analyze the study data. Mean differences between intervention and control groups were used to analyze continuous data.[52] Calculation of the mean differences required the mean, SD, and sample size of each group. If articles did not provide this information, authors were contacted to obtain the data directly at least 3 times by phone and at least 3 times via e-mail. If there was no response the study was excluded. If an outcome presented dichotomous data, relative risks were used for the analysis. If studies had the same population, intervention, control, outcome, and study design, the chi-square statistic was used to test for heterogeneity (ie, differences) between the studies and determine whether a meta-analysis could be completed.[35]

For this EBCPG, the Ottawa Panel has defined a clinically important improvement brought about by an intervention to be ≥30% based on the American College of Rheumatology Pediatric 30, a valid measure for determining JIA disease activity.[53,54] A clinical improvement is quantitatively based on the calculations of the absolute benefit and relative difference in the change from baseline. The calculations for absolute benefit involved subtracting the improvement in the control group from the improvement in the treatment group. To calculate the relative difference, the absolute benefit was divided by the baseline mean (of each group).[33] In the event of dichotomous data, the relative percentage of improvement from baseline was determined by calculating the difference between the percentage of improvement of the intervention and control groups.[33]

Results

Literature search

The literature search yielded 162 references (see Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow sheet in appendix 3). After duplicates were removed, 2 reviewers (L.B., A.G.P.) screened a total of 128 titles and abstracts and assessed 46 of these for eligibility. There was strong agreement between reviewers (>90%). Based on the selection criteria (see table 1), 5 full-text articles were included[55-59] and 41 potential studies were excluded for the subsequent reasons: PA not studied in 7 trials,[60-66] healthy controls in 5 trials,[67-71] no control group in 3 trials,[72-74] not an intervention study in 16 studies,[75-90] 4 review articles,[16,91-93] insufficient statistical data in 1 trial,[94] head-to-head comparison of similar interventions in 3 trials,[95-97] and no control group results in 2 trials.[98,99] Data could not be pooled for meta-analysis because the studies were considered heterogeneous (ie, none shared the same population, intervention, comparator, outcomes, and study design). A more recent search (May 2015) revealed no new studies pertaining to the management of disease using PA in children and adolescents living with JIA.

Study characteristics

The studies selected for these guidelines featured a variety of structured PA programs, and most had an intervention group supervised by clinicians. All 5 studies[55-59] were RCTs. Participants in selected articles had a mean age between 8 and 15 years. One RCT[59] compared a Pilates-based exercise group to a conventional land-based exercise program, which included a combination of stretching and strengthening exercises. Both programs included 50-minute sessions completed twice weekly for 24 weeks. Another RCT[55] investigated the effects of an aquatic exercise program performed once a week for an hour during a 20-week period and compared outcomes with those of a control group receiving usual care and medical treatment. Two other RCTs[56,57] investigated the effects of an aerobic fitness program and compared outcomes with those of a control group. Of these 2 aerobic intervention studies, 1 study[56] assessed the effects of a combined aerobic and resistance training program, which included skipping rope and strengthening exercises, that was performed 3 times a week for a 12-week period and compared outcomes with those of a control group (not described). The other aerobic-based RCT[57] assessed the effects of an aerobic fitness program incorporating dance and martial arts (ie, cardio-karate) that was performed for 45- to 50-minute sessions and compared outcomes with those of a control group following an 18-posture, nonaerobic relaxation program (ie, qigong). Both the experimental and the control (ie, qigong) activity programs were completed 3 times per week over 12 weeks. Finally, 1 RCT[58] evaluated an individualized home exercise program done 3 times weekly along with 1 weekly supervised group exercise program (ie, land-based exercises), with sessions lasting between 20 and 45 minutes, and compared outcomes with those of a wait-listed control group over a study period of 12 weeks. Included studies provided information on the dropout rates, all of which were <20%. Appendix 5 presents extensive details and a summary of included studies.

Excluded outcome measures

The Slaughter equation is not validated for use in children,[100] and results regarding this outcome were excluded posteriori.

Methodologic quality

Four[55,57-59] of the 5 included studies were of high methodologic quality with Physiotherapy Evidence Database scores ranging from 6 to 8. The study by Sandstedt et al[56] (2013) received a score of 5 and was classified as having low methodologic quality. A lower score was assigned because of the lack of random allocation, double-blinding, adequate follow-up, intention-to-treat analysis, and between-group comparisons.

Effectiveness of PA in management of JIA

In the following section we will briefly describe findings from the selected RCTs.[55-59] For more information on the studies, please refer to appendices 6 and 7, as well as figures 1 to 6. A number of clinical improvements were highlighted as a result of the featured treatments. One study[59] reported decreased pain, 2 studies[58,59] demonstrated improved functional status and health-related quality of life, 2 of the studies[55,57] highlighted a decreased number of swollen joints, and 3 studies[56,57,59] reported an increased range of motion (ROM). Two studies[55,58] presented findings highlighting

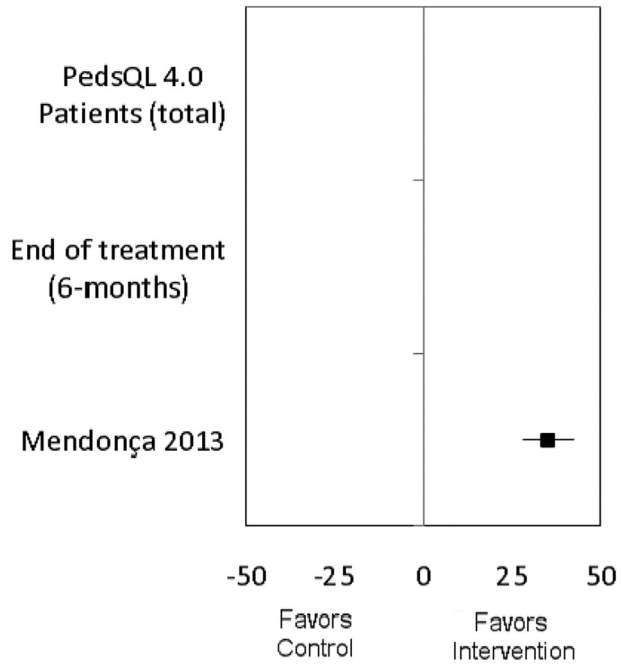

Fig 1 Pilates group versus control group: Health-related quality of life (Pediatric Quality of Life Inventory 4.0 Patients [total]). Abbreviation: PedsQL, Pediatric Quality of Life Inventory.

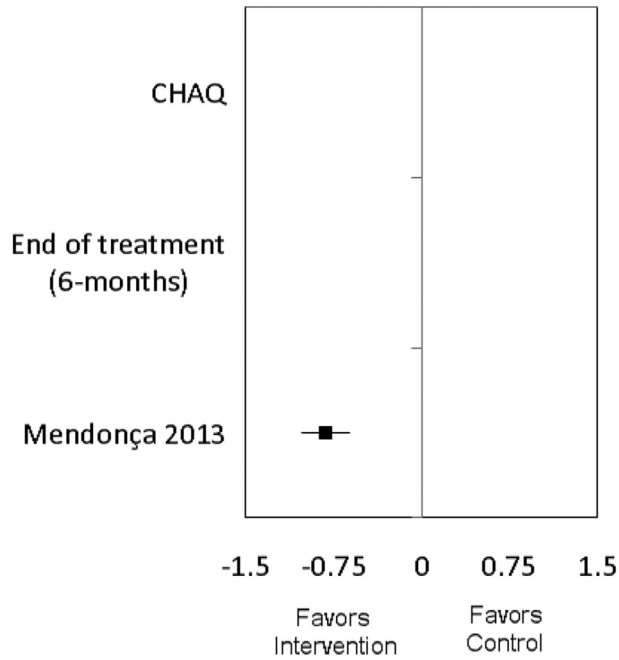

Fig 3 Pilates group versus control group: Functional ability (Childhood Health Assessment Questionnaire). Abbreviation: CHAQ, Childhood Health Assessment Questionnaire.

the effects of PA compared with control groups (ie, no intervention), whereas the other 2[57,59] compared PA interventions to other types of exercise.

