Relationships between psychosocial functioning of the child, parental coping and pain in juvenile idiopathic arthritis: cross-sectional and longitudinal analyses.

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I. ABSTRACT

Chronic pain in juvenile idiopathic arthritis is poorly understood. Although there is a link between pain and disease activity, pain is also modulated by other factors. The psychosocial functioning of the child is linked to his/her pain experience, however direction of causality is unknown. Furthermore, the potential association between parental coping and children's pain has never been explored. The objectives were to evaluate relationships between psychosocial functioning of the child, parental coping, and concurrent pain and future pain report at 6 months. The database "Determinants of outcomes for juvenile arthritis" from the Montreal Children's Hospital, including 95 patients, was used. Hierarchical multiple linear regression was performed. Psychosocial functioning of the child was identified as a correlate of pain, above and beyond disease activity, in the cross-sectional analysis. However, it did not predict future pain. Use of the parental coping pattern "social support" was associated with less concurrent pain.

La douleur chronique dans l'arthrite juvénile idiopathique demeure incomprise. Quoique qu'il y ait un lien entre la douleur et l'activité de la maladie, la douleur est modulée par d'autres facteurs. La fonction psychosociale de l'enfant est liée à son expérience de la douleur, mais la direction de la causalité est inconnue. De plus, l'association potentielle entre l'habileté d'adaptation parentale et la douleur des enfants n'a jamais été explorée. Les objectifs étaient d'évaluer les relations entre la fonction psychosociale de l'enfant, l'habileté d'adaptation parentale, et la douleur concomitante ainsi que la douleur future rapportée à 6 mois. La banque de données "Determinants of outcomes for juvenile arthritis" de l'Hôpital de Montréal pour enfants, qui inclut 95 patients, a été utilisée. La technique de régression linéaire multiple hiérarchique a été appliquée. Dans l'analyse transversale, la fonction psychosociale de l'enfant a été identifiée comme étant un corrélat de la douleur. Par contre, elle n'a pas contribué à prédire la douleur

future. L'utilisation de la stratégie d'adaptation parentale "support social" est associée à une douleur concomitante moindre.

II. INTRODUCTION

Juvenile idiopathic arthritis (JIA) is one of the most common chronic diseases of childhood. Pain is an important symptom experienced by most children with this condition, yet it is still poorly understood. Although there is a direct link between the degree of disease activity and pain, it is likely that pain is modulated by other factors pertaining to the child and his/her environment. Furthermore, the directionality of the association between pain and some of these factors has never been elucidated. The purpose of this study was to identify correlates and predictors of pain in children with JIA. More specifically, the role of psychosocial functioning of the child and parental coping on concurrent and future reports of pain intensity was examined.

This study used data from the study "Determinants of outcomes for juvenile arthritis", which was originally designed to characterize treatment adherence, economic outcomes, disease course, pain and disability as well as health-related quality of life. Several articles have been published from this study, pertaining to treatment adherence, use of complementary and alternative medicine, economic impact, parental coping and quality of life (see Appendix 1). Here, the cross-sectional and longitudinal relationships between the psychosocial functioning of the child, parental coping and pain intensity in children with JIA were evaluated.

III. REVIEW OF THE LITERATURE

1. Juvenile Idiopathic Arthritis

JIA is a chronic inflammatory disease, with a predominant effect on joints. The International League of Associations for Rheumatology (ILAR) defines JIA as an arthritis that begins prior to the 16th birthday, persists for at least 6 weeks and is of unknown etiology. Alternative causes of arthritis must be excluded. JIA represents a heterogenous group of disorders. ILAR revised the classification of JIA for a third time in 2001, which is now used and applied in Canada and most countries (1). The main purpose of the classification is to define relatively homogenous and mutually exclusive categories of JIA, in order to facilitate research and communication among the international pediatric rheumatology community. JIA is the focus of the thesis, as opposed to Juvenile Rheumatoid Arthritis (JRA) defined by the American College of Rheumatology (ACR) (2). JIA is classified into seven categories, each defined by clinical and laboratory criteria, and a list of potential exclusions. The categories are: oligoarthritis, polyarthritis rheumatoid factor negative, polyarthritis rheumatoid factor positive, systemic arthritis, psoriatic arthritis, enthesitis-related arthritis (ERA) and undifferentiated arthritis.

Oligoarthritis is the most common category of JIA and is defined as an arthritis affecting 4 or fewer joints in the first 6 months of disease. It usually affects young girls, and is often associated with antinuclear antibody positivity and a higher risk for the development of chronic anterior uveitis. Children with polyarthritis rheumatoid factor (RF) negative have 5 joints or more involved within the first 6 months of disease. It is more common in girls. Polyarthritis RF positive is common in teenage girls and represents the smallest category of JIA, making up about 5% of all patients. It may be considered as “adult” rheumatoid arthritis with childhood onset and is associated with a poor prognosis. Erosive changes are seen early in the disease course, and rheumatoid nodules and distinct

deformities of the fingers often develop. Systemic arthritis is characterized by unique extra-articular manifestations, including daily fever (quotidian) in addition to the joint symptoms. Most children have a characteristic rash, and some have lymphadenopathy, hepatosplenomegaly or serositis. It has no sex predominance and has a variable age of onset. Psoriatic arthritis is defined as arthritis and psoriasis, or arthritis in association with dactylitis, nail abnormalities or a family history of psoriasis. It is recognized that not all children have psoriasis at the onset of disease, however approximately half of them develop psoriasis after 2 years (3). Girls are affected more than boys, and a bimodal age distribution is described. ERA was first introduced as a category in the ILAR classification of JIA in 1995. It is defined as the presence of arthritis and enthesitis, or arthritis or enthesitis in association with sacro-iliitis/inflammatory spinal pain, presence of HLA-B27, family history of HLA-B27-related disease, or acute anterior uveitis. Enthesitis is tenderness at the insertion of a tendon, ligament, joint capsule or fascia to bone, and is often very painful. ERA is much more frequent in boys, tends to affect older children and teenagers, and is uncommon prior to the 6^{th} birthday. Given the recent introduction of this category, there is a lack of data on its epidemiology and outcomes. However it is presumed, based on studies of related diseases, that most children evolve towards well-defined spondyloarthropathies, such as ankylosing spondylitis, which are diseases characterized by inflammation of entheses, the sacro-iliiac joints and the lumbosacral spine. Children who fulfill criteria in no category or in 2 or more of the above categories are classified with undifferentiated arthritis.

Most of the body of literature on pain in children with chronic arthritis is on JRA. The criteria for the classification of JRA were initially proposed in 1972 by the ACR, and subsequently revised (2). The criteria were widely applied mainly in North America and recognized only three onset types, defined by type of disease within the first 6 months, which are polyarthritis (5 or more joints involved), pauciarthritis (4 or fewer joints involved) and systemic-onset. Children with psoriatic arthritis and spondyloarthropathies were not recognized. In recent

years, the ILAR classification of JIA has gained acceptance internationally, and most published studies now use the term JIA (1). While the term JIA is preferentially used in place of JRA in this thesis, it is acknowledged that the terms are not synonymous and that there are clear and distinct differences. The significance of the recognition of the category ERA vis-à-vis pain may be particularly important. While there are no studies on the pain experience of children with ERA, clinical experience has led some rheumatologists to believe that they have more pain than children belonging to other categories of JIA. Moreover, their pain may be more generalized and not limited to areas of active inflammation (4). The presence of enthesitis, a major feature of the spondyloarthropathies, may play a role in explaining this difference. McGonagle showed with fat-suppressed MRI that early knee synovitis in spondyloarthropathies, but not in rheumatoid arthritis, is associated with prominent and distinct entheseal abnormalities, including soft tissue changes adjacent to entheseal areas outside the joint and bone marrow edema at entheseal insertions (5). This finding may suggest that the mechanism of synovitis in the spondyloarthropathies, including ERA, may be different than in other forms of chronic arthritis.

There are no prevalence studies of JIA. The prevalence of JRA is about 1/1000 children, which makes it one of the most common chronic diseases of childhood (6). However, this likely represents an underestimation of the true prevalence of JIA, in light of the recognition of two distinct conditions, psoriatic arthritis and ERA, and likely better diagnosis of affected children in recent years. Although age of onset is quite variable depending on JIA category, the disease often starts early, with a large peak observed between 1 and 3 years of age. This distribution of age of onset is less impressive for boys, who have a second peak between 8 and 10 years of age (7). Girls are affected twice as commonly as boys, however differences in this ratio are seen according to JIA category.

Although its precise etiology is not known, JIA is a multi-factorial disease where both genetic predisposition and environmental factors are important. The end-result is a shift towards the over-production of pro-inflammatory cytokines, which results in synovitis (inflammation of the synovial membrane of the joints) and an increased production of synovial fluid. The inflammation leads to clinical signs of local warmth, swelling, tenderness, stress pain (pain experienced with movement of the joint) and diminished range of motion of the affected joints. The most commonly reported symptoms are pain, fatigue and morning stiffness. When partially controlled or untreated, JIA results in permanent loss in range of motion, deformities, localized growth disturbances and joint destruction.

Varying degrees of functional disabilities have been reported. In a retrospective cohort study of patients followed in three Canadian pediatric rheumatology centres, Oen demonstrated that, although functional outcome has improved over the past decades, disability develops in a large proportion of patients (8). While most patients with pauciarticular JRA had no or only mild disability on the Childhood Health Assessment Questionnaire (CHAQ) (9), more than half of patients with RF positive polyarthritis and more than one third of patients with systemic arthritis and RF negative polyarthritis developed moderate or severe disability at a median interval of 10 years after onset of disease. The prognosis of JIA is variable, with more than one half of children continuing to have active disease well into adulthood. In the same study, only 37% of patients with systemic, 23% of patients with RF negative polyarticular, 47% of patients with pauciarticular and 6% of patients with RF positive polyarticular JRA achieved remission at 10 years after onset of disease, and the probability of continued active disease into the twenties or thirties was high for patients who were not in remission by 16 years of age. The rate of arthroplasty was high for patients with systemic arthritis and RF positive polyarthritis, who were at considerable risk for serious damage to the hips. These data suggest that outcomes for JIA may not be as good as previously considered.

2. Pain in Juvenile Idiopathic Arthritis

Pain related to JIA is an area of research that has been relatively under-investigated. This may be partly explained by an earlier misconception that children with arthritis experienced little pain, in comparison to adults with rheumatoid arthritis. However Beales, in a qualitative study, showed that children of different age groups were able to adequately describe discomfort in their joints when using developmentally and age-appropriate measures (10;11). In fact, chronic pain is an important symptom experienced by children in all JIA categories. Sherry found that 86% of children reported pain during a routine clinic visit (12). Forty percent of children continue to have pain five years following disease onset according to data from the Cincinnati Juvenile Arthritis Databank (13). Schanberg reported considerable variability in pain ratings. While most children experienced pain of mild-to-moderate intensity when measured on a Visual Analogue Scale (VAS), 25% reported pain in the middle to high ranges (14). The same author, using daily diaries, showed that children reported pain on 70% of days, suggesting that even children with mild disease experience pain almost on a daily basis (15).

The chronic pain of JIA, unlike acute pain, is often accompanied by a variety of reactive features such as mal-positioning of involved joints and abnormal pattern of movements, lack of developmentally appropriate behaviours, depressed mood and restriction in the normal activities of daily living (16). Two studies also suggested that children with JIA develop reduced pain threshold and pain tolerance over time. Using pressure algometry, Hogeweg found that children both with active chronic arthritis and those in remission had reduced pain thresholds not only over inflamed but also over normal joints, in comparison to healthy children (17;18). Similarly, Thastum showed that children with arthritis had reduced pain tolerance compared with healthy children using an experimental cold pain task (19). Children with JIA often continue to experience pain well into adulthood. An outcome study of JIA into adulthood demonstrated

that about half of the adults had pain (20). In addition, patients who experienced pain were not only those with active disease but also a smaller group in remission, suggesting that remission does not always bring resolution of pain. Altogether, these studies suggest that children with JIA may develop an enhanced sensitivity to repetitive noxious stimuli, a process called "central sensitization". In central sensitization, changes in pain processing and amplification of pain occur as a result of prolonged and recurrent activation of the peripheral and central nociceptive nervous systems, which bring structural and functional changes in neuronal pathways (15). Another explanation for the persistence of pain in the context of disease inactivity is the development of joint damage or secondary osteoarthritis (20).

The treatment of pain associated with JIA usually involves controlling the disease with medications aimed at decreasing inflammation, namely nonsteroidal anti-inflammatory drugs (NSAIDs), and medications aimed at suppressing the immune system, such as methotrexate, sulfasalazine, leflunomide and biologic agents (etanercept, infliximab, adalimumab, abatacept). Intra-articular corticosteroid injections can be used when one or several joints are problematic despite adequate systemic treatment. Symptomatic relief of pain is also provided with acetaminophen, heat, warm baths, splints and physiotherapy. Systemic corticosteroids, while usually avoided, may sometimes be used for short periods to treat painful flares, as one waits for other systemic medications to take effect (15). The use of opioids has been limited (21;22). Despite all of these measures, a survey of pediatric rheumatologists found that 77.3% acknowledged that children with arthritis continue to have clinically significant pain (23).

3. Pain measures in Juvenile Idiopathic Arthritis

Several age-appropriate measures of pain that appear to be reliable and valid in children with JIA have been developed since Beales first reported that children

with chronic arthritis are able to describe sensations in their joints (10). Most tools for research and clinical use in JIA are self-report measures of children's pain, rated by the child or a parent. Jaworski also described a behavioural observation method where trained observers code pain behaviours during a 10-minute standard protocol of activities that children are asked to perform (24). However, this pain assessment method is impractical for use in the clinical setting.

The Varni/Thompson Pediatric Pain Questionnaire (PPQ), well documented for its use in JIA, is a multidimensional and comprehensive instrument that uses structured interviews with both the parent and child (25). The tool utilizes several techniques including: (1) the VAS to evaluate present and worst pain intensity in the previous week, (2) the body outline to describe pain location and intensity using a color-coded pain rating scale, (3) and pain descriptors to assess the sensory, affective and evaluative qualities of the child's pain experience. Although not practical for use because of its length, portions of it, such as the VAS, have been used in the clinic setting. The VAS is a 100 mm horizontal line anchored with developmentally appropriate pain descriptors, such as happy and sad faces or "not hurting" and "hurting a whole lot", and without numbers, marks or descriptive words along the line. The VAS has been shown to be reliable and valid in children as young as 5 years, and is the most widely used tool to evaluate pain intensity in JIA (26;27). The body outline is particularly useful in children with arthritis older than 4 years who have pain in multiple locations because it allows for the evaluation of another pain dimension in addition to pain intensity.

Other variations of the VAS include the Oucher Facial Scale and the pain thermometer. The Oucher is a facial scale, consisting of six photographs of a child's face displaying varying degrees of discomfort, along an 11-point 100 mm scale (28). It was shown to be reliable and valid in many pediatric populations over a wide age range. It is simple and easy to administer, and even young children can use it. Versions for White, African-American and Hispanic

populations are available. One problem is that it may evaluate pain affect more than pain intensity. Other facial scales are also available for children. The pain thermometer is a 100 mm vertical scale on which children draw a line corresponding to how much pain they are experiencing (29;30).

Schanberg used daily diaries in order to track pain and related symptoms of fatigue and stiffness on a day-to-day basis, making it possible to analyze relationships between pain and behavioural responses such as activity reduction (31). She demonstrated that the diary method was feasible and well accepted by children older than six years of age. Stinson recently demonstrated the ease of use and validity of the e-Ouch, an electronic version of a chronic pain diary, in adolescents with JIA (32).

4. Relationship between disease activity and pain

Generally, studies have indicated that there is a direct relationship between the degree of disease activity and children's report of pain in JIA. Varni demonstrated a positive correlation between physician's assessment of disease activity and present pain intensity rated by the child on a VAS (25). Similarly, Vandvik reported a positive correlation between a global score of disease severity rated by physicians and children's ratings of pain intensity on the VAS (33). However, these studies and others have shown that disease activity only explained a modest amount of the variance in pain intensity ratings, ranging from 1 to 33% in various regression models, suggesting that other factors may be relevant in explaining children's pain (14;33-42). Thompson reported that disease activity explained only 1% of the variance in present pain and 23% of the variance in worst pain in the previous week measured on the VAS (34). In a large multi-centre study of 388 patients, Malleson showed that disease activity only explained 6.5% of the variance in pain intensity in the previous week measured on the VAS (37). Similarly, Schanberg demonstrated that disease

activity only explained 28% and 33% of present pain intensity measured on the pain thermometer and the Oucher, respectively (40).

Different methodologies used in the assessment of pain may explain the disparate findings in the association between disease activity and pain. Most studies (14;37-41), which assessed pain intensity using a VAS with descriptive words, found modest associations between disease activity and pain, except for Hagglund who failed to show a statistically significant association (36). Some authors assessed pain concurrently (14;38;40;41), while others assessed pain during the past week (37), or month on a VAS (36). Scores for worst pain in the previous week rather than present pain might correlate better with disease activity, because pain is usually more severe when one is involved with daily activities, as compared to when one is at rest in a waiting room or clinic (43). Symptoms of JIA wax and wane over time, and therefore measurement of pain over the past month possibly brings greater variability in pain ratings and also potentially recall bias. This may explain why the regression model developed by Hagglund failed to reach statistical significance (36). Thastum reported that disease activity explained 12% of the variance in pain when children were asked to complete a 3-week pain diary that included a facial scale (35). Disease-related variables explained a small proportion (13%) of variance in pain measured on a body map in a study by Schanberg (14).

Another potential explanation for these disparate findings is the use of proxies to report pain. While in most studies children were asked to rate their pain on self-report measures (14;36;37;40), other studies used parents, mainly mothers, as proxies (38;39). This may be a problem if parents underestimate or overestimate their child's pain. Young children are usually unable to complete self-report measures, and therefore reliance on parental report is necessary. Teenagers, on the other hand, may not communicate well with their parents. For example, Shaw reported wide variation in agreement between adolescents with JIA and their parents with regards to pain, measured on the VAS, and other health-related

variables (44). In addition, children with depressed mood tend to be withdrawn and thus may have difficulty communicating effectively with their parents. Indeed, Palermo found that child depressive symptoms predicted disagreement in pain ratings between children and their parents (45). In the same study, fair agreement was reported for pain frequency, while poor agreement was reported for pain intensity, measured on a facial scale. However, pain was assessed over the previous 4 weeks, which may be problematic given that symptoms of JIA can fluctuate considerably over this time period. Doherty found poor agreement for pain, obtained from a 15 cm VAS, in a small group of 20 children and their mothers, however high agreement for disability, measured on the CHAQ (46). It was postulated that pain, which is highly personal and subjective, is more difficult to evaluate than activities of daily living, which are observable. On the other hand, Toupin found good agreement between the pain perceptions of 50 children aged 9 to 18 years, followed at the Montreal Children's Hospital, and their parents, when pain in the previous week was rated on a 100 mm VAS (47). In the same study, higher levels of agreement for pain were found for those with more severe disease. Few studies have specifically evaluated whether fathers are reliable sources for reporting their children's pain. Garcia-Munitis found moderate agreement in the child-mother dyad for present pain, measured on the VAS, however poor agreement in the child-father dyad (48). Moderate agreement for pain in the previous week measured on the VAS, for both the child-mother dyad and the child-father dyad, were found. Overall, across studies, the results are conflicting. There remains a gap in the medical literature with regards to the use of proxies to report pediatric pain.

Measurement of disease activity is imprecise, with no "gold standard" existing. Hence many approaches have been used, which may explain the different findings with regards to the association between disease activity and pain. The most commonly used measures of disease activity in clinical trials in JIA are a core set of outcome variables identified by Giannini and which include: (1) physician global assessment of disease activity (PGADA) measured on a 10 cm

VAS, (2) parent or patient global assessment of overall well-being measured on a 10 cm VAS, (3) an instrument of functional ability, (4) number of joints with active arthritis or active joint count (AJC), (5) number of joints with limited range of motion, and (6) erythrocyte sedimentation rate (ESR) (49). In the pain regression models, some authors relied on physician global assessment of disease activity (14), while others assessed disease severity (36;40), or AJC (37;41). Malleson reported that the AJC correlated better with pain in younger children (age 8-15 years), whereas in older children (> 16 years) the global assessment correlated better (37). Composite scores were calculated by Ross and Thastum, based on ratings of disease activity and morning stiffness, and based on AJC, morning stiffness and ESR, respectively (35;39). Thompson and Varni used a Disease Activity Index specifically designed for their studies, whereby physicians were asked to score the disease (remission, quiescent, mild, moderate or severe) (34;42). With the use of thermography as an indicator of joint inflammation, Ilowite demonstrated significant correlations between increased temperature in the affected joints and pain intensity ratings on the VAS (38).

Except for the study by Malleson, all regression models were developed based on small populations of patients, ranging from 23 to 100 patients, followed at a single centre (14;33-42). Other limitations that may explain the different findings across studies are the characteristics of the patient populations. For example, more than 50% of patients had inactive disease in the study by Malleson (37), compared to 16% in a study by Schanberg (14). In addition, only Ross, Thastum and Schanberg included patients with psoriatic arthritis and spondyloarthropathies (14;35;39). While most authors studied patient populations including children with variable disease duration, Vandvik only included children recently diagnosed (33).

In summary, many studies have indicated that pain is an important symptom of JIA. However, pain is a complex symptom that is not solely explained by known disease-related variables. Clearly, the experience of pain is modulated by other

factors in addition to clinical and laboratory measures of disease activity. Factors evaluated to date by various authors include the functional status of the child, the psychosocial functioning of the child (mood, stress, emotional distress and pain coping strategies) and the familial environment (parental distress, familial history of pain and family functioning). It is also possible that pain is a manifestation of disease activity and is not well explained by the traditional measures of disease activity, such as AJC, PGADA and ESR. The development of better measures of disease activity and the study of their association with report of pain could be an area of future research.

5. Relationship between the psychosocial functioning of the child and pain

Children with JIA are at risk for psychosocial difficulties, due to the effect of disease on physical appearance, side effects of treatment, disability, increased dependence on family members, disruption of daily life by medical appointments and complex treatment regimen, participation in fewer activities, social isolation, uncertainty about the future and chronic pain. Yet, controversy exists as to whether children with JIA have poorer psychosocial functioning, compared to healthy peers. While some authors (50-53) found decreased levels of social competence with peers and emotional well-being, others (54-59) concluded that children with JIA are well adjusted. LeBovidge completed a meta-analysis including 21 studies published before 2002, and concluded that children with arthritis had significantly higher levels of overall adjustment problems, in comparison to control groups (60). While children were particularly found to be at risk for internalizing problems (i.e., anxiety, depressed mood, social withdrawal), there was no difference in externalizing problems (i.e., hyperactivity, oppositional behaviour, aggressiveness) or self-esteem. She hypothesized that this pattern of internalizing problems might be explained by the physical limitations of the disease, which may constrain acting out behaviours, and female predominance. A concern raised by LeBovidge was the

lack of use of outcome measurement tools validated in JIA. Most authors used the Child Behaviour Checklist (CBCL), as an indicator of psychological adjustment, which contains questions on somatic complaints that may reflect disease process as opposed to behavioural problems. Other methodological problems identified were the retrospective design of most studies, their small sample size, the lack of a uniform method of measurement across studies, and the absence of a control group in some studies.

Several authors examined correlates of psychosocial adjustment in JIA. At the child level, Ungerer and Ding reported that increased level of disability was associated with maladjustment (55;59). While Billings, Timko and Daltroy found more psychosocial dysfunction in those with severe disease (51-53), McAnarney reported that children with mild disease had worse psychosocial functioning (50). McAnarney explained this unexpected finding by suggesting that children with mild disease spend more energy trying to behave and perform in the same way as their healthy peers, in comparison to more disabled children who may be treated as "handicapped". Adolescence is a vulnerable period, when concerns about dependency on parents and body image are often present. Some found that teenagers are at increased risk for psychosocial maladjustment in comparison to younger children (51;52). Ennett investigated the child's perceived burden of illness, and found that more negative disease experiences were associated with diminished sense of self-worth, and perceived poor competence in athletic skills, peer relationships and physical attractiveness (61). At the parental and familial level, as expected, more supportive environments tend to be associated with better adjustment (55;62). Degotardi and Timko investigated the influence of family coping strategies and maternal distress, respectively, on the psychosocial adjustment of the child (see section on parental coping) (53;63).

Although few authors investigated the link between the experience of pain and the psychosocial functioning of children with JIA, studies suggest the presence of

an association. Sandstrom reported that pain measured on the VAS, but not disease activity and functional disability, strongly correlated with depressive symptoms in a cross-sectional study of 36 children (64). Furthermore, pain explained 27% of the variance in depressive symptoms, in a model where peer rejection was also included. Peer rejection moderated the association between pain and depressive symptoms, such that children who experienced high levels of pain and high levels of social rejection reported more depressive symptoms. In a group of adolescents with chronic diseases including JIA, Palermo reported the presence of relationships between the experience of chronic pain, sleep disturbances and depression (65). In addition, in the 1996 National Population Health Survey, Adam reported that depression and pain were more prevalent in Canadian adolescents with arthritis and rheumatism than in healthy adolescents (66).

More recent studies have focused on the concept of health-related quality of life (HRQoL), which is a multi-dimensional construct including both the physical, psychological and social well-being of patients. Generic instruments of HRQoL validated in children with rheumatic diseases include the PedsQL (67) and the Child Health Questionnaire (CHQ) (68); one disease-specific instrument validated in JIA is the Juvenile Arthritis Quality of Life Questionnaire (JAQQ), which was developed by Duffy using a JIA cohort at the Montreal Children's Hospital (69). Sawyer described that high pain intensity ratings predicted worse HRQoL (PedsQL) (70). In a European, cross-sectional, multi-centre investigation of proxy-reported HRQoL of more than three thousands patients with JIA, Oliveira reported that both the physical and psychosocial summary scores of the CHQ were significantly lower than in healthy controls, with the physical well-being domain being the most impaired (71). And while disability was the strongest determinant of physical health, the intensity of pain had the greatest influence on psychosocial health, underscoring the importance of controlling pain to preserve HRQoL. Duffy determined correlations for the four dimensions of the JAQQ (gross motor, fine motor, psychosocial and general

symptoms), total JAQQ score and pain intensity ratings measured on the 100 mm VAS (69). Correlations for the total JAQQ score with pain were very good (r = 0.72). Correlations for the psychosocial dimension with disease activity were low (r = 0.19) but with pain were moderate (r = 0.34). These studies suggest that the psychosocial functioning of children with JIA is related to pain more than disease activity or disability. Shaw described the HRQoL of teenagers with JIA from three age groups (11, 14 and 17 years) using the JAQQ (72). Within the psychosocial dimension of the JAQQ, the biggest psychological problems rated by teenagers were "felt frustrated" and "felt depressed", found in 30.2% and 23.4% of teenagers, respectively. These findings were particularly true for the "oldest" teenagers, with 39% and 63.6% reporting frustration and depression, respectively. Interestingly, adolescents most likely to rate frustration or depression as one of their biggest problems were those with worse pain, greater disease activity, and greater functional disability. Also, the 17-year olds, who appeared to be at greatest risk for depressive symptoms, reported significantly greater pain than the younger groups, suggesting that there may be a strong relationship between depressive symptoms and pain. Dhanani established the minimal change in pain intensity (100 mm VAS) associated with a meaningful change in HRQoL (Quality of My Life scale) (73). She reported that a minimum reduction in pain score of 8.2 mm was associated with improvement in quality of life between two consecutive study visits. Altogether, these studies suggest that the concept of HRQoL in JIA, and more specifically the psychosocial dimension, is closely tied with pain.

As previously mentioned, the chronic pain experienced by children with JIA is likely modulated by many factors, independent of disease status. Varni developed a multidimensional Biobehavioural Model of Pediatric Pain, and hypothesized "a number of factors that may influence pediatric pain perception and behaviour…in an effort to identify potentially modifiable constellation of factors to be targeted for biobehavioural treatment" (74). In the model, pain perception and behaviour are hypothesized to be affected by, and affect (bi-

directional effect) functional status variables, including activities of daily living, school attendance, depressive symptoms, anxious symptoms, behavioural problems and interpersonal relations. Varni found that higher patient-perceived pain intensity assessed by the VAS was associated with higher levels of emotional distress, namely higher depressive and anxious symptoms, lower self-esteem and higher behavioural problems (74). However, due to its cross-sectional design, the study did not address the issue of direction of causality in the relationship between emotional distress and pain intensity.

There are several other studies in the literature suggesting that chronic pain perception and report in JIA is associated with the psychological status of the child. In a cross-sectional analysis, Thompson developed a model whereby child psychological variables (CBCL) and the family environment (Family Environment Scale), together with disease characteristics, explained 34% and 72% of present and worst pain intensity in the past week, respectively, as reported by the child (34). After controlling for disease characteristics, Ross found that greater emotional distress in the child (Child Depression Inventory), maternal distress and greater family harmony, made a substantial impact upon reported pain (75). She hypothesized that family harmony may create an environment which reinforces a child's pain behaviour and report.

Schanberg reported that increased levels of anxiety, but not depressed mood, measured at baseline using a battery of questionnaires, was related to more daily symptoms of pain, fatigue and stiffness recorded on a daily diary over a two-month period (40;76). She also investigated the day-to-day fluctuations in mood, stressful events and disease symptoms using daily diaries, and found that worse mood and more stressful events were predictive of increased daily pain, stiffness and fatigue. She speculated that daily mood and daily stressful events cause alterations in the immune system which in turn bring exacerbations in daily disease symptoms (31). In addition, daily stress, mood and disease symptoms were related to decreased participation in social activities on a day-to-day basis.

The first longitudinal study examining the effects of depressive symptoms on pain intensity reports over time was carried out by Hoff, who used general linear mixed modeling (77). She demonstrated that, in 66 children with JIA of variable disease duration, depressive symptoms (Revised Child Anxiety and Depression Scale) measured at baseline moderated pain intensity ratings (Faces Pain Scale) at 6 and 12 months, but only for those children with initial pain intensity in the mild to moderate range. Thus, depressive symptoms functioned as a risk factor for subsequent disease-related pain in some children.

In summary, although studies suggest that the psychosocial functioning of the child explains a unique and significant proportion of the variance in pain intensity ratings, firm inferences about the direction of the relationship cannot yet be made in view of the cross-sectional study design used by most authors. Although the experience of chronic pain may lead to maladjustment, it is also possible that poor psychosocial functioning predicts more pain. Hoff was the first author to suggest that psychosocial maladjustment predicts higher levels of pain intensity in the future, for some children with JIA. More longitudinal studies, conducted on larger patient populations and with tools validated in JIA, are needed to investigate the direction of the relationship.

6. Parental coping

The relationship between pain coping strategies in the child with JIA and his/her pain experience has already been demonstrated by some authors. Schanberg showed that pain coping strategies of the child, after controlling for disease variables, explained a significant proportion of variance in pain intensity ratings on the pain thermometer, Oucher and body map (14). Children who reported being able to control their pain and who had lesser tendency to catastrophize had lower levels of pain intensity and pain in fewer body locations. Similarly,

Thastum showed that pain-specific beliefs (i.e., the belief that one is able to control pain) and pain coping strategies strongly influenced pain, after controlling for disease variables (35). Children who reported high levels of pain had a tendency to use less positive self-statements and more catastrophizing pain coping strategies. Despite this knowledge, the relationship between parental coping and the pain of children with JIA has never been studied to date.

