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Physical Activity, Adiposity, and Functional Measures in Youth with Juvenile Idiopathic Arthritis Compared to Healthy Controls

by

Colleen Catherine Nesbitt

A THESIS

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Abstract

Objective: To examine habitual physical activity, aerobic capacity, adiposity, and dynamic balance skills in children with JIA, inclusive of knee involvement, compared to age and sex matched healthy controls.

Design: Cohort study with a matched-pair design

Participants: Twenty-five youth with JIA, ages 10-20, (16 female, 9 male) were matched by age and sex to 25 healthy control participants.

Methods: Physical activity data was collected using an ActiGraph accelerometer for 7 days. Aerobic capacity (relative VO_{2peak}) was assessed by a maximal bike test. Adiposity (fat mass index) was evaluated by dual energy X-ray absorptiometry (DXA). Three dynamic balance tests examined balance performance.

Results: No significant difference between groups was found in any of the outcomes after adjusting for multiple comparisons.

Conclusions: Youth with JIA have similar physical activity, aerobic fitness, adiposity, and functional balance ability as their healthy peers. Differences found in physical activity between male groups could have clinical significance.

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Chapter One: **Introduction**

1.1 Problem Statement

Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory disease that affects 1 in 1000 children under 16 years old in Canada.[1, 2] In a 2006 census, an estimated 4350 children ages 5-14 years old were living with juvenile arthritis in Canada.[3] Common symptoms include joint pain, swelling, stiffness, and immobility, in conjunction with muscular weakness, atrophy and contracture.[4] Joint inflammation and systemic symptoms appear in cycles of disease flare and remission.[5] The most affected joint is the knee, followed by the ankle.[5] The aim of treatment is to control the symptoms, preserve the physical joint structures, and prevent long term negative consequences of the disease.[6] Historically, standard practice of care has included pharmacological pain management, rest, and restriction of active physical exercise during flares.[7,8] Habits of inactivity can result from prolonged disease flares and subsequent joint damage, as well as attitudes about physical activity (PA) by parents, physicians, or the patients themselves. [9] Remittent and relapsing symptoms may cause prolonged physical inactivity and a spiral of deconditioning and disability, resulting in an inactive lifestyle.[9] Fear of aggravating disease symptoms causes many patients to delay returning to normal PA patterns.[9] This delay can contribute to or escalate symptoms such as muscle atrophy, muscle weakness, and reduced aerobic capacity.[10]

Patterns of inactivity can affect other aspects of physiology including adiposity, aerobic fitness, and balance skills. Evidence suggests that youth with JIA have increased adiposity, decreased aerobic fitness, and poor balance skills, although diversity in sample populations and methodologies in current investigations prevent the generalization of these conclusions.[4,7,10] The

areas of adiposity and physical function deserve attention as part of a well-focused investigation. As PA decreases and deconditioning occurs, feelings of failure, increased risk of injury, and exacerbation of joint degeneration with PA involvement can occur.[11] PA, experienced as leisure play, sports participation, or social activity, is one of the most important areas of group involvement and peer belonging in a child's life.[12] The social benefits of PA cannot be overemphasized for individuals with JIA, as the primary self- reported concerns of this population are social acceptance and feeling 'left out'.[12, 13]

Emerging evidence suggests PA has no exacerbating effects on disease severity and improves fitness and quality of life.[4] However, children and adolescents with JIA have been consistently found to have decreased physical activity compared to their healthy peers.[3] Most investigations measure minutes spent per day in moderate to vigorous intensity activity, as this allows the activity habits of youth with JIA to be compared to international healthy guidelines for children.[6] Studies are pointing towards the benefits of exercise and PA in youth with JIA for symptom management and increasing health related quality of life, however the best therapeutic program is unknown.[6]

JIA has a heavy societal and individual economic burden. A 2007 study found the total average annual medical cost difference between children with JIA and healthy children was $1686CAN.[14] A study of JIA incidence in Quebec found children visited a physician an average of 17 times in the first year post-JIA diagnosis.[15] While the long-term consequences of JIA are poorly understood, approximately 25% of JIA patients will have active arthritis as adults.[16, 17] With arthritis affecting over 4.6 million Canadians, and those numbers expected to double in the next 30 years, there is great incentive to inform strategies to improve youth JIA health outcomes, and reduce the public health burden through their lifespan.[17]

1.2 Research Purpose

The aim of this project was to examine the differences in physical activity participation, aerobic capacity, adiposity, and balance, in youth with chronic JIA with knee involvement compared to age and sex matched healthy controls. Restrictions on joint involvement and presentation of JIA symptoms were placed on the participants with JIA to avoid confounding factors associated with the heterogeneous characteristics of the disease. A matched design was used to control for confounding by age and sex between the youth with JIA and controls within the study structure.

1.3 Research Objectives

1.3.1 Primary Objectives

1. To examine physical activity, defined as the mean time in minutes per day spent in moderate to vigorous physical activity (MVPA) over 7 days, in youth with JIA including knee involvement, compared to age and sex matched controls participants.
2. To examine the relative aerobic cardiorespiratory fitness, defined as maximum rate of oxygen consumption per mL per kg per minute (relative VO_{2peak}), in youth with JIA including knee involvement compared to age and sex matched healthy control participants.

1.3.2 Secondary Objectives

1. To examine adiposity, defined as fat mass index (FMI), in youth with JIA including knee involvement, compared to age and sex matched healthy control participants.

2. To examine dynamic balance, as assessed by the maximum distance reached on the triple single leg hop (TSLH) test on the dominant and non-dominate leg, expressed as percentage of leg length, in youth with JIA including knee involvement compared to age and sex matched healthy control participants.

1.3.3 Exploratory Objectives

1. To examine physical activity, defined as the mean percentage per day spent in moderate to vigorous activity over 7 days, in youth with JIA including knee involvement, compared to age and sex matched control participants.
2. To examine physical activity, defined as the mean time in minutes per day spent in sedentary and light over 7 days, in youth with JIA including knee involvement compared to age and sex matched control participants.
3. To examine physical activity, defined as the mean percentage per day spent in sedentary and light activity over 7 days, in youth with JIA including knee involvement, compared to age and sex matched control participants.
4. To examine dynamic balance, as assessed by maximum time in seconds achieved on the dominant and non-dominant leg during an eyes-closed dynamic balance (ECDB) test on a foam pad, in youth with JIA including knee involvement compared to age and sex matched healthy control participants.
5. To examine dynamic balance, as assessed by normalized maximum composite reach distances found on a star excursion balance test (SEBT) on the dominant and non-dominant leg in youth with JIA including knee involvement compared to age and sex matched healthy control participants.

6. To compare time spent per day in moderate to vigorous physical activity (min), relative VO_{2peak} (mL/min/kg), fat mass index (kg/m^2), and triple single leg hop (%) outcomes between males with JIA and their same sex healthy peers and between females with JIA and their same sex healthy peers.
7. To graphically assess the association between time spent per day in moderate to vigorous physical activity (min) and each of disease activity (cJADAS10), functional disability (CHAQ), pain (ICOAP), and disease duration (years) in youth with JIA including knee involvement.

1.4 Hypotheses

The above objectives were developed to test the following hypotheses:

1.4.1 Primary Hypotheses

H1: Youth with JIA will participate in significantly fewer minutes of MVPA per day than age and sex matched healthy controls.

H2: Youth with JIA will have significantly decreased aerobic capacity (lower relative VO_{2peak}) than age and sex matched healthy controls.

1.4.2 Secondary Hypotheses

H1: Youth with JIA will have significantly higher fat mass index than age and sex matched healthy controls.

H2: Youth with JIA will jump a lower percentage of their limb length on the triple single leg hop jump on their dominant and non- dominant legs than age and sex matched healthy controls.

1.4.3 Exploratory Hypotheses

H1: Youth with JIA will spend a smaller proportion of their day in MVPA than age and sex matched healthy controls.

H2: Youth with JIA will spend more time per day in SLPA than age and sex matched healthy controls.

H3: Youth with JIA will spend a larger proportion of their day in SLPA than age and sex matched healthy controls.

H4: Youth with JIA will have a shorter maximum time for the eyes closed dynamic balance on their dominant and non-dominant legs than age and sex matched healthy controls.

H5: Youth with JIA will achieve a lower composite score on the star excursion balance test on their dominant and non-dominant legs than age and sex matched healthy controls.

H6: Females and males with JIA will spend less time in MVPA per day, have higher FMI, have decreased aerobic capacity, and achieve a shorter maximum triple single leg hop on both the dominant and non-dominant leg than their healthy same sex counterparts.

H7: A negative association will be observed graphically between time spent in MVPA per day and each of pain, functional disability, disease activity, and disease duration in youth with JIA.

1.5 Research Rationale

This study will inform how JIA impacts the health of youth compared to their peers. It will increase the understanding of the effects of JIA on outcomes that affect participation in sport and recreational activities. Limitations of these activities may negatively influence the psychosocial wellbeing of youth with JIA and impact their health-related quality of life

(HRQoL). Regular PA and exercise has the potential to combat the clinical symptoms of JIA, decrease dependence on pharmacological treatments, and enrich patients' social and psychosocial development. Monitoring adiposity (e.g., fat mass index) provides opportunity for evaluating the trends of adiposity in this population, the risk of secondary chronic disease, and the impact of obesity-related inflammation. Exploring cardiorespiratory fitness and balance can better inform clinical recommendations aimed at improving physical endurance and function in JIA patients. The knowledge gained about the effects of JIA will be used to inform the development and evaluation of a targeted neuromuscular rehabilitation intervention program, aimed at enhancing function, physiological exercise capacity, and health related quality of life in youth with JIA.

1.6 Summary of Thesis Format

This thesis has six chapters, including an introduction, literature review, methods, results, discussion, and conclusion. Chapter One introduces the thesis and includes a problem statement, research purpose, research objectives, research rationale, and summary of the thesis format. Chapter Two contains a literature review, which begins with background information on juvenile idiopathic arthritis including disease characteristics, and management and treatment. Physical activity, adiposity, aerobic capacity, and balance are defined and described for those with JIA and healthy youth. The literature review includes a search strategy, discussion, critique, and summary of the current evidence regarding the physical activity, adiposity, aerobic capacity, and balance outcomes in youth with JIA. Chapter Three describes the methodology of this investigation, including the study design, study population with inclusion and exclusion criteria, procedures, statistical methods, and ethical considerations. Results addressing primary,

secondary, and exploratory objectives, as well as possible confounders are reported in Chapter Four. Chapter Five contains a discussion of the results, including strengths and limitations of the study. The thesis concludes with final statements in Chapter Six, and implications for future research.

Chapter Two: **Literature Review**

2.1 Introduction

2.1.1 Juvenile Idiopathic Arthritis

2.1.1.1 Definition and Prevalence

Juvenile idiopathic arthritis (JIA), previously known as juvenile rheumatoid arthritis, describes a heterogeneous group of seven, clinically distinct inflammatory disease subtypes with onset before the age of 16 years and persistent symptoms for more than six weeks.[5, 18] JIA is the most common childhood rheumatic disease, affecting 0.07-4.01 per 1000 children worldwide, and approximately 1 in 1000 under the age of 16 in Canada.[1 2] JIA is considered a multi-factorial autoimmune disorder with genetic and environmental links but unknown pathogenesis.[18,19] In 2011, The International League of Associations for Rheumatology (ILAR) classified the disease into seven subtypes based on the number of joints involved in the first six weeks of disease and extra-articular symptoms.[19]

2.1.1.2 Disease Characteristics

Active arthritic joints in JIA exhibit swelling, heat, pain, and loss of function.[23] Significant impairment of individuals with JIA can include limited joint range of joint motion, joint stiffness, sleep disturbance, and fatigue.[7] Chronic inflammation can cause growth abnormalities, although general growth retardation is becoming less frequent as availability of treatment improves.[23] Atypical localized growth can include boney overgrowth in affected joints, prematurely fused epiphyses, and leg length discrepancies with the affected limb growing longer. [19] Radiographic damage is found in the joints of all JIA subtypes, with erosion in 25% to 75% of

affected children and joint space narrowing in 14% to 79%, depending on subtype.[20] Systemic and rheumatoid- factor positive polyarticular arthritis exhibit the worst damage.[20]

The presentation of joint inflammation and disease symptoms follow a common pattern of fluctuating periods of disease flare and remission across the subtypes of JIA.[21] Definitions of disease flare and remission are displayed below and are based the American College of Rheumatology (ACR) pediatric core set of six variables (Table 2.1 and Table 2.2).[21] Guzman et al. simplified the below definition as a reoccurrence of systemic manifestations, enthesitis, uveitis, or a physician global assessment of greater than or equal to 10mm.[22] A serious flare is one that requires treatment intensification.[22] This is a definition analogous to the one for adult rheumatoid arthritis.[22] Note that there is no universal definition for defining a flare without reference to a patient's previous condition.

Table 2.1 American College of Rheumatology (ACR) clinical flare definition for juvenile idiopathic arthritis (adapted from Ringold and Wallace (2007))[21]

ACR Pediatric Core Set Components	Clinical Flare Definition
1. Physicians' global assessment of overall disease activity 2. Parent or patient global assessment of overall well being 3. Functional ability 4. Number of joints with active arthritis 5. Number of joints with limited range of motion 6. Erythrocyte sedimentation rate	A minimum of 40% worsening in a minimum of 2 out of 6 components, with no one component improving by more than or equal to 30%

Table 2.2 American College of Rheumatology (ACR) criteria for remission in juvenile idiopathic arthritis (adapted from Ringold and Wallace (2007))[21]

Criteria for Remission	Remission Definitions
No active synovitis No fever, rash, serositis, splenomegaly, or generalized lymphadenopathy attributable to JIA No active uveitis Normal ESR and/or CRP Physician's global assessment of disease activity indicates no active disease	*Inactive disease*: patient meets all the remission criteria
	Clinical remission on medication: 6 consecutive months of inactive disease on medication
	Clinical remission off medication: 12 consecutive months of inactive disease of all anti-arthritis and anti-uveitis medication

The 7 subtypes defined by the ILAR in 2011 include oligoarticular JIA (oJIA), seropositive (rheumatoid factor positive) polyarticular JIA (pJIA), seronegative (rheumatoid factor negative) polyarticular JIA (pJIA), systemic-onset JIA (sJIA), enthesitis-related arthritis (ERA, psoriatic JIA (PsJIA), and undifferentiated JIA.[19, 23] Although these guidelines allow for consistency internationally, problems continue to arise with classification, leaving many designated as undifferentiated JIA.[19] Most research focuses on the oJIA and pJIA, as they make up the most common subtypes and have fewer systemic symptoms.[19] These subtypes are briefly outlined below.

Oligoarticular Juvenile Idiopathic Arthritis (oJIA) is characterized by arthritic involvement of one to four joints in the first six months of the disease.[5,23,]In European and North

American populations, oJIA can account for 50-80% of JIA diagnosis. oJIA predominantly affects young girls. A cross-sectional study in 2007 by the Toronto Hospital for Sick Children reported that 78% of those with the oligoarticular subtype were female.[24] The knee joint is most commonly affected, followed by the ankles.[23] oJIA is exclusive of extra-articular symptoms such as psoriasis and IgM rheumatoid factor, although it carries a high risk of uveitis (i.e., inflammation of the eye) that can cause severe visual impairment.[5,19] Children with oJIA often report restricted mobility and pain in affected joints.[5, 19] Age of onset of oJIA is significantly younger than the other JIA subtypes, peaking between 1 and 3 years of age.[19, 23] oJIA has shorter disease duration than other JIA subsets, however 64% of cases are expected to progress into adulthood.[24] The ILAR discriminates two types of oligoarticular arthritis: persistent and extended.[5] Persistent oJIA occurs if the number of affected joints remains 4 or less during the disease course.[25] It is generally the mildest form of JIA. [25] If the total number of affected joints exceeds four after the initial diagnosis window of 6 months, the diagnosis changes to extended oJIA. [23] Approximately 50% of youth with oJIA will have extended oJIA. [19]

Polyarticular JIA (pJIA) involves five joints or more. This subtype can be further distinguished into immunoglobulin rheumatoid factor (RF) negative pJIA or immunoglobulin rheumatoid factor (RF) positive pJIA. [23] Polyarthritis affects approximately 20% of children with JIA and, of these, 85% have negative tests for RF, although this prevalence varies across ethnicities. [23] Severe extra-articular symptoms are rare in both kinds of pJIA. [5]

Rheumatoid factor negative pJIA is distinguished by absence of RF factor in blood investigations.[23] Rheumatoid factor negative pJIA onset peaks at ages 1-3 years and then again in adolescence.[23] A young age of onset is associated with less favourable long-term outcomes. [23] This subtype is seen in girls more than boys, with the female predominance greater for those

with older age of onset (10:1) than in the younger onset group (3:1).[23] Other than the number of inflamed joints at diagnosis, rheumatoid factor-negative pJIA is often difficult to distinguish clinically from oJIA.[5] Children that do not show remission of this subtype by age 16 are more likely to have ongoing active arthritis into their early 30s.[23]

Rheumatoid factor positive pJIA is determined if rheumatoid factor is detected in the blood on at least two occasions 3 months apart.[23] This subtype is generally more severe and persistent than rheumatoid factor negative pJIA, and shares similar serology, immunogenic profile, and clinical phenotype as adult rheumatoid arthritis.[23] The mean age of onset is 9 to 11 years (range 1.5-15 years). Rheumatoid factor positive pJIA is seen in girls more than boys, with reported ratios ranging from 4:1 to 3:1 (girl:boy) in different investigations.[24] This subtype is most prevalent in non-Caucasian ethnicities (e.g., accounts for 51% of all JIA cases in Indigenous Canadians). [24]

2.1.1.3 Diagnosis

There is no definitive laboratory test to determine presence of JIA, therefore it is diagnosed based on clinical examination and exclusion.[25] In addition, joint pain is confounded by differential diagnoses including growing pains, Lyme disease, viral infection, Faber's disease, idiopathic inflammatory myothpathies, and post-streptococcal reactive arthritis.[25]

Laboratory tests can support a JIA diagnosis and provide insight into subtype specificity. Blood work can reveal high erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), although levels are variable even in children with active JIA.[25] Tests for rheumatoid factor

protein cannot diagnosis JIA, but can distinguish between ILAR classifications of subtypes once the diagnosis has been determined.[23]

2.1.1.4 Management and Treatment

Persistent disease activity is the most important determinant of poor overall health outcomes for youth with JIA, including quality of life.[20] Unlike in adult arthritis, spontaneous remission of JIA occurs.[16,17] Depending on subtype of JIA, probability of remission within 10 years of onset varies 30% to 35%.[16,17] A 2005 Canadian study estimated 65% to 70% of youth with JIA will require treatment into adulthood, although a 2015 Danish study estimated a range of 41-78%.[9,20] The rate of disease remission is highest in oligoarticular arthritis (approximately 50%) and lowest in rheumatoid factor-positive polyarticular arthritis (approximately 5%).[20] No predictive factor for disease latency in adulthood has been identified.[20] Sustained remission off medication for more than 5 years is still unattainable for most.[26] Although inactive disease is ideal, acceptable disease control is a valid alternative treatment goal.[26]

Current guidelines for treatment of JIA call for the integration and collaboration of a multidisciplinary team including, but not limited to, rheumatologists, physiotherapists, occupational therapists, ophthalmologists, and pediatricians.[23] Parents are an important part in the circle of care, influencing the child's treatment pathway and adherence.[23] Parent and patient education are important aspects of treating a child with JIA.[23]

Management of JIA begins with pharmacological therapies to control symptoms.[26] Standard practice of care for JIA has been pharmacological pain management, rest, and restriction of active physical exercise.[7] Currently, evidence points to a 'window of opportunity' for early and aggressive drug treatment against articular damage.[26] This 'top-down' medication

regime employs the use of newer biological drugs more often and at earlier stages of the disease.[27] The development of biologic disease-modifying anti-rheumatic drugs (DMARDS) has revolutionized the management of JIA by improving the efficacy, decreasing toxicity, and increasing tolerability of treatments.[19, 26] Methotrexate is the most widely used DMARD for JIA and is administered via subcutaneous injections or taken orally. [19] It is recommended as an initial therapy for all subtypes of JIA to control peripheral arthritis, following a trial of non-steroidal anti-inflammatory drugs (NSAIDS) in youth with oJIA.[26] It is usually tolerated quite well.[26] In times of acute flare-up, glucocorticoids (GCs) are routinely used to efficiently manage inflammation.[26] Prolonged therapy with GC agents has been significantly associated with increased obesity, insulin resistance, hypertension, and the development of metabolic syndrome.[26] Despite these side effects, they have gained acceptance as a short-term 'bridge therapy' prior to prescribed long acting agents taking effect.[26]

Physical therapy and occupational therapy are important aspects in the management of JIA to reduce pain, long term morbidity, and psychological impacts of JIA.[5,19, 26] Physical therapy aims to preserve range of motion, improve muscle strength and endurance, minimize pain and inflammation, and limit strain on arthritic joints. [6] Treatments include thermotherapy, kinesiotherapy (including range of motion exercises, strengthening, and motor patterning), massage, and electrical stimulation.[6, 23]

In addition to physical outcomes, it is important to recognize the mental impact that JIA and associated chronic pain can have on the child or adolescent and their families.[26] Psychologists should be included in the multidisciplinary team in the management of individuals with JIA.[26]

2.1.2 Physical Activity

A 2008 review investigating adolescents with JIA defined physical activity (PA) as a "behaviour that is characterized by any bodily movement that results in energy expenditure above the basal level".[28] This includes all leisure and non-leisure pursuits.[29] Habitual PA is defined as PA that is carried out within the context of daily living.[30] Physical fitness can influence PA. Physical fitness is a set of attributes that relate to an individual's ability to perform physical activity.[31] PA can be categorized based on intensity into sedentary, light, moderate, and vigorous activity. These exertion levels can be determined based on percentage of an individual's maximum heart rate (HRmax), metabolic equivalents (METS), and/or rate of perceived exertion (RPE).[32] One MET is equivalent to a resting metabolic rate, which utilizes 3.5mL O_2/kg/min.[32] Therefore 6 METS can be interpreted as 6 times the resting metabolic rate.[32] METS may vary for different activities depending on an individual's age, fitness level, and health status.[32]

The Canadian 24-hour Movement Guidelines for Children and Youth recommends all healthy youth between 5 and 17 years old accumulate at least 60 minutes of moderate to vigorous physical activity (MVPA) per day.[33] Canada's 2016 Report Card on Physical Activity for Children and Youth found only 5% of school-aged children met Canada PA recommendations.[34] In individuals 18-39 years old, only 19% met Canadian Physical Activity Guidelines for Adults of 150 minutes of MVPA per week.[34] Those who achieve the recommendations of 60 minutes or more of MVPA per day have better weight control and are less likely to suffer chronic illness in adulthood.[6] The Canadian Sedentary Behavior Guidelines also recommends limiting screen time to 2 hours or less per day for those ages 5-17 years old.[33, 34] Thirty- one percent of 12 to 17 year olds met the guidelines for sedentary activity and screen time usage.[34]

2.1.2.1 Physical Activity and Youth with JIA

The main objectives of the current treatment guidelines for JIA during a flare are to control inflammation and pain, and improve quality of life.[35] Conventionally, physicians warned against PA during flares in order to limit strain, pain and swelling in affected arthritic joints. [36] Youth with JIA are often discouraged from activity and sports participation due to real or perceived limitations imposed by their disease.[37] Fear of injury or lack of self-confidence on the part of the child/adolescent and/or their parents, may prevent vigorous activity.[38] In addition to time and cost constraints, individuals with JIA mention disease symptoms such as pain and fatigue as interfering with PA.[13] Persistent symptoms of the disease cause many youth with JIA to have difficulties with endurance sports due to increased submaximal energy expenditure, to experience biomechanical deficits in neuromuscular control, and to encounter exercise-induced pain from pro-inflammatory cytokine release.[12, 39]

In a 2006 Canadian national survey on leisure activity in children with JIA, data indicated that only 33% participated in physical activity daily and 70% participated in PA only once weekly.[3] Markula-Patjas et al. report that 53% of youth with JIA reported limited participation in school PA. [21, 40] Norgaard et al. and Herlin et al. reported a similar trend in the Danish population, finding that in their sample of 68 adolescents with JIA, 38% were not active in sports, citing pain and shortness of breath.[41] In Canada, 61% of parents noted their child's need for assistance as the most likely explanation for limited PA.[3] However, Klepper and Takken et al., consistently reported that children and adolescents could participate safely in PA, even weight-bearing exercise.[42]

Children with low physical activity during growth can experience delays in fundamental motor skills, muscle atrophy, diminished aerobic capacity, and decreased bone density.[43, 44, 45] In

addition, inactivity increases risk for chronic health conditions, such as obesity, hypertension, diabetes, cancer, coronary disease, and osteoporosis in adulthood.[27, 43, 45] Inactivity in children with chronic illnesses is likely a more permanent state than in their healthy peers, as a sedentary lifestyle can put them even further behind in normal physical development.[42] Much like adults with rheumatoid arthritis, children and adolescents with JIA may need more rigorous training to prevent risks of chronic illness associated with a sedentary lifestyle.[46]

Encouraging youth with JIA to participate in PA is becoming a major focus of treatment.[47] In 2002, the Exercise and Physical Activity Conference Arthritis Working Group recommended children with JIA can engage in moderate aerobic and strengthen exercises.[47] Following this, the Canadian Pediatric Society and Canadian Academy of Sport and Exercise Medicine have published recommendations supporting regular physical activity in children with arthritis, including guidelines for involvement in impact and competitive sport.[47]

2.1.3 Adiposity

Adiposity refers to the fat content of an individual's body composition. The term overweight or obese refers to an accumulation of body fat that may impair health.[48] There has been a significant increase in youth aged 12-17 years old classified as overweight or obese, increasing from 19.5% in 2005 to 23.1% in 2014.[49] Specifically, 6.2% of youth in this age group were classified as obese and 16.9% were classified as overweight, based on self-reported heights and weights.[49] The prevalence of excess weight in all Canadian youth has nearly doubled over the last four decades, putting many youth at risk for secondary chronic conditions, and comorbidities into adulthood.[49] Overweight and obese children have an increased risk of becoming overweight adults.[50] Co-morbidities associated with obesity include dyslipidemia,

insulin resistance, increased risk of cardiovascular disease, increased systolic blood pressure, and increased levels of inflammatory markers.[51]

2.1.3.1 Adiposity and Youth with JIA

The most common clinical measure for adiposity is body mass index (BMI). BMI is calculated as weight in kilograms divided by height in meters squared, and in children is standardized and classified using Z-scores (Z-BMI) or percentiles.[40] Although widely used in literature and in practice, BMI cannot distinguish between fat mass and lean (non-fat) mass and therefore doesn't accurately capture fat content.[52, 53] In children with JIA, even BMI adjusted values can be confounded by height, as some in this population have stunted growth.[12] Adiposity has also been investigated in children with JIA with measures including fat mass index, lean mass index, total fat percentage, waist circumference, truncal fat, and sums of skinfolds.[40, 54, 55, 56] Dual Energy X-ray absorptiometry (DXA) has also been used to capture measures of adiposity.[54] DXA has strong correlation with other gold standard measurements such as underwater weighing and isotope dilution, and has reported excellent precision when evaluating total adiposity.[33,54]

Fat mass index (FMI) is calculated by dividing total fat mass (kg) by height squared (m^2). FMI can be used to differentiate between gain in fat versus gain in fat free mass during times of rapid body composition changes (e.g., puberty), and is useful to differentiate adiposity independent of fat-free mass.[54, 55]

Children and adolescents with JIA are at increased risk of weight gain due to patterns of inactivity and medication use.[57] Prolonged glucocorticoid steroid use increases visceral fat deposition and increases body fat mass.[40] Biologics have also been linked to excessive weight gain.[57] As well, chronic inflammation, such as that associated with JIA disease flares, is

increasingly seen as significantly contributing to the risk of obesity and metabolic syndrome. [58] In youth with JIA, obesity may be of increased concern, as it has been shown adipocytes overproduce pro-inflammatory cytokines contributing to low-grade inflammation.[18]

In adults with rheumatoid arthritis, cardiovascular mortality rates are 50% higher than the general population, making it the leading cause of death in the RA population.[59] Adults with RA show signs of accelerated atherosclerosis which have been speculated to be attributed to increased body weight, decreased physical activity, and side effects of common medication, among other risk factors.[59] Due to the overlaps seen in the pathogenesis of RA, atherosclerosis, and JIA, concern is growing that youth with arthritis may share similar increased cardiovascular risks.[59, 60] Monitoring adiposity in youth with JIA has never been more important.

2.1.4 Functional Outcomes

Physical fitness is a multidimensional concept that includes all the attributes people possess to perform activity, such as cardiorespiratory endurance, strength, flexibility, and balance.[61] Cardiorespiratory endurance, also defined as aerobic fitness or aerobic capacity, is the ability to perform whole-body exercise for extended periods at moderate to high intensities.[62]

The 2007-2009 Canadian Health Measures Survey testing youth from 6-19 found aerobic fitness was higher in boys than girls, and decreased with age among both sexes.[47] Globally, there is a recognized decrease in aerobic fitness in youth.[63] This trend is not explained completely by increases in childhood obesity, suggesting trends in decreasing physical activity may contribute to decreased aerobic fitness.[63] Aerobic fitness has been positively associated to with time spent in vigorous physical activity.[64]

Dynamic balance can be defined as the ability to perform a prescribed movement while maintaining a stable position.[65] Balance skills are fundamental to execute technical movements in sports, as well as tasks of daily living.[65] Increased motor competence has been found to be linked to an increased ability to balance in children 4-6 years old and 9-10 years old.[64, 66] Low aerobic fitness and poor balance are functional outcomes that are highly linked to low physical activity participation and weight gain.[64, 66]

2.1.4.1 Functional Outcomes and Youth with JIA

Impairments in physical fitness result in decreased participation in higher intensity physical activities, decreased participation in sports, and an overall decrease in quality of life.[67,] Low aerobic fitness is a significant risk factor for comorbidity.[67,68] Maintaining a minimum aerobic capacity is important in order to perform daily activities.[92] Starting at age 18, aerobic capacity begins to naturally decline.[92] Adolescents with attenuated aerobic fitness are at risk of reaching minimal functional aerobic capacity as many as 20 years earlier than healthy peers.[67, 69] This would significantly affect an individual's functional mobility and health-related quality of life as he or she ages.[67]

Dynamic balance tests such as hop tests and star excursion balance tests have been developed to gauge readiness to return to activity after injury or surgery, most notably for those with anterior cruciate ligament injuries.[70] These tests assess dynamic knee stability while giving indications of overall function of the knee joint.[71] No research has investigated how these tests could clarify any deficits seen in children with JIA, or how they could be used as a tool in rehabilitation programs. In adults with knee osteoarthritis, inflammation disturbs the proprioceptive receptors of the joint, causing decreased balance skills.[72] This same mechanism

could be at work in the joints of youth with JIA, putting them at an increased risks of both sustaining injury and avoiding physical activity.[73] In addition, the symptoms of JIA cause progressive joint deterioration and deformation, which could also affect balance ability.[74]

The objective of this literature review is to examine the existing research on current trends in physical activity, adiposity, and functional outcomes, including aerobic fitness and balance, in youth with JIA compared to control or reference data. A critical appraisal of the existing body of knowledge is included.

2.2 Methods

2.2.1 Data Sources

Four databases were searched for relevant articles in August 2017: Medline (OVID), PubMed, Embase, and CINHAL. Searches were sorted by relevance. Reference lists of the selected articles were searched for any relevant studies that may have been missed in the database search.

Table 2.3 Medical subject headings and text words used for article extraction

Medical Subject Headings (MeSH) *also used as text words in each search	Text words (tw)
1. juvenile idiopathic arthritis	11. juvenile rheumatoid arthritis
2. Arthritis, Juvenile	12. child arthritis
3. physical activity	13. activity
4. exercise	14. Body Weight
5. Motor Activity	15. Fat
6. Body Composition	16. VO_{2max}
7. Adiposity	17. Athletic performance
8. Obesity	18. Fitness
9. Aerobic fitness	19. Hop
10. Balance	20. Single leg hop
	21. Star excursion balance test

2.2.2 Search Terms

A. Juvenile Arthritis: 1 OR 2 OR 11 OR 12

B. Physical Activity: 3 OR 4 OR 5 OR 13

C. Adiposity: 6 OR 7 OR 8 OR 14 OR 15

D. Aerobic Fitness: 9 OR 16 OR 17 OR 18

E. Balance: 10 OR 19 OR 20 OR 21

F. Physical Activity in youth with JIA: (1 OR 2 OR 11 OR 12) AND (3 OR 4 OR 5 OR 13)

G. Adiposity in youth with JIA: (1 OR 2 OR 11 OR 12) AND (6 OR 7 OR 8 OR 14 OR 15)

H. Aerobic Fitness in youth with JIA: (1 OR 2 OR 11 OR 12) AND (9 OR 16 OR 17 OR 18)

I. Hop ability in youth with JIA: (1 OR 2 OR 11 OR 12) AND (10 OR 19 0R 20)

2.2.3 Search Strategy

Each search was sorted by relevance and every title returned was reviewed. If the title indicated that the study addressed juvenile idiopathic arthritis in the context of the variable (physical activity, adiposity, aerobic fitness, or hop distance), then the abstract was used to determine if the study was appropriate to include in the literature review.

2.2.4 Study Selection Criteria

Inclusion Criteria:

1. Population included youth under 25 years old with juvenile idiopathic arthritis
2. English Language
3. Peer-reviewed article
4. Study's primary outcome variables included:
    - Physical activity as defined as time spent in physical activity per day, in youth under 25 with JIA compared to a control sample or reference data
    - Aerobic fitness defined by a measurement of maximum oxygen consumption in mL/ min (VO_{2max} or VO_{2peak}) during a graded exercise test in youth under 25 with JIA compared to a control sample or reference data
    - Adiposity defined as measures of fat mass in youth under 25 with JIA compared to a control sample or reference data.

- Balance ability in youth under 25 with JIA compared to a control sample or reference data

5. Research design included reviews, randomized control trails, quasi-experimental, pre-experimental, cohort, case-control, cross-sectional, or case series.

Exclusion Criteria:

1. Non-English language
2. Full article not retrievable
3. Study assessed an exercise intervention
4. Case studies

2.2.5 Data Extraction

Data were extracted from all articles that met study inclusion criteria. Study design, study population, method applied for finding primary outcome variables, and the results of each test specific to the variables of interest (physical activity, adiposity, aerobic fitness, or hop distance) were extracted.

2.2.6 Critical appraisal methods

Studies were critically appraised for bias and misclassification based on the study's stated purpose and final outcomes, study design, participant selection, and statistical analysis.

2.3 Results

Searches were conducted separately for each outcome variable of interest in this scientific review. Using the above search strategy, the following articles were found from all electronic databases in relation to each outcome variable after title and abstract review:

A. PA and JIA: 161 articles

B. Adiposity and JIA: 47 articles

C. Aerobic and JIA: 57 articles

D. Hopping and JIA: 0 articles

Searches related to hopping abilities of youth with JIA returned no articles. The search terms were altered to look for any investigations into balance and youth with JIA compared to a control sample or reference data, using the additional text word “dynamic”. This second search returned three articles.

After assessing the full text for eligibility based on inclusion and exclusion criteria, as well as duplicates, the following number of articles were included in the review for each outcome variable.