The study by Tarakci et al[58] (2012) evaluating the effects of an individualized home exercise program was rated as a level 1 study (1 RCT, N=81, high quality). The authors reported clinically important and statistically significant improvements (grade A) in functional ability (Child Health Assessment Questionnaire) and quality of life (self-report and parent report of Pediatric Quality of Life Inventory) at the end of the 3-month treatment period. However, no clinical benefit was noted for functional status, measured by the 6-minute walk test, or for pain, according to the 100-cm visual analog scale, 3 months after intervention.

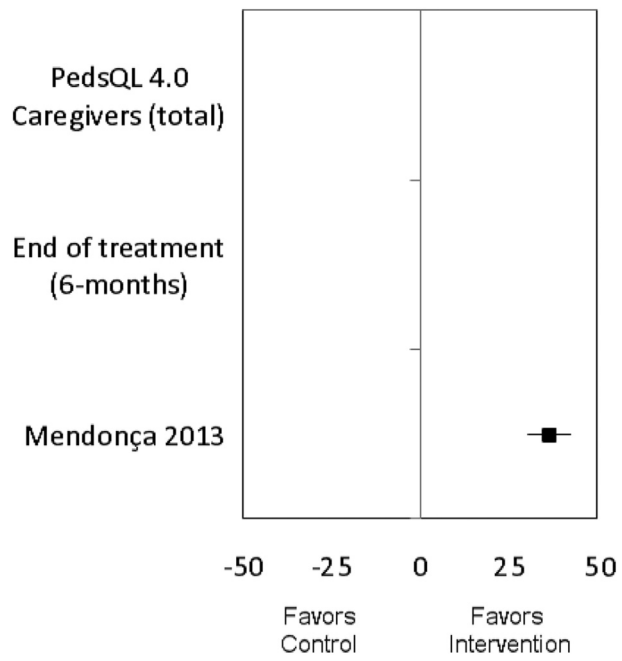

Fig 2 Pilates group versus control group: Health-related quality of life (Pediatric Quality of Life Inventory 4.0 Caregivers [total]). Abbreviation: PedsQL, Pediatric Quality of Life Inventory.

The study conducted by Takken et al[55] (2003) featuring an aquatic fitness training program was rated as a level 1 study (1 RCT, N=44, high quality). Findings demonstrated clinically important and statistically significant improvements for joint status (reduced number of swollen and tender joints) at the end of the 6-month treatment (grade A) (see fig 5) and 3 months after the start of the treatment (grade C). However no clinical improvement in functional ability (Child Health Assessment Questionnaire), health-related quality of life (Juvenile Arthritis Quality of Life Questionnaire), physical health-related quality of life (Child Health Questionnaire—Physical), psychosocial health-related quality of life (Child Health Questionnaire—Psychosocial), ROM (Pediatric Escola Paulista de Medicina Range of Motion Scale), and JIA disability (Juvenile Arthritis Functional Assessment Scale) was noted after intervention involving the aquatic fitness training program.

The study evaluating the effectiveness of an exercise program by Sandstedt[56] (2013) was rated as a level 1 study (1 RCT, N=48, low quality). Clinically important improvements (grade C+) were reported for muscle torque (Nm) of right hip abduction measured using a dynamometer. However no other improvement in muscle torque (ie, right- and left-side elbow extension, elbow flexion, hip flexion, hip extension, knee extension, dorsiflexion, and shoulder abduction, as well as left hip abduction) was reported after the exercise program.

The study conducted by Mendonça et al[59] (2013) assessing the effects of a Pilates program was rated as a level 1 study (1 RCT,

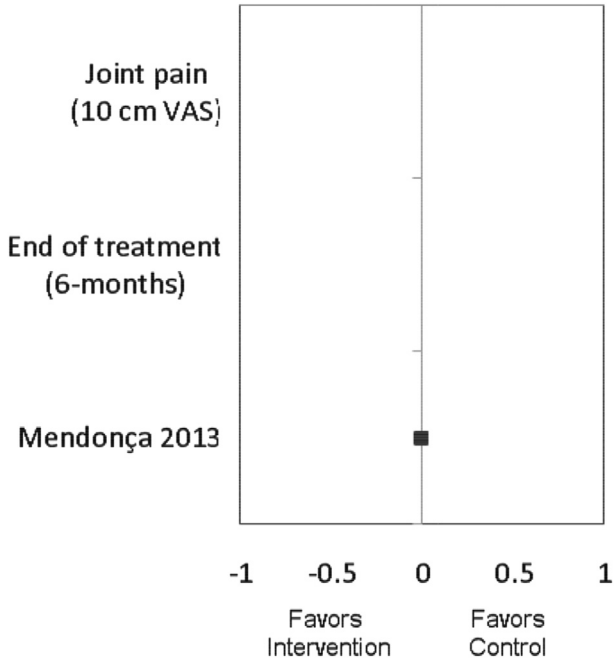

Fig 4 Pilates group versus control group: Pain intensity (joint pain [10-cm visual analog scale]). Abbreviation: VAS, visual analog scale.

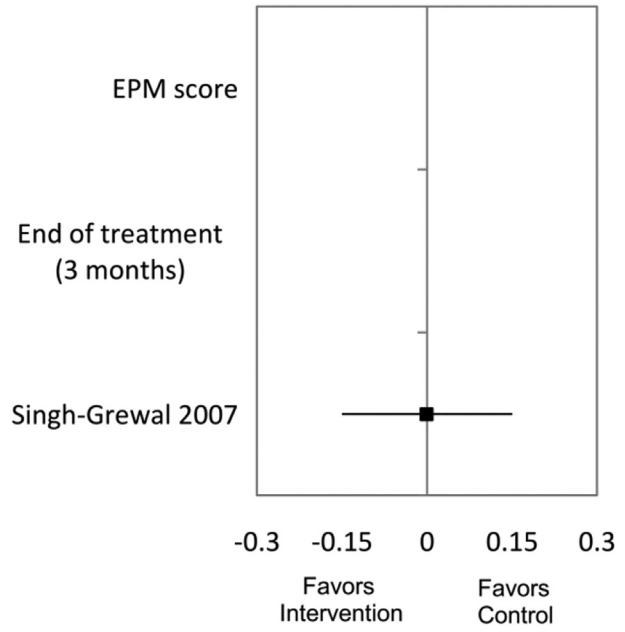

Fig 6 Cardio-karate aerobics group versus control group: ROM (Escola Paulista de Medicina score). Abbreviation: EPM, Escola Paulista de Medicina (ROM).

N = 50, high quality). The findings highlighted clinically important and statistically significant improvements (grade A) in health-related quality of life (self-report and parent report of Pediatric Quality of Life Inventory 4.0 for the physical, psychosocial, and total scores) (see figs 1 and 2), pain intensity (10-cm visual analog scale) (see fig 4), functional ability (Child Health Assessment Questionnaire) (see fig 3), and joint ROM (Pediatric Escola Paulista de Medicina Range of Motion Scale) at the end of 6 months of treatment. However, the authors did not report any improvement in physical health–related quality of life as perceived by caregivers (Pediatric Quality of Life Inventory 4.0 caregivers: physical).

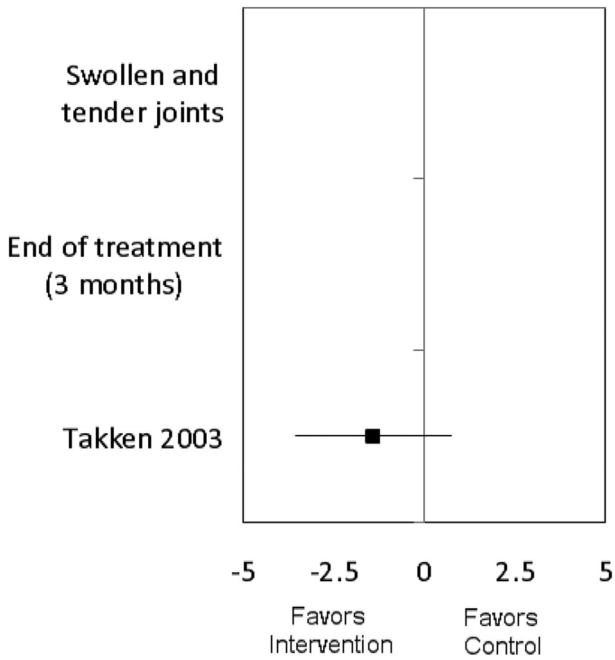

Fig 5 Aquatic aerobic fitness training versus control group: Swollen and tender joints.