Parents of children with JIA face multiple stressors, including the time of initial diagnosis, uncertainty about the future, helping their ill child to achieve normal developmental milestones, the strain of ongoing care and handling of complex treatment regimen, unpredictable exacerbations and hospitalizations, and financial strain (63). Thus, they may be at risk for psychological distress. While several studies did not support the presence of increased parental distress (52;54;78;79), Vandvik reported that more than two thirds of parents experienced moderate to severe family difficulties, including parental health problems, family conflict and lack of social support, and that more than half reported recent stressful events (80). Manuel showed that mothers had more psychological symptoms than a normative group (81). Bernatsky found that the economic impact of JIA on families was substantial, with a difference in annualized average direct medical costs of $1,686 for children with JIA followed in two Canadian medical centres, including the Montreal Children's Hospital, versus controls (82). It may be anticipated that this financial strain is associated with parental distress, although this has not been evaluated. Mothers were found to be at increased risk for psychological distress in comparison to fathers, in various studies, possibly because mothers are often the primary caregivers (53;83-85).

Wallander and Varni developed a model to explain the differential adaptation of parents of chronically ill children, in terms of risk and resistance factors. Risk factors include disease characteristics of the child, functional care strain, and psychosocial stressors (illness-related stressors, daily hassles and major life events) (86). Resistance factors include intra-personal factors, socio-ecological

factors (family environment and support, income) and stress-processing factors (cognitive appraisal and coping strategies). Coping is defined as "constantly changing cognitive and behavioural efforts to manage specific external and internal demands that are appraised as taxing or exceeding the resources of a person" (87). A variety of instruments are available to evaluate parental coping, some of which were specifically designed for parents of children with chronic illnesses. Various factors influence the use of specific coping strategies. Cavallo used the Coping Health Inventory for Parents (CHIP), which is reviewed later, to describe the parental coping strategies of a cohort of children with JIA followed at the Montreal Children's Hospital (88;89). Parents of children with greater psychosocial impairment (psychosocial dimension of the JAQQ) tended to use strategies related to understanding the medical situation better, whereas parents of children with severe disease (total JAQQ score) showed a decrease in the use of coping strategies aimed at maintaining social support and family integration, and understanding the medical situation better.

Just as having a child with JIA may be a stressor for parents, the family environment (family functioning, parental distress and parental coping) may affect the child's outcomes. With respect to the psychosocial functioning of the child, Wagner demonstrated that increased parental distress was significantly associated with greater child depressive symptomatology (90). Similarly, Timko reported that good psychological functioning of the mother predicted better adjustment and social integration of the child with JIA (53). She also showed that mothers who engaged more in social activities with cohesive families had less distressed children. Several other authors reported on the beneficial effect of good family functioning (family support and resources, family cohesiveness) on the child's adaptation to JIA (51;62;91-93). Using a quantitative interview process, Degotardi described the association between different types of family-level coping and psychosocial adjustment of teenagers with JIA, and found that emotion-focused approaches (impulsive outbursts and diminished awareness of others' feelings) were associated with adolescent acting-out behaviours (63).

There was a significant trend for better adjustment with problem-focused (planning of specific actions to deal with the stressors) and appraisal-focused (family's interpretation of arthritis-related stressors) coping strategies. Chaney examined the association between various areas of family functioning (adaptability and cohesion, stressors and coping) and medication compliance (94). Families in which mothers reported a greater number of coping behaviours had children who demonstrated higher levels of compliance. However, an association with disease activity was not found.

With respect to pain in JIA, although the specific role of parental coping has never been studied to date, Ross reported that family harmony (Family Environment Scale), together with increased child anxiety and increased maternal distress, significantly predicted pain (39). The author explained this unexpected finding by hypothesizing that greater family harmony creates an environment which is responsive to a child's pain behaviour. Thompson examined the way family members interact with one another, and proposed a model in which family relationships, psychological functioning of the child and disease-related variables were significantly associated with present and worst pain intensity (34).

In summary, parental coping has been the focus of a small number of studies, and preliminary findings indicate the need to further investigate its impact on children's outcomes. To date, no studies addressed the influence of parental coping on the experience of pain in JIA.

7. Relationship between demographic and disease-related variables, and pain

The effect of demographic and disease-related variables on pain is unclear. Most authors statistically controlled for the effects of age, disease duration, category of JIA (or JRA) and gender, in regression models.

Age of the child

In a qualitative study of children with JIA aged 6-11 and 12-17 years, Beales suggested that cognitive development impacts on pain perception and report (10). Although children of all ages used similar words (e.g., "aching") to describe the sensations in their joints, older children (12-17 years) often attributed a more unpleasant and stronger meaning to their joint sensations because of their greater understanding of internal pathology, in comparison to younger children (6-11 years). Older children were more distressed by their joint sensations and therefore more likely to interpret them as painful, resulting in increasing pain intensity as the children's age increased. However, the data was not statistically analyzed, and thus conclusions could not be drawn.

The data on the effect of age on pain is conflicting. Hagglund (36) found that age was a significant predictor of pain, with older children reporting more pain, and Schanberg (14) showed that age explained 2% of the variance in pain intensity. However, many other authors reported no effect of age on pain (33;39;43). Malleson, in a study including patients with a wider age range (8-32 years), showed a small effect of age on pain only in the age group 8-15 years, but not in the age group 16 years and older (37).

Disease duration

Study findings regarding the effect of disease duration on pain are contradictory. Schanberg reported that, in a model where disease activity explained 28% and

33% of the variance in pain intensity measured on the pain thermometer and Oucher, respectively, disease duration only explained 1% (14). While Schanberg found no significant effect of disease duration on pain, Hagglund and Malleson reported different findings (36;37). Hagglund showed an inverse relationship between disease duration and pain intensity in a univariate analysis, indicating that children diagnosed more recently with JRA reported higher levels of pain. However, this association was not retained in the final multivariate regression model. On the other hand, Malleson found a direct relationship in a model where disease duration explained 14.3% of the variance in pain intensity. A possible explanation is that the patient population in the latter study included much older patients (age range 8-32 years) with longer disease durations.

Category of JIA

There have been no studies investigating the link between pain and category of JIA. Using the ACR classification of JRA, Ross found that children with polyarthritis experienced more pain than children with pauciarthritis and systemic arthritis (39). Thompson reported that children with polyarthritis and systemic arthritis had more pain than children with pauciarthritis, and that category of JRA explained 8% of the variance in present pain intensity, but not in worst pain intensity (34). In Malleson's study, although patients with polyarthritis RF positive described more pain, category of JRA was not retained in the final model (37). Vandvik found no significant difference for present and worst pain intensity by category of JRA, psoriatic arthritis and ankylosing spondylitis (33). Hence, it is still unknown as to whether children belonging to certain categories of JIA, especially those with ERA, experience more pain than others.

Gender

Although idiopathic musculoskeletal pain syndromes predominantly affect girls over boys in a ratio of approximately 4 to 1 in all series (95), the effect of gender on pain in the JIA literature is less clear. Abu-Saad found no significant

difference in gender with regards to pain intensity (43). Similarly, Vandvik showed no difference in the quality of pain, evaluated with pain descriptors, and intensity of pain, measured on the VAS, between boys and girls (33). On the other hand, Schanberg, with the use of daily diaries over a two-month period, described that school-aged girls with polyarthritis reported more severe daily pain, stiffness, fatigue, and poorer sleep and ability to control pain, than boys (96).

IV. RATIONALE, OBJECTIVES AND HYPOTHESIS

1. Rationale

Clearly, clinical and laboratory measures of disease activity in JIA only explain a modest proportion of the variance in pain intensity. Other factors pertaining to the child or his/her environment have been reported to modulate the experience of pain in JIA. However, the cross-sectional design of most of the studies described does not elucidate the direction of the causality between some of the variables and pain. To our knowledge, Hoff is the only author who performed a longitudinal analysis, which showed the moderating effect of depressive symptoms on pain intensity ratings at 6 and 12 months, in a small sample of children with JIA (77). More studies, conducted with larger number of patients and with tools validated in JIA, are required to investigate further the longitudinal impact of the psychosocial functioning of the child on future pain report.

Furthermore, the potential association between parental coping and the pain experience of children with JIA has never been explored. Parental coping strategies might affect pain report by modeling effective, or ineffective, coping skills in children with JIA. Another way parental coping might influence the experience of pain is by an indirect effect, mediated through its impact on the psychosocial functioning of the child. It is possible that children who live within families that cope poorly are at risk for becoming maladjusted, and this may in turn lead to increased levels of reported pain.

This thesis work is unique in that the association between the psychosocial functioning of the child and pain is evaluated not only in a cross-sectional design, but also longitudinally. A longitudinal analysis of the predictors of pain in JIA has rarely been completed. Furthermore, this is the first study to investigate the potential impact of parental coping patterns on children's pain. Except for the

study by Malleson, the sample size of this research project is larger than that of other studies on pain in JIA. Finally, the study was conducted with the use of the JAQQ (reviewed later), an outcome measurement tool whose validity and responsiveness to change in JIA have been demonstrated.

This research project is potentially important from several perspectives. Chronic pain is an important symptom experienced by most children with JIA, yet it is still poorly understood. For clinicians, understanding the relative importance of factors other than disease activity in explaining the pain experience of children with JIA may influence treatment decisions and management. In addition, the psychosocial functioning of the child may be amenable to psychological intervention, and counselling may help some parents to cope better. These strategies may in turn ultimately decrease the pain perception and experience of children, both concurrently and long-term.

2. Objectives

The objectives are the following:
(1) to examine whether the psychosocial functioning of the child assessed at baseline is associated with pain intensity measured at baseline (cross-sectional analysis) and six months later (longitudinal analysis), above and beyond disease activity and after controlling for demographic and disease-related variables.

(2) to examine whether parental coping assessed at baseline is associated with pain intensity measured at baseline (cross-sectional analysis) and six months later (longitudinal analysis), above and beyond disease activity and after controlling for demographic and disease-related variables.

3. Hypothesis

The hypotheses are the following:

(1) the psychosocial functioning of the child assessed at baseline will explain a unique and significant proportion of the variance in pain reported at baseline, above and beyond disease activity and after controlling for demographic and disease-related variables, and this association will be maintained at 6 months.

(2) the use of specific parental coping patterns assessed at baseline will explain a unique and significant proportion of the variance in pain reported at baseline, above and beyond disease activity and after controlling for demographic and disease-related variables, and this association will be maintained at 6 months.

V. METHODOLOGY

1. Research design

Prospective cohort study.

2. Description of the database of "Determinants of outcomes for juvenile arthritis"

This study used data from the database "Determinants of outcomes for juvenile arthritis", for which scientific merit and ethics approval were previously obtained by Dr. Ciarán Duffy, from the Research Institute and the Research Ethics Board of the Montreal Children's Hospital. The study was funded by the Canadian Arthritis Network and the Canadian Institutes of Health Research. The purpose of the study "Determinants of outcomes for juvenile arthritis" is to determine the role of adherence, use of complementary therapies, health-related costs, and parental, psychosocial and disease-related factors on outcomes of quality of life and disease activity. The database is located in the Division of Rheumatology of the Montreal Children's Hospital.

Between September 2001 and November 2003, children with JIA of variable duration and their families were recruited from pediatric rheumatology clinics from two Canadian university-based teaching hospitals (Montreal Children's Hospital – McGill University Health Centre and British Columbia's Children's Hospital in Vancouver). A primary caregiver who accompanied the child was approached by the study coordinator, while waiting with their child for their scheduled clinic visit. To be enrolled in the study, the children had to have a diagnosis of JIA and had to be followed for the duration of the study. In addition, the primary caregiver had to be fluent in either French or English. The time of entry into the study of each child, in relation to duration of disease,

varied. Informed consent for participation was obtained from the primary caregiver. The study terminated in March 2008.

The primary caregiver was asked to complete a battery of questionnaires over a 36-month period. Standardized, validated questionnaires assessing quality of life (JAQQ and CHQ), functional disability (CHAQ), caregiver's psychological distress (Symptom Checklist-90-R (97)), parental coping (CHIP), treatment adherence (parent adherence questionnaire), health-related costs (economic hardship) and demographics (ethnic background, education of parents, family structure), were given at baseline, 6, 12, 18, 24, 30 and 36 months. During completion of the questionnaires, the study coordinator remained available to answer questions. Those unable to complete the questionnaires during the clinic visit were provided with a stamped return envelope. At the baseline visit, medical charts were consulted to determine category of JIA, gender, age of the child, age at disease onset and date of diagnosis. At each visit, information pertaining to disease activity was obtained from the chart and included the AJC, the sum of joint severity score (defined as the sum of scores for joint effusions, joint tenderness or pain on motion, and loss of range of motion) and ESR (erythrocyte sedimentation rate). These data are collected and entered routinely in a specifically designed JIA chart.

In order to ensure patient confidentiality, the names of the patients were replaced by confidential study numbers. The master list, which links the names of the patients and assigned study numbers, is kept in a password protected file, to which only the research coordinator has access.

All data were entered by a data entry clerk in the database, for later incorporation into SPSS. A research assistant verified data entered into the database, by comparing it to the raw data. Discrepancies found were directly corrected in the database.

3. Time points for the cross-sectional and longitudinal analyses

Similar to the study by Hoff (77), it was anticipated that the timeframe within which the psychosocial functioning of the child might influence future pain report is one year or less. Intervals of greater than one year may be too long, because children go through developmental transitions, which may impact psychosocial functioning. For the purpose of this study, the information collected at the baseline and 6-month visits are described and analyzed. The 12-month data was not analyzed because there was a large proportion of missing observations.

4. Measurement of the dependent and independent variables

Dependent variable: pain

The JAQQ, which measures HRQoL, was developed at the Montreal Children's Hospital. The JAQQ is a disease-specific instrument aimed at measuring outcomes in a comprehensive fashion in children with JIA of all age groups and of all categories (69). Parents or children older than 9 years of age themselves can complete it. Its validity, reliability and responsiveness to change in JIA have been established (72;98). It consists of 74 items grouped into 4 dimensions: gross motor function, fine motor function, psychosocial function and general symptoms. At the end of the questionnaire, the caregiver or child is asked to rate pain intensity in the past week as a result of arthritis on a 100 mm horizontal VAS, anchored with "no pain" and "worst pain imaginable". The parent or child is also asked to choose the phrase, which describes pain the best (i.e., no pain, slight pain, moderate pain, severe pain, extreme pain). Children under 10 years of age are asked to rate their pain intensity on a 5 point happy face model (99).

The VAS has been widely used across studies of pain intensity in children with JIA. In the database, data on pain intensity from the VAS was available for a

larger number of patients, than from the phrase or facial scale. Therefore, pain intensity recordings on the VAS at baseline and at 6 months were used as the dependent (continuous) variables. Either the parent or their child recorded pain intensity on the VAS. Information on the proportion of VAS filled in by children was not available from the database.

Independent variables:

-Disease duration:

Participants in the study "Determinants of outcomes for juvenile arthritis" were children of variable disease duration, and not necessarily children recently diagnosed with JIA. Disease duration (in years) was obtained by subtracting the date of diagnosis by a rheumatologist from the date of the baseline visit. The date of diagnosis by a rheumatologist was chosen over the date of onset of symptoms, which may be imprecise. Date of diagnosis is recorded in the JIA chart.

-Category of JIA:

Patients were classified by pediatric rheumatologists at the baseline visit into one of the seven categories of JIA, using the second revision of the ILAR classification: oligoarthritis, polyarthritis RF negative, polyarthritis RF positive, systemic arthritis, ERA, psoriatic arthritis and undifferentiated arthritis (1). If the category of JIA changed between the baseline and 6-month visits, the category of JIA at the 6-month visit was used. Category of JIA is documented in the JIA chart.

The number of patients per independent variable, which is generally considered appropriate to conduct multiple linear regression analysis (MLRA), is about 10 to 20 (100). In order to reduce the number of variables in each model, category of JIA was recoded as a binary variable, oligoarthritis versus all other categories of JIA. Children with oligoarthritis have been reported to have no or mild disability, in comparison to other JIA categories. In addition, oligoarthritis may

have a better prognosis, in terms of proportion of children achieving remission 10 years after onset of disease (8). This type of recoding made the most sense from a clinical standpoint.

-Age of the child:

Age of the child (in years) at the baseline visit was used.

-Gender

-Disease activity:

There is no gold standard for evaluating disease activity. The sum of joint severity score, recorded in the database, may reflect disease damage (i.e., loss of range of motion) in addition to disease activity. AJC and ESR are both included in the core set of outcome variables identified by Giannini and used in many clinical trials (49). ESR is a non-specific marker of inflammation, and thus may be elevated for reasons other than JIA disease activity. Therefore, the AJC at the baseline visit was used as a surrogate marker of disease activity. Although the terms AJC and disease activity are used interchangeably in this thesis, it is understood that they are not the same. The pediatric rheumatologist calculated AJC by summing the number of swollen joints and the number of joints, not swollen, that exhibited warmth, tenderness or stress pain with limitation on movement (possible range 0-77). The AJC is routinely recorded in the JIA chart.

-Psychosocial functioning of the child:

The psychosocial dimension of the JAQQ, which consists of 22 items, was used to evaluate the psychosocial functioning of the child at the baseline visit. The caregiver, or child if older than 9 years, is asked to rate the frequency of psychosocial difficulties experienced on a 7-point Likert scale. The questions are phrased as follows: "How often have you/your child, over the past two weeks, exhibited any of the following behaviours or moods as a result of arthritis or its treatment?". Examples of items include getting teased a lot, feeling frustrated

and feeling depressed. The dimension is patient-specific, meaning that respondents are asked to select up to 5 items that represent the "biggest problems" and may also provide new items. The mean score of the 5 highest scoring items (including the new items) is the dimension score (possible range 0-7). Higher scores indicate poorer psychosocial functioning. Moderate to good parent-child agreement was previously shown (101).

-Parental coping:

Parental coping at the baseline visit was evaluated by the CHIP, on which parents indicate the type of coping behaviours they use in response to their child's chronic illness and on which they rate their perceptions of how helpful these behaviours are on a 4-point Likert scale (102). It consists of a checklist of 45 specific behaviours, which are grouped into 3 coping patterns: (1) Coping pattern I (Family integration, co-operation and an optimistic definition of the situation) focuses on strengthening family life and relationships, and the parents' outlook on life with a chronically ill child, (2) Coping pattern II (Maintaining social support, self-esteem and psychological stability) involves the parents' efforts to develop relationships with others, engage in activities which enhance feelings of individual identity and self-worth plus behaviours to manage psychological tensions and pressures, (3) Coping pattern III (Medical situation) focuses on understanding the health care situation through communication with other parents and consultation with the health care team. The questions are phrased as follows: "For each coping behaviour you used, please record how helpful it was: not helpful (0), minimally helpful (1), moderately helpful (2), extremely helpful (3)". Examples of items include "trying to maintain family stability" (Coping pattern I), "purchasing gifts for myself/others" (Coping pattern II) and "talking with the medical staff" (Coping pattern III). Higher scores indicate that specific behaviours are perceived to be helpful. Coping scale scores are computed for each of the three patterns by an un-weighted summing of a parent's ratings across the behaviour items in each pattern. The possible ranges are as follows: Coping pattern I (0-51), Coping pattern II (0-57), Coping pattern III (0-27).

Information on the identity of the respondent i.e., mother or father, was not available from the database.

Norms for the CHIP are available in samples of parents of chronically ill children. The instrument has shown good validity with significant associations with the Family Environment Scale in patients with cystic fibrosis (103). An additional validity check comes from the finding that high conflict families of children with cerebral palsy scored higher on all three coping patterns than low conflict families (102). This suggests that coping behaviours are developed in response to stressful situations. Cavallo used data from the study "Determinants of outcomes for juvenile arthritis" to evaluate the coping behaviour patterns of parents of children followed at the Montreal Children's Hospital (88;89).

5. Sample size

Data on pain intensity from both the baseline and 6-month visits were available for a total of 95 patients (83 from Montreal and 12 from Vancouver), which represent the study population, called the **Total Cohort**. In order to increase the sample size available for data analysis, the cross-sectional analysis was rerun on all patients for whom data were available from the baseline visit. This group, called **Baseline Cohort**, comprised 157 patients. The **Baseline Cohort** included not only all patients belonging to the **Total Cohort**, but also patients for whom data on pain intensity were available only from the baseline visit. The longitudinal analysis was also rerun on all patients for whom data were available from the 6-month visit. This other group, called the **Month 6 Cohort**, included 112 patients. The **Month 6 Cohort** included not only all patients belonging to the **Total Cohort**, but also patients for whom data on pain intensity were available only from the 6-month visit. It is understood that the patient populations comprising the three cohorts are different. The cohorts are described diagrammatically in Appendix 2. The analyses performed on the **Baseline**

Cohort and **Month 6 Cohort** were exploratory, as explained in the next section. To our knowledge, except for the study by Malleson, the sample size of this project is larger than other study populations from which pain regression models were developed (37). The number of patients per independent variable was appropriate to conduct MLRA, as explained in the next section.

6. Statistical evaluation

Descriptive and univariate analysis

Descriptive statistics, including means and standard deviations for continuous variables and frequencies and proportions for categorical variables, were used to describe the patient population. Transformation of variables was performed, if necessary. Pearson correlations were used to identify simple correlations between all variables in the dataset. Univariate analysis was conducted to determine which variables are significantly associated with pain intensity at baseline and 6 months. Residual plots were examined for any violations of assumptions required for MLRA.

The relationship between the psychosocial functioning of the child and pain

Hierarchical MLRA was used to determine the amount of additional variance in pain ratings explained by the psychosocial functioning of the child, above and beyond disease activity, and after controlling for the potential confounding effects of demographic and disease-related variables. Separate models were developed for each of the two pain outcomes in the **Total Cohort**: (1) pain intensity at baseline visit (cross-sectional analysis), (2) pain intensity at 6-month visit (longitudinal analysis). Given that most previous studies have controlled for gender, age of the child, disease duration and JIA category, these variables were entered in Step 1, regardless of their statistical significance. For each model, AJC was entered in Step 2. Psychosocial functioning was entered in Step 3. In the longitudinal analysis, pain at baseline visit was not forced in the model

because the objective is to identify statistically significant predictors of future pain reports at 6 months, as opposed to change in pain intensity between the baseline and 6-month visit.

-Exploratory analyses:

Additional analyses were performed. First, the cross-sectional analysis was rerun on the **Baseline Cohort**, and the longitudinal analysis was rerun on the **Month 6 Cohort**. The results were compared to those obtained from the **Total Cohort**, to establish generalizability.

Second, in the longitudinal analysis, the choice of the dependent variable was changed from **pain intensity at 6-month visit** to **change in pain intensity** between the baseline and 6-month visits. Here, the influence of the baseline psychosocial functioning of the child on change in pain intensity, rather than future pain report at 6 months, was explored. Change in pain intensity was computed by subtracting baseline pain intensity ratings from 6-month pain intensity ratings. The independent variables were entered in the same steps as previously described. Pain intensity at baseline visit was not forced in the model. According to study findings reported by Glymour, in analyses of change in status, adjustment for baseline status may introduce bias (104).

Third, the possible presence of an interaction between the psychosocial functioning of the child and disease activity was examined on the **Total Cohort,** in both the cross-sectional and longitudinal analyses. It was hypothesized that the psychosocial functioning of the child moderates the influence of disease activity on reported levels of pain measured at baseline, and that this moderating effect is maintained at 6 months. Here, the strength of the relationship between disease activity and pain could depend on the level of psychosocial functioning of the child, such that children with high disease activity experience more pain when poor psychosocial functioning is present, in comparison to well-adjusted children. The interaction term was computed by multiplying AJC with the

psychosocial functioning of the child. The independent variables were entered in the same steps as previously described. The interaction term was entered in Step 4.

The number of patients per independent variable in the various regression models (maximum of 7 variables) exceeded 10, which is generally considered appropriate to conduct MLRA.

The effect of parental coping

Hierarchical MLRA was used to determine the amount of additional variance in pain ratings explained by parental coping, above and beyond disease activity, and after controlling for the potential confounding effects of demographic and disease-related variables. Separate models were conducted for each pain outcome in the **Total Cohort**: (1) pain intensity at baseline visit (cross-sectional analysis), (2) pain intensity at 6-month visit (longitudinal analysis). For each model, gender, age of the child, disease duration and JIA category, were entered in Step 1, and AJC in Step 2. The three parental coping patterns were entered altogether in Step 3. In the longitudinal analysis, pain at baseline visit was not forced in the model, for the reason mentioned above.

-Exploratory analyses:

First, the cross-sectional analysis was rerun on the **Baseline Cohort**, and the longitudinal analysis was rerun on the **Month 6 Cohort**. The results were compared to those obtained from the **Total Cohort**, for the reason mentioned above.

Second, in the longitudinal analysis, the choice of the dependent variable was again changed from **pain intensity at 6-month visit** to **change in pain intensity**. Here, the influence of baseline parental coping patterns on change in pain intensity, rather than future pain report at 6 months, was explored. The independent variables were entered in the same steps as previously described.

Pain intensity at baseline visit was not forced in the model, for the same reason mentioned above.

The use of specific parental coping strategies may have an indirect effect on pain intensity report, potentially mediated through their impact on the psychosocial functioning of the child (direct causal pathway). It is also possible that the psychosocial functioning of the child acts as a confounding factor in the relationship between parental coping and pain. Here, the psychosocial functioning of the child was controlled for in an exploratory analysis. The demographic and disease-related variables and AJC were entered in the same steps as previously described. However, the psychosocial functioning of the child was entered together with the parental coping patterns in Step 3.

The number of patients per independent variable in the various regression models (maximum of 8 variables) exceeded 10, which is generally considered appropriate to conduct MLRA.

All analyses were conducted using SPSS version 16.0.

7. Scientific and ethical approval

Scientific approval to conduct the study was obtained from the Montreal Children's Hospital Research Institute. Extension of the original approval from the Research Ethics Board for the study "Determinants of outcomes for juvenile arthritis" was obtained. Permission to use the database was granted by Dr. Ciarán Duffy and Dr. Debbie Feldman, co-principal investigators of the study "Determinants of outcomes for juvenile arthritis" and owners of the database.

VI. RESULTS

1. Description of dependent and independent variables

The set of dependent and independent variables, their type and coding, are displayed in Table 1, 2A and 2B.

Table 1: Dependent variables

Variable	Dependent/ Independent	Type, range, unit	Coding, decimals
Pain (baseline visit)	Dependent	Continous, 0-100 mm	2 decimals
Pain (6-month visit)	Dependent	Continuous, 0-100 mm	2 decimals
Change in pain intensity	Dependent	Continuous, 0-100 mm	2 decimals

Table 2A: Independent variables

Variable	Dependent/ Independent	Type, range, unit	Coding, decimals
Gender	Independent	Binary	0=M, 1=F
Age	Independent	Continuous, 0-18 year	0 decimal
Disease duration	Independent	Continuous, 0-18 year	2 decimals
JIA category	Independent	Binary	0=oligo, 1=other
AJC	Independent	Continuous, 0-77	0 decimal

Table 2B: Independent variables (cont.)

Psychosocial functioning of the child	Independent	Continuous, 0-7	2 decimals
Coping pattern I (Family integration)	Independent	Continuous, 0-51	0 decimal
Coping Pattern II (Social support)	Independent	Continuous, 0-57	0 decimal
Coping Pattern III (Medical situation)	Independent	Continuous, 0-27	0 decimal

As previously explained, category of JIA was recoded as a binary variable. Oligoarthritis was coded as 0 and all other categories as 1. The frequencies and percentages of all JIA categories and binary variable in the **Total Cohort** are shown in Table 3. The JIA category oligoarthritis was the largest, and included almost one half of the patient population.

Table 3: Frequency and percentage of JIA categories in Total Cohort

All JIA categories			**Binary variable**		
	n	**%**		**n**	**%**
Oligoarthritis	44	46.3	**Oligoarthritis**	44	46.3
Polyarthritis RF-	20	21.1	**Other**	51	53.7
			Total	95	100.0
Polyarthritis RF+	4	4.2			
Systemic arthritis	8	8.4			
ERA	6	6.3			
Psoriatic arthritis	9	9.5			
Undifferentiated	4	4.2			
Total	95	100.0			

2. Descriptive analysis

Missing observations

The frequency of missing observations in the **Total Cohort**, **Baseline Cohort** and **Month 6 Cohort** are shown in Table 4. The percentages of patients for whom data on some independent variables were missing were, 5.3% in the **Total Cohort**, 8.9% in the **Baseline Cohort** and 8.0% in the **Month 6 Cohort**. As the percentages were small, imputation techniques for missing values were not performed.

Table 4: Frequency of missing observations

	Total Cohort n = 95	**Baseline Cohort n = 157**	**Month 6 Cohort n = 112**
Pain (baseline visit)	0	0	---
Pain (6-month visit)	0	---	0
Age	0	0	0
Disease duration	0	0	0
Gender	0	0	0
Category of JIA	0	0	0
AJC	0	0	0
Psychosocial function	0	1	1
Coping pattern I (fam int	5	12	9
Coping pattern II (soc su	5	14	9
Coping pattern III (med s	5	12	9

Description of Total Cohort, Baseline Cohort and Month 6 Cohort

The mean, median, standard deviation, minimum and maximum of the dependent variables are shown in Table 5. Overall, children reported pain of mild intensity, with a mean of 14.16 mm at baseline visit and of 14.66 mm at 6-month visit in the **Total Cohort**. However, the ranges were large (baseline visit 0.00-79.00 mm; 6-month visit 0.00-90.00 mm). The mean of pain intensity at 6-month visit

was slightly higher than that of baseline visit. Overall, the three cohorts were similar in terms of their means and standard deviations. However, pain intensity at baseline visit in the **Total Cohort** had slightly smaller mean and standard deviation, in comparison to the **Baseline Cohort**, probably explained by its smaller range of values (Total Cohort 0.00-79.00 mm; Baseline Cohort 0.00-96.08 mm). The mean of change in pain intensity between both visits (exploratory analysis) was small, with a large standard deviation (mean 0.49 mm; standard deviation 27.03 mm).

Table 5: Descriptive analysis of the dependent variables

Statistics	**Pain (baseline visit)**		**Pain (6-month visit)**		**Change in pain intensity**
	Total Cohort	**Baseline Cohort**	**Total Cohort**	**Month 6 Cohort**	**Total Cohort**
Mean (mm)	14.16	16.60	14.66	14.13	0.49
Median (mm)	7.84	7.92	3.00	3.50	0.00
Standard deviation (mm)	19.58	22.23	23.08	22.89	27.03
Minimum (mm)	0.00	0.00	0.00	0.00	-72.40
Maximum (mm	79.00	96.08	90.00	91.18	90.00

The frequencies and percentages of all independent, categorical variables are shown in Table 6. The majority of patients were female, with a ratio of girls to boys of about 3 to 1. Almost one half of patients had oligoarthritis, and the other half belonged to other categories of JIA. As shown in Table 2, the smallest JIA categories were ERA, polyarthritis RF positive and undifferentiated arthritis. Overall, the three cohorts were similar.

Table 6: Descriptive analysis of the independent, categorical variables

Variables	Statistics	Total Cohort	Baseline Cohort	Month 6 Cohort
Gender	**Male** (n (%))	24 (25.3)	51 (32.5)	28 (25.0)
	Female (n (%))	71 (74.7)	106 (67.5)	84 (75.0)
JIA category	**Oligoarthritis** (n (%)	44 (46.3)	69 (43.9)	53 (47.3)
	Other (n (%))	51 (53.7)	88 (56.1)	59 (52.7)

The mean, median, standard deviation, minimum and maximum of the independent, continuous variables are shown in Table 7 and 8. Patients from the **Total Cohort** had a mean age of 9.29 years (range 2-18). Patients had disease of variable duration with a mean of 3.89 years (range 0.08-12.35). They had, on average, one active joint. However, some patients had inactive disease (range 0 to 8). Psychosocial difficulties in the child were reported, with a mean score of 2.21 on the JAQQ (range 0.00-5.40). Each of the three parental coping patterns was reported to be helpful by parents. Overall, the characteristics of the three cohorts were similar. However, the **Baseline Cohort** had slightly larger mean and standard deviation of AJC, in comparison to the **Total Cohort** and **Month 6 Cohort**, probably explained by its larger range of values (Baseline Cohort 0-29; Total Cohort and Month 6 Cohort 0-8).

