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Secondary Consequences of Juvenile Idiopathic Arthritis in Youth with Knee Joint Involvement Compared to Healthy Controls

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Research article

Keywords: Physical Activity, Adiposity, Aerobic Capacity, Dynamic Balance

Posted Date: January 14th, 2020

DOI: https://doi.org/10.21203/rs.2.20823/v1

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Abstract

Background: Juvenile Idiopathic Arthritis (JIA) is the most common childhood rheumatic disease. Given the heterogeneity of JIA and advances in treatment approaches, there is a persistent lack of consensus regarding the secondary consequences of JIA. This study assessed body structure and function and physical activity outcomes in youth with JIA compared to their healthy peers.

Methods: Youth with JIA (n=25; 10-20 years old) and age and sex matched healthy peers (n=25) participated in two data collections (one week apart) (Ethics ID# REB15-3125). Day 1 testing included a triple single leg hop test (TSLH) and an incremental bike test. Participants then recorded their physical activity for one week using the waist worn ActiGraph. Day 2 testing consisted of a dual-energy x-ray absorptiometry scan. Outcomes included: moderate to vigorous physical activity (MVPA), peak oxygen uptake (VO2peak), maximal TSLH distance (% leg length), and fat mass index (FMI). Data were assessed for normality and outliers. Pair differences were analyzed in R (R Core Team, Austria) using t-confidence intervals (CI) or the Hodges-Lehmann method with Bonferroni correction. A significant difference was accepted if CIs excluded zero. The effect of sex on outcomes was examined using pair difference medians and first and third quartiles.

Results: CIs for all study outcomes contained zero and did not meet criteria for significant differences between pairs. However, based on the large lower limit and small upper limit of the CIs for MVPA (median -18.6min 97.5%CI [-44.3,2.0]), a larger sample might have concluded that youth with JIA perform substantially less MVPA than their healthy peers. Further, based on pair difference point estimates and interquartile ranges, sex may be a confounder with regards to physical activity participation and may be an effect modifier of the TSLH.

Conclusions: The results of this study provide further evidence on the consequences of JIA on physical activity participation in youth. These findings highlight the importance of considering the effects of sex, particularly with regards to physical activity and TSLH outcomes. Further research across JIA subtypes is needed to inform the targeted exercise therapy programs to restore healthy patterns of physical activity participation.

Background

Juvenile Idiopathic Arthritis (JIA) is the most common chronic childhood rheumatic disease, affecting 0.07–4.01 per 1000 youth worldwide, and approximately 1 in 1000 children in Canada [1, 2]. JIA is diagnosed following the onset of persistent joint inflammation of one or more joints for at least six weeks in children under the age of 16 years old [1–3]. Other differential diagnoses have to be excluded before JIA can be confirmed [4]. JIA may be classified into seven, clinically distinct inflammatory disease subtypes, described by the number of joints involved, extra-articular manifestations, and presentation of systemic symptoms [5]. While the long-term consequences of JIA are poorly understood, it is linked to

high societal and economic burden, and approximately 25% of JIA patients will have active arthritis as adults [6].

Symptoms of JIA may include joint pain, swelling, stiffness, and immobility, as well as muscular weakness, atrophy and contractures, which occur in cycles of disease flare and remission [7]. Remittent and relapsing symptoms, as well as fear of aggravating disease symptoms, can cause prolonged physical inactivity resulting in deconditioning and disability, leading to an inactive lifestyle [8]. Resultant inactivity may contribute to or escalate disease symptoms, which has been associated with long-term health consequences including insulin resistance, hypertension, and metabolic syndrome [9].

Current research evidence on the secondary consequences of JIA, indicates that youth with JIA engage in less physical activity, particularly with regards to moderate to vigorous physical activity (MVPA) [8], have decreased aerobic fitness [10], have greater adiposity [11], and display movement abnormalities and balance deficits [12, 13] compared to their healthy peers. However, due to the heterogeneity of JIA, the diversity in sample populations and research methods, as well as substantial advances in pharmacological disease management over the past decade [14], a consensus on the consequences of JIA across disease subtypes has not been achieved.