The study conducted by Singh-Grewal et al[57] (2007) evaluating the effects of an aerobic training program (ie, cardio-karate) was rated as a level 1 study (1 RCT, N = 69, high quality [8/10]). Clinically important improvements (grade C+) were noted for reduced active joint count (mean ± SD (range)) and ROM (Escola Paulista de Medicina Range of Motion Scale) at the end of 3 months of treatment (see fig 6); however, differences were not statistically significant. The aerobic training program did not result in improvements in submaximal oxygen uptake, physical function (Child Health Assessment Questionnaire), or health-related quality of life measured by the visual analog scale (10cm).

Delphi results

Nine of the 11 experts were sent a Delphi questionnaire, since the parent and the child with JIA would comment on patient preference and the feasibility of the recommendations once they were finalized. The response rate for completing the first round of the Delphi questionnaire was 88.9% (8/9). On average, experts found the literature search to be thorough, and the objectives and selection criteria to be clear. The level of disagreement between experts was highest for the clarity and the practical application of the guidelines. Expert agreement for the level of clarity of specific interventions (ie, Pilates exercise vs control, land-based home exercise group vs control, exercise training vs control) was low at 63%.

All experts who completed the first round of Delphi questions moved on to complete the second corresponding round for a response rate of 100% (8/8). In this second round, there was consensus on questions pertaining to the clarity of the content in general and its practical application (agreement ranging from 88% [7/8] to 100% [8/8]).

Based on the other experts' (ie, health professionals and researchers) final recommendations, the child with JIA and the parent concluded (with 100% agreement) that all recommendations were usable and feasible.

Discussion

This Ottawa Panel EBCPG developed recommendations based on 4 high-quality RCTs (Physiotherapy Evidence Database score, ≥6) that evaluated the effects of structured PA interventions in JIA. There were a total of 16 positive recommendations (12 for grade A, 3 for grade C+), 30 neutral recommendations (26 for grade C, 4 for grade D), and 1 negative recommendation (1 grade D+) represented in this EBCPG. Most structured PA programs were both clinically important and statistically significant (grade A). Overall findings suggest that certain structured physical activities improve at least 1 health outcome in JIA. Specifically, Pilates improves quality of life, functional ability, and ROM and decreases pain (grade A); a home exercise program improves quality of life and functional ability (grade A); an aquatic aerobic fitness program decreases the number of active joints (grade A); and cardio-karate (an aerobic exercise) improves ROM and decreases the number of active joints (grade C+).[55,57-59]

Unlike existing clinical practice guidelines in JIA,[18,19] ours is the first to focus exclusively on structured PA interventions and their effects in managing JIA. In addition, the present EBCPG has used a rigorous and quantitative grading system and assessed the methodologic quality of studies to ensure inclusion of high-quality studies. The use of such methods may have helped to limit the risk of bias associated with subjective grading. Some of the existing EBCPGs support the use of structured PA in mitigating the effects of JIA; however, the recommendations are based in part on findings reported in abstracts or supplementary publications,[19] and in 1 case a single RCT,[18] which may limit the validity of the actual recommendations. To best understand the effects of the studied structured PA interventions, we chose to retain only studies highlighting differences between independent control groups. In addition to the 2 RCTs,[55,57] identified by previous EBCPGs,[18,19] the recent systematic literature review (January 1966 to May 2015) conducted by the Ottawa Panel found 3 additional RCTs,[56,58,59] 2 of which were of high quality, and offered several positive recommendations.[58,59]

Of the studied interventions, Pilates was the most clinically effective in reducing disease-related pain, as well as improving function and quality of life among those living with JIA.[59] This program was also effective in increasing ROM.[59] According to our findings, cardio-karate was the exercise best suited to help increase ROM.[57] Participation in Pilates and cardio-karate done either at home or at a gym or community center may require the purchase of specialized equipment or incur registration fees, or both. Families of lower socioeconomic status may find it more challenging to afford these expenses, making this type of activity less accessible to them. Lower household income has shown to be associated with lower participation in PA in JIA.[101] Despite the social benefits of engaging in group and team PA, children and adolescents living with active JIA may prefer to take part in home-based PA to avoid potentially missing scheduled exercise classes or sport practices. Alternatively, exercises adjusted to individual physical tolerance, which include functional activities, stretching, strengthening and posture exercises, can be performed at home to improve functional ability and quality of life.[58] Aquatic aerobic exercises are recommended for swollen or tender joint management[55] and have been identified as a preferred PA among children and adolescents living with physical disabilities.[102] However, participation in water-based activities may, for some families, be limited because of the lack of accessibility/poor proximity to proper facilities (ie, community pools) or the inability to afford entry or registration fees, or both. In addition, certain children not accustomed to water may be fearful.

Although there is no evidence the included structured PA interventions exacerbate JIA symptoms,[16,55-59] clinicians must consider disease status when making recommendations. In fact, recent recommendations underline how those living with JIA can participate in PA if the disease symptoms and associated clinical presentations (eg, cardiac insufficiency, cervical instability) are well managed, and that involvement in impact and competitive sports can be performed within pain limits despite active arthritis or impairment.[13] Furthermore, after a disease flare, those with arthritis are encouraged to gradually return to full activity[13] in an effort to limit deconditioning secondary to reduced PA.

The creation of EBCPGs focused on structured PA programs may help health care professionals, and patients with JIA and their families use the highest-quality evidence available to choose the best therapeutic activities. However, to facilitate evidence-based clinical practice, effective implementation methods must be developed to meet the needs of these specific knowledge users. This is why the Ottawa Panel has begun to develop an evidence-based education program for children and adolescents with JIA known as People Getting a Grip on Arthritis for juvenile idiopathic arthritis (PGrip-JIA) (www.arthritis.ca/peoplegettingagrip), disseminating effective interventions based on high-quality evidence. The complete version of the PGrip-JIA program will be disseminated online through The Arthritis Society website and through social media in order to facilitate the transfer of knowledge on effective and therapeutic structured PA used in JIA.[103] Since this program will be available online free of charge and in an easy-to-understand video format, PGrip-JIA will be practical, affordable, and accessible for children and adolescents with JIA and their parents. Moreover, additional components, such as parental or family support and involvement in the structured PA intervention,[104,105] environmental modification (ie, school or home),[104] incorporation of motivational strategies,[106] and provision of proper information on the intervention (online or in print) to promote self-management,[107,108] may help facilitate uptake of the recommendations. Lastly, understanding and experiencing the benefits of structured PA, such as pain relief,[59] may help to encourage engagement and long-term adherence to PA.[109] However, further intervention studies are needed to properly examine the long-term effects of the identified structured PA interventions on the child's arthritis. In addition to disease-related outcomes, it may also be beneficial to assess the potential effects of PA interventions on improving knowledge acquisition of PA, motivation to engage in PA, and actual participation in the PA program.

Study limitations

Limitations of Ottawa Panel EBCPG

In an attempt to include as many pertinent studies as possible, we chose to retain for our systematic review quasi head-to-head comparison studies.[57,59] This may, because of the nature of the design, have caused an underestimation of the effects of the PA intervention. This Ottawa Panel EBCPG is not focused on a specific subtype, degree of severity, or level of chronicity for JIA; therefore, clinical applications may be more difficult. The present

clinical practice guideline focused uniquely on evidence from studies incorporating structured PA (ie, that are repetitive, regimented, and may require supervision and guidance by an instructor) and not generalized to all PA (ie, structured and unstructured activities). To detect clinically important improvement, we applied a standard minimal clinically important difference score of 30% to all outcome results within and across studies to assess whether treatment resulted in a clinically important effect.[53,54] However, because of the differences in minimal clinically important differences between outcome measures within the same study and across studies, application of a standard minimal clinically important difference may have precluded detection of any improvement. Although valid and reliable, certain outcome measures may lack in responsiveness, which may result in the underestimation of treatment effects.[110,111]

Limitations of primary included studies

In the retained studies, there is a consistent lack of information related to the cost of participation for each structured PA and to the auditing process specific to each intervention. Many of the selected studies[55,56,58] did not report on the rate or underlying causes of participant dropout. Certain studies did not report on specific details related to the intervention process such as information on exercise intensity,[56,59] the number of recommended exercise repetitions, and/or the target muscle(s).[55,57] Such details may be helpful to clinicians and researchers to improve treatment and favor its implementation.