Table 7: Descriptive analysis of the demographic and disease-related variables, and AJC

Variables	Statistics	Total Cohort	Baseline Cohort	Month 6 Cohort
Age (yrs)	**Mean**	9.29	10.07	9.47
	Median	9.00	10.00	9.50
	Standard deviation	4.40	4.39	4.43
	Minimum	2	2	2
	Maximum	18	18	18
Duration (yrs)	**Mean**	3.89	3.95	4.12
	Median	2.72	2.98	3.28
	Standard deviation	3.31	3.31	3.56
	Minimum	0.08	0.08	0.08
	Maximum	12.35	12.99	15.61
AJC	**Mean**	1.12	1.89	1.10
	Median	0.00	1.00	0.00
	Standard deviation	1.79	3.93	1.72
	Minimum	0	0	0
	Maximum	8	29	8

Table 8: Descriptive analysis of psychosocial functioning of the child and parental coping patterns

Variables	Statistics	Total Cohort	Baseline Cohort	Month 6 Cohort
Psychosocial	**Mean**	2.21	2.34	2.19
	Median	2.20	2.20	2.00
	Standard deviation	1.21	1.30	1.22
	Minimum	0.00	0.00	0.00
	Maximum	5.40	6.00	5.40
Coping pattern I (fam int)	**Mean**	38.73	38.38	38.93
	Median	40.00	40.00	40.00
	Standard deviation	8.57	8.89	8.59
	Minimum	6	6	6
	Maximum	51	51	51
Coping pattern II (soc sup)	**Mean**	32.64	33.49	33.01
	Median	32.00	34.00	33.00
	Standard deviation	11.73	11.81	11.41
	Minimum	2	2	2
	Maximum	57	57	57
Coping pattern III (med sit)	**Mean**	16.90	16.58	16.83
	Median	17.00	17.00	17.00
	Standard deviation	5.82	6.11	5.85
	Minimum	3	3	3
	Maximum	27	27	27

3. Histograms and transformation of variables

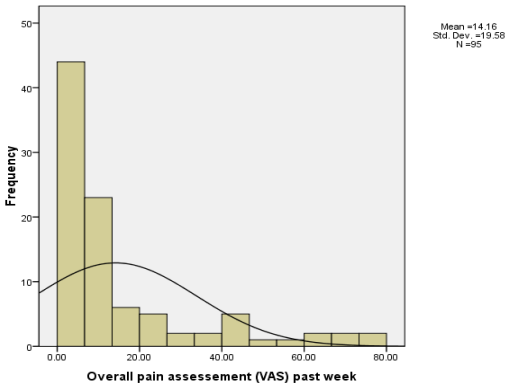
Histograms of the dependent and independent, continuous variables on the **Total Cohort** are shown in Figures 1-15. The histograms of pain (baseline visit), pain

(6-month visit) and AJC indicated a floor effect caused by a large proportion of patients with no reported pain (0.00 mm) and inactive disease (AJC = 0). Their distribution was positively skewed, rather than normal. Log transformation with base e (ln (pain + 1) and ln (AJC + 1)) decreased the skewness and improved the normality of their distribution, although the floor effect persisted. The floor effect reflects the natural history of JIA, and therefore was considered to be inevitable. The skewness and kurtosis statistics are reported with the figures.

Histograms of disease duration and psychosocial functioning of the child indicated that their distribution was positively skewed, with large proportions of patients with short disease duration and good psychosocial functioning. Log transformation with base e (ln (duration + 1) and ln (psychosocial + 1)) decreased the skewness and improved the normality of their distribution, however only to a small extent.

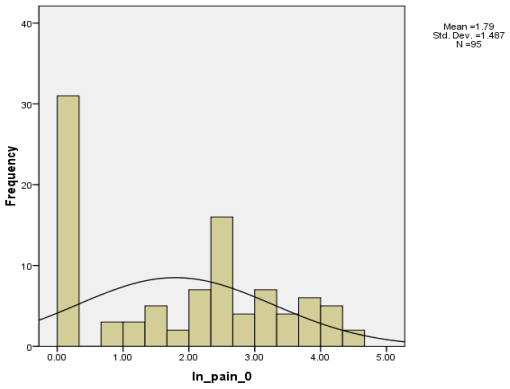
Histograms of the other independent, continuous variables (age, family integration, social support and medical situation) approximated a normal distribution, and therefore transformation was not performed.

Figure 1: pain (baseline)



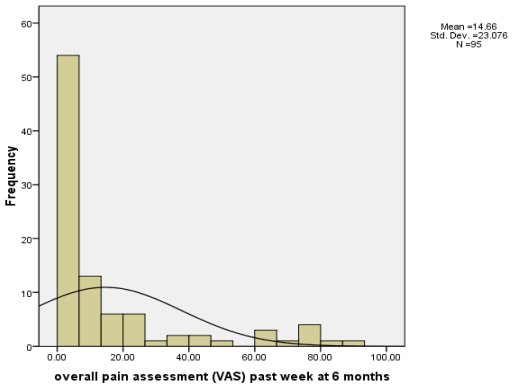
skew 1.765; kurt 2.444

Figure 2: ln pain (baseline)



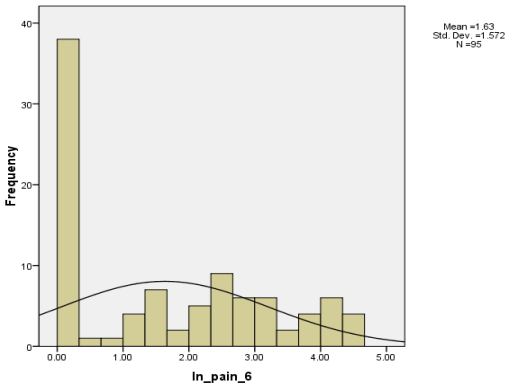
skew 0.043; kurt –1.390

Figure 3: pain (6-month)



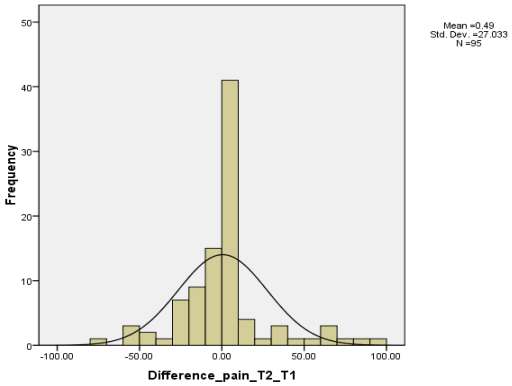
skew 1.871; kurt 2.460

Figure 4: ln pain (6-month)



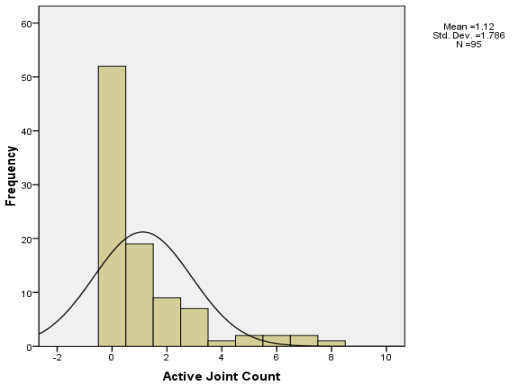
skew 0.330; kurt -1.344

Figure 5: change in pain intensity



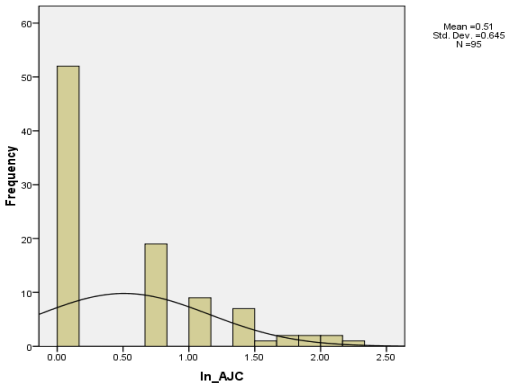
skew 0.773; kurt 2.666

Figure 6: AJC



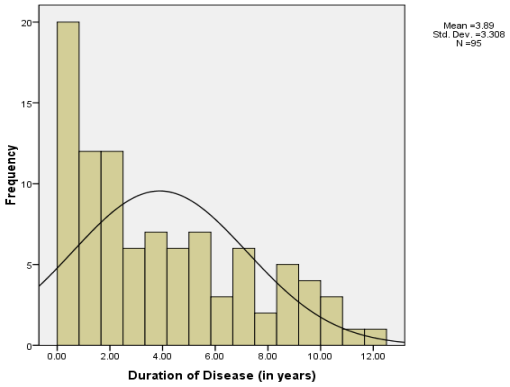
skew 2.078; kurt 4.130

Figure 7: ln AJC



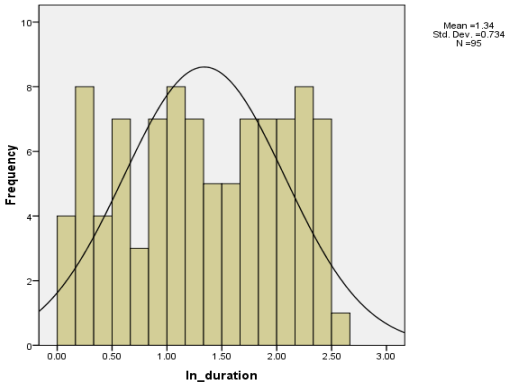
skew 0.977; kurt -0.167

Figure 8: duration



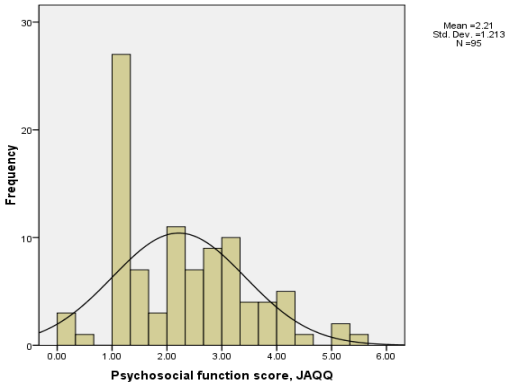
skew 0.734; kurt –0.590

Figure 9: ln duration



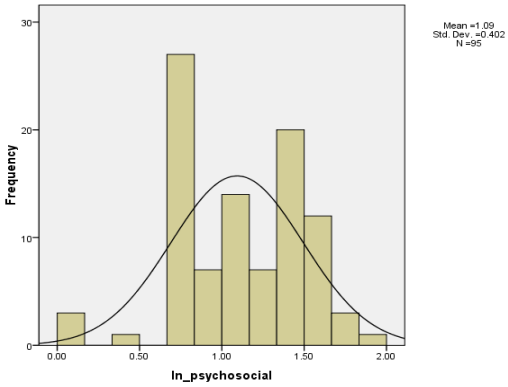
skew –0.097; kurt –1.212

Figure 10: psychosocial



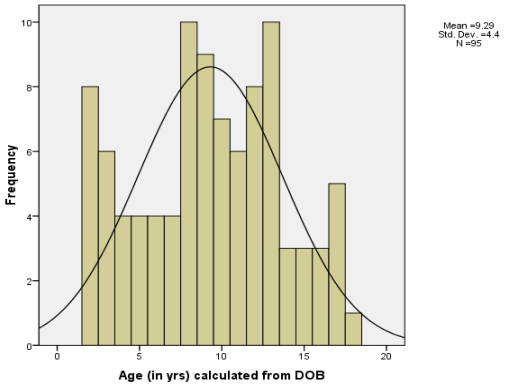
skew 0.441; kurt –0.387

Figure 11: ln psychosocial



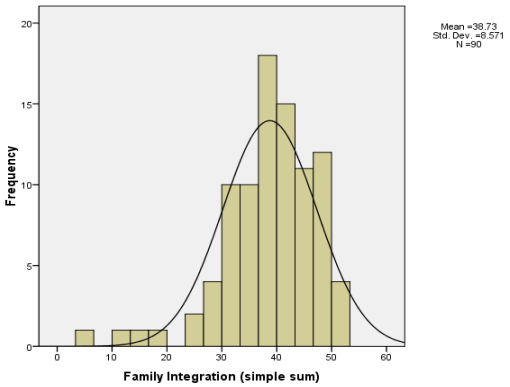
skew –0.439; kurt 0.003

Figure 12: age



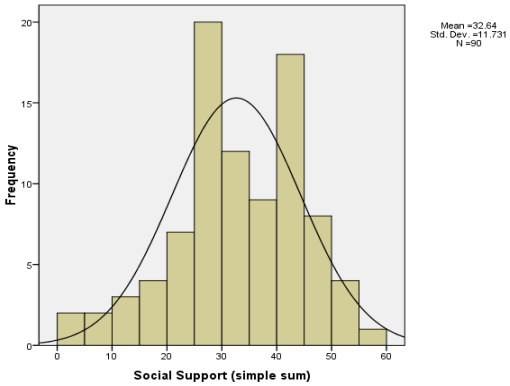
skew –0.039; kurt –0.870

Figure 13: family integration



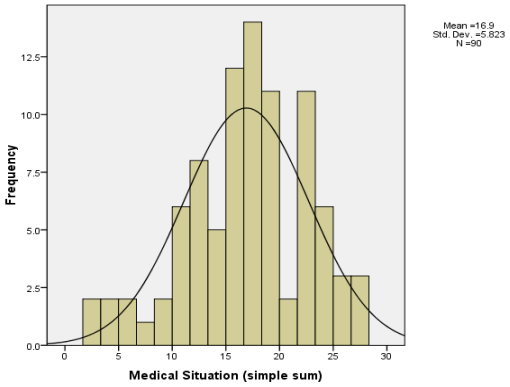
skew –1.304; kurt 2.693

Figure 14: social support



skew –0.443; kurt 0.013

Figure 15: medical situation



skew –0.385; kurt –0.243

Histograms on data from the **Baseline Cohort** and **Month 6 Cohort** were also produced, and log transformation with base e of the same variables was performed (data not shown). The histograms were similar to those obtained from the **Total Cohort**.

The mean, median, standard deviation, minimum and maximum of transformed variables on the **Total Cohort** are shown in Table 9.

Table 9: Descriptive analysis of transformed variables

Variable	Mean	Median	Standard deviation	Minimum	Maximun
Ln pain (baseline)	1.79	2.18	1.49	0.00	4.38
Ln pain (6-month)	1.63	1.39	1.57	0.00	4.51
Ln AJC	0.51	0.00	0.64	0.00	2.20
Ln duration	1.34	1.31	0.73	0.08	2.59
Ln psychosocial	1.09	1.16	0.40	0.00	1.86

4. Correlational analysis

Pearson correlation coefficients were obtained to identify simple correlations between all variables on the **Total Cohort** (see Appendix 3). There were 90 patients in whom data on all variables were available. The variables, which were significantly correlated with each other (p value ≤ 0.05), are shown in Table 10. The direction of the correlation (negative) between change in pain intensity and the psychosocial functioning of the child at baseline visit was unexpected, however the strength was weak ($r = -0.216$). The other statistically significant correlations were logical from a clinical standpoint.

Table 10: Correlations in Total Cohort

Variable 1	Variable 2	Interpretation
Pain (baseline)	**AJC** **Ln AJC**	Patients with higher AJC have more pain at baseline.
	Ln pain (6-month)	Patients with more pain at baseline have more pain at month 6.
	Psychosocial **Ln psychosocial**	Patients with worse psychosocial function have more pain at baseline.
Ln pain (baseline)	**AJC** **Ln_AJC**	Patients with higher AJC have more pain at baseline.
	Pain (6-month) **Ln pain (6-month)**	Patients with more pain at baseline have more pain at month 6.
	Psychosocial **Ln psychosocial**	Patients with worse psychosocial function have more pain at baseline.
	Coping pattern II (soc sup)	Patients whose parents use social support have less pain at baseline.
Pain (6-month)	**Ln AJC**	Patients with higher AJC have more pain at month 6.
Ln pain (6-month)	**AJC** **Ln AJC**	Patients with higher AJC have more pain at month 6.
Change in pain intensity	**Pain (baseline)** **Ln pain (baseline)**	Worsening pain over a 6-month period is associated with less pain at baseline.
	Pain (6-month) **Ln pain (6-month)**	Worsening pain over a 6-month period is associated with more pain at month 6.
	Psychosocial **Ln psychosocial**	Worsening pain over a 6-month period is associated with better psychosocial function at baseline.
Age	**Duration** **Ln duration**	Older patients have had longer disease duration.

Table 10 (cont.)

Coping pattern I (fam int)	**Coping pattern II (soc sup)**	Parents who use family integration also find other coping patterns useful.
	Coping pattern III (med sit)	
Coping pattern II (soc sup)	**Coping pattern III (med sit)**	Parents who use social support also use medical situation.

Pearson correlation coefficients were also obtained to identify simple correlations between all variables of the **Baseline Cohort** (142 patients) **and Month 6 Cohort** (103 patients) (see Appendix 3). Additional significant correlations, not found in the **Total Cohort**, are presented in Table 11 and Table 12. All correlations were logical from a clinical standpoint.

Table 11: Correlations in Baseline Cohort

Variable 1	Variable 2	Interpretation
Gender	**JIA category**	There is a positive correlation between being a girl and having oligoarthritis.
Age	**JIA category**	There is a positive correlation between being older and having other JIA categories.
	Coping pattern II (soc sup)	Patients whose parents use social support are older.
JIA category	**AJC** **Ln AJC**	Patients with other JIA categories have higher AJC.
	Coping pattern II (soc sup)	Patients whose parents use social support belong to other JIA categories.
AJC **Ln AJC**	**Psychosocial** **Ln psychosocial**	Patients with higher AJC have worse psychosocial function.

Table 12: Correlations in Month 6 Cohort

Variable 1	Variable 2	Interpretation
Ln duration	**Ln AJC**	Patients with longer disease duration have lower AJC.
Gender	**JIA category**	There is a positive correlation between being a girl and having oligoarthritis.
Ln AJC	**Coping pattern II (soc sup)**	Patients whose parents use social support have lower AJC.

5. Simple linear regression analysis

Because transformation of the dependent variables resulted in substantial improvement in the normality of their distribution, only their transformed versions were evaluated in the simple linear regression analysis (SLRA). The effects of each untransformed and transformed, independent variables were investigated.

From the **Total Cohort**, simple linear regression (SLR) models were produced for ln pain (baseline visit), ln pain (6-month visit) and change in pain intensity. Then, SLR models were produced for ln pain (baseline visit) in the **Baseline Cohort** and for ln pain (6-month visit) in the **Month 6 Cohort**.

Total Cohort – ln pain (baseline visit)

The parameter estimates, standard errors, t statistics, p values and R^2 values obtained from the cross-sectional analyses evaluating ln pain (baseline visit) in the **Total Cohort** are shown in Table 13. The independent variables that were significantly associated (p value ≤ 0.05) with ln pain (baseline visit) included AJC, psychosocial functioning of the child, social support, ln AJC and ln psychosocial functioning of the child. These variables explained 20.7%, 12.9%, 6.3%, 23.8% and 15.1%, respectively, of the total variance in ln pain (baseline

visit). There was an inverse relationship between social support and ln pain (baseline visit). The remaining variables were not significant and each explained less than 3.0% of the total variance.

Table 13: SLRA on Total Cohort – ln pain (baseline visit)

Variable	Coefficient (unstand.)	Standard error	t stat.	p value	R^2 value
Gender	-0.433	0.350	-1.237	0.219	0.016
Duration	-0.056	0.046	-1.213	0.228	0.016
Age	0.024	0.035	0.687	0.494	0.005
JIA category	-0.170	0.307	-0.555	0.581	0.003
AJC	**0.379**	**0.077**	**4.922**	**<0.001**	**0.207**
Psychosocial	**0.441**	**0.119**	**3.715**	**<0.001**	**0.129**
Coping pattern I	-0.015	0.018	-0.827	0.410	0.008
Coping pattern II	**-0.032**	**0.013**	**-2.424**	**0.017**	**0.063**
Coping pattern III	-0.013	0.027	-0.484	0.630	0.003
Ln AJC	**1.127**	**0.209**	**5.396**	**<0.001**	**0.238**
Ln duration	-0.327	0.207	-1.575	0.119	0.026
Lnpsychosocial	**1.440**	**0.354**	**4.073**	**<0.001**	**0.151**

Total Cohort – ln pain (6-month visit)

The results of the longitudinal analyses evaluating ln pain (6-month visit) in the **Total Cohort** are shown in Table 14. The independent variables that were significantly associated (p value ≤ 0.05) with ln pain (6-month) included AJC and ln AJC. These variables explained 4.4% and 7.7%, respectively, of the total variance in ln pain (6-month). The remaining variables were not significant and each explained less than 3.0% of the total variance.

Table 14: SLRA on Total Cohort – ln pain (6-month visit)

Variable	Coefficient (unstand.)	Standard error	t stat.	p value	R^2 value
Gender	-0.259	0.372	-0.697	0.488	0.005
Duration	-0.059	0.049	-1.197	0.234	0.015
Age	0.002	0.037	0.048	0.962	0.000
JIA category	0.206	0.325	0.634	0.528	0.004
AJC	**0.184**	**0.089**	**2.064**	**0.042**	**0.044**
Psychosocial	0.176	0.133	1.318	0.191	0.018
Coping pattern I	0.009	0.020	0.441	0.660	0.002
Coping pattern II	0.004	0.014	0.251	0.803	0.001
Coping pattern III	0.042	0.029	1.457	0.149	0.024
Ln AJC	**0.678**	**0.243**	**2.789**	**0.006**	**0.077**
Ln duration	-0.311	0.220	-1.414	0.161	0.021
Lnpsychosocial	0.549	0.402	1.367	0.175	0.020

Total Cohort – change in pain intensity

The results from the exploratory analyses evaluating change in pain intensity in the **Total Cohort** are shown in Table 15. The independent variables that were significantly associated (p value ≤ 0.05) with change in pain intensity included psychosocial functioning of the child and ln psychosocial functioning of the child. These variables explained 4.6% and 4.7%, respectively, of the total variance in change in pain intensity. There was an inverse relationship between the psychosocial functioning of the child and change in pain intensity. The remaining variables were not significant and each explained less than 3.0% of the total variance.

Table 15: SLRA on Total Cohort – change in pain intensity

Variable	Coefficient (unstand.)	Standard error	t stat.	p value	R^2 value
Gender	-4.459	6.400	-0.697	0.488	0.005
Duration	-0.004	0.847	-0.005	0.996	0.000
Age	0.309	0.636	0.486	0.628	0.003
JIA category	5.831	5.559	1.049	0.297	0.012
AJC	-2.352	1.551	-1.516	0.133	0.024
Psychosocial	**-4.758**	**2.258**	**-2.107**	**0.038**	**0.046**
Coping pattern I	-0.021	0.344	-0.061	0.952	0.000
Coping pattern II	0.368	0.249	1.480	0.142	0.024
Coping pattern III	0.390	0.505	0.772	0.442	0.007
Ln AJC	-4.021	4.329	-0.929	0.355	0.009
Ln duration	-0.066	3.821	-0.017	0.986	0.000
Lnpsychosocial	**-14.574**	**6.811**	**-2.140**	**0.035**	**0.047**

Baseline Cohort – ln pain (baseline visit)

The results from the cross-sectional analyses (exploratory) evaluating ln pain (baseline visit) in the **Baseline Cohort** are shown in Table 16. In addition to the statistically significant associations identified from the cross-sectional analysis in the **Total Cohort**, age was also found to be associated with ln pain (baseline visit). The variables age, AJC, psychosocial functioning of the child, social support, ln AJC and ln psychosocial functioning of the child each explained 3.1%, 7.0%, 14.7%, 3.0%, 17.8% and 17.0%, respectively, of the total variance in ln pain (baseline visit). The remaining variables were not significant and each explained less than 3.0% of the total variance.

Table 16: SLRA on Baseline Cohort – ln pain (baseline visit)

Variable	Coefficient (unstand.)	Standard error	t stat.	p value	R^2 value
Gender	-0.462	0.253	-1.826	0.070	0.021
Duration	-0.013	0.036	-0.361	0.719	0.001
Age	**0.060**	**0.027**	**2.223**	**0.028**	**0.031**
JIA category	0.176	0.241	0.730	0.466	0.003
AJC	**0.101**	**0.029**	**3.420**	**0.001**	**0.070**
Psychosocial	**0.443**	**0.086**	**5.158**	**<0.001**	**0.147**
Coping pattern I	-0.004	0.014	-0.275	0.784	0.001
Coping pattern II	**-0.022**	**0.010**	**-2.075**	**0.040**	**0.030**
Coping pattern III	0.003	0.021	0.149	0.882	0.000
Ln AJC	**0.793**	**0.137**	**5.785**	**<0.001**	**0.178**
Ln duration	-0.130	0.168	-0.776	0.439	0.004
Lnpsychosocial	**1.522**	**0.271**	**5.609**	**<0.001**	**0.170**

Month 6 Cohort – ln pain (6-month visit)

The results from the longitudinal analyses (exploratory) evaluating ln pain (6-month visit) in the **Month 6 Cohort** are shown in Table 17. The statistically significant associations identified were the same as those found from the longitudinal analyses in the **Total Cohort**. The variables AJC and ln AJC each explained 5.4% and 9.3%, respectively, of the total variance in ln pain (6-month visit). The remaining variables were not significant and each explained less than 2.0% of the total variance.

Table 17: SLRA on Month 6 Cohort – ln pain (6-month visit)

Variable	Coefficient (unstand.)	Standard error	t stat.	p value	R^2 value
Gender	-0.309	0.337	-0.916	0.361	0.008
Duration	-0.024	0.041	-0.589	0.557	0.003
Age	0.007	0.033	0.219	0.827	0.000
JIA category	0.162	0.293	0.551	0.583	0.003
AJC	**0.207**	**0.083**	**2.494**	**0.014**	**0.054**
Psychosocial	0.139	0.121	1.150	0.253	0.012
Coping pattern I	0.002	0.018	0.118	0.906	0.000
Coping pattern II	0.001	0.014	0.099	0.921	0.000
Coping pattern III	0.027	0.026	1.039	0.301	0.011
Ln AJC	**0.742**	**0.221**	**3.360**	**0.001**	**0.093**
Ln duration	-0.235	0.196	-1.199	0.233	0.013
Lnpsychosocial	0.457	0.371	1.231	0.221	0.014

Residual plots

Residual plots (studentized residuals against unstandardized predicted values) were produced for the SLR models obtained from the cross-sectional analyses on the **Total Cohort**. Overall, the assumptions of linearity, normality and homoscedascity were not violated, although a floor effect persisted caused by a large proportion of patients with no pain (ln pain = 0), as shown in Figures 16-25. The residual plots of ln disease duration and ln psychosocial functioning of the child did not differ substantially from the residual plots of the untransformed variables. However, the residual plot of ln AJC showed an improvement in linearity, normality and homoscedascity, in comparison to the residual plot of the untransformed variable. As shown in Figures 26-27, the residuals were negative at values of AJC between 6 and 8. Ln AJC resulted in improvement of the normality. A floor effect persisted, caused by a large proportion of patients with no active joints. Residual plots for the categorical variables were not produced.

