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**EARLY SELF-REPORTED PAIN IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) IS
RELATED TO LONG-TERM OUTCOMES. RESULTS FROM THE NORDIC JIA COHORT
STUDY.**

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ABSTRACT

Objective. To study self-reported pain early in the disease course of juvenile idiopathic arthritis (JIA) as predictor of long-term disease outcomes.

Methods. Consecutive cases of JIA with disease onset 1997-2000 from defined geographical areas of Norway, Sweden, Finland and Denmark were prospectively enrolled in this population-based cohort study. Self-reported, disease-related pain was measured on a 10 cm visual analogue scale (VAS pain). Inclusion criteria were a baseline visit with pain score six months after disease onset, followed by an eight-year study visit. Remission was defined according to Wallace preliminary criteria. Functional disability was measured by Childhood Health Assessment Questionnaire (CHAQ) and Child Health

Questionnaire (CHQ-PF50) if age <18 and Health Assessment Questionnaire (HAQ) if age ≥18 years.

Damage was scored using the Juvenile Arthritis Damage Index (JADI).

Results. The final study cohort consisted of 243 participants, and 120 (49%) had oligoarticular onset.

At baseline 76% reported VAS pain >0 compared to 57% at eight-year. Half of those who reported baseline pain also reported pain at eight-year, but at a lower intensity. Compared to no pain, higher pain intensity at baseline predicted more pain at eight-year, more functional disability, more damage and less remission off medication. Baseline pain predicted more use of DMARDs/biologics during the disease course. Participants with oligoarticular JIA reporting pain at baseline were more likely to develop extended oligoarticular or other unfavorable JIA categories.

Conclusion. Early self-reported, disease-related pain among children and adolescents with JIA is common and seems to predict persistent pain and unfavorable long-term disease outcomes.

SIGNIFICANCE AND INNOVATIONS

Pain is a frequent complaint, tends to persist, and affects health-related quality of life for children and adolescents with juvenile idiopathic arthritis (JIA).

In this study, we show for the first time that early pain report is associated to long-term non-remission, functional impairment, more use of DMARDs/biologics, and for those with oligoarticular JIA, development into extended disease.

The study adds to the increasing amount of evidence establishing the importance of pain assessment in routine care of children and adolescents with JIA.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a diverse chronic disease with onset before 16 years of age. This most common rheumatic disease among children is characterized by at least six weeks of continuous arthritis in one or more joints of unknown cause (1). The incidence rate in the Nordic countries is reported to be about 15-22/100.000 children (2-4). JIA is a heterogeneous disorder classified into seven categories based on defined criteria occurring during the first six months after disease onset (5). Among the different categories, and within each category, the disease course and outcome differ markedly (6). Persistent oligoarticular JIA has the best prognosis of all JIA categories (7). Extended oligoarticular JIA has a more unfavorable outcome, similar to polyarticular disease (8, 9). Predicting outcome is challenging, and several studies have focused on associations between long-term outcome and clinical characteristics and biomarkers, such as the nature of joint involvement, the intensity of acute-phase response and the existence of autoantibodies and genetic variables (10). As none of those predictors are perfect, and in order to tailor treatment to reach the target of clinical remission, there is a need for more prospective longitudinal studies to evaluate early predictors using validated and multidimensional measures (10). More patient-centered measurements have been demanded for assessment of the course and outcome of JIA (11). Among the six core variables endorsed by the American College of Rheumatology (ACR) (12), only the parent/patient assessment of overall well-being can be defined as a patient-reported measure. Patients, parents and clinicians have pointed to more specific quality of life measures, and especially pain, as important measures when evaluating the course and outcome of JIA (11).

