Safety and Feasibility of a Six Week Resistance Training Program in Children with Juvenile Idiopathic Arthritis

A Thesis Submitted to the
College of Graduate Studies and Research
in Partial Fulfillment of the Requirements
for the Degree of Masters of Science in the
Department of Kinesiology
University of Saskatchewan
Saskatoon

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ABSTRACT

BACKGROUND Chronic pain is a common condition in children with juvenile idiopathic arthritis (JIA), affecting their ability to participate in physical activity, a necessary and integral part of a child's growth and maturation. Resistance training specifically displays a paucity of research in children with JIA, and could potentially be a beneficial form of exercise training for this population. The purpose of this study was to determine the safety, feasibility, and effects of a six week resistance training program on pain in children with JIA. **METHODS** Seven JIA patients (8-18 years) participated in a home-based, three days per week exercise training program. Pain was measured using an electronic pain diary (PinGo©) for Android tablets. Participants answered questions initially a week prior to training, once a day on non-exercise days and three times a day (before exercise, after exercise, and end of day) on exercise days for a total of seven weeks. Secondary outcome measures included muscle size, muscle strength, and functional ability, measured at baseline and following the 6 week exercise program. Statistical analyses included attaining the average number of exercise sessions completed, pain changes over the seven weeks (averaged over the initial week and then biweekly) via repeated measures ANOVA, dependent t tests between before and after exercise pain intensity and affect, and dependent t tests between secondary outcomes. **RESULTS** Seven participants completed an average of 13.0 ± 3.6 exercise sessions out of a possible 18. The repeated measures ANOVA revealed no significant differences between pain scores over the seven weeks within each individual ($p>0.05$). When all participants were pooled dependent t tests before and after exercise showed no differences in pain intensity or pain affect ($p>0.05$). Secondary measures revealed a significant difference between vastus lateralis thickness before compared to after training ($p<0.05$). **CONCLUSIONS** The results of this study suggest that a 6 week home-based resistance training program was tolerable in children with JIA and did not cause a clinically

significant increase in pain or any other adverse events. The uniqueness of this exercise program was that it was home-based, allowing children to undertake this emerging form of healthcare within their home environment. As well, the training program was able to significantly improve aspects of fitness in this population. Further research of resistance training in children with JIA is necessary to attain definitive results of its effects and optimal levels of resistance exercise in this population.

ACKNOWLEDGMENTS

I would once again like to thank everyone for the help I have received throughout this project as without all of them none of this would have been possible.

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CHAPTER 1 SCIENTIFIC FRAMEWORK

1.1 Introduction

Juvenile idiopathic arthritis (JIA) is amongst the most common chronic conditions of childhood and the most common class of rheumatic disease affecting children (Weiss and Ilowite. 2007). JIA can have physical and psychosocial implications for the afflicted child's life both now and into their long term futures as adults. Effects of arthritis include pain, reduced aerobic and anaerobic capacity, lower quality of life, decreased functionality, depressive traits, low self-esteem and less participation in social activities (Schanberg and Sandstrom. 1999; Leegaard et al. 2013; Bomba et al. 2013). In Canada, JIA affects approximately one in 1000 children (Petty et al. 2004). There is no cure for JIA, but multi-faceted therapies that include more advanced pharmacologic treatments have substantially improved disease outcomes and attenuated the negative disease sequelae (Hayward and Wallace. 2009).

The current paradigm of caring for JIA patients includes not only anti-inflammatory and immunomodulatory drug therapies but also attentiveness to life style factors that can reduce pain and inflammation and improve function and quality of life. The efficacy of each component of a comprehensive, multi-faceted treatment program for children with arthritis should be supported by evidence generated by scientific research.

Children with JIA are less physically active relative to their healthy peers, and consequently their current and long term musculoskeletal health and function and quality of life can be compromised (Giannini and Protas. 1993; van Brussel et al. 2011).

The benefits of resistance training in children have been well documented and have led to recommendations from The Canadian Society for Exercise Physiologists and The Center for

Disease Control and Prevention of three days a week of resistance exercise for children aged 5 to 17 years. Recommended strengthening exercises within these guidelines included gymnastics and push-ups that target multiple muscles of the body. Resistance training in healthy children can significantly increase muscle cross-sectional area (CSA) and strength with no detrimental health impacts (Payne et al. 1997). Establishing optimal skeletal muscle mass in childhood is of great importance for optimal growth and development. Muscular fitness has a significant impact on improving overall fitness, bone health, body image and obesity (Lee et al. 2012; Rauch et al. 2004; McCabe and Ricciardelli. 2003).

The effects of physical activity and physical fitness have been examined in JIA patients in the past with no resultant adverse effects demonstrated (Takken et al. 2008; Sandstedt et al. 2013). However most studies have concentrated on aerobic exercise and thus less is known about the effects and safety of resistance training in this population. As well, comprehensive measures of pain have not been considered in previous exercise training research in children with JIA. This could give a more detailed understanding of the potential effects of resistance training, be it positive or negative. Therefore, although research has examined the effectiveness of increasing physical activity *via* aerobic exercise programs in children with JIA (Takken et al. 2008; Klepper. 2003), to our knowledge none has examined the safety, feasibility and effectiveness of a home-based resistance training program in children with JIA.

This study collected pilot data on a resistance training program in children with JIA. Specifically, the study examined the safety and feasibility of a home-based six week resistance training program, and collected pilot data on the influence of that program on pain, inflammation, muscle strength, muscle thickness, and function.

1.2 Review of Literature

1.2.1 JIA

One of the most prevalent chronic musculoskeletal childhood diseases in Canada is juvenile arthritis, affecting approximately one in 1000 children (Petty et al. 2004). The cause of JIA is unknown. Children with JIA have inflamed joints that can have adverse effects on growth and function, either promoting abnormal growth in the inflamed joint(s) or attenuating overall growth due to systemic inflammation. JIA is not a single disease but comprises seven diverse subtypes that are distinguished by different clinical and laboratory features (Petty et al. 2004).

1.2.1.1 Diagnosis

JIA is defined as arthritis in one joint or more for six weeks or longer beginning in a child younger than age 16 years of age. JIA is not a single disease but encompasses seven distinctive subtypes; according to the International League of Associations of Rheumatology (ILAR) they are: systemic, oligoarticular, polyarticular rheumatoid factor positive, polyarticular rheumatoid factor negative, enthesitis related, psoriatic, and undifferentiated (Petty et al. 2004) (Appendix 1). Genetic and environmental influences are speculated to contribute to the disease etiology, and could differ among individual subtypes of the disease.

1.2.1.2 Epidemiology

Reported incidence and prevalence of JIA vary greatly, due to differences in diagnostic criteria used and methodological procedures employed by researchers to identify the disease. Population based research in North America and Europe has shown annual incidence rates (the number of new cases every year) ranging from seven to 21 per 100,000 children (Borchers et al.

2006). Prevalence (the number of total cases at a point in time) studies in developed areas including North America, Europe and Australia have reported prevalence ranging from 16 to 400 per 100,000 (Borchers et al. 2006; Ravelli and Martini. 2007). A meta-analysis of epidemiological JIA studies placed the prevalence rate at 132/100,000 with 95% confidence intervals at 119 and 145 (Oen and Cheang. 1996). Issues with diagnosis of JIA and developing criteria for defining what is JIA compared to similar other pediatric rheumatological disorders still exist, so exact prevalence rates continue to be difficult to determine.

Oligoarticular JIA is the most common subtype in European and North American populations accounting for approximately 50% of all cases, again dependent upon diagnostic criteria used (Borchers et al. 2006). In Asian, African and Native North American populations polyarticular rheumatoid factor negative JIA accounts for the majority of JIA cases (Borchers et al. 2006). When disease subtypes are aggregated, JIA affects more females than males. This holds true for oligoarticular and polyarticular arthritis but males predominate in enthesitis related JIA. There is no sex predilection in systemic onset JIA. The age of onset also differs with disease subtype, with the youngest average age of onset being in oligoarticular JIA and the oldest average age being in enthesitis related and psoriatic JIA (Borchers et al. 2006). Generally the peak onset age range is between 1 and 2 years followed by a smaller peak between 9 to 15 years (Berntson et al. 2003).

1.2.1.3 Etiology

Although the etiology of JIA is unknown, evidence suggests a possible interaction between environment and genetic factors. Research using genetic testing and sibling recurrence risk analysis in family studies has suggested that genetic predisposition may play a role in

disease pathogenesis (Prahalad 2004; Thompson et al. 2004). Specific human leukocyte antigen alleles and cytokine reduction regulating genes are associated with certain subtypes of JIA (Murray et al. 1998; Thomson et al. 2002). As well, polymorphisms of the regulatory region of the interleukin 6 (IL6) gene, the 5´ flanking region of the macrophage inhibitory gene, and tyrosene phosphatase N22 have all been associated with JIA (Hinks et al. 2005; Donn 2004; Rosen et al. 2003).

Research examining the environmental influence on JIA has implicated viruses including rubella and parvovirus B19 as being the triggers of chronic arthritis onset (Lang and Shore, 1990). Rubella acts by targeting lymphocytes which can lead to persistent infection within the synovium and subsequent inflammation. There is also evidence of bacterial heat shock proteins acting as disease triggers (Weiss and Ilowite. 2007).

1.2.1.4 Pathogenesis

Although disease etiology of JIA is not well understood, the underlying pathogenic mechanisms are becoming clearer. Initially lymphocytes, macrophages, plasma cells and dendritic cells infiltrate the synovium of a single joint or numerous joints. Clusters of differentiation (CD), including CD4 and CD8 (glycoproteins found on the surface of the infiltrating immune cells), tend to remain in the synovium (Murray et al. 1996). These cells can aggregate leading to inflammation of the synovium. As well, fibroblasts and macrophages tend to proliferate within the synovium leading to inflammation (Grom and Hirsch. 2000).

Research into cytokine patterns in JIA has also shown common sequelae amongst individuals with JIA. For clinical purposes cytokines are divided into two types, one and two. Type one includes interferon gamma γ (IFNγ) and transforming growth factor beta (TGFβ),

whereas type two encompasses the interleukins (IL). The type of cytokine profile can have a profound influence on disease pathogenesis. In JIA, a type one cytokine profile within the synovium predominates, such that the ratio of IFNγ to IL6 within the inflamed synovium of JIA patients is greater than in non-autoimmune arthropathic joints (controls) (Scola et al. 2002). That being said, circulating levels of cytokines differ considerably among JIA patients, even among those with the same disease subtype (Borchers et al. 2006). Nevertheless, patients with systemic JIA show higher concentrations of IL1 and IL6, and these concentrations positively correlate with disease activity (Yilmaz et al. 2001). However, similar correlations have not been shown in other disease subtypes. Finally, tumor necrosis factor alpha (TNF-α) is elevated in patients with JIA, and the extent to which inflammation occurs is positively correlated with TNF-α levels (Grom et al. 1996).

Disease progression can significantly differ amongst children with JIA. Many patients experience a remission period (inactive disease) with no flare ups and minor pain, whereas others can experience protracted inflammation and pain (active disease). Clinical remission has been seen in 40 to 60% of JIA patients, leaving about half of children with prolonged active disease (Oen. 2002; Ravelli. 2003). Predictors for long term JIA without remission include greater severity or temporal extension at onset of disease, symmetrical disease, rheumatoid factor positivity, hip or wrist involvement in early stages, JIA subtype and early radiographic abnormalities (Ravelli and Martini. 2003). Although numerous predictors have been identified to allow pediatric rheumatologists to make conjectures as to disease progression, prognosis continues to remain relatively unpredictable.

Three generally accepted and frequently used terms to label disease patterns of JIA are monophasic, polycyclic and persistent. The first of these describes a subtype of JIA that lasts for

a maximum of 24 months, subsequent remission, and does not return. The second term refers to any subtype of JIA that has multiple cycles of disease activity and inactivity. Persistent describes JIA that lasts for a period of longer than 24 months (Singh-Grewal et al. 2006). After following children with oligoarticular, polyarticular, systemic, and spondyloarthropathies (comparable to enthesitis related JIA) for ten years, Fantini et al (2003) found 28% had monophasic, 10% had polycyclic, and 62% had polycyclic.

1.2.1.5 Treatment

Although there is currently no known cure for JIA, remission is the ultimate goal. Non-steroidal anti-inflammatory drugs (NSAIDS) are the first line of therapy in most children with JIA, although often more aggressive pharmacotherapeutic measures that are anti-inflammatory and immunomodulatory are required to limit disease progression and induce remission. Intra-articular corticosteroid therapy is commonly used to treat oligoarthritis. Low dose methotrexate is a common second line therapy for JIA and appears to be effective and well tolerated in 60 to 70% of JIA patients (Murray and Lovell. 2002). Leflunomide, a lymphocyte proliferation inhibitor, has a similar efficacy and safety profile as methotrexate (Silverman et al. 2005).

Biological agents targeting inflammatory cytokines, including TNF-α, interleukin (IL)-1 and IL-6 have also been evaluated in JIA. Both randomized control trials (RCTs) and observational studies have demonstrated etanercept (Enbrel®), a TNF-α inhibitor, to be effective in patients who did not tolerate or respond well to methotrexate (Lovell et al. 2000; Horneff et al. 2004). Other biological agents effective in treating JIA, particularly polyarticular and enthesitis related subtypes, are infliximab and adalimumab, both TNF- α inhibitors (Borchers et al. 2006;

Horneff. 2013). In patients with systemic JIA, biologically-based therapies targeting IL-1 (kineret) and IL-6 (tociluzimab) are more effective than anti-TNF agents (Horneff. 2013).

In exceptional circumstances autologous stem cell transplantation has been used to treat refractory JIA. Approximately half of the JIA stem cell transplant recipients achieved complete remission, although potential side effects including infectious morbidity or mortality occur in about 15% of cases (De Kleer et al. 2004).

Optimal treatment regimens for children with JIA are multi-faceted and include, in addition to pharmacotherapy, physical therapy, occupational therapy, and psychological intervention. Physical and occupational therapists may prescribe strengthening and range of motion exercise programs, splints, perform manual therapy including joint mobilizations, massage, use modalities including transcutaneous electrical nerve stimulation or intramuscular stimulation and/or use acupuncture (Rhodes. 1991). Therapists also provide education about energy conservation, pacing, activity or environmental modifications, self-management of pain and coping skills development. A meta-analyses examining psychological interventions (beyond solely educating) in children with JIA found improvements in pain, function, psychological status, coping and self-efficacy (Astin et al. 2002). All of this plays a crucial role in the child's overall health and these health professionals are an integral part of the treatment team.

1.2.1.6 Summary

JIA is a common rheumatological disease affecting many children in Canada and worldwide. Although modern science does not understand the exact triggers of the disease, it is thought to have both environmental and genetic influences. Modern medicine is also not

currently capable of curing the disease, although numerous avenues have been explored to attenuate negative sequelae that occur with JIA.

1.2.2 Pain

According to the International Association for the Study of Pain, "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage". Chronic pain is a dynamic variable and of major concern in children with JIA because it may significantly affect an individual's health related quality of life (Hunfeld et al. 2001). The brain is a modifiable and adaptable structure that is constantly making changes to better adjust to the world around it; a concept referred to as neuroplasticity (Kidd et al. 1996). Children who experience pain show long term changes in pain perception and related behaviours, as the brain's nervous system makes adaptations to this pain. When inflammation occurs in a joint, many patients experience hyperalgesia (an increased pain perception to a noxious stimulus) and allodynia (pain on a normally innocuous stimulus) (Kidd and Urban. 2001). In children with JIA, pain is a clinically significant symptom and effectively reducing pain in children with JIA is an essential responsibility of the child's treatment providers (Schanberg et al. 1997).

When referring to pain three distinct themes exist, of which require elaboration; nociceptive pain (pain resulting from activation of nociceptors due to real or perceived damage to tissues), neuropathic pain (pain resulting from damage to or changes within the peripheral or central nervous system) and pain perception (the emotional and behavioural response to physiological information).

1.2.2.1 Nociception and Nociceptive Pain

A nociceptor is a pain receptor within the periphery that is usually polymodal, meaning it responds to differing types of stimuli including mechanical, thermal or chemical. Nociception within the periphery involves four distinct events that allow a message to be communicated from the periphery to the central nervous system. The first of these is transduction, where a stimulus generates depolarization (via sodium channels) of the first order peripheral neuron. The next step is that the depolarization needs to be sufficient enough to create an action potential, referred to as transformation. Subsequently, this action potential must be proliferated from the peripheral terminal to the central terminal. Finally, the action potential must cause the release of neurotransmitters at the synaptic terminal to allow the same process to occur in the second order neuron (Fishman et al. 2010). This occurs for detection of any stimulus, be it noxious or innocuous. Nociceptors aimed at protecting the organism from noxious stimuli have a higher threshold than low intensity stimuli receptors (Kidd and Urban. 2001). Chronic inflammation or tissue damage, like that in juvenile arthritis, leads to the depolarization of nociceptive neurons and can result in nociceptive pain. Ongoing nociception and nociceptive pain from chronic inflammation can also cause changes within the peripheral and central nervous system and may result in neuropathic pain either alone or in conjunction with nociceptive pain (Latremoliere and Woolf. 2009).

1.2.2.2 Neuropathic Pain

Neuropathic pain occurs due to damage to or changes within the peripheral or central nerves. As repeated pain signals are sent from the primary afferent neurons to the dorsal horn of the spinal cord, changes can occur along this pathway that can alter pain sensation (Woolf and

Mannion. 1999). In patients with chronic pain where nociceptors are firing frequently, neurons within and surrounding the area can develop a greater number of sodium channels which reduces the thresholds of peripheral nerves (peripheral sensitization). This can lead to ectopic nerve firing, allodynia and hyperalgesia (Schaible et al. 2002; Hogeweg et al. 1995). Inflammatory mediators and cytokines, present in chronic inflammation, can lower thresholds of nociceptors (Woolf and Mannion. 1999)

Glutamate is the principal neurotransmitter released in primary afferent neurons to allow depolarization at the dorsal horn. Increases in the amount of glutamate released can initiate phosphorylation of glutamate receptors and increase the excitability of the dorsal horn. This is one component of central sensitization and leads to lowered pain thresholds (Woolf and Mannion. 1999).

Central sensitization can also occur simultaneously via other avenues. Inhibition of pain signals occurs in healthy individuals through select inhibitory transmitters. With nerve injury, these transmitters and their receptors can be down-regulated allowing less inhibition to occur and an increased nociceptive response (Woolf and Salter. 2000). Sprouting of sympathetic axons into the dorsal root ganglion may also result in pain sensation with sympathetic activity (Woolf and Mannion. 1999). Therefore there are ample ways that the nervous system can modify itself in the presence of chronic pain that result in amplified nociceptive activity.

1.2.2.3 Inflammatory Pain

Inflammatory pain displays sensitization and pain in similar pathways as previously described. However, way as mentioned above, but yet there are also inimitable alterations that can occur. In JIA, inflammatory markers including ions (potassium and hydrogen), bradykinin,

prostaglandins, histamine, 5-hydroxytryptamine, ATP, nitric oxide, cytokines, leukotrienes and growth factors all infiltrate the synovium causing swelling to occur. These inflammatory mediators can act on nociceptors directly to initiate pain, cause the release of additional algogenic (pain inducing) substances, or modify the response properties of primary afferent neurons causing sensitization within the periphery (Kidd and Urban. 2001).

Again, due to changes within the periphery and sustained activation of primary afferent nerve fibres, central sensitization can occur after chronic inflammation. Glutamate receptors within the central terminal of the primary afferents can again be phosphorylated due to increased glutamate released within the area. As well, inflammation causes increases in neuropeptides and neurotrophic factors within central terminals. These lead to an increase of calcium ions within higher order areas and phosphorylation of receptors (Kidd and Urban. 2001). Although full understanding of inflammation and pain remains to be discovered, the differences that occur with inflammatory pain could affect the results of research in these populations, especially due to the long lasting vicissitudes demonstrated within the peripheral and central nervous system.

1.2.2.4 Pain Perception

Pain perception, a process by which pain is recognized and interpreted, is a subjective experience that can vary greatly among and within individuals temporally. Although it continues to be a poorly understood phenomenon, the strength and unpleasantness of the pain is not solely determined by the amount of tissue damage as endogenous attenuation or facilitation can occur for varying reasons (McGrath. 1994). Specifically in children, pain perception becomes very complex as it entails physiological, psychological, behavioural, environmental, cultural and developmental factors (Morton. 1997; McGrath. 1994).

From an early age children are able to communicate pain through descriptive words like 'hurt'. Pain is evaluated by a child's previous experiences of pain sensations, using past experiences as a framework. At about 5 years of age children are able to better describe their pain and by 7 years children develop an understanding of the quality of this pain (McGrath and Gillsepie. 2001). As children develop they are better able to assess, describe and develop strategies to cope with their pain, also using more abstract concepts to describe their pain (McGrath. 1994). Previous research has also pointed to children who experience mild injuries reporting less pain as they age (McGrath. 1990). Also interesting to note is that gender could play a role in pain perception and reporting, especially in Western societies where males are expected to suppress pain symptoms and females may be encouraged to discuss them (McGrath. 1990).