A 2006 Canadian national survey on leisure activity in children with JIA indicated that only 33% of individuals reported participation in physical activity daily and 70% reported participation in physical activity only once weekly [15]. Further, Nørgaard and Herlin reported that 38% of adolescents with JIA were not active in sports, citing pain and shortness of breath [16], with Canadian parents noting their child's need for assistance as the most likely explanation for limited physical activity [15]. Conversely, Milatz et al. reported an increase in participation in school sports over 15 years (2000–2015) by youth with JIA [17], illustrating the likely positive consequences of more effective treatment options on physical activity participation in youth with JIA. Similarly, results on fat mass indicate that particularly females with JIA were more likely to have higher adiposity [11, 18], while a large longitudinal study by Schenck et al. [19] revealed no significant differences in the body mass index or rates of obesity in over 5000 children and adolescent with mild JIA disease activity in Germany. These findings illustrate the challenges in defining the secondary consequences of JIA and highlight the need for further characterization of this population.

The aim of this study was to examine physical activity participation, aerobic capacity, adiposity, and dynamic balance ability in youth ages 10–20 years old with JIA with knee involvement, compared to age and sex-matched healthy peers. It is anticipated that this information will help to clarify the secondary consequences of JIA for a sub-group of local patients to inform strategies to improve youth JIA health outcomes.

Methods

Study design

This is a prospective cohort study with a matched pair design conducted between July 2016 and November 2017.

Participants

Participants with JIA (JIA group) were recruited by their clinician in collaboration with the local pediatric outpatient rheumatology clinic and an external outpatient rheumatology clinic. Participants who gave consent / assent were contacted by phone by the research team for a screening interview and to book a testing session. Healthy control participants (CON group) were recruited using an online research study portal and through friends and family of participants. Inclusion criteria for participants with JIA included: age 10-20 years old; a diagnosis of JIA by a physician with bilateral or unilateral knee involvement; and active or inactive disease at the time of testing. Patients were not eligible if systemic symptoms were present, if medications had changed during the three weeks prior to testing, or if they had active ankle joint involvement. The CON group had no history of JIA or other rheumatological diseases. Exclusion criteria for all participants included: contraindications as indicated on the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) [20]; previous lower extremity musculoskeletal injury within 3 months prior to testing that resulted in time loss (work, school, or sport); diagnosis of any other arthritides; pregnancy. Ethics approval was granted by the Conjoint Health Research Ethics Board (Ethics ID: REB15-3125).

Data Collections

This study was performed as part of a larger study on the secondary consequences of JIA including dynamic balance, fitness, movement biomechanics and body composition outcomes. Data collections for each study participant were conducted on two separate days. On day 1 participants with JIA were assessed by a pediatric rheumatologist (SB) to record disease history and disease activity and by a pediatric physiotherapist (JB). All participants completed surveys on demographics and knee function and completed a series of testing stations: anthropometrics; dynamic balance; aerobic capacity; and movement biomechanics. Following day 1, participants were provided with an ActiGraph GTX+ (ActiGraph Inc., USA) to measure physical activity and were instructed on the appropriate use. Participants then recorded physical activity for seven consecutive days. Day 2 testing was conducted one week after day 1 testing and involved a body composition assessment by a trained researcher using dual-energy absorptiometry (DXA, Hologic QDR 4500A, Hologic Inc., USA).

Outcomes

Physical activity was measured using the body worn ActiGraph. The ActiGraph has demonstrated excellent validity and classification accuracy for MVPA in adolescents with and without disability [21]. Participants were asked to wear the device for seven consecutive days during waking and sleeping hours

and to follow their regular schedule and activities during this time. The ActiGraph was waist mounted on the right hip using an elastic strap. Participants completed an activity monitor log to record physical activity during non-wear times; i.e. when the ActiGraph was removed for showers or swimming. Participants recorded their average rate of perceived exertion (RPE) using the Pictorial Children's Effort Rating Table (PCERT) for any activities completed without the ActiGraph [22]. Time spent in any activities for which participants recorded an RPE of 5-10 was included in minutes of MVPA. This is a conservative non-wear time estimate, in line with the definition of MVPA by the Canadian 24-hour Movement Guidelines [23]. If RPE was not recorded, participants were contacted for follow up. If RPE could not be obtained, Ridley's Compendium of Energy Expenditures for Youth was used to estimate RPE [24] and MVPA was defined as ≥4 metabolic equivalents [25]. The total MVPA duration was then divided by the number of valid days and expressed as the average time spent in MVPA per day over the wear period.