E. PA and JIA: 12 articles

F. Adiposity and JIA: 8 articles

G. Aerobic and JIA: 9 articles

H. Balance and JIA: 3 articles

2.3.1 Current Evidence on Physical Activity Trends in Youth with JIA

The literature search resulted in identification of 11 studies investigating PA levels in the JIA population compared to a control population. In the earliest study found, Henderson et al.

used two accelerometers to capture data in the vertical and horizontal planes, as well as a 3 day activity diary to determine activity levels.[75] It found mean recorded physical activity in the diary was significantly lower in youth with JIA (at that time defined as juvenile rheumatoid arthritis) versus healthy peers of a similar age (CON).[75] However, bodily movement counts, as captured by the Caltrac actigraphs, was not significantly different between the two groups. The children with JIA spent more hours sleeping [mean (sd) = 11.0hr (0.7) (JIA) and 10.3(1.0) (CON), p=0.02] and less hours in strenuous activities per day than the control group [mean (sd) = 0.2(0.3) (JIA) and 0.7 (1.4) (CON), p< 0.01].[75] Studies by Lein et al. in 2005 and Felin et al. in 2007 report decreased PA in a JIA population, however, they only evaluated weight-bearing physical activity.[27] Tarakci et al. also reported their JIA sample spent significantly less time in PA than age and sex matched controls as reported by a 1 day activity diary and converted into MET/day [mean (sd) = 34.27 MET/day (3.35) (JIA) and 39.01 MET/day (3.10) (CON), p<0.0001].[76]

In 2008, Lelieveld et al. used a 3-day activity diary to compare the physical activity habits of 30 youth with JIA with reference data from 106 controls of similar age [mean (sd) age 17.0 (0.6) and 16.7 (0.9) years, respectively).[28] They reported that 23% of the JIA group met public health recommendations of 60 minutes or more of moderate to vigorous physical activity (MVPA) per day, while 66% of the controls met the recommendations.[28] Overall, youth with JIA spent significantly less time (in hours) versus controls in activities with moderate [mean (sd) = 0.29 (0.53) vs 0.73 (0.77), p <0.01] and high intensity [mean (sd) = 0.36 (0.49) vs 0.61 (0.59), p <0.05], as well as in competitive sport [mean (sd) = 0.07 (0.18) vs 0.36 (0.50) , p<0.01].[28]

Two studies in 2014 used activity diaries to evaluate PA.[46, 77] Gueddari et al. used a one day activity diary to record activity every hour.[46] PA habits of 50 youth with JIA (mean age

11.5) were compared to 50 controls (mean age 10.4).[46] They found 30% of youth with JIA completed 60 minutes of MVPA per day.[46] They spent a mean of 60 min/day on low intensity PA and 15 min/day doing moderate intensity PA activities.[46] Limenis et al. mailed out activity questionnaires to a random sample of 50 youth with JIA, asking for details on the time and type of PA completed in the last 7 days.[77] The mean PA score calculated from the questionnaires returned by the JIA sample was significantly lower the mean scores from two previous studies on healthy youth that used the same questionnaire and methodology.[77]

Hulsegge et al. used PA questionnaires to compare the PA levels of youth 7-15 years old with JIA to control statistics from Australian national databases.[78] PA levels were evaluated with the Adolescent Physical Activity Recall Questionnaire, which asks about hours of participation in organized and non-organized sport over the course of a week. When they stratified the results seasonally, they found only 57.1% of children with JIA met PA recommendations of 60 minutes or more of MVPA in the summer, which dropped to 35.7% in the winter. Matched data from the control database showed that in healthy youth, 78.7% met the recommendations in summer, and 72.3% in winter. [78] This study also tested functional movement skills in a series of running, jumping, and throwing tests, and found no difference in the proportion of children with JIA that had mastered these skills compared to healthy controls.[78]

As advances in wearable fitness technology have been made, two recent studies have employed accelerometers to measure PA in youth with JIA. Bohr et al. and Norgaard et al. used the ActiGraph accelerometer to compare youth with JIA, respectively, with healthy children reference data collected in The European Youth Heart Study (EYHS) (2004) and in The Copenhagen School Child Intervention Study (CoSCIS) (2012).[9,44] Both studies matched control data to their participants by age and sex.[9,44] Over 7 days of PA monitoring, Bohr found 45% of

boys with JIA and 19% of girls participated in 60 minutes or more of MVPA. This was lower than the 61% and 39% of healthy boys and girls that reached 60 minutes of MVPA, respectively.[9] Children and adolescents with JIA spent significantly less minutes in moderate activity [mean (sd) 48.4min (24.7)] compared to controls [mean (sd) 53.8min (no standard deviation reported), (p=0.0001)]. This was also the case for vigorous activity where youth with JIA spent a [mean (sd) of 24.7min (16.3)] versus controls who accumulated 26.5min (no standard deviation reported), (p=0.00015). This trend was substantiated by Norgaard et al.[44] The children with JIA accumulated less time in moderate intensity activity [mean (sd) 97.1min (40.4)] compared to controls [mean (SD) 117.2min (23.5)], and less time in high- intensity activity [mean (sd) 31.3min (19.4)] compared to controls [mean (SD) 38.6min (7.7), (p=0.002)].[44]

Finally, Bos et al. compared the PA habits of 76 youth with JIA and 131 controls with a 7-day activity diary.[79] Only 4% of those with JIA engaged in MVPA for 60 minutes a day, while 16% of controls met that standard.[79] The JIA sample spent a mean (sd) of 1.3 (0.8) hours/ day in MVPA versus 1.8 (0.2) hours/ day by controls.[79]

Several of the studies considered disease and lifestyle factors that may affect PA. Gueddari et al. found no significant relationships between levels of PA and disease duration, disease activity, functional ability, and pain.[46] Interestingly, Bos et al. found increasing pain correlated with more time spent per day in MVPA.[79] This conflicted with results from Norgaard et al., and Limenis et al. who found decreased PA, specifically MVPA, correlated with increased functional disability, number of active joints, disease activity, and decreased well-being. [,44, 77,] Norgaard et al. reported youth with rheumatoid factor positive polyarticular JIA had the lowest measures of accelerometer reported PA.[44]

2.3.1.1 Critical Appraisal of Current Literature on Physical Activity Trends in Youth with JIA

Measuring PA is a difficult task for researchers.[27] Doubly labelled water and direct calorimetry are gold standard measurement techniques to determine energy expenditure, however, these are expensive, not readily available, and cannot discriminate time spent in different intensities of activity.[27] They also do not provide information on the type of activity performed. None of the included studies used these methods. The most common tools remain questionnaires and activity diaries, which are uncomplicated, inexpensive, and attempt to capture PA data in a variety of ways.[46] However, these have varying levels of validity in the JIA and youth populations, and are prone to over-reporting bias.[7,27,] In addition, spontaneous activity performed in short bouts, as is characteristic of children, is difficult to capture in questionnaires.[27] Many of the studies have a sample population that spans the transition into adulthood, yet the questionnaires used are specific to either adults or children.[80] The variety of questionnaires used limits the ability to compare results from different investigations. Each study above that utilized an activity diary had to estimate intensity of activity. This was done either by a scoring system created for that specific questionnaire, or by using a reference chart that assigned different intensities or METs to different activities. The heterogeneity restricts the ability to address if children and adolescents with JIA are meeting the global and national recommendations of 60 minutes of MVPA per day implicated for lifelong wellness.

The use of objective tools to measure PA is growing. Good to excellent reliability and validity has been established in objective activity monitors such as accelerometers and pedometers in healthy children.[63] Those results are extending to populations with chronic disease.[30] Activity monitors allow researchers to have a quantifiable, minute by minute 'count'

of their participants' movements, without the cost and time requirements of direct observation.[45] Accelerometery has the potential to capture the four key aspects of PA (e.g., frequency, intensity, time, and type of activity).[3, 76] However, studies using accelerometry with JIA cohorts either lack control comparison groups or did not gather control PA data concurrently with JIA data collection.[9,44,75,81] In addition, use of the Caltrac activity monitor, as seen in Henderson et al., requires study participants to reliably note the movement counts at the beginning and end of each day so that PA can be measured.[75] It does not allow for the determination of PA intensity throughout the day.[75] Instead, PA intensity is calculated much like the diary method, by connecting recorded activities to pre-determined calculations of METS.[75] Studies by Norgaard et al. and Bohr et al. used ActiGraph activity monitors.[9,44] However each study imputed activities where the device was taken off (e.g., swimming) and/or was predicted to not capture the data accurately (e.g., cycling and horseback riding) with different methods.[9,44] Different estimation procedures can over or underestimate the amount of PA making comparison between studies impossible. In the case of these two studies, both authors reported time spent in imputed activities was not significant and did not affect the overall outcome. Unfortunately, these claims were not supported by statistical evidence.[9,44]

Several studies used control data from previously collected studies on healthy youth. While these studies matched with similar age and gender, most failed to mention how the matches were made (e.g., 3:1, 1:1). In addition, many did not mention if control data were collected within a reasonable time frame of the JIA data, making the comparisons vulnerable to various environmental confounders such as season or natural weather patterns (e.g., smoke, monsoon).

JIA cohort sample sizes in the above studies ranged from 23 to 133. It is difficult to determine if these samples hold statistical power based on the diverse methods used to collect PA data, and lack of sample size calculations in all but one publication.[28]

2.3.1.2 Summary of Evidence on Physical Activity Trends in Youth with JIA

Overall, there is sufficient evidence to conclude that individuals with JIA participate in less PA then their peers, specifically avoiding MVPA and spending more time in sedentary activity or sleeping.[45] In addition, fewer children and adolescents with JIA meet the World Health Organization International Guidelines of 60 minutes of MVPA per day than their healthy peers. [7] Several organizations, such as the Canadian Academy of Sports Medicine and the American Academy of Pediatrics provide guidelines for sport participation by adolescents with JIA, however, there is currently no consensus on what kind of PA is optimal for promoting positive disease outcomes.[39,82] This could be due to the fact that no disease characteristic (e.g., pain, disease activity) have been consistently linked to impaired PA participation. Many youth with JIA cite fear of pain or worsening of condition as reasons to avoid PA.[20] Their parents reflect these concerns.[20] However, lower levels of PA have been associated with more severe and bothersome joint pain, more joint swelling, decreased range of motion (ROM), and higher disease activity.[11,44,77,83] Furthermore, exercise programs have been shown to improve energy levels, self-efficacy, and quality of life in JIA.[84] Importantly, a systematic review of exercise programs targeting youth with JIA found none of the regimes reported exercise exacerbated the patient's arthritis symptoms.[23, 84, 85] In addition to the familiar benefits of exercise, youth with JIA may reap additional benefits from exercise including anti-inflammatory effects, as has been

seen in adults with rheumatoid arthritis.[77] PA could be a useful therapeutic modality to counteract inflammation and improve disease symptomatology in children with JIA.

2.3.2 Current Evidence on Adiposity Trends in Youth with JIA

The literature search revealed 8 studies that investigated adiposity in the JIA population compared to controls. Early studies by Mortensen et al. and Haugen et al. indicate reduced body weight in individuals with polyarticular JIA compared to control data ($p=0.05$ and $p=0.001$, respectively).[86, 87] In a 2011 study, Amine et al. found 41.4% of children with JIA (age 2-16) were overweight, 22.4% were obese, and 36.2% were of normal weight as assessed with BMI matched on age and sex to French reference curves of healthy youth. A total of 60% of their JIA cohort was overweight.[29] Similar results were found in following studies using various methods to measure adiposity. Caetano et al. used DXA scanning to compare a sample of 42 girls with JIA to sex-matched healthy controls and found the JIA cohort had higher median Z-BMI scores.[54] Using skinfold measurements, Gronlund et al. found 30% of their JIA cohort, ages 3-10, were obese or overweight, compared to 12.5% of the age and sex matched control cohort. [88] Markula-Patjas et al. used fat mass percentage from DXA scanning to conclude significantly more youth in their sample of 49 with polyarticular JIA were overweight or obese than age and sex matched controls.[40] Interestingly, in the most recent cross sectional study, Jednacz et al. found the BMI of their sample of 30 youth with JIA (11-17 years old) was significantly lower than 20 healthy controls of similar age and sex distribution (18.6 ± 2.2 vs 20.1 ± 2.3, $p=0.0302$). The authors also found the JIA cohort had lower percent body fat, but was not statistically significant.[89]

The above studies had JIA sample sizes ranging from 15-58 participants. The majority of their results are in contrast to a large longitudinal study (2003-2012) by Schenck et al. in Germany. Schenck et al. compared the BMI of over 5000 children and adolescents with JIA to the general German population under 18 years of age and found no difference in the prevalence of overweight or obese youth in the two populations.[29] However, over the course of the study, over half of those with JIA reported no functional limitations, and disease severity scores indicated mild disease activity.[29]

Several investigations considered factors that may influence fat mass in youth with JIA. High dose GC's, male sex, higher functional limitations, low level of physical activity, high pain levels, greater number of active joints, and longer disease duration were all linked to increased weight or fat mass.[29,40, 54, 57, ,86, 87, 88, 90] However, Schenck et al. found a high prevalence of central and peripheral obesity even in youth with lower levels of inflammation.[29] Obesity is likely linked to factors other than disease severity or activity.

2.3.2.1 Critical Appraisal of the Current Literature on Adiposity in Youth with JIA

An important consideration when measuring adiposity in this population is the confounding effects of pharmacological treatments. In times of acute flare-ups, glucocorticoids (GCs) are routinely used to efficiently manage inflammation.[29] Prolonged therapy with GC agents has been significantly associated with increased obesity, insulin resistance, and hypertension, as well as the development of metabolic syndrome.[29, 52] The studies cited used samples with a mix of active and inactive disease, in various phases of pharmalogical therapy. Most studies were unable to stratify by medication use due to small sample sizes.

Many of the current studies have used small sample sizes and targeted populations, limiting the ability to generalize the results. Generally, there has been good use of control groups, with most cohort studies matching on age and sex. When control groups are not included, authors tend to use BMI reference curves from longitudinal population studies.[29] This can be misrepresentative, as adolescents with JIA can experience growth retardation. [86] Using BMI as an outcome also fails to account for fat mass versus lean mass, which can be a critical distinction in children at various stages of maturation.[91]

2.3.2.2 Summary of Evidence on Adiposity Trends in Youth with JIA

Past investigations continue to use heterogeneous methods of measurement to determine adiposity, which hinders the comparative value of the results. In addition, many investigations fail to account for potentially important covariates such as disease subtype, pubertal stage and medication use.[40, 54] Obesity in children and adolescents with JIA may be of increasing concern, due to increased risk of comorbidities into adulthood, and adipocyte effects on systemic inflammation.[35] There is a general understanding from the literature that youth with JIA have more fat mass than their healthy peers, although there is limited evidence to support that the difference is clinically significant, or universal to each JIA subtype.

2.3.3 Current Evidence on Functional Outcomes in Youth with JIA

A literature search was undertaken for studies relating to aerobic capacity and balance in children with JIA. The literature search provided two reviews and seven original articles directly investigating maximal oxygen uptake (VO_{2peak}) through graded exercise testing in the JIA

population versus healthy controls.[67] Three studies explored balance in youth with JIA compared to a control cohort.[72]

Nine original papers were found investigating aerobic capacity in children and adolescents with JIA, the majority of which are detailed and analyzed by two reviews on the topic. A 2002 systematic review and meta-analysis on aerobic capacity by Takken and colleagues is widely referenced for attenuated VO_{2peak} in JIA patients.[92] They found five studies that investigated aerobic fitness in youth with arthritis, at that time defined as juvenile rheumatoid arthritis (JRA).[92] Studies by Malleson et al. found no difference in VO_{2max} between age and sex matched controls and children with JRA (ages 8-17).[92] On the contrary, separate studies by Giannini and Protas, Golebiowska et al., and Takken et al., found impaired aerobic fitness in their JIA cohorts.[92] Each study used different ages, JIA subtypes, and control groups. Malleson et al., Giannini and Protas., and Giannini and Protas., compared youth with JRA matched by sex and similar age to healthy controls.[92] Takken et al. and Golebiowska et al. used predicted VO_{2peak} values from reference data, with Takken et al. matching on age and sex from a Dutch database.[92]

After conducting a meta-analysis on the five studies, Takken et al. reported the JIA population had VO_{2peak} 21.8% (95 % CI: 13.7, 29.9; $p < 0.0001$) lower than healthy controls. [92] The wide confidence interval of this result should be noted; all authors found a large range of aerobic capabilities in their subjects with JIA.[92] Regardless, the 22% deficit is still heavily referred to, as this is the only meta-analysis that has been done on this topic.

In 2007, Klepper conducted a second review of the literature regarding exercise and fitness in children with juvenile arthritis.[7] She cited two new studies since the 2002 review by Takken et al., both reporting significant impairments in aerobic fitness in the JIA cohorts versus

healthy cohorts.[7, 28, 67] Using a graded bicycle test to measure VO_{2peak}, Van Brussel et al. found 62 patients with JIA had a mean VO_{2peak} 69.8% of that found from VO_{2peak} measures for reference data from healthy controls. [7, 67] Lelieveld et al., operating out of the same laboratory, found similar results in their investigations conducted in the same year.[93] Relative VO_{2peak} (VO_{2peak} mL/kg/min) was significantly different between those with JIA and the controls, overall, in boys, and in girls [mean (sd) = 41.97 (7.18) (JIA boys) vs 50.84 (0.05) (CON boys), and 30.78 (4.56) (JIA girls) vs 39.22 (0.07) (CON girls), $p < 0.01$ for all comparisons].[93]

Two studies were not captured by the above reviews. Metin et al. compared 34 youth with JIA with no hip, knee, or ankle restrictions, ages 7-16 years old, to 21 healthy, sedentary controls, 11-15 years old.[68] After completing a cycle ergometer test, relative VO_{2peak} was significantly different between the controls and the individuals with JIA (mean (SD: 29.1(5.2) and 33.9(5.4), respectively, $p<0.01$).[68] Metin et al. also compared across JIA subtypes, noting unexpectedly that those with enthesitis-related arthritis had significantly higher VO_{2peak} than those with systemic JIA, pJIA, and oJIA.[68] Enthesitis-related arthritis is characterized by inflammation of ligament insertions, and can escalate to include spine arthritis.[19] It should be noted, however, the different subtypes had very low sample sizes when stratified.[68] The second study, a 2012 investigation by van Pelt et al., compared the aerobic capacity of youths with JIA, stratified into age groups, with age and sex matched standardized scores from a database of age and sex- related Dutch youth.[31] Interestingly, the VO_{2peak} of the JIA only differed significantly from standardized scores when grouped all together, and not when separated by age group, subtype, disease duration, or gender.[31] This suggests larger sample sizes in the subgroups may be needed to see significant differences.

Consistently, the literature indicated that disease severity, disease subtype, and sex affected aerobic capacity. Malleson et al. found increased disease severity associated with decreased aerobic fitness. Takken et al. and van Brussel et al. both report patients with oligoarticular arthritis had VO_{2peak} measures similar to healthy controls. Those with more severe disease subtypes, such as psoric arthritis, systemic arthritis, and polyarticular rheumatoid factor positive arthritis, had significantly impaired fitness.[67, 92] Both Lelieveld et al. and van Brussel et al. found girls with JIA had greater deficits in relative VO_{2peak} scores when compared to their healthy sex-matched peers, than boys with JIA.[28, 67]

Three studies were found investigating balance in youth with JIA compared to healthy controls.[72] Houghton and Guzman (2013) compared the results of 25 children with JIA with lower extremity arthritis in single-leg static balance, and bilateral static and dynamic balance tests to 36 healthy children.[72] They used a Biodex Balance System, right and leg single leg balance, bilateral static balance, and bilateral dynamic balance at two different instability levels.[72] Single leg balance was significantly impaired. Forty percent of the subjects with JIA did not complete the single leg balance testing, while all controls were able.[72] For the bilateral dynamic balance test at very unstable levels, mild impairments were found in the youth with JIA versus controls for overall stability index [mean (sd) = 1.871 (1.176) (JIA) and 1.472 (0.676) (CON), p=0.050], respectively, anterior/posterior [mean (sd) = 1.283 (0.77) and 0.978 (0.465), respectively, p=0.031] and medial/lateral stability indices [mean (sd) = 1.079 (0.763) and 0.828 (0.390), respectively, 0.49].[72] No difference was found in static bilateral balance.[72] The deficits seen in the JIA cohort, especially in single leg balance, are noteworthy as they were outperformed by a control group with a younger median age.[72] The authors reported low correlation between lower limb strength and bilateral and unilateral balance.[72] They did not find

associations between balance and pain, functional impairment, or active joints on the day of testing.[72]

In 2017, Patti et al. compared the balance of 17 children with JIA and 39 controls, ages 9-16.[74] Healthy controls were excluded if they participated in a regular exercise program.[74] While the youth stood in the "Romberg test position" with feet together and eyes closed, postural sway was measured using the FreeMed posturography system.[74] Those with juvenile arthritis exhibited significantly lower postural sway than controls.[74] Patti et al. also administered a battery of fitness tests and was able to show correlations between balance and fitness outcomes but could not conclude if the correlations were meaningful.[74]

A second study in 2017 by Merker et al. found contrasting results.[94] Merker et al. compared three groups of 36 subjects: those with inactive lower limb arthritis, those with active lower limbs arthritis, and age and sex matched controls.[94] Each group completed tests on a bipedal balance board. Balance index outcomes did not differ between youth with active or inactive arthritis.[94] When compared to the control group, those with active or inactive JIA scored significantly lower on two out of three balance indices, indicating better stability and motor control.[94] The authors speculated this could be due to long-term physiotherapy and daily coordination training prescribed to the JIA cohort to combat abnormal gait patterns and joint movement.[94]

2.3.3.1 Critical Appraisal of the Current Literature on Functional Outcomes in Youth with JIA

Maximal oxygen consumption (VO_{2max}), based on a graded exercise test, is the gold standard measure for cardiorespiratory or aerobic fitness or capacity.[61] Maximal exercise tests have been found to be reliable in children and adolescents with JIA.[61, 92] A true VO_{2max} is

measured at the end of an effort where an oxygen consumption plateau is reached; however this characteristic plateau is only observed in a minority of children.[61, 92] Instead, objective and subjective criteria, such as reporting a rate of perceived exertion of 10, ceasing exercise despite strong verbal encouragement, and/ or heart rate greater than 180 beats per minute is used to as a terminus for a pediatric maximal exercise tests.[95] Due to this addition subjective endpoints, maximal aerobic tests in children are referred to as measuring VO_{2peak}, not VO_{2max}.[95] Although all the studies included in the meta-analysis by Takken et al. in 2002 used a graded VO_{2peak} test, none clearly define their criteria for ending the exercise test.[92] This would limit comparison of the results, and may underestimate aerobic capacity in children with JIA if the test was terminated too early.[92] In addition, Takken et al. noted that none of the studies included in their systematic review determined if the differences in VO_{2peak} values between JIA and healthy cohorts were clinically relevant.[92] Further, small sample sizes, especially when authors chose to stratify results, limit the power of the statistical comparisons between children with JIA to their healthy counterparts.

Currently, there is no gold standard measurement for assessing balance in adolescents.[96] The three studies described above to test balance in adolescents with JIA all did so with different measures. All three studies used electronic, mechanical balance systems of various expense and sophistication. The advantage of these systems is they provide consistent measurements, although the reliability of platform devices for measuring balance have been reported as high and poor.[65] However, he expense of these systems limit their use in clinical settings.[96] In addition, neither a system nor a set of outcome measures has been adopted for wide-spread investigative use, limiting the ability to compare results across studies. Heterogeneous protocols for testing across studies may contribute to any discrepancy seen in the results.[65]

In addition to the diverse protocols, the authors tested youth with JIA with various ages, subtypes, disease severities, and levels of physical fitness. Only Merker attempted to stratify results by disease activity.[94] Patti et al. did not explicitly state if their sample had lower extremity arthritis when they were tested, and Houghton and Guzman recognized their control comparison group was significantly younger than the JIA cohort.[72, 74] Finally, small samples sizes require us to interpret the results with caution. Houghton and Guzman's investigation has been criticized for indicating significant results when the actual measurements between the two populations were not very distinct, and could lack clinical relevance.[97]

2.3.3.2 Summary of Current Evidence on Functional Measures in Youth with JIA

A graded VO_{2max} test is recognized as the gold standard measure of aerobic capacity, and these tests are relatively easy to administer. This is advantageous when comparing results from different investigations, however, the termination point of the test must be clearly defined in children.[92] The last systematic review analyzing aerobic capacity, as found by testing VO_{2max}, did so in 144 youth with JIA and 145 controls between the age of 4 to 19. It found the children with JIA had 22% lower aerobic capacity than healthy youth.[92] It should be noted that there was a wide confidence interval, indicating a range of aerobic capabilities in the JIA population.[92] Since that review, several other studies have been conducted, all finding a deficit in VO_{2peak} in the adolescents with JIA.[28, 67, 92] It is important to recognize that throughout all these tests to maximum effort, no adverse events were reported in patients with JIA.[7, 92] This suggests youth with arthritis are capable of vigorous maximal efforts without adverse effects. What is lacking from current evidence is consistency, clarity in methodology, and larger cohorts to determine causal factors of attenuated aerobic capacity.

There is a paucity of research investigating balance deficits in the JIA population, particularly of studies assessing dynamic balance through hopping skills. The general understanding that the JIA population struggles with balance, especially on affected limbs, is mainly based on clinical experience. Different devices and protocols of testing limit conclusions about adolescent balance in general and this problem is magnified in the JIA population. Studies remain too few and results too varied to make any definitive conclusions about the balance abilities of youth with JIA.

Dynamic balance tests have been used to assess the functional status of the knee after surgery and rehabilitation programs.[71] The triple hop test can also predict lower extremity strength and power in adolescent populations.[70] These outcomes are of critical to consider when determining the appropriate physical activity recommendations for children with JIA. Clarifying balance defects in this population could lead to changes in physiotherapy programs, including the emphasis of neuromuscular and proprioceptive training to improve function and decrease sports-related injuries.[72] It is of critical importance that investigators continue to build the evidence for balance tests that are easily administered in clinic to ensure direct applicability to front line treatment strategies.

2.4 Summary of Conclusions

Overall, this literature review revealed several gaps in the knowledge of the abilities of youth with JIA. Although it seems clear from recent studies those with JIA engage in less PA, and in particular, less moderate or vigorous physical activity, than their healthy peers, there is little consensus on the current status of adiposity, aerobic capacity, and balance skills in this population. There are several pervasive deficits common throughout the literature, including

small heterogeneous samples, varying methodologies of measurement that prevent comparison, and ambiguous or nonexistent control for confounders or effect modifiers. Accomplishing a large homogenous sample in JIA studies is challenging due to the complex manifestations of the disease, personalized medication regimes, and varying ages of the patients. However, with the advances in pharmacological management of JIA, clinicians require current information on the capabilities of their patients. New, convenient methods of measuring habitual PA, current increases in child and adolescent adiposity, outdated evidence regarding aerobic capacity, and newly emerging investigations into balance, all demonstrate an urgent need for a well-designed investigation addressing these aspects in the JIA population.

Chapter Three: **Methods**

3.1 Study Design

This is a cohort study with a matched pair design, examining outcomes of physical activity, adiposity, aerobic fitness, and balance in youth with juvenile idiopathic arthritis (JIA) compared to age and sex matched healthy controls. Age matches were made within 18 months. Data collection occurred from July 2016 to November 2017. This study was approved by The University of Calgary Conjoint Health Research Ethics Board (Ethics ID: REB15-3125). This study is a part of a larger, ongoing cohort study examining health and clinical outcomes in individuals with JIA compared to healthy age and sex matched controls more broadly (i.e., imaging, serum biomarkers, fatigue, pain, quality of life, and biomechanics).

3.2 Study Population

The study population includes male and female youth, aged 10-25 years old. JIA patients were recruited in collaboration with the outpatient Rheumatology clinic in the Alberta Children's Hospital (ACH) and the Richmond Road Diagnostic and Treatment Centre Rheumatology Clinic, Calgary, Alberta. Eligible participants were identified by their physician or physiotherapist and consent to contact was obtained by the research team. Control participants were recruited from the online Healthy Infants and Children Clinical Research Program (HICCUP), and through JIA study participant and study personnel contacts (e.g., friends).

3.2.1 Inclusion criteria for JIA participants:

- Diagnosis of JIA, with bilateral or unilateral knee involvement
- No change in medication for three weeks prior to testing

3.2.2 Exclusion criteria for JIA participants:

- Within less than two months of commencement of disease modifying anti-rheumatic drugs
- Systemic symptoms (e.g., fever, rash)
- Previous, lower extremity musculoskeletal injury within 3 months prior to testing that resulted in time loss (work, school, or sport)
- Contraindications to exercise indicated by their physician or the Physical Activity Readiness Questionnaire (PAR-Q)
- Current medical problem(s) that prevents participation in the functional testing (e.g., neurological or respiratory disorders)
- History of lower extremity surgical intervention
- Pregnancy

3.2.3 Inclusion criteria for control participants:

- No history of JIA or any other rheumatological disease

3.2.4 Exclusion criteria for control participants:

- History of intra-articular knee injury or lower extremity surgical intervention
- Diagnosis of any arthritides
- Contraindications to exercise indicated by their physician or the PAR-Q
- Pregnancy
- Previous, lower extremity musculoskeletal injury within 3 months prior to testing that resulted in time loss (work, school, or sport)

- Current medical problem that prevents participation in the functional testing (e.g., neurological or respiratory disorders)

Consent to contact was obtained from individuals with JIA and their parent/guardian if under age 18. After consent to contact was obtained, potential participants were contacted via telephone by the research coordinator to complete a screening interview and finalize their eligibility. Eligible participants were sent an email to book their study appointments.

3.3 Data Collection

Data collection occurred over a year and a half at the Vi Riddell Movement Assessment Centre at the ACH, and the Faculty of Kinesiology, University of Calgary. Testing occurred on two separate days, one week apart. Surveys, clinician assessments, balance testing, biomechanical testing, blood work, ActiGraph distribution, and aerobic testing occurred on day one at the C.H. Riddell Movement Assessment Centre at the Alberta Children's Hospital. Day one testing took an average of three and a half hours. Measurements included physician and physiotherapy clinical evaluations, i.e. Childhood Health Assessment Questionnaire (CHAQ); American College of Rheumatology (ACR) core, a ActiGraph GT3X+ device to assess time spent and levels of physical activity (e.g., light, moderate, vigorous), a triple single leg hop test (TSLH), eyes-closed dynamic balance (ECDB) test, and star excursion balance (SEBT) test to assess dynamic balance, and a VO_{2peak} test to assess aerobic cardiorespiratory fitness. Following testing, participants were given an ActiGraph GT3X+ device to monitor physical activity. Participants were instructed on the appropriate way of wearing the ActiGraph by fastening the device around the waist with an elastic strap above the right anterior inferior iliac spine (Figure 3.1). The ActiGraph was worn at all times, even when sleeping, and returned after one week,

when the second round of data collections were conducted. On day two, a dual x-ray absorptiometry (DXA) scan to assess fat mass index and body composition and a pain survey was conducted for all participants at the Roger Jackson Centre for Health and Wellness at the University of Calgary. Control participants completed a physiology assessment evaluating knee function.

The protocols for the DXA scan and the ActiGraph monitor were based on those used in other studies in the Sport Injury Prevention Research (SIPRC) Centre, the Faculty of Kinesiology at the University of Calgary and can be viewed in Appendix A and Appendix B.

Figure 3.1: Placement of the ActiGraph GT3X+ accelerometer on the right hip

3.3.1 Outcome Measures

The primary outcomes for this study were physical activity participation and aerobic fitness. Specifically, physical activity was defined as the mean time (min) spent in moderate to vigorous activity physical activity (MVPA) per day. Time spent in MVPA per day was examined, as activity at these intensities has been linked to health benefits in youth.[63] In addition, examining MVPA time in minutes per day allows the results from this study to be readily compared to world and national health guidelines. Aerobic capacity was measured as relative VO_{2peak} (mL/kg/min), as found with a bike test to volitional fatigue. VO_{2max} tests are accepted as the most accurate measure of cardiorespiratory or aerobic, fitness.[68] A post-hoc power analysis was used to estimate power for these two primary outcomes. The secondary outcomes were body composition, defined as fat mass index (FMI) and dynamic balance, defined as maximum distance reached on the TSLH test on the dominant and non-dominate leg (normalized to leg length). These two outcomes have been found to be significantly different between youth with previous knee injury and non-injured youth, and therefore were considered important to investigate in this population.[108] Exploratory outcomes were mean percentage (%) of time spent in MVPA per day, mean time (min) spent in sedentary and light physical activity (SLPA) per day, mean percentage (%) of time spent in SLPA per day, maximum time achieved on the dominant and non-dominant leg during an eyes-closed dynamic balance (ECDB) test on a foam pad, normalized maximum composite reach distances assessed on a star excursion balance test (SEBT) on the dominant and non-dominant leg, the effects of sex on primary and secondary outcomes, and the graphical association between time spent per day in MVPA by youth with JIA and each of pain, functional disability, disease duration, and disease activity. A sedentary lifestyle prevents the development of the cardio-respiratory system, muscle strength,

coordination, and key social skills, therefore monitoring SLPA is important in adolescents.[9] ECDB and the SEBT have been validated in youth populations as field-based balance measures.[95]

3.3.1.1 Physical Activity Participation

Physical activity participation was assessed using the ActiGraph GT3X+ device over seven consecutive days worn during waking and sleeping hours. The ActiGraph accelerometer is mounted by an elastic strap around the waist at the right hip and collects data in three axes, vertical, horizontal, and perpendicular, at a frequency of 30 Hz. The device is not waterproof and must be removed if submerged in water (i.e., showering, swimming).

Although the ActiGraph GT3X+ has not been validated in children with juvenile idiopathic arthritis, it has previously demonstrated excellent validity and classification accuracy for MVPA in children and adolescents with disability (cerebral palsy) and without disability.[30,44]

Each subject was instructed to complete out a monitor log (Appendix C) specifying times they removed the device during the seven days of wear. This log was used to discriminate non-wear time from wear time. To account for physical activity during non-wear time, each subject was instructed to complete out the monitor log (Appendix C) specifying times the Actigraph was taken off and put back on for activities that may not be detected by the accelerometer (e.g., weight-lifting, stationary biking, horseback riding), when the ActiGraph was removed for safety purposes (e.g., rock-climbing, martial arts), or to when it was removed for a water activity (e.g., swimming, water polo). For each session of activity during which the monitor was removed, participants were asked to determine their average Rate of Perceived Exertion (RPE) for the exercise session completed without the monitor. This was determined using the Pictorial

Children's Effort Rating Table (PCERT) (Appendix D), validated in healthy children 11 to 15 years old.[97] The PCERT is a scale from 1 to 10 depicting different levels of exertion using simple phrases and a sketch of a boy displaying body language and facial features to match various levels of exercise. This method has demonstrated higher correlation with heart rate, minute ventilation and oxygen uptake in children compared to the Borg scale.[97] The scale has been validated in healthy children 11-15 years old.[97] The PCERT had a higher correlation than the Borg Category-Ratio Perceived Exertion (Borg CR-10) Scale with physical effort of 9 to 11 year olds over three treadmill tests to volitional fatigue.[97]

The Canadian 24-hour movement Guidelines for Children and Youth – Glossary of Terms provided direction on classifying the activity in the appropriate level of intensity based on the RPE recorded by the study participant. [98] The Guidelines state "on a scale relative to an individual's personal capacity (e.g., Rating of Perceived Exertion), moderate-intensity physical activity is usually represented by 5-6 on a scale from 1-10".[98] For this investigation, time spent in any activity for which participants recorded a 5 to 10 RPE was included in minutes of MVPA. Participants were contacted if any discrepancies in wear time or activity intensity appeared between the ActiGraph and the log. If participants did not respond to repeat attempts for clarification or description of the RPE of activity, approximate metabolic equivalents (METS) values from the Compendium of Energy Expenditures for Youth (Ridley 2008) were assigned based on the activities reported.[101] The Compendium of Energy Expenditures for Youth gives METs for each activity, followed by reasoning and references for the derivation. The following METs classification scheme for exercise intensity was adopted to discriminate between sedentary/ light activity and moderate/ vigorous activity, based on Trost et al.[101] Sedentary and

light physical activity (SLPA) was defined as < 4 METs.[101] Moderate and vigorous physical activity (MVPA) was defined as > or equal to 4 METs.[101]

When the ActiGraph was returned, the device was analyzed using the Actilife© software. Low frequency extension was enabled to increase the accelerometer sensitivity to very low amplitude activities. This increases the accuracy of data collection in populations that take light steps.[101]

Age-specific algorithms for the pediatric population developed by Evenson et al. were used to apply cut-offs to differentiate the intensity of activity.[101] Evenson algorithm cut-points are defined in movement counts detected by the ActiGraph device per minute. Sedentary activity is detection of less than or equal to 100 counts per minute, light is greater than 100 and less than 2295, moderate activity is greater than or equal to 2296 and less than 4011 counts per minute, and vigorous activity is defined as greater than or equal to 4012 counts per minute.[101] A 2011 study by Trost et al. compared five sets of independently developed and peer-reviewed youth-specific ActiGraph algorithms, only Evenson algorithm cut-points performed well in healthy children of all ages tested across all four levels of physical activity intensity to classify energy expenditure in standardized activity trials.[101]

Monitor logs were used to determine wear time, non-wear time, and duration and intensity of activities while the monitor was removed (e.g. swimming, contact sports). When logs were not returned even upon follow-up with the participant, the Choi 2011 algorithm was used to determine wear and non-wear time in accordance with SIPRC SOP. (Appendix B) To capture all episodes of physical activity by our participants, two separate analyses were carried out: (a) an imputed analysis, using ActiGraph-detected activity with imputed self-reported activity while the device was removed), (b) a non-imputed analysis using ActiGraph-detected activity only and

excluding activities during non-wear time. For the imputed analysis, total wear time was adjusted corresponding with additional activity time. ActiGraph count data and graphs generated using Actilife© were consulted to confirm actual time the device was removed. RPE was used to classify any exercise into sedentary/light or moderate/vigourous activity. Due to the limitations of self-reported activity recall in children, ActiGraph-measured activity was used where any discrepancies occurred between the count data or graphs, and the activity reported.

Subject data were included if the participant had worn the device for 5 to 7 days, with at least one weekend day. The total wear time for each day needed to be equal to or exceeded 10 hours. If the participant wore the device for longer than 7 days, the 7 days for analysis were chosen from the days with the longest amount of wear. If wear time was similar, then the days closest to the date the ActiGraph was received were prioritized. The season of wear was recorded for future consideration and catalogued as summer (April-September) or winter (October – March).

SIPRC Standard Operating Procedure (SOP) for the ActiGraph GT3X+ Accelerometer providing detailed step-by-step instructions for participants and data analyzers is included in Appendix B.

3.3.1.2 Adiposity

Adiposity in this investigation was determined by computing the participant specific fat mass index (FMI). FMI is calculated by dividing total fat mass (kg) by height (m^2), with the units kg/m^2. FMI was determined with Dual Energy X-ray Absorptiometry (DXA) (DXA, Hologic QDR 4500A, Hologic Inc., Waltham, Mass., USA). Using a three-component model of body composition, a whole-body scan was employed to assess total body fat mass using a multi-

component model of body composition. DXA is a gold standard technique for measuring body composition.[102 103]

Before the scan, we recommended the participants abstain from eating for three hours before or exercising 12 hours before the appointment time, and arrive in a normally hydrated state. The patient was asked to lie on the scan bed and remain still for the duration of the scan (i.e. five minutes) (Figure 3.2). The DXA was calibrated prior to each scan using the SIPRC Standard Operating Procedure (SOP) (see Appendix A). An individualized feedback form was provided to each participant detailing body mass index, body fat and lean mass indices, and bone mineral density. Participants were provided resources and study contact information if he or she required more information.

Figure 3.2 Participant undergoing a Dual-Energy X-ray Absorptiometry (DXA) scan

3.3.1.3 Functional Outcomes

3.3.1.3.1 Aerobic Fitness

Aerobic fitness was assessed using an incremental maximal VO_{2peak} fitness test, conducted on a cycle ergometer (Ergoline©). Aerobic fitness was defined as the relative maximal rate of oxygen consumption (VO_{2max}) in mL/ kg/min. A higher rate of oxygen consumption per kilogram indicates increased efficiency and increased aerobic capacity.[68] VO_{2max} tests are accepted as the most accurate measure of cardiopulmonary, or aerobic, fitness.[68] A true VO_{2max} is measured at the end of an effort where an oxygen consumption plateau is reached.[61, 92] However, this characteristic is only observed in a minority of children, therefore subjective observations (e.g., reporting of maximal RPE and volitional fatigue) are used to determine the end of a child VO_{2max} test. [61,92] For this reason, youth VO_{2max} tests are typically referred to as VO_{2peak} tests.[94]

A CSEP-Certified Exercise Physiologist (CSEP-CEP) was present at each testing session and monitored each participant, providing verbal encouragement. Participants started at 0 Watts and resistance was increased by 20 Watt intervals every 2 minutes until volitional fatigue. Starting at 0 Watts provided participants with a warm-up prior to harder levels, and provides a low starting point to allow for varying abilities. The protocol took approximately 15-20 minutes. The test was declared completed when the participant could no longer continue despite enthusiastic encouragement, a steady, maximal heart rate was reached, and/or reported an RPE of 10 on the PCERT exercise scale. To obtain measures of energy expenditure, participants were fitted with a light-weight portable indirect calorimeter (COSMED K5). The K5 requires the participant to wear a face mask that allows for measurement of respiration rate and expired air gas analysis. Face masks were available in various sizes and the appropriate size was identified

for every participant. The participants were also fitted with a Garmin® premium heart rate monitor, worn around the chest (Figure 3.3). All equipment in direct contact with participants was cleaned with warm water and disinfectant wash. After completing the test, the participants were asked to perform an active recovery by continuing to cycle at light intensity to decrease heart rate back to resting levels.