Part of the reason for children perceiving different levels of pain with chronic inflammation is due to pain coping strategies used. Children living with JIA develop strategies to minimize or deal with their pain, including adaptive cognitive strategies, rest and distraction (Schanberg et al. 1997). In a group of 100 JIA patients who were studied for coping strategies and rational thinking, those who employed better coping strategies and rational thinking reported lower pain intensity (Schanberg et al. 1997). Conversely, catastrophizing about pain (a negative set of emotional and cognitive processes to cogitate pain) has also been associated with increased disability and function in activities of daily living (Edwards et al. 2006). The Behavioural Model of Pediatric Pain developed by Varni et al (1996) also suggests there is a significant relationship between pain perception and functional status, and that pain coping strategies play a key role within this model.

Individual emotional factors can also play a strong role in pain perception. Recent research has demonstrated the influence of depressed moods on increasing pain perception (Berna et al. 2010). McGrath (1994) states that anxiousness, fear, frustration, anger and sadness can also have a strong influence on pain. Therefore, there are a multitude of factors that can affect pain perception and subsequent pain reporting.

1.2.2.5 Current Theories of Pain

Pain continues to be a poorly understood and very complex phenomenon, although numerous experts in the area have developed theories to cogitate the numerous aspects of pain and the way in which processes interact. Developed by Ronald Melzack and Patrick Wall in 1965, the Gate Control Theory of pain sought to explain how pain perception can differ drastically between and within people for a given noxious stimuli. The theory postulated that there ascending signals from the periphery and descending excitatory and inhibitory signals from the central nervous system needed to be integrated in order for pain to be perceived. Therefore, several physiological influences could affect pain perception, along with psychosocial and environmental influences (Melzack. 1999).

More recently, a more comprehensive theory of describing pain was developed by Melzack, labeled the neuromatrix theory, building off the gate control theory. This contemporary theory proposes pain as a multidimensional experience where the body establishes a 'neuromatrix' of itself from genetic and sensory influences. As sensory inputs arrive from the periphery to the central nervous system, they are processed and contrasted to this established neuromatrix. If the input differs from the body's established neuromatrix, pain is perceived. This theory is also unique it that it considers pain to be an output rather than a reflex or reaction.

Therefore, an individual has numerous influences, including biological, social, psychological and environmental, that can affect the self-neuromatrix and consequently effect if pain is perceived and outputted (Melzack. 1999).

1.2.2.6 Exercise Induced Hypoalgesia

Resistance training, in addition to increasing muscular fitness, decreases pain response in certain populations (Cote and Hoeger-Bement. 2010; Koltyn and Umeda. 2006). Via a mechanism labeled exercise induced hypoalgesia (EIH), acute bouts of resistance training in healthy adults are effective in increasing pain tolerance locally and distant to the exercised muscle. In a meta-analysis Naugel et al (2012) examined numerous studies on EIH in both healthy adult populations and chronic pain populations. These researchers divided the meta-analysis into three separate training modalities: aerobic exercise, isometric exercise, and dynamic resistance exercise. The latter two types of exercise are both forms of strength training, where isometric involves a static contraction with no change in joint angle and dynamic resistance involves strength training that produces movement within a joint or numerous joints. The meta-analysis of isometric training in healthy adults revealed large positive effect sizes for pain threshold and pain intensity (1.27 and 0.83, respectively). The length of these exercises ranged from 90 seconds to 12 minutes and intensity ranged from 15% maximal voluntary contraction up to 100% maximal voluntary contraction. Three of the isometric exercise studies in this meta-analysis measured pain threshold 15 minutes post exercise and found a medium to large effect size for improving pain threshold. The results of the healthy adult meta-analyses in reference to dynamic resistance exercise were mean effect sizes of 0.99 (SD 0.18) and 0.83 (SD 0.37) for pain threshold and pain intensity, respectively. The dynamic resistance exercise studies were all 45 minutes in length working at 75% of one repetition maximum and included resistance

exercises for the whole body (Naugel et al. 2012). One study examining the lasting effects of EIH after dynamic resistance exercise demonstrated improvements in pain threshold 30 minutes post exercise, but levels returned to baseline after one hour (Pertovaara et al. 1984). Other researchers have demonstrated small to medium effect sizes up to fifteen minutes post dynamic resistance exercise, but did not extend the analysis further temporally (Koltyn and Arbogast. 1998; Focht and Koltyn. 2003).

From Naugel et al's same meta-analysis, chronic pain populations were also analyzed. The chronic pain conditions researched using strength training (all isometric training) were shoulder myalgia and fibromyalgia syndrome patients. For individuals with shoulder myalgia, isometric training demonstrated a reduction in pain perception, although for those with fibromyalgia syndrome pain perception was increased overall. However, when only including low to moderate intensity isometric exercise in fibromyalgia patients, pain threshold was improved. This demonstrates that pain response to exercise can differ significantly between type of disease, training modality, and intensity of training. This research also showed that the duration of exercise can have a significant impact on EIH (Naugel et al. 2012).

Although reasons for EIH are still unclear, there are a number of proposed explanations. The first of these and most widely accepted suggests that the activation of the endogenous opioid system elicited with exercise causes a decrease in pain perception (Naugel et al. 2012). Nonopioid systems have also been speculated to be involved including the endocannabinoid system and the release of neurotransmitters including serotonin and norepinephrine (Naugel et al. 2012). Also it has been speculated that due to overlapping areas of pain regulation and blood pressure within the central nervous system, an increase in blood pressure during exercise can lead to blocking of nociception and decreased pain perception (Cote and Hoeger-Bement. 2010;

Koltyn and Umeda. 2006). Type and duration of exercise could determine the pain signaling pathway that is activated (Naugel et al. 2012).

Children continue to be an understudied population and as such there are currently, to our knowledge, no studies examining EIH in children. Along with that, there has been no research examining the effects of resistance training on comprehensively measured pain in children with JIA.

1.2.2.7 Chronic Pain Measurement in JIA

Chronic pain is a complex and multidimensional health problem requiring careful assessment. Solely measuring pain intensity (frequently done in the past) will not give a complete description of the pain an individual is experiencing. Many children who live with JIA experience pain as a regular part of their lives (Leegaard et al. 2013). It is also speculated that daily pain could be a major contributor to the decreased amount of physical activity observed in JIA patients (Schanberg et al. 2003; Schanberg et al. 2005). Pain perception is also correlated with anxiety, depression, psychological distress, sleep disturbances and decreased quality of life. (Margetic et al. 2005; Schanberg et al. 1996; Bloom et al. 2001; Schanberg et al. 1997; Sawyer et al. 2004).

Children are capable of self-reporting pain from a very early age with the proper age-adapted tool (Von Baeyer and Spagrud. 2006). By the age of 8 to 9 years, the majority of children are capable of self-reporting pain intensity on numeric rating scales or visual analog scales (Von Baeyer and Spargrud. 2006; Srouji et al. 2010). Previous research has demonstrated a number of effective tools for measuring self-reported pain in school-aged children. The first of these includes a visual analog scale (VAS), typically used to measure pain intensity. It entails a

horizontal line allowing patients to select a spot on the line best representing their pain. Most severe pain would be on the far right and no pain would be on the far left of the line (Srouji et al. 2010). The Adolescent Pediatric Pain Tool, a more comprehensive assessment of pain analyzing intensity, location and quality, has also been used extensively in chronic pediatric pain research (Crandall and Savedra. 2005). Although the Adolescent Pediatric Pain Tool is more thorough than simply measuring pain intensity, there are still components missing that are required in order to attain a complete picture of pain.

Three dimensions to pain perception are necessary in order to truly measure pain in its multidimensional nature; the sensory-discriminant aspect (pain intensity), the affective-motivational aspect (pain affect and/or unpleasantness), and the cognitive-evaluative aspect (pain interference with daily life) (von Baeyer and Spagrud. 2006). Although all three dimensions positively correlate, it is necessary to measure each as they have separate components to them and contribute differently to pain perception (Stinson et al. 2008). Along with this, children develop a vocabulary as they age and as such they are capable of using words to describe their pain. Pain assessment tools should incorporate this developmental uniqueness to allow individuals to describe their pain accordingly (Job et al. 2002).

Pain intensity is the most widely analyzed aspect of pain and therefore recent research has aimed to understand a clinically significant change in pain intensity via a VAS. Dhanani et al (2002) established that a decrease in pain intensity of 8.2 units and an increase of 19.0 units is clinically significant in children with rheumatologic conditions. To our knowledge, research examining clinically significant changes in pain affect and pain interference has yet to be performed.

There are also other associations with pain that are necessary in a comprehensive pain analysis, as these factors can affect pain perception. Mood has demonstrated a strong correlation with pain; negative mood is associated with higher pain scores (Schanberg et al. 2005). It has also been well documented that children with arthritis experience sleep difficulties. Recent longitudinal evidence points to sleep disturbances as being a predictor of the next day's pain as opposed to pain being a predictor of sleep disturbances (Lewandowski et al 2010). Bromberg et al (2012) were also able to show that positive mood can act as a moderator between sleep disturbance and increased pain, demonstrating that these pain associated variables most likely interplay and need to be taken into account when measuring pain.

Juvenile arthritis related variables are also important to analyze when measuring pain, as these variables can have an effect on reported pain. These variables include stiffness and fatigue, both associated with pain, which can also have an impact on participation in social and school activities. Increased stiffness, fatigue and pain are negatively associated with participation in social and school activities, which many times includes physical activity (Schanberg et al. 2005).

In recent years, real time data capture (RTDC) has been employed to measure pain in children. RTDC is a pain measurement tool whereby patients report their pain via pain diaries (Stinson. 2009). This method assesses current levels of pain as opposed to recalling pain within the last seven days for instance. Therefore recall bias can be negated and reports are able to be completed in the patient's naturalistic environment such as at home or at school. Compliance can also be improved through the use of RTDC devices because it allows a simple screen tap in order to report pain, therefore reducing response times (Stinson et al. 2006). As well, data can be time stamped to potentially discern temporal effects on pain. With this method researchers are able to formulate within-subject and between-subject comparisons and attain more accurate treatment

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response measures (Stinson, 2009). Chronic pain in children with JIA is an extremely variable measure and therefore it is necessary to analyze in real time in order to get a proper representation of each patients pain (Tupper et al. 2012).

1.2.2.8 Summary

Pain is a common and variable symptom seen in children with JIA. It can have a nociceptive, neuropathic and perceptive influence. Factors that affect pain can be receptors, ion channels, inflammatory mediators, past pain experiences, age and adaptive strategies. The measurement of chronic pain requires a multifaceted approach in order to tease out each patient's pain and other variables affecting that pain. As children over 8 years are capable of self-reporting pain intensity using a VAS, RTDC provides a comprehensive means of measuring pain in children.

1.2.3 Growth and Development in Children

Physical growth of a child naturally occurs from birth through to adulthood. Growth is an intricate process that varies among individuals. As well, a single individual undergoes variation in the amount of growth from year to year. General growth curves show large increases at two stages of this growth period. The first occurs from birth through to the first two years of life and the second peak occurs during the adolescent growth spurt phase of an individual's life. Characteristic of this second phase (puberty) is a change in hormones in both males and females allowing the body to increase in height and weight, leading to the terms 'peak height velocity' and 'peak weight velocity', respectively. During this time the body also experiences shifts in relative proportions of tissue mass, including that of lean tissue and fat.

Each child experiences these pubertal changes at a unique timing, sequence and tempo. The pubertal timing of individual's leads to children classically being grouped into early, average or late matures. However, although timing differs, there are similar characteristics of puberty that exist within and between the sexes. Females on average tend to experience peak height velocity at 12 years of age compared to 14 years of age in males (Tanner and Whitehouse. 1976). Peak weight velocity tends to occur about half a year after peak height velocity in both boys and girls (Iuliano-Burns et al. 2001). Reasons for this are the rise in whole body growth hormone and insulin like growth factor 1, as well as marked increases of sex steroid production from the gonads. The release of these hormones appears to be regulated by hypothalamic neurons of the central nervous system that allow the release of gonadotropin-releasing hormone (Malina et al. 2004). As well, research has linked a minimum amount of leptin (hormone released by adipose cells to decrease appetite) necessary for puberty to initiate, as the body needs enough fat to undergo this process (Malina et al. 2004). Growth can therefore have genetic, hormonal and environmental influences. This can play a significant role on a child's physiological response to exercise.

1.2.3.1 Muscle Mass and Strength Development in Childhood

Puberty significantly affects the overall structure of a child and also specific tissue development. The peak of lean tissue mass growth occurs just before peak weight velocity and just after peak height velocity in both males and females, whereas peak fat mass velocity occurs just after peak weight velocity (Iuliano-Burns et al. 2001). In mid childhood (6-8 years of age) muscle mass accounts for 42% and 40% of total body mass in males and females, respectively. When nearing completion of puberty muscle mass accounts for 54% and 42% of total body mass in males and females, respectively (Malina. 1986). Therefore, both pubertal timing and sex can

have a significant effect on an individual's muscle mass development. This trend can also be seen in muscle strength. During the growth period muscle cross sectional area has a moderate to strong correlation to strength (Davies et al. 1985). Peak strength velocity appears to be nearest to peak weight velocity in pubertal timing (Blimkie. 1989). Although strength differences slightly favour males over females in childhood, this difference becomes much more apparent during and post puberty (Malina and Roche. 1989). Just as is the case with muscle mass, pubertal timing and sex both play significant roles in the strength of a child.

With resistance training programs of sufficient threshold, damage occurs to muscle that needs to be repaired for hypertrophy to occur. In healthy individuals (children included), protein catabolism during training is repaired after each training session if adequate amounts of nutrition and rest are provided, meaning the individual is in an anabolic state. In prepubertal children, gains in strength are majority manly due to neurological adaptations such that neurons are able to fire more efficiently and synchronously (Falk and Eliakim. 2003). As androgen levels change during puberty, adolescents (especially in males) are able to hypertrophy results from normal growth and maturation. However, this also means adolescents due to growth, but are also able to better respond to resistance training and this has an additive effect on hypertrophy to a greater extent (Behm et al. 2008). Usually, increases in muscle size (hypertrophy) are associated with increases in muscle strength (Behm et al. 2008).

1.2.3.2 Development of the Pain System

The neural system of a child undergoes significant growth and development within the first 5 years of life and continues, albeit with slower progression, up until around 16 years of age. By 7 years of age, 95% of the adult size of the central nervous system is attained (Malina et al.

2004). At birth, functional maturation of nociceptive pathways needs to occur to allow proper responses to stimuli. Infants who receive a noxious prick on the foot tend to move their entire body rather than just their foot. During normal growth nociceptive firing thresholds of an infant and child are lower than that of an adult. As well, a fully mature neural system is less excitable than that of an immature system (Fitzgerald. 2005). Therefore biological age, specific to neurological development, can lead to differences in pain perception and nociception.

1.2.3.3 Summary

Growth is a process continually occurring from birth to adulthood (Faigenbaum. 2000). The timing, tempo and sequence of growth events can depend on genetic, hormonal and environmental factors. Physiological systems within the body tend to grow at different times and rates. These variables need to be considered when investigating exercise training programs in children as biological age can have an impact on responses to training.

1.2.4 Physical Activity in Children

The current physical activity guidelines for children aged 5 to 17 is 60 minutes of moderate to vigorous physical activity (MVPA) each day according to the Canadian Society for Exercise Physiologists (CSEP. 2013). This amount of MVPA is prescribed as it is associated with health benefits. Nader et al (2008) objectively analyzed (via accelerometers) the MVPA of 1023 children aged 9 to 15 with the United States National Institute of Health. The results from this study were that 9 year old children participated in approximately 180 minutes of MVPA on weekends and weekdays. As the children aged these levels decreased, such that 15 year olds participated in only 49 minutes of MVPA on weekdays and 35 minutes on weekends. This leaves teenagers with JIA at a much higher risk of being under the recommended 60 minutes of MVPA

per day because even healthy children of their cohort already appear to be under that threshold. Other than age, correlates of decreased physical activity in children include sex (female), ethnicity (non-caucasians), perceived activity competence (inverse), depression and previous physical activity (inverse) (Sallis et al. 1999). Consequences of reduced MVPA include compromised musculoskeletal health and higher risk for chronic diseases including obesity and cardiovascular disease.

1.2.5 Resistance Exercise in Children

Conventionally, it was thought that children should not perform resistance exercise as it could affect their growth plates and stunt their growth. However, not only has research demonstrated resistance training to be safe in this age group, it is also beneficial to numerous areas of muscular fitness and health, including muscular endurance and strength (Payne et al. 1997). Fitness programs for children should include strength training in order to promote health and also decrease risk of injury (Faigenbaum et al. 2009). There has also been evidence of resistance training benefits to include increased cardiorespiratory fitness and improved body composition, blood lipid profiles, motor performance and self-esteem (Faigenbaum. 2000; Faigenbaum and Kang. 2006; Watts et al. 2005; Malina. 2006; Fripp and Hogdson. 1987). Nevertheless, there has been minimal research on the effects of resistance training in children with JIA.

1.2.6 Decreased Physical Activity in JIA

JIA patients are less physically active during the growing years subsequently compromising their musculoskeletal health (Giannini and Protas. 1993; van Brussel et al. 2011). A key reason for this divergence in physical activity compared to their healthy peers could be the

amount of daily pain experienced, such that daily pain is shown to be predictive of attenuated physical activity levels (Bromberg et al. 2012). Due to joint inflammation, neuropathic changes can often occur within the central and peripheral nervous system (Woolf. 2011). These physiological alterations can last even into times of remission. Therefore, because children with JIA potentially live with pain most days of their lives, it is of great importance to treat this pain and potentially improve an individual's quality of life (Katz. 2002).

In the past, JIA patients have been instructed to not partake in physical activity under the belief that it will make the disease symptoms worse and most notably increase their pain (Gualano et al. 2010). JIA patients are also more likely to have a sedentary lifestyle due to a number of predisposing factors including fatigue, joint stiffness, chronic pain, and synovitis (Gualano et al. 2010). The effects of this decreased physical activity can be seen objectively in the attenuated anaerobic and aerobic capacities. Anaerobic capacity (measured using a Wingate test on a cycle ergometer) and aerobic capacity (measured using maximal oxygen uptake on a cycle ergometer) are both significantly reduced in JIA patients compared to healthy children, with the difference more pronounced in certain subtypes of JIA than others (van Brussel et al. 2007). Reduced isometric strength of the quadriceps has also been reported in JIA patients compared to healthy controls (Giannini and Protas. 1993). This reduced strength is not only due to the decreased physical activity of JIA patients, but also a result of local inflammation and the glucocorticosteriods used to treat arthritic sequelae (Gualano et al. 2010). It is now well accepted that exercise is beneficial to children, including those with JIA. However, although the potential to improve numerous health and fitness variables is present, it has yet to be examined the safety, feasibility and effectiveness of a home-based resistance training program in children with JIA.

1.2.7 Exercise Training Interventions in JIA

1.2.7.1 Exercise and Pain

In rheumatic adult populations exercise training can improve pain symptoms (van den Ende et al. 2000; O'Reillya. 1999; Roddy et al. 2005). Research using exercise programs for pediatric populations that present with pain, although limited in number, have shown promising results. Specifically, in those with juvenile arthritis, less has been examined on an exercise program's effects on pain. A Cochrane review was performed by Takken et al (2008) examining the use of RCTs to determine the effects of exercise training programs on numerous variables. All of the studies incorporated used aerobic training rather than resistance training with none of the three reviewed studies finding significant changes. Following this, a study published in 2012 by Tarakci et al had participants perform strengthening, range of motion, stretching, and postural exercises for 12 weeks, and compared them to a standard care control group. Pain intensity was measured using the Childhood Health Assessment Questionnaire (CHAQ), with no significant differences existing between the control and exercise groups, but both having significant decreases in pain between pre and post measures.

Two solely based resistance training studies in children with JIA have been presented as abstracts and discussed by Klepper (2003) in a review article. The first of these noted a reduction in pain after an eight week resistance training program in six children with JIA compared to controls (Fisher et al. 2001). Pain for the aforementioned study was self-reported before and after the program as a decrease, neutral, or increase. The second study by Velazquez et al (1999) also noted significant hypoalgesia (pain reduction) after resistance training. Neither of these studies measured pain comprehensively and results from these studies have not been published other

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than in abstract form, leaving the methodological understanding of each study uncertain. However, although mechanical movement from resistance training could activate nociceptors and lead to pain perception, it could be such that repetitive resistance training leads to changes within inflammatory markers and a subsequent attenuation of pain.

1.2.7.2 Exercise and Inflammation

Although acute bouts of exercise cause microtrauma and subsequent low-grade inflammation, chronic exercise shows opposite adaptations and is anti-inflammatory in nature through a multitude of different mechanisms. Chronic inflammation is defined as a two to four-fold elevation in circulating levels of pro-inflammatory and anti-inflammatory cytokines and acute phase proteins (Bruunsgaard H. 2005). The stress that occurs during exhaustive and moderate exercise activates the hypothalamic-pituitary-adrenal axis, which results in glucocorticoid (immune suppressor) suppression. After resistance exercise, cortisol (a glucocorticoid and anti-inflammatory) rises in healthy people (Tremblay et al. 2004). Because JIA is autoimmune in nature, resistance exercise could help to initiate similar responses within the body that would ultimately reduce inflammation.

