Early Disease Course and Predictors of Disability in Juvenile Rheumatoid Arthritis and Juvenile Spondyloarthritis: A 3 Year Prospective Study

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ABSTRACT. Objective. To describe the 3 year disease course in early juvenile rheumatoid arthritis (JRA) and juvenile spondyloarthritis (JSpA), to compare the health status after 3 years of followup with that of normal controls, and to investigate the relationship between physical function at followup and disease characteristics recorded during the first 6 months.

Methods: One hundred and ninety-seven children (median age 6.6 yrs) with JRA and JSpA and disease duration <1.5 years were examined by a pediatric rheumatologist every 6 months for a median of 3.1 years. Controls were randomly selected from the National Population Register. Physical and psychosocial health was assessed by means of the Child Health Questionnaire and the Childhood Health Assessment Questionnaire (CHAQ). Disease course was analyzed by analysis of variance for repeated measurements.

Results. Health status and disease activity improved over time. Treatment with disease modifying antirheumatic drugs was started in 58% of the patients at baseline. Patients with persistent oligoarthritis had the most favorable disease course. The patients with juvenile ankylosing spondylitis (JAS), syndrome of seronegative enthesopathy and arthropathy (SEA), and rheumatoid factor (RF) positive polyarthritis had the poorest health status. A significant improvement for the whole group was observed after 3 years in all measures of disease activity and health status, except pain. Patients had poorer physical function and general health and more pain than controls. Predictors of reduced physical function at followup were a high CHAQ disability index and a poor well-being assessed during the first 6 months.

Conclusion. Health status and disease activity improved over time in patients under medical treatment. The patients with JAS/SEA and RF positive polyarthritis had poorer health than the patients in other subtypes. A high disability index and a poor well-being at baseline predicted reduced physical function after 3 years. (J Rheumatol 2005;32:1122–30)

Key Indexing Terms:
JUVENILE RHEUMATOID ARTHRITIS
DISABILITY
PROGNOSIS
DISEASE PROGRESSION
RISK FACTORS

Juvenile rheumatoid arthritis (JRA) and juvenile spondyloarthritis (JSpA) are a potential cause of disability among children. Medical regimes that are effective in treating childhood arthritis have recently been developed1–5, but treatment must be started at an early stage of disease to be effective in preventing joint damage and loss of physical function6. Thus it is important to recognize at an early stage patients who will develop severe disease.

Studies have shown that about 40% of children with JRA and JSpA develop functional disability after 10-15 years6,7. Not much is known about the development of disability during the first years of the disease. Most of the studies are retrospective outcome studies, which focus on an endpoint for a given measure at the time of followup. There are currently few prospective studies and none of them include serial measurements over time, which would measure the clinical course of the disease and reveal the disease process leading to the outcome at followup. Repeated measurements can also increase the predictive ability of a variable8.

Further, to our knowledge, health status in early JRA and JSpA has not been compared with that of the general population.

We therefore conducted a prospective study of the course of JRA and JSpA based on repeated assessments every 6 months during a 3 year followup. The aims were to describe the early disease course as measured by internationally standardized and accepted instruments in children with JRA and JSpA, to identify predictors of 3 year functional outcome among disease variables measured during the first 6 months of followup, and to compare the physical and psychosocial short-term outcome in JRA and JSpA with controls from the normal Norwegian population.
MATERIALS AND METHODS

Patients and controls. Two hundred and twenty-seven patients with JRA or JSpA and less than 18 months of disease duration attended the Department of Rheumatology, Rikshospitalet University Hospital, Oslo, from March 1995 to December 1999. One hundred and ninety-seven (87.2%) JRA and JSpA patients [age 1 to 16 yrs (median 6.6), median disease duration of 3.7 mo, 61.4% girls] participated in the study and were examined by a pediatric rheumatologist every 6 months for 3.2 ± 0.4 years.