Figure 16: age

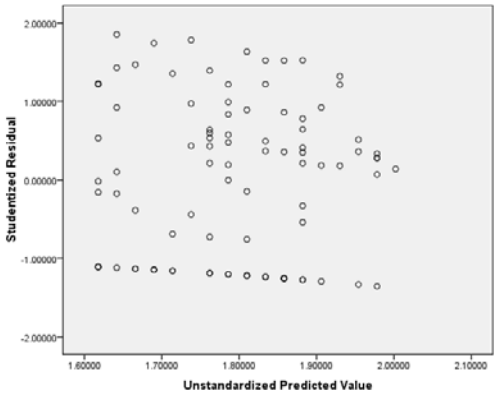


Figure 17: family integration

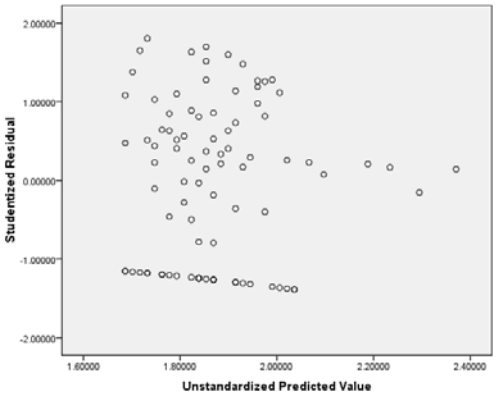


Figure 18: social support

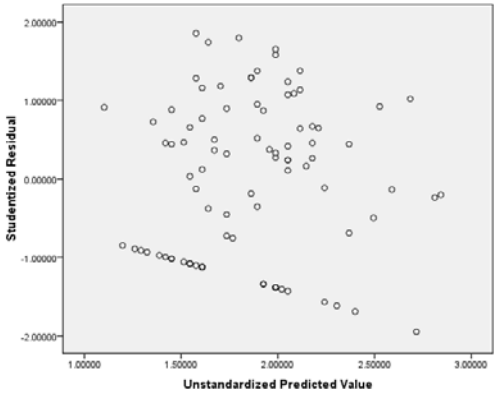


Figure 19: medical situation

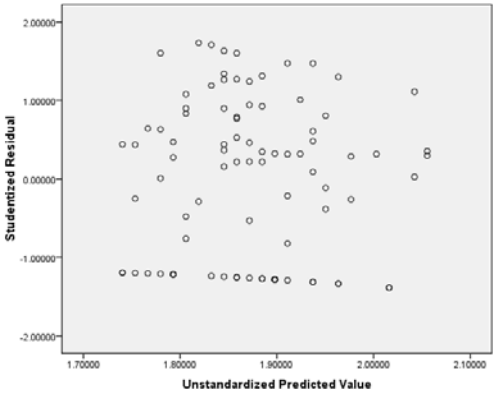


Figure 20: duration

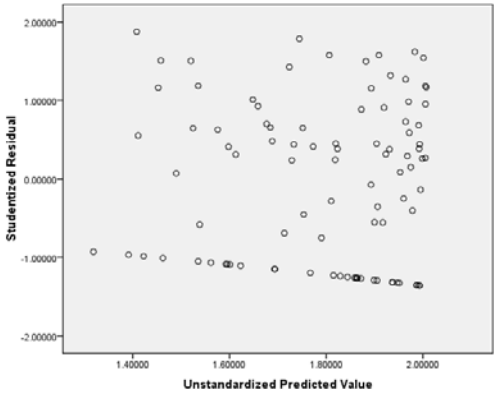


Figure 21: ln duration

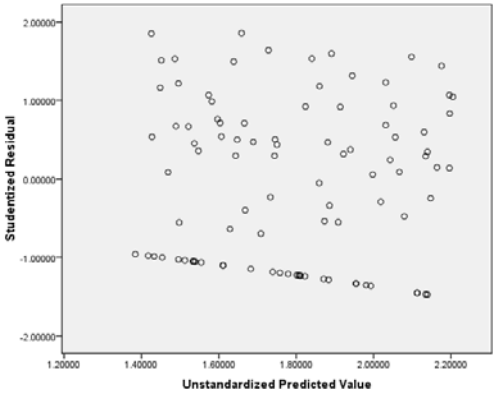


Figure 22 : psychosocial

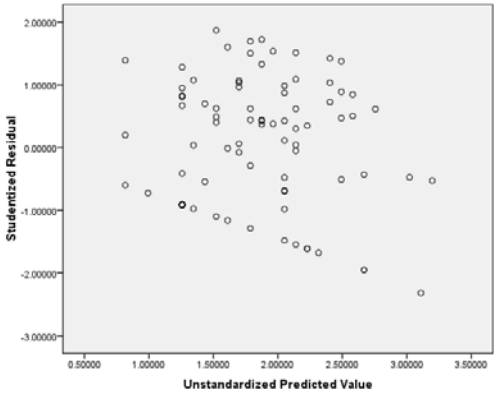


Figure 23 : ln psychosocial

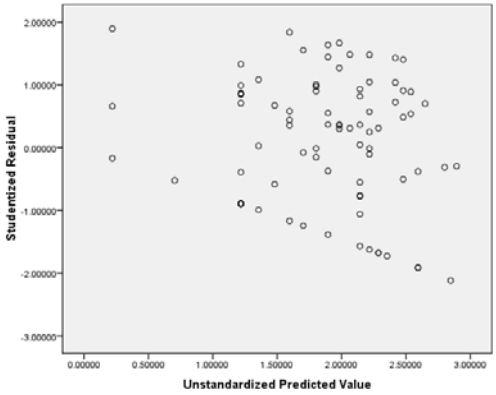


Figure 24: AJC

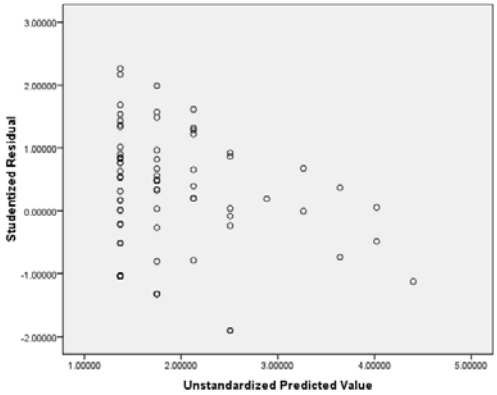


Figure 25: ln AJC

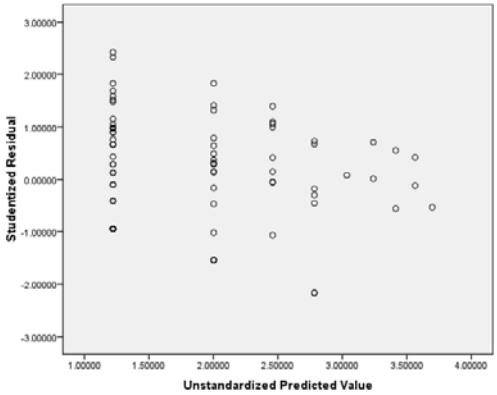


Figure 26: residuals vs AJC

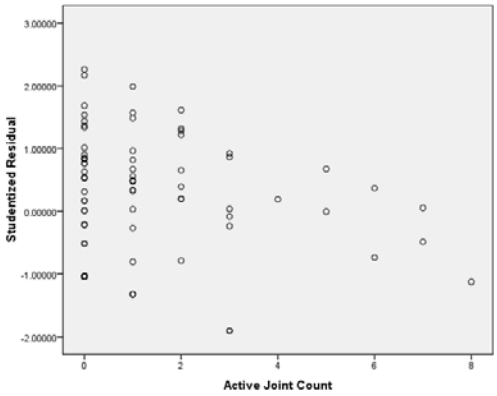
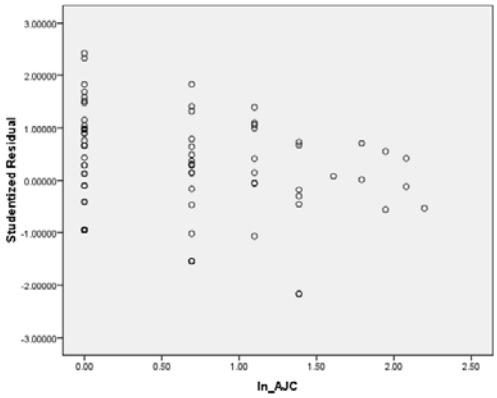


Figure 27: residuals vs ln AJC



Therefore, for the MLRA to be described in the next section, ln AJC was chosen as the independent variable. The other independent, continuous variables were kept untransformed.

Residual plots were also produced for other SLR models obtained on the **Total Cohort**, with ln pain (6-month visit) and change in pain intensity (data not shown). Overall, the residual plots were similar to the ones presented above, and confirmed the choice of the independent, continuous variables mentioned in the previous paragraph.

6. Multiple linear regression analysis - Evaluation of the association between the psychosocial functioning of the child and pain

Here, the relationship between the psychosocial functioning of the child and pain is described. First, the results of the MLRA on the **Total Cohort** are presented, including the cross-sectional and longitudinal analyses. Finally, the results of the exploratory analyses, as outlined in the section Statistical Evaluation, are presented.

Cross-sectional analysis - Total Cohort

A MLRA model was built to evaluate the cross-sectional relationship between the psychosocial functioning of the child and pain intensity reported at baseline visit in the **Total Cohort**. A hierarchical approach was used to determine the amount of additional variance in pain ratings explained by the psychosocial functioning of the child, above and beyond disease activity, and after controlling for demographic and disease-related variables. The total number of patients included in the model was 95, and thus there were no missing observations. The dependent variable was ln pain (baseline visit). The independent variables were entered in the following steps, regardless of their statistical significance:

Step 1: disease duration, gender, age and JIA category

Step 2: ln AJC

Step 3: psychosocial functioning of the child.

The full model is the following, and the statistically significant unstandardized β coefficients (p value ≤ 0.05) are in bold:

ln pain (baseline visit) = 0.408 – 0.058(duration) – 0.379(sex) + **0.073(age)** – 0.452(JIA category) + **1.046(ln AJC)** + **0.420(psychosocial).**

The R^2 value, R^2 change, F change statistic and p value of each step, as well as the F statistics and p values of the full model are shown in Table 18.

Table 18: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.055	0.055	1.318	0.269	1.318	0.269
Step 2	0.286	0.231	28.746	<0.001	7.129	<0.001
Step 3	0.399	0.113	16.537	<0.001	9.734	<0.001

The unstandardized β coefficients, standard errors, t statistics, p values and 95% confidence intervals of the full model (step 3) are shown in Table 19.

Table 19: coefficients and confidence intervals of full model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Duration	-0.058	0.044	-1.314	0.192	-0.146	0.030
Gender	-0.379	0.290	-1.305	0.195	-0.956	0.198
Age	**0.073**	**0.033**	**2.207**	**0.030**	**0.007**	**0.138**
JIA category	-0.452	0.252	-1.792	0.077	-0.954	0.049
Ln AJC	**1.046**	**0.196**	**5.328**	**<0.001**	**0.656**	**1.437**
Psychosocial	**0.420**	**0.103**	**4.067**	**<0.001**	**0.215**	**0.625**

The full model was significant (p value < 0.001). The independent variables collectively explained 39.9% of the total variance in pain (baseline visit). AJC explained 23.1% of the total variance in pain. The psychosocial functioning of the child significantly contributed another 11.3% to the variance in pain, above and beyond disease activity. The variables that were significantly associated with pain (baseline visit) included age, AJC and psychosocial functioning of the child. In comparison to the univariate analyses, the demographic characteristic, age, became significant.

The assumptions of linearity, normality and homoscedascity were verified. The residual plot of studentized residuals versus unstandardized predicted values of ln pain indicated the presence of a floor effect, caused by a large proportion of patients with no pain. However, it also demonstrated that there were no major violations of the assumptions (Figure 28). Furthermore, a histogram of the studentized residuals showed a normal distribution (Figure 29).

Figure 28: residual plot

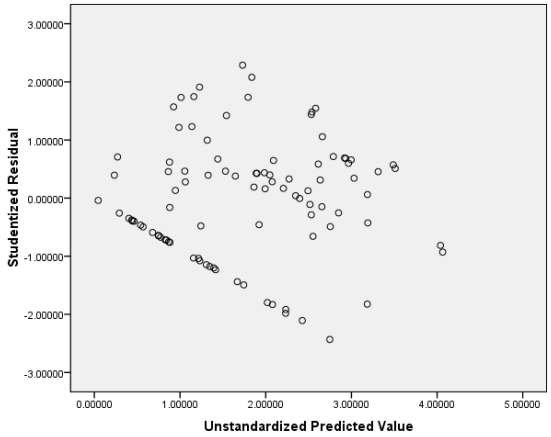
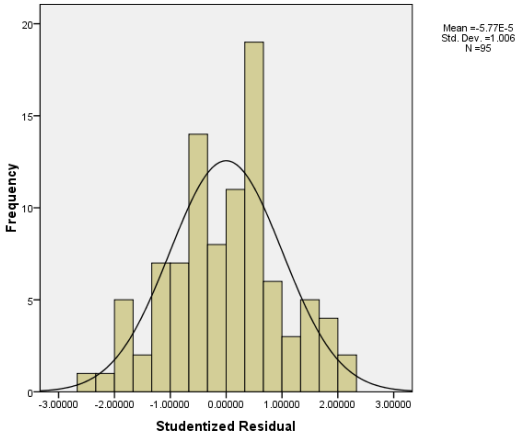


Figure 29: histogram



Partial regression plots of the independent variables were produced. The plots indicated that the associations between age, AJC and psychosocial functioning of the child, and pain (baseline visit), were linear (Figures 30-32). There were no influential points.

Figure 30: partial regression plot (age)

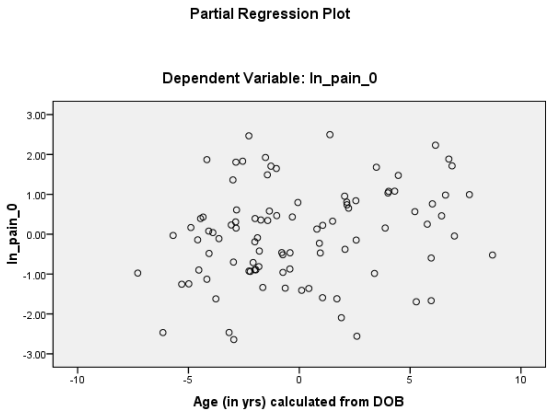


Figure 31: partial regression plot (ln AJC)

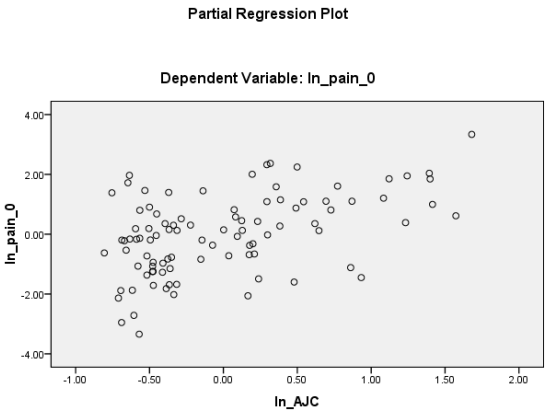
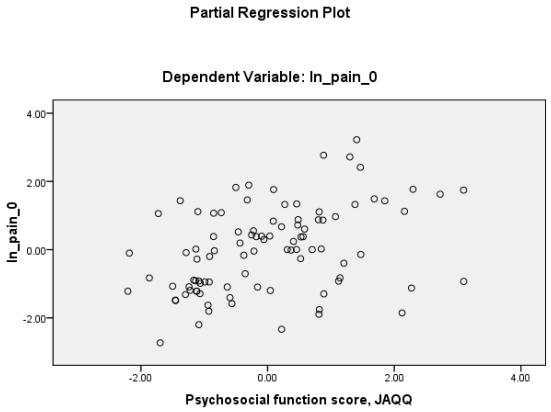


Figure 32: partial regression plot (psychosocial)



An outlier diagnosis was run on the model in order to identify influential points. Values of the Cook's distance were within normal limits i.e., less than 1, meaning that no case resulted in large change in the regression coefficients when removed from the analysis (Appendix 4). Leverage values were below the cutoff (2p/N = 0.13), indicating that no case had unusual combination of values for the independent variables (Appendix 4). The cases that resulted in the 5 largest positive and 5 largest negative changes in regression coefficients, when removed

from the model, were identified by looking at DfBetas (Appendix 4). None of the cases listed resulted in relative changes in the regression coefficients of greater than their standard errors, and therefore none of the patients were removed from the final model.

A collinearity diagnosis was run on the model (Appendix 4). The values of tolerance, condition index and variance proportions indicated that there was no collinearity between the independent variables in the model.

The analysis was rerun without the independent variables gender, disease duration and JIA category. The reduced model was the following:
Ln pain (baseline visit) = -0.058 + 0.045(age) + **1.066(ln AJC)** + **0.405(psychosocial).**

The reduced model summary statistics, coefficients and confidence intervals are shown in Tables 20 and 21, and are overall similar to those from the full model. The independent variables collectively explained 35.3% of the total variance in pain (baseline visit). The variables that were significantly associated with pain (baseline visit) included AJC and psychosocial functioning of the child. The main difference is that the variable age did not significantly contribute to the total variance in pain, and its regression coefficient became non significant. Overall, the regression coefficients were similar to those obtained in the SLRA performed earlier on the Total Cohort (Table 13), indicating that there were no confounding factors.

Table 20: reduced model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.005	0.005	0.472	0.494	0.472	0.494
Step 2	0.247	0.242	29.585	<0.001	15.101	<0.001
Step 3	0.353	0.106	14.959	<0.001	16.581	<0.001

Table 21: coefficients and confidence intervals of reduced model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Age	0.045	0.029	1.552	0.124	-0.012	0.102
Ln AJC	**1.066**	**0.196**	**5.448**	**<0.001**	**0.677**	**1.454**
Psychosocial	**0.405**	**0.105**	**3.868**	**<0.001**	**0.197**	**0.612**

The interpretation of the reduced model is complex because both the dependent variable and AJC were log transformed with base e.

AJC was significantly associated with pain at baseline visit, when adjusted for all other variables in the model. Patients with a high AJC experienced more pain than those with a low AJC. Doubling the number of active joints increased pain by 109% on the VAS, while keeping all other variables constant, based on the following calculations. For high values of baseline pain, the effect of doubling the AJC brings pain outside its expected range (0-100 mm). In these instances, pain should be predicted at 100 mm.

$\beta' = (\beta \ln AJC) * \ln(2) = 1.066 * \ln(2) = 0.7389$

$\exp(\beta') = 2.0936$ = the effect on pain of doubling the AJC.

The psychosocial functioning of the child was significantly associated with pain at baseline visit, when adjusted for all other variables in the model. Worsening of psychosocial functioning by 1 point on the JAQQ increased pain by 49.9% on the VAS, while keeping all other variables constant, based on the following calculation. Similarly, for high values of baseline pain, the effect on pain of increasing the psychosocial score by 1 point brings pain outside its expected range (0-100 mm). In these instances, pain should be predicted at 100 mm.

$\exp(\beta \text{ psychosocial}) = \exp(0.405) = 1.4993$

Longitudinal analysis – Total Cohort

A MLRA model was built to evaluate the longitudinal relationship between the psychosocial functioning of the child measured at baseline and pain intensity reported 6 months later in the **Total Cohort**. A hierarchical approach was again used. The total number of patients included in the model was 95, and thus there were no missing observations. Here, the dependent variable was ln pain (6-month visit). Pain reported at baseline visit was not controlled for. The independent variables were entered in the same steps as described above.

The full model is the following:

ln pain (6-month visit) = 1.004 – 0.053(duration) – 0.160(sex) + 0.028(age) + 0.078(JIA category) + **0.602(ln AJC)** + 0.156(psychosocial).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 22 and 23. The full model was not significant (p value 0.131). The independent variables collectively explained 10.4% of the total variance in pain (6-month visit). However, AJC was the only variable whose regression coefficient was statistically significant, and it explained 6.5% of the total variance in pain intensity. The psychosocial functioning of the child did not significantly contribute to the total variance, above and beyond disease activity. In comparison to the univariate analyses, no additional variable became significant.

Table 22: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.025	0.025	0.582	0.677	0.582	0.677
Step 2	0.090	0.065	6.320	0.014	1.757	0.130
Step 3	0.104	0.014	1.363	0.246	1.697	0.131

Table 23: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.053	0.057	-0.923	0.359	-0.167	0.061
Gender	-0.160	0.375	-0.426	0.671	-0.905	0.586
Age	0.028	0.043	0.659	0.511	-0.057	0.113
JIA category	0.078	0.326	0.239	0.812	-0.570	0.725
Ln AJC	**0.602**	**0.254**	**2.375**	**0.020**	**0.098**	**1.106**
Psychosocial	0.156	0.133	1.167	0.246	-.109	0.421

The residual plot indicated the presence of a floor effect, caused by a large proportion of patients with no pain. However, it also demonstrated that there were no major violations of the assumptions required for MLRA (Figure 33). Furthermore, a histogram of the studentized residuals approximated a normal distribution (Figure 34).

Figure 33: residual plot

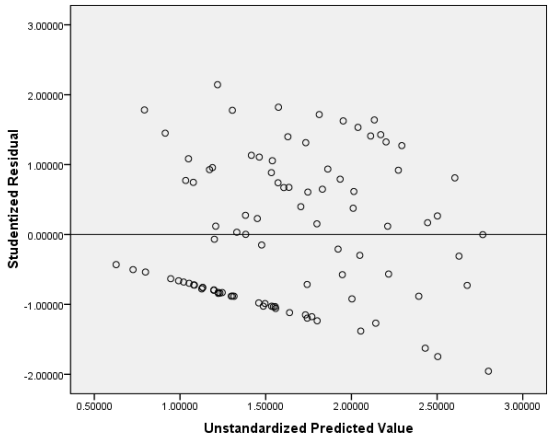
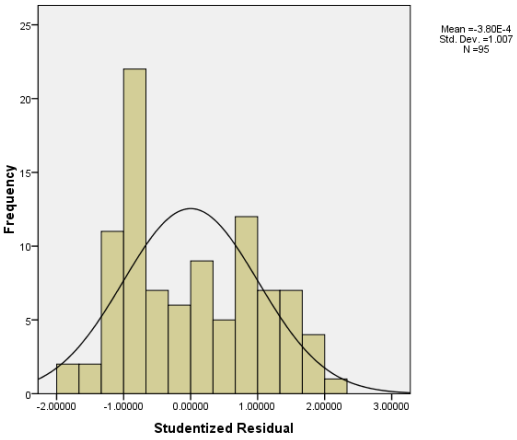
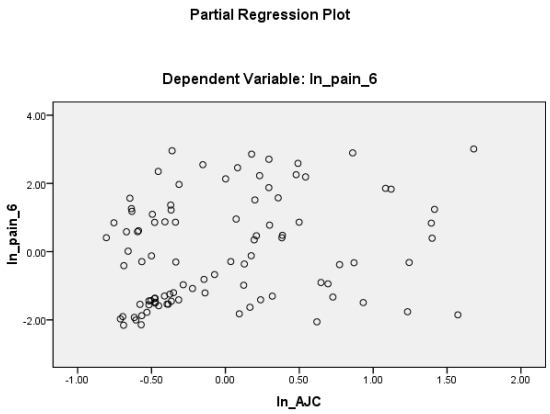


Figure 34: histogram



Partial regression plots demonstrated that the association between ln AJC and ln pain was linear (Figures 35). There were no influential points.

Figure 35: Partial regression plot
(ln AJC)



Similarly to the cross-sectional analysis, multiple linear regression diagnostics for influential points and collinearity were performed. Cook's distances, leverage values, DfBetas and collinearity diagnosis are shown in Appendix 5. Problems were not identified, and none of the patients were removed from the final model.

The analysis was rerun including only ln AJC. The reduced model was the following:
ln pain (6-month visit) = 1.289 + **0.678(ln AJC)**.

The reduced model summary statistics, coefficients and confidence intervals are shown in Tables 24 and 25, and are overall similar to those from the full model. The main difference is that the model became statistically significant (p value 0.006), with AJC explaining 7.7% of the total variance in pain (6-month visit).

Table 24: reduced model summary

R^2 value	**F stat.**	**Sign. of F stat.**
0.077	7.777	0.006

Table 25: coefficients and confidence intervals of reduced model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Ln AJC	0.678	0.243	2.789	0.006	0.195	1.160

AJC was significantly associated with pain at 6-month visit. Patients with a high AJC experienced more pain than those with a low AJC. Doubling the number of active joints increased pain by 60.0% on the VAS, based on the following calculations:

β' = (β ln AJC) * ln(2) = 0.678 * ln(2) = 0.4699

exp(β') = 1.5999 = the effect on pain of doubling the AJC.

Exploratory analysis: Baseline Cohort

In order to establish generalizability, the cross-sectional analysis was rerun on the **Baseline Cohort**. The results were compared to those obtained from the cross-sectional analysis on the **Total Cohort**. A similar approach to that described above was used. The only difference was the total number of patients included in the model i.e., 156 as opposed to 95. There was only one missing observation from the **Baseline Cohort** (1/157, 0.6%).

The full model is the following:

ln pain (baseline visit) = 0.286 – 0.040(duration) – 0.214(sex) + **0.088(age)** – 0.439(JIA category) + **0.649(ln AJC)** + **0.388(psychosocial).**

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 26 and 27, and compared to those obtained from the cross-sectional analysis on the **Total Cohort**. The models obtained from the **Baseline Cohort** and **Total Cohort** were similar. The only difference is that, in the **Baseline Cohort**, the variable JIA category approached but did not reach statistical significance (ß -0.439; p value 0.051). Overall, performing the analysis on a larger sample did not provide more information.

Table 26: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.053	0.053	2.106	0.083	2.106	0.083
Step 2	0.217	0.164	31.508	<0.001	8.326	<0.001
Step 3	0.320	0.103	22.629	<0.001	11.711	<0.001

Table 27: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.040	0.035	-1.136	0.258	-0.109	0.029
Gender	-0.214	0.226	-0.946	0.346	-0.661	0.233
Age	**0.088**	**0.027**	**3.222**	**0.002**	**0.034**	**0.141**
JIA category	-0.439	0.223	-1.968	0.051	-0.879	0.002
Ln AJC	**0.649**	**0.135**	**4.793**	**<0.001**	**0.381**	**0.916**
Psychosocial	**0.388**	**0.082**	**4.757**	**<0.001**	**0.227**	**0.550**

Checking for violation of regression assumptions and multiple linear regression diagnostics were also completed. Similarly to the cross-sectional analysis on the **Total Cohort**, problems were not identified (data not shown).

Exploratory analysis: Month 6 Cohort

The longitudinal analysis was rerun on the **Month 6 Cohort** to establish generalizability**.** The results were compared to those obtained from the longitudinal analysis on the **Total Cohort**. A similar approach to that described above was used. The only difference was the total number of patients included in the model i.e., 111 as opposed to 95. There was only one missing observation from the **Month 6 Cohort** (1/112, 0.9%).

The full model is the following:

ln pain (6-month visit) = 1.174 – 0.005(duration) – 0.227(sex) + 0.014(age) – 0.060(JIA category) + **0.704(ln AJC)** + 0.081(psychosocial).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 28 and 29, and compared to those obtained from the longitudinal analysis on the **Total Cohort**. The models obtained from the **Month 6 Cohort** and **Total Cohort** were similar. Again, the model was not significant (p value 0.085). AJC remained the only variable whose regression coefficient was statistically significant.

Table 28: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.011	0.011	0.294	0.881	0.294	0.881
Step 2	0.096	0.085	9.848	0.002	2.224	0.057
Step 3	0.100	0.004	0.440	0.509	1.917	0.085

Table 29: coefficients and confidence intervals of full model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Duration	-0.005	0.050	-0.094	0.925	-0.104	0.094
Gender	-0.227	0.347	-0.654	0.514	-0.916	0.461
Age	0.014	0.039	0.361	0.719	-.064	0.093
JIA category	-0.060	0.301	-0.199	0.843	-0.656	0.537
Ln AJC	**0.704**	**0.234**	**3.002**	**0.003**	**0.239**	**1.169**
Psychosocial	0.081	0.122	0.663	0.509	-0.161	0.322

Checking for violation of regression assumptions and multiple linear regression diagnostics were also completed. Similarly to the longitudinal analysis on the **Total Cohort**, problems were not identified (data not shown).

Exploratory analysis: change in pain intensity

A MLRA model was built to evaluate the longitudinal relationship between baseline psychosocial functioning of the child and change in pain intensity, rather than future pain report at 6 months. A hierarchical approach was again used to determine the amount of additional variance of change in pain intensity explained by the psychosocial functioning of the child, above and beyond disease activity, and after controlling for demographic and disease-related variables. The analysis was performed on the **Total Cohort** which included 95 patients. The dependent variable was change in pain intensity. The independent variables were entered in the same steps as described above.

The full model is the following:

Change in pain intensity = 12.148 – 0.085(duration) – 3.700(sex) + 0.040(age) + 5.950(JIA category) – 3.635(ln AJC) **– 4.639(psychosocial).**

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 30 and 31. Although the full model was not significant (p value 0.373), the psychosocial functioning of the child had a statistically significant regression coefficient. The independent variables collectively explained only 6.9% of the total variance of the change in pain intensity. The psychosocial functioning of the child significantly contributed 4.2% to the total variance, above and beyond all other variables. In comparison to the univariate analysis, no additional variable became significant.

Table 30: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.016	0.016	0.368	0.831	0.368	0.831
Step 2	0.028	0.012	1.054	0.307	0.505	0.772
Step 3	0.069	0.042	3.945	0.050	1.092	0.373

Table 31: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.085	1.003	-0.085	0.933	-2.077	1.907
Gender	-3.700	6.570	-0.563	0.575	-16.756	9.357
Age	0.040	0.747	0.053	0.958	-1.444	1.523
JIA category	5.950	5.709	1.042	0.300	-5.396	17.295
Ln AJC	-3.635	4.441	-0.818	0.415	-12.461	5.191
Psychosocial	**-4.639**	**2.336**	**-1.986**	**0.050**	**-9.282**	**0.003**

The residual plot indicated the presence of a floor effect, caused by a large proportion of patients with no pain. However, it also demonstrated that there were no major violations of the assumptions required for MLRA (Figure 36). The histogram of the studentized residuals approximated a normal distribution (Figure 37), and showed that many patients experienced small change in pain intensity over a 6-month period .

Figure 36: residual plot

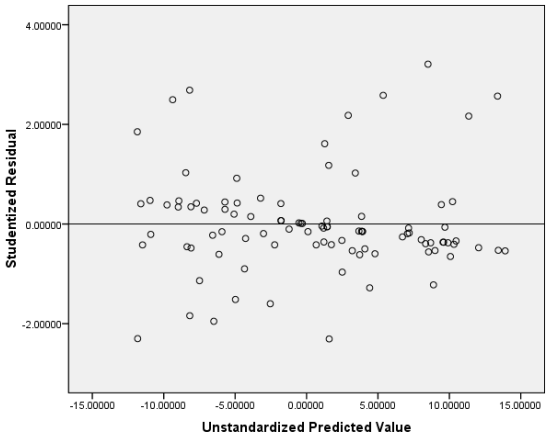
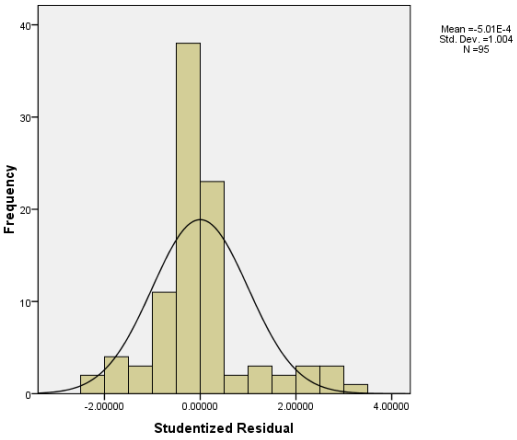
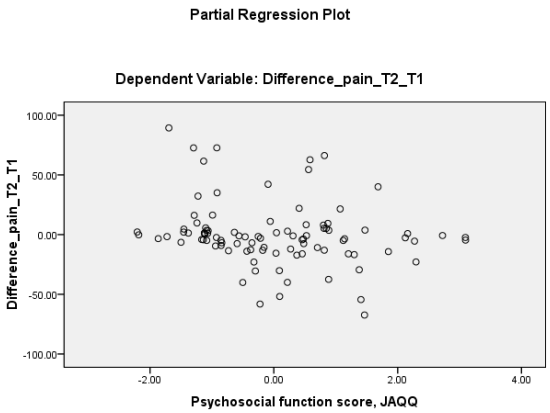


Figure 37: histogram



Partial regression plots demonstrated that the association between the psychosocial functioning of the child and change in pain intensity was linear (Figures 38). The plot also indicated the possible presence of a few influential points.

Figure 38: partial regression plot (psychosocial functioning of the child)



Multiple linear regression diagnostics for influential points were performed (Appendix 6). There was one case with a leverage value above the cutoff (2p/N = 0.13), indicating the presence of unusual combination of values for the independent variables of that particular case. However, no problems were identified from the Cook's distances and DfBetas, and therefore none of the

patients were removed from the final model. A collinearity diagnosis was run on the model, and problems were not identified (Appendix 6).

Even though the full model did not reach statistical significance, the analysis was rerun including only the psychosocial functioning of the child. The reduced model was the following:
Change in pain intensity = 11.032 – **4.758(psychosocial).**

The reduced model summary statistics, coefficients and confidence intervals are shown in Tables 32 and 33. In comparison to the full model, the reduced model became statistically significant (p value 0.038), and the psychosocial functioning of the child significantly contributed 4.6% to the total variance of change in pain intensity.

Table 32: reduced model summary

R^2 value	**F stat.**	**Sign. of F stat.**
0.046	4.439	0.038

Table 33: coefficients and confidence intervals of reduced model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Psychosocial	-4.758	2.258	-2.107	0.038	-9.242	-0.274

The psychosocial functioning of the child was significantly associated with change in pain intensity. The change in pain intensity was 11.032 mm for those with a psychosocial score of 0, and for each increase of 1 point on the psychosocial scale, the change in pain intensity decreased by 4.758 mm.

Exploratory analysis: interaction between psychosocial functioning of the child and disease activity)

A MLRA model was built to evaluate the moderating effect of the psychosocial functioning of the child on the association between disease activity and pain reported at baseline visit on the Total Cohort. The presence of a moderating effect in the longitudinal analysis (ln pain (6-month visit)) was not tested for. The interaction term was computed by multiplying ln AJC by the psychosocial function score. The dependent variable was ln pain (baseline visit). The independent variables were entered in the same steps as described above, and the interaction term was entered in Step 4, as follows:

Step 1: disease duration, gender, age and JIA category

Step 2: ln AJC

Step 3: psychosocial functioning of the child

Step 4: interaction ln AJC * psychosocial functioning of the child.

The full model is the following:

ln pain (baseline visit) = 0.414 – 0.059(duration) – 0.378(sex) + **0.073(age)** – 0.449(JIA category) + 1.003(ln AJC) + **0.416(psychosocial)** + 0.018(interaction (ln AJC * psychosocial)).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 34 and 35. The interaction term did not help explain any additional variance in pain (baseline visit), above and beyond all other variables, and its regression coefficient was not statistically significant. Thus, there was no moderating effect of the psychosocial functioning of the child on the association between disease activity and pain reported at baseline visit.