Pain is a frequent complaint among children and adolescents with JIA (13, 14). Pain perception is highly subjective and different self-reported measures are used to detect pain frequency and intensity (15, 16). Pain assessment in young children is especially challenging because pain reports are dependent on the parents' assumption of their child's pain (17). There are both unidimensional and multidimensional tools available for parent and child/adolescent assessment of pain in JIA (16). Among the unidimensional tools, the visual analogue scale (VAS) is a commonly used and validated

scoring instrument (18, 19). The pathogenesis of pain in children and adolescents with JIA is multifactorial, including both biological and psychosocial factors (16, 20). Pain is a distressing symptom, and several studies have elucidated the relationship between pain, functional disability and health-related quality of life (21-24), but information about pain, as a predictor of long-term disease outcome is lacking.

In our Nordic population-based JIA cohort with comprehensive and prospectively sampled data, we have previously studied different aspects of JIA (2, 8). In this project, we aimed to study self-reported pain early in the disease course and the association to long-term disease outcomes.

PATIENTS AND METHODS

Patients. The Nordic JIA cohort is a population-based cohort study. Consecutive cases of newly diagnosed JIA from defined geographical areas of Norway, Sweden, Finland and Denmark with disease onset from January 1, 1997, to June 30, 2000, were prospectively included. Disease onset was defined as the day the child fulfilled the criteria for active arthritis according to information given by the parents/patient or by a physician. Participants were included consecutively and as soon as possible after the diagnosis was determined. However, the first extensive baseline visit was scheduled to six months after disease onset. This time point was chosen to enable classification of the disease into a JIA category, according to the International League Against Rheumatism (ILAR) Edmonton criteria (5). We have no registration of onset symptoms in the database. Detailed description of data collection and patient enrollment has previously been published (2, 8). In the present study participants were included if they had at least a baseline visit six months after disease onset with available pain scores, and participation in the eight-year follow-up visit. At both visits, we had data from clinical examinations, disease activity measures, previous and ongoing medication, damage and remission status, as well as results from blood tests. Health-related quality of life was reported by the children or by their parents.

Measures. Self-reported, disease-related pain intensity during the previous week was measured on a 10 cm visual analogue scale (VAS pain) (0 = no pain and 10 = worst possible pain) by the children if age ≥ 9 years or by the parents if younger. VAS pain was assessed with the question; “How do you rate your/your child’s pain due to your/his or her illness in the past week?” As in previous studies on pain in JIA, pain analyses were explored both by categorization of VAS pain into =0, >0-3, >3-7 and >7-10, and dichotomized into =0 (no pain) or >0 (15, 24-26). We performed sub-analyses on VAS pain scores in participants <9 years and ≥ 9 years to look for any discrepancies between parent- and patient-reported pain (27). Self-reported physical disability questionnaires were the disease-specific and validated Childhood Health Assessment Questionnaire (CHAQ) (0 = no difficulty and 3 = unable to do) if age <18 years (28, 29), and the Health Assessment Questionnaire (HAQ) (0 = no difficulty and 3 = unable to do) if age ≥ 18 years (30). Children ≥ 9 years filled in the CHAQ and for those <9 years, parents filled in. For children <18 years, the parent form of the generic health-related quality of life instrument, the Child Health Questionnaire (CHQ-PF50), was answered by the parents, yielding a physical summary score (PhS) and a psychosocial summary score (PsS) (0-100, 0 = worst, mean 50, SD ± 10) (28, 31, 32). This instrument is designed to capture the child’s physical and psychosocial well-being independent of his/her disease and it is comparable to norm scores from the general U.S. population. For the remainder of the paper CHQ refers to CHQ-PF50. Damage was scored by experienced pediatric rheumatologists using the Juvenile Arthritis Damage Index (JADI) assessment of articular damage (JADI-A) (scale 0–72, 0 = no damage) and extraarticular damage (JADI-E) (scale 0-17, 0 = no damage) (8, 32). Damage was defined as either JADI-A and/or JADI-E >0. As in previous studies, CHAQ/HAQ and JADI were dichotomized into 0 (no disability, no damage) or >0 (8, 24, 33). Physical and psychosocial summary scores of CHQ were dichotomized into <40 (poor health) or ≥ 40 (better health) (28, 31). Remission was defined according to the preliminary criteria described by Wallace et al. (34). Remission status was dichotomized into Remission off medication or Not in remission off medication (33). The latter included; Active disease, Inactive disease not yet in remission and in Remission on medication.