Conclusions

Our findings based on the Ottawa Panel's recommendations support the use of structured exercises and PA such as Pilates, cardio-karate, home and aquatic exercises to help with disease management among children and adolescents (21y and younger) living with JIA. Pilates showed improvement in a higher number of outcomes. The Ottawa Panel recommends Pilates exercise as an effective PA (compared with conventional exercises) for JIA management of functional ability, joint ROM, and pain intensity, as well as physical, psychosocial, and overall health-related quality of life. Cardio-karate aerobic exercise is only recommended for clinical benefit of active joints and ROM. An individualized home exercise program involving strengthening, stretching, postural and functional exercises is recommended as clinically appropriate for JIA management of functional ability and patient quality of life. Aquatic aerobic fitness training is recommended for long-term ($\geq$6mo) management of swollen and tender joints. The incorporation of these recommendations by health care professionals in individualized treatment plans may help optimize care and improve health among children and adolescents living with JIA. Although PA in general has been shown to be beneficial to the health of children, little is known of the efficacy of habitual PA (in terms of intensity and duration) in JIA, which includes both structured and unstructured activities. Future clinical practice guidelines may benefit from analyzing evidence from highly rated experimental studies investigating the effects of habitual PA in pediatric rheumatology.

Suppliers

a. Microsoft Excel; Microsoft Corp.

b. Review Manager software (version 5.3); Cochrane Informatics & Knowledge Management Department. Available at: http://tech.cochrane.org/revman.

Keywords

Arthritis, juvenile; Exercise; Exercise therapy; Practice guideline; Rehabilitation

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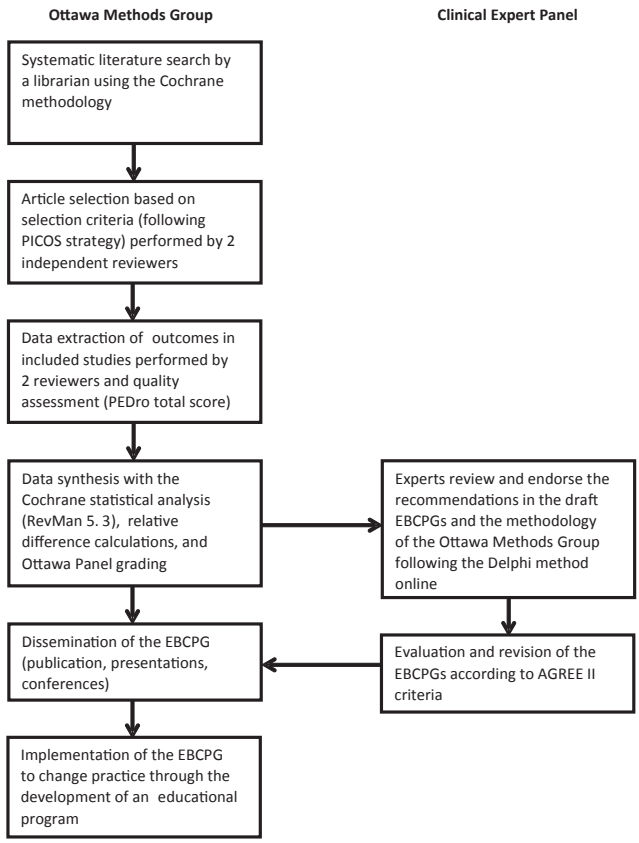
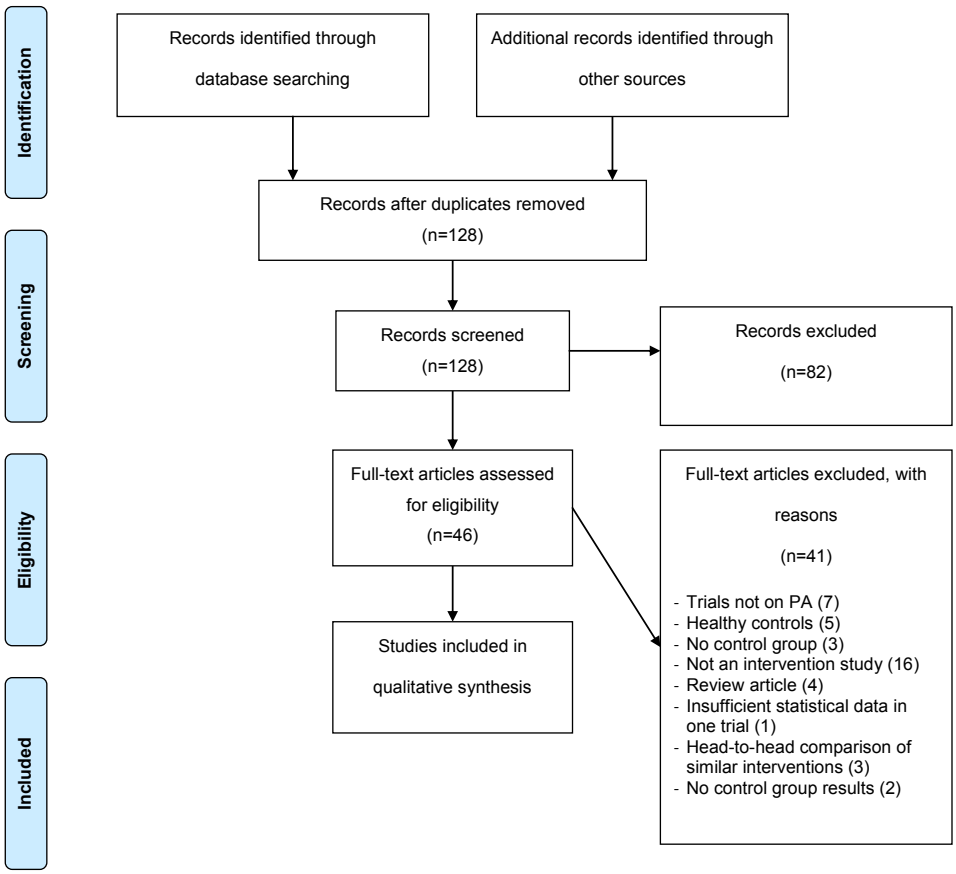


Appendix 1 Flow Diagram of EBCPGs Development Process
Abbreviations: AGREE, Appraisal of Guidelines for Research and Evaluation; PEDro, Physiotherapy Evidence Database; PICOS, population, intervention, comparator, outcomes, and study design.

Appendix 2 Full Search Strategy for MEDLINE

1. arthritis, juvenile/ or arthritis, psoriatic/
2. (juvenile adj2 arthritis).tw.
3. 1 or 2
4. clinical trial.pt.
5. randomized controlled trial.pt.
6. random$.tw.
7. (double adj blind$).tw.
8. placebo$.tw.
9. meta-analysis.pt,sh.
10. (meta-anal: or metaanal:).tw.
11. (quantitativ: review: or quantitativ: overview:).tw.
12. (methodologic: review: or methodologic: overview:).tw.
13. (systematic: review: or systematic: overview:).tw.
14. review.pt. and medline.tw.
15. exp cohort studies/
16. (cohort or longitudinal or prospective).tw.
17. exp case-control studies/
18. (retrospective or case-control).tw.
19. controlled clinical trial/
20. (controlled adj2 trial$).tw.
21. or/4-20
22. therap$ exercise$.tw.
23. exp exercise therapy/
24. (passive adj2 exercis$).tw.
25. mobilizing exercis$.tw.
26. ((strength$ or resistance or aerobic) adj exercis$).tw.
27. (continuous passive motion or movement device).tw.
28. exp exercise/
29. exp sports/
30. exp exercise movement techniques/
31. (sport* or aqua* or swim*).tw.
32. (Taichi or "tai chi" or taiji or "tai ji" or yoga or pilates).tw.
33. or/22-32
34. plyometric exercise/ or plyometric.tw.
35. 33 not 34
36. manual therap$.tw.
37. exp manipulation orthopedic/
38. (manipulation adj (therap$ or joint)).tw.
39. mobilization.tw.
40. or/36-39
41. 3 and 21
42. 35 or 40
43. 41 and 42



Appendix 3 Study Flow Diagram (Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA])

Appendix 4 Delphi Questionnaire

Endorsement of the Ottawa Panel Guidelines

Dear Ottawa Panel Experts,

You are invited to participate in a Delphi survey, conducted by Sabrina Cavallo & Dr. Lucie Brosseau, to obtain consensus on a recently developed clinical practice guideline (CPG) on the use of physical activity (PA) for the management of Juvenile Idiopathic Arthritis (JIA). The Ottawa Methods Group (OMG) was responsible for applying the Ottawa Panel methodology for developing this draft of the CPG. The purpose of this guideline is to identify 1) Randomized Control Trials (RCTs) assessing the efficacy of PA interventions for JIA; 2) the strength of the evidence; 3) the most effective PA interventions and formulate strong recommendations for the appropriate use of PA in management of JIA.