Table 34: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.055	0.055	1.318	0.269	1.318	0.269
Step 2	0.286	0.231	28.746	<0.001	7.129	<0.001
Step 3	0.399	0.113	16.537	<0.001	9.734	<0.001
Step 4	0.399	0.000	0.006	0.938	8.250	<0.001

Table 35: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.059	0.045	-1.305	0.195	-0.148	0.031
Gender	-0.378	0.293	-1.292	0.200	-0.959	0.204
Age	**0.073**	**0.033**	**2.190**	**0.031**	**0.007**	**0.140**
JIA category	-0.449	0.258	-1.743	0.085	-0.961	0.063
Ln AJC	1.003	0.589	1.704	0.092	-0.167	2.174
Psychosocial	**0.416**	**0.118**	**3.522**	**0.001**	**0.181**	**0.650**
Interaction	0.018	0.227	0.077	0.938	-0.433	0.468

Checking for violation of regression assumptions and multiple linear regression diagnostics for influential points did not identify problems (data not shown). A collinearity diagnosis indicated the possible presence of collinearity between ln AJC and the interaction term (Appendix 7).

7. Multiple linear regression analysis - Evaluation of the association between parental coping and pain

The relationship between the use of the three parental coping patterns and pain is described. First, the results of the MLRA on the **Total Cohort** are presented, including the cross-sectional and longitudinal analyses. Here, additional

analyses were also performed in order to evaluate the separate effect of each parental coping pattern. Finally, the results of the exploratory analyses, as outlined in the section Statistical Evaluation, are presented.

Total Cohort – cross-sectional analysis

A MLRA model was built to evaluate the cross-sectional relationship between the three parental coping patterns and pain intensity reported at baseline visit in the **Total Cohort**. A hierarchical approach was used to determine the amount of additional variance in pain ratings explained by the three parental coping patterns, above and beyond disease activity, and after controlling for demographic and disease-related variables. The total number of patients included in the model was 90, and thus there were only 5 missing observations (5/95, 5.2%). The dependent variable was ln pain (baseline visit). The independent variables were entered in the following steps, regardless of their statistical significance:

Step 1: disease duration, gender, age and JIA category

Step 2: ln AJC

Step 3: three parental coping patterns (family integration, social support, medical situation).

The full model is the following:

ln pain (baseline visit) = 2.151 – 0.022(duration) – 0.412(sex) + 0.049(age) – 0.295(JIA category) + **1.049(ln AJC)** – 0.011(family integration) – 0.021(social support) + 0.020(medical situation).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 36 and 37. The model was significant (p value < 0.001). The independent variables collectively explained 29.7% of the total variance in pain (baseline visit). However, AJC was the only variable significantly associated with pain (baseline visit), and it helped explain 23.1% of the total variance in pain. The three parental coping patterns did not

significantly contribute to the total variance in pain, above and beyond disease activity. In comparison to the univariate analysis, the regression coefficient of the parental coping pattern, social support, became not significant.

Table 36: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.037	0.037	0.817	0.518	0.817	0.518
Step 2	0.268	0.231	26.543	<0.001	6.159	<0.001
Step 3	0.297	0.028	1.085	0.360	4.268	<0.001

Table 37: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.022	0.050	-0.446	0.657	-0.123	0.078
Gender	-0.412	0.322	-1.280	0.204	-1.053	0.229
Age	0.049	0.037	1.314	0.193	-0.025	0.123
JIA category	-0.295	0.291	-1.011	0.315	-0.874	0.285
Ln AJC	**1.049**	**0.229**	**4.574**	**<0.001**	**0.593**	**1.505**
Coping I	-0.011	0.024	-0.444	0.659	-0.058	0.037
Coping II	-0.021	0.016	-1.260	0.211	-0.053	0.012
Coping III	0.020	0.031	0.655	0.514	-0.041	0.081

The residual plot indicated the presence of a floor effect, caused by a large proportion of patients with no pain. However, it also demonstrated that there were no major violations of the assumptions required for MLRA (Figure 39). Furthermore, a histogram of the studentized residuals approximated a normal distribution (Figure 40).

Figure 39: residual plot

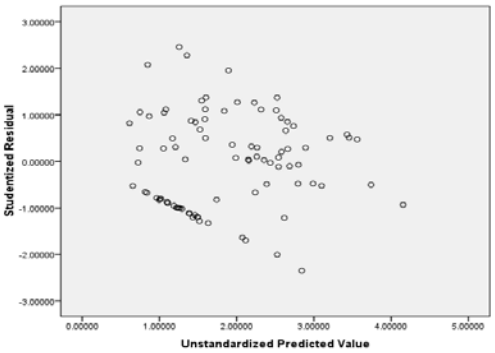
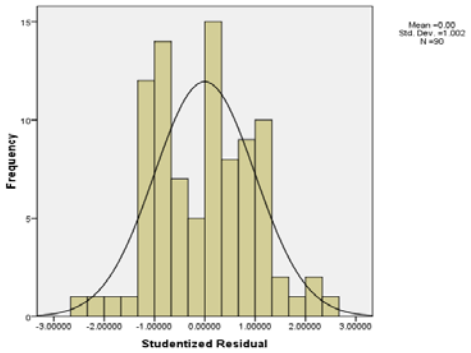
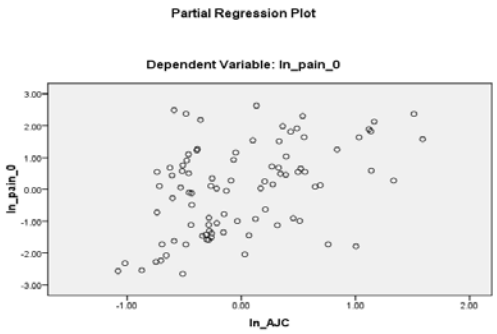


Figure 40: histogram



Partial regression plots demonstrated that the association between ln AJC and ln pain was linear (Figure 41). There were no influential points.

Figure 41: partial regression plot
(ln AJC)



Multiple linear regression diagnostics for influential points and collinearity were performed. Cook's distances, leverage values, DfBetas and collinearity diagnosis are shown in Appendix 8. Problems were not identified, and none of the patients were removed from the final model.

In the previous model, the three parental coping patterns were entered all together in Step 3. In order to evaluate the separate effect of each parental coping pattern, additional analyses were performed by entering the coping patterns, one at a time, in Step 3. There were, therefore, three additional models

analysed. The results of the analyses are not shown however, each of the three parental coping patterns did not significantly contribute to the total variance in pain (baseline visit), above and beyond all other variables, and their regression coefficients were not statistically significant. AJC remained the only variable significantly associated with pain (baseline visit), in each of the three models.

Total cohort – longitudinal analysis

A MLRA model was built to evaluate the longitudinal relationship between the three parental coping patterns and pain intensity reported at the 6-month visit in the **Total Cohort**. A hierarchical approach was again used. The total number of patients included in the model was 90, and thus there were only 5 missing observations (5/95, 5.2%). The dependent variable was ln pain (6-month visit). The independent variables were entered in the same steps as described above.

The full model is the following:

ln pain (6-month visit) = 1.230 – 0.036(duration) – 0.216(sex) + 0.015(age) – 0.100(JIA category) + **0.731(ln AJC)** – 0.026(family integration) – 0.010(social support) + 0.054(medical situation).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 38 and 39. The model was not significant (p value 0.207). The independent variables collectively explained only 12.2% of the total variance in pain (6-month visit). The three parental coping patterns did not significantly contribute to the total variance in pain, above and beyond disease activity. AJC remained the only variable significantly associated with pain (6-month visit), and it explained 6.9% of the total variance in pain.

Table 38: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.022	0.022	0.472	0.756	0.472	0.756
Step 2	0.091	0.069	6.409	0.013	1.683	0.148
Step 3	0.122	0.031	0.946	0.422	1.405	0.207

Table 39: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.036	0.060	-0.591	0.556	-0.155	0.084
Gender	-0.216	0.385	-0.562	0.576	-0.983	0.550
Age	0.015	0.045	0.345	0.731	-0.073	0.104
JIA category	-0.100	0.348	-0.288	0.774	-0.793	0.593
Ln AJC	**0.731**	**0.274**	**2.666**	**0.009**	**0.185**	**1.277**
Coping I	-0.026	0.028	-0.911	0.365	-0.082	0.031
Coping II	0.010	0.020	0.511	0.611	-0.029	0.049
Coping III	0.054	0.037	1.467	0.146	-0.019	0.127

Checking for violation of regression assumptions and multiple linear regression diagnostics were also performed. Similarly to the cross-sectional analysis on the **Total Cohort**, problems were not identified (data not shown).

In order to evaluate the separate effect of each parental coping pattern, additional analyses were performed by entering the coping patterns, one at a time, in Step 3. The results of the analyses are not shown however, each of the three parental coping patterns did not significantly contribute to the total variance in pain (6-month visit), above and beyond all other variables, and their regression coefficients were not statistically significant. AJC remained the only variable significantly associated with pain (6-month visit), in each of the three models.

Exploratory analysis: Baseline Cohort

In order to establish generalizability, the cross-sectional analysis was rerun on the **Baseline Cohort**. The results were compared to those obtained from the cross-sectional analysis on the **Total Cohort**. A similar approach to that described above was used. The only difference was the total number of patients included in the model i.e., 143 as opposed to 95. There were 14 missing observations from the **Baseline Cohort** (14/157, 8.9%).

The full model is the following:

ln pain (baseline visit) = 1.508 – 0.025(duration) – 0.242(sex) + **0.077(age)** – 0.250(JIA category) + **0.683(ln AJC)** + 0.010(family integration) **– 0.032(social support)** + 0.020(medical situation).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 40 and 41, and compared to those obtained from the cross-sectional analysis on the **Total Cohort**. Similarly to the **Total Cohort,** the model on the **Baseline Cohort** was significant (p value < 0.001). The independent variables collectively explained 23.9% of the total variance in pain (baseline visit). However, in addition to AJC, the variables age and social support became significantly associated with pain (baseline visit). Although the three parental coping patterns taken together did not significantly contribute to the total variance in pain, above and beyond disease activity, the regression coefficient of social support became significant. Overall, performing the analysis on a larger sample provided more information.

Table 40: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.048	0.048	1.723	0.148	1.723	0.148
Step 2	0.203	0.156	26.771	<0.001	6.990	<0.001
Step 3	0.239	0.036	2.127	0.100	5.274	<0.001

Table 41: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.025	0.039	-0.650	0.517	-0.102	0.051
Gender	-0.242	0.252	-0.957	0.340	-0.741	0.258
Age	**0.077**	**0.030**	**2.552**	**0.012**	**0.017**	**0.137**
JIA category	-0.250	0.252	-0.993	0.322	-0.749	0.248
Ln AJC	**0.683**	**0.149**	**4.595**	**<0.001**	**0.389**	**0.977**
Coping I	0.010	0.020	0.497	0.620	-0.030	0.050
Coping II	**-0.032**	**0.013**	**-2.391**	**0.018**	**-0.058**	**-0.006**
Coping III	0.020	0.025	0.812	0.418	-0.029	0.069

The residual plot indicated the presence of a floor effect, caused by a large proportion of patients with no pain. However, it also demonstrated that there were no major violations of the linearity, normality and homoscedascity assumptions (Figure 42). Furthermore, a histogram of the studentized residuals approximated a normal distribution (Figure 43).

Figure 42: residual plot

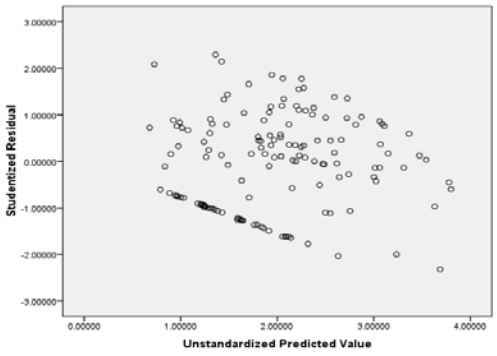
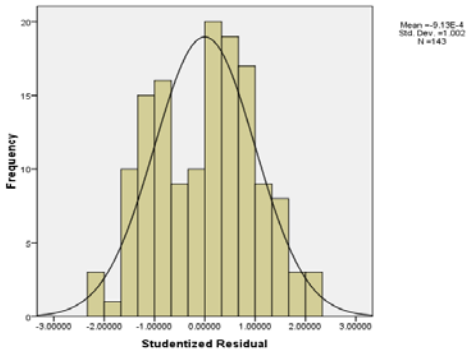


Figure 43: histogram



Partial regression plots of the independent variables were produced. The plots indicated that the association between age, ln AJC and social support, and ln pain were linear (Figure 44-46). There were no influential points.

Figure 44: partial regression plot (age)

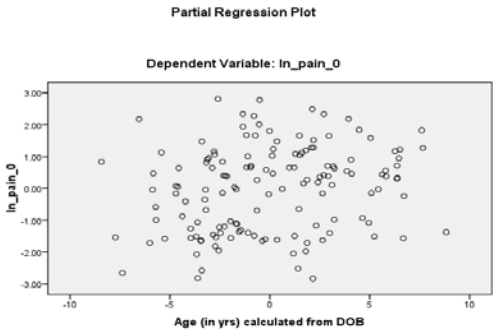


Figure 45: partial regression plot (ln AJC)

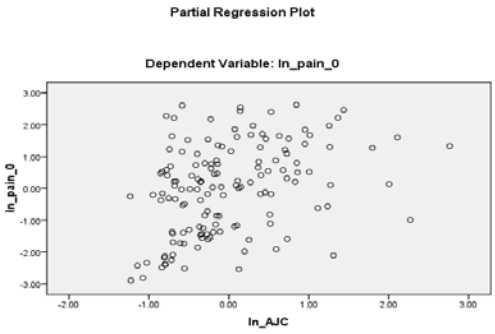
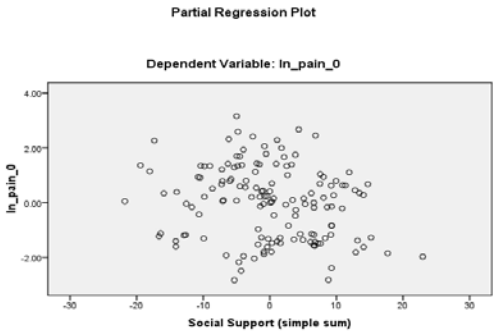


Figure 46: partial regression plot (social support)



Multiple linear regression diagnostics for influential points were performed (Appendix 9). There were a few cases with leverage values above the cutoff (2p/N = 0.11). However, no problems were identified from the Cook's distances and DfBetas, and therefore none of the patients were removed from the final model. A collinearity diagnosis was run on the model, and problems were not identified (Appendix 9).

The analysis was rerun including only age, ln AJC and social support. The reduced model was the following:

Ln pain (baseline visit) = 1.701 + **0.059(age)** + **0.710(ln AJC) – 0.023(social support).**

The reduced model summary statistics, coefficients and confidence intervals are shown in Tables 42 and 43. The reduced model was significant (p value < 0.001). The independent variables collectively explained 21.9% of the total variance in pain (baseline visit). The three variables remained significantly associated with pain (baseline visit). The main difference is that, in comparison to the full model, social support significantly contributed 3.2% to the total variance in pain, above and beyond disease activity. Overall, the regression coefficients were similar to those obtained in the SLRA performed earlier on the Baseline Cohort (Table 16), indicating that there were no confounding factors.

Table 42: reduced model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.028	0.028	4.004	0.047	4.004	0.047
Step 2	0.187	0.159	27.424	<0.001	16.089	<0.001
Step 3	0.219	0.032	5.663	0.019	12.971	<0.001

Table 43: coefficients and confidence intervals of reduced model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Age	0.059	0.025	2.297	0.023	0.008	0.109
Ln AJC	0.710	0.138	5.136	<0.001	0.437	0.983
Coping II	-0.023	0.010	-2.380	0.019	-0.042	-0.004

Age was significantly associated with pain at baseline visit, when adjusted for all other variables in the model. Increasing age by 1 year increased pain by 6.1% on

the VAS, while keeping all other variables constant, based on the following calculation:

$\exp(\beta \text{ age}) = \exp(0.059) = 1.0608$

AJC was significantly associated with pain at baseline visit, when adjusted for all other variables in the model. Patients with a high AJC experienced more pain than those with a low AJC. Doubling the number of active joints increased pain by 63.6% on the VAS, based on the following calculations:

$\beta' = (\beta \ln \text{AJC}) * \ln(2) = 0.710 * \ln(2) = 0.4921$

$\exp(\beta') = 1.6358$ = the effect on pain of doubling the AJC.

The coping pattern social support was significantly associated with pain at baseline visit, when adjusted for all other variables in the model. Increasing the score by 1 point on the CHIP (indicating increased perceived helpfulness of social support) decreased pain by 2.3% on the VAS, while keeping all other variables constant, based on the following calculation:

$\exp(\beta \text{ social support}) = \exp(-0.023) = 0.9773$

In order to evaluate the separate effect of each parental coping pattern, additional analyses were performed by entering the coping patterns, one at a time, in Step 3. Again, family integration and medical situation did not significantly contribute to the total variance in pain (baseline visit), above and beyond all other variables, and their regression coefficients were not statistically significant (data not shown). On the other hand, social support significantly contributed 2.8% to the total variance in pain, above and beyond all other variables, and its regression coefficient was statistically significant, as shown in Tables 44 and 45. Therefore, evaluating the separate effect of social support provided more information, in that this parental coping pattern was found to be linked to the pain experience of children with JIA. The parental perceived usefulness of social support was associated with a decrease in pain intensity reported at baseline visit.

Table 44: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.048	0.048	1.723	0.148	1.723	0.148
Step 2	0.203	0.156	26.771	<0.001	6.990	<0.001
Step 3	0.231	0.028	4.941	0.028	6.816	<0.001

Table 45: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.022	0.038	-0.573	0.567	-0.098	0.054
Gender	-0.276	0.247	-1.119	0.265	-0.765	0.212
Age	**0.069**	**0.029**	**2.354**	**0.020**	**-0.011**	**0.127**
JIA category	-0.237	0.251	-0.943	0.347	-0.733	0.260
Ln AJC	**0.719**	**0.145**	**4.964**	**<0.001**	**0.433**	**1.006**
Coping II	**-0.022**	**0.010**	**-2.223**	**0.028**	**-0.041**	**-0.002**

Exploratory analysis: Month 6 Cohort

The longitudinal analysis was rerun on the **Month 6 Cohort** to establish generalizability. The results were compared to those obtained from the longitudinal analysis on the **Total Cohort**. A similar approach to that described above was used. The only difference was the total number of patients included in the model i.e., 103 as opposed to 95. There were 9 missing observations from the **Month 6 Cohort** (9/112, 8.0%).

The full model is the following:

ln pain (6-month visit) = 1.457 + 0.000(duration) – 0.365(sex) + 0.012(age) – 0.208(JIA category) + **0.869(ln AJC)** – 0.034(family integration) + 0.014(social support) + 0.052(medical situation).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 46 and 47, and compared to those obtained from the longitudinal analysis on the **Total Cohort**. The models obtained from the **Month 6 Cohort** and **Total Cohort** were similar. Again, the model was not significant (p value 0.065). The independent variables collectively explained only 14.1% of the total variance in pain (6-month visit). The three parental coping patterns did not significantly contribute to the total variance in pain, above and beyond disease activity. AJC remained the only variable significantly associated with pain (6-month visit). Therefore, performing the analysis on a larger sample did not provide more information.

Table 46: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.014	0.014	0.342	0.849	0.342	0.849
Step 2	0.110	0.096	10.492	0.002	2.398	0.043
Step 3	0.141	0.031	1.116	0.346	1.923	0.065

Table 47: coefficients and confidence intervals of full model

	β	**Standard error**	**t stat.**	**Sign. of t stat.**	**95% CI (lower)**	**95% CI (upper)**
Duration	0.000	0.051	-0.004	0.997	-0.102	0.102
Gender	-0.365	0.353	-1.035	0.303	-1.066	0.335
Age	0.012	0.041	0.301	0.764	-0.069	0.094
JIA category	-0.208	0.317	-0.656	0.513	-0.837	0.421
Ln AJC	**0.869**	**0.248**	**3.501**	**0.001**	**0.376**	**1.361**
Coping I	-0.034	0.026	-1.300	0.197	-0.086	0.018
Coping II	0.014	0.018	0.770	0.443	-0.022	0.050
Coping III	0.052	0.034	1.534	0.128	-0.015	0.119

Checking for violation of regression assumptions and multiple linear regression diagnostics were also performed. Similarly to the longitudinal analysis on the **Total Cohort**, problems were not identified (data not shown).

The separate effect of each parental coping pattern was not investigated.

Exploratory analysis: change in pain intensity

A MLRA model was built to evaluate the longitudinal relationship between baseline parental coping and change in pain intensity, rather than future pain report at 6 months. Given that family integration and medical situation were not previously shown to be associated with either pain at baseline visit or 6-month visit, only the effect of social support was evaluated in this model. A hierarchical approach was again used to determine the amount of additional variance of change in pain intensity explained by the use of the social support, above and beyond disease activity, and after controlling for demographic and disease-related variables. The analysis was performed on the **Total Cohort** which included 90 patients. There were only 5 missing observations (5/95, 5.3%). The dependent variable was change in pain intensity. The independent variables were entered in the same steps as previously described.

The full model is the following:

Change in pain intensity = -7.980 – 0.397(duration) – 3.153(sex) + 0.258(age) + 3.704(JIA category) – 3.260(ln AJC) + 0.286(social support).

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 48 and 49. The full model was not significant (p value 0.759). None of the independent variables, including social support, contributed significantly to the total variance of change in pain intensity.

Table 48: full model summary

	R^2 value	R^2 change	F change stat.	Sign. of F change	F stat.	Sign. of F stat.
Step 1	0.016	0.016	0.337	0.852	0.337	0.852
Step 2	0.026	0.010	0.878	0.351	0.445	0.816
Step 3	0.039	0.013	1.149	0.287	0.563	0.759

Table 49: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.397	1.069	-0.371	0.711	-2.524	1.730
Gender	-3.153	6.897	-0.457	0.649	-16.871	10.564
Age	0.258	0.781	0.330	0.742	-1.295	1.811
JIA category	3.704	6.266	0.591	0.556	-8.758	16.166
Ln AJC	-3.260	4.756	-0.685	0.495	-12.720	6.200
Coping II	0.286	0.267	1.072	0.287	-0.245	0.817

Exploratory analysis: confounding effect of the psychosocial functioning of the child

In the analysis on the **Baseline Cohort,** it was shown that the parental coping pattern social support was associated with pain reported at baseline visit. Here, the potential confounding effect of the psychosocial functioning of the child was explored. The analysis was performed on the **Baseline Cohort** which included 142 patients. There were 15 missing observations (15/157, 9.6%). The demographic and disease-related variables, and AJC were entered in the same steps as previously described. However, the psychosocial functioning of the child was entered together with social support in Step 3.

The full model is the following:

ln pain (baseline visit) = 0.935 – 0.054(duration) – 0.174(sex) + **0.098(age)** – 0.335(JIA category) + **0.554(ln AJC) – 0.025(social support) + 0.433(psychosocial)**.

The summary statistics, regression coefficients and confidence intervals of each step and of the full model are shown in Tables 50 and 51. The full model was significant (p value < 0.001). The independent variables collectively explain 35.3% of the total variance in pain (baseline visit). AJC explained 15.4% of the total variance. Social support together with psychosocial functioning of the child explained another statistically significant 15.5%, above and beyond disease activity. In comparison to the previous analysis on the Baseline Cohort, which excluded the psychosocial functioning of the child, there was no major change in the regression coefficient of social support (-0.025 versus –0.022). Therefore, there was no confounding effect of the psychosocial functioning of the child on the association between social support and pain.

Table 50: full model summary

	R^2 value	**R^2 change**	**F change stat.**	**Sign. of F change**	**F stat.**	**Sign. of F stat.**
Step 1	0.044	0.044	1.563	0.188	1.563	0.188
Step 2	0.198	0.154	26.183	<0.001	6.717	<0.001
Step 3	0.353	0.155	16.061	<0.001	10.450	<0.001

Table 51: coefficients and confidence intervals of full model

	β	Standard error	t stat.	Sign. of t stat.	95% CI (lower)	95% CI (upper)
Duration	-0.054	0.036	-1.491	0.138	-0.125	0.018
Gender	-0.174	0.229	-0.758	0.450	-0.627	0.280
Age	**0.098**	**0.028**	**3.516**	**0.001**	**0.043**	**0.152**
JIA category	-0.335	0.232	-1.444	0.151	-0.793	0.124
Ln AJC	**0.554**	**0.137**	**4.032**	**<0.001**	**0.282**	**0.826**
Coping II	**-0.025**	**0.009**	**-2.713**	**0.008**	**-0.042**	**-0.007**
Psychosocial	**0.433**	**0.084**	**5.135**	**<0.001**	**0.267**	**0.600**

Checking for violation of regression assumptions and multiple linear regression diagnostics were also performed. Similarly to the analysis previously done on the Baseline Cohort, problems were not identified (data not shown).

VII. DISCUSSION

In recent years, there has been a growing interest from the pediatric rheumatology community to better characterize the pain experience of children suffering from JIA, to develop improved pain measurement tools adapted according to age and developmental level for use in clinical practice and research, and to study the treatment of pain. Despite these efforts, 77.3% of North American pediatric rheumatologists from CARRA (Childhood Arthritis and Rheumatology Research Alliance) believe that "there are children with arthritis who continue to have moderate to severe pain despite adequate disease modifying therapy and NSAIDs" (23). It has been well established that the chronic pain of children with JIA is not solely explained by the activity of the disease, and that other factors in part modulate their pain experience.

One of these factors may be the psychosocial functioning of the child. Numerous studies have demonstrated the link between this and pain however, the direction of causality has not been well evaluated in longitudinal studies. Hoff is the only author who showed that depressive symptoms were a risk factor for subsequent pain at 6 and 12 months, but only for children whose initial pain intensity ratings were in the mild to moderate range (77).

Preliminary findings indicate that the family environment may affect children's outcomes, including their psychosocial functioning, adherence to medications and pain (34;39;53;63;84;90;94). Another factor, parental coping, has been the focus of only a small number of studies. Indeed, Cavallo demonstrated that there were associations between the use of specific parental coping patterns and, severity of disease and psychosocial functioning of children with JIA (88;89). However, the potential impact of parental coping on children's pain has never been studied to date. This study presented here aimed to evaluate the relationship between the psychosocial functioning of the child and pain not only

in a cross-sectional study design, but also longitudinally. Furthermore, the potential association between parental coping and children's pain was explored.

The study findings failed to fully support the proposed hypotheses. In this cohort of 95 patients, the psychosocial functioning of the child was found to be a correlate of pain in the cross-sectional analysis, similar to findings reported by Varni (74), but did not predict pain in the longitudinal analysis. Together with AJC and age, it explained a significant proportion (39.9%) of the total variance in pain intensity ratings at the baseline visit. A modest proportion (11.3%) of the total variance was accounted for by the psychosocial functioning of the child alone. These results imply that, after controlling for age and a surrogate marker of disease activity (AJC), poor psychosocial functioning is associated with somewhat higher pain intensity ratings. However, in the longitudinal analysis, disease activity was identified as the sole predictor for future pain intensity reported at 6 months. It accounted for a small (6.5%), albeit statistically significant, proportion of the total variance in future pain. All other variables, including the psychosocial functioning of the child, were not identified as predictors of future pain reported 6 months later. Here, the change from a non-significant full model to a significant reduced model is probably explained by the fact that the reduced model had a smaller number of degrees of freedom. Performing the analyses on larger patient populations, albeit partially different from the Total Cohort in terms of composition, did not identify additional correlates and predictors of concurrent and future pain reports, respectively. Although it had been hypothesized that the psychosocial functioning of the child might moderate the association between disease activity and pain, this was not confirmed. When evaluating the relationship between the psychosocial function of the child and change in pain intensity, the reduced model demonstrated an inverse association. This finding may indicate that the relationship between these two variables is, in fact, curvilinear.

Parental coping overall was not found to impact children's pain, either concurrently or longitudinally. However, when exploratory analyses were run on larger patient populations, it was observed that the parental coping pattern social support contributed a small, but statistically significant, proportion (3.2%) to the total variance in pain reported at baseline, above and beyond disease activity. The psychosocial functioning of the child was not identified as a confounding factor of this association. This suggests that patients, whose parents use strategies aimed at maintaining social support, self-esteem and psychological stability (Coping pattern II), experience less pain. This finding is in accordance with results reported by Cavallo, where parents of patients with mild disease (total JAQQ score) showed an increase in the use of all coping strategies, including social support (88;89). It remains to be determined whether, although statistically significant, this small change in R^2 value is clinically important.

Among potential confounding factors, age was the only demographic characteristic found to be associated with pain. Although not retained in the reduced model presented above, age was identified as a correlate of pain in the cross-sectional analysis evaluating the psychosocial functioning of the child. In the cross-sectional analysis evaluating the separate effect of the parental coping pattern, social support, older age was again found to be associated with higher pain intensity ratings. These findings are in accordance with the qualitative data described by Beales (10;11). Although it is possible that certain classes of medications, such as corticosteroids and NSAIDs, may affect the psychosocial function of a subset of patients with JIA, the use of these medications were not considered as possible confounders in this study. The confirmation of a direct link between these medications and the psychosocial function of children with JIA remains to be proven.

The cohort of patients was representative of other JIA populations followed in tertiary care centres and described in the medical literature, in terms of age and gender (7). As expected, about 50% of patients belonged to the JIA category

oligoarthritis. Similar to Malleson's study, the large proportion of patients with no active disease was not surprising, given that many had disease of longstanding duration with treatments already in place (37). However, in contrast to what has been reported in other studies, the means of pain intensity reported at the baseline and 6-month visits (14.16 mm and 14.66 mm, respectively) were unexpectedly small. For example, Schanberg described a mean of 36.6 mm for present pain measured on the VAS (40). It may well be that, in this database, the proportion of patients with recently diagnosed JIA, who are expected to experience more pain while waiting for treatment to work, was small. Another potential explanation is that patients were enrolled into the study "Determinants of outcomes for juvenile arthritis" after the year 2000. Biologic agents, found to be very effective in the treatment of JIA, started to be used in some patients after the year 2000 in Canada.

One of the main strengths of this study was its relatively large sample size. Although JIA is one of the most common chronic diseases of childhood, pediatric rheumatological disorders are not frequent and therefore, unless one conducts a multi-centre study, it is difficult to collect data on large populations. Another asset based in the underlying cohort study was the prospective collection of data, which allows one to determine the direction of relationships. Furthermore, the psychosocial functioning of the child and pain were both assessed by the JAQQ, a HRQOL measurement tool well validated in JIA (98).