Ethical issues. Medical research ethical committees from each participating country gave their approval according to national practice and regulations in accordance with the Declaration of Helsinki. Written informed consent was obtained from children ≥ 16 years and if aged < 16 years, from their parents.

Statistical analysis. We used descriptive statistics with median and interquartile ranges (IQR) for continuous variables, and absolute frequency, percentage with 95% confidence interval (CI) for categorical variables. To evaluate the predictive value of pain at baseline for outcome measures after eight years and medication during the disease course, model-based absolute risks were estimated after binominal regression using the post-estimation command `lincom` in STATA. Sex adjustment was weighted 0.7 for girls to mimic the distribution in the population. In additional analyses, we also adjusted for age. To estimate absolute risks, we used the mean age at onset of 6.8 years. We used logistic regression to estimate odds ratio (OR) with 95% CI using VAS pain as a continuous variable. In further analyses, we made receiver operator characteristic (ROC) curves based on measures of sensitivity and specificity. The area under the curve (AUC) was calculated with 95% CI, and with the following interpretations; an area of 0.5 or lower were considered as no discrimination, ≥ 0.7 to < 0.8 as acceptable discrimination, ≥ 0.8 to < 0.9 as excellent discrimination, ≥ 0.9 as outstanding discrimination (35). Statistical analyses were carried out using STATA version 14, software (STATA Corp., College Station, Texas, USA).

RESULTS

Clinical characteristics of the study group

Of the 500 patients included from the four Nordic countries, 440 participated in the eight-year follow-up. Due to lack of baseline pain scores, all Finnish participants ($n = 138$) and additional 59 participants from the other countries were excluded. The final study population consisted of 243 children (Figure

1) with a median baseline visit of seven and a final follow-up visit of 97 months (Table 1). Among these, 70% were female, 49% had oligoarticular disease, median age was 6.3 years at onset and 14.9 years at follow-up (Table 1). The diagnostic delay was short, median interval between disease onset and diagnosis of arthritis by a physician was 50.5 days, interquartile range (IQR) 14-101 days. Of these 243 participants, intraarticular corticosteroid injections had been given to 91, and for 34 of these within the last three months of the baseline visit (results not shown). At this baseline visit, none of the participants used biologics, but 20 used systemic steroids. Methotrexate was used by 31 of the participants, and of those 8 had cumulative doses ≥ 100 mg. The 60 participants that did not participate in the eight-year study did not differ significantly in the proportion of oligoarticular JIA or with respect to sex, and had a median follow-up of 47 months (range 5-83 months). At their last registered visit, 30 (50%) had a pain assessment, including 21 with VAS pain >0 and nine with VAS pain $=0$. Participants excluded from the present study due to lack of pain data at baseline had lower median age (5.1 versus 6.3 years) and the proportion of boys was slightly higher (39% versus 30%). There was no difference in the proportion of oligoarticular JIA at onset and remission status at eight years between the included and excluded participants.

Pain scores

More participants reported VAS pain >0 at the baseline visit (76%) than at eight years (57%). The mean pain intensity score (VAS pain) of those reporting pain were higher at baseline, 3.0 (95% CI 2.6-3.3) than at eight years, 2.4 (95% CI 2.0-2.8). The distribution of pain intensity scores at the baseline visit and at the eight-year follow-up is shown in Supplementary Figure 1. For participants <9 years at baseline, 118 of 159 (74%) had a parent-reported pain score >0 with a mean intensity of 2.7 (95% CI 2.3-3.0), while 67 of 84 (79%) participants ≥ 9 years had a patient-reported pain score >0 , mean intensity of 3.5 (95% CI 2.9-4.1). Among participants with pain measures both at baseline and eight years ($n=204$), 50% reported VAS pain >0 at both visits, and 19% reported no pain at both visits (Figure 2). We divided this group into participants <9 and ≥ 9 years at baseline. Participants <9

years had parent-reported pain scores at their first visit and patient-reported pain scores at their last visit, and 48% reported VAS pain >0 at both visits. Participants ≥ 9 years had only patient-reported pain scores, and 55% reported VAS pain >0 at both visits (results not shown).