MVPA was analyzed using ActiLife (v6.13.3, ActiGraph Inc., USA). Data were collected at 30Hz, at 10 second epochs. Age-specific algorithms by Evenson et al. [25,26] were chosen due to their superior ability to predict energy expenditure in youth across physical activity intensity levels [25]. Here, moderate activity was defined as ≥2296 counts/minute and <4011 counts/minute and vigorous activity as ≥4012 counts/minute [25]. Physical activity data were included if the participant had worn the device for 5-7 days, including at least one weekend day, and for >10 hours per day. If the participant wore the device for >7 days, the days with the longest wear time were included for analysis. Every effort was made to include information on self-reported activities and participant follow up was performed to clarify physical activity participation if self-report data did not correspond with ActiGraph data.

Aerobic capacity was determined using the relative peak oxygen consumption ($VO_{2\ peak}$; mL/kg/min) during an incremental maximal fitness test using a cycle ergometer (Ergoline GmbH, Germany). Participants started at 0W and resistance was increased in 20W intervals every 2 minutes until volitional fatigue, a plateau in maximal heart rate, and/or a reported RPE of 10 on the PCERT scale [22]. Respiratory gases were collected and analyzed using the COSMED K5 portable metabolic system (COSMED, Italy).

Adiposity was determined using DXA and expressed as a fat mass index [FMI; fat mass/height (kg/m^2)]. Participants were asked to lie supine on the scan bed and remain still for the duration of the scan. The DXA was calibrated prior to each scan as per the manufacturer's recommendations and all procedures were consistent with the official positions of the International Society of Clinical Densitometry [27].

Dynamic balance was assessed using a triple single leg hop test (TSLH). This test evaluates neuromuscular control, force generating capacity, and knee stabilization [28,29] and has shown moderate correlation to the Global Rating Scale (r=0.44) [30] and Lower Extremity Functional Scale (r=0.26) [31]. Participants performed a practice trial followed by two test trials in which participants performed three consecutive single-leg hops with the goal of jumping as far as possible [32]. For a trial to be included, the

landing following the last jump had to be solid without excessive movement or twisting of the foot. The maximum distance across trials was recorded for each leg and expressed with respect to % leg length.

Further, self-reported physical disability was assessed using the Childhood Health Assessment Questionnaire (CHAQ) [33]. The CHAQ captures the health and functional status of patients across eight domains using a score of 0 and 3 (higher scores indicate greater functional disability). Disease activity was determined by clinical exam and scored using the Juvenile Arthritis Disease Activity Score (cJADAS10) [34]. cJADAS is a sensitive continuous score of disease activity developed for use with individuals with JIA [34]. cJADAS comprises measures of active joint count (10 joints), physician global assessment of disease activity, and evaluation of the child's wellbeing.

Data Analysis

Matched pairs were assigned based on closest age in months (≤18 months difference between pairs) and sex. Statistical analyses were performed using R (R Core Team, Austria). Demographics data were summarized using medians, and minimum and maximum values for numerical data, and frequencies and percentages for categorical data by group (JIA, CON), sex (male, female) and matched pairs. Pair differences between individuals in the JIA and CON groups for primary (MVPA, Aerobic Fitness) and secondary (FMI, TSLH) outcomes were graphed to assess for normality and outliers. To evaluate differences between normally distributed matched pair outcomes, t-confidence intervals (CI) corrected by the Bonferroni Correction ([1-alpha/(2*number of tests)]% CI) were reported. If the pair differences were not normally distributed, the medians and CIs ([1-alpha/(2*number of tests)]% CI) were determined using the Hodges-Lehmann method. A statistical difference was determined if the CI excluded zero. Further, the effect of sex on the primary and secondary outcomes were examined using medians and first and third quartiles for each study group and the respective pair differences, due to the small sample.