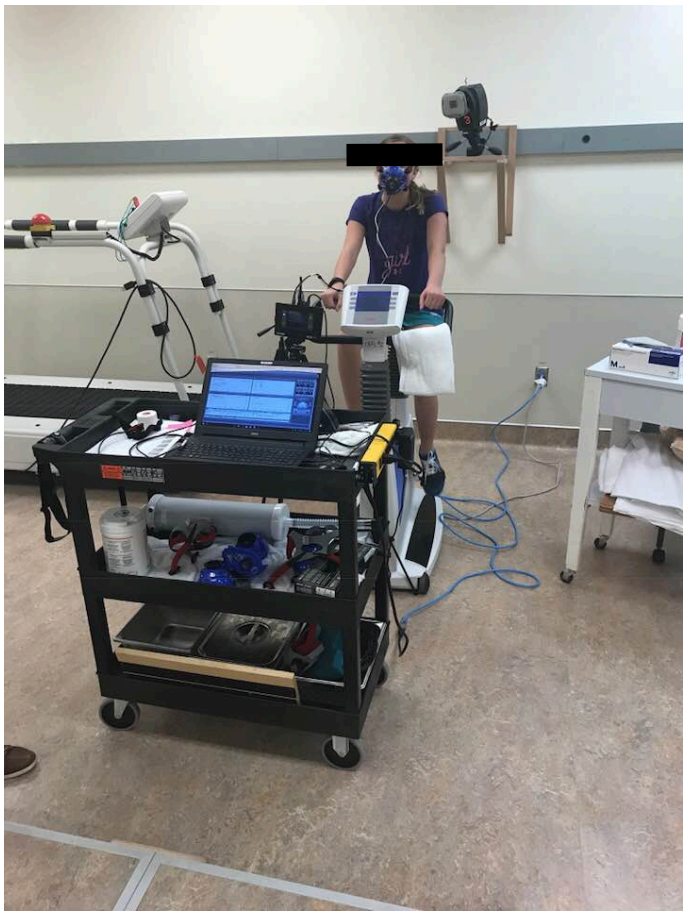

Figure 3.3 Participant undergoing VO_{2peak} testing

3.3.1.3.2 Star Excursion Balance Test (SEBT)

The Functional Movement Systems ® Y-Balance Test Kit was used for the SEBT. This model consists of a central platform where the stance leg is placed, and three plastic pipes are attached at the central platform that extend in the anterior, posteromedial, and posterolateral directions. The posterior pipes are positioned 45 degrees apart from each other. The anterior pipe is 135 degrees from the posterior pipes. A sliding reaching block is attached to each pipe. Pipes are marked at increments 1 cm apart. The research assistant verbally and visually demonstrated the test before the participant was given one trial attempt in all three directions with each foot. Only one practice trial was permitted after verbal and visual demonstration by research personnel, to decrease chance of fatigue and increase safety, as well as due to time constraints. The participant completed the test barefoot, the supporting foot placed on the center platform with toes behind the red line. Once the subject was balanced, he or she would reach forward with the non-stance leg pushing the sliding block forward until a maximum reach was hit. Hands were required to remain on the subject's hips (Figure 3.4). Participants could return their foot to the center and rest their foot downtown momentarily to regain their balance before proceeding to reach in the posterolateral and posteromedial directions. The trial was repeated if: [105]

- The non-stance leg touched down during the reach or before returning back to the center from each direction
- Participant removed his or her hands from his or her hips
- Participant removed the stance foot from the center platform
- The reaching leg pushed the sliding block without control past their maximum reach distance

The reach distance in each of the three directions for each leg was recorded to the nearest centimeter. Three test trials were conducted per leg. Maximum composite reach distance was used to assess balance performance on the dominant and non-dominant leg. Maximum reach distance in each direction was normalized to 3xleg length as measured from ASIS joint to pointed big toe by a physiotherapist and expressed as a percent using the formula: Maximum composite reach distance = ((maximum reach anterior + maximum reach posteriomedial + maximum reach posteriolateral)/ (3*leg length))*100. Normalization of reach distances allows the scores to be compared among individuals or groups.[106] Maximum composite scores allow individual's overall performance on the test to be compared.[106]

The Y balance device has a strong inter-rater and intra-rater reliability (0.85-0.89 ICC and 0.97-1.00 ICC, respectively) in a study with 15 collegiate soccer players.[106] Low composite reach distances have been correlated to risk of lower limb injury in adolescent basketball players and has shown the ability to differentiate between healthy youth and those with ankle instability, anterior cruciate ligament reconstruction, and patellofemoral pain syndrome.[106]

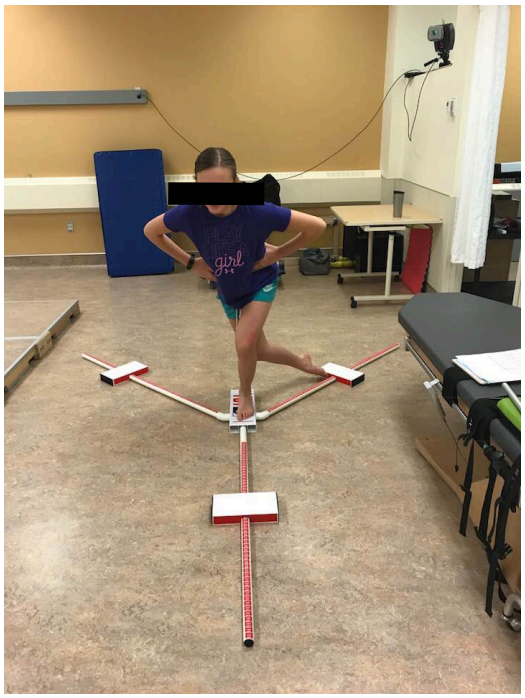

Figure 3.4 Star Excursion Balance Test (SEBT) conducted on the Functional Movement Systems Y- Balance test kit

3.3.1.3.3 Eyes closed dynamic balance (ECDB) test

The ECDB test on the foam pad was developed to provide an easy, affordable, and reliable clinical measure of dynamic balance.[96] The reliability of the ECDB test has been assessed in high school adolescents (ICC =0.46).[96]

This test is conducted balancing with a single leg on a high-density foam (50kg/m^3) Airex® Balance Pad with eyes closed. The participant was given a 15 second practice session on each foot to familiarize themselves with the test after verbal and visual demonstration by research personnel. The test was conducted three times on each foot, alternating feet in between trials. The participant was instructed to complete the test barefoot. The participant was instructed to place one foot on the middle of the foam pad while keeping his or her hands on his or her hips.

The non-standing leg was then raised so the knee was flexed at 90 degrees and the femur was parallel to the floor. The research assistant started the time as soon as the subject closed their eyes. The trial time in seconds was recorded, to $1/100^{th}$ of a second. The maximum time allowed for each test was 180 seconds. If the participant failed to hold the balance for a minimum of 2 seconds, the trial was void and he or she was asked to repeat it. Three complete trials on each were conducted and balance times recorded. Time was stopped upon loss of balance, which included:

- One or both hands removed from the hips
- Eyes open
- Free leg touches down, or uses static leg for support
- Balance on the pad is kept but pad moves from original position, or the static leg raises from the pad

To increase the safety of the test, the participants alternated legs between trials and were allowed to raise their leg to 90 degrees before closing their eyes. Modifications were applied to both JIA patients and controls.

3.3.1.3.4 Triple Single Leg Hop (TSLH)

Dynamic balance was assessed with the triple single leg hop test (TSLH). This test evaluates neuromuscular control, force generating capacity, and knee stabilization.[107] It has been validated and used to assess functional knee capacity longitudinally after ACL injury rehabilitation or surgery in healthy youth.[107] The test has been moderately correlated with other scales of lower limb function such as the Global Rating Scale (r =0.44), and the Lower Extremity Functional Scale (r =0.26).[107]

The TSLH test is performed as three consecutive single-leg hops, with the goal of jumping as far as possible.[107] For the trial to be included, the landing from the final hop had to be solid with the non-hopping leg elevated, without extra small hops, unbalanced movements, or twisting of the foot. After a practice trial on each leg, each participant performed two trials on each leg, alternating feet between trials. The maximum distance across trials was recorded for each leg and expressed as a percentage of leg length [(distance jumped/ leg length) *100].

3.3.2 JIA Participant Characteristics

3.3.2.1 Level of Disease Activity

No single measure can capture all facets of JIA's effects on a child's life, therefore clinical measures include a number of global assessment scales, pain scales, active joint counts, and laboratory tests. In order to aid consistency in disease evaluation across physicians, reduce sample size required in research, and provide patients with a greater understanding of their own disease activity, these variables are often 'pooled' into a single measure.[108]

The Juvenile Arthritis Disease Activity Score (JADAS) is composed of four variables taken from the ACR Pediatric Core Set: physician's global assessment, parents' global assessment, active joint count (AJC), and an acute phase reactant.[108] In order to facilitate immediate rating of disease activity in a clinical setting, the 3-measure clinical JADAS (cJADAS) was derived and validated by McErlane et al. in 2013.[108] The cJADAS excludes a laboratory test for CRP or ESR that is present in the original JADAS, and consists of the physician assessment of disease, the parent assessment of disease, and active joint count.[108] Three derivations of the cJADAS exist, named for the number of joints included in the AJC: cJADAS10, cJADAS27, and cJADAS71.[108] Total scores range from 0-30, 0-47, and 0-971,

respectively.[108] The cJADAS is calculated as the sum of its components: AJC (71, 27, or 10 joints) + physician global assessment (10cm visual analog scale (VAS)) + parent global assessment (10cm VAS).[109] The cJADAS27, which specifies which joints are included in the count, has been criticized for excluding important joints such as the temporomandibular joint.[110] The cJADAS71 is time-consuming.[110] In comparison, the cJADAS10 may have the greatest applicability in a busy clinical setting, due to its simplicity of use.[109] It is quick, and includes any joint involved to a maximum of 10 with no weighting of joints.[109,110]

In this investigation, the study physician (kept consistent for all participants with JIA) was asked to conduct a clinical assessment to determine the physician global assessment (10cm VAS) and the number of active joints. This information was then entered into the clinical assessment form. (Appendix E) Parents were asked to fill the parent global assessment on a 10cm VAS.

In 2014, Consolaro et al. determined disease status cut offs in the cJADAS, defining inactive disease (ID), low disease activity (LDA), moderate disease activity (MDA), and high disease activity (HDA)[111] (Table 3.1). Cut-offs were distinguished into those for oligoarticular and polyarticular arthritis, and excludes those patients with systemic JIA or active systemic symptoms.[108,111]

Table 3.1 : Disease state classification cut offs based on disease activity scores found using the clinical Juvenile Arthritis Disease Activity Score (cJADAS10) [111]

Disease State	Oligoarticular	Polyarticular
Inactive disease	<1	<1
Low disease activity	<1.5	<2.5
Moderate disease activity	1.5-4	2.51-8.5
High disease activity	>4	>8.5

3.3.2.2 Physical Function

The Childhood Health Assessment Questionnaire (CHAQ) is the most common tool by physicians and clinical trials to assess physical function in patients with JIA.[112] It has been specifically developed for the juvenile arthritis population, and has been determined to be valid, reliable, and sensitive.[112] The CHAQ captures the health and functional status of patients' in two components, disability and discomfort.[113] Disability is assessed over eight domains covering aspects of daily living, for example: dressing, grooming, grip, walking etc.[113] Discomfort is rated on a 10mm VAS pain scale anchored by 0 (no disability) and 10 (severe disability).[113] The total score is between 0 and 3, with higher scores indicating greater functional disability.[112] In 2001, Dempster et al. correlated the survey values to other measures of disease severity to determine median CHAQ scores that distinguish levels of functional disability.[113] They found CHAQ scores of 0, 0.13, 0.63, and 1.75 correspond to no, mild, mild-to- moderate, and moderate disability respectively. [113] All participants filled out the CHAQ on the first day of testing. (Appendix F).

3.3.2.3 Disease History

History of ankle, knee, hip arthritis, and unilateral or bilateral arthritis was noted. When physician assessments were missing, participant disease history was gathered through retrospective examination of patient charts or interviews with clinicians.

3.3.2.4 Pain

Pain is one of the most common symptoms in JIA, and is often cited by patients as one of the main symptoms limiting psychosocial function and decreasing quality of life.[114] Recent studies have shown that 31% of JIA patients reported pain in the severe range over a 2-month period.[114] The Intermittent and Constant Osteoarthrosis Pain (ICOAP) questionnaire was designed to evaluate the two kinds of pain experienced in osteoarthritis: constant and intermittent pain.[115] Its total score is useful as a measure of the overall pain severity experienced by adults with osteoarthritis.[115] Eleven items on the ICOAP measure both pain intensity and effect of pain on quality of life.[115] Five items address constant of pain and six deal with intermittent pain.[115] Each item is addressed on a five-point Likert scale from 0 to 4. The ICOAP has shown good internal consistency, test-retest reliability, and construct validity, even when applied across other cultures.[115] It has been recommended by osteoarthritis experts and the Osteoarthritis Research Society International.[115] The ICOAP has not been validated for use in the JIA population, however, its use could provide a valuable tool to compare the pain experienced by youth with JIA. All participants filled out the ICOAP on the second day of testing, after the week with the ActiGraph activity monitor. (Appendix G)

3.4 Statistical Analysis

3.4.1 Descriptive Statistics

Statistical analyses were performed using STATA (v14.2, Collage Station, Texas, USA). In the case of missing data, the participant and their matched pair were removed from the analysis for the outcome. Data were visually assessed for normality/ symmetry, and measures of central tendency were reported. For continuous data, means and standard deviations were reported for normally distributed data and medians and ranges were reported for skewed data. Categorical data was presented as total number and percent. Sex, age, weight, height, BMI, and CHAQ functional disability score were reported for both the control and JIA group, stratified by sex where appropriate. JIA subtype, disease duration, bilateral involvement, joint involvement, active joint count, and disease activity were reported for the JIA group.

Pair differences between the JIA and control group for primary, secondary, and exploratory outcomes were graphed to assess for normality and outliers. To account for the matched paired design, the mean pair differences (95% CI) for normally distributed data were determined using paired t-tests. The Wilcoxon signed-rank test (95% CI as determined by the Hodges-Lehmann treatment) was used to determine median differences and 95% CI's for pair difference distributions that were skewed. The Hodges- Lehmann treatment effects estimator estimates a median by looking at all possible means between pair differences. A median based on means is derived for the distribution of pair differences and a confidence interval is built around that median.

As there are two primary objectives (mean time per day spent in MVPA (min) and relative VO_{2peak} (mL/kg/min)), a significance level alpha of 0.025 was used for statistical tests, derived from a Bonferroni correction (a priori alpha/ number of tests: 0.05/ 2 = 0.025). A

significance level of alpha 0.025 was determined for the two secondary outcomes fat mass index [FMI (kg/m^2) and maximum TSLH distance (%)] on the dominant and non-dominant leg.

3.4.2 Exploratory Analysis

3.4.2.1 Primary and Secondary Objectives

The effect of sex on the primary and secondary outcomes of time spent per day in MVPA and aerobic capacity, as well as FMI and distance of TSLH were examined. Median (ranges) were reported for each study group and sex. Mean (95% CI) or median (95% CI) pair differences are reported. To account for the matched paired design, the mean pair differences (95% CI) for normally distributed data were determined with paired t-tests. The Wilcoxon signed-rank test (95% CI as determined by the Hodges-Lehmann treatment) was used to determine median differences and 95% CI's for pair difference distributions that were skewed. The relationship between the amount of time spent per day in MVPA and pain, disease duration, functional ability (CHAQ score), and disease activity (cJADAS10 score) was explored graphically for the JIA cohort.

3.5 Ethical Considerations

This study occurred in the context of the larger investigation entitled "Exercise Capacity in Juvenile Idiopathic Arthritis". JIA and control participants under 18 were required to have written consent from a parent or guardian, as well as sign a child assent form. (See Appendix H and Appendix I , respectively). Written consent was required from participants over 18 signed (Appendix H). Participants and their parents/ guardians were informed of their right to end participation in the study when desired with no repercussions. Testing was not completed on an

individual if he or she did not feel comfortable with the measurement (i.e., waist circumference, weight, aerobic test).

Each participant was assigned an identification (ID) number upon enrolling and all data relating to an individual were tracked with a study ID. All data was stored in a hard-copy version in a locked filing cabinet in the Alberta Children's Hospital Paediatric Research Office, and in password- protected electronic format online in Research Electronic Data Capture (REDCap) with access only by investigators and coordinators. All research assistant helping with data collection obtained a TCPS2 certification to ensure proper ethical standards were followed.

During testing, participants were regularly asked for verbal assessment of their well-being, as well as monitored with a pain and fatigue survey before the aerobic test. Each participant was encouraged to rest as much as they needed, and were offered water and snacks. All participants were required to complete a PAR- Q+ form and be cleared by a CSEP-CEP in order to participate in the bicycle ergometer VO_{2peak} aerobic test. All VO_{2peak} tests were monitored by a CSEP-CEP.

The use of the DXA bone scan involves exposure to ionizing radiation. The estimated dose of radiation from DXA machine is 0.001mSv or about three hours of background radiation.[116] The actual health risks from exposure to low x-ray doses are difficult to determine. Any radiation exposure involves some risk to the participant, however the dose used for whole body DXA is minimal and may be deemed negligible. All imaging was conducted by a trained and qualified operator.

Chapter Four: **Results**

4.1 Study Participants

In total, 62 participants consented to participate in the study, 30 children with JIA (JIA) and 32 healthy controls (CON). The primary analysis was based on 25 matched pairs (matched on age and sex). Ages matching was within 18 months based on date of birth. The 25 matched pairs included 32 females (64%) and 18 males (36%) (n=50). Ages range from 10 to 20 years old with a median age of 15. Table 4.1 summarizes participant demographics.

The participants with JIA demonstrated primarily bilateral disease presentation (20 (80%)). All participants with JIA had a history of knee involvement, three (12%) had a history of hip involvement, and nine (36%) had a history of ankle involvement. A median disease duration of 6.6 years (range 3 months to 15 years) was recorded. At time of testing, the youth with JIA had a median of one active joint (range 0-3), with a median clinical Juvenile Arthritis Disease Activity Score (cJADAS10) of 1.8 (range 0-4.1) out of ten. The majority of participants with JIA, 16 or 64%, had inactive to low disease activity, based on Consolaro et al.'s cJADAS10 cut offs for disease activity.[111] Only four participants (16%) had scores that would identify them as having moderate to high disease activity.[111] Self-reported functional disability, as measured with the Childhood Health Assessment Questionnaire (CHAQ), was low, ranging from zero to 0.6 on a scale from zero to three, with three being high disease activity. Dempster et al. found CHAQ scores of 0.13 to 0.63 corresponded to mild to moderate disease.[113]

We were unable to recruit control participants to match five JIA participants (Table 4.1). In addition, we were unable to recruit seven participants with JIA to match seven healthy controls. See Table 4.1 for unmatched participant demographics. The unmatched JIA and CON

group participants were younger than their matched counterparts. Importantly, the unmatched JIA participants did not differ on disease activity scores.

Table 4.1 Median (range) of matched participant characteristics by study group and sex (M= male, F=female) in youth with arthritis (JIA) and healthy controls (CON)

Variable	Matched		Unmatched	
	JIA (n=25) median (range) or frequency (percent)	CON (n=25) median (range) or frequency (percent)	JIA (n=5) median (range) or frequency (percent)	CON (n=7) median (range) or frequency (percent)
Sex (female, %)	32 (64%)		4 (80%)	6 (85%)
Age (years)	15.1 (10.6-20.0)	15.1 (10.0-19.8)	M (1): 13.3 F: 14.5 (14.5-14.4)	M (1): 11.6 F: 13.9 (10.2-20.2)
Weight (kg)	M: 64.2 (48.5-101.5) F: 51.2 (28.5-66.0)	M: 53.0 (34.0-77.0) F: 54.0 (34.0-87.0)	M (1): 45.0 F: 55.0 (51.5-78.5)	M (1): 36.0 F: 54.0 (26.5-72.0)
Height (cm)	M: 175.0 (160.0-195.1) F: 161.3 (133.5-175.0)	M: 170.2 (142-182.5) F: 162.95 (143.8-175.0)	M (1): 162.0 F: 163.0 (162.5-170.5)	M (1): 146.6 F: 160.2 (136.4-177.1)
BMI	M: 19.0 (16.0-31.3) F: 19.5 (15.9-25.3)	M: 18.9 (14.9-23.8) F: 20.1 (16.4-32.0)	M (1): 17.2 F: 20.8 (19.3-27.0)	M (1):16.1 F: 18.6 (19.4-27.0)
Functional Disability (CHAQ) (0-3)	M: 0.15 (0-0.6) F: 0.12 (0-0.5)	M: 0 (0) F: 0 (0-0.1)	M (1): 0.13 F: 0.4 (0-0.9)	M (1): 0.25 F: 0 (0)
Disease Course Oligoarticular Polyarticular Enthesitis Related Arthritis	 14 (56%) 9 (36%) 2 (8%)	N/A	 0 (0%) 4 (80%) 1 (20%)	N/A
Disease Duration (years)	6.8 (0-15)	N/A	4 (1-10)	N/A
Bilateral Involvement	20 (80%)	N/A	5 (100%)	N/A
Joint Involvement Knee Ankle Hip	 25 (100%) 11 (44%) 4 (16%)	N/A	 5 (100%) 5 (100%) 1 (20%)	NA/
Disease Activity (cJADAS10) (0-10)	1.9 (0-9)	N/A	3.7 (0.5-10)	N/A
Active Joint Count (0-10)	1 (0-3)	N/A	2 (0-26)	N/A

BMI= body mass index, cJADAS = Clinical Juvenile Disease Activity Score, CHAQ = Childhood Health Assessment Questionnaire

4.2 Physical Activity Outcome Measures

Physical activity data were collected for 46 participants, 24 CON and 22 JIA. Two participants with JIA returned the ActiGraph without wearing it, and one CON participant returned the device with inadequate wear time to make an evaluation of PA. One youth with JIA was lost to follow up and did not obtain a device. Typical reasoning for not wearing the ActiGraph included forgetfulness and annoyance with the elastic band. Twenty-three pairs of completed PA data were compared. Before evaluating PA outcomes, the total time of activity recorded by the ActiGraph and imputed from activity logs was compared between the JIA and CON matched pairs. Although the control cohort had more time collected on their activity than the JIA group median (range) 9472.0min (5652-10080) versus 9169min (4545-10080), respectively, there was no significant difference between the groups. The median pair difference (JIA-CON) was -74min (95% CI -733, 165).

PA outcomes are described (medians and ranges) by study group (JIA vs. CON) (Table 4.2). All outliers were identified visually on graphically and included in analysis. The Wilcoxon-signed rank test was used to assess the matched- pair difference distributions that deviated from normal. Medians are reported with 95% confidence intervals (CI) created with the Hodges-Lehmann treatment. When matched- pair differences were normally distributed, paired t-tests were used to evaluate pair differences. Means and 95% confidence intervals were reported.

Table 4.2 Paired t-test mean difference and 95% CI or median difference and 95% CI by the Hodges- Lehmann treatment for physical activity (PA) outcomes in children with arthritis (JIA) and healthy controls (CON)◊

PA Outcome Measure	JIA (n=22) Median (range)	CON (n=22) Median (range)	Mean or Median Pair Difference (JIA - CON) (95% CI)
Mean MVPA per day (min)	45.1 (18.0-111.9)	72.0 (25.7-190.6)	-13.8 (-31.1, -9.0)*
Mean percent of day spent in MVPA (%)	3.3 (1.4-7.8)	5.2 (1.8-14.3)	-1.6 (-3.0, -0.2)†*
Mean SLPA per day(min)	1290.8 (852.4-1400.2)	1282.0 (1027.0-1414.3)	1.9 (-27.4, 32.9)
Mean percent of day spent in SLPA (%)	96.8 (92.1-98.6)	94.7 (85.7-98.2)	1.2 (0.5, 2.2)*

*p <0.05
◊ table created with imputed PA data
†mean pair difference reported, evaluated with paired-test
MVPA = moderate to vigorous physical activity, SLPA= sedentary to light physical activity

4.2.1 Moderate to Vigorous Activity

Children with JIA spent a median of 14 minutes less in MVPA [95% CI (-31.1, -9.0), p= 0.03]. In addition, those with JIA spent a smaller proportion of their day in MVPA than controls [mean difference= -1.6%; 95% CI -3.0, -0.2, p= 0.03] (Table 4.2). Once multiple comparisons are considered, (a-priori alpha α <0.025), these results are not statistically significant.

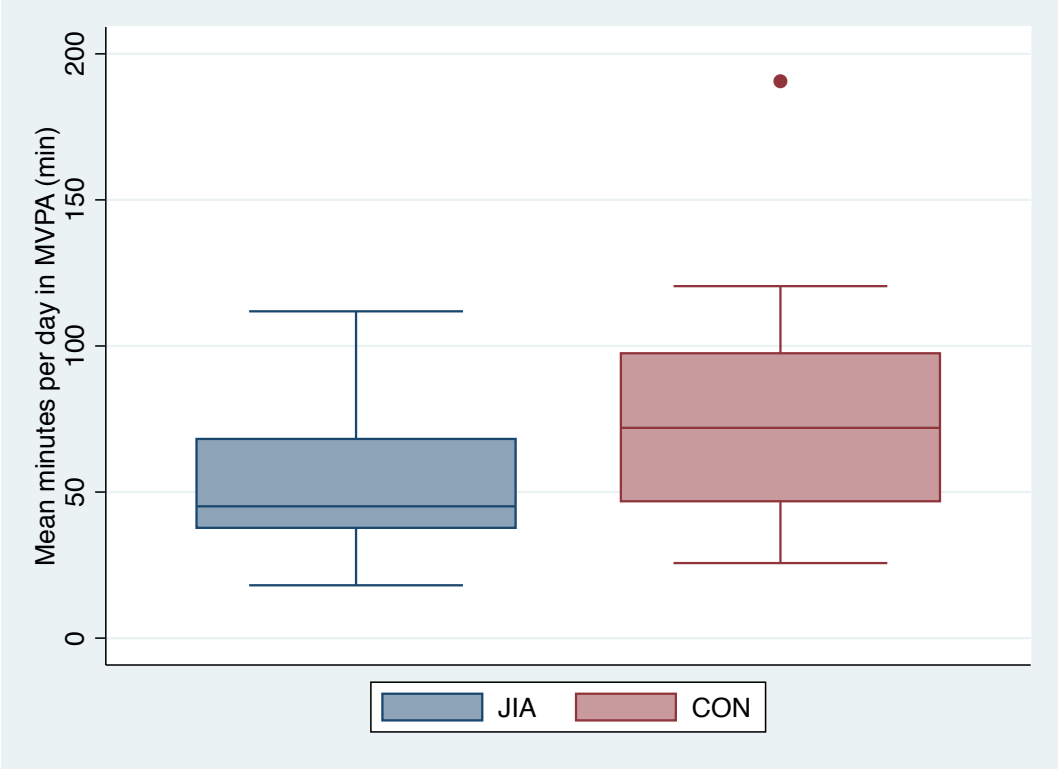

Figure 4.1 Mean minutes per day in moderate to vigorous physical activity (MVPA) (min) in healthy controls (CON) and youth with JIA (JIA)

One outlier in the control cohort logged a mean of 120.5 minutes per day of MVPA (Figure 4.1). This subject participated in four hours of ballet for three nights of the seven days, accumulating over 200 minutes of MVPA on those three days. On another night, she participated in swimming for 110 minutes (1.8 hours). The removal of the outlier and her pair reduces the width of the confidence intervals around the pair differences in time and proportion spent in MVPA between JIA and CON cohorts. With the outlier and her pair removed, the median difference in time spent in MVPA per day becomes -13.3 min (95% CI -26.6, -5.15, p =0.06). (Figure 4.2). The median difference in proportion of day spent in MVPA becomes -1.3% (95% CI -2.5, -0.02, p=0.05).

The Canadian 24-hour Movement Guidelines for Children and Youth recommends all healthy youth between 5 and 17 years old accumulate at least 60 minutes of moderate to vigorous physical activity (MVPA) per day.[33] Sixty-eight percent (17) of the CON cohort and 40% (10) of JIA participants met these guidelines based on mean minutes in MVPA per day over 5 to 7 days. Of the controls, 62% (10) of the females and 78% (7) of the males met the guidelines. In the JIA cohort, 38% (6) of the females and 44% (4) of the males accumulated at least 60 minutes of MVPA per day.

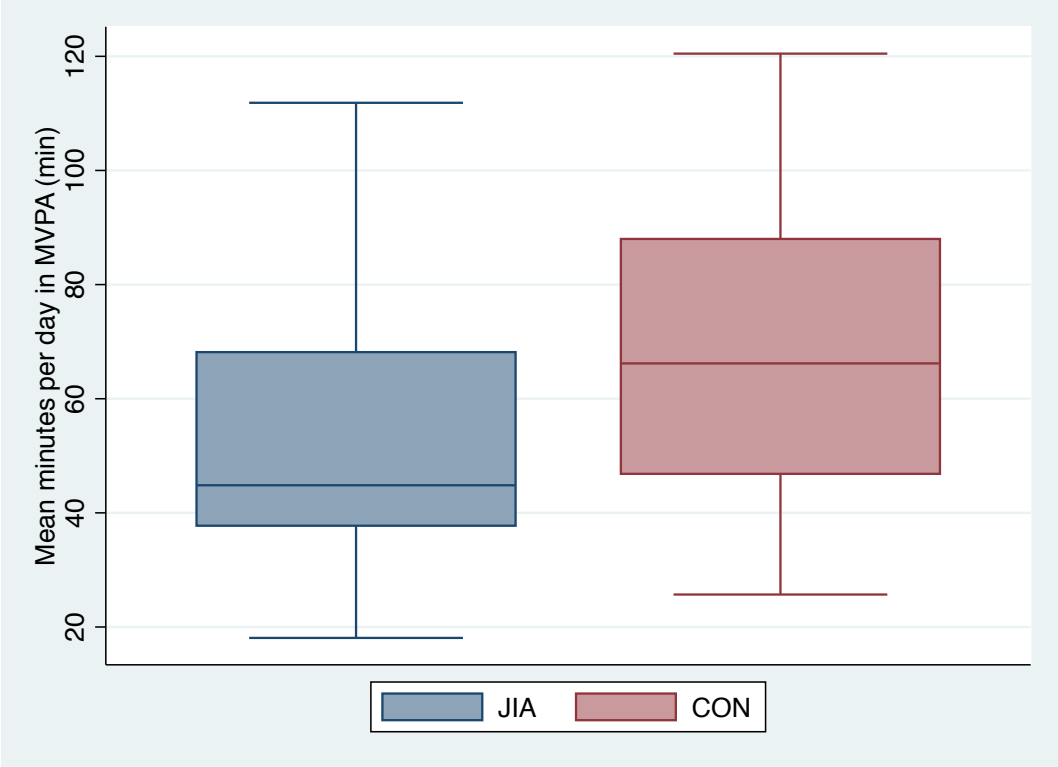

Figure 4.2 Mean minutes per day in moderate to vigorous physical activity (MVPA) (min) in healthy controls (CON) and youth with JIA (JIA), control outlier and matched pair removed.

4.2.2 Sedentary to Light Physical Activity

When the mean minutes per day in SLPA was investigated, no significant difference was found between the two cohorts median difference (JIA-CON) [1.9min (-27.4, 32.9)]. However, when examining the median difference for the proportion of the day spent in SLPA, the results indicate a significant difference between groups [1.2%; 95% CI: 0.5, 2.2, p=0.04].

Outliers for mean minutes per day spent in SLPA can be observed in the CON and JIA groups (Figure 4.3). The JIA outlier had no imputed light activities, and otherwise had typical ActiGraph data. The low mean minutes spent in SLPA in the CON outlier can be explained by a low number of hours per day recorded by the ActiGraph. This is why considering proportion of day in SLPA is informative (Figure 4.4). The control outlier observed in Figure 4.4 is the participant that imputed a large amount of MVPA, as described above, and therefore has a low proportion of time spent per day in SLPA. These outliers are included in the final analysis.

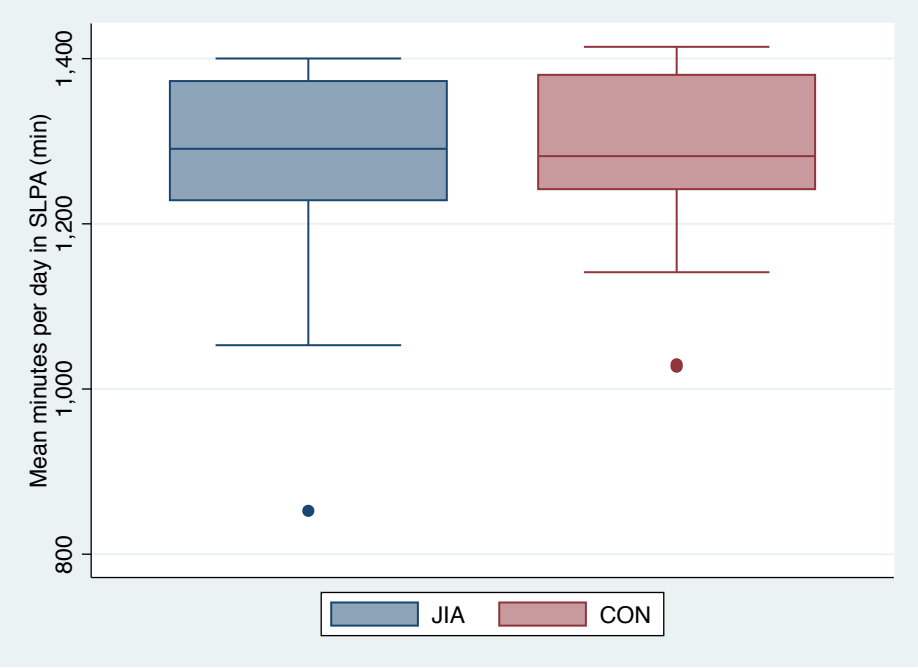

Figure 4.3 Mean minutes per day in sedentary to light physical activity (SLPA) (min) in healthy controls (CON) and youth with JIA (JIA)

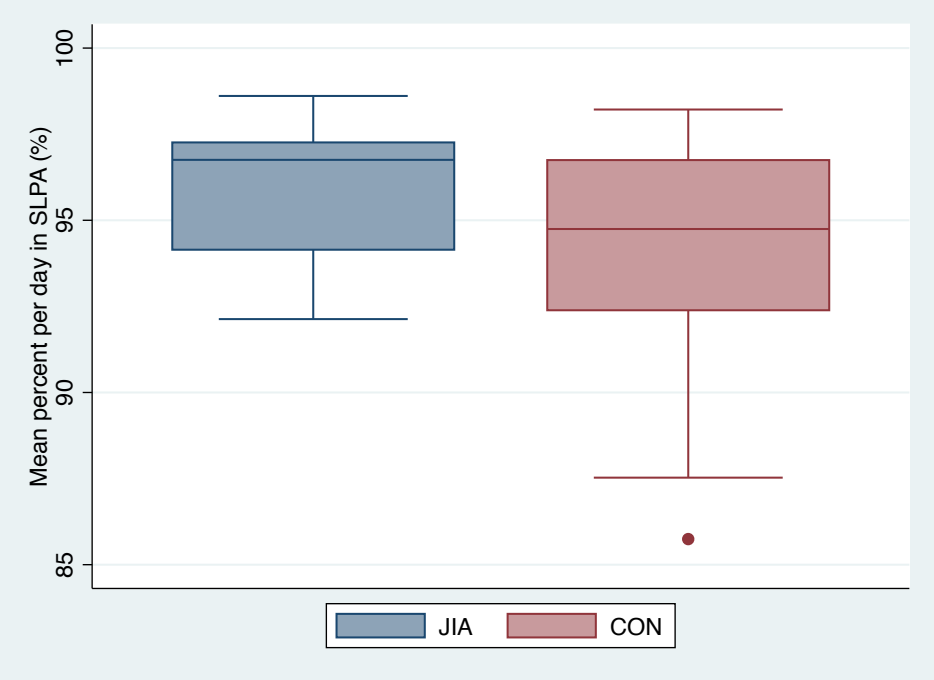

Figure 4.4 Mean proportion (%) per day in sedentary to light physical activity (SLPA) in healthy controls (CON) and youth with JIA (JIA)

4.2.3 Physical Activity Imputation, Adult and Child Algorithms

4.2.3.1 Physical Activity Imputation

Descriptive statistics were used to evaluate the effect of including imputed physical activity obtained from activity monitor logs in the analysis of PA outcomes. Imputed activities were compared to participant PA data collected only from the ActiGraph, referred to as "not imputed" data. PA data was collected for 47 participants, 24 CON and 23 JIA. Data was imputed for 15 (30%) participants, 10 (67%) CON and 5 (22%) JIA.

The total time of activity tracking in the JIA and CON groups was compared to evaluate the effect of including imputed data. When the matched pair difference of total time of NI data between JIA and CON is evaluated, there is no difference in total wear time collected between

groups [median difference 161min; 95% CI -313, 345]. A visual examination of the box plots from imputed and not imputed data demonstrates the imputation method did increase the median time included in activity tracking outcomes for the CON cohort (Figure 4.5 and Figure 4.6). Some participants on the CON side benefited with the addition of over 500 minutes, or a mean of 1.2 hours over 7 days. Two control participants recorded over 5 hours of lake and swimming activities on four days, and another control subject participated in swimming and ballet classes for which the ActiGraph was removed.