Thirty (13.3%) out of the 227 patients with JRA or JSpA did not participate. Eighteen parents of these children chose not to participate, 4 parents did not know the Norwegian language well enough, and 8 patients were excluded due to incomplete data. The participants were comparable to the non-participants with regard to age, gender, disease subtype, and disease duration (data not shown).

One hundred and eighty-five patients had JRA according to the American College of Rheumatology criteria and 12 had juvenile spondyloarthropathy (JSpA) [3 with juvenile ankylosing spondylitis (JAS) 10, 4 syndrome of seronegative enthesopathy and arthropathy (SEA) 11, and 5 juvenile psoriatic arthropathy (JPsA) 12]. No patient with JPsA had sacroiliitis. Diseased deviation of 10 in the general US population 16. The PhS and PsS in a population and then dividing these by the standard deviations for the US population (standardization). These standardized concept scores are then weighted according to how much they contribute to the PhS/PsS (using factor score coefficients for each concept score from the same US population) and added together (raw score). The raw score, which is a deviation from a mean of 0, is computed into the final PhS/PsS by multiplying this raw score with 10 (the standard deviation in the US population) and adding this product to 50 (the mean in the US population). We used the parent form of the questionnaire consisting of 50 questions (CHQ-pf50). The 2 questionnaires, which have been translated and culturally adapted to Norwegians 15, 17 were administered to one or both parents of all the children. Parents completed the questionnaires without any help from a health professional.

Clinical and laboratory data. The patients were examined by one of 5 pediatric rheumatologists (BF, DS, OV, GL, or AMS). The clinical examination included registration of number of joints with swelling, tenderness, and limited range of motion, number of active (swelling or both tenderness and limited range of motion) joints, an arthritis severity index 19, 20, morning stiffness (hours), and physician’s global assessment of disease activity (on a 5-point Likert scale, where 1 = inactive, 2 mild, 3 moderate, 4 severe, and 5 very severe). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured by standard methods. Antinuclear antibody (ANA) titer ≥ 32, measured by indirect immunofluorescence using mouse liver sections as substrate, was considered positive. Positive IgM rheumatoid factor (RF) was defined as titer ≥ 64 by the Rose-Waaler test. HLA-B27 was determined by serologic testing 19.

Statistical analyses. Differences between participants and non-participants and between patients and controls were measured by the independent sample t test. The chi-squared test was used for categorical variables. The concept scores general health, bodily pain, and the summary scores (PhS, PsS) from the CHQ were close to normally distributed. We also did a Mann–Whitney test on these variables, which gave the same results as the independent sample t test, but we chose to present the t test. The differences between baseline and 3 year followup were normally distributed and tested by the paired samples t test. One-way analysis of variance (ANOVA) was used to compare patients with active disease, patients in remission, and controls.

To study disease course, we performed an ANOVA for repeated measurements on each of the study variables (CHAQ, PhS, PsS, pain, global assessment of well-being, physician’s global assessment of disease activity, number of active and mobility restricted joints, and ESR as dependent variables). Disease subtype and months of followup (0, 6, 12, 18, 24, 30, 36) were used as fixed factors and identification numbers as random factors (nested to disease subtype). Residuals were normally distributed. Scheffé correction for multiple comparisons was used. The analysis tells if there is a difference in mean estimated level for each subgroup during the 3 years and if there is a change over time for the total patient group. We used ANOVA to examine if each subgroup within each variable improved during the 3 years (corrections for multiple comparisons were not performed).