Results

A total of 62 youth participated in this study. Fifty participants met the criteria for matched pairs (JIA n = 25, female n = 16, male n = 9; CON n = 25, female n = 16, male n = 9). No matches were identified for the remaining 12 participants (JIA n = 5, CON n = 7) who were then excluded from matched pairs analysis. Male participants had predominantly oligoarticular JIA (67%), while female participants had either oligoarticular or polyarticular JIA (50% respectively). The median disease duration across participants was 6.4 years [range 0, 14]. Participants with JIA recorded low scores for active joints [female, n = 14, median 0 joints (range 0, 1); male, n = 7, median 1 joint (range 0, 3)], joints with limited range of motion [female, n = 14, median 0 joints (range 0, 1); males, n = 7, median 1 joint (range 0, 3)], physician global assessment of disease activity [female, n = 13, 0 (range 0, 1); male, n = 7, 0.6 (range 0, 2.5) out of 10] and parent global assessment of disease activity [female, n = 13, 0 (0, 2); male, n = 4, 0.9 (0, 8) out of 10]

(Table 1). At the time of testing, participants reported active joint involvement for the knee (38%), temporomandibular joint (14%), shoulders (5%) and fingers (5%).

Physical Activity

Three pairs were excluded from the physical activity analysis (< 5 days of ActiGraph wear-time). Fifteen participants (CON n = 10; JIA n = 5) self-reported physical activity and RPE data on the monitor logs, which were included in the final analysis. Paired differences in combined ActiGraph and self-report physical activity data did not meet the criteria for a significant pair difference in MVPA as the confidence intervals included zero [median − 18.6 min 97.5% CI (-44.3, 2.0)] (Table 2). However, based on the large lower limit and small upper limit of CIs the sample size may actually have an effect on this; a larger sample might have given a significant result. Specifically, 75% of healthy males and 64% of females accumulated at least 60 minutes of MVPA per day as recommended by the World Health Organization and Canadian 24-hour Movement Guidelines for Children and Youth. Only 38% of male youth with JIA and 29% of females accumulated the equivalent amount of MVPA.

Aerobic capacity

Two pairs were excluded from the VO_{2peak} analyses (did not consent, lost to follow up). Both JIA and CON group participants displayed similar VO_{2peak} values with no significant differences between pairs [mean − 0.13 ml/kg/min 97.5%CI (-5.5, 5.2)] (Table 2).

Adiposity

Three pairs were excluded from the adiposity analyses (DXA malfunction, lost to follow up) due to missing data. Youth in the JIA and CON groups had similar FMI with no significant differences observed between pairs [median 0 kg/m^2 98.33% CI (-0.8, 0.9)] (Table 2).

Dynamic balance

All participants completed the TSLH. There were no significant differences between pairs, with CIs for both outcomes including zero [median − 12.0% leg length 98.33% CI (-80.4, 56.4)] (Table 2).

Effect of sex

Data stratification suggested a potential effect of sex on study outcomes. The point estimates and spread of the differences of study outcomes between matched pairs generally did not show similarities between males and females (Table 3, Table 4). Matched pair differences for males (Table 4) were generally larger than for females (Table 3), where male youth with JIA had a 2.3x greater deficit in MVPA compared to females. Further, median pair differences indicated opposite responses for male and female matched pairs for aerobic capacity and adiposity. Sex may be an effect modifier of TSLH distance in youth with JIA. The median pair difference of TSLH for female participants was 33.2% of leg length, while it was 70.3% for males (Table 3, Table 4). This might suggest that females with JIA performed better than their controls, whereas males performed substantially worse. Therefore, sex likely affects body structure and function outcome comparisons, particularly as male and female youth with JIA had similar levels of disease activity.

Discussion

The findings of this study did not meet the criteria for a statistically significant difference in daily MVPA between youth with JIA with knee involvement and mild disease activity compared to their age and sex-matched healthy peers. However, an observed median difference of 18 minutes less MVPA per day for youth with JIA may be considered clinically relevant. Youth with and without JIA did not appear to differ in aerobic capacity, dynamic balance or adiposity. However, data stratification highlighted the potential effects of sex as a confounder on analyses of physical activity participation and as an effect modifier for dynamic balance.