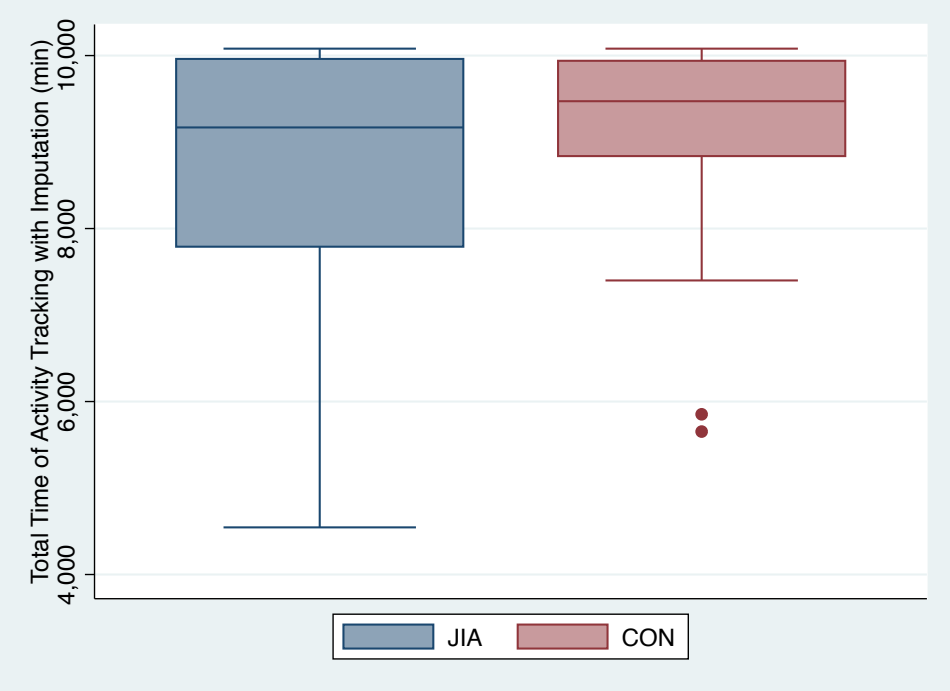

Figure 4.5 Total wear time with imputation (min) in youth with JIA (JIA) and healthy controls (CON)

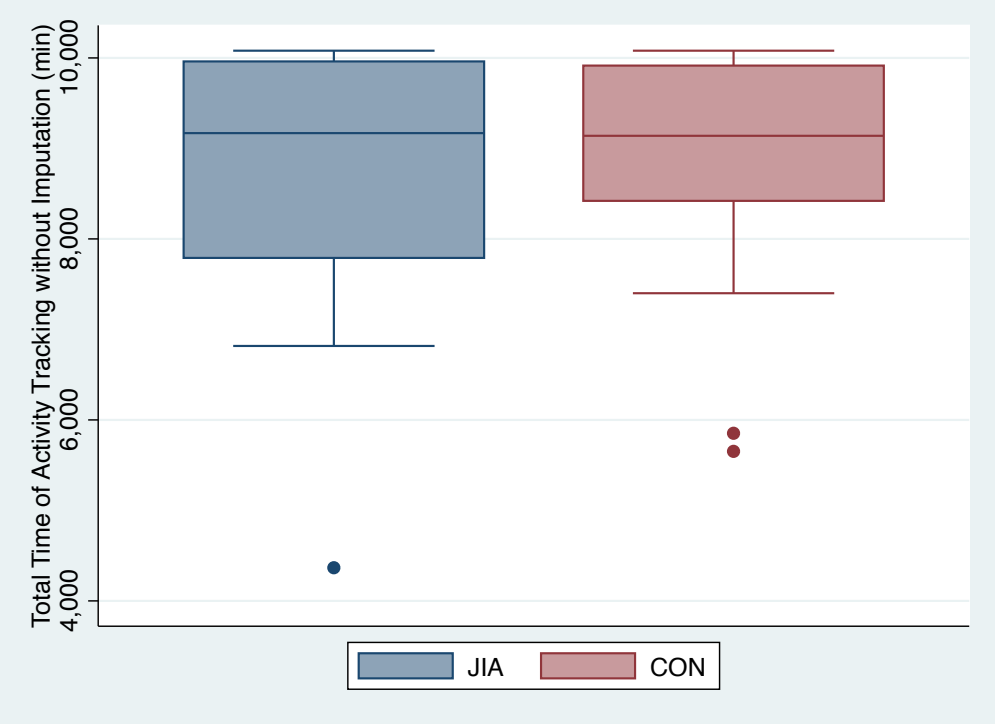

Figure 4.6 Total wear time without imputation (min) in youth with JIA (JIA) and healthy controls (CON)

Not imputed physical activity outcomes are described by median and range, stratified by study group (Table 4.3). The Wilcoxon-signed rank test was used to assess the matched-pair difference distributions that deviated from normal. Medians are reported with 95% confidence intervals (CI) created with the Hodges- Lehmann treatment. When matched- pair differences were normally distributed, paired t-tests were used to evaluate pair differences. Means and 95% confidence intervals are reported. See Table 4.3 to compare PA outcomes using imputed and not imputed data.

Table 4.3 Paired t-test mean difference and 95% CI or median difference and 95% CI by the Hodges- Lehmann treatment comparing imputed and not imputed data for physical activity (PA) outcomes in children with JIA (JIA) and healthy controls (CON)

Data Handling Procedure	PA Outcome Measure	JIA (n=22) Median (range)	CON (n=22) Median (range)	Mean or Median Pair Difference (JIA - CON) (95% CI)
Imputed	Mean MVPA per day (min)	45.1 (18.0-111.9)	72.9 (25.7-190.6)	-13.8 (-31.1, -9.0)*
	Mean percent of day spent in MVPA (%)	3.3 (1.4-7.8)	5.5 (1.8-14.3)	-1.6 (-3.0, -0.2)†*
	Mean SLPA per day(min)	1290.8 (852.4-1400.2)	1282.0 (768.0-1414.3)	1.9 (-27.4, 32.9)
	Mean percent of day spent in SLPA (%)	96.8 (92.1-98.6)	94.5 (85.7-98.2)	1.2 (0.5, 2.2)*
Not Imputed	Mean MVPA per day (min)	44.3 (18.1-105.4)	48.4 (12.5-100.6)	-1.3 (-14.9, 12.3)
	Mean percent of day spent in MVPA (%)	3.2 (1.4-7.5)	3.6 (1.0-8.8)	-0.02 (-1.0, 1.0)†
	Mean SLPA per day(min)	1282.9 (852.5-1400.2)	1278.1 (768.0-1414.3)	1.9 (-55.5-50)
	Mean percent of day spent in SLPA (%)	96.8 (92.6-98.6)	96.5 (91.1-99.0)	0.07 (-0.9, 1.1)

*p <0.05
†mean pair difference reported, evaluated with paired-test
MVPA = moderate to vigorous physical activity, SLPA= sedentary to light physical activity

When the physical activity data that was not imputed was evaluated, no difference was found between matched pairs for all PA outcomes (Table 4.3). Trends between groups remained the same as those found with imputed data. CON participants spent more time per day in MVPA and a greater proportion of their day in MVPA than JIA participants. CON participants also spent fewer minutes of their day in SLPA, and less proportion of their day in lower-intensity activities than youth with JIA.

In Figure 4.7 and 4.8, the impact of imputed data on the two groups' time spent in MVPA can be visually assessed. The CON group has a noticeable increase in the median minutes spent in MVPA per day. The appearance of the outlier when imputed data is considered (Figure 4.7) is consistent with the imputation of the ballet and swimming lessons for the control participant. Although subtle, in the JIA group the distribution shifts up when imputed data is included.

A similar distribution shift is seen when proportion per day in MVPA is examined (Figure 4.7 and 4.8). However, it should be noted, the control outliers in Figure 4.9 and 4.10 are not the same participant. The outlier in 4.9 benefited from the ability to impute her PA, while the outlier in 4.9 completed their MVPA while wearing the ActiGraph device.

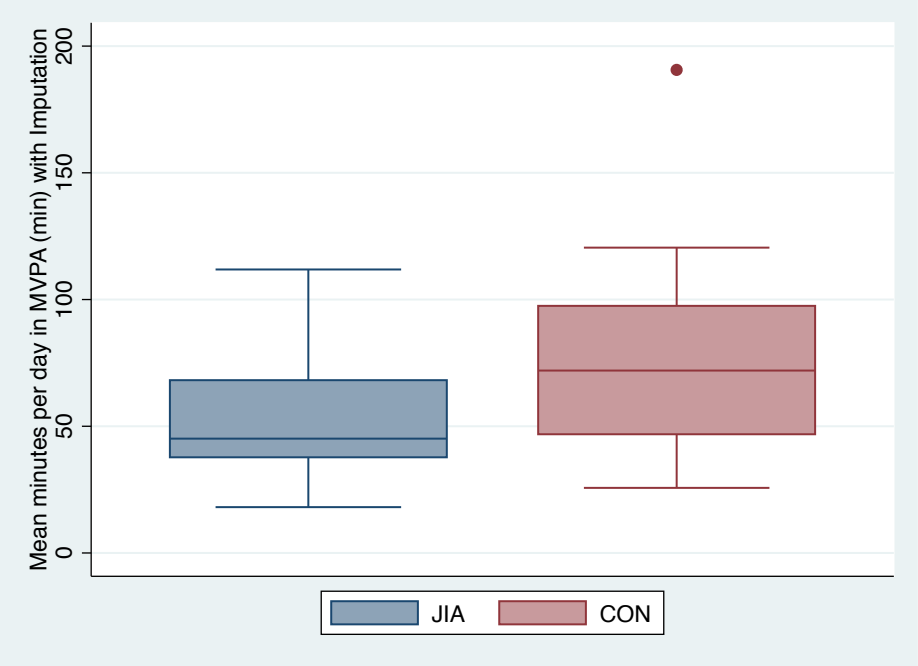

Figure 4.7 Mean minutes per day spent in moderate to vigorous (MVPA) with imputed data in youth with JIA (JIA) and healthy controls (CON)

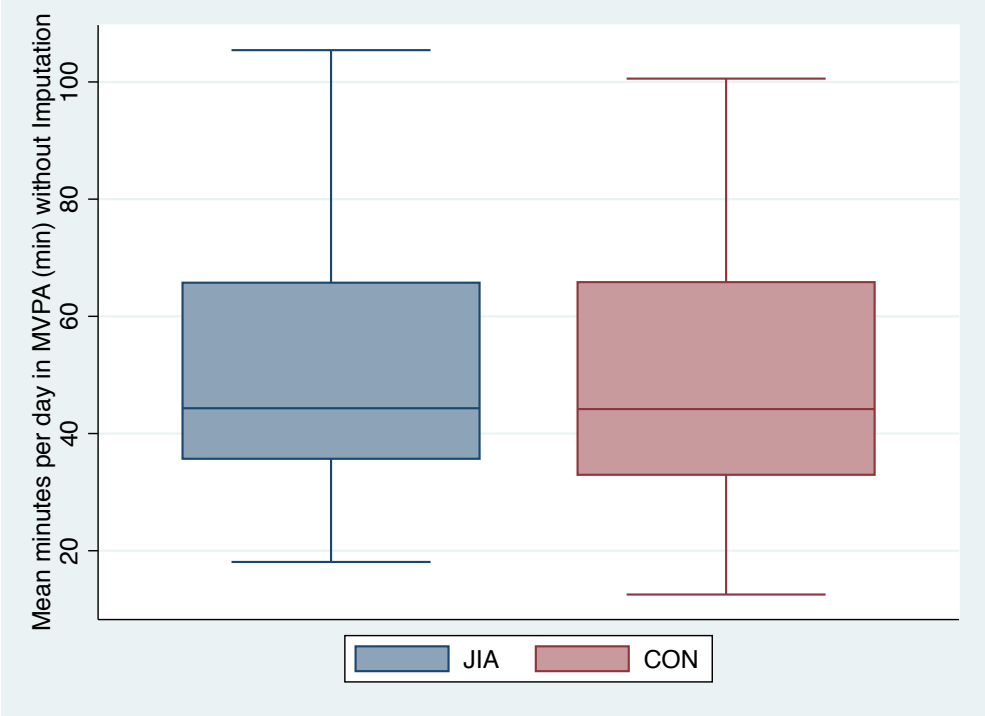

Figure 4.8 Mean minutes per day spent in moderate to vigorous (MVPA) without imputed data in youth with JIA (JIA) and healthy controls (CON)

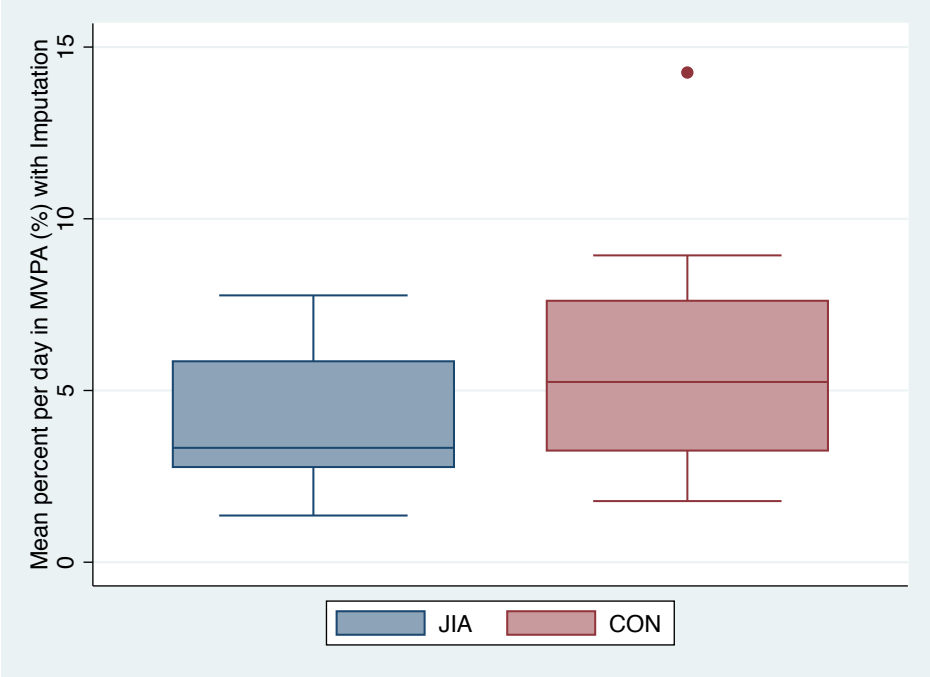

Figure 4.9 Mean proportion (%) per day spent in moderate to vigorous (MVPA) with imputed data in youth with JIA (JIA) and healthy controls (CON)

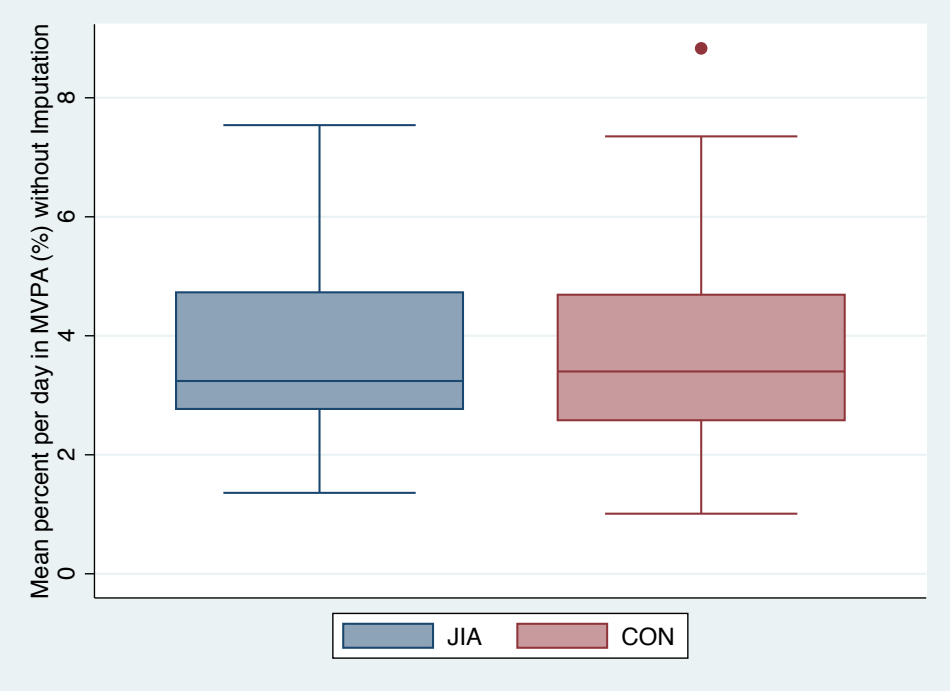

Figure 4.10 Mean proportion (%) per day spent in moderate to vigorous (MVPA) without imputed data in youth with JIA (JIA) and healthy controls (CON)

Imputed and non-imputed mean time spent in SLPA per day was examined in the study groups. The JIA cohort median time spent in SLPA per day was very similar with or without with the inclusion of imputed data (Figure 4.11 and Figure 4.12). In the CON group, the median amount of time spent in SLPA per day did not change, however the distribution shifted to less time in SLPA in response to the imputation of MVPA (Figure 4.11 and 4.12) Figure 4.13 and 4.14 illustrate a shift in the JIA and CON distribution with the inclusion of SLPA, as the mean proportion of time spent per day in SLPA decreases with the imputation of MVPA activities.

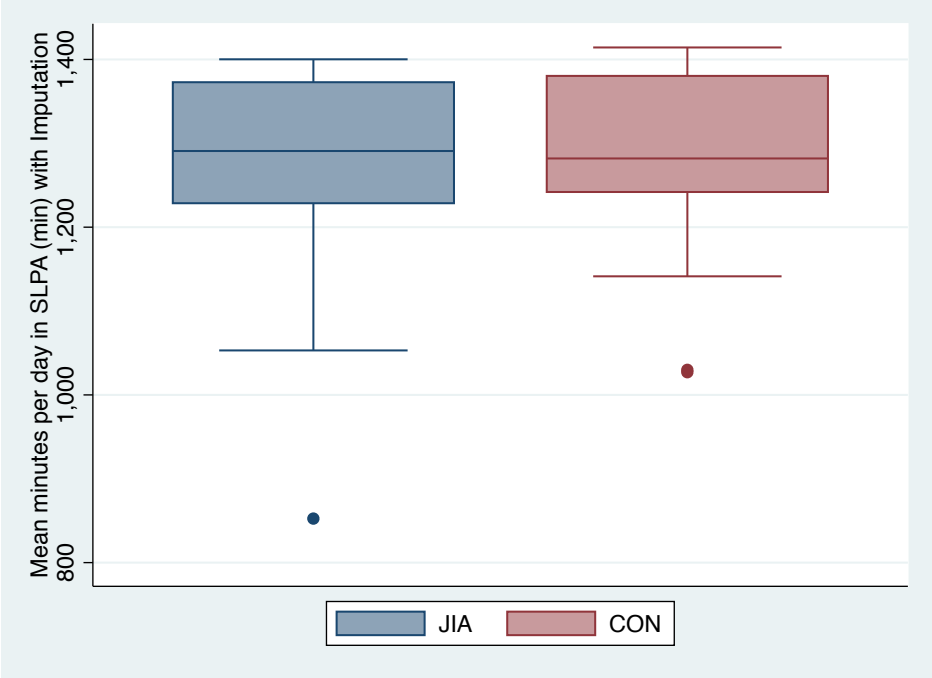

Figure 4.11 Mean minutes per day spent in sedentary to light physical activity (SLPA) with imputed data in youth with JIA (JIA) and healthy controls (CON)

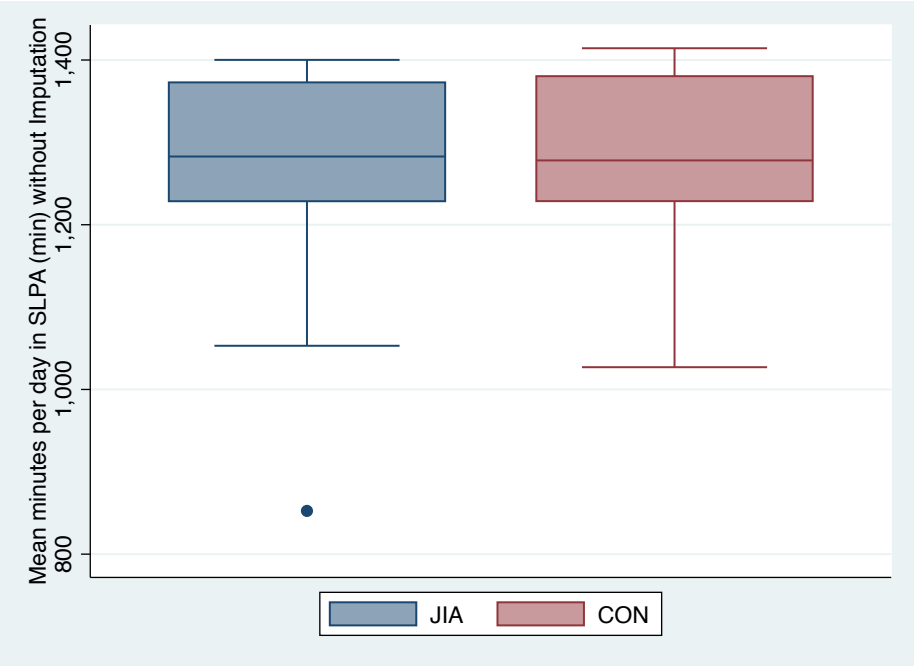

Figure 4.12 Mean minutes per day spent in sedentary to light physical activity (SLPA) without imputed data in youth with JIA (JIA) and healthy controls (CON)

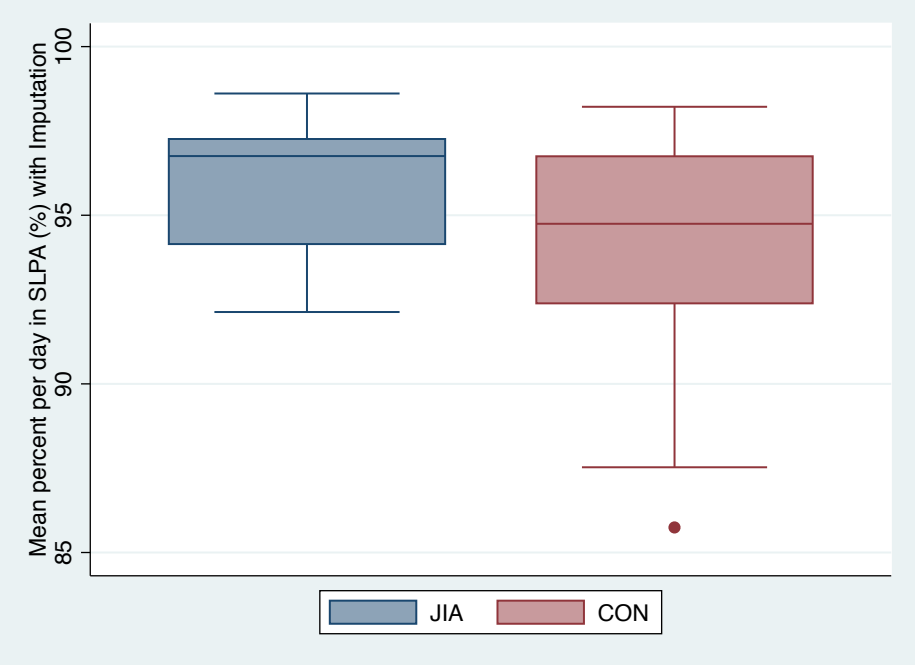

Figure 4.13 Mean proportion (%) per day spent in sedentary to light physical activity (SLPA) with imputed data in youth with JIA (JIA) and healthy controls (CON)

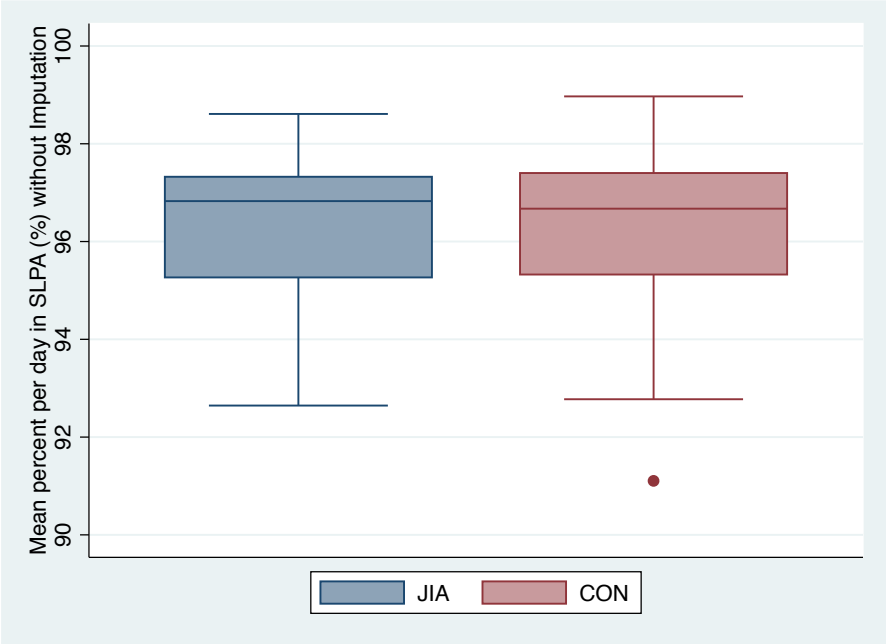

Figure 4.14 Mean proportion (%) per day spent in sedentary to light physical activity (SLPA) without imputed data in youth with JIA (JIA) and healthy controls (CON)

4.2.3.2 Adult and Child Algorithm Use

In this investigation, PA intensity level was determined by the Evenson et al. cut-points, established for children under 18 years old. [100] One matched pair included participants over 18 years old, with ages ranging from 19.5 to 20.1. To maintain homogeneity in our investigation, Evenson et al. algorithms were used initially to evaluate the PA of the adult participants. The ActiGraph data was then analyzed with the adult algorithm in order to ensure no significant changes occurred. An algorithm established by Troiano et al. (Troiano Adult (2008)) for adults was applied, in alignment with SIPRC protocol (see Appendix B).[63] Table 4.4 compares the pair difference for the mean time and proportion spent in MVPA and SLPA for both child and adult algorithms.

Table 4.4 Median (range) and pair differences comparing child and adult algorithms for physical activity (PA) outcomes in a participant with arthritis (JIA) and a healthy control (CON)

Algorithm Used	PA Outcome Measure	JIA (n=1) Median (range)	CON (n=1) Median (range)	Pair Difference (JIA - CON)
Evenson et al. (2008) - Child	Mean MVPA per day (min)	37.7	33.0	4.8
	Mean percent of day spent in MVPA (%)*	2.7	2.3	0.4
	Mean SLPA per day(min)	1372.8	1407.0	-34.2
	Mean percent of day spent in SLPA PA (%)	97.3	97.7	-0.4
Troiano et al. (2008) - Adult	Mean MVPA per day (min)	42.6	37.1	5.5
	Mean percent of day spent in MVPA (%)*	3.0	2.7	0.3
	Mean SLPA per day(min)	1397.3	1342.2	55.1
	Mean percent of day spent in SLPA PA (%)	97.0	97.3	-0.3

MVPA = moderate to vigorous physical activity, SLPA = sedentary to light physical activity

Overall, more time was allocated to MVPA in the two when adult algorithms were used (Table 4.4). The largest discrepancy between the algorithms is the pair difference in the mean minutes of SLPA minutes per day. The adult algorithm allocates 64.5 minutes less time in SLPA for the CON participant. This could be explained by the subject participating in a number of activities that were classified as light with the child algorithm and moderate with the adult algorithm.

A sensitivity analysis on the final PA outcomes was conducted using the adult and child MVPA and SLPA means and percentages for the above pair. The median pair differences and 95% CI did not change for the mean time spent in MVPA per day, or the mean percent of day spent in MVPA or SLPA. The median pair difference for the mean time spent in SLPA per day did not change after adult algorithms were implemented for the appropriate pair, however the confidence interval did widen [1.9min (95% CI -48.8, 28.4)].

4.3 Functional and Physical Measures

Univariate analyses were used to investigate all primary, secondary, and exploratory outcomes for functional and physical measures. Median (range) were reported by study group for all functional and physical measures (Table 4.5). CON and JIA pair difference (JIA-CON) distributions of relative aerobic capacity (ml/kg/min), TSLH distance on the dominant and non-dominant leg, and SEBT on the dominant were found to be normal and paired t-tests were used to created 95% CI around mean pair differences. FMI, SEBT on the non-dominant foot, and ECDB on the dominant and non-dominant foot were found to have pair differences with a right skew, and the Wilcoxon-signed Rank test was used to assess the between group differences for

significance. The Hodges-Lehmann treatment was used to create 95% CI for median pair differences. Median or mean pair differences and 95% CI were reported (Table 4.5).

Table 4.5 Functional and physical outcomes paired t-test mean difference and 95% CI or median difference and 95% CI by the Hodges- Lehmann treatment in children with arthritis (JIA) and healthy controls (CON)

Physical or Functional Outcome Measure	JIA Median (range)	CON Median (range)	Mean or Median Pair Difference (JIA - CON) (95% CI)
Relative VO_{2peak} (mL/ kg/ min)	39.0 (27.3-66.9)	44.6 (25.5-60.0)	-0.7 (-5.0, 3.7)† N=23
FMI (kg/m^2)	4.4 (2.3-15.1)	4.4 (1.7-12.3)	-0.1 (-0.6, 0.7) N=24
TSLH Distance as Percentage of Dominant Leg (%)	487.8 (335.9-654.8)	518.5 (380.1-643.7)	1.2 (-46.9, 49.2)† N=25
TSLH Distance as Percentage of Non-dominant Leg (%)	481.5 (332.5-629.3)	503.2 (362.7-697.3)	-4.1 (-52.0, 43.9)† N=25
SEBT Dominant Foot normalized composite reach distance (%)	80.7 (63.9-92.0)	77.6 (62.5-86.9)	3.6 (-0.6, 7.8)† N=25
SEBT Non- dominant Foot normalized composite reach distance (%)	78.8 (63.1-94.2)	76.9 (64.4-85.3)	0.5 (-1.6, 6.3) N=25
Dominant Foot Unipedal Dynamic Balance Maximum Time (sec)	4.9 (2.34-18.65)	6.71 (2.6-23.2)	-1.7 (-2.7, 0.5) N=24
Non-dominant Foot Unipedal Dynamic Balance Maximum Time (sec)	4.1 (2.68-11.13)	5.7 (3.51-15.64)	-0.9 (-2.8, -0.01) N=24

†mean pair difference reported, evaluated with paired-test
N= number of matched pairs, FMI = fat mass index, TSLH = triple single leg hop, SEBT = star excursion balance test, JIA= youth with arthritis, CON= healthy controls

4.3.1 Adiposity

Median measures of fat mass index (FMI) (kg/m^2) between the cohorts were similar and a similar distribution of FMI was seen between those with JIA and the healthy controls (see Table 4.5). The median matched-pair difference between groups was not statistically significant [$-0.1 kg/m^2$; 95% CI -0.3, 0.4]. Forty- six DXA scans were performed; for two participants, the machine was under maintenance and two participants were lost to follow up. Due to lack of literature on normative values of FMI for youth, whole body fat percent based on age and sex was used to describe the nutritional status of the study population.[118] One (2%) control youth was classified as underweight, 40 (87%) were classified as normal (22 JIA, 18 CON), and three (7%) (1 JIA, 2 CON) were classified as overweight.[118] Two outliers of note were observed, one male with JIA and one female control (Figure 4.15). Their body fat percent classified them as obese, with FMI of 15.1 kg/m^2 and $12.3 kg/m^2$ respectively.[117] Four participants did not undergo a DXA scan.

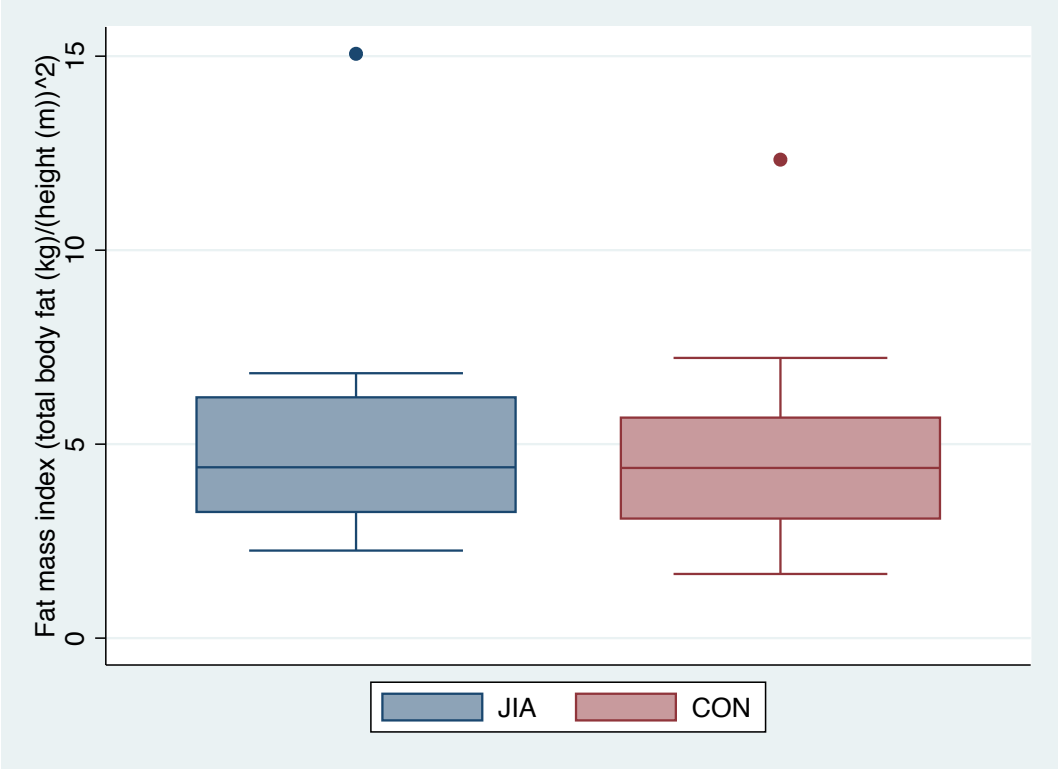

Figure 4.15 Fat mass index (FMI) [fat (kg)/ height (m2)] in youth with JIA (JIA) and healthy controls (CON)

4.3.2 Aerobic Capacity

The median relative VO_{2peak} was lower in the JIA cohort 39.0mg/kg/min (95% CI 27.3-66.9) compared to the CON cohort 44.6mL/kg/min (95% CI 25.25-60.0), however, the mean matched pair difference between groups was not statistically significant [-0.7 mL/kg/ min; 95% CI -5.0, 3.7, p=0.80]. A similar spread of the data was observed in the two samples, indicating a wide range of abilities within both cohorts (see Figure 4.16). This was confirmed by classifying the relative VO_{2peak} scores into normative percentiles based on age and sex.[117] Forty-eight VO_{2peak} tests, 25 for control participants and 23 for youth with JIA were performed. One participant with JIA was lost to follow up and another did not consent. Fifty-two percent (25) of the participants were classified in the 50th and 75th percentile (11 JIA, 14 CON). Six (12%)

reached the 90th percentile (3 JIA, 3 CON), and three (6%) of the participants demonstrated superior aerobic capacity for their age and sex, reaching the 95th percentile (1 JIA, 2 CON). In contrast, 11 (23%) participants demonstrated lower aerobic capacity, and classified in the 25th (two), 15th (five), 10th (two), and 5th (two) percentiles (7 JIA, 4 CON). Of note are three participants (6%), one JIA and two CON who demonstrated very low aerobic capacity, being classified in the 2nd percentile.

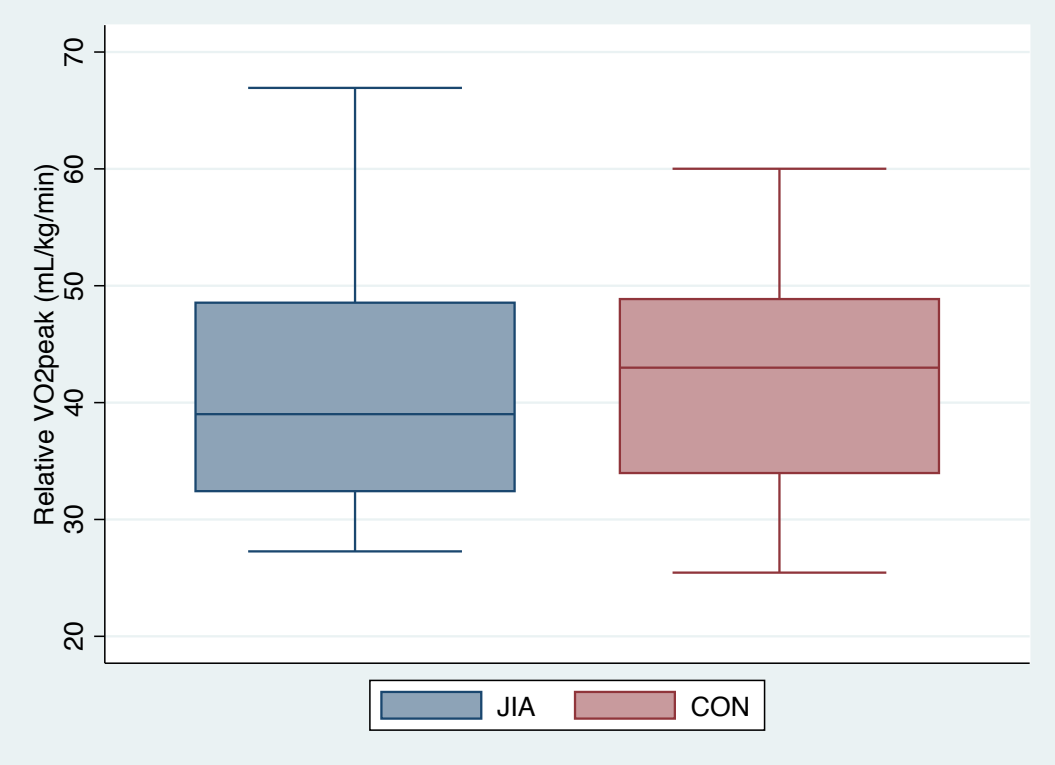

Figure 4.16 Relative VO_{2peak} (mL/kg/min) in youth with JIA (JIA) and healthy controls (CON)

4.3.3 Triple Single Leg Hop (TSLH)

The TSLH distance achieved by each participant was normalized by dividing maximum distance hopped by leg length. Median pair differences (JIA-CON) revealed the CON cohort covered slightly more distance in their TSLH than the JIA cohort while hopping on dominant and non-dominant legs. In both cohorts, the median dominant leg performance was slightly better than the non-dominant (Table 4.5). However, mean differences between groups were not significant for either leg (dominant [1.2%; 95% CI -46.9, 49.2], non-dominant [-4.05%; 95% CI -52.0, -43.9]) (Table 4.5).

4.3.4 Eyes Closed Dynamic Balance (ECDB)

Maximum time over three trials on the dominant and non-dominant foot were found for the single leg Eyes Closed Dynamic Balance (ECDB) on a foam pad. The median ECDB maximum balance time was higher for dominant and non-dominant legs in the CON cohort (Table 4.5). Both groups balanced longer on their dominant legs versus the non-dominant leg (Table 4.5). The median of the matched-pair difference between groups was not significant on either the dominant [-1.7sec; 95% CI -2.7, 0.5] or non-dominant leg [-0.9sec; 95% CI -2.8, -0.01]. The analysis for the EDCB included 24 pairs, as one JIA participant with visual impairment was unable to complete the test.