You have been approached to be a member on the Ottawa Panel of Experts, because you have been identified as a content expert. As a member of the Ottawa Panel of Experts participating in this survey, you will be a co-author on this publication (attached PDF) and will be responsible for endorsing the draft CPG. If you feel you are not the correct person for this, we would kindly ask you to refer a colleague who is best suited to be a content expert.

You can find a draft of the purpose, methods, results, and recommendations in the clinical practice guideline (CPG) file which is attached as a PDF (pg1-95). Once you have read the CPG document please take a moment to fill out this survey.

Please send us back the completed survey by August 15th 2014 and if you have any questions do not hesitate to contact me at:

Lucie.Brosseau@uottawa.ca

Thank you,

Sabrina Cavallo & Dr. Lucie Brosseau

Information and Instructions

Title: Ottawa Panel Evidence-Based Clinical Practice Guidelines for Physical Activity in the Management of Juvenile Idiopathic Arthritis

Aim of the Guideline: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatologic disease in children and has immense implications on a child's physical health and psychosocial integration. JIA is diagnosed if symptoms are experienced for a minimum of 6 consecutive weeks before 16 years of age and differential diagnoses have been excluded (Petty et al, 2004). Common symptoms associated with JIA include joint pain, fever, rash, and limited ability to participate in physical activity. However, several systematic reviews and CPGs have identified physical activity as an effective and safe way to manage JIA, but the scientific evidence available does not provide strong and detailed information about the recommendations for therapeutic applications. Further, many of the reviews and CPGs are now outdated, and there is a strong need for evidence-based clinical practice guidelines. The Ottawa Panel aims for rigorous guideline development with more quantitative methods, which focused on providing detailed recommendations about the effectiveness, safety, and therapeutic application-prescription for physical activity as a management strategy for JIA. Furthermore, this CPG will serve to supplement currently available non-pharmacologic treatment options.

Your role as an expert: You have been identified as an expert in Juvenile Idiopathic Arthritis or physical activity in children and have been invited to contribute to an expert consensus panel (known as the Ottawa Panel Experts) as a panelist. As an expert you will be asked to provide your opinion on the reporting of this guideline and its recommendations. You will also be responsible for endorsing the draft guideline.

This is the second round of the Delphi survey, and if it is needed we will add a third round.

Round 1(July 7th): *Completed. It included questions about the CPG and the recommendation reporting.*

Round 2 (August 5th): *Will require you to review and comment on the revised guideline (revisions in green). The survey will need to be completed by* ***August 15th****.*

Instructions: Once you have read a draft of the Ottawa Panel Guideline (the PDF is attached) please provide your feedback on this survey. This survey is separated into 2 parts: part 1 asks questions on the reporting of the guideline and whether the objectives, target populations, and the way the guideline was developed are clear to the readers. Part 2 asks questions on the recommendations and whether you agree or disagree with the stated recommendations. Where possible please provide your comments so that we can incorporate them into our next draft to develop a high-quality guideline.

Contact Information: Dr. Lucie Brosseau may be contacted by email at: Lucie.Brosseau@uottawa.ca.

PART 1: Guideline Reporting (pages 7–25 of attached PDF)

For questions 1 to 6 please check one of the boxes and please comment if you check unclear for any of the questions.

Q1: Are the overall objectives of the guideline clearly described? (Please check one of the following options.) **Likert Scale Options: 1 – 5 (Not Clear – Very Clear); Comments Section Provided.**

Q2: Is the target population to whom the guideline is meant to apply clearly described? **Likert Scale Options: 1 – 5 (Not Clear – Very Clear); Comments Section Provided.**

Q3: Is the literature search relevant and complete? **Likert Scale Options: 1 – 5 (Strongly Disagree – Strongly Agree); Comments Section Provided.**

Q4: Are the criteria for selecting the evidence (table 1: selection criteria) clearly described? **Likert Scale Options: 1 – 5 (Strongly Disagree – Strongly Agree); Comments Section Provided.**

Q5: Did you find the guidelines well-structured and easy to understand? **Likert Scale Options: 1 – 5 (Strongly Disagree – Strongly Agree); Comments Section Provided.**

Q6: Do you think the target audience can easily apply this guideline to their practice? (If you disagree, please comment.) **Likert Scale Options: 1 – 5 (Strongly Disagree – Strongly Agree); Comments Section Provided.**

PART 2: Recommendation reporting (pages 35–96 of attached PDF)

Questions 7 to 11 will be about the recommendations for the management of JIA. Please select either yes or no for each of the questions. If you check 'no' please comment why.

Q7: Pilates group vs Control (standard workout) (Level I, RCT):

A) Is the recommendation clear? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

B) Do you agree with this recommendation? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
C) Are the results in the guidelines interpreted according to your understanding of the data? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

Q8: Cardio-karate aerobic exercise vs Control (Qigong) (Level I, RCT):

D) Is the recommendation clear? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
E) Do you agree with this recommendation? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
F) Are the results in the guidelines interpreted according to your understanding of the data? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

Q9: Individualized home exercise vs Control (waiting list) (Level I, RCT):

G) Is the recommendation clear? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
H) Do you agree with this recommendation? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
I) Are the results in the guidelines interpreted according to your understanding of the data? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

Q10: Exercise strength training vs Control (Level I RCT):

J) Is the recommendation clear? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
K) Do you agree with this recommendation? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
L) Are the results in the guidelines interpreted according to your understanding of the data? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

Q11: Aquatic aerobic fitness training vs Control (usual care and medical treatment) (Level I RCT):

M) Is the recommendation clear? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
N) Do you agree with this recommendation? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**
O) Are the results in the guidelines interpreted according to your understanding of the data? (If no, please comment why) **Yes/No Response Option; Comments Section Provided: "If no, please comment"**

Appendix 5 Characteristics of included studies

Author/Year	Sample Size	Population Details	Disease Duration (y)	Age (y)	Treatment	Comparison Group	Concurrent Therapy	Sessions per Week No. of Weeks	Follow-Up	PEDro Score
Mendonça et al,[59] 2013	60 screened; 50 completed Gr 1: 25/25 completed Gr 2: 25/25 completed	Inclusion: Aged 8—18y, oligoarticular, polyarticular, and systematic subtypes of JIA (clinical diagnosis — ILAR), 6mo prior receive local and/or systemic arthritis-related therapy consisting of nonsteroidal anti-inflammatory drugs, disease modifying anti-rheumatic drugs, immunosuppressive medication, and/or steroids. Exclusion criteria: Significant cardiac, pulmonary, or metabolic comorbidity or had an active disease that required modified therapy during study.	Gr 1: 4.5±2.1 Gr 2: 3.3±2.1	Gr 1: 11.8±3.4 Gr 2: 11.0±3.9	Gr 1: Pilates exercises that followed the Canadian Stott-Pilates methodology and included floor exercises, exercises with the Reformer, the Stability Chair, the Cadillac, the Ladder Barrel. (adapted to age group)	Gr 2: Conventional program including warmup, workout (6—10 repetitions in supine, prone, and seated positions, and stretching exercises), and cool down	Medication used before start of the study	2 sessions/wk 24wk 50min/session	At the end of treatment (6mo)	8/10
Sandstedt et al,[56] 2013	54 screened/ 48 completed Gr 1: 28/33 completed Gr 2: 20/21 completed	Inclusion criteria: Polyarticular or extended oligoarticular arthritis with a treatment involving methotrexate, TNF-blockers, and/or prednisone as well as needing multiple injections of corticosteroid in lower extremities. Ages 9—21y. Exclusion criteria: N/A	Gr 1: 6.1 (1.2—16.5) Gr 2: 4.8 (1—13.4)	Gr 1: 13.3 (8.8—19.9) Gr 2: 14.9 (8.8—20.6)	Gr 1: Fitness training program; rope skipping, muscle strength, core exercise, free weights exercises for arms. Leisure-time PA was documented in a diary.	Gr 2: Control (was not described in the article)	Methotrexate, TNF blockers, and/or prednisone and corticosteroid injections in lower body	3 sessions/wk 12wk total 20min/session	At the end of treatment (3mo) and at 3mo follow-up (6mo from baseline)	5/10