Baseline pain scores and long-term outcome measures

The association between baseline pain scores subdivided into four categories of pain intensity, and long-term outcome measures are shown in Table 2. Participants reporting VAS pain >0 at the baseline visit, more frequently reported pain and functional disability (CHAQ/HAQ >0) at the eight-year follow-up. A distinct dose-response was observed with increasing pain intensity at baseline. Using VAS pain as a continuous variable, we observed increased odds ratio for the different long-term outcomes. Functional disability as presented by CHQ PhS, demonstrated similar results. Participants reporting pain at baseline, more frequently were not in remission off medication at follow-up, compared to those reporting no baseline pain. A similar association between increasing pain intensity at baseline and long-term remission status was observed, but the dose-response relationship tended to level out at the most extreme pain intensities. Participants reporting no pain at baseline, rarely reported pain (28%) and functional disability (18%) at eight years, and 74% were in remission off medication. In all analyses, we adjusted for sex, and additional adjustment for age did not change the results. Similar to the results on long-term remission, pain and functional disability, baseline pain was associated with the use of DMARDs and biologics during the eight-year disease course (Supplementary Table 1). In contrast to the other eight-year outcome measures, psychosocial health assessed with CHQ PsS, did not show association to baseline pain score (results not shown). The predictive ability of baseline pain was also analyzed using receiver operator characteristic (ROC) curves, giving acceptable discrimination between early pain scores and long-term outcomes of pain, functional

disability and not being in remission at eight years, but no clear discrimination was observed for long-term damage (Figure 3).

Baseline pain scores and long-term outcomes in the oligoarticular category

Among participants with oligoarticular JIA reporting VAS pain >0 at the baseline visit, 48% (95% CI 38-60%) developed extended oligoarticular disease or other JIA categories during the course of the disease compared to 30% (95% CI 16-44%) of those reporting no pain (Table 3). Also, a higher proportion of participants with VAS pain >0 at baseline, was not in remission off medication, 65% (95% CI 55-76%), and reported pain, 61% (95% CI 50-73%) at eight years, compared to those reporting no pain at baseline. In contrast, 70% (95% CI 56-84%) of those reporting no pain at baseline remained in the persistent oligoarticular JIA category at the eight-year follow-up. The associations were strengthened using VAS pain as a continuous variable. In all analyses, we adjusted for sex, and additional adjustment for age did not change the results.

DISCUSSION

Among participants in the population-based Nordic JIA study, a higher proportion reported disease-specific pain seven months after disease onset, and the pain was of higher intensity compared to the eight-year follow-up. Half of the participants reporting pain at baseline also reported pain at eight years. Self-reported pain early in the disease course predicted more pain, more functional disability, more damage, more use of DMARDs/biologics, and more long-term disease activity at eight years. In addition, participants with oligoarticular JIA and VAS pain >0 at baseline, more often developed an extended disease or other unfavorable JIA categories.