4.3.5 Star Excursion Balance Test (SEBT)

Maximum reach for the three directions of the star excursion balance test (SEBT) were normalized over leg length. In both cohorts, the median dominant leg SEBT performance was slightly higher than the non-dominant leg. (Table 4.5). The median normalized reach distance

was higher on dominate and non-dominant legs for the JIA cohort. However, the median pair differences of the dominant and non-dominant were not significantly different (Table 4.5).

4.4 Functional and Physical Outcomes Stratified by Sex

The effect of sex on MVPA, aerobic capacity, adiposity, and triple single leg hop (TSLH) distance was examined between youth with JIA (JIA) and healthy controls (CON) (Table 4.6). Outcomes are described (medians and ranges) by study group (JIA vs. CON) (Table 4.6). The Wilcoxon-signed rank test was used to assess the matched- pair difference distributions that deviated from normal. Medians are reported with 95% confidence intervals (CI) created with the Hodges- Lehmann treatment, where possible. Due to low sample size, it was inappropriate to create 95% CI's by the Hodges-Lehmann treatment in males; therefore, interquartile ranges (IQR) are reported. When matched- pair differences were normally distributed, paired t-tests were used to evaluate pair differences. Means and 95% confidence intervals were reported.

In addition to the above, the amount of time spent in MVPA per day and pain, disease duration, and self-reported functional disability (CHAQ score) was explored graphically for the JIA cohort.

Table 4.6 Functional and physical outcomes paired t-test mean difference and 95% CI or median difference and 95% CI by the Hodges- Lehmann treatment in children with arthritis (JIA) and healthy controls (CON), stratified by sex

Outcome	Females		Mean or Median Pair Difference (JIA - CON) (95% CI)	Males		Median Pair Difference (JIA - CON) (IQR)
	JIA Median (range)	CON Median (range)		JIA Median (range)	CON Median (range)	
Mean MVPA per day (min)	44.3 (18.1-111.9)	66.0 (25.7-190.6)	-11.1 (-50,0, 12.0) N=14	52.1 (28.4-73.5)	83.0 (30.1-112.5)	-25.9 (50.5) N=8
Relative VO_{2peak} (mL/ kg/ min)	37.7 (29.7-51.2)	37.6 (25.5-52.1)	0.8 (-1.7, 5.0) N=15	45.6 (27.3-66.9)	49.1 (35.5-60.0)	-5.2 (19.45) N=8
FMI (kg/m^2)	4.7 (3.1-6.7)	5.3 (3.4-12.3)	-0.5 (-1.7, 0.7) N=14	3.1 (2.3-15.1)	2.6 (1.7-4.2)	0.3 (1.9) N=8
TSLH Distance as Percentage of Dominant Leg (%)	500.2 (405.6-643.2)	484.7 (380.1-611.6)	6.5 (-41.5, 96.3)† N=16	486.8 (335.9-649.1)	541.8 (460.8-643.7)	-25.9 (127.9) N=9
TSLH Distance as Percentage of Non-dominant Leg (%)	496.0 (332.5-625.6)	455.7 (362.7-600.0)	34.5 (-11.0, 59.8) N=16	490.7 (355.8-629.4)	537.2 (490.5-697.3)	-44.6 (116.4) N=9

†mean pair difference reported, evaluated with paired-test
N= number of matched pairs, IQR= Inter- Quartile Range, MVPA = moderate to vigorous physical activity, FMI = fat mass index, TSLH = triple single leg hop, JIA= youth with arthritis, CON= healthy controls

Due to low sample size, it was inappropriate to create 95% CI's by the Hodges-Lehmann treatment in males and therefore, interquartile ranges (IQR) are reported. When MVPA participation is examined by sex, it is clear that both males and females with JIA are accumulating less time per day in higher intensity activity than their healthy peers of the same

sex. (Table 4.6) While some were very active, females with JIA are spending a median of 11 minutes less in MVPA per day than healthy females (95% CI -50,0, 12.0) (Table 4.6). Males with JIA are spending a median of 26 minutes less in MVPA per day per day than healthy males (IQR 50.5). Females with JIA are spending the least median amount of time in MVPA out of all the groups examined. The relationships above can be clearly observed in Figure 4.17. Figure 4.17 also indicates the healthy male participants had higher variability in the time per day spent in MVPA, compared to males with JIA. Female distributions are quite similar in both groups.

The crude association between groups for time spent per day in MVPA is described by the median difference (95% CI) [-13.8 (-31.1, -9.0)]. The sex stratum specific median pair differences (JIA-CON) are quite different. The female JIA-CON median difference (95% CI) is less than crude median pair difference [-11.1 (-50,0, 12.0)], and male JIA-CON median difference (IQR) is more than the crude median pair difference [-25.9 (50.5)] (Table 4.5 and Table 4.6). It appears sex is an effect modifier and should be considered when examining MVPA in youth with JIA compared to healthy controls.

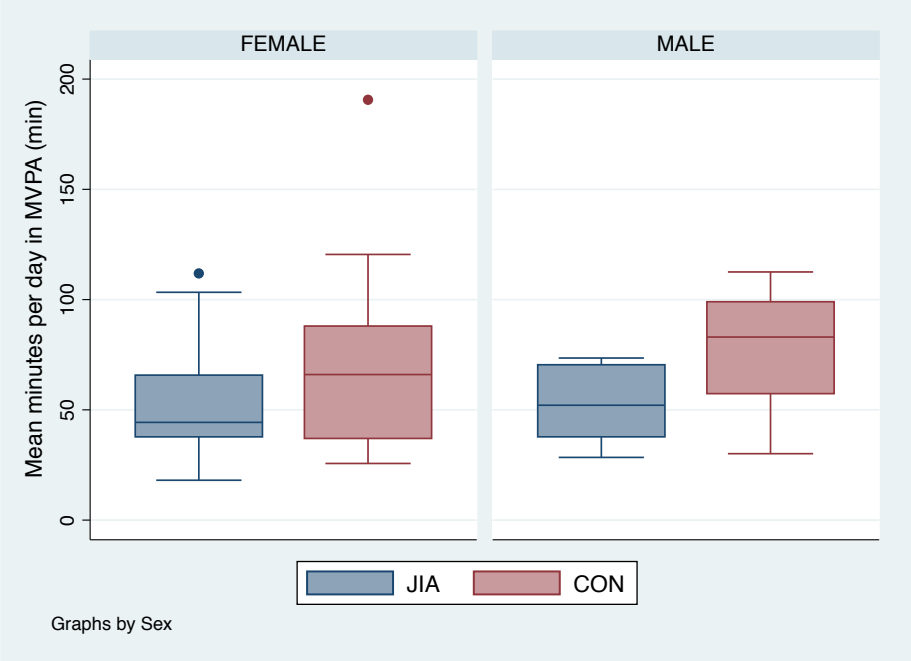

Figure 4.17 Mean time in moderate to vigorous physical activity (MVPA) per day (min) in females (matched pairs= 14) and males (matched pairs =8) with JIA (JIA) and healthy controls (CON)

Comparisons of aerobic fitness by sex show females with JIA have a higher relative VO_{2peak} [median difference (95%CI) 0.8 mL/kg/min (-1.7, 5.0)] than female controls (Table 4.6). In contrast, males with JIA have a relative VO_{2peak} deficit of 5.2 mL/kg/min compared to their healthy peers [median difference (IQR) -5.2 (19.45)], although a wide variability in the male youth with JIA is seen (Table 4.6) This difference is distinct in Figure 4.18. Two outliers in the male controls can be observed. The high outlier reached a VO_{2peak} that classified him in the 95th percentile for his age and sex. The low outlier reached a VO_{2peak} that classified him in the 5th percentile for his age and sex. The rest of the group was between the 50th and 75th percentiles, therefore these two participants stand out. Again, we observe that the female distributions of aerobic capacity are more alike than the male distributions. The males with JIA have high variability in their VO_{2peak} scores, while healthy males are tightly grouped, besides the two

outliers. The deficit observed in relative VO_{2peak} between JIA and CON cohorts when the sexes are grouped together may be a result of decreased aerobic capacity in males with JIA (Table 4.5). A larger sample size would be required to the confirm the evidence presented here.

The crude association between groups for relative VO_{2peak} was [mean difference (95% CI), -0.7 (-5.0, 3.7)]. The sex stratum specific median pair differences found were quite dissimilar, with each stratum estimate lying on either side of the crude estimate (Table 4.6). It appears sex is an effect modifier that should considered when examining aerobic capacity in youth with JIA compared to healthy controls.

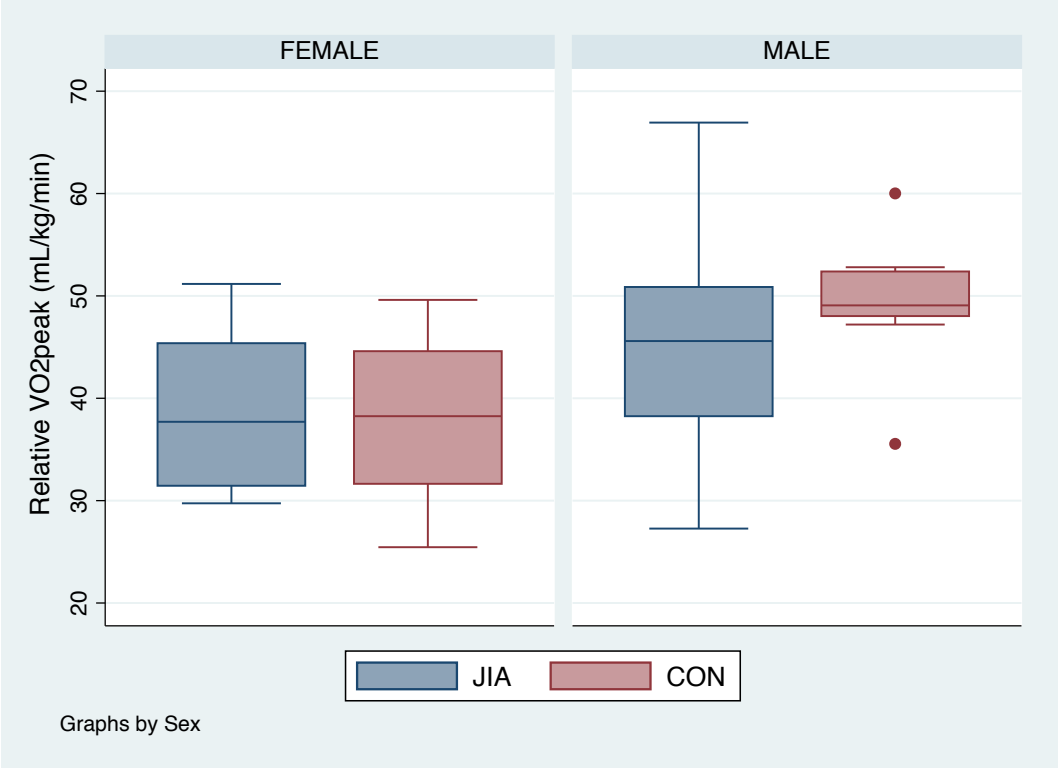

Figure 4.18 Relative VO_{2peak} (mL/kg/min) in females (matched pairs=15) and males (matched pairs=8) with JIA (JIA) and healthy controls (CON)

Examination of fat mass index (FMI) by sex reveals that females with JIA had slightly lower adiposity than healthy female [median difference (95% CI) -0.5 (-1.7, 0.7)]. This result must take into consideration the outlier in the female healthy controls (Figure 4.19). This participant was the only female classified as obese. The males with JIA had higher adiposity than the control males [median difference (IQR) 0.3 (1.9)], however an outlier in the male JIA group must be considered. (Figure 4.19). This participant was the classified as the only male classified as obese. Here the distributions show a similar range for FMI between JIA and CON participants in both males and females. (Figure 4.19) Overall, males had lower fat mass indices than females (Table 4.6).

The crude association between groups for relative FMI was, median difference (95% CI), -0.1 (-0.3, 0.4). The sex stratum specific median pair differences found were quite dissimilar, with each stratum estimate lying on either side of the crude estimate (Table 4.6). It appears sex is a modifier that should be considered when examining adiposity in youth with JIA compared to healthy controls.

Figure 4.19 Mean fat mass index ((total body fat (kg)/ (height (m))^2) in females (matched pairs=14) and males (matched pairs=8) with JIA (JIA) and healthy controls (CON)

Finally, maximum distance achieved on a triple single leg hop (TSLH) test on the dominant and non-dominant leg, presented as percentage of the corresponding leg length, was compared by sex between the study groups. Interestingly, females with JIA had higher median jump distance than female controls on both the dominant [mean difference (95% CI) 6.5% (-41.5, 96.3)] and non-dominant leg [median difference (95% CI) 34.5% (-11.0, 59.8)]. This trend was not reproduced in the males. Males with JIA had large deficits in TSLH performance on the dominant [median difference (IQR) -25.9 (127.9)], and non-dominant leg [median difference (IQR) -44.6 (116.4)], compared to their same-sex healthy peers. Males with JIA demonstrated a wide range of hopping abilities on their dominant leg (Figure 4.20). Healthy females had the lowest TSLH distance medians of for dominant and non-dominant legs out of all the groups

examined (Table 4.6). All groups had higher medians for jumps made on their dominant compared to non-dominant leg except males with JIA.

The crude association between groups for TSLH distance as percentage of leg length was, mean difference (95% CI), 1.2 (-46.9, 49.2) on the dominant leg and mean difference (95% CI), -4.1(-52.5, 43.9) on the non-dominant leg. The sex stratum specific median pair differences found were quite dissimilar, with each stratum estimate lying on either side of the crude estimate (Table 4.6). It appears sex is an effect modifier that should be considered when examining dynamic balance in youth with JIA compared to healthy controls.

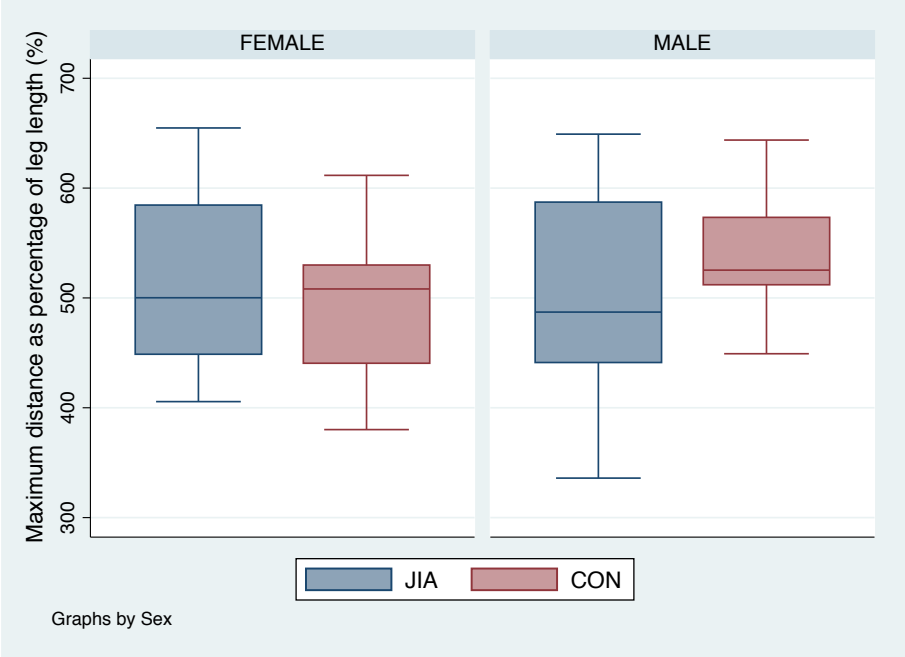

Figure 4.20 Triple single leg hop maximum distance as the percentage of leg length (%) on the dominant leg in females (matched pairs=16) and males (matched pairs=9) with JIA (JIA) and healthy controls (CON)

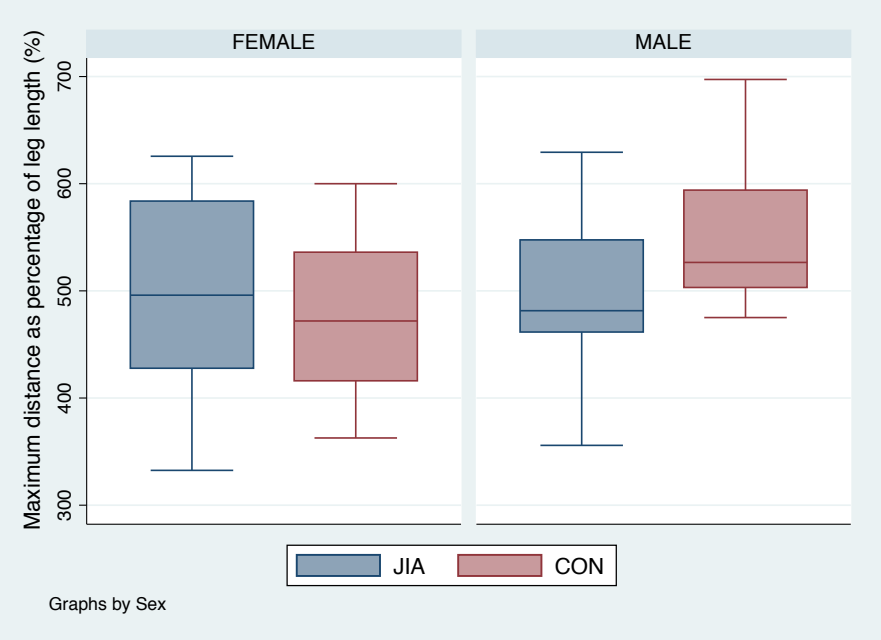

Figure 4.21 Triple single leg hop maximum distance as the percentage of leg length (%) on the non- dominant leg in females (matched pairs=16) and males (matched pairs=9) with JIA (JIA) and healthy controls (CON)

4.4.1 Association between Disease Characteristics and Physical Activity in youth with JIA

In JIA participants, there appears to be no association between mean time spent per day in MVPA and disease activity (Figure 4.22), disease duration (Figure 4.23), functional disability (Figure 4.24), or pain (Figure 4.25).

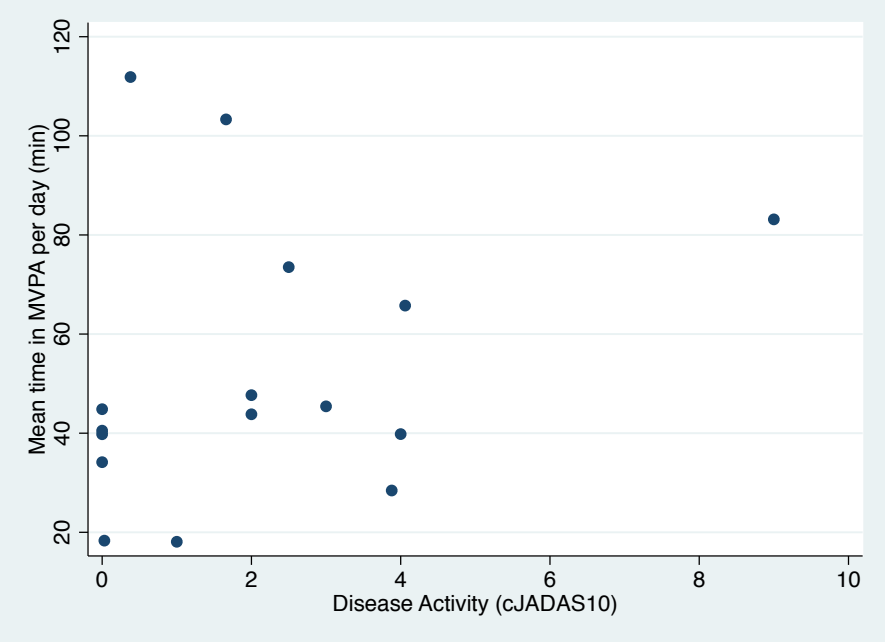

Figure 4.22 Mean time in moderate to vigorous physical activity (MVPA) per day (min) compared to disease activity as measured by the clinical Juvenile Arthritis Disease Activity Score (cJADAS10) in youth with JIA.

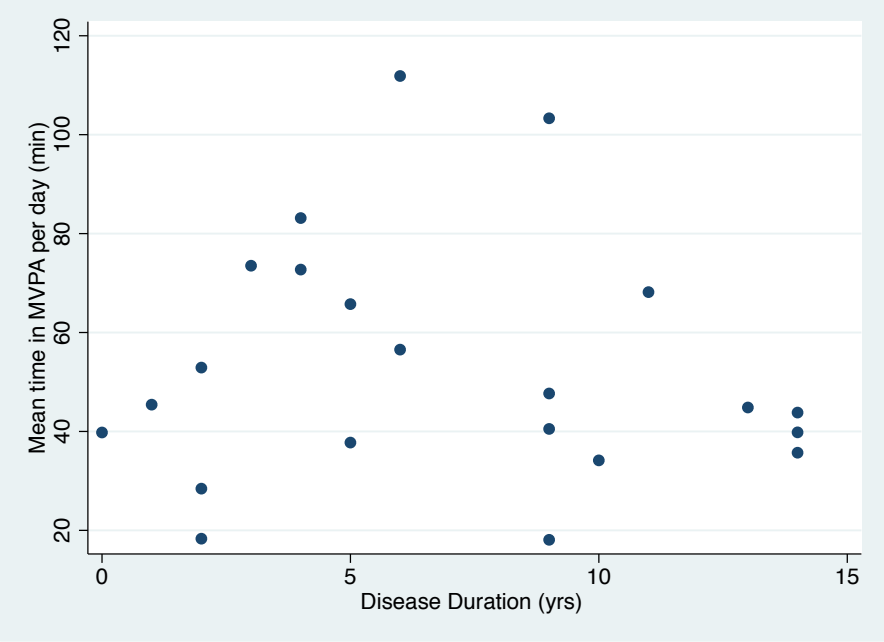

Figure 4.23 Mean time in moderate to vigorous physical activity (MVPA) per day (min) compared to disease duration (years) and youth with JIA.

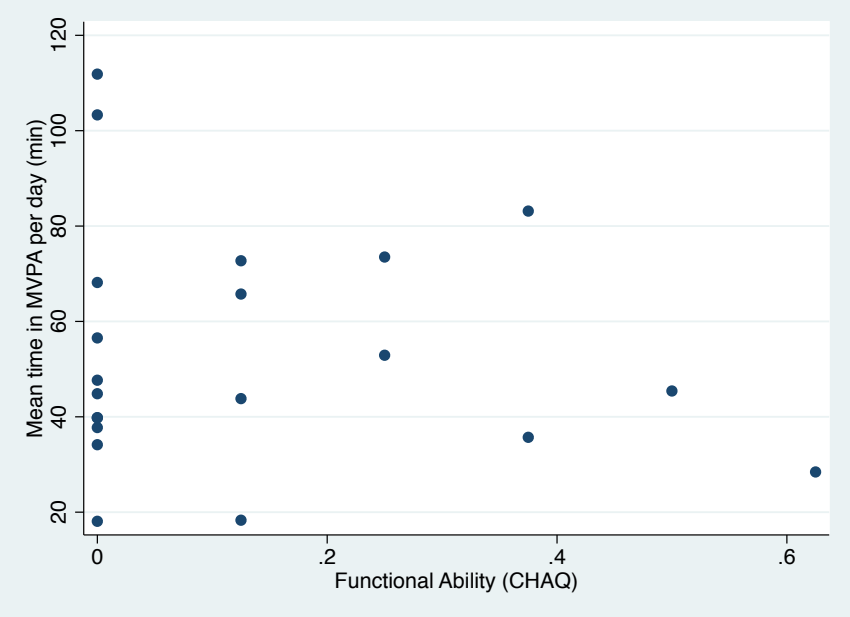

Figure 4.24 Mean time in moderate to vigorous physical activity (MVPA) per day (min) compared to functional ability as measured by the Childhood Health Assessment Questionnaire (CHAQ) in youth with JIA.

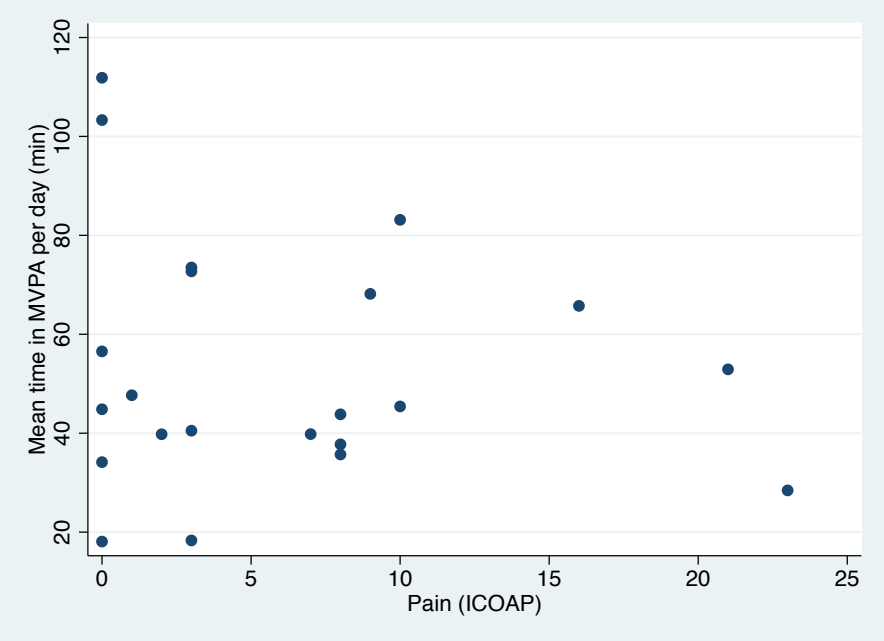

Figure 4.25 Mean time in moderate to vigorous physical activity (MVPA) per day (min) compared to pain as measured by the Intermittent and Constant Osteoarthrosis Pain (ICOAP) scale in youth with JIA.

4.5 Effect size and Power

Effect size and power were explored for the two primary outcome variables, time spent per day in MVPA and aerobic capacity found as relative VO_{2peak} (mL/kg/min). No previous literature on these outcomes reported standard deviations of the paired differences, which are required to conduct traditional sample size calculations. Therefore, the standard deviations of each of the JIA and the healthy control groups from previous investigations were used to estimate the potential standard deviation of the mean difference between matched pairs. The standard deviation of the difference was calculated for several values of potential correlation values between the two groups for each primary outcome. Then, power calculations were completed for each of the two primary outcomes: mean time spent in MVPA (min) per day and aerobic capacity defined as relative VO_{2peak} (mL/kg/min), based on the collected sample size of 25 matched pairs.

An investigation by Norgaard et al. compared the mean minutes of MVPA accumulated per day between youth with JIA (n=61) and age and sex matched healthy controls from reference databases (n=2055).[44] PA was assessed using accelerometry. The mean and standard deviation that they found for the JIA group was 97.1 (40.4) minutes and for the control groups was 117.2 (23.5) minutes. Based on these means and standard deviations, and for all potential values of correlation (from -1 to +1), a biostatistician was able to estimate potential standard deviations of the difference within matched pairs based on statistical formulas for standard deviation of the difference between two random variables (see graph Appendix J). For detecting a difference between groups of at least 20.1, if 80% power is desired, a standard deviation of the mean difference between pairs should be 34.4 minutes, which could correspond to a correlation within pairs of 0.527.

Lelieveld et al. examined the aerobic capacity in 22 youth with JIA compared to 27 age and sex matched healthy controls.[93] Aerobic capacity was assessed with a VO_{2peak} test to volitional fatigue on a bike. The mean and standard deviation for the JIA group was 35.36 (7.95) mL/kg/min and for the control group was 43.98 (5.85) mL/kg/min. Based on these standard deviations, and for all potential values of correlation (from -1 to +1), a biostatistician was able to estimate potential standard deviations of the difference within matched pairs (see graph in Appendix K). For detecting a difference between groups of at least 8.62, and given that correlation cannot be less than -1, the maximum standard deviation within pair differences that could be observed is 13.8, which would then yield a minimum power of 85%.

After the conclusion of data collection for 25 matched pairs, standard deviations were estimated for the within paired differences for each primary outcome for this study. The standard deviation for MVPA was 24.66, which is less than 34 minutes (as estimated a-priori for an 80% power), which could indicate this study was well-powered for this outcome. The standard deviation between pairs for relative VO_{2peak} was 10.09mL/kg/min, which is less than 13.8mL/kg/min (as estimated a-priori for an 85% power), which could indicate that our project is well-powered for this outcome.

4.6 Summary of Results

The results from this investigation indicate youth with JIA spend less time per day in moderate to vigorous activity, however this result is not significant after adjusting for multiple comparisons. An exploratory finding indicates youth with JIA spend more time per day in sedentary to light activity then their healthy peers. No difference between the JIA and CON groups was found for physical and functional outcomes. However, results from exploratory

analysis reveal sex is an effect modifier that must be taken into consideration when comparing youth with JIA and healthy controls in physical activity participation, and physical and functional outcomes.

Chapter Five: **Discussion**

The primary objective of this study was to examine physical activity (PA), defined as the mean time in minutes per day spent in moderate to vigorous activity over 7 days, in youth with JIA including knee involvement, compared to age and sex matched healthy controls. To the best of our knowledge, this is the first study to objectively measure the PA of youth with JIA inclusive of knee involvement, and to compare the results to data gathered concurrently in age and sex matched healthy controls.

Overall, the youth with JIA participated in less moderate to vigorous physical activity (MVPA) per day than their matched healthy peers, although this result was not significant after adjustment for multiple comparisons. Youth with JIA spent a larger proportion of their time in sedentary to light (SLPA) physical activities than matched youth controls. In addition, the participants with JIA exhibited similar dynamic balance abilities, aerobic capacity performance, and adiposity measures when compared to their healthy peers. These results were seen in a JIA cohort reporting relatively mild disease activity, pain, and functional disability.

5.1 Participant characteristics

Most youth with JIA in this study had oligoarticular, n=14 (56%), or polyarticular arthritis, n=9 (36%), and were female n=16 (64%). This is in alignment with the subtype and sex distribution seen in much of the literature on youth with JIA.[19, 24, 76] Most participants had mild disease activity (low cJADAS10), high functional ability (low CHAQ scores), and low active joint counts (Table 4.1). These proportions are consistent with the disease characteristics of most participants in studies evaluating PA in the JIA population.[24, 28]

To our knowledge, no previous investigation into PA has based study inclusion criteria on affected joints. Few investigations report details on unilateral, bilateral, or specific joint involvement, therefore it is not possible to compare the joint involvement history of our JIA cohort to previous studies.

The CON and JIA participants that were unable to be matched did not vary from those that were included in final analysis (Table 4.1). Every opportunity should be taken to recruit matches and contribute their data to the overall results.

5.2 Physical Activity Participation

5.2.1 Moderate to Vigorous Activity

Youth with JIA participated in less moderate to vigorous physical activity (MVPA) per day than age and sex matched healthy controls. These results are in accordance with previous studies of PA in adolescents with JIA, including recent studies utilizing accelerometery.[42, 43, 44] The studies that objectively measured PA mined large reference databases for control PA outcomes to compare to the youth with JIA recruited for the study.[9,44] Bohr et al. and Norgaard et al. used the ActiGraph to track the habitual PA of children with JIA, ages 7 to 20 and 10 to 16 years old respectively.[9,44] Compared to age and sex- comparable healthy youth reference data, both authors found those with JIA participated in significantly less moderate and high intensity PA.[9,44] Neither study required participants with JIA to have lower limb arthritis, nor did they use healthy PA data that was collected within the same year as the study was performed. A mean difference between groups was not reported in either study.[9,44]

In this investigation, it was found that youth with JIA spent a smaller percentage of their day in MVPA than controls. This supports the results seen in time spent in MVPA per day.

Arguably, proportion of day is the more informative measure, as it adjusts for time discrepancies that can occur when using activity monitoring devices and gives a holistic view of how PA is distributed over the day. Past investigations do not usually focus on reporting proportions as national and health guidelines for physical activity and sedentary behavior are often detailed in minutes per day.[33]

This investigation's primary outcome was time spent in MVPA per day, as activity at these intensities has been linked to health benefits in youth.[63] In addition, examining MVPA time in minutes per day allows the results from this study to be readily compared to world health guidelines. The World Health Organization and Canadian 24-hour Movement Guidelines for Children and Youth recommend all healthy adolescents between 5 and 17 years old accumulate at least 60 minutes of MVPA per day.[33] Just under 7% of adolescent Canadians meet these guidelines.[63] In this investigation, 68% (n=17) of controls and 40% (n=10) of youth with JIA accumulated at least 60 minutes of MVPA per day. These are higher proportions than those found by Lelieveld et al. in a JIA cohort with similar disease characteristics.[28] Lelieveld et al. found 23% of participants with JIA and 66% of controls met the guidelines.[28] Compared to Lelieveld et al.'s investigation, which focused on 15-18 year olds, this study included younger participants (ages 10-20).[28] This could explain the observed discrepancy in MVPA, as PA levels decrease with age.[63] The high proportions of youth meeting the guidelines in this study compared to previous studies could be due to the method of recruitment. Controls and participants with JIA chose to participate in the study after being approached by their friends and family or physicians. The activities in the study may have appealed to youth who were more active themselves, as explained in limitation.

Exploratory analysis stratifying males and females in the study groups determined that sex is an effect measure modifier when comparing time spent per day in MVPA in youth with JIA and healthy controls. The magnitude of the median pair difference between males with JIA and their healthy peers was much larger than between females with JIA and female controls. Compared to controls, males with JIA spent 26 minutes less per day in MVPA, while females with JIA spent 11 minutes less per day of MVPA compared to their same-sex peers. Unfortunately, the small sample size of matched pairs for male participants in this investigation prohibits definitive conclusions being drawn about the male JIA population compared to male controls. However, these findings highlight a potential oversight in the existing literature, where sex is rarely stratified in studies reporting on PA in the JIA population. When data is stratified based on sex, the between sex pair-differences are not reported. Therefore, the results from this study cannot be compared to previous investigations. By ignoring sex when reporting on PA habits in children with JIA, investigators may overlook sub-populations that are failing to maintain an active lifestyle, as well as neglect key characteristics necessary to include in targeted exercise interventions.

It is recognized that males spend more time in PA than females at any age.[63] In this study, females in both JIA and CON groups spent less time in MVPA than their male counterparts. Recently, a similar pattern was reported by Bohr et al. [9] That investigation found 45% of the boys with JIA spent 60 minutes or more a day in MVPA, compared to 19% of the girls with JIA. [9] In controls, 61% of the males met the guidelines compared to 39% of the females.[9] In this study, females with JIA accumulated the least amount of time in MVPA per day compared to healthy females, males with JIA, or healthy males. This result is especially relevant when females make up the majority of children diagnosed with JIA.[23]

Arthritis of the hip and ankles has previously been shown to decrease PA participation, although in studies with small sample sizes.[44, 50] Four (16%) of the JIA participants had a history of hip involvement and eleven (44%) had ankle involvement. This could suggest that the mean time in MVPA per day found in this study is lower than if participants had only knee involvement.

As with any study monitoring PA, a risk of surveillance bias exits. Participants may have engaged in more PA than is habitual due to wearing the ActiGraph device. Involved parents could have also pushed their child to do more while under scrutiny from the study. As both those with JIA and their peers were subject to the same PA tracking methods, this bias would have occurred non-differentially, and would be unlikely to affect the difference seen between groups for time spent per day in MVPA.

There seemed to be little impact of disease activity, disease duration, pain, or functional ability on mean time spent in MVPA per day in children with arthritis. This is similar to results from studies by Tarakci et al., Limenis et al., and Gueddari et al., but contradicts evidence presented by Norgaard et al. and Bos et al.[9, 44, 46, 76, 77] The associations seen in this may be explained by the low severity of disease activity, pain, and functional disability in the participants with JIA.

5.2.2 Sedentary to Light Physical Activity

When mean time spent in sedentary and light physical activity (SLPA) per day was evaluated, youth with JIA spent more time per day in lower intensity activities than controls. In addition, the median proportion of the day the JIA group spent in SLPA was significantly higher than the control group. As mentioned above, examining proportion of time spent in SLPA may

be more informative than exclusively looking at minutes per day. This method would allow normalization of time spent in MVPA and SLPA and facilitate easy comparison within and between individuals.

The results of this study are consistent with previous investigations that have found children with JIA spent more time sleeping, being sedentary, and in light activities than healthy youth.[28, 38, 77, 93] Cavallo et al. found adolescents with JIA spent less time in leisure activities such as play and outings with friends than healthy controls, which points to a preference for sedentary activities.[3] A sedentary lifestyle prevents the development of the cardio-respiratory system, muscle strength, coordination, and key social skills, therefore sedentary habits in youth with JIA should continue to be the focus of investigation.[9]

The method of PA imputation in this study did not allow for discrimination between sedentary and light activity, or time spent sleeping. However, even if the youth with JIA were involved in light PA, low intensity pursuits do not have the same evidence for healthy benefits in youth as MVPA.[9]

5.3 Imputation

In this investigation, participants recorded type, duration, and intensity of any activities done without the ActiGraph device in monitor logs. To be conservative, any activities with a reported RPE of 5-10 were classified as minutes spent in moderate or vigorous activity, and any activities with a reported RPE of 1-4 were classified as minutes spent in sedentary or light activity. This is in accordance with the Canadian 24-hour movement Guidelines for Children and Youth – Glossary of Terms, which defines moderate intensity activity as any activity for which

participants recorded a 5-6 on a scale from 1-10.[99] It was decided to group MVPA and SLPA to reduce the chance of misclassification errors due to recall bias from participants.

Every effort was made to include information on activities written by the participants. When RPE was not provided, even after follow up, approximate metabolic equivalents (METS) values from the Compendium of Energy Expenditures for Youth were assigned based on the activities reported.[100] All activities requiring at least 4 METS were classified as MVPA, and all under 4 METS were classified as SLPA. There has been some controversy around selecting MET intensity thresholds for youth. It has been reported that children with chronic arthritis may have higher metabolic demand in endurance exercises due to biomechanical deficits and systemic symptoms, no previous studies have suggested a method for adjusting METS when comparing youth with JIA and controls.[4, 28, 46, 76] In addition, the participants in this study do not have systemic symptoms, therefore METS during PA were assumed to be comparable. The above MET intensity thresholds were chosen as they closely approximated the thresholds used in original calibration studies with the ActiGraph accelerometer.[100, 101] This information was then combined with the data from the ActiGraph to create a complete picture of the participants PA habits.