(*continued on next page*)

Appendix 5 (*continued*)

Author/Year	Sample Size	Population Details	Disease Duration (y)	Age (y)	Treatment	Comparison Group	Concurrent Therapy	Sessions per Week No. of Weeks	Follow-Up	PEDro Score
Singh-Grewal et al,[57] 2007	80 screened; 69 completed Gr 1: 35/41 completed Gr 2: 34/39 completed	Inclusion criteria: Diagnosed with JIA, aged 8—16y, considered stable by their rheumatologist and unlikely to require modification of therapy during the study. Exclusion criteria: Significant cardiac, pulmonary, or metabolic comorbidity, moderate or severe hip pain while walking, f3h/wk of PA (excluding physiotherapy pool programs) and unable to cooperate with training or testing.	N/A	Gr 1: 11.7±2.5 Gr 2: 11.5±2.4	Gr 1: Experiment: Aerobic program of cardio-karate (similar to dance and martial arts). HR>75% of maximal HR. 10-min warmup, 30-min workout with progressively increasing intensity, 10-min cool down (passive stretching).	Gr 2: Control: Qigong program (nonaerobics), relaxation program similar to tai chi. 18-posture program avoiding elevated HR or aerobic training, postures repeated 8 times	No medication restrictions, but stable doses throughout the experiment	3 sessions/wk (1 supervised and 2 unsupervised) 12-wk program 30min/session	2wk after end of treatment (3mo)	8/10
Takken et al,[55] 2003	54 screened/54 completed Gr 1: 27/27 completed Gr 2: 27/27 completed	Inclusion criteria: JIA diagnosis, a phase of remission without medication for ≤6mo in the absence of joint pain, tenderness, and/or morning stiffness, and a normal range for the rate of erythrocyte sedimentation. Ages 5—13y. Exclusion criteria: Systemic disease	N/A	Gr 1: 8.66±2.29 Gr 2: 8.88±1.86	Gr 1: Aerobic aquatic training program consisting of a warmup, aerobic conditioning, rest period, 2nd conditioning, and cool down. Low-intensity swimming, aquatic	Gr 2: Control group; assessment only group (no exercise)	Usual care and medical treatment	1 session/wk 6mo (20wk, ~20 sessions total) 1h/session	At the end of treatment (3mo and 6mo)	6/10

(*continued on next page*)

Appendix 5 (*continued*)

Author/Year	Sample Size	Population Details	Disease Duration (y)	Age (y)	Treatment	Comparison Group	Concurrent Therapy	Sessions per Week No. of Weeks	Follow-Up	PEDro Score
		including a fever, low levels of hemoglobin, and a general feeling of malaise, exercise contraindication (as determined by a medical specialist), bone marrow transplant recipient, and not feeling confident in water.			aerobics, play, flexibility exercises or ball games for the warmup, rest, and cool-down phases. High-intensity swimming, diving, walking through the water, aqua jogging or splashing with the legs for conditioning phases. Duration and intensity increased gradually.					
Tarakci et al,[58] 2012	93 screened; 81 completed Gr 1: 43/47 completed Gr 2: 38/46 completed	Inclusion criteria: Diagnosed with JIA in accordance with the ILAR criteria, aged 5—17y, on stable dosage of medication/ treatment. Exclusion criteria: Presence of active joints in the exacerbation period, neurologic disease, metabolic disorder, decompensated organ failure, intra-articular	Gr 1: 5.31±3.05 Gr 2: 6.50±3.83	Gr 1: 10.02 (3.44) Gr 2: 10.82±4.00	Gr 1: Land-based home exercise program; individual exercise program included ROM, strengthening, stretching (20—30s), and posture exercises at home (eg, Theraband, walking, squats, stairs).	Gr 2: Control (waiting list)	Medication from before study	Supervised once a week at hospital, unsupervised at home daily for 3 consecutive days 12wk (3mo) Minimum of 20min to 45-min maximum	End of treatment at 3mo	7/10

(*continued on next page*)

Appendix 5 (*continued*)

Author/Year	Sample Size	Population Details	Disease Duration (y)	Age (y)	Treatment	Comparison Group	Concurrent Therapy	Sessions per Week No. of Weeks	Follow-Up	PEDro Score
		steroid injection or surgery in any joint, >2h regular weekly exercise, and uncooperative with exercise or measurement.			Gradual increase in number and difficulty of repetitions (up to 15 reps); participants wrote in a diary, reviewed weekly.					

NOTE. Values are mean ± SD, mean (range), or as otherwise indicated.
Abbreviations: Gr, group; ILAR, International League of Associations for Rheumatology; N/A, not available; HR, heart rate; TNF, tumor necrosis factor.

Appendix 6 Clinically significant effects of PA interventions on health outcomes: pain, function, quality of life, active disease, and ROM

Outcome	Study (Study Design)	Study Groups: Intervention (I) and Control (C)	Measure	No. of Patients	Baseline Mean	End of Study Mean	Absolute Benefit	Relative Difference in Change From Baseline (%)	Mean Difference (95% CI)
Pain	Mendonça (level I, RCT)	I: Pilates exercises	10-cm VAS—joint pain Lower better EOT: 6mo	25	2.3	0	−2.5	−96	MD: 0* CI Low: 0* CI High: 0* *Not estimable
		C: Conventional program		25	2.9	3.1			
Functional status	Mendonça (level I, RCT)	I: Pilates exercises	CHAQ Lower better EOT: 6mo	25	0.9	0.08	−0.82	−91	MD: −0.82 CI Low: −1.02 CI High: −0.62
		C: Conventional program		25	0.9	0.9			
	Tarakci (level I, RCT)	I: Individualized home exercise	CHAQ Lower better EOT: 3mo	43	0.63	0.19	−0.42	−65	MD: −0.45 CI Low: −0.70 CI High: −0.20
		Control		38	0.66	0.64			
Health- related quality of life	Mendonça (level I RCT)	I: Pilates exercises	PedsQL 4.0 patients: physical Higher better EOT 6mo	25	50.5	90.5	40.9	79	MD: 37.90 CI Low: 29.20 CI High: 46.6
		C: Conventional program		25	53.5	52.6			
	Mendonça (level I RCT)	I: Pilates exercises	PedsQL 4.0 patient: PSCS Higher better EOT: 6mo	25	45.7	80.1	41.7	86	MD: 36.30 CI Low: 28.72 CI High: 43.88
		C: Conventional program		25	51.1	43.8			
	Mendonça (level I RCT)	I: Pilates exercises	PedsQL 4.0 patient: total Higher better EOT: 6mo	25	47.4	82.2	39.6	80	MD: 35.30 CI Low: 28.32 CI High: 42.28
		C: Conventional program		25	51.7	46.9			
	Mendonça (level I, RCT)	I: Pilates exercises	PedsQL 4.0 caregiver: PSCS Higher better EOT: 6mo	25	44.4	80.4	50	97	MD: 36.10 CI Low: 28.59 CI High: 43.61
		C: Conventional program		25	58.3	44.3			

(*continued on next page*)

Appendix 6 (*continued*)