Another theory suggests that exercise triggers the efferent vagus nerve, which inhibits pro-inflammatory cytokine release (Tracey. 2005). Adding to this, a higher amount of adipose tissue is seen to contribute to higher levels of TNF-α, a cytokine associated with inflammation. Not only can repeated bouts of exercise decrease the amount of adipose tissue and, in turn, suppress TNF-α, muscle fibres can also be stimulated to produce interleukins which act as anti-inflammatory cytokines within the body (Petersen and Pedersen. 2005). Moreover, working skeletal muscle is a major source of whole body production of IL- 6, a cytokine signaling

protein, which is the main reason why it is elevated after acute bouts of exercise (Woods et al. 2009). IL-6 can have both anti-inflammatory and pro-inflammatory effects depending on where the cytokine is produced and the subsequent effect it has on other substrates. Obese children, children with JIA and adults with rheumatoid arthritis show elevated baseline levels of IL-6 (Bastard et al. 1999; Rosen et al. 2003; Schoels et al. 2013). Children with JIA are also at a greater risk of osteoporosis, largely due to an imbalanced homeostasis of cytokines like IL-6 affecting bone formation and resorption (Dhamrait et al. 2003). By exercising and potentially increasing circulating levels of IL-6 derived from skeletal muscle, children with JIA could possibly increase the anti-inflammatory properties of this cytokine and decrease inflammation, although this has yet to be studied.

Children with JIA have a decreased aerobic fitness, measured on average at a 21.8% lower absolute VO_{2peak} (Houghton. 2008). With that said, a few studies have shown an inverse correlation between VO_{2peak} levels and C-reactive protein, a marker of inflammation (Katja et al. 2005; Pitsavos et al 2005; Kondo et al. 2005). Adamopoulos et al (2001) found that, in patients with heart disease, monocyte chemoattractant protein (a marker of inflammation) decreased the same amount in both a group taking pravastatin (a drug to decrease monocyte chemoattractant protein) and exercising compared to a group taking a placebo and exercising. This demonstrates that in certain circumstances exercise may be as effective as certain pharmaceuticals aimed at reducing inflammation.

Previous research examining the effects of exercise on inflammation in JIA has found conflicting results. Takken's (2008) review paper on RCTs using aerobic exercise in children with JIA reports no difference in number of joints with swelling between control and exercise groups. Conversely, pilot studies examining the effects of group resistance exercise in JIA have

reported modulated levels of pro-inflammatory mediators after JIA patients performed resistance training programs (Fisher. 2001; Valasquez. 1999). Again, both of these studies were only presented as abstracts and the specific pro-inflammatory mediators analyzed were not reported. It appears that the nature of exercise being performed could influence its effects on inflammation, and resistance training has demonstrated small, but promising results. No study to date has examined the effects of resistance training in children with JIA on inflammation via a non-invasive method.

1.2.7.3 Exercise and Muscle Parameters

Exercise, especially resistance training, has a profound influence on muscle development. Specific to increasing strength and muscle mass, healthy children over 6 years of age are recommended two to three days of strength training a week at 70 to 85% one repetition maximum for two to five sets per exercise to see benefits. It is also recommended that these exercises are targeted at larger muscle groups (Strong et al. 2005).

Specifically, children with JIA have been studied using both aerobic and anaerobic exercise training programs. A four month aquatic aerobic exercise training program showed no significant differences in the intervention versus control group, but this training was only done once a week (Takken et al. 2003). It has been suggested that a minimum of two exercise sessions a week is needed to show significant improvements (Minor. 2003). As well, the absence of significant differences also suggests that physical activity is not detrimental to JIA patient. Singh-Grewal et al (2007) used a three month, three times per week, aerobic land-based training program with progressing intensity and compared it to a standard Qigong (similar to tai chi) training program that did not significantly raise heart rate. The results showed that both groups

improved their physical function, but there was no difference in VO_{2peak} between the two groups. This may seem peculiar due to the higher intensity of the aerobic training group, but the adherence was much less in the aerobic training group which would rationalize this result. An increase in anaerobic leg power was also shown in a three month pilot study training program, but energy cost of locomotion and aerobic capacity did not significantly improve (Singh-Grewal et al. 2006). The final study performed was an uncontrolled study by Klepper (1999) where an eight week, three times per week exercise training program showed significant improvements in nine minute walk-run time and articular severity index (a measure of joint swelling, pain on motion and tenderness).

Aquatic training, thought to be better for JIA patients because of less weight bearing and joint impact, has been a novel form of exercise training for JIA patients. Epps et al (2005) wanted to compare a land based physiotherapy program to a combined hydrotherapy/land based physiotherapy program and found that both groups had similar increases in strength and aerobic capacity, but the retention of these benefits after the programs ended lasted longer in the combined hydrotherapy/land-based physiotherapy group.

Resistance exercise training programs for JIA patients have shown conflicting results as well. The two abstracts previously mentioned that used resistance training to target muscle strength only examined muscles of the lower extremities (Klepper. 2003). Oberg et al (1994) trained their participants twice a week for three months using gymnastics and pool training. They compared the participants to age and sex matched controls. No differences were found between the groups in quadriceps strength after the three months. Conversely, quadriceps and hamstring strength and endurance improved in a group of JIA patients who performed eight weeks of resistance training three times per week (Fisher. 2001). The dichotomy between the two studies

demonstrates a need for more definitive research and measurement outcomes to determine if resistance training improves muscular fitness in children with JIA. Klepper (2003) has suggested six weeks is the minimum duration necessary for children with JIA to participate in exercise training in order to see improvements.

1.2.7.4 Exercise and Functional Ability

A growing body of evidence is now suggesting that those with rheumatoid arthritis should be exercising to improve their symptoms. In a study of 50 adults with rheumatoid arthritis in at least one hand, it was found that exercise specific to the hand and physical therapy was able to improve hand pain, joint tenderness, activities of daily living scores and range of motion (Buljina et al. 2001). More recent research looked at the use of dynamic exercise (combined aerobic and resistance training) to improve the health and quality of life of people with arthritis. Baillet et al (2009) used a four week dynamic exercise training program to try to improve the arthritic symptoms of 25 older adults with arthritis. The program significantly improved health assessment questionnaire scores and aerobic fitness, but these results were only seen just after the training program finished and did not last six or 12 months after. This would suggest that physical activity is necessary on a regular basis in order to improve arthritic symptoms in this population.

In studies measuring functional ability in children with JIA after exercise training programs, again conflicting results are found. Fisher (2001) reported significant improvements in functional status, timed task performance, and disability in the training group relative to the control group. However, Takken et al (2001) saw no significant changes in functional ability (measured via CHAQ) or health related quality of life (measured via juvenile arthritis quality of

life questionnaire) after a 15 week aquatic training program. Bacon et al (1991) measured functional tasks in children with JIA after completing an aquatic exercise training regimen, finding no significant differences in function after the training program. A Cochrane review also revealed no significant changes in functional ability between exercise and control groups (Takken et al. 2008), and each of those individual studies also reported no significant differences between training and control/standard care groups (Epps et al. 2005; Singh-Grewal et al. 2007; Takken et al. 2003). Therefore although research has shown improvements in function with exercise training, the effectiveness of resistance training on function in JIA continues to not be well understood. As well, no studies have examined the effects of resistance training on functional ability as measured via the CHAQ, a tool explained in more detail later on.

1.2.7.5 Summary

Children with JIA are less physically active relative to their healthy counterparts. Resistance exercise is capable of improving muscular fitness in children and could beneficial in patients with JIA; however, research utilizing resistance exercise in children with JIA is very limited. Previous research in healthy adult populations has shown evidence for EIH, although clinical populations with chronic pain show varying results. However, this intermittent phenomenon has yet to be examined in JIA. There has yet to be research using a home-based resistance training program in children with JIA while measuring pain, inflammation, muscle thickness, muscle strength and functional ability.

1.3 Purpose and Hypotheses

1.3.1 Purpose

There is currently a gap in the literature with regards to the effectiveness of resistance training in children with JIA. The purpose of this pilot study, defined as a 'small study for helping to design a further confirmatory study' (Arnold et al. 2009), was multifold. The first aim was to determine if home-based resistance training in JIA is a feasible and safe form of exercise training for this population. Feasibility studies encompass studies that aim to estimate parameters including standard deviations, approximate participant numbers and willingness of participants, and adherence rates (Arain et al. 2010). To understand if the program was safe for this population, an absence of adverse events and no significant increases in pain would be interpreted as safe.

Another aim was to understand the temporally sensitive effects of resistance training on pain in children with JIA in order to inform further definitive research. As well, the research aimed to collect pilot data on the effects of resistance training on daily pain, inflammation, muscle strength, muscle thickness and functional ability. The final aim was to objectively determine the baseline physical activity levels of the participants in this study.

1.3.2 Hypotheses

Hypothesis 1: A six week resistance training program would be both feasible and safe in children with JIA (safety is operationalized as exercise that does not significantly increase pain from pre to post exercise and/or cause adverse events. A clinically significant increase in pain intensity was considered as 19.0 units and a clinically significant decrease was considered as 8.2 units, which are discussed in greater detail in the results and discussion).

Hypothesis 2: Inflammation would decrease after the six week resistance training program.

Hypothesis 3: Muscle strength and muscle thickness would increase after the six week resistance training program.

Hypothesis 4: Functional ability would improve after the six week resistance training program

Hypothesis 5: Pain before exercise would be significantly correlated to ratings of perceived exertion (RPE) of exercise.

CHAPTER 2 METHODS

2.1 Participants

Seven children (four females, three males) between the ages of 8 and 18 with JIA who attended the Pediatric Rheumatology Clinic at Royal University Hospital (RUH) were enrolled in this study. Twenty patients were approached about the study, five of whom expressed no interest, five cancelled their appointments and decided to not participate, one was deemed ineligible because of a lack of pain within the last six months and two patients lived too far away to participate. Exclusion criteria consisted of any contraindications to exercise including recommendation by a specialist to not exercise, low hemoglobin levels, heart conditions and/or an absence of any JIA related pain within the last six months. As well, if the participant was not at a minimum grade one English level they were not able to participate. Participants with active or inactive disease of any of the seven subtypes of JIA were eligible to enroll. Participant descriptives are described in detail in section 3.1.

2.2 Training Program

The intervention was a combined body weight and resistance band training program lasting a total of six weeks. The uniqueness of this exercise program was that it was home-based, allowing children to undertake this emerging form of healthcare within their natural environment. Children with JIA (or their parents) have reported distance of travel to a supervised exercise program, scheduling conflicts and a lack of time all as reasons for not adhering to an exercise program (Takken. 2008; Long and Rouster-Stevens. 2010). By allowing children to perform the exercises at home, at a time suitable to their schedule, it was felt this that could improve adherence would be improved.

The participants were instructed to exercise three times per week for approximately 40 minutes each session in a circuit style of training. The program consisted of a five minute warm up, 25 minutes of resistance training, and an eight minute cool down. The initial warm up was done with body weight only and consisted of a series of arm circles, side steps, marching on the spot while raising hands, elbows to knees, jumping over a line, jumping jacks and reaching to the sky and then touching the toes. Subsequently, the primary part of the program was completed, with each exercise having a 15 to 20 second rest in between. Each exercise session was completed with a cool down, consisting of stretches for the hamstrings, quadriceps, gluteals, hip flexors, abdominals, latissimus dorsi and pectoralis major. The program was developed by Cameron Van Oort (certified personal trainer and kinesiologist) and Dr. Susan Tupper (physiotherapist) to target the entire body; as musculoskeletal fitness has been shown to be compromised throughout the body in children with JIA (Burnham et al. 2008; Giannini and Protas. 1993; Roth et al. 2004). As well, it was felt that exercises with only body weight and a resistance band would be easy to administer as children may not be at the right size for adult machines and these training tools may not be economically feasible for a large scale study. Finally, a position paper by Behm et al (2008) recommended matching the exercises to the abilities of the children when starting on a resistance training program. Therefore we chose exercises were chosen that children as young as 8 would be able to perform and that also required minimal feedback.

Over the six weeks the program was designed to progress biweekly via increases in number of repetitions and difficulty of exercises. This was employed to prevent boredom, increase adherence and improve muscle adaptation. As well, children were instructed to be able to increase resistance for exercises by moving their foot placement further away from the middle

of the resistance band for certain exercises or by using a higher step in the case of the step-up.

All programs were displayed through video in a disc provided to participants so that each session could be followed verbally and visually at home, either on their television or computer.

Video 1-The first two weeks of the resistance training program consisted of three sets of eight repetitions of the following exercises.

1)   The first exercise being performed was squats with the band under the sole of each foot and the handles in the hands while resting on the shoulders. Ideally for this exercise the participant went into 90 degrees of flexion at the knee, but if it was not possible then they were allowed to go to a depth that was possible for them. The tempo was 2/0/2 seconds (eccentric/isometric/concentric). If they were not capable of this either then the exercise could be done without the resistance band.

2)   Body weight stationary lunges. The knee opposite to the lunging leg was to come within six inches of the floor on the downward portion and the exercise was to be performed at the same tempo as the squat (eight repetitions for each leg). Again, if the participant was not capable of this they were able to go down to a point that they were capable of.

3)   Step ups on a stair or chair. The height of the chair or stair was up to the participant, but meant to be at a degree of difficulty they felt possible while staying in a pain free range for the individual's joints. The tempo was 2/1/1.

4)   Thirty second plank. The participant's forearms and toes were in contact with the ground and their body was held rigid in a straight line. If this was not comfortable, the individual was instructed to place a pillow(s) under their forearms or drop to their knees to allow less pressure on the forearms.

5)   Seated rows. The individual was sitting with the resistance band fastened around a stable object and they were pulling the handles of the band toward their chest at a tempo of 2/0/1. The degree of difficulty depended on how far they chose to sit away from the stable object.

6)   Bicep curl with combined shoulder press. The hands were in supination and the individual bent at the elbow starting from full extension in order to curl the resistance band and then press the handles of the resistance band up performing a shoulder press. If the hand positioning was painful they were able to rotate their hands. As well, if putting the arms above the shoulders was painful then the participant could perform front deltoid raises instead in a separate motion.

7)   Push-ups on the floor. The children performed push-ups either from the knees or toes. As well, participants could be on their hands or knuckles (to keep wrists from bending if there was wrist pain). If all of this was not a possibility, the child could perform push-ups against the wall while standing and position themselves a distance from the wall that was challenging, but didn't cause pain.

Pictures of each of these exercises are shown in Appendix 2.

If the grip on the band was painful for any of these exercises the participant was able to wrap towels around the handles so that their hand could be in a more open position.

Variations in these exercises were performed as weeks progressed so that each individual was challenged. The squats were altered by where the band was positioned under the feet in order to increase the tension. The lunges progressed from stationary, to returning to a feet together stance, and finally to a walking lunge. The step ups increased the height of the step and eventually had participants come up on their toes in the final two weeks. The core exercise was

standard throughout the six weeks, but if the participant was only able to do it on their knees initially they were asked to progress to their toes eventually. As well, participants were asked to hold the plank for a maximum of 30 seconds, and if they were not able to at first then the exercise was intended to progress to a full 30 seconds by the end of the six weeks. For the upper body exercises, the seated row progressed further away from the stable object. The position of the feet on the resistance band for the bicep curl/shoulder press could have been wider as to cause the resistance band to increase tension in the resistance band and increase the difficulty of the exercise. Finally, the push-ups progressed from the knees to feet, and the hands could have been placed closer together if greater difficulty was necessary. For the upper and lower body exercises (six in total) the number of repetitions increased by two every second week to increase the volume (therefore weeks three and four were ten repetitions and weeks five and six were 12 repetitions for each set). The modifications were also shown in the take home instructional exercise video incase participants needed extra guidance.

Participants were all shown the exercises before they began the six week exercise program. The demonstrations were done in person by Cameron Van Oort, the same individual who is demonstrating the exercises in the videos. Each participant was also asked to demonstrate the exercise to see if they were able to perform it properly. Resistance band selection was also done at that point in time to tailor the resistance to each individual's ability. There were two different options of resistance bands, both purchased from TheraGear® (TheraGear Canada Ltd. Mission, BC). The green resistance band provided eight to 12 pounds resistance and the pink provided 13 to 19 pounds resistance. As the participant performed the exercises, they were asked which band made each exercise difficult, but not too difficult to not be able to complete the exercise for a total of eight repetitions. Participants were also watched during exercises to note

their level of difficulty. Although, in this study, no participant felt any of the seven exercises to be excessively difficult such that they could not complete them at the time of demonstration, if that was the case then the exercise(s) potentially would have been changed to accommodate that. However, modifications to exercise were allowed and we therefore felt that the exercises were appropriate to a wide range of children with varying forms of JIA.

2.3 Pain Measurement

Pain was measured at the end of the day for the week preceding the exercise program and once daily (end-of-day) on non-exercise days and three times a day (before exercise, after exercise, end-of-day) on exercise days throughout the six week time course of the exercise regimen. Due to the necessity of comprehensively measuring pain, this study used a tablet application (PinGo©; Tupper 2012) developed by Dr. Susan Tupper, Cameron Van Oort, Rahnuma Kazi and Dr. Ralph Deters in the Department of Computer Science, University of Saskatchewan. The PinGo© application was developed based off previous work by Dr. Tupper (Tupper. 2012). Each child was loaned a tablet with the PinGo© app installed for the seven week period. Once a day pain reports were seen as time-driven (end of day) whereas before and after exercise reports were event-based (Stinson et al. 2008).

The application had different questions depending on the series selected (before exercise, after exercise or end-of-day). Initially the child selected the time of day that they were answering the questions (i.e. before exercise, after exercise, end-of-day questions). The app then had a map of the child's body where they could select each body region that had pain at that point in time and other locations of pain that they had experienced throughout the day (other pain locations could only be selected in the end-of-day questionnaire). They then reported their pain intensity

using a VAS, with a range from zero being no pain to 100 being the most pain possible. Subsequently a question was answered on pain affect by having the participant select a face on the Facial Affective Scale that they felt most representative of how their pain was presently affecting them (McGrath et al. 1996). This scale had nine different faces with the first face being the least unpleasant face and the ninth being the most unpleasant face. After this, pain interference was reported to measure how the pain interfered with the participant's daily life (using sliding VAS scales). The measurement of pain interference was modified based off of the Brief Pain Inventory measure originally developed by Cleeland et al (1989). Following that, a question asking the participant to choose from a list of 26 words describing their pain experience was answered (pain descriptives). The descriptive words were adapted to children with JIA from the previous developed and validated Adolescent Pediatric Pain Tool (Savedra et al. 1993). They were able to choose as many words that they felt fit at that time. The next three questions used separate VAS scales to measure self-reported stiffness, fatigue, emotional valence (mood) and emotional activation (alertness/degree to which participant felt awake).

After these initial questions, the subsequent questions would vary depending on the time of day the questions were being answered. For the end-of-day questions, the next question asked the pharmacological treatments the child had used for pain (if any) since the last diary entry and how well those treatments worked (pain relief measured via a VAS). After this, non-pharmacological treatments were reported and its respective pain relief (via VAS). Finally an open texting field for the participant to tell what they felt necessary marked the completion of the end-of-day questions.

For the before exercise questionnaire, the next question following emotional activation was an open texting field for the participant to say whatever they felt necessary. This marked the completion of the before exercise questionnaire.

The after exercise questionnaire was more lengthy and went into detail about specific exercises. The first question following the emotional activation was their ratings of perceived exertion (RPE) for the exercise program based on the Omni RPE scale developed and validated by Robertson et al (2005). This tool was a pictorial gradient ranging from zero to ten (zero being the easiest exercise and ten being the hardest). Following that the participants answered multiple questions similar for each of the seven exercises. First, they answered if they were able to complete the exercise as described in the video through a dichotomous 'yes' or 'no' answer. Then participants were asked how many repetitions were completed for each set and if they had to modify the exercise in any way. Subsequently, did they have increased pain during the exercise ('yes' or 'no') and if so, what was the pain intensity via VAS. Once these questions were answered for each of the seven exercises, another open texting field was provided to mark the completion of the after exercise questionnaire.

All VASs were a standard ten centimeters long. Not only did this app allow a very detailed outcome measure, adherence to the exercise program was also tracked as each questionnaire was time stamped, including the before and after exercise questionnaires. Once each questionnaire was complete, data was stored in a separate file on the tablet, not allowing participants to see their previous answers and influence their subsequent inputs. Errors with missing questions were avoided by developing the app so the advance/next button did not appear until each question was completed.

PinGo© was based off a RTDC tool developed by Stinson et al (2006) (e-Ouch©) that measured pain intensity, affect and interference, as well as stiffness and fatigue in children with JIA. The use of electronic diaries to report pain has been suggested to be valid, feasible and highly acceptable in the JIA population (Stinson et al. 2008). Stinson et al (2008) compared a RTDC tool (similar to PinGo©) to recall measures of pain scores (which is most commonly used), and found that there were moderate to high positive correlations between the two, demonstrating construct validity of the tool. This aforementioned study was performed in children and adolescents with arthritis and also showed divergent validity, such that the tool was not measuring erroneous aspects of pain (Stinson et al. 2008). Stinson et al (2006) also demonstrated in a study with JIA patients that their version of an electronic pain diary was easy to learn, easy to use and the participants were satisfied. For a detailed outline of instructions given to participants on how to use the PinGo© application refer to Appendix 3.