The ability to impute PA was crucial, as previous evidence indicated non-weight bearing activities such as swimming and cycling were often recommended for children with JIA.[27] The ActiGraph must be removed during swimming, and cycling effort has been previously found to be underestimated in previous studies using accelerometry.[44]

Other studies objectively measuring PA have employed imputation.[9, 44] Norgaard et al. mathematically adjusted for underestimation of accelerometer counts obtained during cycling, cycle racing, and horse riding, but cited a cycling study to explain how activities of swimming

and bathing were estimated.[44] Bohr et al. adjusted for swimming activity done without the activity monitor, but their methods were not explained. [9] Both studies reported time spent in imputed activities was not significant and did not affect the overall outcome.[9, 44]

In contrast to the above studies, the imputation method used in this study was designed to conform with definitions of activity intensities specified by the Canadian 24-hour movement Guidelines for Children and Youth. The physical activity monitor log was designed to be easily understood by younger populations. No participants in this study reported being confused with the method of tracking their activity, while those that did not complete the log cited forgetfulness.

Physical activity data were imputed for 30% (15) of the participants. Over half (67%) of participants that logged imputed data were controls. In the control participants, the main activity imputed was swimming, followed by lake activities (e.g., waterskiing, paddle-boarding), and then dance (ballet). The five (22%) youth with JIA that required PA imputation did so due to swimming activities. Addition of imputed activity did alter the relationships observed compared to when only ActiGraph data were considered. The differences between MVPA and SLPA activity between groups was smaller without imputed activity, indicating a loss of information when participant activity is limited to only what is recorded on the ActiGraph device. This indicates that it is imperative to include the option for participants to record activity, to ensure a complete picture of activity in youth is gathered. To limit recall bias, recorded activities can be compared to ActiGraph data, and discrepancies can be resolved through follow up, as was done in this study.

It is interesting to note that comparatively few participants with JIA chose to take part in non-weight bearing activities. Many exercise programs designed for youth with JIA purposively

employ non-impact exercises, to minimize the potential for aggravating joint pain.[8] However, there could be a discrepancy between activities that may be deemed most beneficial for those with JIA, and those activities that youth with JIA habitually participate in.

5.4 Adiposity

There was no difference between adiposity, measured as fat mass index (FMI) [whole body fat (kg)/ (height (m)^2], in children with JIA compared to healthy youth control participants. This is consistent with a large longitudinal study done in Germany by Schenck et al. that found no difference in the BMI of over 5000 children with JIA compared to the youth population. [29] They expressed this finding in a low functional disability, low disease activity JIA cohort, much like the one represented in this study.[29]

Comparison of FMI median pair differences in JIA and CON cohorts stratified by sex show females with JIA have lower adiposity than the control females, however this comparison is limited by the presence of an outlier in the control females. This result contradicts a previous investigation by Caetano et al. They found significantly higher FMI in girls with polyarticular and oligoarticular JIA, ages 6 to 19 years old, compared to age and sex matched controls ($p<0.001$).[54] In contrast, males with JIA had a higher median fat mass index than control males, as well as a larger median pair difference between the male groups compared to the female groups. The small sample size of matched males prevents definitive conclusions from being drawn about the males with JIA compared to male controls, especially with the presence of an outlier in the males with JIA. However, these results may indicate males with JIA are at greater risk of developing secondary chronic conditions associated with increased adiposity including hypertension, diabetes mellitus, and cardiovascular diseases. [54]

5.5 Functional Outcomes

5.5.1 Aerobic Capacity

While a higher median aerobic capacity (relative VO_{2peak}) was found in healthy controls, no significant difference was seen when compared to youth with JIA. This contradicts a meta-analysis in 2002 by Takken et al. who found that children with JIA had a 22% deficit in VO_{2peak} compared to healthy reference data.[42] These findings also challenge more recent data from van Pelt et al., who found reduced aerobic capacity in adolescents and young adults with JIA, both in remission and with active disease when compared to healthy reference data.[31]

The youth with JIA had a median deficit of 0.7mL/kg/min compared to their peers. Although slight, this could have considerable long-term consequences.[42] After age 18, there is a 0.41mL/kg/min decline in VO_{2max}, when not maintained by physical training. Deficits in adolescents with JIA would be accelerated compared to their healthy peers, increasing the risk of disability in the later years of life. In the healthy population, women have a 30% lower VO_{2max} compared to men, which indicates aerobic capacity outcomes in females with JIA could be vital to establish in childhood.

The females with JIA in this study had a higher median relative VO_{2peak} than their female healthy matches. This result is unusual and could be explained by selection bias during recruitment of active females with JIA, as explained in limitations. Males with JIA had a lower relative VO_{2peak} than male healthy controls. They did, however, demonstrate a wide variability in aerobic capacity, which may obscure the true association, especially in a cohort with a small sample size.

5.5.2 Balance

No significant differences were seen between CON and JIA cohorts in balance performance on any of three dynamic balance tests. When group medians are compared, youth with JIA performed worse on the unipedal dynamic balance on both the dominant and non-dominant leg compared to controls. This is consistent with results from a study in 2013 by Houghton and Guzman, which found single leg balance was deficient in children with JIA compared to controls. In that study, 40% of participants with JIA did not complete the single leg balance test. In this investigation, only one male with JIA (4%) was unable to complete the test.

Interestingly, adolescents with JIA were superior to controls in the star excursion balance test on both dominant and non-dominant legs, as well as at completing the triple single leg hop on the dominant leg. This trend was readily apparent after stratifying for sex; median differences for triple single leg hop performance indicated females with JIA could jump farther than healthy female controls on both dominant and non-dominant legs. Merker et al. found similar findings when comparing groups of children with arthritis to healthy controls.[94] That investigation found those with JIA demonstrated better stability and motor control while balancing on a bipedal balance board.[94] It was speculated this could be due to long-term physiotherapy and coordination training prescribed to the JIA cohort. [94] This conclusion may apply to the participants with JIA in this study, who regularly attend physiotherapy. However, if training during physiotherapy teaches better balance, the results would be expected to be similar for both males and females with JIA. Instead, the males with JIA were outperformed by their healthy peers in the hop test on both the dominant and non-dominant legs. It is important to consider that the discrepancy seen between male cohorts may have origins in the differences in time spent in moderate to vigorous physical activity. Males with JIA healthy males could have improved their balance performance

while participating in regular PA, leaving males with JIA behind, even if they participated in regular physiotherapy.

5.6 Exploratory Analysis

Results from exploratory analysis indicate that females with JIA spend less time per day MVPA, but have higher aerobic capacity, superior balance performance, and slightly lower adiposity measures than female controls. In contrast, males with JIA spent less time per day in moderate to vigorous physical activity (MVPA), and had lower relative VO_{2peak}, higher adiposity, and performed worse on the dynamic balance test compared to male controls.

It is interesting to consider why these trends appears. Males with JIA differ the most from their healthy counterparts in dynamic balance performance and mean time spent per day spent in MVPA (Table 4.6). These two outcomes may be related; males in JIA may avoid intense physical activity due to poor balance skills, or less time spent in MVPA may lead to deficits in balance. Females with JIA obtained a median time per day in MVPA much closer to healthy females. Perhaps time spent in MVPA has a helped bring functional and physical outcomes in females with JIA on par with healthy females. If so, emphasis on accumulating time in MVPA could be the key to maintaining normal function in youth with JIA.

5.7 Limitations

This study has some limitations. Participants were recruited from the outpatient Rheumatology clinic in the Alberta Children's Hospital (ACH) and the Richmond Road Diagnostic and Treatment Centre and were first approached by their attending physicians or physiotherapists. This method could drive selection bias. While all youth that met the inclusion

criteria were to be informed of the study, clinicians may have been more inclined to recruit patients with low disease activity and athletic interests. Targeted recruiting often occurs to prevent overburdening a population inundated with many ongoing research requests. In addition, the study content may have appealed to those that were confident in their ability to complete the required movements, and interested in their athletic capacity. This may have resulted in a more active study sample, and increased the mean time spent in MVAP per day in each participant. In addition, an active sample would have higher relative VO_{2peak}, decreased FMI, and increased balance performance than the representative population. Controls participants were recruited through word of mouth, as family or friends of the participants, and through a local database for healthy children interested in participating as controls in scientific research. The same self-selection bias could occur in this cohort, as a study investigating movement skills and physical activity active likely appeals to active youth. While this recruitment method likely does not influence comparison of the groups, it may limit the generalizability of the results to less active youth.

The method of physical activity imputation categorized sedentary and light, and moderate and vigorous activity into two groups. While this maintained the investigations ability to compare moderate to vigorous levels of activity to worldwide health standards, it does not discriminate patterns of sedentary behaviour. Canada's 24-hour Movement Guidelines for Children and Youth recommend no more than 2 hours of screen time and limiting periods of sitting. [33] It would be informative to know if these recommendations are being met in the JIA population. Although evidence has indicated health risks from participating in MVPA are not affected by sedentary time in children, this effect is not continued into adulthood. [120]

Even with the combination of objective and self-report PA tracking techniques, recall bias cannot be ruled out completely. While the Pictorial Children's Effort Rating Table (PCERT) used to quantify RPE has been found to reliability reflect exertion levels in children immediately after exercise it is unknown if each participant completed the log promptly.[97] In addition, children tend to overestimate the duration and intensity of exercise, which could lead to an overrepresentation of time spent per day in MVPA.[121] In this investigation, this could differentially benefit the control participants, as they recorded more imputed activities. This would result in an overestimation of the difference in the amount of time spent in MVPA per day between the JIA and CON groups. Extensive follow up was done to clarify the reported RPE and activities for any substantial portions of time the controls had been without the ActiGraph. Unfortunately, there is a risk that this bias was not completely mitigated. Therefore, a larger sample size would be required to make definitive statements on the magnitude of the difference in MVPA participation between groups.

Four participants did not have a DXA scan: 2 control females, 1 control male, and 1 male with JIA. The participants were between the ages of 14 and 17. BMI measures calculated from weight and height were 21.5, 18.2, 20.4, and 18.4 respectively. This classifies them as "healthy weight" according to American age and sex BMI percentiles, which is consistent with the majority of the participants. Selection bias from attrition was deemed to be negligible.

Pubertal stage was not measured in this investigation, which could affect interpretations of aerobic capacity. [68] However, Metin et al. has argued that most studies investigating VO_{2peak} in the JIA population do not account for puberty, therefore comparison between studies is not affected if the measure is lacking. [68] In addition, although pubertal stage may be important to reach the oxygen consumption plateau at the end of an exercise test, the majority of children do

not achieve this characteristic leveling off. [68] Metin et al. argues that finding reliable aerobic fitness measures in children can be accomplished by having definitive subjective endpoints to the test, and keeping these endpoints consistent across testing sessions. [68]

Through exploratory analysis, sex could be observed to be an effect modifier for all primary and secondary outcomes. Statistical analysis to determine if confounding occurred on outcomes stratified by sex was not undertaken due to small sample sizes. Other factors could have affected the primary outcome of time in MVPA. Season, socio-economic status, depression, quality of life, and pattern of joint involvement have all been found to impact regular PA, and were not assessed.[76, 78]

The conclusions of this study are limited by sample size. None of the results found were statically significant, which increases the risk of type two error (the probability of concluding there is no difference between JIA and CON cohorts when in fact significant differences exist). Confidence intervals for each outcome indicated a wide range of capabilities and characteristics across participants, and a wide range of possible pair-differences between groups.

5.8 Strengths

This study is the first to use accelerometry to measure the PA of youth with JIA inclusive of knee arthritis, and to compare concurrently to healthy controls matched by age and sex. Previous literature has compared objectively monitored PA of children with JIA to reference data of healthy controls collected a few years before. This can increase the likelihood of diverse methodologies surrounding administration of the activity monitors device, PA imputation, and data analysis. In addition, PA data gathered at different time points can be influenced by

environmental events (i.e. harsh weather, pollution) and yearly activity trends (i.e. Pokemon Go).[76,122]

Selecting for children with knee involvement and exclusive of systemic symptoms ensured any results of this investigation would directly relate to the effect of lower extremity arthritis. This is in contrast to previous studies, where conclusions were often confounded by samples with the presence of systemic symptoms or by heterogeneous joint involvement. [28, 75, 45, 46, 75, 77] In addition, matching youth with JIA by age and sex controls eliminates some variability between individuals that could confound the results. Most previous research into

Clinical evaluations of the youth with JIA were conducted by the same physician and physiotherapist over the course of the study. The physiotherapist for the CON cohort collaborated with the physiotherapist from the JIA cohort to ensure measures were taken consistently. The same CSEP-Certified Exercise Physiologist supervised and determined the endpoint for each maximal aerobic test. Research personnel were trained to give the same instructions for administration of the ActiGraph device and balance tests.

Controversy exists when defining end points to maximal aerobic tests in children.[61] Many do not exhibit the same oxygen consumption plateau seen that indicates the conclusion of adult tests. [61, 92] The same CSEP-Certified Exercise Physiologist was present at each aerobic test and determined the end of the test based on volitional fatigue despite consistent encouragement, a plateau in maximal heart rate, and/or reported an RPE of 10 on the PCERT exercise scale. Consistency of personnel ensured each participant received the same encouragement and limited variability in end point determination. Taken over several seconds, peak VO_2 has been demonstrated to be an index of maximal exercise, even without the characteristic plateau endpoint.[68]

This study employs gold standard methods for measuring aerobic capacity and adiposity, and the latest technology for collecting PA.[68, 103 104] Accelerometers are ideal for capturing children's spontaneous PA and avoiding recall bias inherent to self-report measures.[3] Study personnel conducted detailed follow up to clarify self-report data. In addition, efforts were made to utilize balance measures that could easily be employed in a physicians' office, to ensure any unique findings could have clinical applications.

Chapter Six: **Conclusions**

6.1 Summary of Findings

The literature review preceding this study identified a gap in knowledge about the current physical and functional status of children with JIA compared to their healthy peers. In addition, investigations lacking control populations and control of confounders obscured the true relationships between JIA and healthy youth in measures of physical activity, aerobic capacity, adiposity, and balance. This study has used sophisticated methods of measurement to investigate these outcomes, while considering the effect of sex on the comparisons between youth with JIA and healthy controls.

Twenty-five children with juvenile idiopathic arthritis (JIA) and 25 age and sex matched healthy controls participated in this investigation. No significant difference was found between time spent per day in moderate to vigorous physical activity (MVPA) or sedentary to light physical activity (SLPA), aerobic capacity, adiposity, or balance performance between the two groups after adjusting for multiple comparisons. However, a significant difference was found in the proportion of time spend per day in SLPA between youth with JIA and healthy controls. There appears to be no relationship between time spent in moderate to vigorous activity per day and disease activity, disease duration, pain, or functional disability in children with JIA.

Results from exploratory analysis indicate females with JIA spend less time per day in MVPA, but have higher aerobic capacity, superior balance performance, and lower adiposity measures than female controls. In contrast, males with JIA spent less time per day in moderate to vigorous physical activity (MVPA), had lower relative VO_{2peak}, had higher adiposity, and performed worse on the dynamic balance test compared to male controls. These results are limited by low sample size, but are important to indicate directions for future studies.

6.2 Public Health Implications

Recently, the goal of treatment for JIA has been to achieve inactive joint disease and promote normal joint function including bone stability, range of motion, coordination, and strength.[6] This study suggests that at times of low disease activity, normal function is achieved; the participants with JIA equaled controls in all physical and functional tasks. The results of this study join others that conclude youth with JIA are falling short of their healthy peers in moderate and high intensity physical activity participation.[47] Limited MVPA can hinder healthy growth and development, facilitate social isolation and depression, and increase the risk of long term health consequences.[4, 120]

Although there was no statistically significant difference found in the median time spent in MVPA per day between the JIA and CON cohorts, the median pair difference may hold clinical significance. Ekelund et al. found time in MVPA was significantly and inversely associated with cardio-metabolic risk factors in children and adolescents, regardless of time spent in sedentary activity.[120] An increase of 10 minutes in MVPA had small but measurable effects on waist circumference and fasting insulin.[120] In children with chronic disease, such as juvenile arthritis, 10 minutes more moderate to high intensity PA could have remarkable health repercussions.[10]

This study supports a previous research that indicates youth with JIA spend a large portion of time in sedentary and light activity. Patterns of inactivity in children with chronic illnesses are more consequential than in healthy children, as a sedentary lifestyle can further exacerbate deficiencies in normal physical development.[42] In addition it can lead to chronic

secondary health conditions as adults.[120] It is important to keep tracking sedentary patterns in this population to encourage physical activity and mitigate health risks.

Females with JIA spent less time in MVPA per day then their healthy female counterparts, but this median difference was smaller in magnitude than the difference seen between males with JIA and male controls. In addition, females with JIA performed better than healthy females in physical and functional tests. If time spent in MVPA is assisting females with JIA to rival their healthy peers in physical and functional outcomes, there may be large public health implications. Targeted exercise therapy to manage JIA could decrease dependence on expensive pharmaceuticals, increase quality of life in patients, and reduce the short and long term public health burden of juvenile arthritis.

6.3 Recommendation for Future Research

The conclusions in this study are limited by a small sample size. Future research with a larger sample is warranted, as important trends between sexes were established. Larger sample size may facilitate multivariable analysis to consider potential confounding by season, age, sports participation, socio-economic status, quality of life, and psychosocial factors. In addition, a larger sample could reveal the effects of JIA disease characteristics such as joint involvement, disease activity, pain, and functional disability on physical activity participation and functional and physical outcomes. These associations could clarify barriers to PA facing male and females with JIA.

Future research should focus on elucidating the effect of sex on physical activity participation, aerobic capacity, adiposity, and dynamic balance in youth with JIA. Understanding the difference between males and females is critical to developing targeted treatment plans.

Future studies should be deemed incomplete without stratifying the two sexes. The results of this investigation have demonstrated that males with JIA may require different strategies to achieve optimal outcomes. They are an important group to consider in future studies, even in a disease that preferentially affects young women.[19]

Overall, the participants with JIA in this study exhibited dynamic balance skills above what was expected. It would be interesting to investigate if training at regular physiotherapy sessions heightens an individual's dynamic joint proprioception and augments balance abilities.

Future investigations should confirm the finding that females with JIA have better functional and physical outcomes compared to female controls with a larger sample size. Selection bias for active females, as well as small group sizes may explain the results of this study.

This study contains important information for those wishing to design targeted exercise therapy programs for children with JIA. Overall results from this study indicate youth with JIA demonstrate no significant differences between their healthy peers with regards to physical and functional capabilities, therefore exercises can be weight-bearing and require aerobic fitness, coordination, and balance skills. Evaluation of ActiGraph data showed that youth with JIA are demonstrating no preference for non-weight bearing physical activities. Future studies should consider which activities were popular amount those with JIA when designing targeting exercise programs or, alternatively, develop knowledge translation techniques to inform youth with JIA of non-weight- bearing PA that would facilitate safe accumulation of high intensity exercise.

While females with JIA in this investigation did not show deficits to their female counterparts, they still accumulated the lowest amount of MVPA out of any group or sex. Therefore, any program aimed at increasing this type of activity in youth with JIA should

incorporate females. This is especially important to ease the burden of this disease, as the majority of those diagnosed are young girls. In addition, males with JIA demonstrated large deficits in PA participation, and functional and physical outcomes. Future studies should investigate if there are disease specific aspects that are preferentially affecting the PA of males with JIA.

The Alberta Children's Hospital (ACH) rheumatology clinic has a strong treatment plan focused on helping their patients manage pain and maintain normal childhood activities. However, clinicians should be aware that, despite achieving positive outcomes, patients with JIA are not participating in moderate to high intensity activities to their fullest capacity. Future rehabilitation programs and clinical recommendations should emphasize the accumulation of time spent in moderate and vigorous activities, especially in females. Including of this type of physical activity could improve the immediate quality of life and long term health of youth with JIA.

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APPENDIX A: STANDARD OPERATING PROCEDURE (SOP) FOR ACTIGRAPH GT3X+ ACCELEROMETER

Sport Injury Prevention Research Centre
UNIVERSITY OF CALGARY

Standard Operating Procedure (SOP) for Actigraph GT3X+ Accelerometer

All ActiGraph activity monitors are designed to monitor human activity and record energy expenditure (calories spent during normal activity, METs, everyday activity, and exercise). Additionally, these devices can also function as a very accurate sleep assessment tool. While collecting day-to-day energy expenditure data, the device should be affixed securely to the body's center-of-mass to ensure the most accurate caloric measurements.

The GT3X+ based activity monitors provide objective measurements of human activity and are used in many research and clinical applications. They include both a micro-electro-mechanical system (MEMS) based accelerometer and an ambient light sensor.

Contents:

Review Update: September 2015

Author: Clodagh Toomey

Version: 1.0

Logistics/Instructions for participants

This section contains the information you need to give to the participant and tips to improve compliance.

i. Tracking Actigraphs

- A sticker should be placed on the back of each monitor to identify the monitor code e.g. AG01 in addition to lab contact details in the case where the monitor has been lost.
- A second small sticker should be place on top of the actigraph beside the USB cap to highlight how the monitor should be worn
- Monitors should be logged in and out via an excel database with the following variables:
    - Monitor Code
    - Serial number
    - Participant ID
    - Date initialized/activated
    - Stop time
    - Researcher
    - Monitor returned
    - Monitor log complete
    - Date/time removed (self-report)
    - Battery life
    - Notes

ii. Pre-data collection

- To achieve a minimum of 5 valid days of data collection, the participant is asked to wear the monitor for 7 full consecutive days if possible (a valid day is defined as 10 valid hours)
- The participant will complete a monitor log to fill in a start and end wear time and any period of time where the device is removed for more than 5

minutes (see **Appendix A**). This will be an important cross check for validating wear time.

- Participants are instructed on how to wear the monitor while shown the instructions for wear sheet (see **Appendix B**)
    - The ActiGraph will be given to the participant already threaded onto the elastic belt. Participants should be instructed to wear the ActiGraph with the blue sticker facing up, the elastic belt fastened around the waist and the monitor positioned over the right hip bone.
    - The ActiGraph can be worn either over or under clothing, whichever is most comfortable to the participant. The meter does not need to be in direct contact with the body. However, it is essential that the ActiGraph be positioned snugly enough against the body that it cannot flop around.
    - Participants will be instructed to wear the unit all day and night. Some slight re-positioning of the device is allowable if the participant has trouble sleeping e.g. if they sleep on their right side, they may slightly reposition to the front
    - The only times they should remove the monitor are if the monitor would become completely wet (e.g. swimming, showering). These times should be logged.
    - Show participants an example report of the output
    - Organize a pick-up time and location for returning the device. If collection or drop-off is not possible, give a stamped, addressed and padded envelope for return mail.
- Some useful examples of what to tell the participant:
    - *"We would like you to wear a movement monitor for 7 days. It is similar to a pedometer, except it measures general movement."*
    - *"To the best of your ability, go about your usual days -- don't do anything different."*
    - *"Leave next to your clothes to remind you to put it back on after showering"*
    - *"It runs on a watch battery and isn't a tracking device. It can't tell what type of activity you are doing or where you are."*
    - *"It's really small, I've worn it myself and after a little while I forgot I was even wearing it."*

iii. Post-data collection

- Thank the participant for completing the research and let them know they will receive their physical activity report via email
- Log the return date into the master database
- Wash the waist band after each use by hand (warm soapy water) or cold cycle. Drip dry
- Download the data and charge for next use. Ensure stickers are intact.

Using Actilife Software

i. Initializing a monitor

This section contains information on how to set up the monitor to begin recording data. For an online tutorial, click here

1. Open Actilife software. Download the latest version of software if you are prompted to do so. Always work under the latest version to ensure compatibility between computers when using the datavault.
2. Open the actigraph USB cap using the key provided and plug in using USB cable. The monitor should appear under devices. Ensure the battery level is at least 3.85V (>80%) or initialization will not be allowed.
3. Select the check box for the device and click on "Initialize – Regular Initialization" in the toolbar.
4. Select your initialization parameters. First input the recording time by selecting a start time and date and a stop time and date. For a 7 day data collection period, it is recommended to set the device to record 8 or 9 days to allow time to make up for periods of non-wear.
5. Set Sample Rate to 30Hz. Under LED options and wireless options, nothing is selected. Idle sleep mode is set to disabled.
6. Enter subject info including participant ID, sex, height weight, DOB and race. 'Limb' is set to waist and 'Side' is set to right.
7. Select 'Initialize 1 device'
8. Check that initialization is complete under 'status' and check recording parameters again under devices before plugging out. You can hover over icons under "mode" to determine if the features you need are activated.
9. Safely remove device, plug out and close cap firmly

ii. Downloading data

This section contains information on how to download the data to your computer after the participant has worn the actigraph. See online tutorial here

1. Open Actilife software
2. Open the actigraph and plug in using the USB cable. The monitor should be recognized and appear under devices. Confirm that the device contains data for this wear period
3. Click the download option in the toolbar and a new window will open
4. Download naming convention should be set to <Subject Name><Start Date>
5. For Download Options, ensure 'Create AGD File' is checked Epoch length should be set to 10 seconds and # of Axis should be set to 3. Ensure boxes for 'Steps', 'Lux', 'Inclinometer' and 'Low Frequency Extension' are also checked. You can also edit any participant information here under 'Add biometric and user information' here.
6. Select 'Download All Devices'
7. The progress bar in the main window will show you when the download is complete. Under 'Status' should read 'finished downloading'
8. Click the 'finished downloading' hyperlink and select 'Export GT3X file'. A new window will open. Ensure 'Create AGD', 'Create CSV', 'Create DAT' and 'Low Frequency Extension' are selected. Then click in 'Export RAW Files'
9. These files will save to Actigraph>Actilife>Downloads in your Documents folder

iii. Wear Time Validation

The next step in the analysis process is to set the appropriate wear time for the downloaded data. This is done using a combination of wear period algorithms and using the monitor log provided by the participant.

1. Click on the Wear Time Validation tab
2. 'Define a Non-Wear Period' should be set to Choi (2011). Minimum Length (90 minutes), Small Window Length (30 minutes) and Spike Tolerance (2 minutes). Select 'Use Vector Magnitude'
3. For 'Optimal Screen Parameters', nothing is selected
4. Uncheck all Data Sets and check the one(s) you wish to analyze. If it is not there, click on 'Add Dataset' and find the AGD file in the downloads folder

5. Hit Calculate and a new window will open
6. At the end of the window, under 'All Periods' contains a list of Wear and Non-Wear periods as calculated using the Choi algorithm. You will need to cross-check these periods with the monitor log provided by the participant. Normally, shower periods are not recognized if the monitor is off for periods shorter than 90 minutes. Also, a very inactive period (often evening time or during sleep) can be detected in error as a Non-Wear period.
7. Go to the first Non-Wear period. If the participant has not recorded this date and time as a Non-Wear period, click on 'Set As Wear' if appropriate. Scroll down and continue this process for all Wear and Non-Wear periods. Use best judgement call to change between 'Wear' and 'Non-Wear' as appropriate. Also note beginning and end of wear period provided by the participant as the device may continue recording past this time depending on set-up.
8. Click on 'Save' and select the next dataset or click on 'Save and Close'

iv. Scoring and Exporting

We now wish to analyze the selected data period and select appropriate algorithms to apply cut-offs for calculation of energy expenditure, METs and exercise intensity. Recommendations are provided below but can be altered depending on the population in question. See https://help.theactigraph.com/entries/21452826 for more details.

1. Click on the 'Scoring' tab
2. On the left, under Algorithms, ensure the following boxes are checked:
    - Energy Expenditure
    - METs
    - Cut Points and MVPA
    - Bouts
    - Sedentary Analysis
3. The following algorithms are recommended for use for an **adult population**:
    - Energy Expenditure – Freedson VM3 (2011)
    - METs – Freedson Adult (1998)
    - Cut Points and MVPA – Troiano Adult (2008)
4. The following algorithms are recommended for use for **a pediatric population**:
    - Energy Expenditure – Freedson VM3 (2011)
    - METs – Freedson (2005)

- Cut Points and MVPA – Evenson Children (2008)

5. Under Filters, check 'Exclude Non-Wear Times from Analysis'
6. Select your required dataset from list or go to 'Add Dataset'
7. Click on 'Calculate'
8. Click on 'Export' in right bottom corner
9. Select required excel files for analysis and hit export. Name your file. It is better to do an export in bulk, selecting numerous datasets so they will all be contained in one excel file
10. One Summary file and one data file with numerous tabs will be saved under CSVFiles in your Actilife folder

Creating a report

1. The type of report you want to create will be based on the research study in question. An example report form is in **Appendix C**.
2. To create the graph, a screen grab is taken from the 'Graphing' tab in Actilife software for the relevant days. Use the clipping tool in Windows software. Ensure the checked box for 'Equal Activity Scales' is selected and set in the region 1500-3000 counts, dependent on the activity level for the individual.
3. Create a table in excel to include date, day, wear time (hrs), activity kcals, average kcals/hr, steps and sedentary, light, moderate and vigorous time presents as mins and %. Calculate total and average values. You can also choose to graph these values in a pie chart a % of total time
4. To allow the participant to interpret these values, show how they compare to Canadian physical activity guidelines and refer to the Canadian Society for Exercise Physiology website

Additional Information

This section contains additional useful information on specification and functionality of the Actigraph device. This information and more is available by accessing the Actigraph GT3X manual.

Steps: Step counts are accumulated on a per-epoch basis and are based on accelerometer data collected on the vertical axis. An algorithm present in the device firmware filters out the accelerometer's baseline noise level to help accurately accumulate the steps-per-epoch.

Inclinometer : The post-processed inclinometer feature helps users identify the orientation of the device and, more importantly, when the device itself was taken off. Each epoch is flagged with a number (1 through 4) to indicate the orientation of the device during that epoch.

Important: The inclinometer feature is only valid if the device is worn on the hip with Axis 1 upward facing.

Interpretation of Inclinometer Code (Stored with each Epoch)

0 Device Off (Not Being Worn)
1 Subject Standing
2 Subject Lying Horizontal
3 Subject Sitting

Low Frequency Extension: The Low Frequency Extension (LFE) option, though not a mode or channel, is another data collection option during post-processing for the GT3X+ and wGT3X+. The standard proprietary filter algorithm used in ActiGraph products is used to eliminate any acceleration noise outside of the normal human activity frequency bandwidth. This filter is customized to work with ActiGraph's Energy Expenditure Algorithms. The LFE option, when enabled, increases sensitivity to very low amplitude activities allowing for the study of population groups who move slowly or take very light steps (for example, the elderly). For more details, contact ActiGraph at support@theactigraph.com.

Data Collection: Initialize time options/selections have been reduced significantly due to the new data collection method used by the GT3X+ and beyond devices. During initialization, the user is now only required to select the desired raw data sample frequency (30Hz up to 100Hz in 10Hz increments). Data is automatically collected from all on-board sensors in raw data format. The data recorded includes:

Vertical Axis Activity Acceleration Data (Axis 1)
Horizontal Axis Activity Acceleration Data (Axis 2)
Perpendicular Axis Activity Acceleration Data (Axis 3)
Ambient Light (Lux)

Unlike previous ActiGraph products, the wGT3X+ and wActiSleep+ do not filter or accumulate data into epochs. Raw data is collected at the selected sample rate and is post-processed in the ActiLife. Because these devices collect data from all sensors at all times, users can generate native ActiLife *.agd files containing any desired combination of parametric data at a later time. This helps facilitate backward compatibility and enhances the flexibility of the data by allowing users to compare data to studies which use different filter techniques or accumulation sizes (e.g., 1 second epochs versus 60 second epochs).

Water Resistance: The wGT3X+ and wActiSleep+ are water resistant in accordance with IEC 60529 IPX7, or immersion in one (1) meter of water for up to 30 minutes

Battery: All ActiGraph devices use a lithium ion rechargeable battery that has a maximum voltage of approximately 4.20 volts. At 3.1 volts the devices enter a low voltage mode state (HALT mode).

Low Voltage Mode (HALT): ActiGraph devices enter a "Low Voltage Mode" (or HALT) state when the battery discharges beyond a point of being able to power the device. In this mode, all important variables and data are stored in flash memory to secure the device download. Because the device's internal clock stops in HALT mode, the device cannot be recharged and redeployed; the device must be downloaded and reinitialized to continue use.

Recharging and LED Decoding: Recharging is automatic and is accomplished by connecting the device to a standard USB port. Charging time will depend on the battery life, but typically will not exceed four hours for a fully depleted battery to become fully charged. Once the battery is completely charged, the green LED will remain illuminated. If the battery voltage drops below 3.1 volts while in use, the device will not have sufficient power to collect data and will warn the user through a series of coded flashes. The battery level, reported in volts, can be viewed at any time by starting the ActiLife software and plugging in the device.

Appendix A

Monitor Log

Wear the physical activity monitor for seven (7) consecutive days. In the table below, write down the dates and days on which you wear the monitor. Note the times, including "a.m." or "p.m.", that you put it on and take it off during each day. Also note the reason you took it off. Below is a sample entry:

Date	Day	Time Off	Time On	Reason
e.g. July 15th 2015	Wednesday	7.30 AM	8.30AM	Swimming
Monitor Off (complete):				
Date	Day	Time Off		

OFFICE USE ONLY Actigraph ID_____

Start Date and Time:_____

Participant ID:_____ Valid

How to Wear the Physical Activity Monitor

This small activity monitor records general movement and allows us to get a better understanding of your overall activity level. We will not be able to tell what kind of specific activity you are doing, only the intensity and duration of physical activity. At first, the belt may feel slightly awkward, but after a few hours, you will not notice it as much. It is extremely important for our study that you wear the monitor correctly. Please follow these instructions carefully:

- ✓ Wear the monitor attached to the belt around your waist, **just above your right hipbone**
- ✓ Wear the monitor so that the sticker is facing **up**
- ✓ Wear the monitor snug against your body. If you have to, you can adjust the end of the strap to make it tighter. Or, to loosen the belt, push more of the strap through the loop. **Wear the monitor tight enough so that it does not move when you are being active**
- ✓ The monitor can be worn underneath or on top of your clothes or in your belt loop
- ✓ Keep the monitor on all day and all night for a 7 day period
- ✓ **Do not submerge in the water** (swimming, bathing etc.) You can remove for showering but remember to put it back on as soon as possible and keep record of each occurrence in your monitor log
- ✓ Do not let anyone else wear it

Details for dropping off/collection of monitor_____

If you have any questions related to the monitor, please call or email:

_____

There is no ‘ON’ or ‘OFF’ switch that you need to worry about. The activity monitor runs on a battery and is programmed to run continuously from when we give it to you. Please do not try to open the monitor

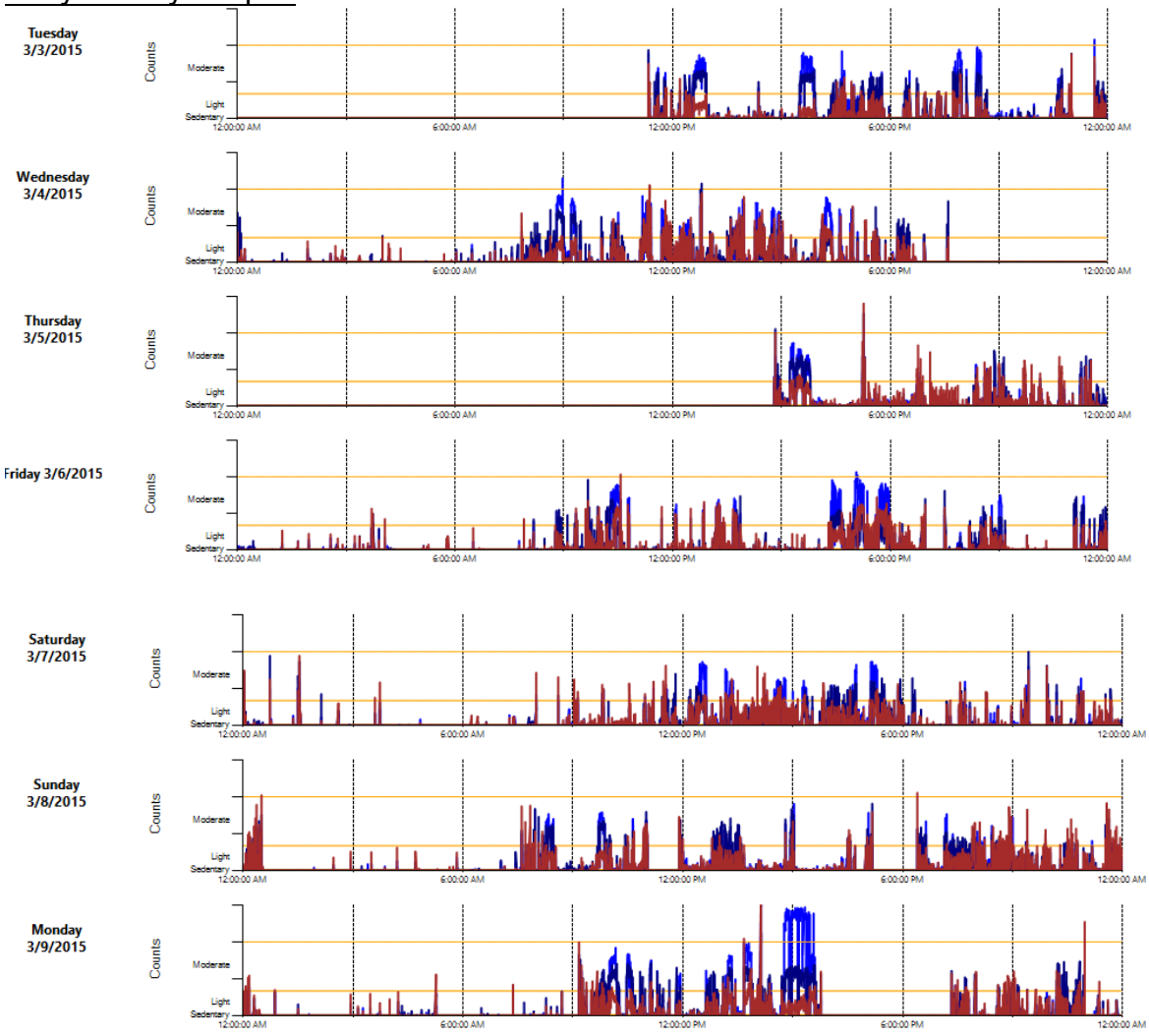
Physical Activity Report

Name:

Days: 7

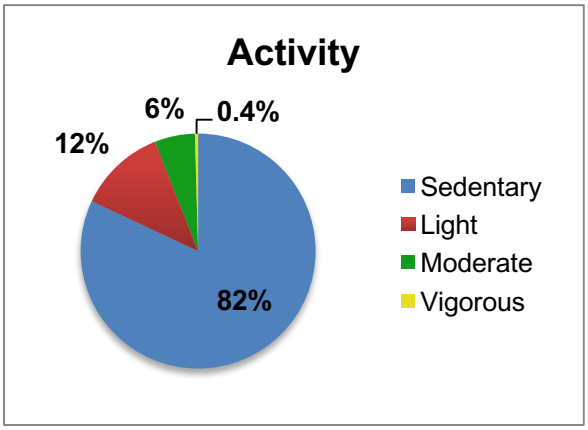
Sport Injury Prevention Research Centre
UNIVERSITY OF CALGARY

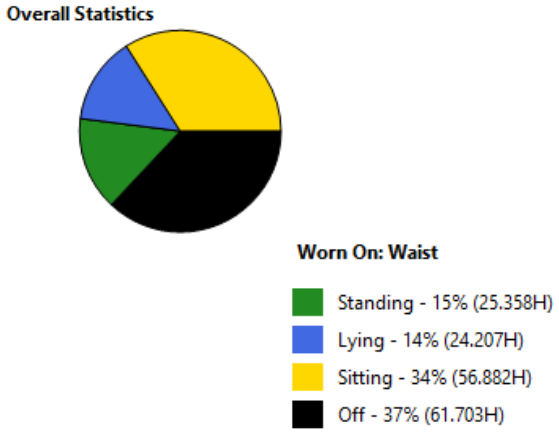
Daily Activity Graphs



Date	Day	Wear (hrs)	Activity kcals	Avg kcals/hr	Steps	Sedentary (min)	Sedentary (%)	Light (min)	Light (%)	Moderate (min)	Moderate (%)	Vigorous (min)	Vigorous (%)
3-Mar	Tue	12.7	548.38	42.18	11276	580.0	76.4	101.7	13.4	77.2	10.2	0.2	0.0
4-Mar	Wed	19.6	535.49	22.31	10256	964.0	81.8	145.8	12.4	67.7	5.7	0.5	0.0
5-Mar	Thur	9.2	236.81	9.87	4263	439.5	79.8	81.3	14.8	30.2	5.5	0.0	0.0
6-Mar	Fri	24.0	591.62	24.65	11502	1243.8	86.4	110.0	7.6	85.8	6.0	0.3	0.0

7-Mar	Sat	24.0	392.71	16.36	9216	1230.0	85.4	154.2	10.7	55.8	3.9	0.0	0.0
8-Mar	Sun	24.0	423.56	17.65	8434	1181.7	82.1	216.8	15.1	41.5	2.9	0.0	0.0
9-Mar	Mon	20.5	817.04	34.04	14956	1006.2	82.0	128.0	10.4	56.3	4.6	36.5	3.0
Total		**133.9**	**3545.61**	**167.07**	**69903**	**6645.2**		**937.8**		**414.5**		**37.5**	
Average		**19.1**	**506.52**	**23.87**	**9986**	**949.3**	**82.0**	**134.0**	**12.1**	**59.2**	**5.5**	**5.4**	**0.4**





Interpretation

- Basal metabolic calories are the amount of calories your body burns at rest to maintain normal body functions and are calculated based on your age, height, weight and gender. **Activity kcals**: the calories you burned actively all along your day i.e. when walking, running.
- **Step count:** The number of steps recommended for adults have been estimated as:
  - 7,000 to 13,000 steps/day for adults age 20-50y (Tudor-Locke, 2004)
    - Your average daily step count is **9,986**
- Canadian Physical Activity Guidelines suggest that for health benefits, adults aged 18-64 years should accumulate at least 150 minutes of **moderate-vigorous aerobic physical activity** per week
    - You accumulated in **452 minutes** of moderate-vigorous activity over 7 days
- Guidelines also recommend adding muscle and bone strengthening activities using major muscle groups, at least 2 days per week. The intensity of this type of activity is likely not detected accurately using accelerometry devices. If you partake in this type of activity, bear in mind that it may not be reflected in your report.
- Health research recommends minimizing the time you spend being sedentary each day.