Outcome	Study (Study Design)	Study Groups: Intervention (I) and Control (C)	Measure	No. of Patients	Baseline Mean	End of Study Mean	Absolute Benefit	Relative Difference in Change From Baseline (%)	Mean Difference (95% CI)
	Mendonça (level I, RCT)	I: Pilates exercises	Peds QL 4.0 caregivers: total Higher better EOT: 6mo	25	43.1	81.9	52.6	103	MD: 36.40 CI Low: 30.31 CI High: 42.49
		C: Conventional program		25	59.3	45.5			
	Tarakci (level I, RCT)	I: Individualized home exercise	Peds QL—Self-Report Higher better EOT: 3mo	43	63.58	85.58	20.61	33	MD: 23.16 CI Low: 14.44 CI High: 31.88
		Control		38	61.03	62.42			
	Tarakci (level I, RCT)	I: Individualized home exercise	Peds QL—Parent Report Higher better EOT: 3mo	43	63.41	86.17	21.67	34	MD: 21.13 CI Low: 12.32 CI High: 29.94
		Control		38	63.95	65.04			
Active disease	Singh-Grewal (level I, RCT)	I: Cardio-karate aerobics group	Active joints, mean ± SD (range) Lower better EOT: 3mo	35	3.5	2.2	−0.9	−30	MD: 0.10 CI Low: −2.65 CI High: 2.85
		C: Qigong group		34	2.5	2.1			
	Takken (level I, RCT)	I: Aquatic aerobic fitness training	Swollen/tender joints Lower better EOT: 3mo	27	2.5	2.2	−1	−37	MD: −1.4 CI Low: −3.54 CI High: 0.74
		Control		27	2.9	3.6			
	Takken (level I, RCT)	I: Aquatic aerobic fitness training	Swollen/tender joints Lower better EOT: 6mo	27	2.5	1.11	−2.09	−77	MD: −2.49 CI Low: −4.40 CI High: −0.58
		Control		27	2.9	3.6			
ROM	Mendonça (level I, RCT)	I: Pilates exercises	pEPM-ROM Lower better EOT: 6mo	25	0.5	0.09	−0.41	−117	MD: −0.11 CI Low: −0.2 CI High: −0.02
		C: Conventional program		25	0.2	0.2			
	Singh-Grewal (level I, RCT)	I: Cardio-karate aerobics group	EPM ROM score Lower better EOT: 3mo	35	0.1	89.1	−0.1	−197	MD: 0.00 CI Low: −0.15 CI High:0.15

(*continued on next page*)

Appendix 6 (*continued*)

Outcome	Study (Study Design)	Study Groups: Intervention (I) and Control (C)	Measure	No. of Patients	Baseline Mean	End of Study Mean	Absolute Benefit	Relative Difference in Change From Baseline (%)	Mean Difference (95% CI)
		C: Qigong group		34	0	0.1			
	Sandstedt (level I, RCT)	I: Exercise strength training	Hip abduction, right side (Nm) Higher better Follow-up: 3mo	26	26.5	29.6	10.4	32	MD: −3.70 CI Low: −9.67 CI High: 2.27
		Control		19	40.6	40.6			

Abbreviations: CHAQ, Childhood Health Assessment Questionnaire; CI, confidence interval; EOT, end of treatment; EPM, Escola Paulista de Medicina; MD, mean difference; PedsQL, Pediatric Quality of Life Inventory; pEPM-ROM, Pediatric Escola Paulista de Medicina Range of Motion Scale; PSCS, psychosocial; VAS, visual analog scale.

Appendix 7 EBCPGs Related to PA Program Interventions for the Management of JIA

1. Mendonça et al[59] (2013)—EBCPGs related to Pilates exercise (N=25) versus conventional exercise (warmup; supine, prone, and seated positions; stretching exercises; cool down; N=25) (level I RCT). The Pilates method of exercise attempts to achieve mind, body, and spirit coordination through a series of yoga, dance, and martial arts–inspired movements. This intervention was delivered twice a week for 50 minutes per session over a period of 24 weeks. Exercise intensity was not explicitly specified in the study. At 6 months (end of treatment), statistically significant evidence was found supporting the implementation of Pilates exercise to provide clinically important benefits (grade A) for functional ability (Childhood Health Assessment Questionnaire [CHAQ]) (mean difference [MD]=−.82; 95% confidence interval [CI], −1.02 to .62), joint ROM (Pediatric Escola Paulista de Medicina Range of Motion Scale [pEPM-ROM]) (MD=−.11; 95% CI, −0.2 to −.02]), pain (labeled as "pain intensity" in study) (10-cm visual analog scale [VAS]–joint pain) (MD is not estimable), and health-related quality of life (physical (Pediatric Quality of Life Inventory [PedsQL] 4.0 patients: physical) (patients: MD=37.9; 95% CI, 29.2–46.6), psychosocial (PedsQL 4.0 patients: psychosocial) (patients: MD=36.3; 95% CI, 28.72–43.88) (PedsQL 4.0 caregivers: psychosocial) (caregivers: MD=36.1; 95% CI, 28.59–43.61), and total (PedsQL 4.0 patients: total) (patients: MD=35.3; 95% CI, 28.32–42.28) (PedsQL 4.0 caregivers: total) (caregivers: MD=36.4; 95% CI, 30.31–42.49) for children and adolescents with JIA. For physical health-related quality of life (PedsQL 4.0 caregivers: physical) (MD=38.8; 95% CI, 32.01–45.59) as perceived by caregivers, no benefit was demonstrated. This study also received a Physiotherapy Evidence Database (PEDro) Scale rating of 8 out of 10, verifying that high-quality methods were used. Therefore, based on the gathered evidence, the Ottawa Panel recommends Pilates exercise as an effective PA compared with conventional exercises for JIA management of functional ability, joint ROM, and pain intensity, as well as physical, psychosocial, and overall health-related quality of life.
2. Singh-Grewal et al[57] (2007)—EBCPGs related to cardio-karate aerobic exercise program (N=35) versus a control (qigong program [nonaerobics]; N=34) (level I RCT) (see appendix 6). Cardio-karate comprises dance and martial arts movements, whereas qigong, which is similar to tai chi, promotes bodily relaxation through the repetition of 18 postures. The cardio-karate sessions were delivered 3 times a week (once supervised, twice unsupervised) for 30 minutes per session over a period of 12 weeks. The exercise intensity was gradually increased from low to moderate/high as the session progressed. At 3 months (end of treatment), study findings showed that aerobic exercise is clinically beneficial (grade C+) in reducing the number of active joints (MD=0.1; 95% CI, −2.65 to 2.85) and improving ROM (Escola Paulistade Medicina [EPM] score) (MD=0; 95% CI, −.15 to .15), but differences were not found to be statistically significant. For (1) submaximal oxygen consumption ($\dot{V}o_2$submax) 1.5km/h: absolute (L/min) (MD=0; 95% CI, −.05 to .05), (2) ($\dot{V}o_2$submax 3.0km/h: absolute (L/min) (MD=0; 95% CI, −.05 to .05), (3) peak oxygen consumption (Vo_2peak): absolute (L/min) (MD=−0.1; 95% CI, −.34 to .14), (4) Vo_2peak: relative (mL/kg/min)

(MD = −1.4; 95% CI, −5.37 to 2.57), (5) peak power (watts: 10s) (MD = 17; 95% CI, −44.93 to 78.93), (6) peak power (watts: 30s) (MD = 11; 95% CI, −47.78 to 69.78), (7) functional ability (labeled as "physical function" in study) (CHAQ) (MD = .01; 95% CI, −.16 to .18), and (8) quality of life (10 cm VAS) (MD = −0.3; 95% CI, −1.11 to .51), there was no observed benefit of aerobic exercise training. For $\dot{V}o_2$submax 1.5km/h: relative (mL/kg/min) (MD = −0.6; 95% CI, −1.36 to .16), $\dot{V}o_2$submax 3.0km/h: relative (MD = −0.6; 95% CI, −1.38 to .18), and health-related quality of life (10-cm VAS) (MD = −0.7; 95% CI, −1.55 to .15), the outcomes favored the control; therefore, no benefit for aerobic exercise use was demonstrated. In addition, the PEDro Scale rating for this study was 8 out of 10, indicating high-quality methodology. Therefore, based on the evidence, cardio-karate aerobic exercise is only recommended for clinical benefit of active joints and ROM.