2.4 Inflammation

Inflammation was assessed non-invasively pre and post the six weeks exercise training program using ultrasound (General Electric Canada of Mississauga, Canada); a safe and non-invasive method for detecting synovial membrane inflammation (Collado et al. 2012). The effectiveness of this method is two-fold in that it measures inflammation with no ionizing radiation and is comparable to MRI for measuring synovitis (Szkudlarek et al. 2001).

This ultrasound assessment was performed by Dr. A. Rosenberg, pediatric rheumatologist, at the Royal University Hospital. Participants were examined at joints with current or previous inflammation for fluid, synovitis, synovial thickening and inflammation. Fluid was determined via B-mode ultrasound and described the absence or presence of fluid,

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usually indicative of active inflammation. Synovitis was determined via Colour Doppler ultrasound and indicates inflammation of the synovial membrane by the detection of blood flow within the membrane. Synovial thickening, measured via B-mode ultrasound, is determined in the absence of fluid or synovitis and can indicate changes from previous inflammation but does not typically indicate active inflammation. Inflammation was a global conclusion based off of the previous three variables. Each participant's inflammation, fluid, synovial thickening and synovitis were scored and reported semi-quantitatively on a zero to four scale (averaged across joints if multiple joints were measured), where zero is not present at all and four is maximally present.

2.5 Anthropometry

Anthropometric measurements of height and weight were performed twice for each time point and the average of those two was used. Height was measured to the nearest 0.1 cm on a wall mounted stadiometer (Holtain Ltd. of Crymych, Dyfed, UK.) and weight was measured to 0.1 kg on a weight scale (Toledo Scale Company of Canada, Windsor, ON). Age was measured in years and decimal places (calculated by the number of days after the most recent year and divided by 365.25).

2.6 Muscle Thickness

To assess muscle hypertrophy, muscle thickness (cross sectional area) of the vastus lateralis (VL) and the biceps brachii (BB) were measured using B-mode ultrasound placed over the muscle belly of each muscle (General Electric Canada of Mississauga, Canada). The muscle belly of the VL was located by measuring from the top of the greater trochanter to the lateral epicondyle of the femur and taking the 70% mark between those two points, starting at the

proximal end. This was done with the participant seated on a table with a relaxed and fully

extended leg. To locate the muscle belly of the BB a measurement was taken from the anterior

aspect of the acromion process of the scapula to the proximal aspect of the cubital fossa with the

arm in a 90 degree flexed position. Again starting from the proximal end, 70% of that distance

was considered the muscle belly of the BB. For this measurement the participant was standing

with their arm relaxed and supinated, so that the muscle belly of the BB was visible. For both the

VL and BB, a transparent piece of paper with a cut out the size of the ultrasound head was then

placed over the marked area, with the halfway point of the cutout at the muscle belly (70% area

previously located). The cutout area was traced and the ultrasound was taken over that area. For

each of the measurements the dominant arm and leg (determined by asking the participant which

arm and leg are used to normally throw and/or kick a ball) were used. Measurements were

completed four times for each muscle, taking the average of the two closest measurements. The

ultrasound was performed with consistent minimal pressure being applied to each muscle to

avoid compression of the muscle. Transparent papers were kept after each participant did

baseline testing until they came back to do post testing, with anatomical landmarks as well as

birthmarks on that anatomical site being marked down on the transparent paper to reference for

the post testing and allow the same spot to be located for measurement (Chilibeck et al. 2004).

All measurements were performed by Cameron Van Oort.

Ultrasound is an imaging technique that uses sounds higher than that audible by the

human ear to send frequencies into a certain area of the body to have sounds reflected back,

providing a relatively detailed image. The B-mode ultrasonography technique that was used for

this study produces a two-dimensional image derived using a 12 megahertz linear-array probe

(General Electric Canada of Mississauga, Canada). Muscle thickness was defined as the distance

from the muscle-subcutaneous fat interface to the bone-muscle interface. This method is reliable and valid, with correlation coefficients of 0.998 for reliability and 0.999 for validity when compared to the gold standard of MRI (Reeves et al. 2003). The minimum generalizability coefficient when using the ultrasound for numerous muscle groups is 0.92 (Ishida. 1992).

2.7 Muscle Strength

Leg extension strength of the dominant leg and elbow flexion of the dominant arm were tested using the Humac NORM Dynamometer (CSMi, Stoughton MA, USA) and Humac 2009 computer program. This was performed before and after the six week exercise training program. Participants were placed in a seated position with shoulder and abdominal straps securing them to the chair and the anatomical axis of rotation was lined up with dynamometer's axis of rotation. Before each of the measurements each participant performed three warm up repetitions. This was done to ensure participants became accustomed to the machine, the researcher's verbal instructions and also served as a warm up. They then completed four maximal voluntary contractions (MVC) with one minute between each contraction to allow full recovery. The highest torque recorded from of the MVCs was used for analysis. Location of the seat in relation to the dynamometer was written down during pre-testing in order to test the participant in the same position for post-testing. Therefore rotation scale, back angle, fore/aft position, dynamometer height, dynamometer rotation and location of the monorail were recorded to allow post-testing to commence in a similar position.

The Humac NORM dynamometer applies a constant velocity while adjusting the resistance to the strength of the individual. Both the knee extension and elbow flexion MVCs were performed at a concentric speed of 60 degrees per second (1.05 radians/sec). All

measurements were reported in Newton metres, a measure of perpendicular force on a moment

arm in keeping with that of the dynamometer. A high one week test-retest reliability (0.82 - 0.97)

has been shown in previous literature (Pincivero et al. 1997).

2.8 Functional Assessment

The Childhood Health Assessment Questionnaire (CHAQ) was used to assess self-

reported functional ability before and after the six weeks of training (Singh et al. 1994). The

questionnaire is divided into three portions; a disability index, discomfort index, and health

status. Klepper et al (2003) deemed children 8 years and older capable of self-administering the

CHAQ without any specific training.

Each question on the disability index was reported on a scale of zero to three. Answering

zero means the child does the task without any difficulty, whereas answering three means the

child is unable to perform that task. Therefore, a higher score means the child has a greater

disability and less functional capacity. If the task is beyond that child because they are not at that

developmental age, then the question is marked 'not applicable'. If the child requires an aid in

order to perform the task, whether it is a device or another person, the minimum score for that

activity is a two, representing 'with much difficulty'. This initial part of the CHAQ (disability

index) is divided into eight subcategories including dressing and grooming, arising, eating,

walking, hygiene, reach, grip and activities. There are numerous questions for each of these

subcategories. A score is given for each of the eight subcategories, which is determined by

taking the highest scoring item in each category. For example, if in the eating category a child

had a score of zero for 'lift up a cup to mouth' and for 'open a new cereal box' but had a two for

'cut his/her own meat', then the score for that category would be a two. Once this is done for each

subcategory, the scores are averaged and the child will have a final score between zero and three. The score obtained from these categories is the disability index.

Each participant's discomfort index and health status were measured using a ten centimeter VAS where the child answers how much pain they have had in the past week due to their arthritis and how they feel they are doing knowing all the different things in their daily lives that they have to do and how their arthritis can affect that. The distance from the left end of each scale to the point the child marked was then measured in centimeters to the nearest 0.1cm. That value was multiplied by 0.3 and a score was given from zero to three. In the end, a score was obtained for disability index and health status (discomfort index was omitted as pain was measured throughout the study more comprehensively) (Singh et al. 1994).

This test has been shown to be reliable and valid in children with JIA and has been tested against healthy children who score zero in both the disability and discomfort index (Singh et al. 1994). It also correlates significantly (p<0.0001) with established disease activity measures (Klepper. 2003). Singh et al (1994) reported CHAQ scoring as being more sensitive to change than morning stiffness or active joint count, while Feldman et al (1995) report the responsiveness of the CHAQ to change as being moderate to good.

2.9 Baseline Physical Activity

Baseline physical activity was objectively measured in participants using accelerometers over a seven day period in conjunction with end-of-day pain measurement for the week preceding initiation of the exercise program. To gain a valid representation of physical activity for children a four to nine day period of measurement is needed, with at least one weekend day (Trost et al. 2005). Participants wore the ActiGraph GT3X+ (Actigraph© of Pensacola, FL,

United States) accelerometer around their waist during waking hours. Participants were instructed to take the device off while swimming, bathing, showering or participating in contact sports as it is not recommended that the device stay submerged in water for long periods of time or be worn during contact sports. The device was located at their right hip just anterior and medial to the anterior superior iliac spine. It was fastened in this location using an elastic belt. The placement as close to the centre of mass as possible will not take into account low intensity activities like painting or writing, but it is recommended for the best estimation of true energy expenditure as it measures whole body movements (McIver et al. 2005; Godfrey et al. 2008). All of this information was given to the participants orally and they were instructed to contact one of the researchers if they had questions about the device. The accelerometers were borrowed from the accelerometer pool at the University of Saskatchewan in the College of Kinesiology.

Along with the accelerometer, children were given an accelerometer log to write down times of day when they wore or did not wear the accelerometer, along with reasons as to why. This log consisted of a seven day schedule, with two weekend days. It asked the children to note when they woke up, when they put on the accelerometer, when they took off the accelerometer, when they went to bed and any other times they took off the accelerometer and why. A final question asked if this was a typical day for the participant or not, and if not then why. The log was meant to aid in reminding the child to wear the device each morning and also to understand if there were periods of physical activity that were missed due to removal of the device. Please see Appendix 4 for details of the accompanying sheet to the accelerometer.

The ActiGraph GT3X+ accelerometer is a tri-axial measuring tool which will measure movements in the vertical, anterior-posterior (horizontal), and medio-lateral direction. It has been shown to be a valid tool for measuring physical activity in children (Robusto and Trost. 2012).

This device uses a high-sensitivity proportional integrating measure mode, which can measure both direction and intensity of movement by measuring the peizoelectrical charge created from the compression of the crystals inside the device. These accelerations are converted into a signal referred to as 'counts', which can be compared between individuals and to reference standards to get an estimate of energy expenditure and minutes of sedentary, light, moderate and vigorous physical activity (Cliff et al. 2009).

This particular type of accelerometer is set to a sampling rate of 30 Hertz and measures motion within the normal human range and nothing outside of that. The user can pre-define the epoch (time interval) length in which they want the accelerometer to measure, which in the case of the Actigraph accelerometers, the options were 1, 2, 3, 5, 10, 15, 30, or 60 seconds. Due to the nature of physical activity in children being short bursts of about three seconds of exercise, the epoch length was set at three seconds (Rowlands. 2007). No higher than fifteen second epoch lengths is recommended for field based research in children (Trost et al. 2005).

The ActiLife version 6.4.5 software (Actigraph© of Pensacola, FL, United States) was used to initialize the devices, as well as download the collected data from the accelerometers. Uploading the data from the accelerometer was done as soon as possible when the device was retrieved. The same computer was also used as to prevent disturbances that can occur between computer time offsets (Yildirim et al. 2011).

Data reduction was performed to remove excessively long zero counts from the data that could be due to the participant removing the accelerometer because of sleeping purposes, shower, swimming, or contact sport activity (Robertson et al. 2011). However, not all zero counts should be omitted from the data as some may be due to sedentary behavior rather than

non-wearing time (Yildirim et al. 2011). It was decided time periods of greater than 20 minutes with consecutive zero counts were to be removed from the data due to the likelihood that the accelerometer was removed from the participant (Esliger et al. 2005; Yildirim et al. 2011). The ActiLife software allowed cut points to be set for sedentary, light, moderate and vigorous physical activity. Those cut points were set based off the Puyau et al (2002) calibration study of physical activity monitors in children.

Wear time was calculated by subtracting non-wearing time from a 24 hour period (Yildirim et al. 2011). For this study a minimum wearing time of seven hours was needed in order to consider that a valid day of data collection. Previous literature has shown that the reliability between seven and ten hours (standard amount of wear time) of wear time does not significantly differ (Corder et al. 2008; Penpraze et al. 2006).

Although it was intended to collect accelerometer data for seven days, a minimum of four days was considered necessary (with at least one weekend day) in order to qualify that participant's accelerometry data into the analysis. This is standard protocol when using accelerometers with children (Stone et al. 2009; Robertson et al. 2011). Therefore a minimum of four days with at least seven hours of data for each day was necessary to qualify that participants accelerometer data.

Because participants were given a log and the accelerometer to wear, when there were no counts in a time period and participants had logged the reason why they removed the device, the activities reported in that period were classified into sedentary, light, moderate or vigorous physical activity based off Telford et al (2004) physical activity study in children. If this non-

wear time was considered moderate to vigorous physical activity (MVPA), it was then added to the minutes of MVPA retrieved from the accelerometer.

The minutes attained from the accelerometer and those reported in the log were added together to get total minutes of MVPA. Total minutes of MVPA were then divided by the number of valid days of accelerometer wearing to attain mean minutes of MVPA per day. This measurement was used to compare the participants in this study to that of healthy children from a childhood physical activity study published by Nader et al (2008). MVPA was used as opposed to counts so that researchers, physicians and health practitioners not familiar with the use of accelerometers could better understand the activity levels of these participants.

2.10 Closing Questionnaire

At the end of the study each participant answered a standardized questionnaire on whether they liked the exercise program, if they would like to see changes within the exercise program, if they felt it improved their quality of life as a whole, if they liked using the tablet device, and if there were other questions they would have liked to see on the tablet application. These questions were read to each participant by a researcher and the researcher wrote down the answers accordingly. If the participant did not understand the question it was then worded in a way that made it easy for the participant to comprehend. As an example, for the quality of life question the child would be asked if they felt the exercise program made their life better and easier. See Appendix 5 for the questionnaire.

2.11 Statistical Analysis

Adherence to the program was analyzed in Microsoft Excel by using the number of after exercise questionnaires completed. If adverse events were reported by participants it was noted and reported in the results. Graphs of daily pain intensity, pain affect, and pain interference per participant were created on Microsoft Excel to depict the variability of those variables for each participant in the study.

All other data were entered into SPSS data entry and analyzed using SPSS software version 20© (IBM Corporation of Armonk, New York). End-of-day pain intensity, pain affect and pain interference scores were averaged over the initial baseline week, the first two weeks of training, the middle two weeks of training and the final two weeks. The main effect of time was then tested between the averages using repeated measures ANOVA for the whole group. Pain intensity change scores from before to after exercise (for each occasion in each subject) were computed by subtracting the pain intensity before the exercise from the pain intensity after the exercise. Occasions (a single time point pain measure of an individual) were then used to determine the number that decreased below 8.2 units and the number that increased above 19.0 units (clinically relevant decrease and increase in pain intensity in pediatric rheumatic populations) for any of the participants (Dhanani et al. 2002). As well, dependent t-tests were run for each individual between before and after exercise pain intensity and pain affect scores. Pearson's correlation was used to assess the relationship between pain intensity before the exercise and RPE of the exercise (aggregated and within individuals). Pearson's correlation was also run individually to assess the relationship between end-of-day pain intensity with stiffness, fatigue and mood. Descriptive statistics were assessed in SPSS and reported in the results section. To analyze the secondary measures of this study, paired-samples dependent t-tests were

employed to compare before and after intervention scores of inflammatory variables, muscle

strength of the knee extensors and elbow flexors, muscle thickness of the VL and BB, disability

index of the CHAQ and health status of the CHAQ. Significance was considered acceptable at an

alpha level of $p<0.05$. G*Power (G*Power© of Dusseldorf, Germany) was used to calculate the

necessary sample size for a definitive study to achieve a power of 80%.

The analysis of the Actigraph GT3x accelerometers was performed on ActiLife version

6.4.5 software (Actigraph© of Pensacola, FL, United States). From this an average amount of

MVPA per day was attained for each participant.

CHAPTER 3 RESULTS

3.1 Demographics

Results are presented as means ± standard deviation (SD). In total seven participants (four females, three males) were included in this pilot study. Three participants had seronegative polyarticular JIA, three had oligoarticular JIA and one had enthesitis related arthritis. Before starting the exercise program four participants had active disease and three participants had inactive. Upon completion of the six week training program one participant had active disease and the other six had inactive JIA. The average age for female participants in the study was 14.9 ± 3.0 and 15.0 ± 3.3 for before and after training, respectively. Males' age was 13.5 ± 2.2 and 13.6 ± 2.4 for before and after training, respectively. The height of female participants was 161.6 ± 11.6 and 161.2 ± 10.4 before and after training, respectively. The height of our male participants was 153.9 ± 17.2 and 155.0 ± 17.5 before and after training, respectively. On average, the female height-for-age fell just below the 50th centile and males were between the 15th and 25th centile, compared to World Health Organization (WHO) growth reference charts. The weight of our female participants was 62.8 ± 19.4 and 62.8 ± 19.8 before and after training, respectively. The weight of our male participants was 42.8 ± 15.4 and 43.0 ± 16.1 before and after training, respectively. Body mass index (BMI) of the female participants was 24.05 and 24.17 before and after training, respectively. BMI of the male participants was 18.67 and 18.15 before and after training, respectively. The female and male BMI's placed them between the 85th and 95th centiles and 50th and 75th centiles, respectively. Table 1 displays the demographics of the participants.

Table 1: Demographics of participants

Variable	Before	After
Age (yrs)-females	14.9 ± 3.0	15.0 ± 3.3
Age (yrs)-males	13.5 ± 2.2	13.6 ± 2.4
Height (cm)-females (n=4)	161.6 ± 11.6	161.2 ± 10.4
Height (cm)-males (n=3)	153.9 ± 17.2	53.9 ± 17.2
Height (cm)-combined (n=7)	158.27 ± 13.50	158.59 ± 12.95
Weight (kg)-females (n=4)	62.8 ± 19.4	62.8 ± 19.8
Weight (kg)-males (n=3)	42.8 ± 15.41	43.0 ± 16.1
Weight (kg)-combined (n=7)	54.21 ± 19.51	54.31 ± 19.83
BMI (kg/m^2)-females (n=4)	24.1	24.7
BMI (kg/m^2)-males (n=3)	18.7	18.2

No significant differences existed between before and after training values.

3.2 Baseline physical activity

Baseline physical activity is depicted in figure 1, with a comparison of each participant to the recommended 60 minutes of MVPA per day (bold black line). Reference lines of physical activity for healthy children between the ages of 9 and 15 years are also shown in the figure, reproduced from Nader et al (2008). One female and one male participant met the recommended 60 minutes of MVPA per day and there was only one participant (a male) within the averages for healthy children of his age. All other participants were under the recommended 60 minutes of

MVPA for their age and were also less than their age-matched peer averages for minutes of

MVPA per day.

Figure 1: Baseline MVPA in children with JIA relative to their healthy peers.
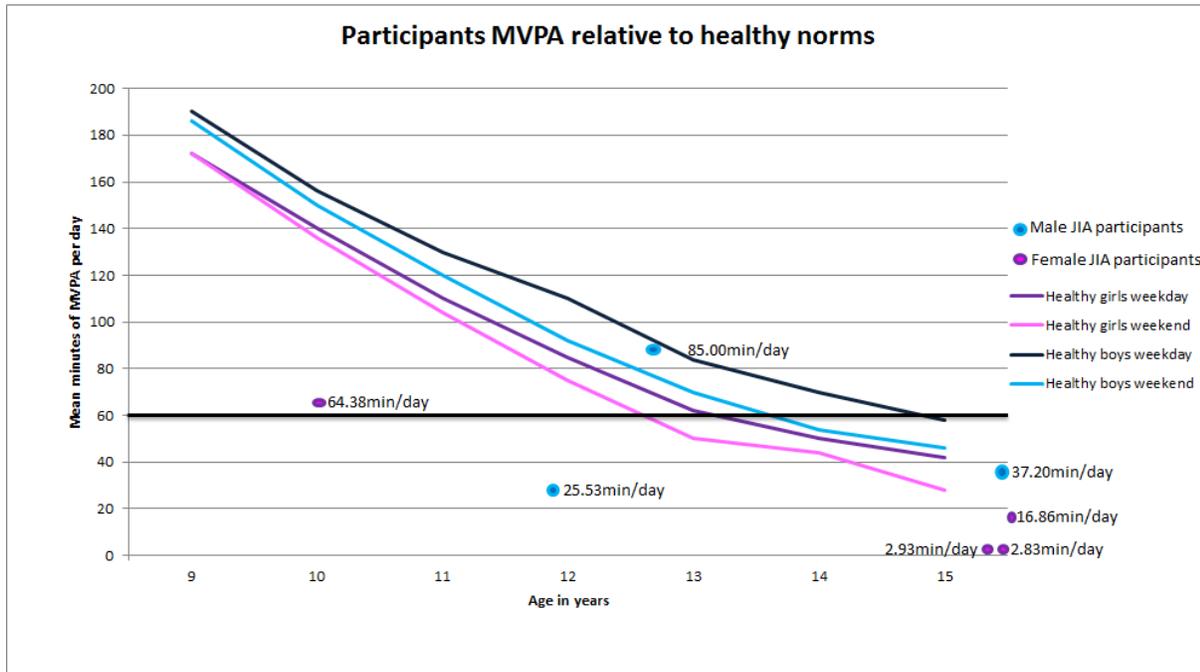
3.3 Hypothesis 1-Feasibility of Study

The average number of exercise sessions completed was 13.0 ± 3.6 out of a possible 18 (72.2%), determined by identifying the number of after exercise pain entries questionnaires answered by each participant. Using that same standard, zero of the seven participants completed all 18 exercise sessions; the highest number was 17 completed by two participants. The average number of before exercise pain questionnaires completed was 12.7 ± 3.4. The average number of daily pain questionnaires completed was 36.0 ± 10.1 out of a possible 49. The highest number of daily pain questionnaires completed was 47 by one of the participants. No adverse events were

reported from any participant by way of either contacting any of the researchers or reporting adverse events via notes on the tablet. As well, no dropouts occurred in this study.