A multiple linear regression analysis was performed to identify predictors of the CHAQ disability index at 3 year followup (dependent variable). The CHAQ score, parent’s global assessment of child’s well-being, physician’s global assessment of disease activity, number of active and mobility restricted joints and ESR were chosen as possible predictors (independent variables) calculated as the area under the curve (AUC) 20 between baseline and 6 months. These variables were chosen because they have been shown to be the most important factors for defining improvement in juvenile arthritis 21. In addition we included pain. Variables with p value < 0.10 in the univariate analysis were analyzed as possible predictors in the multivariate analysis. Highly intercorrelated independent variables (r > 0.7) were avoided in the analysis. Backward and forward regression methods were used. Residuals were normally distributed. Missing data were replaced with the variable from the previous or the next visit. For all the analyses, p values < 0.05 (2-tailed tests) were considered statistically significant. All statistical analyses were performed by the SPSS software program (SPSS Inc., Chicago, IL, USA) versions 10.0/11.0.
Table 1. Demographic and clinical characteristics of patients with JRA and JSpA (n = 197). * Values refer to the numbers of subjects (%) unless otherwise stated.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>121 (61.4)</td>
</tr>
<tr>
<td>Males</td>
<td>76 (38.6)</td>
</tr>
<tr>
<td>Age at baseline, yrs (SD)</td>
<td>6.9 (4.2)</td>
</tr>
<tr>
<td>Disease subtypes</td>
<td></td>
</tr>
<tr>
<td>Oligoarticular, persistent</td>
<td>95 (48.2)</td>
</tr>
<tr>
<td>Oligoarticular, extended</td>
<td>16 (8.1)</td>
</tr>
<tr>
<td>Polyarticular, RF negative</td>
<td>55 (27.9)</td>
</tr>
<tr>
<td>Polyarticular, RF positive</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Systemic</td>
<td>14 (7.1)</td>
</tr>
<tr>
<td>JAS/SEA</td>
<td>7 (3.6)</td>
</tr>
<tr>
<td>Juvenile psoriatic arthritis</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Disease duration at baseline, mo (SD)</td>
<td>4.7 (6.5)</td>
</tr>
<tr>
<td>HLA-B27-positive</td>
<td>43 (21.9)</td>
</tr>
<tr>
<td>ANA positive</td>
<td>96 (48.7)</td>
</tr>
<tr>
<td>RF positive</td>
<td>8 (4.1)</td>
</tr>
</tbody>
</table>

* Patients with JRA and JSpA and a disease duration < 1.5 years admitted to hospital between March 1995 and December 1999. JAS: juvenile ankylosing spondylitis. SEA: syndrome of seronegative enthesopathy and arthropathy in children.

RESULTS

Demographic and clinical data for the patients are shown in Table 1. The patient group comprised 95 patients (48.2%) with persistent oligoarthritis, 16 patients (8.1%) with extended oligoarthritis, 55 patients (27.9%) with RF negative polyarthritis, 5 patients (2.5%) with RF positive polyarthritis, 14 patients (7.1%) with systemic arthritis, 7 patients with JAS (n = 3)/SEA (n = 4) (3.6%), and 5 patients with persistent oligoarthritis, 16 patients (8.1%) with oligoarticular, extended oligoarthritis, 55 patients (27.9%) with RF negative polyarthritis, 5 patients (2.5%) with RF positive polyarthritis, 5 patients (2.5%) with JPsA. The mean disease duration at baseline was 4.7 ± 6.5 months and the mean symptom duration at baseline was 10.1 ± 9.9 months.

Changes over time in health status and disease activity.