The strength of our study is the longitudinal and population-based design, a robust international cohort, and the use of validated and multidimensional outcome measures. The novelty in looking at associations between early pain report and long-term remission status, medication, and development into more unfavorable disease categories, is also a major strength. Some limitations must be recognized. The exclusion of all the Finnish participants reduced the number of study participants, but did not change the population-based design of the study. The missing early pain scores from the other countries might have skewed the remaining cohort, but the distribution of JIA categories and the remission status were comparable among those with or without early pain scores. Even though the VAS pain instrument is disease-specific, we cannot rule out that other musculoskeletal co-conditions, such as generalized joint hypermobility, specific onset symptoms or differences in timing of diagnosis, might have influenced the child's/parent's pain rating. However, this is a challenge to all pain research. Since pain is a subjective descriptor, our cohort is close to population-based, and trained pediatric rheumatologists ascertained the JIA diagnosis, we do not think that this will seriously disturb the interpretation of our results. Similarly, we cannot ascertain the nature of "bodily pain" the participants scored when filling out this question in the CHQ questionnaire. However, we only used this question in accordance with the CHQ instructions, as one of many items describing a summary of physical function, and not as a pain measure. Parents reporting their child's pain for children <9 years constituted a majority of pain reports at the baseline visit, but a small minority at the eight-year follow-up. We cannot rule out some element of parent/child discordance, although the sub-analyses on pain-reports according to age at baseline seem to indicate that this was not a major problem. This is in accordance with a study from 2006, showing moderate agreement between parent's and child's pain rating (17). Our results are not directly comparable, because the parent/child pain reports are not from the same visit. The early pain scores from the baseline study visit seven months after disease onset, were given by participants both off and on medication, but only few had started disease-modifying anti-rheumatic drugs (DMARDs).

Consistent with previous research, we found pain as a frequent complaint among the participants in our study cohort (14, 16, 36). We found a reduction in number of participants reporting pain from baseline (76%) to the eight-year follow-up (57%). A quite similar reduction was found by Lovell et al in 1989 demonstrating pain frequency of 60% at baseline, 50% at one-year follow-up and 40% at five-year follow-up (37). In a recent 30-year follow-up study of JIA in Norway, 66% of the participants reported pain of some degree (24).

In accordance with other studies, the intensity of pain was mainly in the mild to moderate range (19, 37, 38). Our results on early pain intensity with mean VAS pain 3.0 are consistent with a recent cross-sectional study in children and adolescents with JIA from southeastern region of the United States, showing mean VAS pain of 2.6 (13). Our results on pain intensity at the eight-year follow-up appear to be lower compared to other studies (14, 39). These studies are, however, skewed to the severe end of the spectrum of JIA, whereas our population-based study included the full disease spectrum. Also, to compare studies on pain, age and disease duration must be taken into account.

Even in the biologic era with generally good disease control, persistent pain during the course of the disease remains a concern (26, 40, 41). Half of our participants reporting pain seven months after disease onset also reported pain at the eight-year follow-up, indicating high pain persistency. This is in agreement with other studies showing that a significant number of children and adolescents with JIA continue to report pain during the course of disease and into adulthood (14, 24, 42). It is of notice that the proportion of pain persistence is fairly similar whether the parents report their child's pain, or the pain was self-reported at baseline. Pain persistence despite seemingly good treatment response, supports theories that the causes of pain are multifactorial (41, 43). Both psychosocial and biologic factors contribute to these children's subjective experience of pain (38, 44, 45).

Pain as a predictor of unfavorable health-related quality of life in children with JIA is widely studied (21, 23, 46, 47). In a multinational quality of life study from the Pediatric Rheumatology International Trials Organization (PRINTO), pain was found to be a predictor of psychosocial well-being (21). In agreement with our study, previous studies have concluded that pain at presentation was a strong predictor of persistent pain (42, 48). In accordance with our results, pain as a predictor of functional disability was also found in a small cross-sectional study from the United States (49). Except for health-related quality of life outcomes and functional disability, studies that specifically address pain as predictor of other long-term outcomes, such as remission, damage, medication, and changing of JIA categories, are lacking. Our results demonstrate for the first time, that early pain is associated with not achieving remission off medication in a long-term perspective. We also demonstrate, for the first time, that early pain reports predict a higher risk of development into extended oligoarticular or other unfavorable JIA categories during the course of the disease. This suggests that early pain may be an indicator of subclinical disease activity or a marker of a more severe disease category. This is also supported by the fact that a higher proportion of participants with early pain report used DMARDs/biologics during the course of the disease.