3.4 PinGo Analyses

Figures 2 to 7 depict the end-of-day pain intensity (represented in blue), pain affect (represented in red and translated to a ten to 90 scale by increments of ten from a one to nine scale) and pain interference (represented in green) of each participant separately over the seven weeks (participant four has been excluded from the pain analysis as the tablet malfunctioned and data for only the first two days of the study is available). Blanks indicate that individuals did not complete the questionnaire of pain for that day (shown as measurement occasion).

Figure 2: Participant 1 pain intensity, pain affect, and pain interference
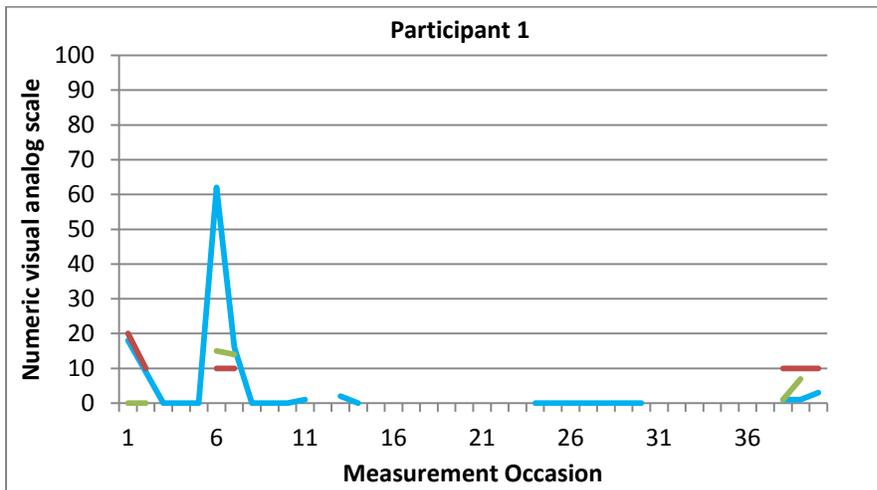
Figure 3: Participant 2 pain intensity, pain affect, and pain interference
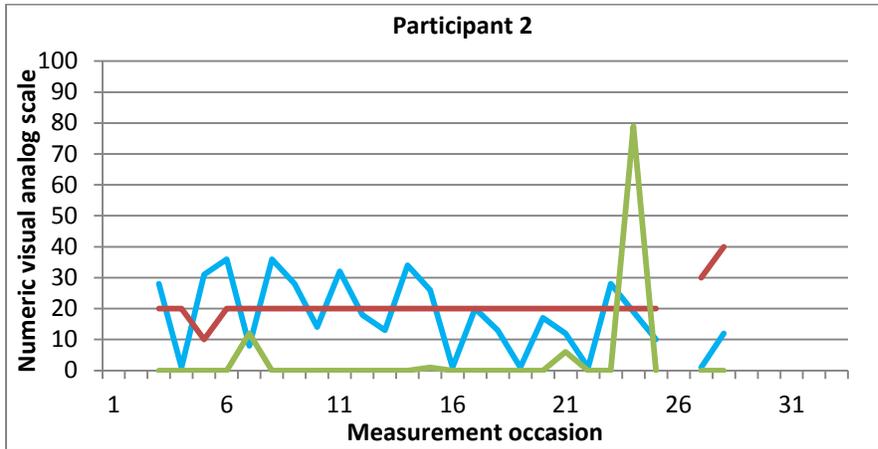
Participant 2

Figure 4: Participant 3 pain intensity, pain affect, and pain interference
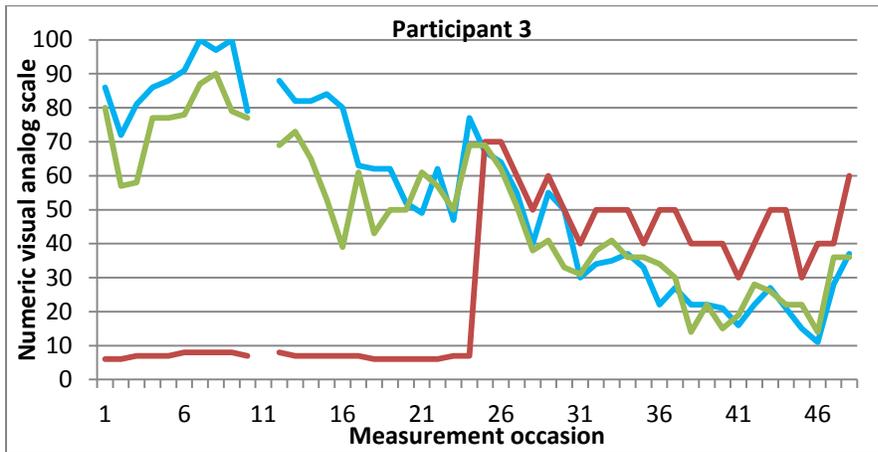
Participant 3

Figure 5: Participant 5 pain intensity, pain affect, and pain interference
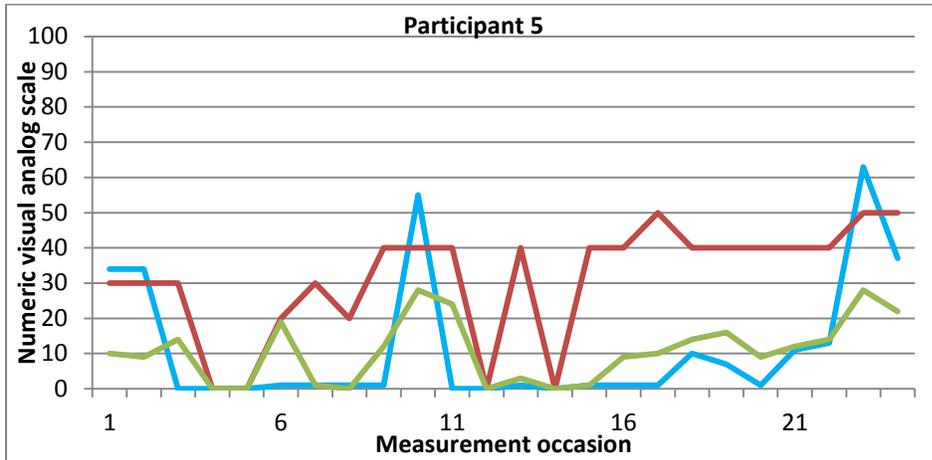
Figure 6: Participant 6 pain intensity, pain affect, and pain interference
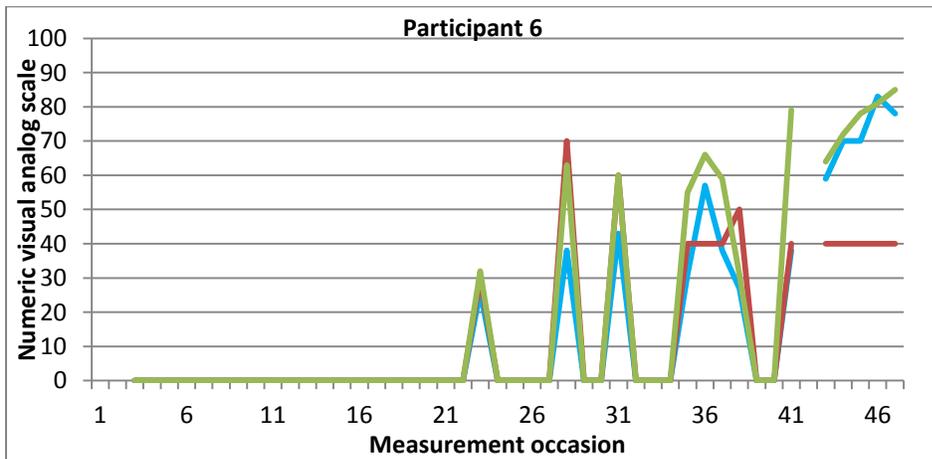
Figure 7: Participant 7 pain intensity, pain affect, and pain interference
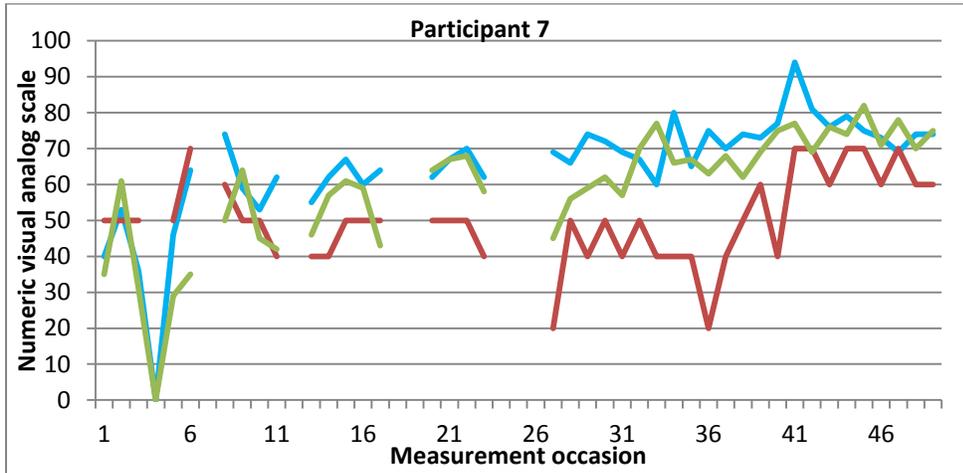
Repeated measures ANOVA of averaged pain intensity, pain affect and pain interference scores for the baseline week, the first two weeks of training, middle two weeks of training and final two weeks of training revealed no significant main effect of time for the group ($p>0.05$).

The average change in pain intensity from before exercise pain intensity to after exercise pain intensity was an increase of pain intensity by 3.0 ± 11.8 units. The number of occurrences (each occurrence is a single exercise session with a respective before and after exercise questionnaire completed) that had a clinically significant decrease in pain intensity of 8.2 units or more was seven with a mean decrease of 19.9 ± 9.1 units. The number of occurrences that had a clinically significant increase in pain intensity of more than 19.0 units or more was seven with a mean increase of 26.7 ± 6.6 units. The total number of occurrences that did not increase or decrease in pain intensity to a clinically significant amount was 60 out of 74. A decrease in pain to any extent occurred in 17 out of the 74 total occurrences and an increase in pain occurred in 31 out of the 74 cases.

When before to after exercise pain intensity and affect were analyzed per participant and aggregated, no significant differences existed for both pain intensity and pain affect ($p > 0.05$).

End-of-day pain intensity was averaged for each of the participants to attain a baseline average, initial two weeks of training average, middle two weeks of training average, and final two weeks of training average. Repeated measures ANOVA for all the participants revealed no significant difference in pain intensity, pain affect, or pain interference over those four time points ($p > 0.05$).

When all occurrences (total of 74) were analyzed together, pain intensity reported before exercise was positively correlated to RPE of the exercise, $r(72)=0.327$, $p < 0.05$ with higher pain intensity being related to a higher RPE. When split by participant, one participant showed a positive correlation between the two variables, $r(15)=0.785$, $p < 0.05$, whereas all others were not significant ($p > 0.05$). Table 2 displays the number of sessions completed by each participant, the range of scores of pain intensity before exercise, the range of scores of pain intensity after exercise and the range of RPE scores of each participant.

Table 2: Pain intensity before, pain intensity after and RPE of participants individually

Participant	Pain intensity before mean (range)	Pain intensity after mean (range)	RPE mean (range)	Number of training sessions completed
1	12.1 ± 26.7 (0-83)	12.9 ± 31.7 (0-92)	7.08 ± 2.4 (2-10)	13

2	7.9 ± 8.8 (0-23)	11.5 ± 15.3 (0-50)	3.7 ± 0.8 (2-5)	10
3	46.9 ± 23.7 (13-88)	52.7 ± 27.1 (0-100)	7.1 ± 0.6 (6-8)	17
5	23.6 ± 17.1 (0-50)	20.4 ± 25.4 (0-68)	6.4 ± 0.5 (6-7)	8
6	27.8 ± 32.2 (0-81)	25.4 ± 32.5 (0-74)	4.5 ± 1.3 (3-7)	17
7	63.8 ± 13.8 (34-87)	68.69 ± 10.1 (56-92)	6.4 ± 0.5 (6-7)	13

Table 3 presents the self-reported measures of stiffness, fatigue, mood, and level of awakeness for both before and after each resistance training session.

Table 3: Stiffness, fatigue, mood and level of awakeness before and after each exercise session.

Variable	Before	After
Stiffness	30.7 ± 24.2	32.6 ± 25.7
Fatigue	43.5 ± 27.7	53.4 ± 28.3
Mood	71.8 ± 23.4	70.7 ± 24.3
Level of awakeness	48.8 ± 29.9	54.0 ± 31.4

T-tests not performed on this data as participants contributed multiple and uneven time points to the data.

Using bivariate correlations, end-of-day pain intensity was significantly correlated to end-of-day stiffness $r(225)=0.864$, $p<0.001$. End-of-day pain intensity was also significantly correlated to end-of-day fatigue $r(225)=0.581$, $p<0.001$ and end-of-day pain intensity was negatively correlated to end-of-day mood $r(225)=-0.637$, $p<0.001$.

3.5 Inflammation

Inflammation, fluid, synovial thickening and synovitis all showed no significant differences between pre and post resistance training program ($p>0.05$). The means and standard deviations of each of the variables are reported in table 4.

3.6 Muscle Strength and Muscle Thickness

Muscle thickness of the vastus lateralis increased from before to after the six weeks of resistance training ($p<0.05$). All other variables did not significantly change for pre to post ($p>0.05$). These variables are displayed in table 4.

3.7 Functional Ability

Functional ability (disability index and health status did not significantly change from pre to post exercise ($p>0.05$). These variables are displayed in table 4 as well.

Table 4: Measures of pre and post 6 weeks resistance training program and required sample size for 80% power

Measures of pre and post 6 weeks training	Pre training	Post training	Required sample size for 80% power
Inflammation (Likert scale) (n=7)	1.00 ± 1.15	0.14 ± 0.38	29
Fluid (Likert scale) (n=7)	1.00 ± 1.15	0.29 ± 0.49	26
Synovial thickening	0.57 ± 1.13	0.57 ± 0.79	Effect size not large

(Likert scale) (n=7)			enough
Synovitis (Likert scale) (n=7)	0.57 ± 0.79	0.14 ± 0.38	46
Vastus lateralis thickness (cm) (n=7)	3.00 ± 0.58	3.18 ± 0.66*	7
Biceps brachii thickness (cm) (n=5)	2.61 ± 0.41	2.87 ± 0.51	8
Leg extension strength (n.m) (n=7)	111.57 ± 42.99	105.00 ± 50.54	22
Elbow flexion strength (n.m) (n=7)	28.29 ± 11.27	30.14 ± 17.99	275
Disability index from CHAQ(0 to 3 continuous scale) (n=7)	0.38 ± 0.70	0.20 ± 0.28	47
Health status from CHAQ (VAS) (n=7)	0.37 ± 0.61	0.21 ± 0.21	131

*Significant difference from pre training.

3.8 Closing questionnaire

All participants reported that they felt the exercise program was enjoyable. Two participants reported that the exercise program became more challenging as the weeks progressed due to the greater number of repetitions required, but that that was a good thing. One participant felt that a baseline level of athleticism was necessary in order to be able to complete

the exercise program, so the thought was that it would not be suitable for a very unfit JIA patient. As well, one participant felt it to be tough at first and that her muscles were sore the following day, but that as the weeks progressed less muscle soreness occurred. A competitive bowler in the study reported that it improved her endurance in bowling competitions so that she was able to last longer into her bowling tournaments, especially if they were to bowl ten to 15 rounds in a day. Finally, two participants reported performing the exercises sometimes with siblings or parents.

Changes that participants felt could have been beneficial to the exercise program as a whole were to add music to the background. One participant who had pain in her left arm for two out of her 14 completed exercise sessions decided to only use her right arm to do the exercises that involved movement of the radiohumeral and ulnohumeral joint. Another participant reported the resistance band rubbing against her skin and causing some skin pain so she decided to wear a long sleeve shirt while exercise which solved the issue. A final modification was push-ups from the wall rather than the floor, employed by one participant for the initial two weeks of the program until she became strong enough to perform them from her knees, after which she progressed to her toes.

PinGo© was overall well-received by the seven participants. Five of the seven participants reported the tool to be difficult/ annoying to use for the initial couple of days because it would lag in the time for the next arrow to come up in order to answer the next question. As well, the dragging of the cursor within the VAS would have a delayed reaction for the first couple of times until the user became accustomed to where their finger should be placed. The length of the questionnaires was reported to be reasonable and each questionnaire was said to be comprehensive enough to understand the pain of each participant.

CHAPTER 4 DISCUSSION

4.1 Safety and Feasibility

The primary purpose of this study was to examine the feasibility, acceptability and safety of a home-based resistance training program in children with JIA. The uniqueness of this exercise program was that it was home-based, allowing JIA children to undertake this emerging form of healthcare within their natural environment. The results presented suggest that the program is safe, feasible and acceptable as indicated by the absence of adverse events from the study participants, non-significant increases in pain, moderate participation rates and qualitative feedback indicating acceptability. Some of the participants reported modifications of an exercise or exercises in order to complete the program, but those participants were able to tailor it so that they could complete the resistance training program that day.

For the purposes of this study and this population an 8.2 unit decrease or a 19.0 unit increase in pain intensity from before to after exercise was considered clinically significant. This is based on the work of Dhanani et al (2002) who analyzed the chronic pain changes in 553 children with rheumatic disease. In the present study seven of the self-reported pain intensity cases (exercise sessions) decreased greater than 8.2 units and seven increased greater than 19.0 units from before to after exercise. As well, 60 of the current cases did not show a clinically significant change in pain intensity (the most widely used measure of pain) from before to after exercise. Although four of the participants in this study demonstrated significant increases in pain from before to after the exercise program, none of these were nearing a clinically significant increase in pain of 19.0 units (Dhanani et al. 2002). This demonstrates that resistance training did

not have a significant immediate effect on pain in children with JIA and is a safe form of exercise that is worth researching in this population.

The analysis of end-of-day pain (when averaged across the baseline week, initial two weeks of training, middle two weeks of training and final two weeks of training) also did not reveal a significant increase in pain from before to after the exercise program. This also demonstrates the safety of a resistance training program in this population as there were no lasting negative effects of the exercise on pain.

The results of this study show that the participants were able to complete 72.2% of prescribed exercise sessions. Takken et al (2001) conducted a pilot study on the effects of a group-based aerobic aquatic training program in children with JIA. The adherence rate was 85% with participants missing the training sessions due to disease, lack of transportation or conflicting social activities. Singh-Grewal et al (2007) reported adherence rates of 56% in their high intensity aerobic exercise experimental group compared to 78% in their control group. A pilot study conducted by Singh-Grewal et al (2006) saw adherence rates of 63% for a supervised circuit training program in children with JIA. Finally, a recent study by Sandstedt et al (2013) had participants perform a 12 week exercise program including jumping jacks, free weight and body weight exercises. Adherence to this program was 70% of the expected value, with five out of 28 participants in the training group dropping out. This present study, unique in that it was home-based indicating less social influence and pressure as the aforementioned studies, demonstrated similar rates of adherence. Therefore home-based resistance exercise appears to be acceptable for children with JIA.

4.2 Pain, Inflammation, Muscle Parameters, Function and Physical Activity

Children with JIA are generally less physically active relative to their healthy peers and typically have compromised musculoskeletal and cardiovascular health (Giannini and Protas. 1993; van Brussel et al. 2011; Lelieveld et al. 2007). Previous research has also shown that children, including those who are healthy, tend to decrease in the amount of physical activity (measured in MVPA) they participate in as they age (Nader et al. 2008; Sallis et al. 2000). The present sample of children also demonstrated attenuated baseline physical activity. Additionally, this study demonstrated RPE of the exercise to be positively correlated to before exercise pain intensity ($p<0.05$). This may signify that performing physical activity or exercise while in pain makes the exercise more difficult and therefore causes a reduced to bereduction in physically active. It may be beneficial to consider evaluating the effects of age-specific unique exercise training programs in children and adolescents with JIA in order to increase their fitness and health.