Table 2. Health status and disease activity over 3 years of followup in 197 children with early JRA and JSpA. Values are mean ± SD.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>6 mo</th>
<th>12 mo</th>
<th>18 mo</th>
<th>24 mo</th>
<th>30 mo</th>
<th>36 mo</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAQ (range 0–3)†</td>
<td>0.52 ± 0.58</td>
<td>0.49 ± 0.55</td>
<td>0.44 ± 0.61</td>
<td>0.47 ± 0.60</td>
<td>0.36 ± 0.51</td>
<td>0.33 ± 0.47</td>
<td>0.35 ± 0.51</td>
<td>0.447</td>
</tr>
<tr>
<td>Physical summary score CHQ‡</td>
<td>38.4 ± 15.3</td>
<td>43.0 ± 12.9</td>
<td>46.0 ± 12.0</td>
<td>44.7 ± 11.6</td>
<td>45.7 ± 11.5</td>
<td>46.2 ± 11.9</td>
<td>46.3 ± 12.4</td>
<td>0.016</td>
</tr>
<tr>
<td>Psychosocial summary score CHQ‡</td>
<td>51.1 ± 7.1</td>
<td>49.5 ± 8.9</td>
<td>52.9 ± 6.9</td>
<td>51.8 ± 8.6</td>
<td>54.2 ± 7.0</td>
<td>53.7 ± 6.7</td>
<td>52.8 ± 7.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pain (10 cm VAS)§</td>
<td>2.5 ± 2.4</td>
<td>2.2 ± 2.4</td>
<td>2.3 ± 2.4</td>
<td>2.5 ± 2.4</td>
<td>2.3 ± 2.4</td>
<td>2.3 ± 2.5</td>
<td>2.3 ± 2.5</td>
<td>0.776</td>
</tr>
<tr>
<td>Patient’s global well-being (10 cm VAS)§</td>
<td>2.6 ± 2.3</td>
<td>2.3 ± 2.2</td>
<td>2.2 ± 2.2</td>
<td>2.4 ± 2.3</td>
<td>1.9 ± 2.0</td>
<td>2.0 ± 2.1</td>
<td>2.0 ± 2.2</td>
<td>0.637</td>
</tr>
<tr>
<td>Physician global disease activity (Likert scale 1–5)*</td>
<td>3.0 ± 0.9</td>
<td>2.3 ± 0.9</td>
<td>2.1 ± 0.9</td>
<td>1.9 ± 0.9</td>
<td>1.9 ± 1.0</td>
<td>1.8 ± 0.9</td>
<td>1.8 ± 1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of active joints (range 0–69)</td>
<td>3.1 ± 3.8</td>
<td>2.1 ± 3.4</td>
<td>1.5 ± 2.5</td>
<td>1.3 ± 2.6</td>
<td>1.5 ± 3.5</td>
<td>1.3 ± 2.9</td>
<td>1.3 ± 3.1</td>
<td>0.098</td>
</tr>
<tr>
<td>No. of joints with LOM (range 0–69)</td>
<td>2.3 ± 2.9</td>
<td>1.6 ± 2.2</td>
<td>1.2 ± 1.8</td>
<td>1.2 ± 2.1</td>
<td>1.5 ± 2.8</td>
<td>1.2 ± 2.8</td>
<td>1.2 ± 2.8</td>
<td>0.300</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>26.2 ± 23.7</td>
<td>16.7 ± 14.8</td>
<td>13.4 ± 12.9</td>
<td>13.2 ± 12.5</td>
<td>13.0 ± 12.5</td>
<td>14.5 ± 22.5</td>
<td>11.3 ± 9.4</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Analysis of variance for repeated measurements, time effect. † CHAQ: Childhood Health Assessment Questionnaire, 0 (no disability), 3 (severe disability). ‡ CHQ: Child Health Questionnaire, a score where 50 ± 10 corresponds to the mean value ± SD in the normal population (> 50 better than mean, < 50 worse than mean). § Scores could range from 0 cm (best) to 10 cm (worst). # Scores could range from 1 (best) to 5 (worst). LOM: limitation of motion.
Figure 1. The disease course in the different disease subtypes during 3 years of followup for the variables Child Health Assessment Questionnaire disability index (range 0-3), physical and psychosocial function measured by the Child Health Questionnaire (50 ± 10 corresponds to the mean value ± SD in the normal population), parent’s global assessment of child’s well-being (0–10 cm VAS), pain (0-10 cm VAS), physician’s global assessment of disease activity (Likert scale 1-5), number of active joints (range 0-69), number of joints with limitation of motion (LOM) (range 0-69) and erythrocyte sedimentation rate (range 0-100 mm/h). The x axis represents the number of months in the study. The y axis represents the measurement scale for each variable. JAS: juvenile ankylosing spondylitis. SEA: syndrome of seronegative enthesopathy and arthropathy in children. JPsA: juvenile psoriatic arthritis.