Even though pain assessment has been highlighted as a quality measure of pediatric arthritis care (50), pain scores are infrequently used as guiding tools in daily care of these patients (41). Our results demonstrate that pain complaints in children with JIA at an early stage in their disease should be taken seriously, not just to relieve ongoing discomfort, but probably also as a sign of ongoing clinical or subclinical disease activity. This emphasizes the importance of pain assessment in routine care of children and adolescents with JIA. In a Canadian study where patients, parents and clinicians were asked what matters most in the care of JIA, pain was one of the five most important factors (11). The active joint count was the only one of these five factors that is included in the pediatric version of the American College of Rheumatology (ACR) core variables for clinical care in children with JIA (12). The association between early pain reports and long-term unfavorable outcome adds to the discussion on the validity of the ACR core variables, and whether pain should be included in these variables.

In conclusion, early self-reported pain in JIA is common, tends to persist, and seems to predict unfavorable long-term disease outcome in several outcome dimensions.

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FIGURE LEGENDS

Figure 1. Flow-chart of the study population. F = female. M = male.

Figure 2. Venn diagram demonstrating pain persistency in the Nordic JIA study cohort. The cohort included 204 participants with pain measures seven months after disease onset and at the eight-year follow-up. Disease-related pain was measured on a 10 cm visual analogue scale (VAS pain) (0 = no pain and 10 = worst possible pain). Continuous circle represents VAS pain >0 at seven months and dashed circle represents VAS pain >0 at eight years.

Figure 3. Receiver operator characteristic (ROC) curves in the Nordic JIA study cohort for different disease outcomes after eight years compared to self-reported disease-related pain (VAS pain) at seven months. Pain was measured on a 10 cm visual analogue scale (VAS pain) (0 = no pain and 10 = worst

possible pain). Remission was defined according to the preliminary criteria described by Wallace et al. (34). Functional disability was measured with Childhood Health Assessment Questionnaire/ Health Assessment Questionnaire (CHAQ/HAQ). Damage was measured with the Juvenile Arthritis Damage Index (JADI), articular and extraarticular. The area under the curve (AUC) values were 0.74 (95% CI 0.67-0.80) for persistent pain, 0.68 (95% CI 0.61-0.75) for not being in remission, 0.71 (95% CI 0.64-0.79) for functional disability and 0.58 (95% CI 0.50-0.67) for joint damage.

Table 1. Clinical characteristics of the juvenile idiopathic arthritis (JIA) study population

Characteristics	Total no. assessed	n (%)
Female sex	243	170 (70)
Oligoarticular JIA at onset	243	120 (49)
Median age at disease onset, years	243	6.3 (2.9-10.3) ^a
Median age at the 8-year follow-up, years	243	14.9 (11.1-18.5) ^a
Disease duration at the baseline visit, months	243	7 (6-9) ^a
Disease duration at the 8-year follow-up, months	243	97 (95-102) ^a
VAS pain ^b >0 at the baseline visit	243	185 (76)
VAS pain ^b >0 at the 8-year follow-up	204	117 (57)

CHAQ/HAQ >0 at the 8-year follow-up	207	80 (39)
CHQ PhS <40 at the 8-year follow-up	132	25 (19)
CHQ PsS <40 at the 8-year follow-up	132	7 (5)
JADI >0 at the 8-year follow-up	203	46 (23)
Not in remission ^c at the 8-year follow-up	236	135 (57)

CHAQ = Childhood Health Assessment Questionnaire, age <18 years; HAQ = Health Assessment Questionnaire, age ≥18 years; CHQ PhS = Child Health Questionnaire physical summary score (0-100); CHQ PsS = Child Health Questionnaire psychosocial summary score (0-100); JADI = Juvenile Arthritis Damage Index assessment of articular damage (JADI-A) and extraarticular damage (JADI-E)

^aInterquartile range

^bSelf-reported pain was measured on a 10 cm visual analogue scale (VAS pain)

^cNot in remission off medication according to the definition by Wallace et al. (34)

Table 2. Association between baseline pain report and long-term outcomes in juvenile idiopathic arthritis (JIA)