3. Tarakci et al[58] (2012)—EBCPGs related to an individualized home exercise program (N = 43) versus a control group (waiting list; N = 38) (level I high-quality RCT). This primarily unsupervised (by health professionals) and individualized aerobic program consisted of strengthening, stretching, postural exercises, and functional activities whose repetitions were gradually increased over time. The intervention was delivered 4 times a week (once supervised at hospital, 3 times unsupervised at home) from 20 to 45 minutes per session over a period of 3 months. The exercise intensity was perceived to increase over time because of the gradual increase in number of repetitions, difficulty of exercises, and duration of session. At 3 months (end of treatment), the individualized home exercise program displayed evidence of clinically important benefits (grade A) in functional ability (CHAQ) (MD = −.45; 95% CI, −0.7 to −0.2), as well as quality of life measured by the PedsQL−Self-Report (MD = 23.16; 95% CI, 14.44−31.88) and PedsQL−Parent Report (MD = 21.13; 95% CI, 12.32−29.94) compared with the control group. No benefits were seen for physical fitness (labeled as "functional status" in study) (6-minute walk test) (MD = −5.74; 95% CI, −46.85 to 35.37) or pain (10-cm VAS) (MD = −11.08; 95% CI, −22.6 to .44). Of note, the 6-minute walk test is usually accepted for use in children as a validated measure; however, this is specifically for joint status and not functional capacity (eg, Vo_2peak). Therefore, results regarding this outcome should be interpreted with caution. This study also received a PEDro Scale rating of 7 out of 10, verifying that high-quality methods were used. In conclusion, based on significant evidence, the Ottawa Panel recommends an individualized home exercise program involving strengthening, stretching, postural and functional exercises as clinically appropriate JIA management of functional ability and patient quality of life.
4. Takken et al[55] (2003)—EBCPGs related to aquatic aerobic training exercises (N = 27) versus a control (usual care and medical treatment; N = 27) (level I high-quality RCT). The aquatic training program included aerobic conditioning through high-intensity swimming and aqua jogging, as well as warmup and cool-down phases consisting of low-intensity swimming, flexibility exercises, and aquatic aerobics. The intervention was delivered once a week for 1 hour per session over a period of 6 months. At 3 months (end of treatment), evidence showed that this intervention was clinically beneficial (grade C) for swollen and tender joints (joint status) (MD = −1.4; 95% CI, −3.54 to .74), but it was not found to be statistically significant. No benefit was found for (1) functional ability (CHAQ) (MD = −.23; 95% CI, −.55 to .09); (2) JIA disability (Juvenile Arthritis Functional Assessment Scale) (MD = −0.1; 95% CI, −.24 to .04); (3) health-related quality of life, measured with the Juvenile Arthritis Quality of Life Questionnaire (JAQQ) (MD = −3.1; 95% CI, −5.8 to −0.4), the Child Health Questionnaire−Physical (CHQ-PhS) (MD = 7.85; 95% CI, 1.58−14.12), and the Child Health Questionnaire−Psychosocial (CHQ-PsS) (MD = 1.96; 95% CI, −2.02 to 5.94); (4) physical fitness, measured with Vo_2peak (MD = .09; 95% CI, −.11 to .29); or (5) ROM (pEPM-ROM) (MD = −.07; 95% CI, −.26 to .12). At 6 months (end of treatment), evidence showed that this intervention was clinically beneficial (grade A) for swollen and tender joints (joint status) (MD = −2.49; 95% CI, −4.4 to −.58). No benefit was seen for (1) ROM (pEPM-ROM) (MD = −.17; 95% CI, −.36 to .02); (2) functional ability (CHAQ) (MD = −.36; 95% CI, −0.7 to −.02); (3) health-related quality-of-life outcome measures such as JAQQ (MD = −3.74; 95% CI, −6.71 to −.77), CHQ-PhS (MD = 10.45; 95% CI, 3.87−17.03), and CHQ-PsS (MD = 4.67; 95% CI, 0.97−8.37); and (4) physical fitness, measured by Vo_2peak (MD = .11; 95% CI, −.09 to .31). The PEDro Scale rating for this study was 7 out of 10, verifying that high-quality methods were used. Therefore, based on the emerging evidence, aquatic aerobic fitness training is recommended for long-term (≥6mo) management of swollen and tender joints.
5. Sandstedt et al[56] (2013)—EBCPGs related to strength training exercises (N = 26) versus an assessment-only control (not described) (N = 19) (level I low-quality RCT). The strength training program incorporated a number of exercises targeting both extremity and core muscles using free weights and skipping rope. The intervention was delivered 3 times a week for 20 minutes per session over a period of 3 months. The exercise intensity was not explicitly stated within the study. At 3 months (end of treatment), evidence demonstrated no benefit for (1) for grip strength (right side) (MD = −35.4; 95% CI, −80.08 to 9.28); and muscle torque (Nm) of (2) shoulder abduction (right side) (MD = −2.2; 95% CI, −7.96 to 3.56); (3) shoulder abduction (left side) (MD = −1.5; 95% CI, −7.05 to 4.05); (4) elbow extension (right side) (MD = −3.5; 95% CI, −9.46 to 2.46); (5) elbow extension (left side) (MD = −3.6; 95% CI, −8.7 to 1.5); (6) elbow flexion (right side) (MD = −7; 95% CI, −13.81 to −.19); (7) elbow flexion (left side) (MD = −8; 95% CI, −14.9 to −1.1); (8) hip extension (right side) (MD = −9.7; 95% CI, −24.69 to 5.29); (9) hip extension (left side) (MD = −8.8; 95% CI, −22.98 to 5.38); (10) hip flexion (right side) (MD = −8.3; 95% CI, −21.38 to 4.78); (11) hip flexion (left side) (MD = −6.9; 95% CI, −17.58 to 3.78); (12) hip abduction (right side) (MD = −11.3; 95% CI, −20.37 to −2.23); (13) hip abduction (left side) (MD = −6.3; 95% CI, −14.95 to 2.35); (14) knee extension (right side) (MD = −12.9; 95% CI, −25.96 to .16); (15) knee extension (left side) (MD = −17.9; 95% CI, −29.35 to −6.45); (16) dorsiflexion (right side) (MD = −2; 95% CI, −5.8 to 1.8); and (17) dorsiflexion (left side) (MD = −1.2; 95% CI, −4.56 to 2.16). In addition, for grip strength (left side) (MD = −36; 95% CI, −76.22 to 4.22), the outcome favored the control; therefore, no benefit for fitness training exercise was demonstrated.

At 3 months' follow-up, evidence demonstrated that there was a clinically important benefit (grade C+), however, without statistical significance for muscle torque (Nm) for hip abduction (right side)

(MD = −3.7; 95% CI, −9.67 to 2.27). Evidence also demonstrated that there was no benefit for muscle torque (Nm) (1) for shoulder abduction (left side) (MD = −3.1; 95% CI, −8.59 to 2.39); (2) elbow extension (right side) (MD = −3.3; 95% CI, −9.06 to 2.46); (3) elbow extension (left side) (MD = −3.3; 95% CI, −8.31 to 1.71); (4) elbow flexion (right side) (MD = −7.2; 95% CI, −14.86 to .46); (5) elbow flexion (left side) (MD = −6.5; 95% CI, −12.91 to −.09); (6) hip extension (right side) (MD = −11.6; 95% CI, −25.17 to 1.97); (7) hip extension (left side) (MD = −8.4; 95% CI, −21.34 to 4.54); (8) hip flexion (right side) (MD = −12.1; 95% CI, −24.95 to 0.75); (9) hip flexion (left side) (MD = −11; 95% CI, −22.49 to .49); (10) hip abduction (left side) (MD = −5.1 95% CI, −13.01 to 2.81); (11) knee extension (right side) (MD = −9.6; 95% CI, −22.32 to 3.12); (12) knee extension (left side) (MD = −12.9; 95% CI, −25.91 to .11); (13) dorsiflexion (right side) (MD = −3.4; 95% CI, −6.84 to .04); and (14) dorsiflexion (left side) (MD = −2; 95% CI, −5.17 to 1.17). The control was favored, and thus no benefit was demonstrated for grip strength on both the left (MD = −38.9; 95% CI, −79.5 to 1.7), and right sides (MD = −42.5; 95% CI, −84.4 to −0.6), as well as for shoulder abduction on the right side (MD = −6.2; 95% CI, −12.16 to .24). The PEDro score for this article (5 out of 10) was lower than the high-quality cutoff. However, this ranking and its implications were taken into account when developing the Ottawa Panel recommendations. In conclusion, because of the lack of positive recommendations and the low PEDro score, no conclusions can be drawn for strength training exercises for JIA management.

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