Pain and stiffness, and pain and fatigue in this sample displayed a very strong ($r=0.864$, $p<0.001$) and strong positive correlations ($r=0.581$, $p<0.001$, $r=0.864$, $p<0.001$), respectively). Previous research has demonstrated that pain, stiffness and fatigue are all significant predictors of reduced participation in school and social activities in children with JIA (Schanberg et al. 2003). As well, mood was has been demonstrated to be a significant predictor of pain, stiffness and fatigue in children with JIA (Schanberg et al. 2005). This study demonstrated a significant negative correlation between mood and pain ($r=-0.637$, $p<0.001$), in support of previous research. Future research would have to determine whether altering one of these variables can have an impact on the other variables, such that if morning stiffness or mood were improved in this population, potentially pain reduction could occur.

The current study suggests that home-based resistance training can be beneficial for muscular fitness. The thickness of the VL significantly increased after the six weeks of exercise training. To our knowledge, this is the first study of its kind to analyze muscle thickness in children with JIA after a strength training program. Although we were not able to directly analyze if this increase was due to changes in muscle fibre cross-sectional area from myofibrillar growth, proliferation and satellite cell activation (muscle biopsy required), these results support the necessity of strength training in this population to improve musculoskeletal fitness. Whether muscle damage (protein degradation) was induced by the program is unknown and it is recommended this should be assessed in future research. As well, the effects of this muscle damage systemically on children with JIA would be an interesting area of research. Nevertheless, these results demonstrate that a home-based, minimal equipment resistance training program can be beneficial in this population. The same results were not seen with respect to the BB, which would require a sample size of eight to achieve 80% power. However, this program used body weight and resistance bands which could have provided greater resistance for the lower body exercises while not stimulating the BB enough to generate hypertrophy. Changing the program or measuring muscles in the upper body different from the BB may have elicited significant results.

Strength gains in children and inexperienced individuals after a resistance training program are primarily due to neurological adaptations, although hypertrophy has been demonstrated in programs lasting as little as four weeks (Behm et al. 2008). However, muscle strength was not altered significantly after training for either elbow flexion and knee extension strength. Elbow flexion strength displayed a required sample size of 275 and knee extension strength required 22. The lack of effect may be due to the study's small sample size, but also the

lack of the specificity of training. The tool used to measure pre and post strength in these individuals was not explicit to the type of training that was performed in this study. The training used resistance tubing and body weight as opposed to machines, and also had participants perform many multi-joint movements per exercise versus a single joint movement such as that of the testing using the dynamometer. Age, sex and motivation of the immature participants in this study could have meant a submaximal effort on the MVC at any time point, which could have affected the results. Finally, children in this study were allowed to perform their training any day of the week and also participated in other activities, potentially not allowing themselves enough rest to recover for post measurements of strength. Therefore it may have been such that strength gains occurred without being detected by the measurements performed here, or that muscular endurance improved whereas MVC did not become significantly greater.

Functional ability and inflammation showed no significant differences after the six weeks of training, again showing that the sample size needs to be increased for definitive research. To determine the effects of resistance training on the disability index and health status using the CHAQ, a required sample size of 41 and 131 participants would be required, respectively. A Cochrane review showed no statistically significant change in functional ability as measured by the CHAQ from before to after an aerobic exercise program (Takken et al. 2008). As well, a plyometric and strength training randomized control trial revealed no significant differences in functional ability between the experimental and control group (Sandstedt et al. 2013). A required sample size of 29, 26 and 46 participants would be necessary to achieve 80% power for inflammation, fluid and synovitis, respectively. The same Cochrane review by Takken et al (2008) revealed no significant differences in number of joints with swelling after aerobic exercise training programs. This is the first study of our knowledge to analyze the effects of a

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home-based resistance training on functional ability and objectively and non-invasively measured inflammation in children with JIA. Future research would need to further these analyses with larger sample sizes.

4.4 Strengths

Despite the widespread understanding that physical activity, including exercises that target muscular strength and fitness, is a necessary component for optimal growth in children, there has been little research on resistance training in JIA. The majority of studies have examined the effects of aerobic training programs on fitness and function in youth with JIA. The present study contributes pilot data from a novel form of home-based exercise training in JIA that could potentially improve pain, disease symptoms and muscular fitness. This study also closely monitored the safety of the exercises (in terms of reporting of adverse events and increased pain with exercise), feasibility (in terms of participation and modification) and acceptability of the exercise regimen.

It was demonstrated that these children were able to safely participate in the program without significantly exacerbating their pain from a clinical standpoint. The exercise program also increased in volume over the six weeks and the children were able to sustain those requirements without adverse events occurring. This demonstrates the necessity for further research to understand the precise effects of a resistance training program in this population.

This home-based resistance training program allowed for exercise in a naturalistic environment where children with JIA could appropriately tailor the program to themselves and the symptoms of their JIA. The program was effective for increasing the size of the leg muscles despite the lack of direct supervision from a trainer and without expensive weights or weight

machines. The program was also able to be completed in a small area of the home with minimal use of extra tools, rendering the program accessible to JIA patients of different socioeconomic status and settlement areas. There were no adverse events from the exercise program and it required no supervision from health professionals. This method of exercise could therefore be useful in a variety of populations, including rural and underprivileged communities.

The children were also able to report their pain in real time once a day on non-exercise days and three times a day when they exercised, allowing an extremely comprehensive analysis of pain. Previous research lends to the reality that pain needs to be measured comprehensively in order to develop a full understanding of a patient's perception of pain (von Baeyer and Spagrud. 2007). The questions in this study gave a comprehensive analysis of each participant's pain while also analyzing JIA specific variables and exercise variables. This permitted an understanding of pain specific to JIA as well as an understanding of the exercise program and how individuals could tailor it to suit themselves.

4.5 Limitations

Although the results of this study are unique as it is the first to our knowledge to analyze the effects of a home-based resistance training program on pain, inflammation, muscular fitness and functional ability in children with JIA, the conclusions are limited by several factors. First, the sample size of this study was such that definitive results cannot be attained. Secondly, the exercise program was a home-based program and therefore not objectively monitored for the completion of exercises in the proper form.

Because this was a safety and feasibility study, it may have not been long enough to find definitive results for multiple variables. A meta-analyses analyzing resistance training programs

in children incorporated studies as little as four weeks and up to 60 weeks. Although significant results could be found with the shorter duration training programs, there was a significant correlation between study duration and resistance training effect (Behringer et al. 2010). Potentially, if the program duration was extended to 12 weeks and an analysis of inflammation, muscle parameters and functional ability was performed at baseline, six and 12 weeks, results could be significant. Furthermore, longitudinal measurements of growth patterns could have been made with a longer study to determine whether muscle hypertrophy was due to growth or resistance training, or a combination of the two.

This study chose to use cut points of clinically significant changes in pain as an increase of 19.0 units or a decrease of 8.2 units, based off the Dhanani et al (2002) study in children with rheumatic disease which was most relevant to this study. However, other research has considered a change in pain on a VAS of approximately ten in either direction to be significant, which could have slightly altered the results (Todd et al. 1996; Gallagher et al. 2001; Powell et al. 2001). Furthermore, recent research suggests that relevant changes in pain should be accounted for on an individual basis, especially because patients experience more pain require greater changes in pain scores to be considered clinically significant (Bird and Dickson. 2001; Emshoff et al. 2011). This highlights the fact that pain is an individual construct that can differ greatly between and within individuals. Due to the limited sample size and scope of this study, factors affecting pain intensity were not equated as covariates of changes in pain. Environmental, genetic, psychological, contextual and developmental variables can all influence self-reported pain and ultimately affect the results of research. Further definitive research should aim to understand all these influences on an individual basis and be able to account for those in the analyses.

The current study also did not aim to determine whether each individual's pain stemmed more from neuropathic or nociceptive mechanisms. It is possible that the exercise could have produced changes in inflammatory mediators or increased inhibitory transmitters (ex: gamma-aminobutyric acid) (Hirose et al. 2004; Binder et al. 2004). Changes in physiological markers including cytokines, TNF-α, gamma aminobutyric acid, α-amino-3-hydroxy-5-methyl-4-isoxazoleproprionic acid receptors and N-methyl-D-aspartate receptors should be examined in future research. As well, cortisol levels in individuals with JIA from before to after exercise training sessions (and potentially pre and post an extended exercise training program) should be examined so as to tease out the influence of physiological stress on pain. Melzack (1999) proposes that chronic pain can originate or proliferate due to elevated levels of cortisol, which has been demonstrated in patients with chronic pain (Van Uum et al. 2008). This would be able to lend information to current theories on pain, especially if exercise training can influence physiological markers of pain.

The primary aim of this study was to understand if a home-based resistance training program was safe and feasible in children with JIA. To understand if this is valid a sample representative of the entire disease is necessary. This study included no children rheumatoid factor positive JIA or systemic JIA. These subtypes of JIA present differently from others and can respond differently to exercise (Takken et al. 2002). Therefore this study is not completely generalizable to children with JIA and it may be that those with systemic JIA or rheumatoid factor positive JIA need to be more closely monitored when performing resistance training.

4.6 Future directions

Children with JIA are less physically active relative to their healthy age-matched peers, rendering their musculoskeletal fitness compromised (Giannini and Protas. 1993). Exercise training, specifically that of resistance training, can have implications on pain threshold (the point at which a noxious stimuli is first recognized) and pain tolerance (the degree of pain an individual perceives with a noxious stimuli). Through a mechanism labeled exercise-induced hypoalgesia, children with JIA who participate in a resistance training program could potentially decrease the amount of daily pain they experience while enhancing their muscular fitness. Although EIH was not tested in this study, future research should aim to examine this phenomenon in children with JIA.

This study was able to demonstrate that resistance exercise is a feasible intervention for children with JIA. Further research, using RCTs for a longer time period and with a larger sample size, could determine the precise effects of a similar intervention. These future studies would require a comprehensive analysis of pain specific to children with JIA. RTDC could be employed in future research while also measuring exercise variables, as has been done in this study. It would also be interesting to determine the effects of pharmaceuticals on resistance training in children with JIA. Ibuprofen, a type of NSAID, has been demonstrated to have no effect on muscle hypertrophy in healthy adults after a six week resistance training program (Krentz et al. 2008). However, this has not been examined in chronic inflammatory populations, nor has there been research determining the effects of resistance training coupled with NSAIDs, methotrexate, etanercept or other biological agents in children with JIA.

To facilitate adherence to the exercise protocol and the completion of pain questionnaires, future research should also consider having children participate in an exercise program with added bonuses to following the exercise regime or peer/parental support. Recently, gamification has been explored as a means of employing electronic gaming components into non-gaming contexts (i.e., exercise) in order motivate individuals to participate in that behavior (King et al. 2013). As electronics such as smartphones and tablets become more widespread and desired, gamification could provide a viable avenue to potentially increase adherence to exercise programs and questionnaire completion by rewarding the individuals via electronic rewards for participation. Furthermore, an additional option to increase adherence could potentially be to have idolized individuals (ex: athletes, singers, actors, etc.) perform the exercise programs on the videos in order to motivate the participants to follow along with the program. However, this type of potential adherence motivator would have to be investigated as some children may respond oppositely to observing an athlete as it may be viewed as something to aspire to or an unattainable goal.

Although the study was underpowered for definitive results, this study sheds light on the effects of resistance training in JIA and provides a greater understanding of the safety of this type of intervention in this population. Clinicians, specifically pediatric rheumatologists and physical therapists, will be able to use the introductory findings of this pilot research in order to understand that this form of exercise is safe in their patients, although its effectiveness is still to be determined. The general consensus is that physical activity is typically beneficial for most pediatric populations with chronic diseases and this study appears to support that (Philpott et al. 2010).

CHAPTER 5 CONCLUSION

Results from this study demonstrate that a home-based resistance training program in children with JIA would appear to be a safe and feasible form of exercise. Although significant effects on pain were not attained from this analysis, further definitive research needs to be performed in order to detect its exact effects on pain. As well, the results from this study demonstrate that resistance training can improve muscular fitness in children with JIA. The methods of this study need to be extended in future research in order to understand the precise benefits of resistance training in JIA.

REFERENCES

1.   Adamopoulos S, Parissis J, Kroupis C et al. 2001. Physical training reduces peripheral markers of inflammation in patients with chronic heart failure. Eur Heart J, 22(9): 791–7.

2.   Arnold D, Burns K, Adhikari N et al. 2009. McMaster Critical Care Interest Group. The design and interpretation of pilot trials in clinical research in critical care. Crit Care Med, 37(Suppl 1): S69-S74.

3.   Arain M, Campbell M, Cooper C et al. 2010. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Med Res Method, 10(67): 1-7.

4.   Astin A, Beckner W, Soeken K et al. 2002. Psychological interventions for rheumatoid arthritis: A meta-analysis of randomized controlled trials. Arth Res, 47(3): 291-302.

5.   Bacon MC, Nicholson C, Binder H et al. 1991. Juvenile rheumatoid arthritis: aquatic exercise and lower-extremity function. Arthritis Care Res, 4(1): 102–5.

6.   Baillet A, Payraud E, Niderprim V et al. 2009. A dynamic exercise programme to improve patients' disability in rheumatoid arthritis: a prospective randomized controlled trial. Rheum, 48(4): 410-5.

7.   Bastard J, Jardel C, Delattre J et al. 1999. Evidence for a Link Between Adipose Tissue Interleukin-6 Content and Serum C-Reactive Protein Concentrations in Obese Subjects. Circulation, 99(16): 2219–22.

8.   Behm D, Faigenbaum A, Falk B et al. 2008. Canadian Society for Exercise Physiology position paper: resistance training in children and adolescents. Appl Physiol Nut Metab, 33(3): 547-61.

9.   Behringer M, von Heede A, Yue Z et al. 2010. Effects of resistance training in children and adolescents: A meta-analysis. Ped, 126(5): 1199-2010.

10.   Berna C, Leknes S, Holmes E et al. 2010. Induction of depressed mood disrupts emotion regulation neurocircuitry and enhances pain unpleasantness. Biol Pysch, 67(11): 1083-90.

11.   Berntson L, Anderssonäre B, Fasth A et al. 2003. Incidence of juvenile idiopathic arthritis in the Nordic countries. A population based study with special reference to the validity of the ILAR and EULAR criteria. J Rheumatol, 30(1): 2275–82.

12.   Binder E, Droste S, Ohl F et al. 2004. Regular voluntary exercise reduces anxiety-related behaviour and impulsiveness in mice. Behav Pain Res, 155(2): 197-206.

13.   Bird S & Dickson E. 2001. Clinically significant changes in pain along the visual analog scale. Ann Emerg Med, 38(6): 639-43.

14.   Blimkie C. 1989. Age and sex associated variation in strength during childhood: Anthropometric, morphologic, neurologic, biomechanical, endocrinologic, genetic, and physical activity correlates. In Gisolfi, C. V. (Ed.) Perspectives in Exercise Science and Sports Medicine: Youth, Exercise and Sports. Indianapolis, Indiana: Benchmark Press.

15.   Bloom B, Owens J, McGuinn M et al. 2001. Sleep and its relationship to pain, dysfunction, and disease activity in juvenile rheumatoid arthritis. J Rheum, 29(1): 169-73.

16.   Bomba M, Meini A, Molinaro A et al. 2013. Body experiences, emotional competence, and psychosocial functioning in juvenile idiopathic arthritis. Rheumatol Int, In Press.

17.   Borchers A, Selmi C, Cheema G et al. 2006. Juvenile idiopathic arthritis. Autoimm Rev, 5(4): 279-98.

18.   Bromberg M, Gil K, Schanberg L. 2012. Daily sleep quality and mood as predictors of pain in children with juvenile polyarticular arthritis. Health Pyschol, 31(2): 202-9.

19.   Bruunsgaard H. 2005. Physical activity and modulation of systemic low-level inflammation. J Leuko Biol, 78(4): 819-35.

20.   Buljina A, Taljanovic M, Avdic D et al. 2001. Physical and exercise therapy for treatment of the rheumatoid hand. Arthritis Rheum, 45(4): 392-7.

21.   Burnham J, Shults J, Dubner S et al. 2008. Bone density, structure, and strength in juvenile idiopathic arthritis: Importance of disease severity and muscle deficits. Arth Rheum, 58(8): 2518-27.

22.   Canadian Society of Exercise Physiologists. 2013. Canadian physical activity guidelines. Retrieved from

http://www.csep.ca/CMFiles/Guidelines/CSEP_PAGuidelines_youth_en.pdf.

23.   Center for Disease Control and Prevention. 2011. How much physical activity do children need? Retrieved from

http://www.cdc.gov/physicalactivity/everyone/guidelines/children.html.

24.   Chilibeck P, Stride D, Farthing J et al. 2004. Effect of creatine ingestion after exercise on muscle thickness in males and females. Med Sci Spor Exer, 36(1): 1781-8.

25.   Cleeland C, Landinsky J, Serlin R et al. 1989. Multidimensional measurement of cancer pain: Comparisons of US and Vietnamese patients. J Pain Symp Manage, 3(1): 23-7.

26.   Cliff D, Reilly J, Okely A. 2009. Methodological considerations in using accelerometers to assess habitual physical activity in children aged 0–5 years. J Sci Med Sport, 12(1): 557-67.

27.   Collado P, Jousse-Joulin S, Alcalde M et al. 2012. Is ultrasound a validated imaging tool for the diagnosis and management of synovitis in juvenile idiopathic arthritis? A systematic literature review. Arthritis Care Res; 64(7): 1011-9.

28.   Corder K, Ekelund U, Steele R et al. 2008. Assessment of physical activity in youth. J App

Phys, 105(3): 977–87.

29.   Cote J and Hoeger-Bement M. 2010. Update on the relation between pain and movement:

Consequences for clinical practice. Clin J Pain, 26(9): 754-62.

30.   Crandall M and Savedra M. 2005. Multidimensional assessment using the adolescent

pediatric pain tool: a case report. J Special Ped Nurs, 10(3): 115–23.

31.   Davies C, Dooley P, McDonagh P et al. 1985. Adaptation of mechanical properties of

muscle to high force training in man. J Phys, 365(1): 277-84.

32.   De Kleer IM, Brinkman DM, Ferster A et al. Autologous stem cell transplantation for

refractory juvenile idiopathic arthritis: analysis of clinical effects, mortality, and transplant

related morbidity. Ann Rheum Dis, 63(10): 1318-26.

33.   Dhanani S, Quenneville J, Perron M et al. 2002. Minimal difference in pain associated with

change in quality of life in children with rheumatic disease. Arth Care Res, 47(5): 501-5.

34.   Dhamrait S, James L, Brull D et al. (2003). Cortical bone resorption during exercise is

interleukin-6 genotype-dependent. Euro J App Phys, 89(1): 21-5.

35.   Donn R, Alourfi Z, Zeggini E et al. 2004. A functional promoter haplotype of macrophage

migration inhibitory factor is linked and associated with juvenile idiopathic arthritis.

Arthritis Rheum, 50(1): 1604–10.

36.   Edwards R, Bingham C, Bathon J et al. 2006. Catastrophizing and pain in arthritis,

fibromyalgia, and other rheumatic diseases. Arth Care Res, 55(2): 325-32.

37.   Emshoff R, Bertram S, Emshoff I. 2011. Clinically important difference thresholds of the visual analog scale: A conceptual model for identifying meaningful intraindividual changes for pain intensity. Pain, 152(10): 2277-82.

38.   Epps H, Ginnelly L, Utley M et al. 2005. Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis. Health Technol Assess, 9(1): 1–59.

39.   Esliger D, Copeland J, Barnes J et al. 2005. Standardizing and optimizing the use of accelerometer data for free-living physical activity monitoring. J Phys Act Health, 3(1): 366–83.

40.   Faigenbaum A. 2000. Strength training for children and adolescents. Clin Sports Med, 19(4): 593-619.

41.   Faigenbaum A and Kang D. 2006. Youth strength training: Facts, fallacies, and program design considerations. ACSM's Certified News, 4-6.

42.   Faigenbaum A, Kraemer W, Blimkie C et al. 2009. Youth resistance training: Updated position statement paper from the National Strength and Conditioning Association. J Strength Cond Res, 23(1): S60-S79.

43.   Falk B and Eliakim A. 2003. Resistance training, skeletal muscle and growth. Pediatr Endocrinol Rev, 1(2): 120-7.

44.   Fantini F, Gerloni V, Gattinara M et al. 2003. Remission in juvenile chronic arthritis: a cohort study of 683 consecutive cases with a mean 10 year followup. J Rheumatol, 30(1): 579–84.

45.   Feldman B, Ayling-Campos A, Luy L et al. 1995. Measuring disability in juvenile dermatomyositis: validity of the childhood health assessment questionnaire. J Rheumatol, 22: 326–31.

46.   Fisher NM, Venkatraman JT, O'Neil K. 2001. The effects of resistance exercises on muscle function in juvenile arthritis [abstract]. Arthritis Rheum, 44(Suppl 9): S276.

47.   Fishman, S Ballantyne J, Rathmell J. 2010. Bonica's management of pain. Text. Lippincott Williams & Wilkins.

48.   Fitzgerald M. 2005. The development of nociceptive circuits. Nature Rev; 6(1): 507-20.

49.   Focht B, Koltyn K. 2003. Alterations in pain perception after resistance exercise performed in the morning and evening. J Strength Cond Res, 23(1): 891–7.

50.   Fripp R and Hogdson J. 1987. Effect of resistance training on plasma lipid and lipoprotein levels in male adolescents. J Ped, 111(1): 926-31.