The numbers of active and mobility restricted joints were lowest in patients with persistent oligoarthritis (p ≤ 0.003 vs extended oligoarthritis, RF negative and RF positive polyarthritis, and systemic arthritis but not different from those with JAS/SEA and JPsA). The highest numbers of active and mobility restricted joints were found in RF positive polyarthritis. This number of active joints was significantly higher than in all other subtypes (p < 0.001 vs all). The number of mobility restricted joints in RF positive polyarthritis was significantly higher than in persistent oligoarthritis (p < 0.001, but not different from extended oligoarthritis, RF negative polyarthritis, systemic arthritis, JAS/SEA, and JPsA).

ESR was lowest in patients with persistent oligoarthritis (p < 0.001 vs extended oligoarthritis, RF negative polyarthritis and systemic arthritis, but not significantly different from RF positive polyarthritis, JAS/SEA, and JPsA), and those with systemic arthritis had the highest ESR (p < 0.001 vs all).

Short-term outcome after 3 years. Table 3 shows that in the total group of JRA and JSpA patients there were statistically significant improvements for most disease variables after 3 years of followup compared with baseline. CHAQ disability index was 0.0 (range 0-2.4) in 51.8% (68.4% in persistent oligoarthritis, 37.5% in extended oligoarthritis, 41.8% in RF negative polyarthritis, 40.0% in RF positive polyarthritis, 28.6% in systemic, 0% in JAS/SEA, and 40% in JPsA).

PhS, general health score, and pain score from the generic CHQ at followup were significantly worse in our patient group compared with those of a group of children from the normal population (Table 4). There was no difference in PsS. We divided patients into those with active disease and those in remission. Poor scores in PhS, general health, and pain were mainly found in patients with active disease. The patients in remission had PhS and pain comparable to controls, but a lower general health (Table 4). After 3 years of followup, 53 (26.9%) of the 197 JRA and JSpA patients were in remission. At baseline 93.4% of the patients used nonsteroidal antiinflammatory drugs (NSAID) and 57.9% had started disease modifying antirheumatic drugs (DMARD). After 3 years 47.2% used NSAID and 40.1% used DMARD.

**Predictors of disability.** We performed a regression analysis looking for predictors of CHAQ disability index after 3 years of followup. The CHAQ score, global assessment of well-being, pain, physician’s global assessment of disease activity, number of active and mobility restricted joints, and ESR during the first 6 months were used as independent variables (calculated as AUC between baseline and 6 mo). There was a high correlation between global assessment of well-being and pain (r = 0.815, p < 0.001). We chose to use well-being in the analysis. The CHAQ score and parent’s global assessment of the child’s well-being during the first 6 months were predictors of CHAQ disability index after 3 years (standardized beta 0.324 and 0.231, p < 0.001 and p = 0.006 respectively, $R^2 = 25.1\%$) (Table 5). We also looked separately at predictors for CHAQ disability index at followup in patients with oligoarthritis ($n = 111$) and included course type as an independent variable. Parent’s global assessment of the child’s well-being during the first 6 months (standardized beta 0.353, p < 0.001) and course type (standardized beta 0.345, p < 0.001) were predictors of disability after 3 years in the patients with oligoarthritis ($R^2 = 22.2\%$) (Table 6). CHAQ score during the first 6 months was the only predictor of CHAQ disability index after 3 years in the 60 patients with polyarthritis (standardized beta 0.636, $p < 0.001, R^2 = 39.4\%$) (Table 7).

**DISCUSSION**

This is the first prospective study with repeated assessments of health status and disease activity at standardized intervals in JRA and JSpA. We found that health status and disease activity improved over time. The patients had worse physical function, general health, and pain than normal controls. The 2 predictors of the CHAQ disability index after 3 years
**Table 3.** Measures of disease activity at first admission and at 3 year followup in 197 children with JRA and JSpA.