Pain scores seven months after disease onset	Clinical characteristics at the eight-year follow-up				
	VAS pain ^a >0	CHAQ/HAQ >0	CHQ PhS <40	JADI >0	Not in remission ^b
VAS pain ^a =0					
n/total	15/54	9/54	3/32	4/53	14/55
% (95% CI) ^c	28 (16-40)	18 (8-28)	11 (1-21)	8 (1-15)	26 (14-37)
VAS pain ^a >0-3					
n/total	53/86	31/86	8/62	25/83	61/95
% (95% CI) ^c	62 (51-72)	35 (25-45)	12 (4-21)	30 (20-40)	64 (54-74)
VAS pain ^a >3-7					
n/total	44/58	34/60	14/38	15/60	52/73
% (95% CI) ^c	74 (63-85)	56 (44-69)	37 (22-52)	25 (14-36)	71 (61-81)
VAS pain ^a >7-10					
n/total	5/6	6/7	0	2/7	8/13
% (95% CI) ^c	90 (66-114)	94 (80-107)	0	28 (-5-61)	61 (35-88)
VAS pain ^a continuous ^d					
OR (95% CI) ^c	1.5 (1.2-1.7)	1.4 (1.2-1.6)	1.4 (1.1-1.7)	1.1 (0.9-1.2)	1.2 (1.1-1.4)

CHAQ = Childhood Health Assessment Questionnaire, age <18 years; HAQ = Health Assessment

Questionnaire, age ≥18 years; CHQ PhS = Child Health Questionnaire physical summary score (0-100); JADI =

Juvenile Arthritis Damage Index assessment of articular damage (JADI-A) and extraarticular damage (JADI-E);

OR = Odds ratio; CI = Confidence interval

^aSelf-reported pain was measured on a 10 cm visual analogue scale (VAS pain)

^bNot in remission off medication according to the definition by Wallace et al. (34)

^cAdjusted for sex, weighted 0.7 for girls

^dAnalyzed with VAS pain as a continuous variable

Table 3. Association between baseline pain report and long-term outcomes in juvenile idiopathic arthritis (JIA) with oligoarticular onset

Pain scores seven months after disease onset	Clinical characteristics at the eight-year follow-up				
	Extend. Oligo./others ^a	VAS pain ^d >0	CHAQ/HAQ >0	JADI >0	Not in remission ^e
VAS pain ^d =0					
n/total	12 ^b /40	10/37	7/37	3/36	11/38
% (95% CI) ^f	30 (16-44)	26 (12-40)	16 (7-26)	7 (0-15)	29 (14-43)
VAS pain ^d >0					
n/total	39 ^c /80	40/65	26/66	19/65	51/78
% (95% CI) ^f	48 (38-60)	61 (50-73)	39 (28-51)	29 (18-40)	65 (55-76)
VAS pain ^d continuous ^g					
OR (95% CI) ^f	1.3 (1.1-1.6)	1.4 (1.1-1.8)	1.4 (1.1-1.8)	1.0 (0.8-1.3)	1.3 (1.0-1.5)

Extend. Oligo. = Extended oligoarticular JIA; CHAQ = Childhood Health Assessment Questionnaire, age <18 years; HAQ = Health Assessment Questionnaire, age ≥18 years; JADI global = Juvenile Arthritis Damage Index assessment of articular damage (JADI-A) and extraarticular damage (JADI-E); Not in remission = Not in remission off medication; OR = Odds ratio; CI = Confidence interval

^aOligoarticular JIA at six months changed to either extended oligoarticular or other JIA categories at the eight-year follow-up

^bOthers were one with enthesitis-associated arthritis and two with undifferentiated arthritis

^cOthers were two with psoriatic arthritis, six with enthesitis-associated arthritis and two with undifferentiated arthritis

^dSelf-reported pain was measured on a 10 cm visual analogue scale (VAS pain)

^eAccording to the definition by Wallace et al. (34)

^fAdjusted for sex, weighted 0.7 for girls

^gAnalyzed with VAS pain as a continuous variable