51.   Gallagher E, Liebman M, Bijur P. 2001. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Ann Emerg Med, 38(6): 633-8.

52.   Giannini M and Protas E. 1993. Comparison of peak isometric knee extensor torque in children with and without juvenile rheumatoid arthritis. Arthritis Care Res, 6(2): 82-8.

53.   Grom A and Hirsch R. 2000. T-cell and T-cell receptor abnormalities in the immunopathogenesis of juvenile rheumatoid arthritis. Curr Opin Rheumatol, 12(1): 420–4.

54.   Grom A, Murray K, Luyrink L et al. 1996. Patterns of expression of tumor necrosis factor α, tumor necrosis factor β, and their receptors in synovia of patients with juvenile rheumatoid arthritis and juvenile spondylarthropathy. Arthritis Rheum, 39(10): 1703–10.

55.   Gualano B, Sa Pinto A, Perondi B et al. 2010. Evidence for prescribing exercise as treatment in pediatric rheumatic diseases. Autoimm Rev, 9(8): 569-73.

56. Hayward K and Wallace C. 2009. Recent developments in anti-rheumatic drugs in pediatrics: treatment of juvenile idiopathic arthritis. Arth Res Ther, 11(1): 216.

57. Hinks A, Barton A, John S et al. 2005. Association between the PTPN22 gene and rheumatoid arthritis and juvenile idiopathic arthritis in a UK population: further support that PTPN22 is an autoimmunity gene. Arthritis Rheum, 52(1): 1694–9.

58. Hirose L, Nosaka K, Newton M et al. 2004. Changes in inflammatory mediators following eccentric exercise of the elbow flexors. Exerc Immunol Rev, 10(1): 75-90.

59. Hogeweg J, Kuis W, Oostendorp R et al. 1995. General and segmental reduced pain thresholds in juvenile chronic arthritis. Pain, 62(1): 11-7.

60. Horneff G. 2013. Update on biologicals for treatment of juvenile idiopathic arthritis. Expert Opin Biol Ther, 13(3): 361-76.

61. Horneff G, Schmeling H, Biedermann T et al. 2004. The German etanercept registry for treatment of juvenile idiopathic arthritis. Ann Rheum Dis, 63(12): 1638–1644.

62. Houghton K. 2008. Aerobic and anaerobic capacity in Juvenile Idiopathic Arthritis: evaluation of the cardiorespiratory response. Int J Rheum, 5(2): 1-46.

63. Hunfeld J, Perquin C, Duivenvoorden H et al. 2001. Chronic pain and its impact of quality of life in adolescents and their families. J Pediatr Psychol 26(3): 145–53.

64. Ishida, Y. 1992. Reliability of B-mode ultrasound for the measurement of body fat and muscle thickness. Amer J Hum Biol, 4(4): 511-20.

65. Iuliano-Burns S, Mirwald R, Bailey D. 2001. Timing and magnitude of peak height velocity and peak tissue velocities for early, average, and late maturing boys and girls. Amer J Hum Biol, 13(1): 1-8.

66.   Job E, Chambers C, Craig K. 2002. An underused resource: the contributions of developmental psychology to the field of pediatric pain. Pediatr Pain Lett, 6(1): 14–7.

67.   Katja B, Laatikainen T, Salomaa V et al. 2005. Associations of leisure time physical activity, self-rated physical fitness, and estimated aerobic fitness with serum C-reactive protein among 3803 adults. Atherosclerosis, 185(2): 381-7.

68.   Katz, N. 2002. The impact of pain management on quality of life. J Pain Symptom Manage, 24(Suppl 1): S38-S47.

69.   Kidd B, Morris V, Urban L. 1996. Pathophysiology of joint pain. Ann Rheum Dis, Review, 55(1): 276-283.

70.   Kidd B and Urban L. 2001. Mechanism of inflammatory pain. Brit J Anesthesia, 87(1): 3-11.

71.   Kim K and Kim D. 2010. Juvenile idiopathic arthritis: Diagnosis and differential diagnosis. Korean J Pediatr, 53(11): 931–935.

72.   King D, Greaves F, Exeter C et al. 2013. 'Gamification': Influencing health behaviours with games. J R Soc Med, 106(3): 76-8.

73.   Klepper S. 2003. Exercise and fitness in children with arthritis: Evidence of benefits for exercise and physical activity. Arthritis Care & Research, 49(3): 435–43.

74.   Klepper S. 2003. Measures of Pediatric Function. Arth & Rheum, 49(5): S5-S14.

75.   Koltyn K and Arbogast R. 1998. Perception of pain after resistance exercise. Br J Sports Med, 32(1): 20–4.

76.   Koltyn K and Umeda M. 2006. Exercise, Hypoalgesia and Blood Pressure. Sports Med, 36(3): 207-14.

77.   Koltyn K and Umeda M. 2007. Contralateral Attenuation of Pain After Short-Duration Submaximal Isometric Exercise. J Pain, 8(11): 887-92.

78.   Kondo M, Nomura M, Nakaya Y et al. 2005. Association of inflammatory marker and highly sensitive C-reactive protein with aerobic exercise capacity, maximum oxygen uptake and insulin resistance in healthy middle-aged volunteers. Circ J, 69(4): 452-7.

79.   Krentz J, Quest B, Farthing J et al. 2008. The effects of ibuprofen on muscle hypertrophy, strength, and soreness during resistance training. Appl Physiol Nut Metab, 33(3): 470-5.

80.   Lang B and Shore A. 1990. A review of current concepts on the pathogenesis of juvenile rheumatoid arthritis. J Rheumatol, 17(21): 1–15.

81.   Latremoliere A and Woolf C. 2009. Central sensitization: A generator of pain hypersensitivity by central neural plasticity. J Pain, 10(9): 895-926.

82.   Lee S, Kim Y, White DA et al. 2012. Relationships between insulin sensitivity, skeletal muscle mass and muscle quality in obese adolescent boys. Eur J Clin Nutr, 66(12): 1366-8.

83.   Leegaard A, Lomholt J, Thastum M et al. 2013. Decreased Pain Threshold in Juvenile Idiopathic Arthritis: A Cross-sectional Study. J Rheum, In Press.

84.   Lelieveld O, van Brussel M, Takken T et al. 2007. Aerobic and anaerobic exercise capacity in adolescents with juvenile idiopathic arthritis. Arth Care Res, 57(6): 898-904.

85.   Lewandowski AS, Palermo TM, De la Mott S et al. 2010. Temporal daily associations between pain and sleep in adolescents with chronic pain versus healthy adolescents. Pain, 15(1): 220–5.

86.   Long A and Rouster-Stevens K. 2010. The role of exercise therapy in the management of juvenile idiopathic arthritis. Curr Opin Rheum, 22(2): 213-7.

87.   Lovell D, Giannini E, Reiff A, et al. 2000. Etanercept in children with polyarticular juvenile rheumatoid arthritis. Pediatric Rheumatology Collaborative Study Group. N Engl J Med, 342(11): 763–9.

88.   Malina R. 1969. Quantification of fat, muscle, and bone in man. Clin Orthop, 65(1): 9-38.

89.   Malina R, Bouchard C, Bar-Or O. 2004. Growth, maturation and physical activity. Human Kinetics. USA. Text.

90.   Malina R and Roche A. 1983. Manual of physical status and performance, in childhood: Vol. 2 Physical performance. New York: Plenum.

91.   Margetic B, Aukst-Margetic B, Bilic E et al. 2005. Depression, anxiety and pain in children with juvenile idiopathic arthritis (JIA). Eur Psych, 20(3): 274-6.

92.   Melzack R. 1999. From the gate to the neuromatrix. Pain, (Suppl 6): S121-S6.

93.   McCabe MP and Ricciardelli LA. 2003. Body image and strategies to lose weight and increase muscle among boys and girls. Health Pyschol, 22(1): 39-46.

94.   McGrath P. 1994. Psychological aspects of pain perception. Archs Oral Biol, 39(Suppl 1): S55-S62.

95.   McGrath P. 1990. Pain in children: Nature, assessment and treatment. Guilford Publications, New York.

96.   McGrath P and Gillsepie J. 2001. Pain assessment in children and adolescents. Handbook of pain assessment, D. C. Turk and R. Melzack, Eds., pp. 97–118, Gilford Press, New York, NY, USA, 2nd edition.

97.   McGrath PA, Seifert CE, Speechley KN et al. 1996. A new analogue scale for assessing children's pain: An initial validation study. Pain, 64(1): 435-43.

98.   McIver, K et al. 2005. Validity of the Actigraph and Actical accelerometers in 3- to 5-year-old children (abstract). Ped Exer Sci, 17(1): 97.

99.   Morton N. 1997. Pain assessment in children. Paed Anaes, 7(4): 267–72.

100.   Murray K, Grom A, Thompson S et al. 1998. Contrasting cytokine profiles in the synovium of different forms of juvenile rheumatoid arthritis and juvenile spondyloarthropathy: prominence of interleukin 4 in restricted disease. J Rheumatol, 25(1): 1388–98.

101.   Murray K and Lovell D. 2002. Advanced therapy for juvenile arthritis. Best Pract Res Clin Rheumatol, 16(1): 361–78.

102.   Murray K, Luyrink L, Grom A, et al. 1996. Immunohistological characteristics of T cell infiltrates in different forms of childhood onset chronic arthritis. J Rheumatol, 23(12): 2116–24.

103.   Nader P, Bradley R, Houts R et al. 2008. Moderate-to-Vigorous Physical Activity From Ages 9 to 15 Years. J Amer Med Assoc, 300(3): 295-305.

104.   Naugel K, Fillingim R, Riley J. 2012. A Meta-Analytic Review of the Hypoalgesic Effects of Exercise. J Pain, 13(12): 1139-50.

105.   Oen K. 2002. Long-term outcomes and predictors of outcomes for patients with juvenile idiopathic arthritis. Best Pract Res Clin Rheumatol, 16(1): 347–60.

106.   Oen K and Cheang M. 1996. Epidemiology of chronic arthritis in childhood. Semin Arthritis Rheum, 26(1): 575–591.

107.   Oen K, Malleson P, Cabral D et al. 2002. Disease course and outcome of juvenile rheumatoid arthritis in a multicenter cohort. J Rheumatol, 29(1): 1989–99.

108. O'Reillya S, Muirb K, Dohertya M. 1999. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. Ann Rheum Dis; 58(1): 15-19.

109. Payne G, Morrow J, Johnson L et al. 1997. Resistance Training in Children and Youth: A Meta-Analysis. Res Quart Exer Sport, 68(1): 80-8.

110. Penpraze, V, Reilly J, MacLean C et al. 2006. Monitoring of physical activity in young children: how much is enough? Ped Ex Sci, 18(4): 483–491.

111. Petty R, Southwood T, Manners P et al. 2004. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheum, 31(2): 390-2.

112. Pertovaara A, Huopaniemi T, Virtanen A et al. 1984. The influence of exercise on dental pain thresholds and the release of stress hormones. Physiol Behav, 33(1): 923–6.

113. Petersen A and Pedersen B. 2005. The anti-inflammatory effect of exercise. J Appl Physiol, 98(4): 1154-62.

114. Philpott JF, Houghton K, Luke A. 2010. Physical activity recommendations for children with specific chronic health conditions: juvenile idiopathic arthritis, hemophilia, asthma, and cystic fibrosis. Clin J Sport Med. 20(3): 167-72.

115. Pincivero D, Lephart S, Karunakara R. 1997. Reliability and precision of isokinetic strength and muscular endurance for the quadriceps and hamstrings. Int J Sports Med, 18(1): 113-117.

116. Pitsavos D, Panagiotakos D, Chrysohoou C et al. 2005. The associations between physical activity, inflammation, and coagulation markers, in people with metabolic syndrome: the ATTICA study. Eur J Cardiovasc Prev Rehabil, 12(2): 151–8.

117. Powell C, Kelly A, Williams A. 2001. Determining the minimum clinically significant difference in visual analog pain score for children. Ann Emerg Med, 37(1): 28-31.

118. Prahalad S. 2004. Genetics of juvenile idiopathic arthritis: an update. Curr Opin Rheumatol, 16(1): 588–94.

119. Puyau M, Adolph A, Vohra F et al. (2002). Validation and calibration of physical activity monitors in children. Obese Res, 10(1): 150-7.

120. Rauch F, Bailey D, Baxter-Jones A, et al. 2004. The 'muscle-bone unit' during the pubertal growth spurt. Bone, 34(5): 771-5.

121. Ravelli A. 2003. Toward an understanding of the long-term outcome of juvenile idiopathic arthritis. Clin Exp Rheumatol, 22(1): 271–275.

122. Ravelli A and Martini A. 2003. Early predictors of outcome in juvenile idiopathic arthritis. Clin Exp Rheumatol, 21(Suppl 31): S89–S93.

123. Ravelli A and Martini A. 2007. Juvenile idiopathic arthritis. The Lancet. 369(9563): 767-78.

124. Reeves N, Maganaris, C, Narici, M. 2003. Ultrasonographic assessment of human skeletal muscle size. Eur J Appl Phys, 91(1): 116-8.

125. Rhodes V. 1991. Physical Therapy Management of Patients with Juvenile Rheumatoid Arthritis. J Amer Phys Ther Assoc, 71(12): 910-9.

126. Robertson W, Stewart-Brown S, Wilcock E et al. 2011. Utility of Accelerometers to Measure Physical Activity in Children Attending an Obesity Treatment Intervention. J Obes, 1:1-8.

127. Robertson RJ, Goss FL, Andreacci JL et al. 2005. Validation of the children's OMNI RPE scale for stepping exercise. Med Sci Sports Exer, 37(2): 290-8.

128. Robusto, K. & Trost, S. 2012. Comparison of three generations of ActiGraph activity monitors in children and adolescents. J Sport Scien, 30(13): 1429-35.

129. Roddy E, Zhang W, Doherty M. 2005. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. Ann Rheum Dis; 64(1): 544-8.

130. Rosen P, Thompson S, Glass D. 2003. Non-HLA gene polymorphisms in juvenile rheumatoid arthritis. Clin Exp Rheumatol, 21(1): 650–6.

131. Roth J, Palm C, Scheunemann I. 2004. Musculoskeletal abnormalities of the forearm in patients with juvenile idiopathic arthritis relate mainly to bone geometry. Arth Rheum, 50(4): 1277-85.

132. Rowlands A. 2007. Accelerometer assessment of physical activity in children: an update. Pediatric Exercise Sciience, 19(1): 252–66.

133. Sallis J, Prochaska J, Taylor W. 1999. A review of correlates of physical activity of children and adolescents. Med Sci Sports Exer, 32(5): 963-75.

134. Sandstedt E, Ander F, Eek M et al. 2013. Muscle strength, physical fitness and well-being in children and adolescents with juvenile idiopathic arthritis and the effect of an exercise programme: a randomized controlled trial. Ped Rheum, 11(7): 1-10.

135. Savedra M, Holzemer W, Tesler M et al. 1993. Assessment of postoperation pain in children and adolescents using the adolescent pediatric pain tool. Nurs Res, 42(1): 5–9.

136. Sawyer G, Whitham J, Roberton D et al. 2004. The relationship between health-related quality of life, pain and coping strategies in juvenile idiopathic arthritis. Rheum; 43(3): 325-30.

137. Schaible H, Ebersberger A, Von Banchet G. 2002. Mechanisms of pain in arthritis. Ann N Y Acad Sci, 966(1): 343-54.

138. Schanberg L and Sandstrom M. 1999. Causes of pain in children with arthritis. Rheum Dis Clin N Am, 25(1): 31–53.

139. Schoels M, van der Heijde D, Breedveld F et al. 2013. Blocking the effects of interleukin-6 in rheumatoid arthritis and other inflammatory rheumatic diseases: systematic literature review and meta-analysis informing a consensus statement. Clin Epi Res, In press.

140. Scola M, Thompson S, Brunner H et al. 2002. Interferon-γ: interleukin 4 ratios and associated type 1 cytokine expression in juvenile rheumatoid arthritis synovial tissue. J Rheumatol, 29(2): 369–78.

141. Schanberg L, Kredich D, Keefe F et al. 1996. Pain coping strategies in children with juvenile primary fibromyalgia syndrome: Correlation with pain, physical function, and psychological distress. Arth Rheum, 9(2): 89-96.

142. Schanberg L, Lefebvre J, Keefe F, et al. 1997. Pain coping and the pain experience in children with juvenile chronic arthritis. Pain, 73(2): 181-9.

143. Schanberg L, Anthony K, Gil K, et al. 2003. Daily pain and symptoms in children with polyarticular arthritis. Arth Rheum, 48(5): 1390-7.

144. Schanberg L, Gil K, Anthony K, et al. 2005. Pain, stiffness, and fatigue in juvenile polyarticular arthritis: Contemporaneous stressful events and mood as predictors. Arth Rheum, 52(4): 1196-1204.

145. Silverman E, Mouy R, Spiegel L et al. 2005. Leflunomide or methotrexate for juvenile rheumatoid arthritis. N Engl J Med, 352(16): 1655–66.

146. Singh G, Athreya B, Fries J. 1994. Measurement of health status in children with juvenile rheumatoid arthritis. Arth Rheum, 37(12): 1761-9.

147. Singh-Grewal D, Wright V, Bar-Or O, et al. 2006. Pilot study of fitness training and exercise testing in polyarticular childhood arthritis. Arth Care & Care, 55(3): 364-72.

148. Singh-Grewal D, Schneider R, Bayer N et al. 2006. Predictors of disease course and remission in systemic juvenile idiopathic arthritis: Significance of early clinical and laboratory features. Arthritis Rheum, 54(5): 1595-601.

149. Singh-Grewal D, Schneiderman-Walker J, Wright V et al. 2007. The effects of vigorous exercise training on physical function in children with arthritis: A randomized, controlled, single-blinded trial. Arth Care Res, 57(7): 1202-10.

150. Singh-Grewal D. 1991. Functional status in juvenile rheumatoid arthritis: sensitivity to change of the Childhood Health Assessment Questionnaire. Arth Rheum, 34(9): S81.

151. Srouji R, Ratnapalan S, Schneeweiss S. 2010. Pain in children: Assessment and nonpharmacological management. Int J Ped; Review: 1-11.

152. Stinson J. 2009. Improving the assessment of pediatric chronic pain: Harnessing the potential of electronic diaries. Pain Res Manage, 14(1): 59-64.

153. Stinson J, Petroz G, Tait G et al. 2006. e-Ouch: Usability Testing of an Electronic Chronic Pain Diary for Adolescents With Arthritis. Clin J Pain, 22(3): 295-305.

154. Stinson J, Petroz G, Stevens B et al. 2008. Working out the kinks: Testing the feasibility of an electronic pain diary for adolescents with arthritis. Pain Res Manage, 13(5): 375-82.

155. Stinson JN, Stevens BJ, Feldman BM, Streiner D, McGrath PJ, Dupuis A, et al. 2008. Construct validity of a multidimensional electronic pain diary for adolescents with arthritis. Pain, 136(3): 281-92.

156. Stone M, Rowland A, Eston R. 2009. Relationships between accelerometer-assessed physical activity and health in children: impact of the activity-intensity classification method. J Sports Sci Med, 8(1): 136-43.

157. Strong WB, Malina RM, Blinkie CJ et al. 2005. Evidence based physical activity for school age youth. J Pediatr, 146(6): 732-7.

158. Szkudlarek M, Court-Payen M, Strandberg C et al. 2001. Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging. Arthritis Rheum, 44(1): 2018–23.

159. Takken T, van Brussel M, Engelbert R, et al. 2008. Exercise therapy in juvenile idiopathic arthritis: a Cochrane review. Eur J Phys Rehabil Med, 44(1): 287-97.

160. Takken T, van der Net J, Helders P. 2001. Do juvenile idiopathic arthritis patients benefit from an exercise program? A pilot study. Arth Care Res, 45(1): 81-5.

161. Tanner J & Whitehouse R. 1976. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child, 51(1):170-9.

162. Taracki E, Yeldan I, Baydogan N et al. 2012. Efficacy of a land-based home exercise programme for patients with juvenile idiopathic arthritis: A randomized, controlled, single-blind study. J Rehabil Med, 44(1): 962-7

163. Telford A, Salmon J, Jolley D et al. 2004. Reliability and validity of physical activity questionnaires for children: The children's leisure activities study survey (CLASS). Ped Exer Sci, 16(1): 64-78.

164.   Thompson S, Moroldo S, Guyer L et al. 2004. A genome-wide scan for juvenile rheumatoid arthritis in affected sibpair families provides evidence of linkage. Arthritis Rheum, 50(1): 2920–30.

165.   Thomson W, Barrett J, Donn R et al. 2002. Juvenile idiopathic arthritis classified by the ILAR criteria: HLA associations in UK patients. Rheumatology, 41(1): 1183–1189.

166.   Todd K, Funk K, Funk J et al. 1996. Clinical significance of reported changes in pain severity. Ann Emerg Med, 27(4): 485-9.

167.   Tracey K. 2007. Physiology and immunology of the cholinergic antiinflammatory pathway. J Clin Inves, 117(2): 289-96.