While the findings of this study did not meet the criteria for a statistically significant difference between pairs, the large lower and small upper limit of the CIs (-44.3 and 2.0 respectively, Table 2) might indicate that, given a larger sample size, youth with JIA could be missing out on clinically relevant level of daily MVPA. These observations are in line with recent studies indicating that youth with JIA spend significantly less time per day in MVPA [8, 35]. The World Health Organization and Canadian 24-hour Movement Guidelines for Children and Youth recommend all healthy adolescents aged 5–17 years old accumulate at least 60 minutes of daily MVPA [6, 23]. However, just under 7% of adolescent Canadians meet these guidelines [36]. In this investigation, 68% of controls and only 32% of youth with JIA accumulated at least 60 minutes of MVPA per day, which is similar to the findings by Lelieveld et al. who reported that 66% of controls and 23% of youth with JIA met current guidelines [37]. The current observation of a median pair difference of 18 minutes less daily MVPA for youth with JIA may be considered clinically relevant as an increase of ten minutes of daily MVPA had a measurable effects on waist circumference and fasting insulin in children and adolescents [38]. Interestingly, stratification by sex indicated that median MVPA pair differences were 2.3x larger for males than females (Table 3, Table 4). While the descriptive summaries have to be treated with caution, due to the small sample of male participants, these findings indicate that sex likely acts as an effect modifier with respect to physical activity participation.

No significant differences in aerobic capacity were observed between healthy controls and youth with JIA (Table 2). This is in contrast to a meta-analysis in 2002 by Takken et al. who reported that children with JIA had a 22% deficit in $VO_{2\ peak}$ compared to reference data [39]. Further, van Pelt et al. identified reduced aerobic capacity in young adults with JIA, both in remission and with active disease when compared to reference data [10]. The comparable levels of aerobic capacity in this study may indicate a successful control of disease activity for participants in this cohort and a generally active population of youth with and without JIA.

Encouragingly, no differences were observed in adiposity between youth with and without JIA. This is consistent with a large longitudinal study by Schenck et al. who found no differences in the BMI for over 5000 youth with JIA compared to the general population [19]. These results were found in a low functional disability, low disease activity JIA cohort, much like the one represented in this study.

No differences in dynamic balance ability (TSLH) were observed between matched pairs. Merker et al. reported similar findings for children with arthritis [40] and speculated that this could be due to long-term

physiotherapy and coordination training prescribed to the JIA cohort. It is interesting that female participants with JIA performed somewhat better than males during the TSLH (females median 33.2% leg length; males − 70.8% of leg length; Table 3, Table 4). Specifically, the magnitude of the differences between males and females indicate that sex might be an effect modifier of the TSLH. These findings highlight the importance of considering sex in research design for studies investigating the consequences of JIA and the response of youth to interventions.

Limitations

This study focused on a subgroup of a youth patient population who have ongoing JIA with knee involvement and no active ankle involvement compared to their matched healthy peers. Consequently, the findings of this study are not generalizable across the population of youth with varying JIA subtypes. Due to sample size considerations, the statistical approach was based on univariate analyses and may not reflect potential interactions amongst covariates. A larger sample size may facilitate multivariable analyses and consideration of potential confounders (e.g. sex, age, JIA subtype, disease severity), which may impact physical activity. Further, the use of PCERT to supplement ActiGraph data during non-wear time may be influenced by recall bias, which may affect resultant MVPA estimates. However, this is the first study in this population to attempt to adjust for limitations of accelerometry and account for non load-bearing activities performed when the device is not worn (e.g. swimming). Further work regarding the validity and reliability of body worn sensors to estimate physical activity in active youth populations is warranted.

Conclusions

The results of this study indicate that youth with JIA are missing substantial time in MVPA and therefore could miss out on the health benefits provided by this level of activity. This study informs research on targeted exercise therapy programs for youth with JIA to restore healthy patterns of physical activity. Furthermore, this investigation reveals that sex should be considered when comparing activity and body structure and function outcomes in youth with JIA. Current work is ongoing to substantiate these findings and quantify the efficacy of exercise interventions to mediate the disease-specific effects.