There are several limitations to this study. First, as previously mentioned, means of pain intensity ratings at the baseline and 6-month visits were small, with many patients reporting no pain. Although inevitable, a floor effect was therefore present in all models. As a consequence, the difference in pain ratings between both time points was small. This may have prevented the identification of correlates and predictors of pain in the cross-sectional and longitudinal analyses, respectively. This may also explain why the longitudinal analyses failed to identify risk factors for future pain reports at 6 months, other than disease

activity, and for change in pain intensity. Second, there were some missing data in the database "Determinants of outcomes for juvenile arthritis" because some parents, or patients, failed to complete all of the questionnaires. From a total of 157 patients, there were only 95 for whom pain data were available at both the baseline and 6-month visits. Similar to Hoff, it would have been interesting to study the 12-month time point however, the amount of data available from that visit was even smaller. Third, parents or children older than 9 years were asked to assess pain over the past week, at both time points. Although this timeframe represents an advantage over assessment of present pain and pain within the past month, an element of recall bias may be present. Both Schanberg and Stinson commented on the problem of recall bias in JIA pain studies, and instead preferred to use daily diaries, in paper and electronic versions, respectively (32;40;76). Fourth, the characteristics of the children/parents enrolled into the underlying cohort study could not be compared to those who were approached by the study coordinator but refused to consent. Although it is possible that an element of selection bias was present, this cannot be verified. As a result, there may be some issues of generalizability of these findings. Finally, maximal use of the pain data available from the database was not done, in that children younger than 10 years were asked to rate their pain on a facial scale. Parents or children older than 9 years were also asked to choose the phrase that described pain the best. Given that only a small proportion of the cohort completed these pain measurement scales, no attempt was made at evaluating those two pain outcomes in regression models.

An important gap in the body of knowledge pertaining to pediatric pain lies in the area of use of proxies for measurement of this subjective symptom. As reviewed earlier, several authors studied agreement in the child-parent dyad, and the results are controversial (44-46). Similarly, the reliance on proxies for assessment of psychosocial functioning could be problematic. It may well be that all perspectives, of the child and parent, are valid, and that one should take into consideration all sources of information available. In this study, it was

decided not to investigate the pain measurement facial scale, filled in by children aged less than 10 years, because of the small number of children who completed them. Hence, reliance on parental report was inevitable in those children, for measurement of both pain and psychosocial functioning. For children older than 9 years, the proportion of VAS and psychosocial scales (JAQQ) filled in by parents versus children was unknown. The agreement in the child-parent dyad was therefore not evaluated, and this represents a weakness to this study. However, Toupin determined the level of agreement between children with JIA aged 9-18 years followed at the Montreal Children's Hospital and their parents concerning quality of life and pain assessed by the JAQQ (47). She found moderate-to-good agreement for pain with an intraclass correlation coefficient of 0.60, and good agreement for psychosocial function with an intraclass correlation coefficient of 0.61. Levels of agreement on pain were higher for those children with more severe disease. Better agreement on psychosocial function was found among younger children. Altogether, the findings reported by Toupin suggest that there seems to be good agreement between the perceptions of children with JIA and their parents concerning pain and quality of life (total JAQQ score), and that the use of parental proxies for an unknown proportion of the cohort may have been appropriate in this thesis project.

Other alternatives considered for the methodology of this project include the evaluation of children recently diagnosed with JIA, as opposed to children with variable disease duration. Children with a recent diagnosis, in whom the appropriate combination of treatment has not yet been found or is not yet effective, may report more pain in comparison to children with longstanding disease. The mean change in pain intensity between the baseline and 6-months visit may be larger in this setting. For the longitudinal analyses, this could have allowed for the identification of additional predictors of pain intensity at 6 months. Although one could argue that the announcement of a new diagnosis of JIA brings stress in many children/parents, which tends to dissipate over time, it may be useful to identify which children are at risk of reporting more pain at

future time points. The proportion of children with a recent diagnosis of JIA was too small in this cohort of patients to carry out such analysis. One should be able to address this question through the study REACCH OUT (105), a Canadian multi-centre registry launched in 2005. The goal of this study is to collect information and study long-term outcomes on a very large number of children recently diagnosed with JIA across the country. Unfortunately, at the time of initiation of this thesis work, the database of REACCH OUT was too small and not yet ready to be used.

Similarly, other techniques of MLRA were considered, including stepwise, forward and backward selection methods. However, as one of the objectives was to determine the amount of additional variance in pain explained by the psychosocial functioning of the child and parental coping, above and beyond disease activity, a hierachical approach was chosen and all variables were forced into the model. For the evaluation of the 6-month pain outcome, the goal was to identify predictors of future pain, in order to aid pediatric rheumatologists targeting those children at higher risk for experiencing pain at future visits. Therefore, it was deemed not necessary to force baseline pain into the models. However, in the exploratory analyses, predictors of change in pain intensity were assessed. Here, an analytic alternative considered but not performed was to adjust for baseline pain.

It is the opinion of several pediatric rheumatologists that children with ERA experience more pain, in comparison to other JIA categories. The fact that JIA category was recoded as the binary variable (oligoarthritis versus all other categories) did not allow for the evaluation of associations between some JIA categories, such as ERA, and pain. Although considered, JIA category was not recoded into the binary variable (ERA versus all other categories), because the number of patients with ERA (n=6) was too small. Even though mothers and fathers may prefer to use different patterns of coping behaviours, separate analyses were not conducted, because the majority of respondents were mothers.

Finally, while not examined, it is likely that the treatment practices in the pediatric rheumatology clinics of Montreal and Vancouver are similar. Therefore, the effect of site of enrolment on pain outcome was not controlled for in the analyses. Furthermore, only 12/95 patients were recruited from Vancouver.

VIII. CONCLUSION

In this study, the only variable which was consistently associated with pain in the cross-sectional and longitudinal analyses was AJC, a surrogate marker of disease activity. The psychosocial functioning of the child was found to be a correlate of pain at baseline however, it did not predict subsequent pain. This may have been due to some limitations reviewed above in the methodology and/or analysis of this study, which precluded the identification of risk factors for future pain. Hopefully, the Canadian multi-centre study REACCH OUT will answer some of the questions raised in this thesis, by virtue of the very large number of children recruited across the country, and the fact that data on long-term outcomes are collected prospectively in children just recently diagnosed with JIA (as opposed to children of variable disease duration). In addition, it will allow for the evaluation of predictors of pain beyond the 6-month time point. Preliminary findings herein indicated that there might be a relationship between parental use of strategies aimed at increasing social support, and the pain experience of children with JIA. More studies are required, which will evaluate how parental coping might affect children's outcomes, including pain.

This work was important from several perspectives. Chronic pain is an important symptom experienced by many children with JIA, yet it is still poorly understood. For clinicians, identifying the relative importance of factors other than disease activity in explaining the pain experience of children with JIA may influence treatment decisions and management. The psychosocial functioning of the child may be amenable to psychological intervention, and counseling may help some parents to better manage their family life. These strategies may in turn ultimately decrease the pain perception and report of children, both concurrently and long-term. More longitudinal studies are needed in order to identify ways professionals, families and children can reduce pain experience over time.

Reference List

(1) Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International league of associations for rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004;31(2):390-2.

(2) Cassidy JT, Levinson JE, Bass JC, Baum J, Brewer EJJ, Fink CW, et al. A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. Arthritis Rheum 1986;29(2):274-81.

(3) Roberton DM, Cabral DA, Malleson PN, Petty RE. Juvenile psoriatic arthritis: followup and evaluation of diagnostic criteria. J Rheumatol 1996;23(1):166-70.

(4) Schanberg LE, Sandstrom MJ. Causes of pain in children with arthritis. Rheum Dis Clin North Am 1999;25(1):31-53.

(5) McGonagle D, Gibbon W, O'Connor P, Green M, Pease C, Emery P. Characteristic magnetic resonance imaging entheseal changes of knee synovitis in spondylarthropathy. Arthritis Rheum 1998;41(4):694-700.

(6) Oen KG, Cheang M. Epidemiology of chronic arthritis in childhood. semin arthritis rheum 1996;26(3):575-91.

(7) Cassidy JT, Petty RE. Textbook of pediatric rheumatology. fourth edition 2001;221.

(8) Oen K, Malleson PN, Cabral DA, Rosenberg AM, Petty RE, Cheang M. Disease course and outcome of juvenile rheumatoid arthritis in a multicenter cohort. J Rheumatol 2002;29(9):1989-99.

(9) Singh G, Athreya BH, Fries JF, Goldsmith DP. Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum 1994;37(12):1761-9.

(10) Beales JG, Keen JH, Holt PJL. The child's perception of the disease and the experience of pain in juvenile chronic arthritis. J Rheumatol 1983;10(1):61-5.

(11) Beales JG, Holt PJL, Keen JH, Mellor VP. Children with juvenile chronic arthritis: their beliefs about their illness and therapy. Ann Rheum Dis 1983;42:481-6.

(12) Sherry DD, Bohnsack J, Salmonson K, Wallace CA, Mellins E. Painless juvenile rheumatoid arthritis. J Pediatr 1990;116(6):921-3.

(13) Lovell DJ, Walco GA. Pain associated with juvenile rheumatoid arthritis. Pediatr Clin North Am 1989;36(4):1015-27.

(14) Schanberg LE, Lefebvre JC, Keefe FJ, Kredich DW, Gil KM. Pain coping and the pain experience in children with juvenile chronic arthritis. Pain 1997;73:181-9.

(15) Anthony KK, Schanberg LE. Pain in children with arthritis: a review of the current literature. Arthritis Care Res 2003;49(2):272-9.

(16) Varni JW, Walco GA. Chronic and recurrent pain associated with pediatric chronic diseases. Comprehensive pediatric nursing 1988;11:145-58.

(17) Hogeweg JA, Kuis W, Oostendorp RAB, Helders PJM. General and segmental reduced pain thresholds in juvenile chronic arthritis. Pain 1995;62:11-7.

(18) Hogeweg JA, Kuis W, Huygen ACJ, De Jong-De Vos Van Steenwijk C, Bernards ATM, Oostendorp RAB, et al. The pain threshold in juvenile chronic arthritis. Br J Rheumatol 1995;34:61-7.

(19) Thastum M, Zachariae R, Herlin T. Pain experience and pain coping strategies in children with juvenile idiopathic arthritis. J Rheumatol 2001;28(5):1091-8.

(20) Zak M, Pederson FK. Juvenile chronic arthritis into adulthood: a long-term follow-up study. Rheumatology (Oxford) 2000;39:198-204.

(21) Connelly M, Schanberg L. Opioid therapy for the treatment of refractory pain in children with juvenile rheumatoid arthritis. Nat Clin Pract Rheumatol 2006;2(12):636-7.

(22) Kimura Y, Walco G. Treatment of chronic pain in pediatric rheumatic disease. Nat Clin Pract Rheumatol 2007;3(4):210-8.

(23) Kimura Y, Walco GA, Sugarman E, Conte PM, Schanberg LE. Treatment of pain in juvenile idiopathic arthritis: a survey of pediatric rheumatologists. Arthritis Care Res 2006;55(1):81-5.

(24) Jaworski TM, Bradley LA, Heck LA, Roca A, Alarcon GS. Development of an observation method for assessing pain behaviors in children with juvenile rheumatoid arthritis. Arthritis Rheum 1995;38(8):1142-51.

(25) Varni JW, Thompson KL, Hanson V. The Varni/Thompson Pediatric Pain Questionnaire. I. Chronic musculoskeletal pain in juvenile rheumatoid arthritis. Pain 1987;28:27-38.

(26) Scott PJ, Ansell BM, Huskisson EC. Measurement of pain in juvenile chronic polyarthritis. Ann Rheum Dis 1977;36(2):186-7.

(27) Varni JW. Evaluation and management of pain in children with juvenile rheumatoid arthritis. J Rheumatol 1992;19(supplement 33):32-5.

(28) Beyer JE, Denyes MJ, Villarruel AM. The creation, validation, and continuing development of the Oucher: a measure of pain intensity in children. J Pediatr Nurs 1992;7(5):335-46.

(29) Dahlquist LM, Gil KM, Armstrong FD, DeLawyer DD, Greene P, Wuori D. Preparing children for medical examinations: the importance of previous medical experience. Health Psychol 1986;5(3):249-59.

(30) Jay SM, Ozolins M, Elliott CH, Caldwell S. Assessment of children's distress during painful medical procedures. Health Psychol 1983;2(2):133-47.

(31) Schanberg LE, Sandstrom MJ, Starr K, Gil KM, Lefebvre JC, Keefe FJ, et al. The relationship of daily mood and stressful events to symptoms in juvenile rheumatic disease. Arthritis Care Res 2000;13(1):33-41.

(32) Stinson JN, Petroz GC, Tait G, Feldman BM, Streiner D, McGrath PJ, et al. e-Ouch: Usability testing of an electronic chronic pain diary for adolescents with arthritis. Clin J Pain 2006;22(3):295-305.

(33) Vandvik IH, Eckblad G. Relationship between pain, disease severity and psychosocial function in patients with juvenile

chronic arthritis (JCA). Scand J Rheumatol 1990;19:295-302.

(34) Thompson KL, Varni JW, Hanson V. Comprehensive assessment of pain in juvenile rheumatoid arthritis: an empirical model. J Pediatr Psychol 1987;12(2):241-55.

(35) Thastum M, Herlin T, Zachariae R. Relationship of pain-coping strategies and pain-specific beliefs to pain experience in children with juvenile idiopathic arthritis. Arthritis Rheum 2005;53(2):178-84.

(36) Hagglund KJ, Schopp LM, Alberts KR, Cassidy JT, Frank RG. Predicting pain among children with juvenile rheumatoid arthritis. Arthritis Care Res 1995;8(1):36-42.

(37) Malleson PN, Oen K, Cabral DA, Petty RE, Rosenberg AM, Cheang M. Predictors of pain in children with established juvenile rheumatoid arthritis. Arthritis Care Res 2004;51(2):222-7.

(38) Ilowite NT, Walco GA, Pochaczevsky R. Assessment of pain in patients with juvenile rheumatoid arthritis: relation between pain intensity and degree of joint inflammation. Ann Rheum Dis 1992;51:343-6.

(39) Ross CK, Lavigne JV, Hayford JR, Dyer AR, Pachman LM. Validity of reported pain as a measure of clinical state in juvenile rheumatoid arthritis. Ann Rheum Dis 1989;48:817-9.

(40) Schanberg LE, Anthony KK, Gil KM, Maurin EC. Daily pain and symptoms in children with polyarticular arthritis. Arthritis Rheum 2003;48(5):1390-7.

(41) Gragg RA, Rapoff MA, Danovsky MB, Lindsley CB, Varni JW, Waldron SA, et al. Assessing chronic musculoskeletal pain associated with rheumatic disease: further validation of the pediatric pain questionnaire. J Pediatr Psychol 1996;21(2):237-50.

(42) Varni JW, Thompson Wilcox K, Hanson V, Brik R. Chronic musculoskeletal pain and functional status in juvenile rheumatoid arthritis: an empirical model. Pain 1988;32:1-7.

(43) Abu-Saad HH, Uiterwijk M. Pain in children with juvenile rheumatoid arthritis: a descriptive study. Pediatr Res 1995;38(2):194-7.

(44) Shaw KL, Southwood TR, McDonagh JE. Growing up and moving on in rheumatology: parents as proxies of adolescents with juvenile idiopathic arthritis. Arthritis Rheum 2006;55(2):189-98.

(45) Palermo TM, Zebracki K, Cox S, Newman AJ, Singer NG. Juvenile idiopathic arthritis: parent-child discrepancy on reports of pain and disability. J Rheumatol 2004;31(9):1840-6.

(46) Doherty E, Yanni G, Conroy RM, Bresnihan B. A comparison of child and parent ratings of disability and pain in juvenile chronic arthritis. J Rheumatol 1993;20(9):1563-6.

(47) Toupin April K, Feldman DE, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning perceived quality of life. Qual Life Res 2006;15:655-61.

(48) Garcia-Munitis P, Bandeira M, Pistorio A, Magni-Manzoni S, Ruperto N, Schivo A, et al. Level of agreement between children, parents, and physicians in rating pain intensity in juvenile idiopathic arthritis. Arthriris Care and Research 2006;55(2):177-83.

(49) Giannini EH, Ruperto N, Ravelli A, Lovell DJ, Felson DT, Martini A. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997;40(7):1202-9.

(50) McAnarney ER, Pless IB, Satterwhite B, Friedman SB. Psychological problems of children with chronic juvenile arthritis. Pediatrics 1974;53(4):523-8.

(51) Billings AG, Moos RH, Miller III JJ, Gottlieb JE. Psychosocial adaptation in juvenile rheumatic disease: a controlled evaluation. Health Psychol 1987;6(4):343-59.

(52) Daltroy LH, Larson MG, Eaton HM, Partridge AJ, Pless IB, Rogers MP, et al. Psychosocial adjustment in juvenile arthritis. J Pediatr Psychol 1992;17(3):277-89.

(53) Timko C, Stovel KW, Moos RH. Functioning among mothers and fathers of children with juvenile rheumatic diseases: a longitudinal study. J Pediatr Psychol 1992;17(6):705-24.

(54) Harris JA, Newcomb AF, Gewanter HL. Psychosocial effects of juvenile rheumatic disease: the family and peer

systems as a context for coping. Arthriris Care and Research 1991;4(3):123-30.

(55) Ungerer JA, Horgan B, Chaitow J, Champion GD. Psychosocial functioning in children and young adults with juvenile arthritis. Pediatrics 1988;81(2):195-202.

(56) Noll RB, Kozlowski K, Gerhardt C, Vannatta K, Taylor J, Passo M. Social, emotional, and behavioral functioning of children with juvenile rheumatoid arthritis. Arthritis Rheum 2000;43(6):1387-96.

(57) Huygen ACJ, Kuis W, Sinnema G. Psychological, behavioural, and social adjustment in children and adolescents with juvenile chronic arthritis. Ann Rheum Dis 2000;59:276-82.

(58) Reiter-Purtill J, Gerhardt CA, Vannatta K, Passo MH, Noll RB. A controlled longitudinal study of the social functioning of children with juvenile rheumatoid arthritis. J Pediatr Psychol 2003;28(1):17-28.

(59) Ding T, Hall A, Jacobs K, David J. Psychological functioning of children and adolescents with juvenile idiopathic arthritis is related to physical disability but not to disease status. Rheumatology (Oxford) 2008;47:660-4.

(60) Lebovidge JS, Lavigne JV, Donenberg GR, Miller ML. Psychological adjustment of children and adolescents with chronic arthritis: a meta-analytic review. J Pediatr Psychol 2003;28(1):29-39.

(61) Ennett ST, DeVellis BM, Earp JA. Disease experience and psychosocial adjustment in children with juvenile rheumatoid arthritis: children's versus mothers' reports. J Pediatr Psychol 1991;16(5):557-68.

(62) Varni JW, Thompson Wilcox K, Hanson V. Mediating effects of family social support on child psychological adjustment in juvenile rheumatoid arthritis. Health Psychol 1988;7(5):421-31.

(63) Degotardi PJ, Revenson TA, Ilowite NT. Family-level coping in juvenile rheumatoid arthritis: assessing the utility of a quantitative family interview. Arthritis Rheum 1999;12(5):314-24.

(64) Sandstrom MJ, Schanberg LE. Brief report: peer rejection, social behavior, and psychological adjustment in children with juvenile rheumatic disease. J Pediatr Psychol 2004;29(1):29-34.

(65) Palermo TM, Kiska R. Subjective sleep disturbances in adolescents with chronic pain: relationship to daily functioning and quality of life. The journal of pain 2005;6(3):201-7.

(66) Adam V, St-Pierre Y, Fautrel B, Clarke AE, Duffy CM, Penrod JR. What is the impact of adolescent arthritis and rheumatism? Evidence from a national sample of Canadians. J Rheumatol 2005;32(2):354-61.

(67) Varni JW, Seid M, Smith Knight T, Burwinkle T, Brown J, Szer IS. The PedsQL in pediatric rheumatology: reliability, validity, and responsiveness of the Pediatric Quality of Life Inventory Generic Core Scales and Rheumatology Module. Arthritis Rheum 2002;46(3):714-25.

(68) Nugent J, Ruperto N, Grainger J, Machado C, Sawhney S, Baildam E, et al. The British version of the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ). Clin Exp Rheumatol 2001;19(4(Supplement 23)):S163-S167.

(69) Duffy CM, Arsenault L, Duffy KNW, Paquin JD, Strawczynski H. The Juvenile Arthritis Quality of Life Questionnaire - development of a new responsive index for juvenile rheumatoid arthritis and juvenile spondyloarthritides. J Rheumatol 1997;24(4):738-46.

(70) Sawyer MG, Whitham JN, Roberton DM, Taplin JE, Varni JW, Baghurst PA. The relationship between health-related quality of life, pain and coping strategies in juvenile idiopathic arthritis. Rheumatology (Oxford) 2004;43(3):325-30.

(71) Oliveira S, Ravelli A, Pistorio A, Castell E, Malattia C, Prieur AM, et al. Proxy-reported health-related quality of life of patients with juvenile idiopathic arthritis: the pediatric rheumatology international trials organization multinational quality of life cohort study. Arthritis Care Res 2007;57(1):35-43.

(72) Shaw KL, Southwood TR, Duffy CM, McDonagh JE. Health-related quality of life in adolescents with juvenile idiopathic arthritis. Arthritis Rheum 2006;55(2):199-207.

(73) Dhanani S, Quenneville J, Perron M, Abdolell M, Feldman BM. Minimal difference in pain associated with change in quality of life in children with rheumatic disease. Arthritis Rheum 2002;47(5):501-5.

(74) Varni JW, Rapoff MA, Waldron SA, Gragg RA, Bernstein BH, Lindsley CB. Chronic pain and emotional distress in children and adolescents. Developmental and behavioral pediatrics 1996;17(3):154-61.

(75) Ross CK, Lavigne JV, Hayford JR, Berry SL, Sinacore JM, Pachman LM. Psychological factors affecting reported pain in juvenile rheumatoid arthritis. J Pediatr Psychol 1993;18(5):561-73.

(76) Schanberg LE, Gil KM, Anthony KK, Yow E, Rochon J. Pain, stiffness, and fatigue in juvenile polyarticular arthritis. Arthritis Rheum 2005;52(4):1196-204.

(77) Hoff AL, Palermo TM, Schluchter M, Zebracki K, Drotar D. Longitudinal relationships of depressive symptoms to pain intensity and functional disability among children with disease-related pain. J Pediatr Psychol 2006;31(10):1046-56.

(78) Gerhardt CA, Vannatta K, McKellop M, Zeller M, Taylor J, Passo M, et al. Comparing parental distress, family functioning, and the role of social support for caregivers with and without a child with juvenile rheumatoid arthritis. J Pediatr Psychol 2003;28(1):5-15.

(79) Myones BL, Williams GF, Billings A, Miller JJ. Social environment in families of children with juvenile arthritis. Arthritis Care Res 1988;1:17-22.

(80) Vandvik IH, Hoyeraal HM, Fagertun H. Chronic family difficulties and stressful life events in recent onset juvenile arthritis. J Rheumatol 1989;16(8):1088-92.

(81) Manuel JC. Risk and resistance factors in the adaptation in mothers of children with juvenile rheumatoid arthritis. J Pediatr Psychol 2001;26(4):237-46.

(82) Bernatsky S, Duffy CM, Malleson P, Feldman DE, St-Pierre Y, Clarke AE. Economic impact of juvenile idiopathic arthritis. Arthritis Rheum 2007;57(1):44-8.

(83) Lustig JL, Ireys HT, Sills EM, Walsh BB. Mental health of mothers of children with juvenile rheumatoid arthritis: appraisal as a mediator. J Pediatr Psychol 1996;21(5):719-33.

(84) Timko C, Baumgartner M, Moos RH, Miller III JJ. Parental risk and resistance factors among children with juvenile rheumatic disease: a four-year predictive study. J Behav Med 1993;16(6):571-88.

(85) Vandvik IH, Eckblad G. Mothers of children with recent onset of rheumatic disease: associations between maternal distress, psychosocial variables, and the disease of the children. Developmental and behavioral pediatrics 1991;12(2):84-91.

(86) Wallander JL, Varni JW. Effects of pediatric chronic physical disorders on child and family adjustment. J Child Psychol Psychiatry 1998;39(1):29-46.

(87) Lazarus RS, Folkman S. Stress, appraisal and coping. Springer 1984.

(88) Cavallo S, Feldman D, Swaine B, Duffy C. Impact of disease severity on parental coping skills in children with juvenile idiopathic arthritis. Arthritis Rheum 2006;54(9 (supplement)):S775.

(89) Cavallo S, Feldman DE, Swaine B, Meshefedjian G, Malleson PN, Duffy CM. Is parental coping associated with quality of life in juvenile idiopathic arthritis? Pediatric Rheumatology 2009;7(7).

(90) Wagner JL, Chaney JM, Hommel KA, Page MC, Mullins LL, White MM, et al. The influence of parental distress on child depressive symptoms in juvenile rheumatic diseases: the moderating effect of illness intrusiveness. J Pediatr Psychol 2003;28(7):453-62.

(91) Wallander JL, Varni JW, Babani L, Tweddle Banis H, Thompson Wilcox K. Family resources as resistance factors for psychological maladjustment in chronically ill and handicapped children. J Pediatr Psychol 1989;14(2):157-73.

(92) Wallander JL, Varni JW. Social support and adjustment in chronically ill and handicapped children. Am J Community Psychol 1989;17(2):185-201.

(93) Helgeson VS, Janicki D, Lerner J, Barbarin O. Brief report: adjustment to juvenile rheumatoid arthritis: a family systems perspective. J Pediatr Psychol 2003;28(5):347-53.

(94) Chaney JM, Peterson L. Family variables and disease management in juvenile rheumatoid arthritis. J Pediatr Psychol 1989;14(3):389-403.

(95) Cassidy JT, Petty R. Textbook of pediatric rheumatology. fourth edition 2001;382.

(96) Schanberg L, Maurin E, Anthony K, Gil K. Girls with polyarticular arthritis report more disease symptoms than boys. Arthritis Rheum 2001;44(supplement 9):S168.

(97) Derogatis LR, Rickels K, Rock A. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976;128:280-9.

(98) Duffy C, Arsenault L, Watanabe Duffy K. Validity and sensitivity to change of the Juvenile Arthritis Quality of Life Questionnaire (JAQQ). Arthritis Rheum 1993;36(supplement):S144.

(99) Maunuksela E, Olkkala K, Korpela R. Measurement of pain in children with self-reporting and behavioural assessment. Clin Pharmacol Ther 1987;42:137-41.

(100) Harrell FE. Regression modeling strategies with applications to linear models, logistic regression, and survival analysis. 1 ed. Springer Series in Statistics; 2001.

(101) Duffy CM, Arsenault L, Duffy KNW. Level of agreement between parents and children in rating dysfunction in juvenile rheumatoid arthritis and juvenile spondyloarthritides. J Rheumatol 1993;20(12):2134-9.

(102) McCubbin HI, Thompson AI. CHIP Coping Health Inventory for Parents. Family assessment inventories for research and practice. 2 ed. The University of Wisconsin-Madison; 1987. p. 175-94.

(103) McCubbin HI, McCubbin MA, Patterson JM, Cauble AE, Wilson LR, Warwick W. CHIP - Coping Health Inventory

for Parents: an assessment of parental coping patterns in the care of the chronically ill child. Journal of marriage and family 1983;45:359-70.

(104) Glymour MM, Weuve J, Berkman LF, Kawachi I, Robins JM. When is baseline adjustment useful in analyses of change? An example with education and cognitive change. Am J Epidemiol 2005;162(3):267-78.

(105) Oen K, Tucker L, Huber A, Miettunen P, Scuccimarri R. Predictors of early inactive disease in a juvenile idiopathic arthritis cohort: The Research in Arthritis in Canadian Children Outcomes Studies I. Arthriris Care and Research 2009.

APPENDIX 1

Determinants of outcomes for juvenile arthritis - Characterizing the Clinical, Quality of Life and Economic Outcomes In Juvenile Idiopathic Arthritis

Abstracts:

1. De Civita, M., Feldman, D., Duffy, CM., & Dobkin, P.L. Adherence in juvenile idiopathic arthritis: Psychometric properties of the PARQ. (abstr). Journal of Psychosomatic Research 2002; 52:396.

2. Ehrmann Feldman D, De Civita M, Dobkin PL, Gibbon M, Karp I, Duffy CM. Characterizing adherence to prescribed exercises in patients with juvenile idiopathic arthritis. Arthritis and Rheumatism 2002; 46:S483.

3. *Bernatsky S, Duffy CM, Clarke A, Malleson P, Penrod J, Gibbon M, Oritz-Alvarez, O, Dobkin P, Feldman D, & De Civita, M. The economic impact of juvenile idiopathic arthritis. Pediatric Rheumatology on line Journal, Sept 2003;43:H79.

4. *Bernatsky S, Clarke A, Malleson P, Dobkin P, Feldman D, De Civita M, Gibbon M, Oritz-Alvarez O, & Duffy CM. The health impact of juvenile idiopathic arthritis (JIA). Pediatric Rheumatology on line Journal, Sept 2003, 43:E:28.

5. Duffy CM, De Civita M, Gibbon M, Dobkin P, Scuccimarri R, Duffy NW K, Geoffrion M, Brownstein A, Ehrmann-

Feldman D. Adherence to treatment in juvenile idiopathic arthritis. Pediatric Rheumatology on line Journal, Sept 2003, 43:H:77.

6. Ehrmann Feldman D, De Civita M, Dobkin P L, Gibbon M, Wilchesky M, & Duffy CM. Adherence to prescribed exercise programs in juvenile arthritis. Med Sci Sports Exerc, 2003; 35;S235.

7. *Bernatsky S, Duffy CM, Penrod JR, Malleson P, Dobkin P, Feldman, De Civita M, Gibbon M, Ortiz-Alvarez O, Clarke A. Health service use in juvenile idiopathic arthritis. Arthritis Rheum 2003,46;S130.

8. Toupin April K, Ehrmann Feldman D, Platt R, Duffy CM. Perceptions of parents and children with juvenile idiopathic arthritis concerning quality of life and adherence to treatment. Canadian Arthritis Network Conference, Montreal, November 2003.

9. Toupin April K, Ehrmann Feldman D, Platt R, Duffy CM. Perceptions of parents and children with juvenile idiopathic arthritis concerning quality of life and adherence to treatment. Canadian Arthritis Network Conference, Montreal, November 2003.

10. Bernatsky S, Duffy CM, Penrod J, St. Pierre Y, Malleson P, Dobkin P, Feldman D, DeCivita M, Gibbon M, Oritz-Avarez O, Clarke A. Economic impact of juvenile idiopathic arthritis. American College of Rheumatology Meeting, San Antonio, October 2004.

11. Toupin April K, Ehrmann Feldman D, Platt R, Duffy CM. Perceptions of parents and children with juvenile idiopathic arthritis regarding quality of life and adherence to treatment. Canadian Arthritis Network Conference, Vancouver, 2004.

12. Ehrmann Feldman D, De Civita M, Dobkin PL, Malleson P, Gibbon M, Meshefedjian G, Duffy CM. Patterns of adherence to treatment in juvenile idiopathic arthritis. Canadian Arthritis Network Conference, Vancouver, 2004.

13. Ehrmann Feldman D**,** Duffy CM, Malleson P, Couture M, Toupin April K. A cross-sectional analysis of CAHC (complementary and alternative health care) use in two pediatric cohorts. Symposium on CAHC, Toronto, December 2004.

14. De Civita M, Ehrmann-Feldman D, Meshefedjian G, Dobkin P, Malleson P, Duffy CM. Caregiver recall of treatment recommendations in juvenile idiopathic arthritis. Arthritis Rheum 2005;52;S539.

15. Toupin April K, Ehrmann Feldman D, Zunzunegui MV, Descarreaux M, Duffy CM. Use and effectiveness of complementary and alternative health care (CAHC) in children with juvenile arthritis and physical disabilities, Focus on Alternative and Complementary Therapies 2005,10 (Supplement 1):54, 2005.

16. Toupin-April K, Ehrmann Feldman D, Zunzunegui MV, Duffy CM. A longitudinal analysis of users of

complementary and alternative health care (CAHC) in children with juvenile idiopathic arthritis. Canadian Arthritis Network Proceedings, Dec 2006.