    - Minimize the amount of time spent in prolonged sitting
    - Break up periods of sitting as often as possible by standing or walking
    - Your average daily sedentary time is **82% of your day**

- If you would like more information please view the Canadian Society for Exercise Physiology website (www.csep.ca/guidelines) or contact me!

APPENDIX B: DUAL-ENERGY X-RAY ABSORPTIOMETRY SCAN ACQUISITION AND ANALYSIS FOR WHOLE BODY ASSESSMENT STANDARD OPERATING PROCEDURE

Sport Injury Prevention Research Centre

Dual-Energy X-Ray Absorptiometry Scan Acquisition and Analysis for Whole Body Assessment

Standard Operating Procedure

Hologic Discovery A

Department of Kinesiology

University of Calgary

Review Update: November 2014

Author: Clodagh Toomey

All instructions and procedures in this document are in line with the International Society for Clinical Densitometry (ISCD) Position Statements[1] and the International Atomic Energy Agency (IAEA) Human Health Series[2]

Table of Contents

[1]Hangartner, T. N., Warner, S., Braillon, P., Jankowski, L. and Shepherd, J. (2013) 'The official positions of the international society for clinical densitometry: acquisition of dual-energy x-ray absorptiometry body composition and considerations regarding analysis and repeatability of measures', *J Clin Densitom*, 16(4), 520-36

[2]Dual energy X ray absorptiometry for bone mineral density and body composition assessment. — Vienna : International Atomic Energy Agency, 2010. p. ; 24 cm. — (IAEA human health series, ISSN 2075–3772 ; no. 15) STI/PUB/1479

1 Daily Calibration check

1.1 Computer/ Program

The computer should be turned on and the QDR program up and running when you enter the room. If not turn the computer on and double click on the QDR program, (note the "System Backup" always seems to be flashing).

1.2 Calibration (10 minute process)

1. Put lead apron on.
2. Click 'QC' – 'Daily QC'
    a. Center Spine Phantom on bed (in wooden box on shelf)
    a. Sticker facing computer
    b. Laser crosshairs need to be in middle of white dot
    c. Click 'continue' – OK'
    d. Remove spine
3. Click QC – 'Step Phantom QC'
    a. Center Large Step Phantom on bed (longitudinally, square with both ends of the bed)
    b. Sticker facing computer (smallest step facing the door)
    c. Laser crosshairs 2cm away from smallest step
    d. Click 'continue' – 'OK'
    e. Remove step
4. Click 'continue' to complete calibration (this next step takes 5 minutes or so).

2 Scan Acquisition

2.1 Contraindications

The scan process should be explained to the participant.

Any contraindications to scanning should also be checked at this point.

Ask subject about any absolute contraindications: these include

- **Pregnancy**
- **Recent radiological or nuclear medicine investigations, or therapies using IV contrasts in the past week**

Or relative contraindications: these include

- metal implants e.g. hip replacements, screws etc (note in analysis)
- Body weight – exceeding 300lbs
- Inability to transfer to/from the scan table safely or lie flat for 5-7 mins

2.2 Pre-Scan Protocol

DXA assumes constant fat-free mass (FFM) hydration of 0.73. Therefore, participants are required to be in a euhydrated (normal hydrated) state for scanning. Food/fluid intake and strenuous exercise will effect hydration status and therefore require standardization.

The following is the ideal pre-scan protocol that should be adhered to where possible. If testing conditions do not allow all conditions to be met, **it is important that the testing conditions are consistent for each scan in the study and any subsequent follow-up scans.**

Standardized conditions:

- After an overnight fast (or fasting for at least 3 hours)
- No strenuous exercise in previous 12 hours
- No alcohol intake in previous 12 hours
- Empty bladder
- Defecate if required

2.3 Subject Preparation/Positioning

Participants should wear loose, comfortable clothing without excessive zippers or buttons. All jewelry, watches, coins, tissues, phones should be removed from the body and pockets.

1. Remove shoes
2. Measure height and body mass if this has not been already done
3. Ask participant to lie on bed within the perimeter line, feet facing computer
4. Arms extended, palms face down. Space should be maintained between the arms and the torso when possible. If necessary, with larger or heavier subjects, the hands may be placed in a lateral position next to the hips (you may need to tuck the thumb under the fingers and/or internally rotate the shoulder).
5. Legs extended, big toes touching (use tape to secure feet together – it is ok to leave socks on).
6. If taller than 195cm, make sure entire foot is within perimeter line. Exclude top of head if needs be.
7. If participant is not lying straight on bed, apply traction at ankles to straighten lumbar spine
8. Ensure head is not tilted, face up with neutral chin. Adjust if necessary.

9. If participant is too wide to fit in the scan field, position ensuring the entire right side is between the boundaries and use hemi-scan analysis after acquisition.

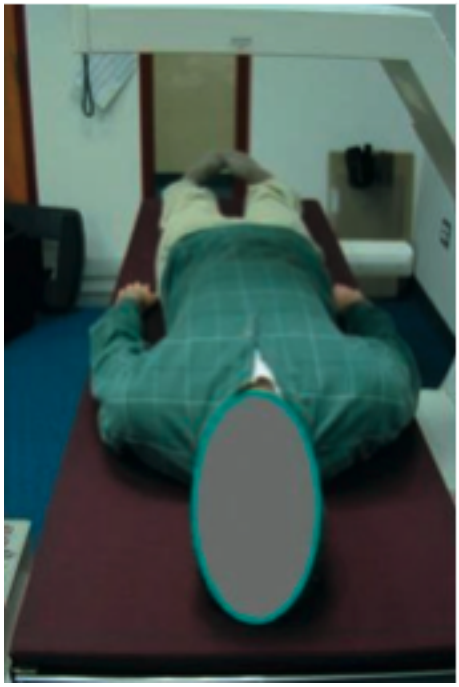


Fig 1. Example of good whole body scan positioning on a Hologic scanner

2.4 Input Patient Information

1. Click ‘Perform Exam’ – ‘New Patient’
2. Input name (In the ‘last name’ field and ‘Patient ID’ field enter study ID number i.e. OA001 to OA200, DOB (check that this is consistent with the follow-up questionnaire), height, weight, sex, ethnicity. Input ID without ‘OA’ under Identifier 2 i.e. 001 to 200
3. If participant has been scanned before, find and select name and click ’ok’. Enter Current Height, Current Weight, scan Operator and Accession Number i.e. ‘001_2’ if second scan for participant OA001
4. Click ‘Whole Body Scan’
5. **Click Start Scan** (3 minute process)
6. Once scan is finished and participant has left, disinfect and wipe down bed for next scan.

3 SCAN ANALYSIS

3.1 Standard Region of Interest (ROI) Analysis

1. Click ‘Analyze Scan
2. Click ‘All Scans’
3. Type in participant name (e.g. OA001) - highlight participant name - click ‘Next’
4. Choose analysis method: ‘Whole Body Fan Beam’ - click ‘Next’
5. Click ‘Regions’
6. Adjust image contrast:
   a. Click ‘sun/moon’ icon
   b. Click ‘black dot’ in triangle to adjust contrast
   c. Click ‘up/down’ arrows to zoom (100 or 150 recommended)
   d. Click ‘sun/moon’ icon to exit

7. Click ‘Line Mode’:
   a. Outline extremities: drag lines outside the soft tissue of hips, calves, arms and trunk
   b. Outline spine: drag inside lines as close to spine as possible; drag top line just below jaw
   c. Outline lumbar spine: drag top line to T12/L1 (last rib attachment); drag bottom line to top of iliac crest

8. Click ‘Point Mode’:
   a. Arm Cut: move the upper vertex of the arm lines to ensure they touch the most medial point of the proximal humerus
   b. Horizontal pelvic cut: ensure top line is a straight line sitting on top of the iliac crests. If crests are not level, maintain the horizontal line using the higher crest as your marker.
   c. Leg cut: move the upper vertex laterally on both sides to ensure that full leg/hip region is within the line. Move lower vertex to correct any problems with lower leg regions. Make sure central line is between toes
   d. Vertical pelvic cut: drag point below pelvis so that lines intersect lateral aspect of pelvic bone and femoral head/neck; drag points on outside lines to adjust further – be mindful not to exclude soft tissue.
   e. Neck Cut; finally position the neck cut at the tip of the lowest bony point of the skull, ensuring neck tissue (e.g. trapezius muscles) remain below the line

9. Click ‘Results’

    a. Check that the Left and Right proportions (area and BMC) of arm, rib, and leg are < 50 points different

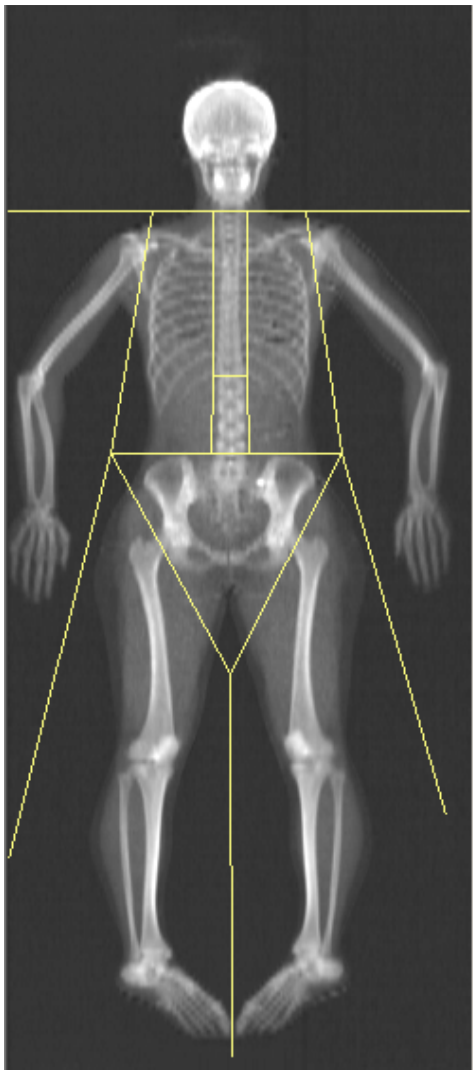


Fig. 2 Standard Segmental Analysis

3.2 Custom Region of Interest (ROI) Analysis

1. Click ‘Subregions’
2. Click **‘+’** to add **L1-L4** ROI (R1)
    a. Move ROI until the bottom line lies just below the L4 vertebrae.
    b. Using ‘Line Mode’, drag the top of the ROI until it is just above the L1 vertebrae.
    c. Drag the sides of the ROI until they lie outside the soft tissue of the abdomen (use ‘Point Mode’ if required)

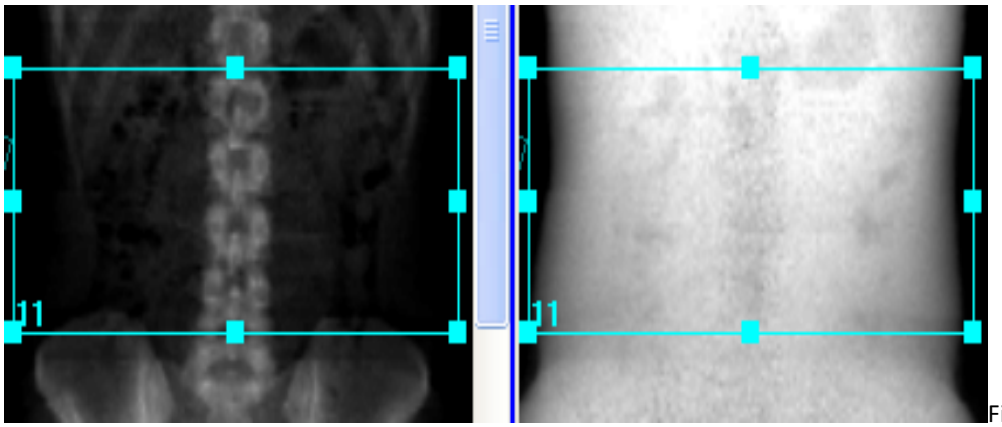
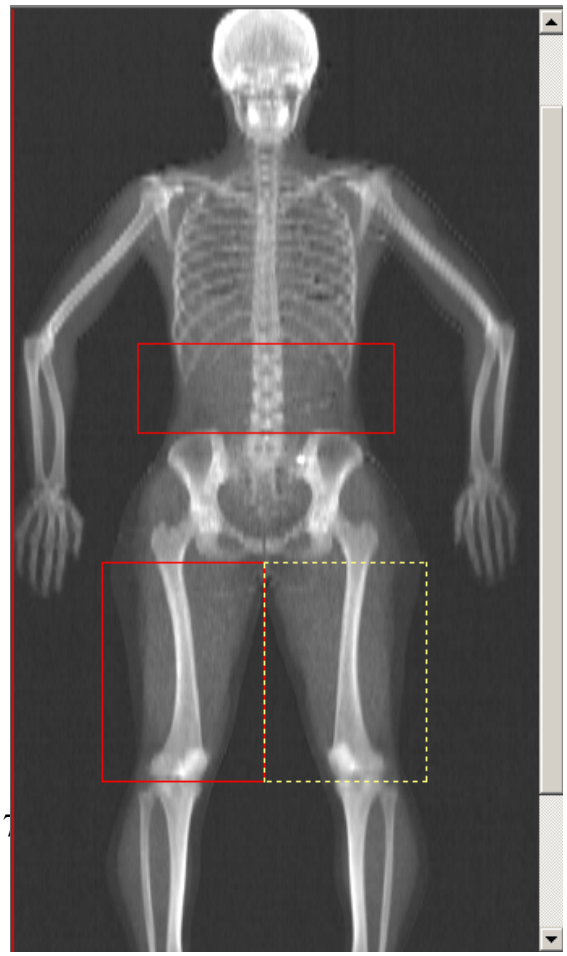


Fig 3. L1-L4 Region of Interest

3. Click **‘+’** to add Right **Upper Thigh** ROI (R2)
    a. Move ROI until the bottom line lies just below the right femur (knee joint line).
    b. Using ‘Line Mode’, drag the top line until it lies inferior to the lesser trochanter. If the lesser trochanter is not visible, use the ischium as your landmark.
    c. Drag the sides of the ROI until the medial side is in line with the pubis and the lateral side lies outside the soft tissue.



d. Repeat step 2 to add **Left Upper Thigh ROI (R3)**
e. Click ‘Results’

Fig 4. Full Custom Segmental Analysis

3.3 Filing

a. Click ‘Close’
b. Click ‘Report’ – ‘Next’
    i. Select ‘Filing’
c. Click ‘Print’ – select printer: HP1102w – Click ‘OK’
d. Click ‘Close’

After you have printed the scan write “testing day report” as well as any metal objects or artefacts that could not be removed (e.g. pacemaker, implant) on the front page and then staple the report together and place on the participants clipboard.

4 Data Extraction

4.1 Export Data

1. All new scans should be exported at the end of each month
2. Make sure all labeling is correct and segmental analysis is complete
3. Attach the pen drive to the USB port on the back of the computer tower
4. Home page tool bar: Click ‘Utilities’
5. Click ‘Database Tools’
6. Click ‘Export’

7. Enter either the Participant Name Range you wish to access (e.g. OA100-OA115) or the scan date range (e.g. 01 Nov 2014 – 30 Nov 2014)
8. Click 'Export'
9. Save in My Computer / Removable disc drive F/ TEAM OA 2014 DXA
10. Name .mdb file (Microsoft Acces file) the date of testing: yearmonthday (I.E. 20140623 OA STUDY DXA)
11. Copy saved .mdb files to ASIS-SMC/ASIS documents/Team OA Prevention/Team OA Data/ DEXA data

4.2 Transfer Data from Access to Excel

1 Open Access file on a Windows operating system
2 Tables listed on left side contain extracted data. The 5 tables of interest for body composition analysis are: 'PATIENT', 'ScanAnalysis', 'SubRegionComposition', 'Wbody' and 'WbodyComposition'
3 A Query Design template is available in the Access file named 'OA_DXAextraction_template' on ASIS. Open this file, select the Query labeled 'OA_bodycomp'(on left, below tables), copy and paste into your new Access file
4 If you need to create a new query, follow steps 5-8. Otherwise, **skip to step 9.**
5 **DESIGNING A QUERY:** Go to 'Create' in top tab and click on 'Query Design'
6 Hold CTRL key and add the 5 tables listed above. Select 'close'
7 Enter the desired fields as shown in Table 1 in Appendix. In the second row, select Table (e.g. PATIENT). In the first row, select Field (e.g. Identifier 1). Continue for the rest of the columns.
8 Select 'Run' in upper tab
9 Select all. Copy and paste results into a blank excel document.
10 Close query and save as 'OA_bodycomp'
11 In excel, select all and sort file by 1. 'Identifier 1' and 2. 'Accession_No'
12 Make sure the correct number of scans are present i.e. no duplicates and Accession_No are labeled correctly (e.g. 001 for 1st scan, 001_02 for second scan. If duplicate scans are present (error in software), check analysis_date and delete oldest record.
13 Sort file by Accession_No. Create a new column labeled 'Scan_No' and type '1' if first scan and '2' if second (follow-up) scan. Sort by 'Scan_No'.
14 Cut all follow-up scans and paste into second tab labeled 'Follow-Up 2'.
15 Sort for import to RedCap by deleting unnecessary columns.

5 Repeatability of Measurement

A standardized approach exists for DXA scanning to ensure the random (non-biological) error is kept to a minimum. Calculation of this precision error is critical in serial measurement of body composition or bone mineral density to monitor the change in body composition through longitudinal or intervention studies. Common sources of variation between scans that affect measurement precision include poor or inconsistent positioning and incomplete data acquisition. It is therefore recommended by the International Society for Clinical Densitometry (ISCD) that each technologist carries out an in vivo precision assessment after having performed approximately 100 scans to determine the precision error for BMD at that facility. A similar recommendation has been made for body composition scanning, without indication of prior technologist scanning experience.

5.1 Precision Assessment

Every DXA technologist should conduct a precision assessment on the instrument and patient population they will be scanning on a regular basis. The details are given below:

- Participants should be informed of the benefits and risks before they are included in a precision assessment.
- Participants that are representative of the study's typical population should be used.
- The scan modes in use for clinical or study needs where the change in the parameter is important for individual participants should be used. For whole body composition studies, this is total bone mineral density (BMD), total bone mineral content (BMC), total fat mass (FM) and total lean tissue mass (LTM).
- Each technologist should scan 30 participants twice or 15 participants three times.
- The participant should be repositioned between each scan by asking them to get off the table and then back on.
- Average BMD, BMC, FM and LTM should be calculated.
- Precision results can be calculated using the DXA precision worksheet located on ASIS and are reported as:

- root mean square standard deviation (RMS-SD), calculated as $\sqrt{((\sum SD^2)/n)}$;
- root mean square coefficient of variance (RMS-CV%), calculated as (RMS-SD/mean);
- Least significant change (LSC) at the 95% confidence interval (CI) was calculated as (RMS-SD*2.77)

Minimum precision standards for individual technologists are as follows:

Parameter	*RMS-CV%*
Total BMD	1.5%
Total BMC	2.0%
Total FM	3.0%
Total LTM	2.0%

Precision is also calculated as the 'least significant change' (LSC) that has to be seen for there to be 95% statistical confidence that the change in the measure is not just due to chance. This can be useful when monitoring change due to a disease state or intervention.

5.2 Strategies to minimize precision error

1. All operators should be formally trained in positioning and analysis for each scan mode used.
2. Participants should be scanned on the same densitometer. Scans from different makes and model systems cannot be quantitatively compared.
3. The same operator should be used for the baseline and follow-up scans.
4. The participant should be positioned using the standardized procedure suggested by the manufacturer or study protocol.
5. The scan mode should not be changed between baseline and follow-up scans. The scan mode that was used for the baseline should always be used for the follow-up.
6. Identical ROIs should be used for each scan and placed consistently. The 'compare' or 'copy' function should always be used if available.

7. Auto-analysis algorithms should be used and checked by the operator, and only modified when necessary and at a minimum.

6 Appendix

6.1 Table1. Creating a Query Design: Recommended Fields

Table (2nd Row)	*Field (1st Row)*
Patient	Identifier 1
Patient	Identifier 2
Patient	Patient_Key
Patient	Birthdate
Patient	Sex
ScanAnalysis	ScanID
ScanAnalysis	Scan_date
ScanAnalysis	Analysis_date
ScanAnalysis	Accession_No
ScanAnalysis	Height
ScanAnalysis	Weight
Wbodycomposition	HEAD_FAT
Wbodycomposition	HEAD_LEAN
Wbodycomposition	HEAD_MASS
Wbodycomposition	HEAD_PFAT
Wbodycomposition	LARM_FAT
Wbodycomposition	LARM_LEAN

Wbodycomposition	LARM_MASS
Wbodycomposition	LARM_PFAT
Wbodycomposition	RARM_FAT
Wbodycomposition	RARM_LEAN
Wbodycomposition	RARM_MASS
Wbodycomposition	RARM_PFAT
Wbodycomposition	TRUNK_FAT
Wbodycomposition	TRUNK_LEAN
Wbodycomposition	TRUNK_MASS
Wbodycomposition	TRUNK_PFAT
Wbodycomposition	L_LEG_FAT
Wbodycomposition	L_LEG_LEAN
Wbodycomposition	L_LEG_MASS
Wbodycomposition	L_LEG_PFAT
Wbodycomposition	R_LEG_FAT
Wbodycomposition	R_LEG_LEAN
Wbodycomposition	R_LEG_MASS
Wbodycomposition	R_LEG_PFAT
Wbodycomposition	SUBTOT_FAT
Wbodycomposition	SUBTOT_LEAN
Wbodycomposition	SUBTOT_MASS

Wbodycomposition	SUBTOT_PFAT
Wbodycomposition	WBTOT_FAT
Wbodycomposition	WBTOT_LEAN
Wbodycomposition	WBTOT_MASS
Wbodycomposition	WBTOT_PFAT
Wbody	WBTOT_AREA
Wbody	WBTOT_BMC
Wbody	WBTOT_BMD
SubRegionComposition	REG1_FAT
SubRegionComposition	REG1_LEAN
SubRegionComposition	REG1_MASS
SubRegionComposition	REG1_PFAT
SubRegionComposition	REG2_FAT
SubRegionComposition	REG2_LEAN
SubRegionComposition	REG2_MASS
SubRegionComposition	REG2_PFAT
SubRegionComposition	REG3_FAT
SubRegionComposition	REG3_LEAN
SubRegionComposition	REG3_MASS
SubRegionComposition	REG3_PFAT

NOTE:

Order is not important. Not all fields are required but are useful for determination of errors/duplicates after extraction. Many may be deleted before import to RedCap. The recommended fields include a full body composition extraction. Additional fields can be added for a full regional bone (BMC and BMD) analysis using ‘Wbody’ and ‘Subregionbone’ tables. Only total BMC and BMD are included in this protocol.

APPENDIX C: PARTICIPANT PHYSICAL ACTIVITY MONITORING LOG

How to Wear the Physical Activity Monitor

This small activity monitor records general movement and allows us to get a better understanding of your overall activity level. We will not be able to tell what kind of specific activity you are doing, only the intensity and duration of physical activity. At first, the belt may feel slightly awkward, but after a few hours, you will not notice it as much. It is extremely important for our study that you wear the monitor correctly. Please follow these instructions carefully:

- ✓ Wear the monitor attached to the belt around your waist, **just above your right hipbone**
- ✓ Wear the monitor so that the yellow sticker is facing **up**
- ✓ Wear the monitor snug against your body. If you have to, you can adjust the end of the strap to make it tighter. Or, to loosen the belt, push more of the strap through the loop. **Wear the monitor tight enough so that it does not move when you are being active**
- ✓ The monitor can be worn underneath or on top of your clothes or in your belt loop
- ✓ Keep the monitor on all day and all night for a 7 day period
- ✓ **Do not submerge in the water** (swimming, bathing etc.) You can remove for showering but remember to put it back on as soon as possible and keep record of each occurrence in your monitor log
- ✓ Do not let anyone else wear it

Details for dropping off/collection of monitor_____

If you have any questions related to the monitor, please call or email:

OFFICE USE ONLY Actigraph ID_____

Start Date and Time:_____

Participant ID: Valid

_____

There is no 'ON' or 'OFF' switch that you need to worry about. The activity monitor runs on a battery and is programmed to run continuously from when we give it to you. **Please do not try to open the monitor.**

Monitor Off (complete):			
Date	Day	Time Off	

Monitor Log

Wear the physical activity monitor for seven (7) consecutive days. Please remove the monitor for swimming, showering or bathing. The **first table** below is to log every time that you take the **monitor off** for **non-exercise activities** such as **showering and bathing**.

TABLE 1: Log every time you take the monitor off

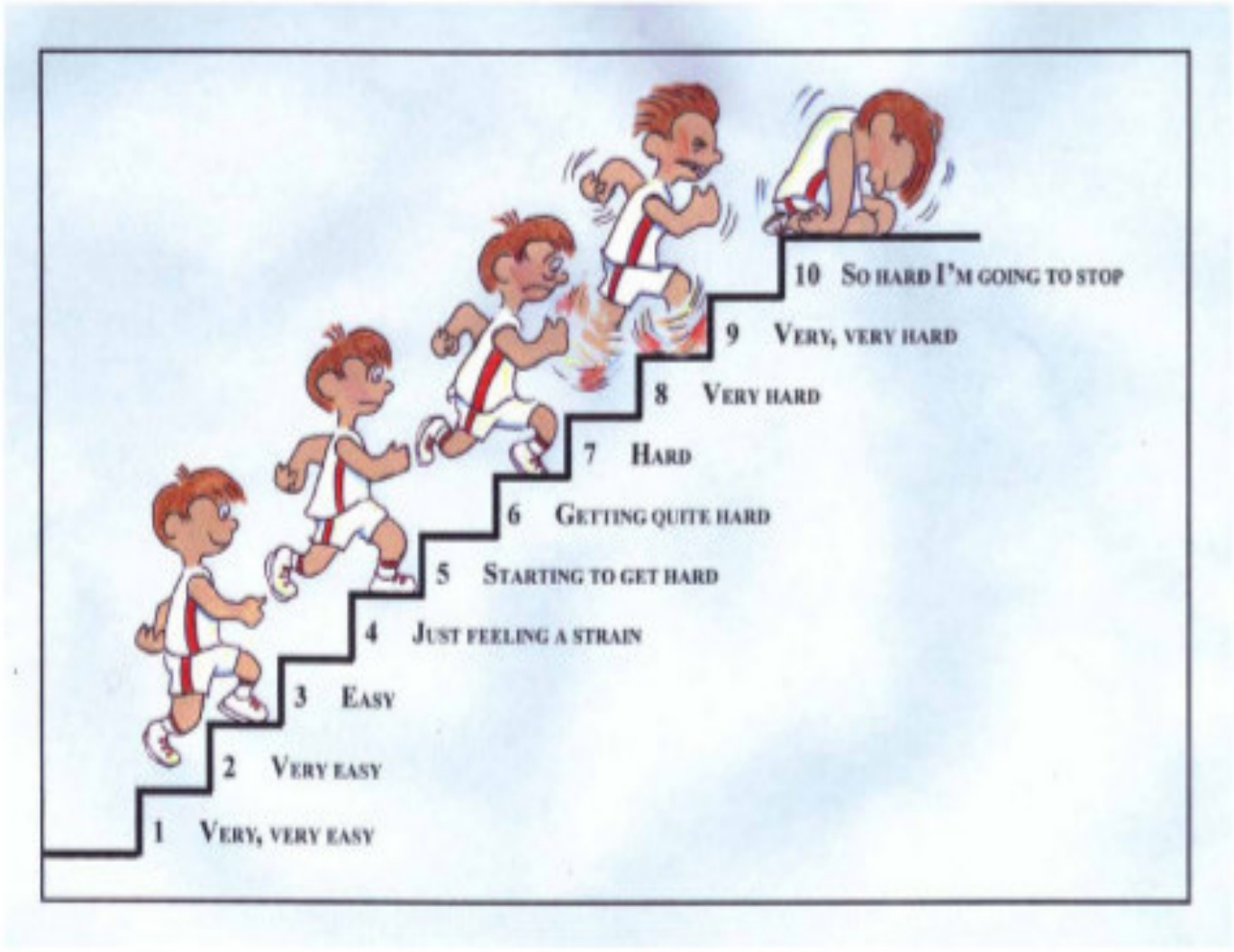
Date	Day	Time Off	Time On	Reason
e.g. July 15th 2016	Wednesday	7.30 AM	7.45AM	Shower

In the **second table** below, write down if there were any **exercise-related activities** that **the monitor may not detect** or require you to **remove your monitor**. Activities in this table may include: swimming, stationary biking, elliptical training, horseback riding, rowing/ canoe/ kayaking, resistance training (weights). In the right hand column, we would like you to note how hard you thought this exercise session was using the scale attached. For example: a slow bike to school may be a 2, while a hard swimming session could be an 8.

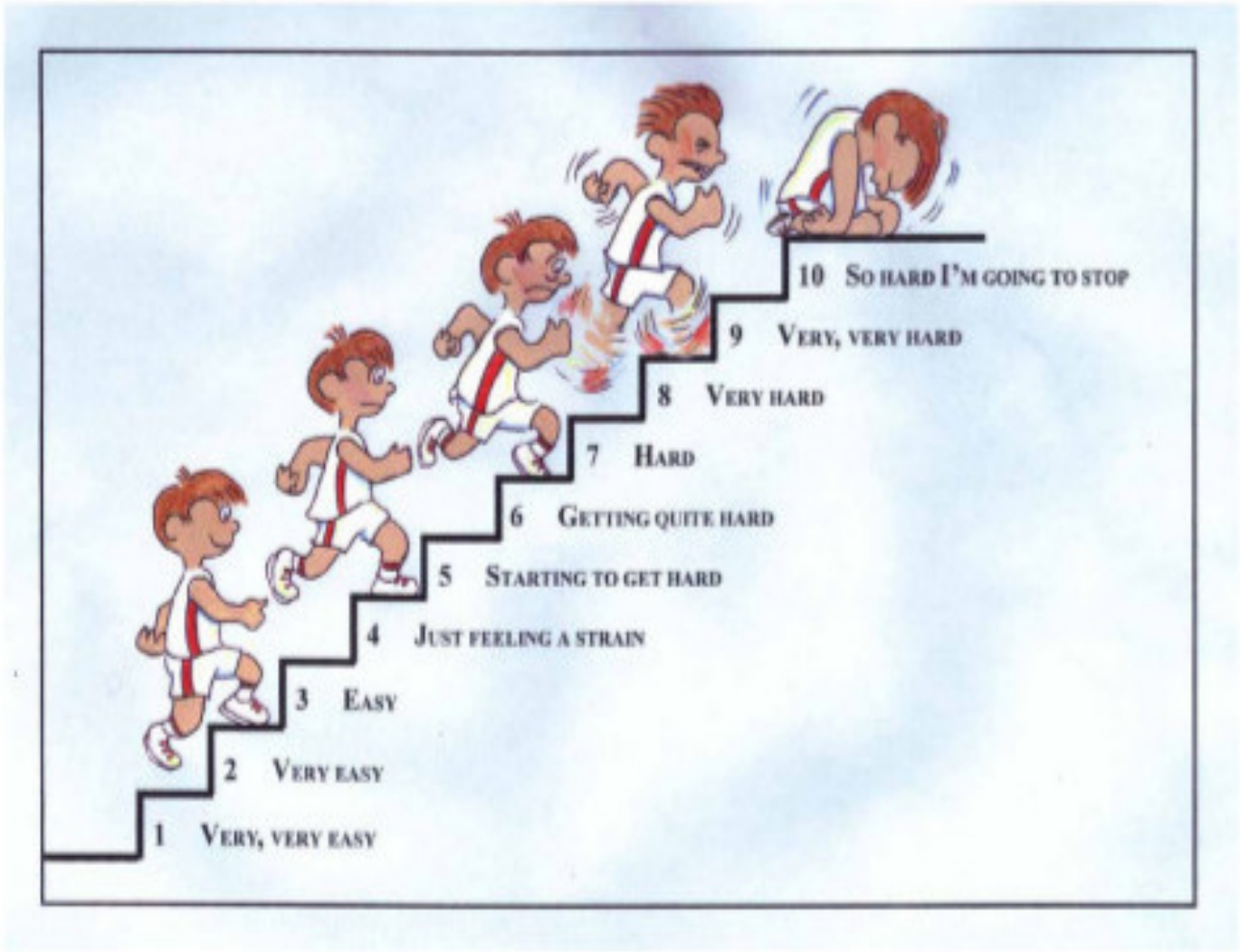
TABLE 2: Log exercise-related activities that the monitor may not detect

Date	Day	Did you take the monitor off?	Activity Start	Activity End	Type of Activity	RPE of Exercise
e.g. July 15th 2015	Wednesday	Yes	7.30 AM	8.30AM	Swimming	7

Please use the scale below to rate how hard you worked during your activity


10 So hard I'm going to stop
9 Very, very hard
8 Very hard
7 Hard
6 Getting quite hard
5 Starting to get hard
4 Just feeling a strain
3 Easy
2 Very easy
1 Very, very easy

APPENDIX D: PICTORIAL CHILDREN'S EFFORT RATING TABLE (PCERT)


10 So hard I'm going to stop
9 Very, very hard
8 Very hard
7 Hard
6 Getting quite hard
5 Starting to get hard
4 Just feeling a strain
3 Easy
2 Very easy
1 Very, very easy

APPENDIX E: PHYSICIAN ASSESSMENT FORM

UNIVERSITY OF CALGARY

ACR Core Measures: Juvenile Idiopathic Arthrits

to be completed by the Study Physician

Alberta Children's HOSPITAL RESEARCH INSTITUTE

Sport Injury Prevention Research Centre, UNIVERSITY OF CALGARY

Rheumatologist (name):			
Date of exam: ____/____/____ (Day / Month / Year)	**ILAR Classification of Diagnosis** _____	**Study Subject ID#** (office use only)	

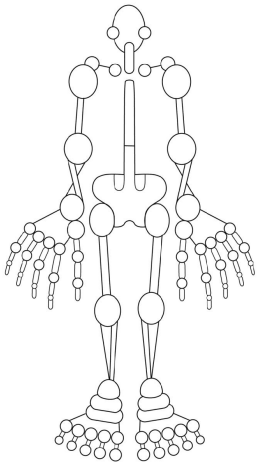
ACR Core Measures: Juvenile Idiopathic Arthrits

Physician Global Assessment of Disease Activity	0: None ——— 10: Maximum Activity				
Parent Global Assessment of Disease Activity	0: None ——— 10: Maximum Activity				
Functional Ability- CHAQ disability index	_____(0-3)	**Erythrocyte Sedimentation Rate (ESR)**		**C-reative Protein (CRP)**	

Active Joint Count

ACTIVE defined as presence of swelling NOT due to currently inactive synovitis or to bony enlargement, or limitation of motion accompanied by heat, paln, or tenderness

R L

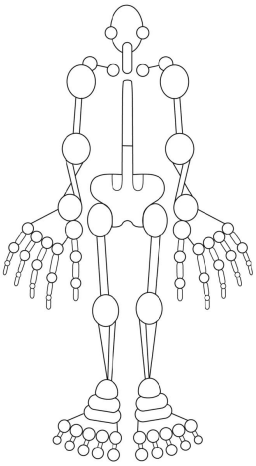


Total # Active Joints: _____

Limited ROM Joint Count

Limited ROM due to Active Arthritis

R L



Total # Joints with Limited ROM: _____

UNIVERSITY OF CALGARY

Rheumatologist Assessment Form

To be filled out by Study Physican

Alberta Children's HOSPITAL RESEARCH INSTITUTE

Sport Injury Prevention Research Centre
UNIVERSITY OF CALGARY

Rheumatologist (name):			
Date of exam: / / (Day / Month / Year)	**ILAR Classification of Diagnosis** _____	**Study Subject ID#** (office use only)	
Date of Diagnosis / / (Day / Month / Year)	**Disease Course**	☐ Oligo ☐ Poly ☐ Systemic	

MEDICATION USE

Please indicate which medication(s) is currently prescribed:

Type	If yes please indicate:	Type	Dose	Frequency	Start Date	Side Effects (If any)
DMARDS	☐ No ☐ Yes					
NSAIDS	☐ No ☐ Yes					
Biologics	☐ No ☐ Yes					
Oral Steroids	☐ No ☐ Yes					
Anti-TNF	☐ No ☐ Yes					
Steroid Injections*	☐ No ☐ Yes					

*For Interarticular injections only: Date of last injection (d/m/y): / / Injection Site(s):

APPENDIX F: CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE (CHAQ)

CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE

In this section we are interested in learning how your child's illness affects his/her ability to function in daily life. Please feel free to add any comments on the back of this page. In the following questions, please check the one response which best describes your child's usual activities (averaged over an entire day) **OVER THE PAST WEEK. ONLY NOTE THOSE DIFFICULTIES OR LIMITATIONS WHICH ARE DUE TO ILLNESS**. If most children at your child's age are not expected to do a certain activity, please mark it as "Not Applicable". **For example, if your child has difficulty in doing a certain activity or is unable to do it because he/she is too young but not because he/she is RESTRICTED BY ILLNESS, please mark it as "NOT Applicable".**

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To do	Not Applicable
DRESSING & GROOMING					
Is your child able to:					
- Dress, including tying shoelaces and doing buttons?	☐	☐	☐	☐	☐
- Shampoo his/her hair?	☐	☐	☐	☐	☐
- Remove socks?	☐	☐	☐	☐	☐
- Cut fingernails?	☐	☐	☐	☐	☐
ARISING					
Is your child able to:					
- Stand up from a low chair or floor?	☐	☐	☐	☐	☐
- Get in and out of bed or stand up in a crib?	☐	☐	☐	☐	☐
EATING					
Is your child able to:					
- Cut his/her own meat?	☐	☐	☐	☐	☐
- Lift up a cup or glass to mouth?	☐	☐	☐	☐	☐
- Open a new cereal box?	☐	☐	☐	☐	☐
WALKING					
Is your child able to:					
- Walk outdoors on flat ground?	☐	☐	☐	☐	☐
- Climb up five steps?	☐	☐	☐	☐	☐

*** Please check any AIDS or DEVICES that your child usually uses for any of the above activities:**

- Cane	☐	- Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)	☐
- Walker	☐	- Built up pencil or special utensils	☐
- Crutches	☐	- Special or built up chair	☐
- Wheelchair	☐	- Other (Specify:_____)	☐

*** Please check any categories for which your child usually needs help from another person BECAUSE OF ILLNESS:**

- Dressing and Grooming	☐	- Eating	☐
- Arising	☐	- Walking	☐

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To do	Not Applicable
HYGIENE					
Is your child able to:					
- Wash and dry entire body?	☐	☐	☐	☐	☐
- Take a tub bath (get in and out of tub)?	☐	☐	☐	☐	☐
- Get on and off the toilet or potty chair?	☐	☐	☐	☐	☐
- Brush teeth?	☐	☐	☐	☐	☐
- Comb/brush hair?	☐	☐	☐	☐	☐
REACH					
Is your child able to:					
- Reach and get down a heavy object such as a large game or books from just above his/her head?	☐	☐	☐	☐	☐
- Bend down to pick up clothing or a piece of paper from the floor?	☐	☐	☐	☐	☐
- Pull on a sweater over his/her head?	☐	☐	☐	☐	☐
- Turn neck to look back over shoulder?	☐	☐	☐	☐	☐
GRIP					
Is your child able to:					
- Write or scribble with pen or pencil?	☐	☐	☐	☐	☐
- Open car doors?	☐	☐	☐	☐	☐
- Open jars which have been previously opened?	☐	☐	☐	☐	☐
- Turn faucets on and off?	☐	☐	☐	☐	☐
- Push open a door when he/she has to turn a door knob?	☐	☐	☐	☐	☐
ACTIVITIES					
Is your child able to:					
- Run errands and shop?	☐	☐	☐	☐	☐
- Get in and out of a car or toy car or school bus?	☐	☐	☐	☐	☐
- Ride bike or tricycle?	☐	☐	☐	☐	☐
- Do household chores (e.g. wash dishes, take out trash, vacuuming, yardwork, make bed, clean room)?	☐	☐	☐	☐	☐
- Run and play?	☐	☐	☐	☐	☐

*** Please check any AIDS or DEVICES that your child usually uses for any of the above activities:**

- Raised toilet seat	☐	- Bathtub bar	☐
- Bathtub seat	☐	- Long-handled appliances for reach	☐
- Jar opener (for jars previously opened)	☐	- Long-handled appliances in bathroom	☐

*** Please check any categories for which your child usually needs help from another person BECAUSE OF ILLNESS:**

- Hygiene	☐	- Gripping and opening things	☐
- Reach	☐	- Errands and chores	☐

PAIN: We are also interested in learning whether or not your child has been affected by pain because of his or her illness. How much pain do you think your child has had because of his/her illness IN THE PAST WEEK? Place a mark on the line below, to indicate the severity of the pain

No pain 0 ├──────────────────────────────────────┤ 100 Very severe pain

GLOBAL EVALUATION: Considering all the ways that arthritis affects your child, rate how he/she is doing by placing a single mark on the line below.