Declarations

Ethics approval and consent to participate: Ethics approval was granted by the Conjoint Research and Biomedical Ethics (Ethics ID: REB15-3125). Each participant provided or consent to be contacted for inclusion in the study and once they arrived for testing.

Consent for Publication: Not applicable

Availability of data and materials: The datasets generated and/or analysed during the current study will be made available through figshare (fishare.com).

Competing interests: None

Funding: This project was supported by the Vi Riddell Pediatric Rehabilitation Research Program, the Cumming School of Medicine and Alberta Health Services. Additional support was received by the Alberta Children's Hospital Foundation and Alberta Innovates Technology Futures

Authors contributions:

As principle author, CN was responsible for study design, recruitment, data acquisition, analysis and interpretation, and construction of the manuscript. GK was responsible for study inception and design, data acquisition, analysis and interpretation, and drafting of the manuscript. CT performed data acquisition and analysis. SE contributed to participant recruitment and data acquisition and analysis. JB conducted participant recruitment and data acquisition. DM contributed to study inception and manuscript review. MT contributed to study inception and design and manuscript revision. CJ contributed to participant recruitment and data acquisition. LMPD conducted data analysis and interpretation and manuscript revision. JR contributed to study inception and design and manuscript revision. SB was responsible for study inception and design, data acquisition and manuscript revision. CE was responsible for study inception and design, data acquisition, data interpretation and manuscript revision. All authors have approved the submitted version of the manuscript and agree to be personally accountable for the author's own contributions and to address any questions related to the accuracy or integrity of any part of the work presented in this manuscript.

Acknowledgements: We would like to thank the participants and their families as well as all the clinicians at the Alberta Children's Hospital and Richmond Road Clinic for their support**.**

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Tables

ıble 1. Matched participants characteristics by group and sex.

	JIA F (n=16)	JIA M (n=9)	CON F (n=16)	CON M (n=9)
rticipant Characteristics				
e [median (range) yrs]	15.3 (10.6, 20.0)	14.9 (12.1, 18.9)	15.7 (10.1, 19.8)	14.5 (11.7, 18.0)
eight [median (range) kg]	52.0 (28.5, 66.0)	61.1 (48.5, 101.5)	52.8 (34.0, 87.0)	51.0 (34.0, 77.0)
ight [median (range) m]	1.61 (1.34, 1.75)	1.75 (1.60, 1.95)	1.63 (1.44, 1.75)	1.70 (1.42, 1.83)
MI [median (range)]	19.5 (16.0, 25.4)	19.0 (16.0, 31.3)	20.3 (16.4, 32.0)	18.9 (14.9, 23.8)
sease Course				
goarticular [n (%)]	8 (50%)	6 (67%)	N/A	N/A
lyarticular [n (%)]	8 (50%)	1 (11%)	N/A	N/A
A [n (%)]	0 (0)	2 (22%)	N/A	N/A
ne since diagnosis	5.5 (0, 14)	6 (1, 14)	N/A	N/A
edian (range) years]				
ysician Global Assessment of Disease Activity (0-10) [median nge)]	n=13, 0 (0, 1)	n=7, 0.6 (0, 2.5)	N/A	N/A
rent Global Assessment of Disease Activity (0-10) [median nge)]	n=13, 0 (0, 2)	n=4, 0.9 (0, 8)	N/A	N/A
tive Joints				
tive Joint Count	n=14, 0 (0, 1)	n=7, 1 (0, 3)	N/A	N/A
nts with limited ROM	n=14, 0 (0, 1)	n=7, 1 (0, 3)	N/A	N/A
MJ [n]	1 out of 14	2 out of 7	N/A	N/A
oulder [n]	0 out of 14	1 out of 7	N/A	N/A
gers [n]	1 out of 14	0 out of 7	N/A	N/A
ee [n]	3 out of 14	5 out of 7	N/A	N/A

ıle (M); Female (F); Youth with juvenile idiopathic arthritis (JIA); Youth asymptomatic for juvenile idiopathic arthritis (CON); Body ıss index (BMI); and Enthesitis Related Arthritis (ERA).

Table 2. Matched pair differences in study outcomes between JIA and CON.