17. Toupin-April K, Ehrmann Feldman D, Zunzunegui MV, Duffy CM. Why do children with juvenile idiopathic arthritis use complementary and alternative health care? Canadian Arthritis Network Proceedings, Dec 2006.

18. Toupin-April K, Ehrmann Feldman D, Zunzunegui MV, Duffy CM. Types of complementary and alternative health care used by children with various physical disabilities and perceived effectiveness. Canadian Arthritis Network Proceedings, Dec 2006.

19. Cavallo S, Feldman D, Swaine B, Duffy C. Impact of disease severity on parental coping skills in children with juvenile idiopathic arthritis. Arthritis Rheum 2006; 54(9 (supplement)): S775.

Articles:

1. Feldman DE, Duffy CM, De Civita M, Malleson P, Philibert L, Gibbon M, Ortiz-Alvarez O, Dobkin PL. Factors associated with the use of complementary and alternative medicine in juvenile idiopathic arthritis Arthritis Rheum. 2004; 15;51(4):527-532.

2. Adams V, St-Pierre Y, Fautrel B, Clarke AE, Duffy CM, Penrod JR. What is the Impact of Adolescent Arthritis and

Rheumatism (AAR)? Evidence from a National Sample of Canadians. J Rheumatology 2005;32 (2):354-361.

3. *De Civita M, Dobkin PL, Ehrmann Feldman DE, Karp I, Duffy CM. Development and preliminary reproducibility and validity of the Parent Adherence Report Questionnaire: A measure of adherence in Juvenile Idiopathic Arthritis: Journal of Clinical Psychology in Medical Settings, 2005;12:1-12.

4. *Toupin April K, Ehrmann Feldman D, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning perceived quality of life. Quality of Life Research 2006;15:655-661.

5. *Toupin April K, Ehrmann Feldman D, Platt RW, Duffy CM. Comparison between children with juvenile idiopathic arthritis (JIA) and their parents concerning adherence to treatment. Arthritis Rheum 2006:55:558-563.

6. Bernatsky S, Duffy CM, Malleson P, Feldman DE, St Pierre Y, Clarke AE. Economic impact of juvenile idiopathic arthritis. Arthritis Rheum 2007;57:44-48.

7. De Civita M, Ehrmann-Feldman D, Meshefedjian G, Dobkin P, Malleson P, Duffy CM. Caregiver recall of treatment recommendations in juvenile idiopathic arthritis. Arthritis Rheum 2007;57:219-225.

8. Ehrmann-Feldman D, De Civita M, Dobkin P, Malleson P, Duffy CM. Perceived adherence to prescribed treatment in

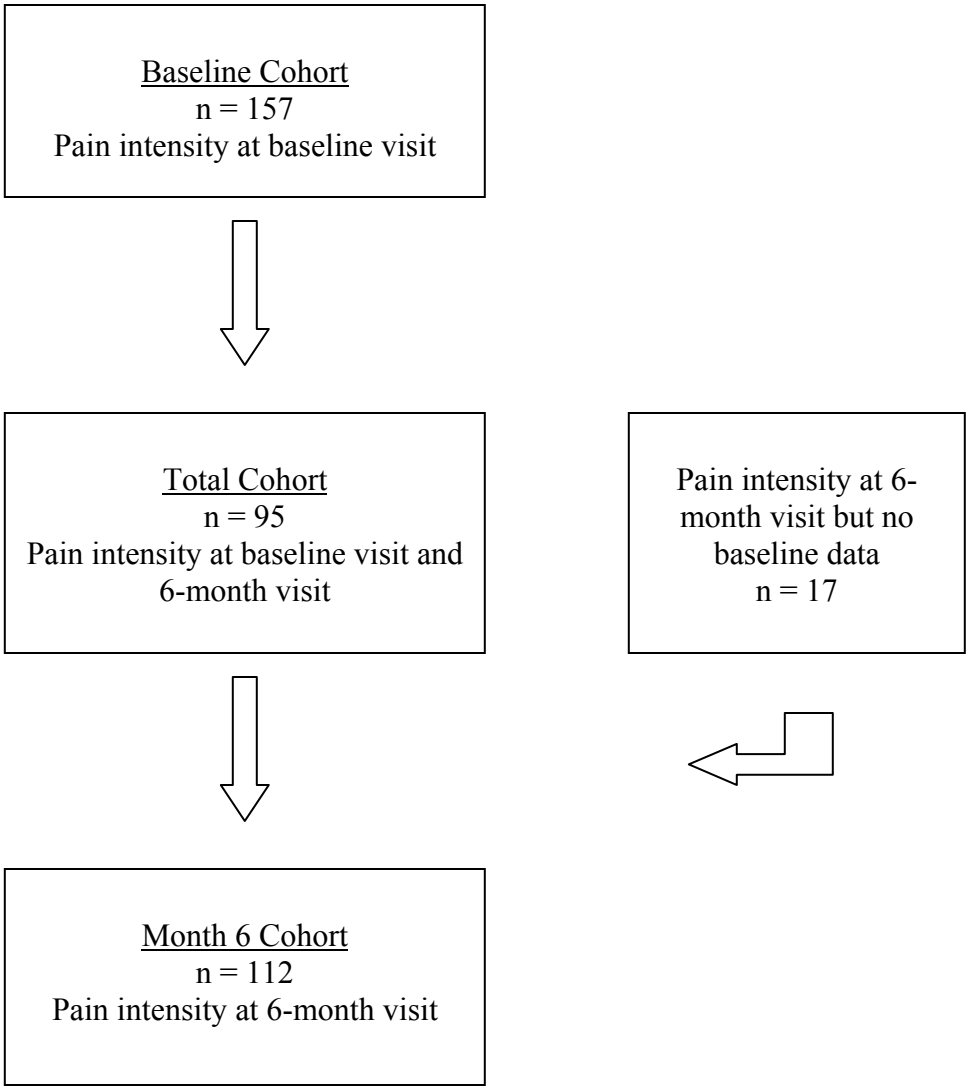
juvenile idiopathic arthritis (JIA) over a one-year period. Arthritis Rheum 2007;57:226-233.

9. Feldman DE, De Civita M, Dobkin P, Malleson P, Meshefedjian G, Duffy CM. Effects of adherence to treatment on short-term outcomes in children with juvenile idiopathic arthritis. Arthritis Rheum 2007;57:905-912.

10. Cavallo S, Ehrmann Feldman D, Swaine B, Meshefedjian G, Malleson PN, Duffy CM. Is parental coping associated with quality of life in juvenile idiopathic arthritis? Pediatric Rheumatology 2009;7:7

APPENDIX 2

Total Cohort, Baseline Cohort and Month 6 Cohort



APPENDIX 3

Correlations - Total Cohort

Correlations[a]

		Overall pain assessement (VAS) past week	ln_pain_0	overall pain assessment (VAS) past week at 6 months	ln_pain_6	Difference pain_T2_T1	Age (in yrs) calculated from DOB	Duration of Disease (in years)	ln_duration	Sex: 0=M,1=F	dx2_ oligovsother	Active Joint Count	ln_AJC	Psychosocial function score, JAQQ	ln_ psychosocial	Family Integration (simple sum)	Social Support (simple sum)	Medical Situation (simple sum)
Overall pain assessement (VAS) past week	Pearson Correlation	1.000	.840**	.195	.379**	-.551**	-.045	-.073	-.110	-.084	-.074	.401**	.414**	.286**	.313**	.012	-.187	.016
	Sig. (2-tailed)		.000	.066	.000	.000	.674	.492	.301	.430	.490	.000	.000	.006	.003	.911	.078	.882
ln_pain_0	Pearson Correlation	.840**	1.000	.214*	.449**	-.420**	.076	-.084	-.123	-.100	-.048	.445**	.481**	.316**	.348**	-.088	-.250*	-.052
	Sig. (2-tailed)	.000		.043	.000	.000	.475	.430	.248	.350	.655	.000	.000	.002	.001	.410	.017	.630
overall pain assessment (VAS) past week at 6 months	Pearson Correlation	.195	.214*	1.000	.852**	.711**	.019	-.078	-.109	-.164	.055	.161	.243*	-.013	-.009	.002	.026	.110
	Sig. (2-tailed)	.066	.043		.000	.000	.861	.466	.304	.122	.609	.131	.021	.900	.929	.982	.810	.303
ln_pain_6	Pearson Correlation	.379**	.449**	.852**	1.000	.453**	-.002	-.123	-.145	-.067	.033	.209*	.280**	.113	.102	.047	.027	.153
	Sig. (2-tailed)	.000	.000	.000		.000	.985	.248	.173	.530	.755	.048	.007	.287	.337	.660	.803	.149
Difference_pain_T2_T1	Pearson Correlation	-.551**	-.420**	.711**	.453**	1.000	.048	-.014	-.014	-.079	.099	-.151	-.090	-.216*	-.232*	-.006	.156	.082
	Sig. (2-tailed)	.000	.000	.000	.000		.653	.898	.896	.458	.352	.155	.399	.041	.027	.952	.142	.442
Age (in yrs) calculated from DOB	Pearson Correlation	-.045	.076	.019	-.002	.048	1.000	.481**	.516**	-.039	.169	-.027	-.033	-.130	-.154	-.100	.110	-.096
	Sig. (2-tailed)	.674	.475	.861	.985	.653		.000	.000	.718	.111	.800	.755	.221	.148	.348	.301	.366
Duration of Disease (in years)	Pearson Correlation	-.073	-.084	-.078	-.123	-.014	.481**	1.000	.953**	.131	.030	-.110	-.151	.086	.055	-.018	.052	-.114
	Sig. (2-tailed)	.492	.430	.466	.248	.898	.000		.000	.218	.777	.301	.154	.420	.606	.870	.628	.284
ln_duration	Pearson Correlation	-.110	-.123	-.109	-.145	-.014	.516**	.953**	1.000	.098	.031	-.136	-.180	.071	.039	-.021	.118	-.117
	Sig. (2-tailed)	.301	.248	.304	.173	.896	.000	.000		.361	.771	.202	.089	.504	.713	.845	.267	.273
Sex: 0=M,1=F	Pearson Correlation	-.084	-.100	-.164	-.067	-.079	-.039	.131	.098	1.000	-.161	.056	.017	.015	.006	-.107	-.072	-.075
	Sig. (2-tailed)	.430	.350	.122	.530	.458	.718	.218	.361		.129	.603	.877	.887	.954	.314	.499	.479
dx2_oligovsother	Pearson Correlation	-.074	-.048	.055	.033	.099	.169	.030	.031	-.161	1.000	.111	.085	.011	.005	.117	.206	.130
	Sig. (2-tailed)	.490	.655	.609	.755	.352	.111	.777	.771	.129		.298	.426	.917	.966	.272	.051	.222
Active Joint Count	Pearson Correlation	.401**	.445**	.161	.209*	-.151	-.027	-.110	-.136	.056	.111	1.000	.949**	.063	.123	.093	-.171	.001
	Sig. (2-tailed)	.000	.000	.131	.048	.155	.800	.301	.202	.603	.298		.000	.554	.247	.383	.106	.996
ln_AJC	Pearson Correlation	.414**	.481**	.243*	.280**	-.090	-.033	-.151	-.180	.017	.085	.949**	1.000	.056	.121	.079	-.196	-.004
	Sig. (2-tailed)	.000	.000	.021	.007	.399	.755	.154	.089	.877	.426	.000		.600	.254	.461	.064	.969
Psychosocial function score, JAQQ	Pearson Correlation	.286**	.316**	-.013	.113	-.216*	-.130	.086	.071	.015	.011	.063	.056	1.000	.978**	-.013	-.031	.059
	Sig. (2-tailed)	.006	.002	.900	.287	.041	.221	.420	.504	.887	.917	.554	.600		.000	.900	.771	.581
ln_psychosocial	Pearson Correlation	.313**	.348**	-.009	.102	-.232*	-.154	.055	.039	.006	.005	.123	.121	.978**	1.000	-.033	-.063	.013
	Sig. (2-tailed)	.003	.001	.929	.337	.027	.148	.606	.713	.954	.966	.247	.254	.000		.756	.553	.904
Family Integration (simple sum)	Pearson Correlation	.012	-.088	.002	.047	-.006	-.100	-.018	-.021	-.107	.117	.093	.079	-.013	-.033	1.000	.601**	.600**
	Sig. (2-tailed)	.911	.410	.982	.660	.952	.348	.870	.845	.314	.272	.383	.461	.900	.756		.000	.000
Social Support (simple sum)	Pearson Correlation	-.187	-.250*	.026	.027	.156	.110	.052	.118	-.072	.206	-.171	-.196	-.031	-.063	.601**	1.000	.488**
	Sig. (2-tailed)	.078	.017	.810	.803	.142	.301	.628	.267	.499	.051	.106	.064	.771	.553	.000		.000
Medical Situation (simple sum)	Pearson Correlation	.016	-.052	.110	.153	.082	-.096	-.114	-.117	-.075	.130	.001	-.004	.059	.013	.600**	.488**	1.000
	Sig. (2-tailed)	.882	.630	.303	.149	.442	.366	.284	.273	.479	.222	.996	.969	.581	.904	.000	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

a. Listwise N=90

APPENDIX 3 (cont.)

Correlations - Baseline Cohort

Correlations[a]

		Overall pain assessement (VAS) past week	ln_pain_0	Age (in yrs) calculated from DOB	Duration of Disease (in years)	ln_duration	Sex: 0=M,1=F	dx2_ oligovsother	Active Joint Count	ln_AJC	Psychosocial function score, JAQQ	ln_ psychosocial	Family Integration (simple sum)	Social Support (simple sum)	Medical Situation (simple sum)
Overall pain assessement (VAS) past week	Pearson Correlation	1.000	.836**	.066	-.029	-.061	-.120	.055	.179*	.327**	.396**	.407**	.051	-.134	.047
	Sig. (2-tailed)		.000	.434	.733	.473	.154	.519	.033	.000	.000	.000	.548	.112	.578
ln_pain_0	Pearson Correlation	.836**	1.000	.162	-.016	-.059	-.114	.061	.253**	.404**	.395**	.422**	-.014	-.171*	.015
	Sig. (2-tailed)	.000		.054	.847	.482	.177	.470	.002	.000	.000	.000	.873	.042	.860
Age (in yrs) calculated from DOB	Pearson Correlation	.066	.162	1.000	.438**	.449**	-.091	.272**	.070	.058	-.091	-.114	.024	.190*	-.036
	Sig. (2-tailed)	.434	.054		.000	.000	.281	.001	.405	.490	.282	.176	.780	.024	.669
Duration of Disease (in years)	Pearson Correlation	-.029	-.016	.438**	1.000	.948**	.070	.040	-.031	-.106	.068	.069	.032	.058	-.039
	Sig. (2-tailed)	.733	.847	.000		.000	.406	.640	.710	.211	.419	.417	.705	.490	.645
ln_duration	Pearson Correlation	-.061	-.059	.449**	.948**	1.000	.042	.044	.006	-.088	.080	.077	.013	.103	-.045
	Sig. (2-tailed)	.473	.482	.000	.000		.623	.600	.945	.300	.345	.362	.875	.222	.591
Sex: 0=M,1=F	Pearson Correlation	-.120	-.114	-.091	.070	.042	1.000	-.245**	-.066	-.080	-.086	-.057	-.155	-.027	-.061
	Sig. (2-tailed)	.154	.177	.281	.406	.623		.003	.434	.344	.308	.499	.066	.748	.470
dx2_oligovsother	Pearson Correlation	.055	.061	.272**	.040	.044	-.245**	1.000	.241**	.249**	.119	.104	.149	.181*	.156
	Sig. (2-tailed)	.519	.470	.001	.640	.600	.003		.004	.003	.158	.220	.076	.031	.064
Active Joint Count	Pearson Correlation	.179*	.253**	.070	-.031	.006	-.066	.241**	1.000	.861**	.263**	.245**	.102	.031	.120
	Sig. (2-tailed)	.033	.002	.405	.710	.945	.434	.004		.000	.002	.003	.228	.716	.157
ln_AJC	Pearson Correlation	.327**	.404**	.058	-.106	-.088	-.080	.249**	.861**	1.000	.224**	.230**	.104	-.057	.120
	Sig. (2-tailed)	.000	.000	.490	.211	.300	.344	.003	.000		.007	.006	.219	.498	.156
Psychosocial function score, JAQQ	Pearson Correlation	.396**	.395**	-.091	.068	.080	-.086	.119	.263**	.224**	1.000	.976**	.098	.032	.163
	Sig. (2-tailed)	.000	.000	.282	.419	.345	.308	.158	.002	.007		.000	.247	.703	.053
ln_psychosocial	Pearson Correlation	.407**	.422**	-.114	.069	.077	-.057	.104	.245**	.230**	.976**	1.000	.071	.000	.118
	Sig. (2-tailed)	.000	.000	.176	.417	.362	.499	.220	.003	.006	.000		.401	.997	.161
Family Integration (simple sum)	Pearson Correlation	.051	-.014	.024	.032	.013	-.155	.149	.102	.104	.098	.071	1.000	.629**	.612**
	Sig. (2-tailed)	.548	.873	.780	.705	.875	.066	.076	.228	.219	.247	.401		.000	.000
Social Support (simple sum)	Pearson Correlation	-.134	-.171*	.190*	.058	.103	-.027	.181*	.031	-.057	.032	.000	.629**	1.000	.513**
	Sig. (2-tailed)	.112	.042	.024	.490	.222	.748	.031	.716	.498	.703	.997	.000		.000
Medical Situation (simple sum)	Pearson Correlation	.047	.015	-.036	-.039	-.045	-.061	.156	.120	.120	.163	.118	.612**	.513**	1.000
	Sig. (2-tailed)	.578	.860	.669	.645	.591	.470	.064	.157	.156	.053	.161	.000	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

a. Listwise N=142

APPENDIX 3 (cont.)

Correlations - Month 6 Cohort

Correlations[a]

		overall pain assessment (VAS) past week at 6 months	ln_pain_6	Age (in yrs) calculated from DOB	Duration of Disease (in years)	ln_duration	Sex: 0=M,1=F	dx2_ oligovsother	Active Joint Count	ln_AJC	Psychosocial function score, JAQQ	ln_ psychosocial	Family Integration (simple sum)	Social Support (simple sum)	Medical Situation (simple sum)
overall pain assessment (VAS) past week at 6 months	Pearson Correlation	1.000	.845**	.068	.025	-.048	-.145	.011	.170	.258**	-.018	-.013	-.005	.024	.092
	Sig. (2-tailed)		.000	.494	.804	.628	.144	.912	.086	.009	.855	.894	.961	.808	.354
ln_pain_6	Pearson Correlation	.845**	1.000	.026	-.057	-.111	-.094	.017	.231*	.313**	.106	.094	.012	.010	.103
	Sig. (2-tailed)	.000		.792	.571	.266	.347	.866	.019	.001	.285	.345	.906	.921	.301
Age (in yrs) calculated from DOB	Pearson Correlation	.068	.026	1.000	.525**	.542**	-.014	.136	-.030	-.041	-.142	-.160	-.064	.152	-.074
	Sig. (2-tailed)	.494	.792		.000	.000	.886	.171	.765	.684	.153	.107	.520	.124	.456
Duration of Disease (in years)	Pearson Correlation	.025	-.057	.525**	1.000	.946**	.170	-.069	-.135	-.163	-.005	-.028	-.024	.086	-.085
	Sig. (2-tailed)	.804	.571	.000		.000	.087	.490	.175	.100	.963	.777	.808	.389	.391
ln_duration	Pearson Correlation	-.048	-.111	.542**	.946**	1.000	.131	-.046	-.166	-.205*	.000	-.032	-.041	.140	-.109
	Sig. (2-tailed)	.628	.266	.000	.000		.188	.648	.094	.038	.994	.750	.680	.159	.272
Sex: 0=M,1=F	Pearson Correlation	-.145	-.094	-.014	.170	.131	1.000	-.203*	.043	.000	-.050	-.045	-.106	-.069	-.081
	Sig. (2-tailed)	.144	.347	.886	.087	.188		.040	.664	1.000	.619	.655	.289	.486	.414
dx2_oligovsother	Pearson Correlation	.011	.017	.136	-.069	-.046	-.203*	1.000	.132	.106	.050	.039	.145	.181	.147
	Sig. (2-tailed)	.912	.866	.171	.490	.648	.040		.185	.289	.619	.695	.143	.068	.137
Active Joint Count	Pearson Correlation	.170	.231*	-.030	-.135	-.166	.043	.132	1.000	.948**	.087	.143	.072	-.168	-.029
	Sig. (2-tailed)	.086	.019	.765	.175	.094	.664	.185		.000	.380	.150	.472	.090	.775
ln_AJC	Pearson Correlation	.258**	.313**	-.041	-.163	-.205*	.000	.106	.948**	1.000	.089	.146	.042	-.202*	-.050
	Sig. (2-tailed)	.009	.001	.684	.100	.038	1.000	.289	.000		.371	.140	.677	.041	.613
Psychosocial function score, JAQQ	Pearson Correlation	-.018	.106	-.142	-.005	.000	-.050	.050	.087	.089	1.000	.979**	-.027	-.042	.046
	Sig. (2-tailed)	.855	.285	.153	.963	.994	.619	.619	.380	.371		.000	.783	.677	.642
ln_psychosocial	Pearson Correlation	-.013	.094	-.160	-.028	-.032	-.045	.039	.143	.146	.979**	1.000	-.034	-.066	.014
	Sig. (2-tailed)	.894	.345	.107	.777	.750	.655	.695	.150	.140	.000		.735	.508	.891
Family Integration (simple sum)	Pearson Correlation	-.005	.012	-.064	-.024	-.041	-.106	.145	.072	.042	-.027	-.034	1.000	.608**	.633**
	Sig. (2-tailed)	.961	.906	.520	.808	.680	.289	.143	.472	.677	.783	.735		.000	.000
Social Support (simple sum)	Pearson Correlation	.024	.010	.152	.086	.140	-.069	.181	-.168	-.202*	-.042	-.066	.608**	1.000	.483**
	Sig. (2-tailed)	.808	.921	.124	.389	.159	.486	.068	.090	.041	.677	.508	.000		.000
Medical Situation (simple sum)	Pearson Correlation	.092	.103	-.074	-.085	-.109	-.081	.147	-.029	-.050	.046	.014	.633**	.483**	1.000
	Sig. (2-tailed)	.354	.301	.456	.391	.272	.414	.137	.775	.613	.642	.891	.000	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

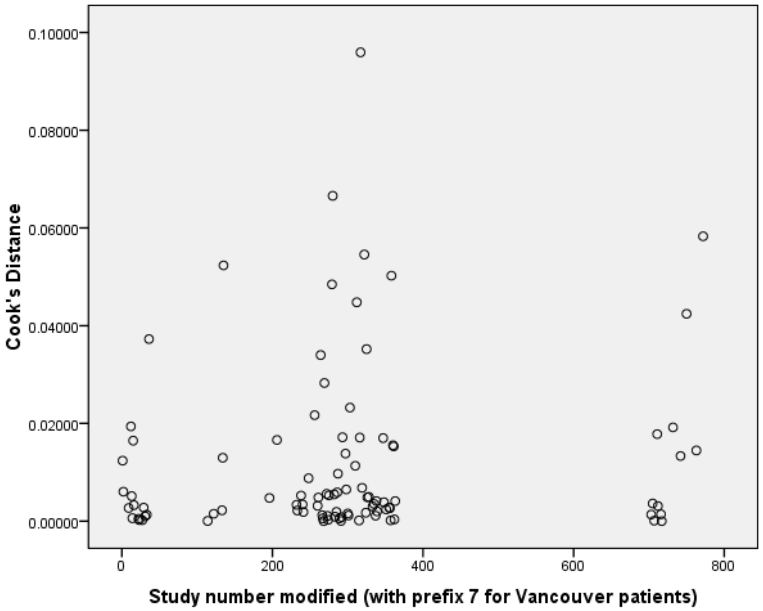
*. Correlation is significant at the 0.05 level (2-tailed).

a. Listwise N=103

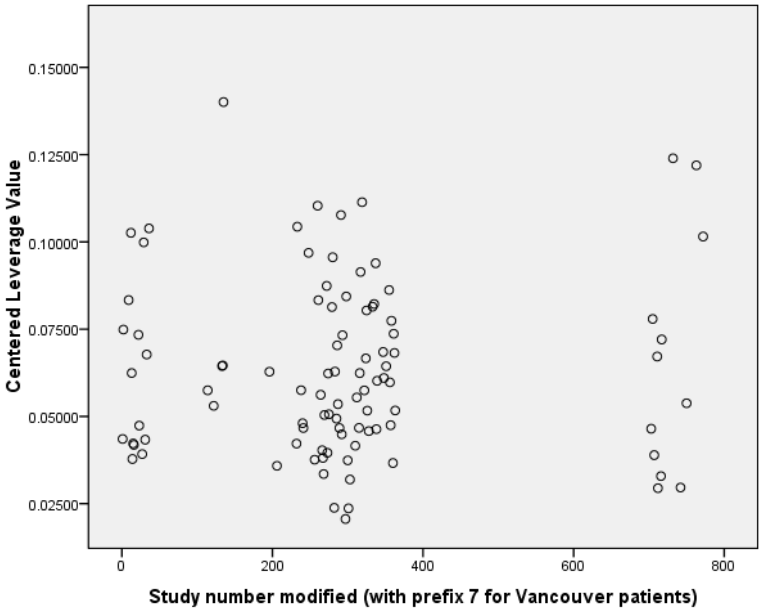
APPENDIX 4

MLRA – Cross-sectional analysis (Total Cohort) : psychosocial functioning

Cook's distance



Leverage value



APPENDIX 4 (cont.)

MLRA – Cross-sectional analysis (Total Cohort): psychosocial functioning

DFBETA (duration)

Extreme Values

			Case Number	Value
DFBETA Duration_Dis_YR	Highest	1	31	.01797
		2	25	.01387
		3	9	.01055
		4	50	.01033
		5	45	.00793
	Lowest	1	83	-.01428
		2	72	-.00941
		3	91	-.00871
		4	30	-.00793
		5	116	-.00700

DFBETA (gender)

Extreme Values

			Case Number	Value
DFBETA sex	Highest	1	87	.12955
		2	182	.09730
		3	107	.07463
		4	86	.07062
		5	173	.05508
	Lowest	1	25	-.10114
		2	160	-.08964
		3	54	-.08482
		4	62	-.05167
		5	61	-.04693

DFBETA (age)

Extreme Values

			Case Number	Value
DFBETA agedob	Highest	1	182	.01073
		2	94	.00925
		3	131	.00781
		4	30	.00692
		5	83	.00589
	Lowest	1	50	-.01027
		2	61	-.00927
		3	9	-.00873
		4	116	-.00762
		5	87	-.00610

DFBETA (JIA category)

Extreme Values

			Case Number	Value
DFBETA dx2_oligo	Highest	1	87	.09148
		2	116	.06949
		3	50	.06300
		4	45	.04952
		5	78	.04409
	Lowest	1	83	-.05322
		2	62	-.05301
		3	25	-.05248
		4	94	-.04964
		5	91	-.04668

DFBETA (ln AJC)

Extreme Values

			Case Number	Value
DFBETA ln_AJC	Highest	1	31	.08481
		2	87	.04731
		3	62	.04672
		4	61	.03766
		5	81	.02834
	Lowest	1	83	-.06580
		2	182	-.05318
		3	148	-.05085
		4	116	-.04883
		5	91	-.04877

DFBETA (psychosocial)

Extreme Values

			Case Number	Value
DFBETA Psychosocial	Highest	1	91	.02984
		2	182	.02897
		3	116	.02325
		4	34	.02076
		5	160	.01702
	Lowest	1	62	-.05807
		2	87	-.04877
		3	61	-.03908
		4	94	-.02543
		5	45	-.02195

APPENDIX 4 (cont.)

MLRA – Cross-sectional analysis (Total Cohort): psychosocial functioning

Collinearity diagnosis

Coefficients[a]

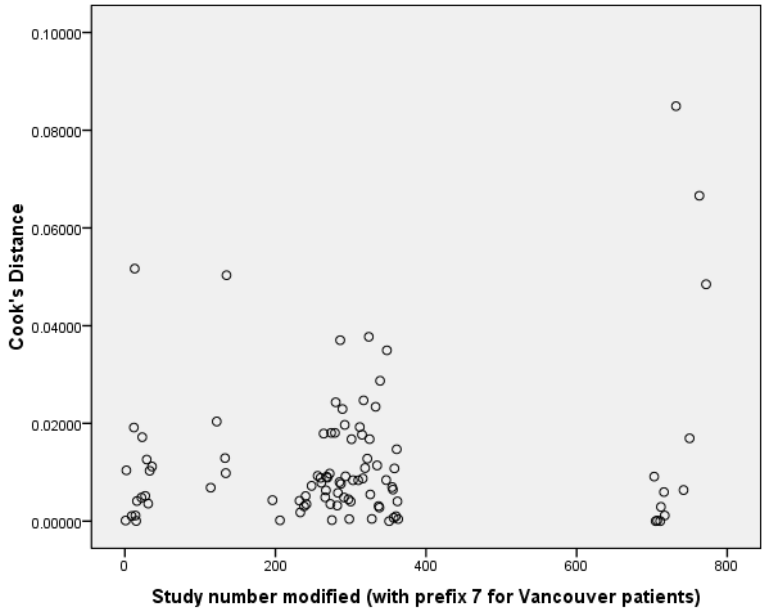
Model		Statistics											
		Unstandardized Coefficients		Standardized Coefficients			95% Confidence Interval for B		Correlations			Collinearity Statistics	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound	Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	2.004	.475		4.216	.000	1.059	2.948					
	Duration of Disease (in years)	-.086	.054	-.191	-1.600	.113	-.193	.021	-.125	-.166	-.164	.737	1.357
	Sex: 0=M,1=F	-.362	.359	-.106	-1.008	.316	-1.076	.352	-.127	-.106	-.103	.943	1.061
	Age (in yrs) calculated from DOB	.059	.040	.175	1.463	.147	-.021	.139	.071	.152	.150	.736	1.358
	dx2_oligovsother	-.288	.311	-.097	-.925	.357	-.907	.331	-.057	-.097	-.095	.952	1.050
2	(Constant)	1.442	.428		3.366	.001	.591	2.294					
	Duration of Disease (in years)	-.038	.048	-.085	-.804	.423	-.133	.056	-.125	-.085	-.072	.711	1.406
	Sex: 0=M,1=F	-.438	.314	-.129	-1.394	.167	-1.063	.187	-.127	-.146	-.125	.941	1.063
	Age (in yrs) calculated from DOB	.051	.035	.152	1.457	.149	-.019	.122	.071	.153	.130	.735	1.360
	dx2_oligovsother	-.421	.273	-.142	-1.538	.128	-.964	.123	-.057	-.161	-.138	.945	1.059
	ln_AJC	1.134	.212	.491	5.361	.000	.714	1.554	.488	.494	.480	.955	1.047
3	(Constant)	.408	.470		.867	.388	-.527	1.342					
	Duration of Disease (in years)	-.058	.044	-.130	-1.314	.192	-.146	.030	-.125	-.139	-.109	.703	1.423
	Sex: 0=M,1=F	-.379	.290	-.111	-1.305	.195	-.956	.198	-.127	-.138	-.108	.938	1.066
	Age (in yrs) calculated from DOB	.073	.033	.216	2.207	.030	.007	.138	.071	.229	.182	.716	1.396
	dx2_oligovsother	-.452	.252	-.152	-1.792	.077	-.954	.049	-.057	-.188	-.148	.944	1.060
	ln_AJC	1.046	.196	.453	5.328	.000	.656	1.437	.488	.494	.440	.943	1.060
	Psychosocial function score, JAQQ	.420	.103	.342	4.067	.000	.215	.625	.359	.398	.336	.963	1.038

a. Dependent Variable: ln_pain_0

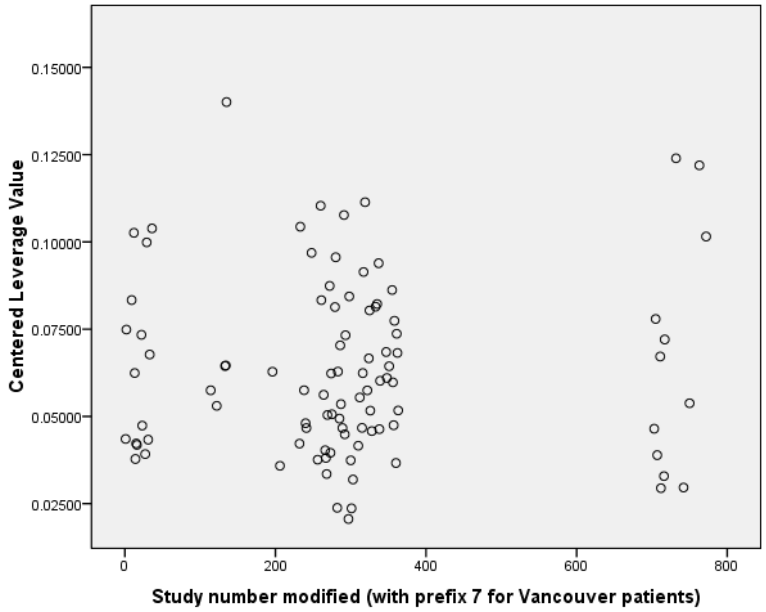
APPENDIX 5

MLRA – Longitudinal analysis (Total Cohort): psychosocial functioning

Cook's distance



Leverage value



APPENDIX 5 (cont.)