Very well 0 ├──────────────────────────────────────┤ 100 Very poor

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APPENDIX G: INTERMITTENT AND CONSTANT OSTEOARTHROSIS PAIN (ICOAP) SURVEY

A Measure of Intermittent and Constant Osteoarthritis Pain, ICOAP: KNEE Version

People have told us that they experience different kinds of pain (including aching or discomfort) in their knee. To get a better sense of the different types of knee pain you may experience, we would like to ask you about any "constant pain" (pain you have all the time) separately from any pain that you may experience less often, that is, "pain that comes and goes". The following questions will ask you about the pain that you have experienced in your knee in the PAST WEEK. Please answer ALL questions.

A) CONSTANT PAIN

For each of the following questions, please select the response that best describes, on average, your *constant knee pain* in the PAST WEEK.

1. In the past week, how intense has your *constant knee pain* been?

☐0	☐1	☐2	☐3	☐4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

2. In the past week, how much has your *constant knee pain* affected your sleep?

☐0	☐1	☐2	☐3	☐4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

3. In the past week, how much has your *constant knee pain* affected your overall quality of life?

☐0	☐1	☐2	☐3	☐4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

4. In the past week, how frustrated or annoyed have you been by your *constant knee pain?*

☐0	☐1	☐2	☐3	☐4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

5. In the past week, how upset or worried have you been by your *constant knee pain*?

☐0	☐1	☐2	☐3	☐4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

B) PAIN THAT COMES AND GOES

For each of the following questions, please select the response that best describes your *knee pain that comes and goes*, *on average*, in the PAST WEEK.

6. In the past week, how intense has your most severe *knee pain that comes and goes* been?

☐0	☐1	☐2	☐3	☐4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

7. In the past week, how frequently has this *knee pain that comes and goes* occurred?

☐0	☐1	☐2	☐3	☐4
Never/ No knee pain that comes and goes	Rarely	Sometimes	Often	Very Often

8. In the past week, how much has your *knee pain that comes and goes* affected your sleep?

☐0	☐1	☐2	☐3	☐4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

9. In the past week, how much has your *knee pain that comes and goes* affected your overall quality of life?

☐0	☐1	☐2	☐3	☐4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

10. In the past week, how frustrated or annoyed have you been by your *knee pain that comes and goes*?

☐0	☐1	☐2	☐3	☐4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

11. In the past week, how upset or worried have you been by your *knee pain that comes and goes*?

☐0	☐1	☐2	☐3	☐4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

THANK YOU!

APPENDIX H: CONSENT FORM FOR PARTICIPANT OVER 18 AND PARTICIPANT GUARDIANS

TITLE: Exercise Capacity in Juvenile Idiopathic Arthritis: A Mixed Methods Study

SPONSOR: Vi Riddell Pediatric Rehabilitation Research Program, Alberta Children's Hospital Foundation; Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary.

Chapter Seven: **INVESTIGATORS:** Carolyn, Emery; Gregor Kuntze; Susanne Benseler; Dianne Mosher; Janet Ronsky; Marinka Twilt; Colleen Nesbitt

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your child's participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

BACKGROUND

Juvenile idiopathic arthritis (JIA) is the most common form of childhood rheumatic disease affecting an estimated 24,000 Canadian children (3 out of every 1000) under the age of 18. JIA is associated with pain, disability, reduced psychosocial wellbeing, and high economic burden on the healthcare system. Exercise therapy may be beneficial to enhance function and wellbeing, reduce pain and inflammation, and minimize the burden of disease. However, little is known about the effects of JIA on health, wellbeing and activity. This information is vital to understand how exercise interventions need to be designed (i.e. type of exercise type, frequency, intensity, and duration) to optimally contribute to the health and wellbeing of JIA patients.

The objective of this research project is to identify the effects of JIA across the spectrum of health, wellbeing, activity, and function. Our long term goal is to improve health and wellbeing and to reduce the personal and financial burden of JIA. The information collected in this study is essential to inform future work on the development of customized and effective physical therapy interventions. This project is an interdisciplinary team effort that combines clinical experts in pediatric rheumatology at the Alberta Children's Hospital and community and epidemiology, rehabilitation and biomechanics and physiology researchers from the University of Calgary. This provides a unique environment to advance knowledge of the effects of JIA and enhance the health and wellbeing of youth in Alberta.

WHAT IS THE PURPOSE OF THE STUDY?

This study investigates the effects of JIA on combined psychosocial, functional, physiological, clinical, structural and healthcare utilization outcomes. This information is critically needed to enable effective exercise program development and evaluation. Mitigating chronic disease through exercise may significantly impact the individual and societal burden by reducing disability for young Albertans and limiting the economic burden of JIA on the Alberta Health Services.

7.1 WHAT WOULD MY CHILD HAVE TO DO?

If you choose to participate in the study you will undergo a short phone interview (approx. 10-15 minutes) with a research coordinator to determine if you are eligible to participate and if you are willing to consent to participating in the study. You will be asked to participate in two testing days: Day 1 will be conducted at the C.H. Riddell Movement Assessment Centre in conjunction with your appointment at the JIA Clinic at the Alberta Children's Hospital; Day 2 will be conducted one week after your initial visit at the Faculty of Kinesiology, University of Calgary. Prior to Day 1 you will be asked to complete the following questionnaires at home:

a) FISSA: is a 31-item participant completed questionnaire of fatigue (~15-20 min).
b) PHQ-9: is a participant completed questionnaire of depression (~5 min).
c) ICOAP: is a participant completed questionnaire of intermittent and constant knee pain (~10 min).
d) KOOS: is a participant completed questionnaire of knee function (~10-15 min).
e) RAOS: is a modified version of KOOS, designed specifically for arthritis (~10-15 min)
f) CHQ-PF50: is a parent completed questionnaire of quality of life (~10-15 min)
g) Healthcare Utilization: is a parent completed self-report form summarizing all healthcare use over the past year.

On Day 1 you will attend the JIA Clinic for your scheduled clinical appointment. After this appointment you will met by a researcher who will take you to the C.H. Riddell Movement Assessment Centre. This is a state of the art lab where the way you move can be recorded and analyzed using a 12 camera motion capture system. Here we will also investigate how you activate your muscles and how much energy you use to move. These data collections will have about 2 hours to complete. These will include:

a) A blood test: to help identify presence of biomarkers (chemicals) that are commonly found in people with JIA.
b) NPRS: to rate your current pain on a scale of 0 to 10.
c) OMNI-RPE: to rate your current level of exertion on a scale of 0 to 10.
d) EQ-5D-5L: to rate your quality of life.
e) Height, weight, and waist circumference.
f) Functional testing:
    - Balancing on one leg: Involves balancing on one leg with your eyes open for 60 seconds. Three repetitions will be done on each leg.

- Walking on a treadmill: Involves walking at a normal speed (1.2m/s) for a total of 6 minutes.
- Running on a treadmill: Involves running on a treadmill at a normal speed (2.5m/s) for 6 minutes)
- Vertical drop jump: Involves five sets of dropping down from a 31cm platform and jumping back up as high as possible times.
- Single leg squat: Involves three sets of squatting with one leg at a time for five repetitions per leg.
- Triple single hop test: Involves two trials of hopping on one leg, three times, trying to get as far as possible.
- Star excursion balance test: Involves balancing on one foot while reaching out as far as possible with the other leg, in three directions.
- Unipedal dynamic balance test: Involves standing on a balance pad with one foot, closing your eyes, and raising your other leg.

NOTE: PLEASE LET US KNOW IF YOU HAVE AN ALLERGY TO ADHESIVES. IF SO, YOU WILL NOT BE ABLE TO COMPLETE FUNCTIONAL TESTS (d) AND (e).

g) Aerobic fitness test: to assess your energy expenditure during cycling on an instrumented cycle ergometer using an indirect calorimeter. For this you will need to wear a face mask while you are doing the cycle exercise.

Before you leave the lab we will provide you with a small, lightweight device called an Actigraph that will measure your physical activity. You will be asked to wear the Actigraph using an elastic belt around your waist for 7 days. At home we also ask you to keep a record of the food and fluid intake for three days (2 weekdays and 1 weekend day). These do not have to be recorded on consecutive days but should reflect your typical eating patterns. You will be given information on how to accuratley complete the diary or how to use the MyFitnessPal mobile app for this. We will schedule an appointment with you to return the Actigraph and the dietary recall form for one week after your first visit.

On Day 2 we will ask you to come to our lab at the Sport Injury Prevention Centre at the University of Calgary. You will be met by a researcher who will provide you with a parking pass and instructions for parking. We will collect the Actigraph and dietary recall forms from you and ask you to take part in a dual-energy X-ray absorptiometry scan (DXA). This scan gives us information on your body composition (adiposity and muscle mass) and your bone mineral density. For the scan you will be asked to lay flat on an exam table while the arm of a machine passes over you from head to toe. This test is a low-dose x-ray and will take about 10 minutes. Outside of the lab we will also conduct a detailed secondary analysis of your MRI scans that were previously performed. This analysis will look at the shape of your knee joint and quantify any injuries and inflammation in your knee joint. This will be done with the help of the

radiologists at the Alberta Children's Hospital and you do not have to do anything else for this.

7.2 WHAT ARE THE RISKS?

There are no expected risks associated with participating in this study. The measurements described above will be done under close supervision and every effort will be made to ensure your safety. As with any physical activity there is the possibility of a muscle pull or strain for the running and jumping tests. The risk of injury will be reduced by careful supervision during the testing procedures.

The blood tests will be done in a standardized fashion as done in any laboratory that withdraws blood. The person taking your blood will either be a trained technician or a physician. You should let the person taking the blood know if you have any allergies. Although very rarely, there is the possibility of local infection within days of having your blood taken. You would need to see a physician for this and be treated with antibiotics. There is also the remote possibility of fainting, which would be related to having a needle. This is unpredictable. This resolves after lying down for a short period. You would recover completely from this.

The estimated dose of radiation from the DXA scan is less than 25 mrads, and from knee x-rays, 20 mrads. No amount of radiation is considered to be completely safe. For the sake of comparison, the dose from a chest x-ray is 25 mrads, from a dental x-ray is 750 mrads, natural living at sea level exposes you to 100 mrads and watching TV one hour per day exposes a person to 1 mrad per year. The actual health risks from exposure to low x-ray doses are difficult to determine. Conservatively, health experts assume radiation health risks are proportional to exposure. This leads to pessimistic estimates of a 0.01% chance of developing cancer due to a 10 000 μSv x-ray dose, compared to a normal lifetime risk of cancer for women in the US of 33% (Reference: Kalender WA. Effective dose values in bone mineral measurements by photon absorptiomentry and computed tomography. Osteoporosis Int 2: 82-87, 1992).

There may be some initial discomfort wearing the physical activity monitor and belt. However, the belt is fully adjustable to fit the individual and minimize any discomfort.

ARE THERE ANY BENEFITS FOR MY CHILD?

If you agree to participate in this study there may or may not be a direct medical benefit to you outside your scheduled appointment at the JIA clinic (JIA patients only). The information we get from this study may help us to optimize physical therapy interventions and exercise guidelines for JIA in the future through pediatric programs and sport. However, you will receive information about your body mass index, bone mineral density, % fat and lean body mass, leg balance, and aerobic fitness.

DOES MY CHILD HAVE TO PARTICIPATE?

No, you do not have to participate. Participation is completely voluntary. If you agree to participate, we require you to sign and return this form to us. Two copies of this form have been provided. Please keep one for your records, and return the other to us.

Your signature on this form indicates that you have understood to your satisfaction the information regarding participation in this research project and agree to be a participant. In no way does this waive your legal rights nor release the investigators, sponsors, or involved institutions from their legal and professional responsibilities.

You are free to withdraw from the study at any time by contacting the Research Coordinator at 403-955-2772 sesau@ucalgary.ca.

WHAT ELSE DOES MY CHILD'S PARTICIPATION INVOLVE?

All of the information collected will remain strictly confidential. Your privacy will be assured. Only the investigators responsible for this study, the research assistants who will be doing the assessments and data analysis, and the University of Calgary Conjoint Health Research Ethics Board will have access to this information. Data will be kept in a secure, either locked, or password protected location, for five years after completion of the study. Confidentiality will be protected by using a study identification number in the database. Any results reported from the study will in no way identify study participants.

WILL WE BE PAID FOR PARTICIPATING, OR DO WE HAVE TO PAY FOR ANYTHING?

Participants will not be paid to participate in the study, and there will be no costs (parking permits will be provided) to the participants.

WILL MY CHILD'S RECORDS BE KEPT PRIVATE?

All of the information collected will remain strictly confidential. Your privacy will be assured. Only the investigators responsible for this study, the research assistants who will be doing the assessments and data analysis, and the University of Calgary Conjoint Health Research Ethics Board will have access to this information. Data will be kept in a secure, either locked, or password protected location, for five years after completion of the study. Confidentiality will be

protected by using a study identification number in the database. Any results reported from the study will in no way identify study participants.

IF MY CHILD SUFFERS A RESEARCH-RELATED INJURY, WILL WE BE COMPENSATED?

In the event that your child suffers injury as a result of participating in this research, no compensation will be provided to you by the Vi Riddell Pediatric Rehabilitation Program, the University of Calgary, the Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

7.3 SIGNATURES

Your signature on this form indicates that you have understood to your satisfaction the information regarding your child's participation in the research project and agree to their participation as a subject. In no way does this waive your legal rights nor release the investigators, or involved institutions from their legal and professional responsibilities. You are free to withdraw your child from the study at any time without jeopardizing their health care. If you have further questions concerning matters related to this research, please contact:

Dr. _____ (403) ___-____

or

Dr. _____ (403) ___-____

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair of the Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Parent/Guardian's Name	Signature and Date
Child's Name	Signature and Date
Investigator/Delegate's Name	Signature and Date
Witness' Name	Signature and Date

The investigator or a member of the research team will, as appropriate, explain to your child the research and his or her involvement. They will seek your child's ongoing cooperation throughout the study.
The University of Calgary Conjoint Health Research Ethics Board has approved this research study.
A signed copy of this consent form has been given to you to keep for your records and reference.

APPENDIX I: CHILD ASSENT FORM

TITLE: Exercise Capacity in Juvenile Idiopathic Arthritis: A Mixed Methods Study

Chapter Eight: **INVESTIGATORS:** Carolyn, Emery; Gregor Kuntze; Susanne Benseler; Dianne Mosher; Janet Ronsky; Marinka Twilt; Colleen Nesbitt

A research study is a way to find out new information about something. This consent form is part of the process to tell you about the research and what you will be asked to do. Please ask if you would like any extra information. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

BACKGROUND

You are being asked to take part in this research study because we are trying to learn more about the effects of Juvenile Idiopathic Arthritis (JIA) on the health, activity and wellbeing of children and adolescents. We are asking you to be in the study because either you have been diagnosed with oligoarticular JIA or because you are healthy and have not had any major injuries. By comparing between the two we can find out what is different and work on reducing those differences with the help of physiotherapists and physicians.

WHAT IS THE PURPOSE OF THE STUDY?

This study investigates the effects of JIA on how you feel, how you move, how fit you are, if you have any JIA symptoms, if your knee has changed and how often you go to the hospital, your doctor or any other health care professional. This information is important to tell us where we may be able to make the biggest difference for young Albertans.

8.1 WHAT WOULD I HAVE TO DO?

Your participation is completely voluntary and you can decide to not take part or to stop at any time. If you want to take part we would ask you to:

- Come to the Alberta Children's Hospital Movement Assessment Lab. We will check with your parents at the start of each session to see if you are happy to come to the lab.
- You will fill out some questionnaires during the study, which will ask questions about your

medical background, your participation in physical activity, your function and if you have any challenges in your daily life. These questionnaires will be emailed to you on the email address you provide on the other side of this form.

- You will participate in testing where a group of researchers will take your height, weight, measure your waist and take a small sample of your blood. Then we will run you through some activity and fitness measurements. For this you will have to wear small measuring devices so we can record your movement, how your muscles are working and how much energy you use.
- We will also ask you to wear an Actigraph, which is a small gadget that measures your activity during one week. During this week we would like you to also write down everything you eat and drink for three days.
- We will then ask you to bring back the Actigraph to our lab at the University of Calgary. When you bring it back we will ask you to take a DEXA scan of your body for about 10 minutes so we know how good your bones are.
- If you have JIA we will also look at MRI scans of your knee to look at the shape of your knee, and any injuries or inflammation in your knee. This will be done with the help of the radiologists and you do not have to do anything else for this.

NOTE: PLEASE LET US KNOW IF YOU HAVE ANY ALLERGIES.

8.2 WHAT ARE THE RISKS?

This study will not hurt you. The activities you do in this study will not be very different from the ones that you do during your physical education classes. We will ask you to do some exercise testing on a bicycle where you will have to work hard but you can stop when you are out of energy. We will also put small measuring tools on your body to look at your movement and muscles when you move. This is a lot like what is done for movies and computer games and should not cause you any pain or discomfort. If you do get injured during any of the activities, a physiotherapist or certified athletic therapist will be available to assess your injuries and give you recommendations for treatment. We will have to get a small sample of your blood but this will be done in the same way as it is done in any other laboratory by a trained technician or a physician. You should let the person taking the blood know if you have any allergies. Although very rarely, there is the possibility of local infection within days of having your blood taken. You would need to see a physician for this and be treated with antibiotics. There is also the remote possibility of fainting, which would be related to having a needle. This is unpredictable. This resolves after lying down for a short period. You would recover completely from this. The DEXA scan uses a very small amount of radiation, much smaller than the amount of radiation you are exposed to in a year living in Calgary. This should pose no risk to your health.

ARE THERE ANY BENEFITS FOR ME?

If you agree to participate in this study there may or may not be a direct medical benefit to you

outside your scheduled appointment at the JIA clinic (JIA patients only). The information we get from this study may help us to optimize physical therapy interventions and exercise guidelines for JIA in the future through pediatric programs and sport. However, you will receive information about your body mass index, bone mineral density, % fat and lean body mass, leg balance, and aerobic fitness.

DO I HAVE TO PARTICIPATE?

No, you do not have to participate. You can stop at any time by contacting the Research Coordinator at 403-955-2772 sesau@ucalgary.ca. If you agree to participate, we need you to sign and return this form to us. Two copies of this form have been provided, one for you and one for us.

WILL MY INFORMATION BE KEPT PRIVATE?

Only the investigators responsible for this study, the research assistants who will be doing the assessments and data analysis, and the University of Calgary Conjoint Health Research Ethics Board will have access to this information. Your data will be kept securely for five years after completion of the study. Any results reported from the study will in no way identify you as a participant.

WILL WE BE PAID FOR PARTICIPATING, OR DO WE HAVE TO PAY FOR ANYTHING?

We will not pay you to participate but we will cover the cost of parking at the Children's Hospital and at the University of Calgary.

IF I INJURE MYSELF DURING THE STUDY, WILL WE BE COMPENSATED?

If you suffer an injury as a result of participating in this research, no compensation will be provided to you by the Vi Riddell Pediatric Rehabilitation Program, the University of Calgary, the Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

8.3 SIGNATURES

Would you like to take part in this study? (Please ✓ one)

_____ Yes, I will be in this research study. _____ No, I don't want to do this.

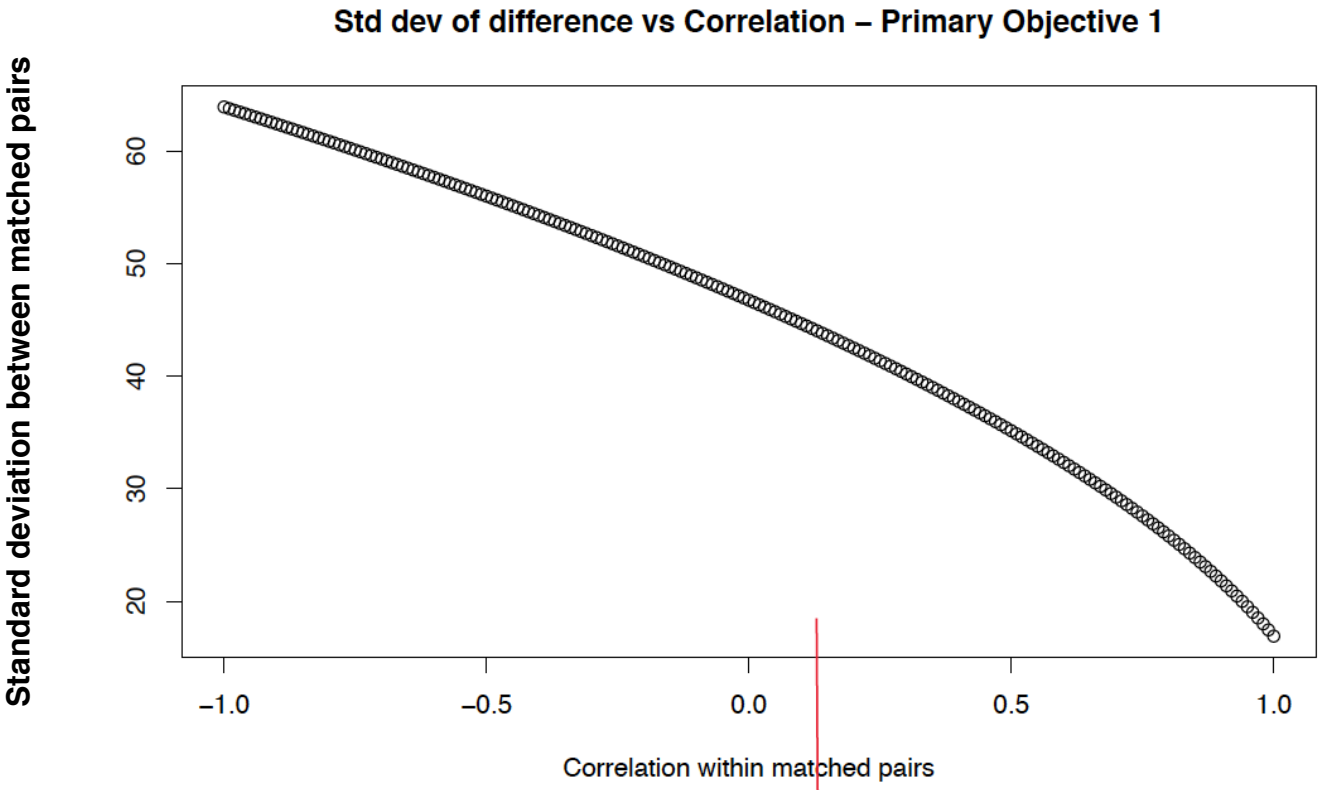
If you have any questions concerning your rights as a possible participant in this research, please contact the Chair of the Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

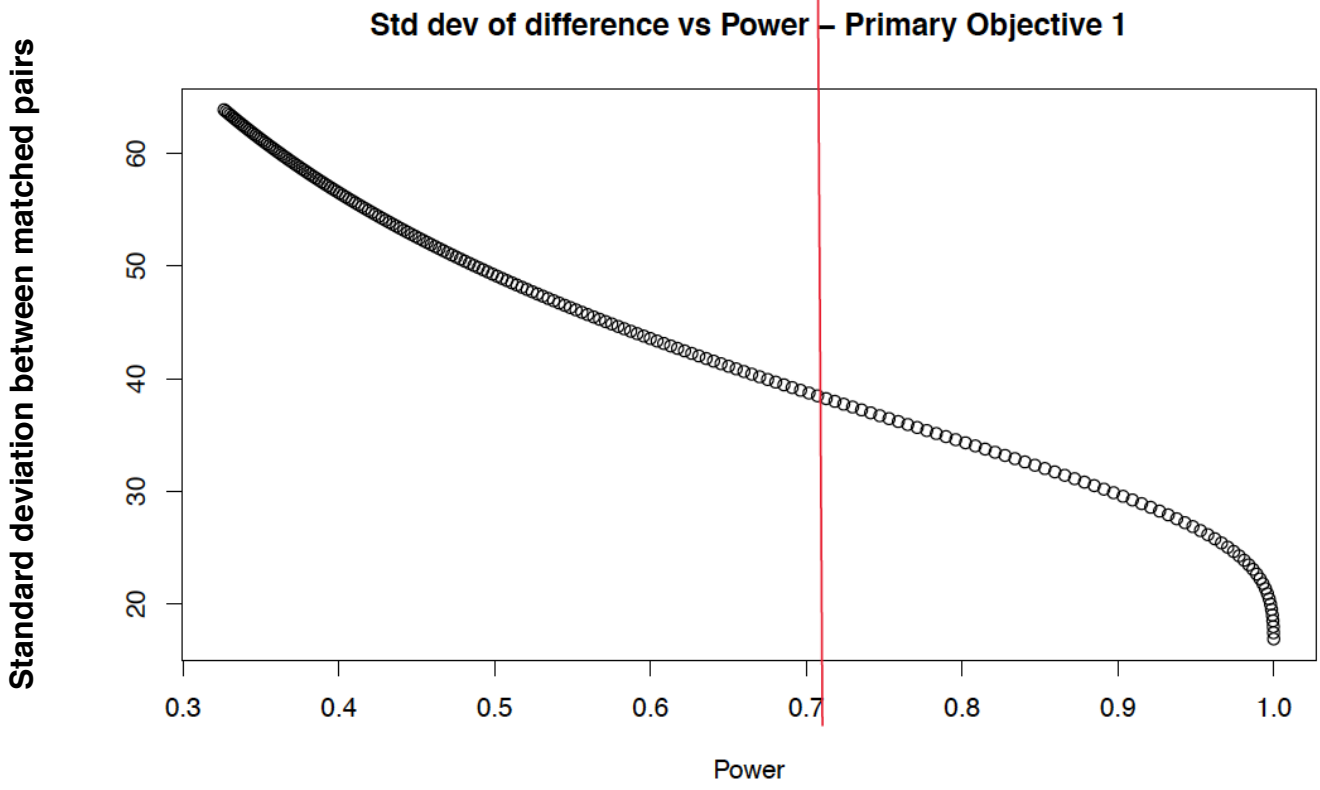
Participant's Name	Signature and Date
Investigator/Delegate's Name	Signature and Date
Witness' Name	Signature and Date

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.
A signed copy of this consent form has been given to you to keep for your records and reference.

APPENDIX J: POST-HOC POWER CALCULATION CORRELATION GRAPH

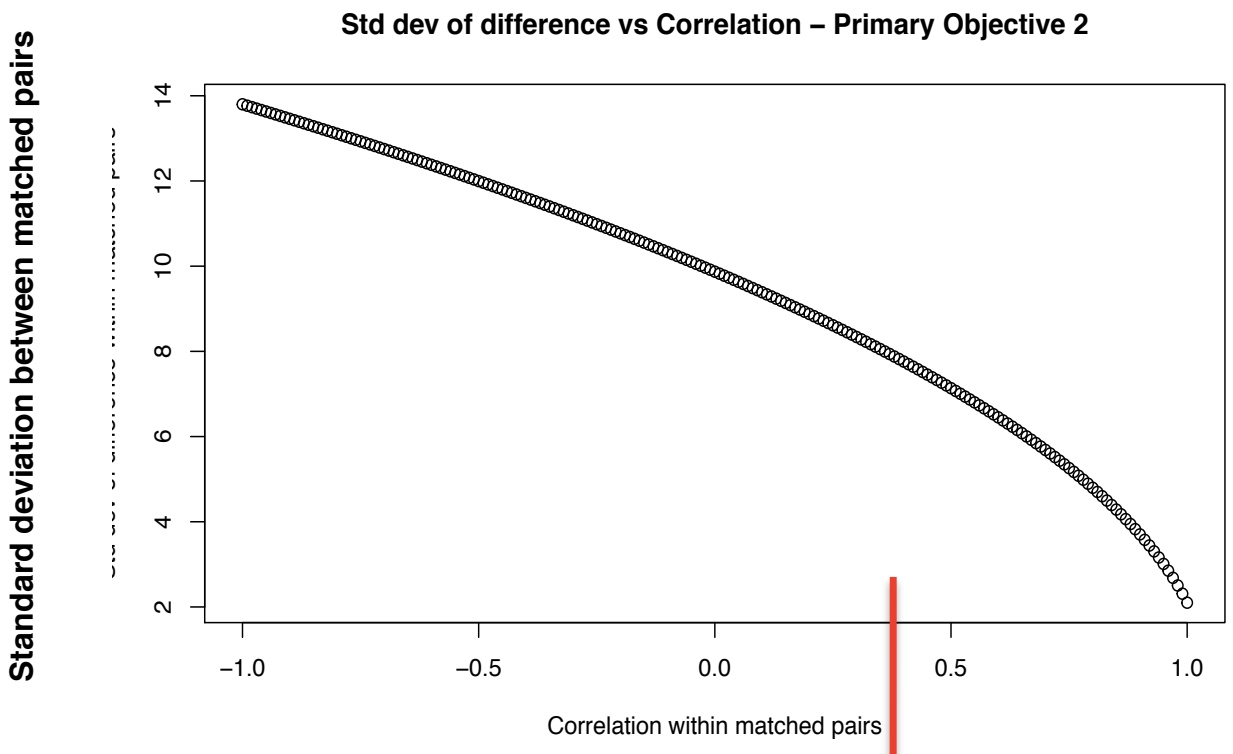
PRIMARY OUTCOME ONE, TIME SPENT PER DAY IN MVPA

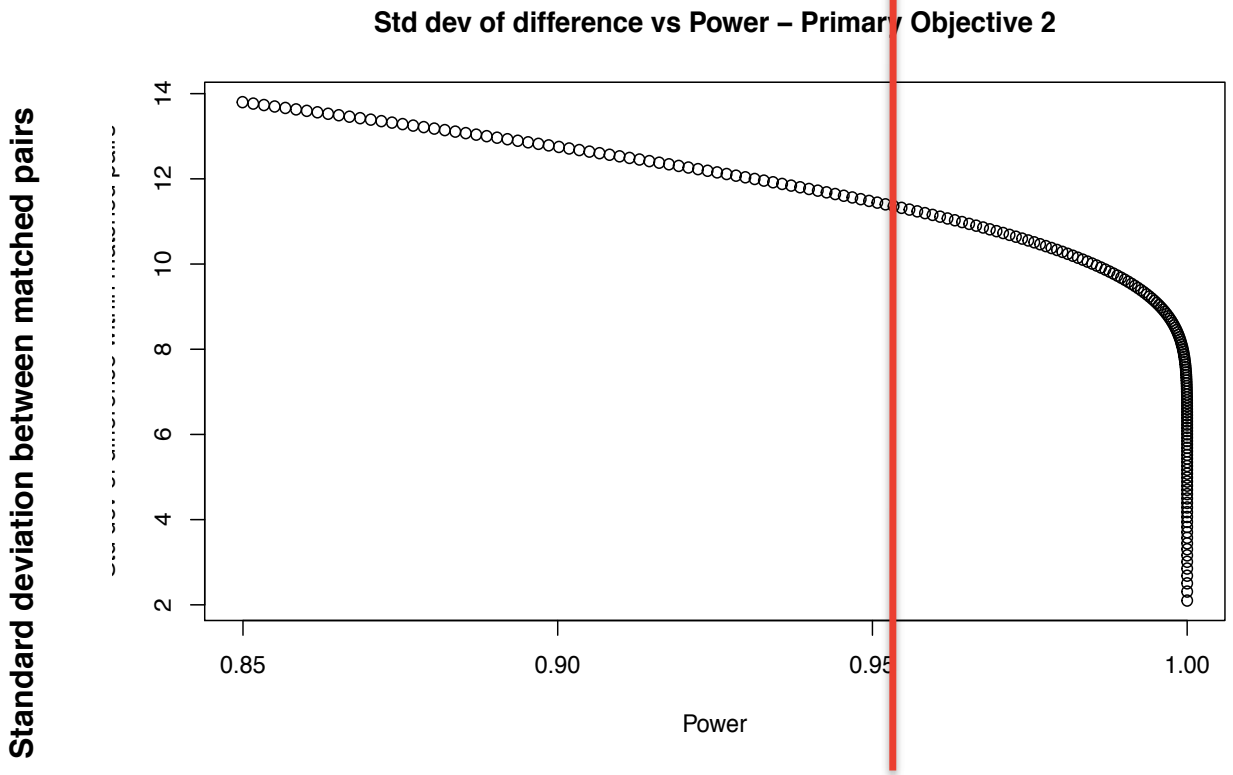

Std dev of difference vs Correlation – Primary Objective 1
Standard deviation between matched pairs
20
30
40
50
60
−1.0
−0.5
0.0
0.5
1.0
Correlation within matched pairs


Std dev of difference vs Power – Primary Objective 1
Standard deviation between matched pairs
20
30
40
50
60
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Power

APPENDIX K: POST-HOC POWER CALCULATION CORRELATION GRAPH

PRIMARY OUTCOME TWO, RELATIVE VO2PEAK


Std dev of difference vs Correlation – Primary Objective 2
Standard deviation between matched pairs
2
4
6
8
10
12
14
–1.0
–0.5
0.0
0.5
1.0
Correlation within matched pairs


Std dev of difference vs Power – Primary Objective 2
Standard deviation between matched pairs
2
4
6
8
10
12
14
0.85
0.90
0.95
1.00
Power