Outcome	JIA	CON	Matched Pair Differences
MVPA per day (minutes) *	n=22	n=24	n=22
[n, median (min, max)]	45.1 (18.1, 111.9)	72.9 (25.7, 190.6)	-18.6 (-44.3, 2.0) †
Relative VO_{2peak} (mL/ kg/ min) *	n=23	n=25	n=23
[n, median (min, max)]	39.0 (27.3, 66.9)	43.0 (25.5, 60.0)	-0.13 (-5.5, 5.2) ‡
FMI (kg/m^2) **	n=24	n=22	n=22
[n, median (min, max)]	4.4 (2.3, 15.1)	4.4 (1.7, 12.3)	-0.0 (-0.8, 0.9) †
TSLH (% of leg length) **	n=25	n=25	n=25
[n, median (min, max)]	479.8 (332.5, 654.8)	517.4 (380.1, 697.3)	-12.0 (-80.4, 56.4) ‡

Data are presented as means or medians (min, max) for each group and mean or median pair differences (JIA-CON) and confidence intervals (CI). * Primary outcome: 97.5% CI reported; ** Secondary outcome: 98.33% CI reported; † median (CI) reported; ‡ mean (CI) reported. Abbreviations: Juvenile idiopathic arthritis (JIA); Healthy matched controls (CON); Moderate to vigorous physical activity (MVPA); Fat mass index (FMI); Triple single leg hop (TSLH).

Table 3. Comparison of outcomes in females with JIA and female controls			
Outcome	**JIA**	**CON**	**Pair Differences** **Median (Q1, Q3)**
MVPA per day (minutes)	n=14	n=15	n=14
[n, median (min, max)]	44.3 (18.1, 111.9)	66.2 (25.7, 190.6)	-11.2 (-48.2, 6.8)
Relative $VO_{2\ peak}$ (mL/ kg/ min)	n=15	n=15	n=15
[n, median (min, max)]	37.7 (29.7, 51.2)	38.7 (25.5, 52.1)	0.8 (-1.9, 5.5)
FMI (kg/m^2)	n=16	n=14	n=14
[n, median (min, max)]	5.0 (3.1, 6.8)	5.3 (3.4, 12.3)	-0.5 (-0.9, 0.5)
TSLH (% of leg length)	n=16	n=16	n=16
[n, median (min, max)]	483.8 (332.5, 654.8)	500.9 (380.1, 611.6)	33.2 (-80.3, 122.1)

Data are presented as means or medians (min, max) for each group and median and interquartile ranges (Q1, Q3) of pair differences. * Primary outcome: 97.5% CI reported; ** Secondary outcome: 98.33% CI reported. Abbreviations: Juvenile idiopathic arthritis (JIA); Healthy matched controls (CON); Moderate to vigorous physical activity (MVPA); Fat mass index (FMI); Triple single leg hop (TSLH).

Table 4. Comparison of outcomes in males with JIA and male controls

Outcome	JIA	CON	Pair Differences Median (Q1,Q3)
MVPA per day (minutes)	n=8	n=9	n=8
[n, median (min, max)]	52.1 (28.4, 73.5)	81.9 (30.1, 112.5)	-25.9 (-47.3,3.3)
Relative $VO_{2\ peak}$ (mL/ kg/ min)	n=8	n=9	n=8
[n, median (min, max)]	45.6 (27.3, 66.9)	49.3 (35.5, 60.0)	-5.2 (-13.0, 12.6)
FMI (kg/m^2)	n=8	n=8	n=8
[n, median (min, max)]	3.1 (2.3, 15.1)	2.6 (1.7, 4.2)	0.3 (-0.3, 1.7)
TSLH (% of leg length)	n=9	n=9	n=9
[n, median (min, max)]	474.3 (335.9, 629.4)	526.5 (449.2, 697.3)	-70.8 (-125.0, 2.85)

Data are presented as means or medians (min, max) for each group and median and interquartile ranges (Q1, Q3) of pair differences. * Primary outcome: 97.5% CI reported; ** Secondary outcome: 98.33% CI reported. Abbreviations: Juvenile idiopathic arthritis (JIA); Healthy matched controls (CON); Moderate to vigorous physical activity (MVPA); Fat mass index (FMI); Triple single leg hop (TSLH).