MLRA – Longitudinal analysis (Total Cohort): psychosocial functioning

DFBETA (duration)

Extreme Values

			Case Number	Value
DFBETA Duration_Dis_YR	Highest	1	31	.02275
		2	108	.01866
		3	148	.01481
		4	9	.01354
		5	28	.01239
	Lowest	1	173	-.01501
		2	83	-.01209
		3	29	-.01114
		4	103	-.01008
		5	25	-.00980

DFBETA (gender)

Extreme Values

			Case Number	Value
DFBETA sex	Highest	1	173	.15262
		2	87	.08489
		3	58	.07153
		4	25	.07149
		5	23	.06899
	Lowest	1	10	-.15060
		2	182	-.11454
		3	99	-.09574
		4	103	-.09054
		5	85	-.07852

DFBETA (age)

Extreme Values

			Case Number	Value
DFBETA agedob	Highest	1	93	.01675
		2	50	.00963
		3	18	.00887
		4	29	.00854
		5	66	.00852
	Lowest	1	148	-.01477
		2	182	-.01263
		3	9	-.01120
		4	58	-.00898
		5	100	-.00766

DFBETA (JIA category)

Extreme Values

			Case Number	Value
DFBETA dx2_oligo	Highest	1	148	.10044
		2	173	.09773
		3	77	.06744
		4	87	.05994
		5	10	.05926
	Lowest	1	66	-.07697
		2	93	-.07692
		3	50	-.05905
		4	18	-.05852
		5	108	-.05845

DFBETA (ln AJC)

Extreme Values

			Case Number	Value
DFBETA ln_AJC	Highest	1	31	.10735
		2	182	.06261
		3	56	.03904
		4	27	.03798
		5	62	.03646
	Lowest	1	148	-.13814
		2	173	-.09659
		3	83	-.05570
		4	69	-.04334
		5	49	-.03973

DFBETA (psychosocial)

Extreme Values

			Case Number	Value
DFBETA Psychosocial	Highest	1	66	.03483
		2	48	.02560
		3	113	.02233
		4	91	.01865
		5	42	.01820
	Lowest	1	62	-.04532
		2	182	-.03410
		3	10	-.03337
		4	87	-.03196
		5	61	-.03080

APPENDIX 5 (cont.)

MLRA – Longitudinal analysis (Total Cohort) : psychosocial functioning

Collinearity diagnosis

Collinearity Diagnostics[a]

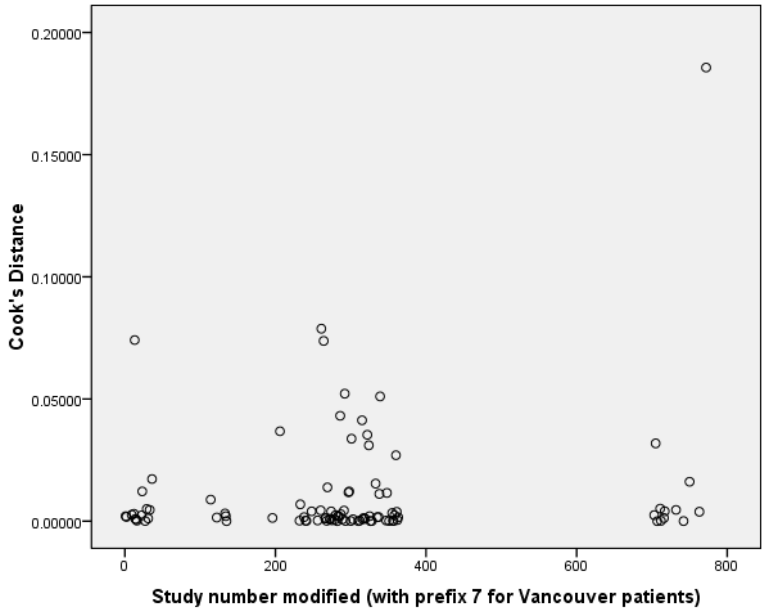
Model	Dimension	Eigenvalue	Condition Index	Variance Proportions						
				(Constant)	Duration of Disease (in years)	Sex: 0=M,1=F	Age (in yrs) calculated from DOB	dx2_ oligovsother	ln_AJC	Psychosocial function score, JAQQ
1	1	3.989	1.000	.01	.01	.01	.01	.02		
	2	.469	2.916	.00	.10	.05	.00	.70		
	3	.316	3.550	.02	.45	.32	.02	.01		
	4	.160	4.998	.08	.34	.26	.36	.24		
	5	.066	7.795	.89	.10	.35	.61	.04		
2	1	4.387	1.000	.00	.01	.01	.01	.01	.01	
	2	.665	2.569	.00	.10	.00	.01	.01	.64	
	3	.450	3.122	.00	.02	.08	.00	.74	.08	
	4	.280	3.955	.02	.37	.39	.02	.02	.19	
	5	.153	5.350	.08	.43	.18	.39	.19	.06	
	6	.065	8.239	.89	.07	.34	.58	.03	.02	
3	1	5.145	1.000	.00	.01	.01	.00	.01	.01	.01
	2	.666	2.780	.00	.10	.00	.01	.01	.62	.00
	3	.452	3.373	.00	.01	.07	.00	.76	.06	.00
	4	.307	4.097	.01	.34	.10	.03	.00	.27	.19
	5	.234	4.689	.00	.03	.49	.00	.07	.00	.43
	6	.148	5.900	.04	.45	.07	.48	.13	.04	.06
	7	.049	10.257	.95	.06	.27	.48	.02	.00	.31

a. Dependent Variable: ln_pain_6

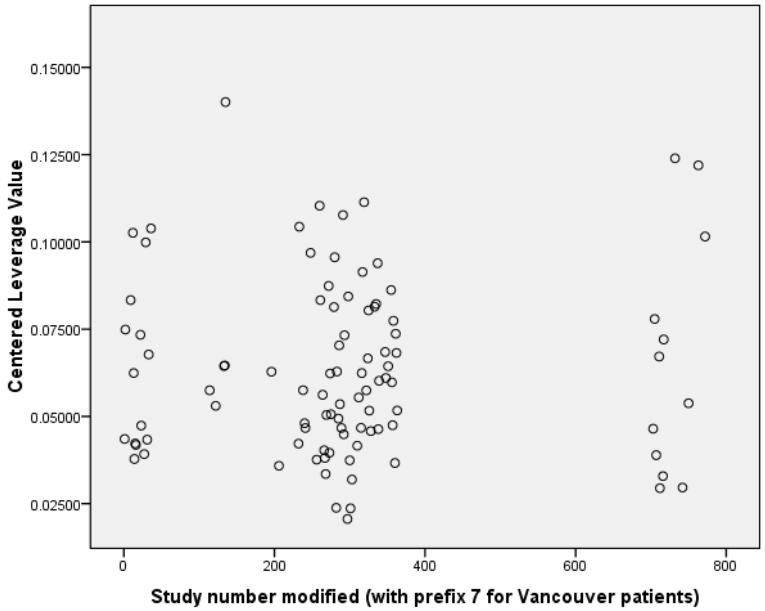
APPENDIX 6

MLRA – Exploratory analysis (change in pain intensity): psychosocial functioning

Cook's distance



Leverage value



APPENDIX 6 (cont.)

MLRA – Exploratory analysis (change in pain intensity): psychosocial functioning

DFBETA (duration)

Extreme Values

			Case Number	Value
DFBETA Duration_Dis_YR	Highest	1	10	.23991
		2	108	.18782
		3	91	.15848
		4	117	.15175
		5	66	.15123
	Lowest	1	50	-.34420
		2	103	-.23548
		3	25	-.21317
		4	85	-.20350
		5	93	-.15052

DFBETA (gender)

Extreme Values

			Case Number	Value
DFBETA sex	Highest	1	49	2.64167
		2	25	1.55469
		3	54	1.34113
		4	50	1.25886
		5	160	1.25006
	Lowest	1	182	-3.92724
		2	10	-3.15977
		3	103	-2.11453
		4	85	-2.10121
		5	99	-1.35839

DFBETA (age)

Extreme Values

			Case Number	Value
DFBETA agedob	Highest	1	50	.34229
		2	93	.26617
		3	66	.16095
		4	18	.13082
		5	103	.10328
	Lowest	1	182	-.43307
		2	71	-.15144
		3	10	-.12182
		4	77	-.11316
		5	49	-.10731

DFBETA (JIA category)

Extreme Values

			Case Number	Value
DFBETA dx2_oligo	Highest	1	182	1.69119
		2	77	1.67564
		3	34	1.36809
		4	10	1.24339
		5	117	1.13161
	Lowest	1	50	-2.09912
		2	66	-1.45481
		3	71	-1.35095
		4	93	-1.22205
		5	18	-.86299

DFBETA (ln AJC)

Extreme Values

			Case Number	Value
DFBETA ln_AJC	Highest	1	182	2.14651
		2	50	.97437
		3	71	.92285
		4	91	.88757
		5	27	.75413
	Lowest	1	49	-2.20577
		2	125	-1.61767
		3	117	-.73049
		4	10	-.70425
		5	36	-.66216

DFBETA (psychosocial)

Extreme Values

			Case Number	Value
DFBETA Psychosocial	Highest	1	66	.65825
		2	50	.45988
		3	48	.31636
		4	71	.30340
		5	113	.26945
	Lowest	1	182	-1.16926
		2	10	-.70016
		3	34	-.69865
		4	91	-.54314
		5	103	-.51574

APPENDIX 6 (cont.)

MLRA – Exploratory analysis (change in pain intensity): psychosocial functioning

Collinearity diagnosis

Collinearity Diagnostics[a]

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions						
				(Constant)	Duration of Disease (in years)	Sex: 0=M,1=F	Age (in yrs) calculated from DOB	dx2_ oligovsother	ln_AJC	Psychosocial function score, JAQQ
1	1	3.989	1.000	.01	.01	.01	.01	.02		
	2	.469	2.916	.00	.10	.05	.00	.70		
	3	.316	3.550	.02	.45	.32	.02	.01		
	4	.160	4.998	.08	.34	.26	.36	.24		
	5	.066	7.795	.89	.10	.35	.61	.04		
2	1	4.387	1.000	.00	.01	.01	.01	.01	.01	
	2	.665	2.569	.00	.10	.00	.01	.01	.64	
	3	.450	3.122	.00	.02	.08	.00	.74	.08	
	4	.280	3.955	.02	.37	.39	.02	.02	.19	
	5	.153	5.350	.08	.43	.18	.39	.19	.06	
	6	.065	8.239	.89	.07	.34	.58	.03	.02	
3	1	5.145	1.000	.00	.01	.01	.00	.01	.01	.01
	2	.666	2.780	.00	.10	.00	.01	.01	.62	.00
	3	.452	3.373	.00	.01	.07	.00	.76	.06	.00
	4	.307	4.097	.01	.34	.10	.03	.00	.27	.19
	5	.234	4.689	.00	.03	.49	.00	.07	.00	.43
	6	.148	5.900	.04	.45	.07	.48	.13	.04	.06
	7	.049	10.257	.95	.06	.27	.48	.02	.00	.31

a. Dependent Variable: Difference_pain_T2_T1

APPENDIX 7

MLRA – Exploratory analysis (interaction term): psychosocial functioning

Collinearity diagnosis

Collinearity Diagnostics[a]

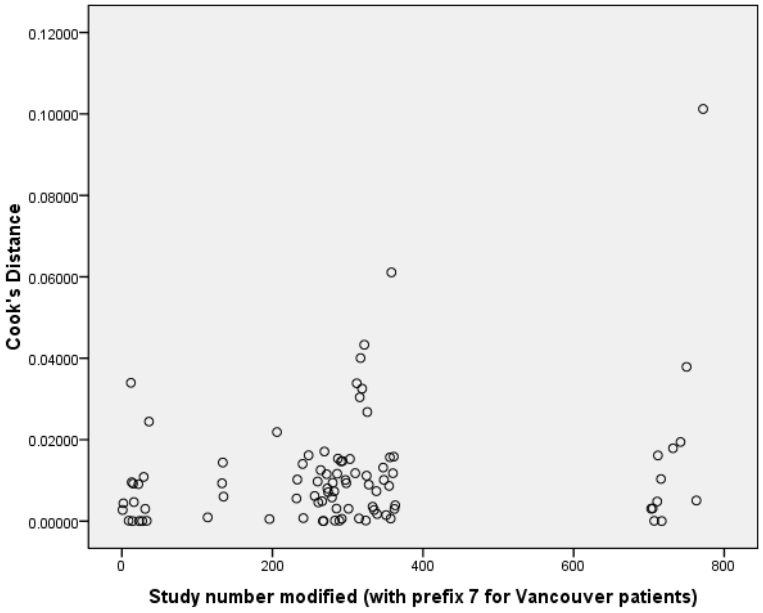
Model	Dimension	Eigenvalue	Condition Index	Variance Proportions							
				(Constant)	Duration of Disease (in years)	Sex: 0=M,1=F	Age (in yrs) calculated from DOB	dx2_ oligovsother	ln_AJC	Psychosocial function score, JAQQ	inter_lnAJC_ psych
1	1	3.989	1.000	.01	.01	.01	.01	.02			
	2	.469	2.916	.00	.10	.05	.00	.70			
	3	.316	3.550	.02	.45	.32	.02	.01			
	4	.160	4.998	.08	.34	.26	.36	.24			
	5	.066	7.795	.89	.10	.35	.61	.04			
2	1	4.387	1.000	.00	.01	.01	.01	.01	.01		
	2	.665	2.569	.00	.10	.00	.01	.01	.64		
	3	.450	3.122	.00	.02	.08	.00	.74	.08		
	4	.280	3.955	.02	.37	.39	.02	.02	.19		
	5	.153	5.350	.08	.43	.18	.39	.19	.06		
	6	.065	8.239	.89	.07	.34	.58	.03	.02		
3	1	5.145	1.000	.00	.01	.01	.00	.01	.01	.01	
	2	.666	2.780	.00	.10	.00	.01	.01	.62	.00	
	3	.452	3.373	.00	.01	.07	.00	.76	.06	.00	
	4	.307	4.097	.01	.34	.10	.03	.00	.27	.19	
	5	.234	4.689	.00	.03	.49	.00	.07	.00	.43	
	6	.148	5.900	.04	.45	.07	.48	.13	.04	.06	
	7	.049	10.257	.95	.06	.27	.48	.02	.00	.31	
4	1	5.607	1.000	.00	.01	.01	.00	.01	.00	.00	.00
	2	1.135	2.223	.00	.03	.01	.01	.01	.02	.00	.02
	3	.465	3.472	.00	.05	.06	.00	.72	.00	.00	.00
	4	.317	4.204	.01	.39	.14	.03	.00	.01	.12	.00
	5	.240	4.834	.00	.02	.40	.00	.03	.01	.36	.00
	6	.154	6.040	.04	.37	.12	.44	.18	.00	.02	.01
	7	.051	10.465	.74	.10	.27	.53	.04	.06	.11	.07
	8	.031	13.495	.21	.02	.00	.00	.02	.90	.39	.89

a. Dependent Variable: ln_pain_0

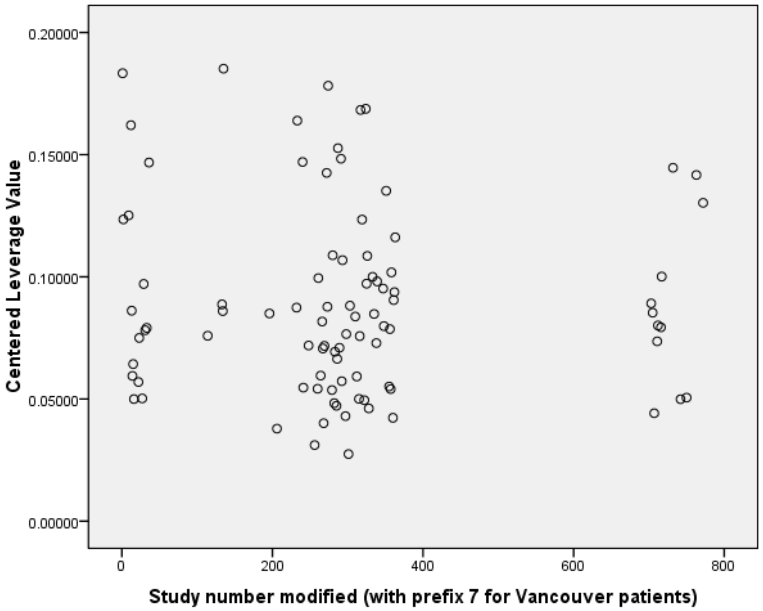
APPENDIX 8

MLRA – Cross-sectional analysis (Total Cohort): parental coping

Cook's distance



Leverage value



APPENDIX 8 (cont.)

MLRA – Cross-sectional analysis (Total Cohort): parental coping

DFBETA (duration)

Extreme Values

			Case Number	Value
DFBETA Duration_Dis_YR	Highest	1	9	.01688
		2	25	.01091
		3	118	.00922
		4	56	.00865
		5	48	.00814
	Lowest	1	83	-.01615
		2	72	-.01130
		3	108	-.00956
		4	30	-.00944
		5	70	-.00931

DFBETA (gender)

Extreme Values

			Case Number	Value
DFBETA sex	Highest	1	182	.15624
		2	86	.10935
		3	87	.09352
		4	107	.06534
		5	116	.05263
	Lowest	1	160	-.10797
		2	88	-.09031
		3	25	-.08041
		4	42	-.07854
		5	54	-.07474

DFBETA (age)

Extreme Values

			Case Number	Value
DFBETA agedob	Highest	1	182	.01851
		2	94	.00784
		3	21	.00696
		4	30	.00685
		5	83	.00664
	Lowest	1	9	-.01466
		2	116	-.01380
		3	50	-.00715
		4	148	-.00694
		5	91	-.00661

DFBETA (JIA category)

Extreme Values

			Case Number	Value
DFBETA dx2_oligo	Highest	1	116	.08404
		2	87	.06248
		3	86	.05609
		4	50	.05275
		5	113	.04912
	Lowest	1	88	-.06735
		2	83	-.06556
		3	34	-.06263
		4	182	-.06077
		5	91	-.05158

DFBETA (ln AJC)

Extreme Values

			Case Number	Value
DFBETA ln_AJC	Highest	1	9	.05784
		2	95	.04989
		3	36	.04416
		4	81	.04342
		5	56	.03857
	Lowest	1	182	-.10277
		2	83	-.06384
		3	91	-.06020
		4	148	-.05469
		5	160	-.04592

DFBETA (family integration)

Extreme Values

			Case Number	Value
DFBETA total_Fam_Integ	Highest	1	182	.01245
		2	88	.00591
		3	87	.00484
		4	62	.00478
		5	25	.00457
	Lowest	1	116	-.00910
		2	9	-.00746
		3	67	-.00565
		4	70	-.00495
		5	155	-.00473

APPENDIX 8 (cont.)

MLRA – Cross-sectional analysis (Total Cohort): parental coping

DFBETA (social support)

Extreme Values

			Case Number	Value
DFBETA total_Soc_Sup	Highest	1	95	.00501
		2	9	.00369
		3	81	.00364
		4	114	.00329
		5	132	.00329
	Lowest	1	87	-.00620
		2	182	-.00500
		3	78	-.00389
		4	25	-.00276
		5	62	-.00237

DFBETA (medical situation)

Extreme Values

			Case Number	Value
DFBETA total_Med_Sit	Highest	1	87	.00859
		2	155	.00837
		3	116	.00807
		4	57	.00570
		5	73	.00499
	Lowest	1	40	-.00791
		2	132	-.00648
		3	72	-.00514
		4	62	-.00482
		5	56	-.00460

APPENDIX 8 (cont.)

MLRA – Cross-sectional analysis (Total Cohort): parental coping

Collinearity Diagnostics[a]

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions								
				(Constant)	Duration of Disease (in years)	Sex: 0=M,1=F	Age (in yrs) calculated from DOB	dx2_ oligovsother	ln_AJC	Family Integration (simple sum)	Social Support (simple sum)	Medical Situation (simple sum)
1	1	3.961	1.000	.01	.02	.01	.01	.02				
	2	.474	2.891	.00	.09	.07	.00	.69				
	3	.335	3.440	.02	.46	.32	.01	.00				
	4	.162	4.939	.08	.34	.27	.36	.26				
	5	.068	7.612	.89	.09	.33	.62	.03				
2	1	4.377	1.000	.00	.01	.01	.01	.01	.01			
	2	.642	2.610	.00	.11	.00	.01	.01	.65			
	3	.459	3.087	.00	.02	.09	.00	.71	.07			
	4	.296	3.844	.02	.38	.37	.01	.03	.20			
	5	.157	5.275	.09	.41	.20	.39	.21	.05			
	6	.067	8.064	.89	.07	.32	.59	.03	.02			
3	1	7.050	1.000	.00	.00	.00	.00	.01	.00	.00	.00	.00
	2	.648	3.297	.00	.09	.00	.00	.01	.60	.00	.00	.00
	3	.463	3.900	.00	.04	.09	.00	.62	.07	.00	.00	.00
	4	.376	4.329	.00	.36	.03	.02	.07	.13	.00	.01	.02
	5	.230	5.532	.00	.01	.69	.02	.28	.01	.00	.01	.02
	6	.125	7.497	.00	.47	.01	.72	.02	.02	.00	.00	.03
	7	.052	11.676	.02	.00	.01	.01	.01	.07	.00	.68	.42
	8	.040	13.266	.35	.00	.10	.10	.00	.06	.07	.07	.44
	9	.014	22.307	.62	.02	.06	.13	.01	.04	.92	.21	.08

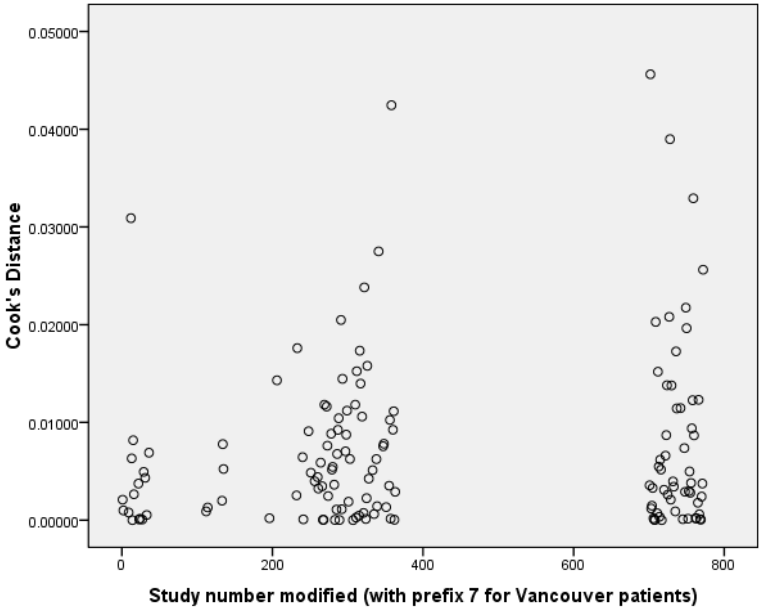
a. Dependent Variable: ln_pain_0

Collinearity diagnosis

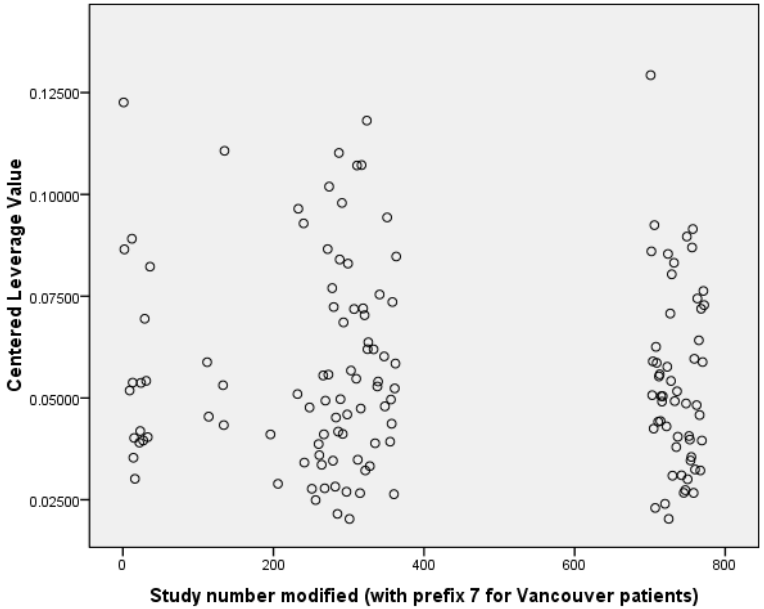
APPENDIX 9

MLRA – Exploratory analysis (Baseline Cohort): parental coping

Cook's distance



Leverage value



APPENDIX 9 (cont.)

MLRA – Exploratory analysis (Baseline Cohort): parental coping

DFBETA (duration)

Extreme Values

			Case Number	Value
DFBETA Duration_Dis_YR	Highest	1	9	.01128
		2	104	.01115
		3	152	.00875
		4	129	.00854
		5	169	.00792
	Lowest	1	70	-.00887
		2	83	-.00819
		3	72	-.00818
		4	153	-.00708
		5	108	-.00629

DFBETA (gender)

Extreme Values

			Case Number	Value
DFBETA sex	Highest	1	86	.06344
		2	182	.05829
		3	144	.05212
		4	87	.04757
		5	141	.04533
	Lowest	1	160	-.05686
		2	9	-.05552
		3	146	-.04781
		4	42	-.04516
		5	54	-.04418

DFBETA (age)

Extreme Values

			Case Number	Value
DFBETA agedob	Highest	1	182	.00856
		2	122	.00518
		3	135	.00511
		4	83	.00421
		5	21	.00402
	Lowest	1	9	-.01025
		2	116	-.00973
		3	129	-.00761
		4	36	-.00712
		5	143	-.00554

DFBETA (JIA category)

Extreme Values

			Case Number	Value
DFBETA dx2_oligo	Highest	1	116	.07376
		2	141	.05170
		3	168	.04396
		4	86	.04270
		5	50	.03540
	Lowest	1	81	-.04473
		2	152	-.04264
		3	83	-.04235
		4	34	-.03876
		5	88	-.03744

DFBETA (ln AJC)

Extreme Values

			Case Number	Value
DFBETA ln_AJC	Highest	1	9	.03450
		2	129	.02964
		3	36	.02939
		4	81	.02484
		5	56	.02386
	Lowest	1	122	-.07884
		2	144	-.05183
		3	68	-.03365
		4	160	-.02831
		5	116	-.02471

DFBETA (family integration)

Extreme Values

			Case Number	Value
DFBETA total_Fam_Integ	Highest	1	182	.00528
		2	122	.00496
		3	34	.00368
		4	140	.00313
		5	87	.00305
	Lowest	1	116	-.00590
		2	9	-.00579
		3	70	-.00499
		4	67	-.00402
		5	143	-.00339

APPENDIX 9 (cont.)

MLRA – Exploratory analysis (Baseline Cohort): parental coping

DFBETA (social support)

Extreme Values

			Case Number	Value
DFBETA total_Soc_Sup	Highest	1	9	.00319
		2	95	.00314
		3	81	.00286
		4	132	.00278
		5	70	.00223
	Lowest	1	159	-.00328
		2	87	-.00321
		3	75	-.00249
		4	122	-.00246
		5	182	-.00209

DFBETA (medical situation)

Extreme Values

			Case Number	Value
DFBETA total_Med_Sit	Highest	1	169	.00825
		2	143	.00617
		3	116	.00518
		4	155	.00472
		5	146	.00457
	Lowest	1	132	-.00524
		2	36	-.00504
		3	167	-.00502
		4	40	-.00419
		5	56	-.00418

APPENDIX 9 (cont.)

MLRA – Exploratory analysis (Baseline Cohort): parental coping

Collinearity Diagnostics[a]

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions								
				(Constant)	Duration of Disease (in years)	Sex: 0=M,1=F	Age (in yrs) calculated from DOB	dx2_ oligovsother	ln_AJC	Family Integration (simple sum)	Social Support (simple sum)	Medical Situation (simple sum)
1	1	3.931	1.000	.01	.02	.01	.01	.02				
	2	.492	2.827	.00	.03	.22	.00	.45				
	3	.359	3.308	.01	.61	.22	.00	.05				
	4	.151	5.095	.11	.29	.29	.30	.47				
	5	.066	7.727	.87	.06	.25	.69	.01				
2	1	4.377	1.000	.00	.01	.01	.01	.01	.01			
	2	.663	2.569	.00	.09	.06	.00	.06	.47			
	3	.434	3.177	.00	.07	.29	.01	.27	.17			
	4	.313	3.742	.01	.45	.12	.00	.29	.30			
	5	.149	5.421	.11	.32	.27	.32	.36	.03			
	6	.065	8.189	.87	.05	.26	.66	.01	.01			
3	1	7.073	1.000	.00	.00	.00	.00	.00	.00	.00	.00	.00
	2	.669	3.253	.00	.07	.05	.00	.07	.47	.00	.00	.00
	3	.437	4.022	.00	.11	.24	.01	.26	.12	.00	.00	.00
	4	.362	4.418	.00	.45	.00	.00	.09	.31	.00	.01	.01
	5	.232	5.521	.00	.00	.52	.00	.51	.01	.01	.02	.03
	6	.118	7.740	.00	.33	.00	.68	.07	.00	.00	.00	.07
	7	.051	11.803	.14	.00	.03	.00	.00	.07	.01	.70	.08
	8	.045	12.571	.16	.01	.05	.22	.00	.00	.05	.04	.74
	9	.013	23.480	.69	.01	.10	.07	.00	.01	.93	.23	.07

a. Dependent Variable: ln_pain_0

Collinearity diagnosis