168.   Tremblay M, Copeland J, Van Helder W. 2004. Effect of training status and exercise mode on endogenous steroid hormones in men. J Appl Physiol, 96(2): 531-9.

169.   Trost, S. McIver K, Pate R. 2005. Conducting accelerometer-based activity assessments in field-based research. Med Sci Sports Exerc, 37(11): 531-43.

170.   Tupper S, Rosenberg AM, Pahwa P et al. 2013. Pain intensity variability and its relationship with quality of life in youths with juvenile idiopathic arthritis. Arth Care Res, 65(4): 563-70.

171.   van Brussel M, van der Net J, Hulzebos E et al. 2011. The Utrecht Approach to Exercise in Chronic Childhood Conditions: The Decade in Review. Ped Phys Ther, 23(1): 2-14.

172.   van den Ende C, Breedveld F, le Cessie S et al. 2000. Effect of intensive exercise on patients with active rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis, 59(1): 615–21.

173.   Van Uum S, Sauvé B, Fraser L, et al. 2008. Elevated content of cortisol in hair of patients with severe chronic pain: a novel biomarker for stress. Stress, 11(6):483-8.

174.   Varni JW, Waldron SA, Gragg RA et al. 1996. Development of the Waldron/Varni Pediatric Pain Coping Inventory. Pain, 67(1): 141–50.

175. Velazquez V, Fisher NM, Venkatraman KM et al. 1999. Effect of resistance exercise on children with juvenile arthritis [abstract]. Arthritis Rheum, 42(Suppl 9): S396-S427.

176. von Baeyer C and Spagrud L. 2006. Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years. Pain, 127(1): 140-50.

177. Watts K, Jones T, Davis E et al. 2005. Exercise training in obese children and adolescents. Sports Med, 35(1): 375-92.

178. Weiss J and Ilowite N. Juvenile idiopathic arthritis. 2005. Rheum Dis Clin North America, 33(3): 441-70.

179. Woods J, Viera V, Keylock T. 2009. Exercise, Inflammation, and Innate Immunity. Immunol Allerg Clin North Amer, 29(2): 381-93.

180. Woolf CJ. 2011. Central sensitization: Implications for the diagnosis and treatment of pain. Pain, 152(Suppl 3): S2-S15.

181. Woolf C and Mannion R. Neuropathic pain: aetiology, symptoms, mechanisms, and management. Pain, 353(1): 1959-64.

182. Woolf C and Salter M. 1999. Neuronal plasticity: Increasing the gain in pain. Science, 288(1): 1765-8.

183. Yildirim M, Verloigne M, de Bourdeaudhuij I et al. 2011. Study protocol of physical activity and sedentary behaviour measurement among schoolchildren by accelerometry - Cross-sectional survey as part of the ENERGY-project. BMC Public Health, 11(1): 182-9.

184. Yilmaz M, Kendirli S, Altintas D et al. 2001. Cytokine levels in serum of patients with juvenile rheumatoid arthritis. Clin Rheumatol, 20(1): 30–5.

Appendix 1-International League of Rheumatology Classification of Juvenile Idiopathic Arthritis

Category	Diagnostic criteria
Systemic	Fever of at least 2 weeks' duration (daily for at least 3 days) and arthritis in ≥1 joint, plus one more of the following: Erythematous rash, generalized lymph node enlargement, hepatomegaly and/or slenomegaly, or serositis Exclusions: a, b, c, d
Oligoarticular	Arthritis affecting ≤4 joints during the first 6 months of disease. There are 2 subcategories: Persistent: affecting no more than 4 joints throughout the disease course Extended: affecting more than 4 joints after the first 6 months of disease Exclusion: a, b, c, d, e
Polyarticular RF(-)	Arthritis affecting ≥5 joints during the first 6 months of disease Test for RF is negative Exclusions: a, b, c, d, e
Polyarticular RF(+)	Arthritis affecting ≥5 joints during the first 6 months of disease 2 or more test for RF at least 3 month apart during the first 6 months of disease are positive Exclusions: a, b, c, e
Psoriatic	Arthritis and psoriasis, or arthritis and at least 2 of the following: Dactylitis, nail pitting or onycholysis, psoriasis in a first-degree relative Exclusions: b, c, d, e
Enthesitis-related	Arthritis and enthesitis, or arthritis or enthesitis with at least 2 of the following: The presence of or a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain The presence of HLA-B27 antigen Onset of arthritis in a male over 6 years of age Acute (symptomatic) anterior uveitis History of anklosing spondylitis, enthesitis related arthritis, sacrolitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative Exclusions: a, d, e
Undifferentiated	Arthritis that fulfills criteria in no category or in 2 or more of the above categories

* Reproduced from Kim & Kim, 2010.

One of the major aims of the ILAR classification is the mutual exclusivity of the subtypes. Therefore, the following list of possible exclusion for each category was defined:

a) Psoriasis or a history of psoriasis in the patient or first-degree relative.

b) Arthritis in an HLA-B27-positive male beginning after the sixth birthday.

c) Ankylosing spondylitis, enthesitis-related arhtiris, sacroiliitis with inflammatory bowel disease or acute anterior uveitis or a history of one of these disorders in a first-degree relative.

d) The presence of IgM rheumatoid factor and at least two occasions at least 3 months a part.

e) The presence of systemic JIA in the patient

RF=Rheumatoid factor

Appendix 2- Pictures for Each of the Seven Resistance Exercises

Exercise 1   Exercise 2   Exercise 3

Exercise 4

Exercise 5   Exercise 6

Exercise 7

Appendix 3- Pain Diary Questions and Practice Vignette

General Electronic Diary Instructions

Now it's your turn to try the diary on the tablet. We will go through the questions slowly the first time so we can talk about what they mean and how to answer them. Then I'll ask you to answer the questions based on a story so you can practice. Some people find this hard to do and others find it fairly easy. I want to know how it is for you. You can ask me questions at any time as we go through it.

The diary will allow you to answer the end-of-day questions once a day and the pre and post exercise questions three times a week. You should try to answer the pre-exercise questions just before you do you exercise and the post-exercise questions right after you do your exercise. When you answer the questions over the next seven weeks, I want you to do this by yourself. Don't ask your friends, teachers or family to answer them for you. These questions are about how you are feeling, so we want you to answer them. If you have any questions about how to answer the diary questions or are having a problem with the diary, I want you or a parent to call me or email me right away and I'll help you.

Let's take a look.

Once you press the icon to enter the diary you will see three boxes labeled "pre-exercise, post-exercise, and end-of-day questions." There are only a couple of differences between the three times of day. The correct one for you to use will be lit up. Open the "end-of-day questions" by pressing "end-of-day questions" now and we'll go through the questions.

End-of-Day Questions

The first question asks you to show on the left body picture where you hurt or have pain. You can choose as many locations as you need to show where you hurt or have pain. Why don't you try and touch all the areas where you have hurt or pain right now. To the right of that body picture is another one where I would like you to select where you have had body pain at any time throughout the day. If you have had no pain at all, click the button "no pain". This question is done for both the front and back of you on separate pages. After you have answered each, click next.

The next question asks you to show how much pain or hurt you have right now. To answer this question, you should move the marker somewhere on this line between "no pain" and "most pain possible" to show how much you hurt. Why don't you try and slide the marker to show how much hurt or pain you have right now. Then click next.

The next question asks you to tell how bad or good your pain is right now. To answer this question, you need to select a face that best matches the amount of pain you have right now. Try and select a face that you feel best matches the way you feel right now. Then click next.

The next questions ask how pain has affected the things you do; your walking and sleeping, seeing your friends, and enjoying life. To answer each of these questions you should slide the mark somewhere on the line, between "doesn't get in the way at all" and "totally got in the way" to show how much pain has affected or interfered with these things in your life. Now why don't you try and touch the screen to show how much pain has affected things you do (or sleep, feelings, seeing friends, enjoying life) right now. Here is where the questions between each time of day are different. In the afternoon, there is a question asking if pain has gotten in the way of

schoolwork and relationships with friends or family and in the evening it asks about pain getting in the way of relationships. Then click next.

The next question asks you to tell us how much your pain got in the way of you sleeping last night. To answer this you need to select "Pain did not get in the way of my sleep last night" or "Pain got in the way of my sleep last night". If you answer that the pain did get in the way of your sleep last night you will be taken to a new page to answer if your pain how it got in the way of your sleep. You will have the option of answering "I had a hard time falling asleep last night because of pain" and/or "My pain woke me up last night". If you answer that your pain woke you up you will be taken to a new page that will ask you if your pain woke you up once or multiple times the previous night. You will answer "My pain woke me up once last night" or "My pain woke me up more than once last night".

The next question asks you to choose words that describe how your pain feels. To answer this question, you should choose the words that best tell how your pain feels right now. The list has many different words and they are grouped in ways that the words are similar. You can select as many words as you feel describe your pain. If none of the words describe your pain, you don't have to select any. Then click next.

The next question asks you to tell how stiff your joints or muscles feel. To answer this question, you should slide the marker somewhere on this line between "not at all stiff" and "most stiffness possible." Why don't you try and slide the marker to show how much stiffness you feel in your joints or muscles right now. Then click next.

The next question asks you how fatigued/tired you feel right now. To answer this question you need to slide the marker somewhere on this line between "not at all fatigued" and "most fatigued

possible". Why don't you try and slide the marker to show how fatigued you feel right now. Then click next.

The next question asks you to tell how good or bad your mood is right now. To answer this question, you should touch the face that best shows how you are feeling inside from "very bad" to "very good." It's not just how your face looks, but how you really feel inside right now. Touch the face now that shows how you are feeling. Then click next.

The next question asks how awake or sleepy you feel. Even though you are awake, sometimes you feel very energetic and sometimes you feel very tired and sleepy. To answer this question, you should slide the marker somewhere on this line between "very sleepy" and "very awake" to show how awake or sleepy you feel right now. Slide the marker now to show how sleepy or awake you feel right now. Then click next.

The next question asks if you took any pain medicines to help with your pain since the last time you answered the diary. If you took pain medicine, touch the yes button and another question will pop up to ask how helpful the medicine was in making your pain feel better. Press the yes button to practice this question. Slide the marker on the line somewhere between "no relief at all" and "complete relief." "No relief" means the medicine didn't help at all and "complete relief" means it took all of your pain away. Slide the marker now to show how much your last pain medicine helped with your pain. If child or adolescent states they have not taken medicine recently, say "For practice think about the last time you took medicine for pain and how much it helped." If you took medicine for pain I want you or a parent to fill in what you took on the medication and treatment log. Mark in what medicine you took, how much you took and when you took it. Then click next.

The next question is similar but it asks about what other types of treatments you tried to help make your pain better. For example, some people try stretches, massage or physiotherapy, or relaxation exercises, hot baths or ice packs to help make pain better. If you tried something other than a medicine to help make pain better, then answer the question about how much it helped just the same as the last. If you tried other things to help with your pain, I want you or a parent to fill in what you did on the medication and treatment log. Mark in what you did and when you did it. Then click next.

Finally, the diary gives you a chance to write anything down about your pain, the study, your activity or your treatments. Touch the white box and a keyboard will pop up. If you wanted to use a different word to describe your pain that wasn't on the list before, you can write that word here. You can also write down if you took medicine or other treatments for pain here instead of on the paper log. You don't have to write anything in here if you don't want to. In that case you just click "I have no extra comments".

After you're finished, a box will pop up telling you that you're done. Press submit and the screen will go blank. Press the home button and it will be returned to the opening screen and it will be ready for the next time.

Post exercise Questions

We will now run through the "post exercise questions" so that you can get a hang of how they are different from "end-of-day questions." For this you need to select "post-exercise questions."

The first ten questions are the same as "end-of-day questions" and so you can answer them in the same way. After asking you about how sleepy or awake you feel, the next questions will ask you about the exercises you just did.

The first of these questions will ask you how hard you felt the exercises that you just did were. There will be pictures with a person looking very energetic to someone who looks exhausted. Underneath this there will be numbers from 0 to 10. 0 means you felt the exercise was the easiest possible and 10 means you felt it was the hardest exercise you ever did. To answer this question you need to select a number that you feel is how hard the exercises were. Then click next.

The next set of questions will ask you about each individual exercise. You will need to answer five questions for each of the seven exercises you did in the video. The first exercise questions you will answer will be on the "squat", then "lunges", followed by "step-ups", "plank", "seated-row", "bicep-curl/shoulder-press", and finally "push-ups." For each of these exercises you will need to answer as follows:

Were you able to complete the exercise as described on the video? To answer this question you need to answer yes or no. Yes means you were able to do the exercise in the same way as the instructor in the video. No means you had to modify (change) the exercise so that it didn't cause you as much pain. After answering this, click the next arrow button.

The next question asks you how many repetitions of the exercise you were able to complete for each of the 3 sets of the exercises. A repetition means that you were able to do the full movement one time (example: one push-up). Ten repetitions means you did the movement ten times. One set counts as the group of repetitions that you performed for one exercise in each circuit. This means that you are doing 3 sets of each exercise, one in the first circuit, one in the second and one in the third. You need to tell me if you did "0-1", "2-5" or "6 or more" repetitions for each of your sets. Then click next.

The next question asks you if you changed the exercise in any way from how it was described in the video. If you answer "yes" to this question then you need to describe how you changed the exercise in the next window by typing it in the open texting box. If you answer "no", you will move on to the next question by clicking the next arrow.

The next question asks you if you had increased pain during while doing that exercise. If you answer "yes" and click the next arrow, then you will be presented with a visual analog scale where you can rank your pain from "no pain" to "most pain possible". If you answer "no" you will move on to the same set of questions with the next exercise after clicking the next arrow.

This will be done for all seven exercises.

Finally, the diary gives you a chance to write anything down about your pain, the study, your activity or your treatments. Touch the white box and a keyboard will pop up. If you wanted to use a different word to describe your pain that wasn't on the list before, you can write that word here. You can also write down if you took medicine or other treatments for pain here instead of on the paper log. You don't have to write anything in here if you don't want to. In that case you just click "I have no extra comments".

After you're finished, a box will pop up telling you that you're done. Press submit and the screen will go blank. Press the home button and it will be returned to the opening screen and it will be ready for the next time.

Before exercise

We will now run through the "before exercise" questions so that you can get a hang of how they are different from "end-of-day questions" and "post-exercise" questions. For this you need to select "before exercise".

The initial set of questions are the same as "end-of-day questions" and so you can answer them in the same way. It will not ask you how much your pain affected the things you do or did that day and it will also not ask you if your pain got in the way of your sleep.

The last question will be asking you about how sleepy or awake you feel. After this the final question will be an open texting box. The diary gives you a chance to write anything down about your pain, the study, your activity or your treatments. Touch the white box and a keyboard will pop up. If you wanted to use a different word to describe your pain that wasn't on the list before, you can write that word here. You can also write down if you took medicine or other treatments for pain here instead of on the paper log. You don't have to write anything in here if you don't want to. In that case you just click "I have no extra comments".

After you're finished, a box will pop up telling you that you're done. Press submit and the screen will go blank. Press the home button and it will be returned to the opening screen and it will be ready for the next time.

You are now ready to begin your exercises.

Practice Vignette

Now let's practice with the diary again by going through a story.

It's first thing in the morning. You day is complete and you are getting ready to go to bed.

Right now you have pain in your (name a body location where the youth typically feels pain), and at some other point in the day you also had pain in your (name a body location where the youth typically feels pain). Wait for youth to touch the correct body location and move to the next page. If necessary, prompt child again to press the next button to move forward in the survey. They will do this for the front and back of themselves.

Where would you slide the marker if I said that you only had a little bit of pain? (Youth should slide marker to the left indicating a lower level of pain). Show me again where you would slide the marker if you were having a lot of pain (youth should slide the marker to the right indicating a higher level of pain.) Okay, let's move to the next question.

Which face would you select if your pain was feeling really bad and hurting you a lot? (Youth should select the face that looks most upset or at least very upset). Show me which face you would select if you had a great day and your pain did not affect you much. (Youth should select a face with a smile on it

You have a medium amount of pain that is getting in the way of doing some things, but not very much. Where would you slide the mark to show how much your pain is interfering or getting in the way of you doing things? (Youth should slide marker below the midway line) Where would you slide the marker if I said that it was really getting in the way of doing things? (Youth should slide marker to the right indicating a higher level of general interference)

When you went to bed last night your pain affected your sleep. Which button do you select? (youth should select pain got in the way of sleep). Which would you select if you fell asleep right away, but your pain woke you a couple of times in the night? (Youth should select pain woke me up only and then select that it woke them up multiple times).

Now we're at the page where you get to choose the words that best describe how your pain feels. You can describe your pain any way you want right now.

Where would you place the marker if throughout the day your joints and body felt really stiff. (youth should select close to most stiffness possible). If you felt very flexible that day where would you place the marker? (youth should select close to not stiff at all).

If you felt tired all day where would you place the marker? (youth should place the marker close to most tired possible). Rather, if you felt very energetic during the day where would the marker go (youth should place the marker close to not at all tired).

When you woke up you were feeling not really in a good or bad mood – just kind of neutral. Where would you place the marker to show this? (Youth should place marker near the middle).

Now you feel wide awake and really energetic. Where would you slide the marker to show feeling awake? (Youth should slide marker to most awake possible).

You didn't use any medication this morning for pain. (youth should select "no" button and move to the next page). But you did some stretches to try to make the pain in your (name body part) better. The stretches helped a little. Where would you slide the marker to show that the stretches helped a bit? (youth should place the marker to the left of midline)

Now you can type whatever you want in the open box.

We will now go over a few of the questions in the after exercise questionnaire to make sure you understand.

If you felt very tired after doing the exercises that day, which number would you select? (Youth should select a high number in the 8 to 10 range). If the exercises were not hard at all and you felt it was easy, which number would you select? (Youth should select in the 0 to 3 range).

If you were not able to complete the exercises the same way you were shown in the video, what would you select? (Youth should select "no")

If you were able to finish 7 repetitions for set 1, 4 for set 2, and 3 for set 3, which buttons would you select? (Youth should select 7 under set 1, 4 under set 2, and 3 under set 3).

If you changed the exercise from the way it was shown in the video because it hurt your knees so you didn't bend down as far, which button would you select? (Youth should select "Yes") Youth should then type that they didn't bend down as far.

While doing the exercise you felt a lot more pain in your knee. Which button would you select? (Youth should select "Yes") Youth should then drag the marker closer to the most pain possible side.

This will finish off the tutorial of how to use the app. Do you have any questions?

Pharmacological treatment log

Here you/your parent will fill in what medicine you took, how much you took, and when you took it.

Non-pharmacological treatment log

Here you will fill in if you used treatments not prescribed by your doctor. You will need to write what you did/took to treat, when you did it, and how much you used if it was a medicine.

Example pages

Body Location: Front

Menu

Places I have pain RIGHT NOW

No pain on the front

No Pain

Pain Diary © 2012

Stiffness question

Menu

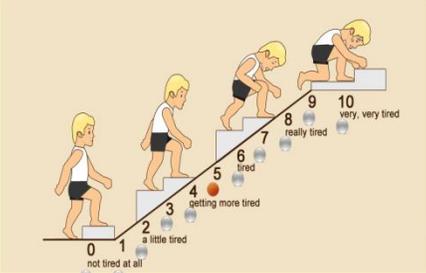Drag the mark to show how STIFF you are rigth now.

Not at all stiff ———————————————— Most stiffness possible

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Rate of perceived exertion

Menu

How tired does your body feel during exercise?

10 very, very tired
9
8 really tired
7
6 tired
5
4 getting more tired
3
2 a little tired
1
0 not tired at all

PInGo Pain Diary © 2012

List of words to describe the p…

Menu

Touch the words that best describe how your pain feels right now.

Sore	Pinching	Tiring
Aching	Tingling	Sickening
Pins and needles	Biting	Sad
Stinging	Burning	Cruel
Squeezing	Sharp	Punishing
Pounding	Cold	Fearful
Pulling	Scraping	Uncomforta…
Itching	Cutting	Miserable
Beating	Jumping	Horrible
Pricking	Flashing	Unbearable
Throbbing		None of these words

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Appendix 4- Accelerometer Log

Participant ID:_____

ACCELEROMETER LOG-PinGo study

	Weekday 1	Weekday 2	Weekday 3	Weekday 4	Weekday 5	Week**end** 6	Week**end** 7
Date (day/month/year)							
Time you woke up (circle am or pm)	--------- am/pm	--------- am/pm	--------- am/pm	--------- am/pm	--------- am/pm	--------- am/pm	--------- am/pm
Time in the morning you put on the accelerometer	--------- am	--------- am	--------- am	--------- am	--------- am	--------- am	--------- am
Time at night when you took off the accelerometer	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm
Time you went to bed	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm	--------- pm

Other times you didn't wear the accelerometer and why?							
Was this a typical day for you? (yes/no) If no, why not?	(yes/no)	(yes/no)	(yes/no)	(yes/no)	(yes/no)	(yes/no)	(yes/no)

Appendix 5: Closing Questionnaire

Participant ID:_____

Closing Questionnaire

1. Did you enjoy the exercise program?

2. Would you like to see anything different about the exercise program?

3. Do you feel it improved your quality of life (well-being) as a whole?

4. Did you enjoy using the app/tablet?

5. Was there anything about the tablet you would like changed?