<table>
<thead>
<tr>
<th>Measures of Disease Activity</th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAQ (range 0–3)*</td>
<td>0.5 (0.6)</td>
<td>0.4 (0.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Parent’s assessment of child’s pain (0–10 cm VAS)†</td>
<td>2.5 (2.4)</td>
<td>2.3 (2.5)</td>
<td>0.586</td>
</tr>
<tr>
<td>Parent’s assessment of child’s fatigue (0–10 cm VAS)†</td>
<td>2.4 (2.5)</td>
<td>2.4 (2.5)</td>
<td>0.857</td>
</tr>
<tr>
<td>Parent’s global assessment of child’s well-being (0–10 cm VAS)†</td>
<td>2.6 (2.3)</td>
<td>2.0 (2.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Morning stiffness (range 0–5 h)</td>
<td>0.5 (0.5)</td>
<td>0.2 (0.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Physician’s global assessment of disease activity (Likert scale 1–5)‡</td>
<td>3.0 (0.9)</td>
<td>1.8 (1.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of swollen joints (range 0–66)</td>
<td>3.0 (3.8)</td>
<td>1.2 (3.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of tender joints (range 0–68)</td>
<td>1.5 (2.7)</td>
<td>0.8 (2.5)</td>
<td>0.004</td>
</tr>
<tr>
<td>No. of joints with limited range of motion (range 0–69)</td>
<td>2.3 (2.9)</td>
<td>1.2 (2.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of active joints (range 0–69)</td>
<td>3.1 (3.8)</td>
<td>1.3 (3.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Arthritis severity index (range 0–668)§</td>
<td>8.6 (9.9)</td>
<td>4.6 (12.4)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* CHAQ: Childhood Health Assessment Questionnaire, 0 (no disability), 3 (severe disability). † VAS: Visual analog scale, scores could range from 0 cm (best) to 10 cm (worst). ‡ Scores could range from 1 (best) to 5 (worst). § Scores could range from 0 (best) to 668 (worst).

**Table 4.** Health status in JRA and JSpA patients after 3 years of followup compared with controls.

<table>
<thead>
<tr>
<th>CHQ scores</th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total N = 173/180</td>
<td>Active Disease N = 124</td>
</tr>
<tr>
<td>Physical summary score*</td>
<td>47.1 ± 12.0†</td>
<td>44.2 ± 12.7‡</td>
</tr>
<tr>
<td>Psychosocial summary score*</td>
<td>53.5 ± 6.9</td>
<td>53.2 ± 7.0</td>
</tr>
<tr>
<td>General health§</td>
<td>64.2 ± 19.1†</td>
<td>61.1 ± 19.5‡</td>
</tr>
<tr>
<td>Pain§</td>
<td>65.1 ± 29.6†</td>
<td>58.4 ± 29.6‡</td>
</tr>
</tbody>
</table>

* According to the parent-completed Child Health Questionnaire (CHQ) the summary scores are computed as scores where 50 ± 10 corresponds to the mean value ± SD in the normal population (> 50 better than mean, < 50 worse than mean). † p < 0.001 for independent t test between total patient group and controls. ‡ p < 0.001 for the difference between patients with active disease and controls. § General health and pain range from 0 to 100, where 0 means poor health status and 100 means excellent health status. # p = 0.001 for the difference between patients in remission and controls.

**Table 5.** The relationship between the Child Health Assessment Questionnaire (CHAQ) disability index at 3 year followup and measures of disease activity in JRA and JSpA (n = 197). Measures of disease activity are analyzed as area under the curve (AUC) between first admission and 6 months.*

<table>
<thead>
<tr>
<th>Measures of disease activity†</th>
<th>Univariate Analysis</th>
<th>Multiple Regression Analysis‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Area Under the Curve During the First 6 mo (SD)</td>
<td>Pearson’s Correlation Coefficient with CHAQ</td>
</tr>
<tr>
<td>CHAQ</td>
<td>92.4 (107.2)</td>
<td>0.478</td>
</tr>
<tr>
<td>Parent’s global assessment of child’s well-being</td>
<td>4648.7 (4356.5)</td>
<td>0.447</td>
</tr>
<tr>
<td>Physician’s global assessment of disease activity</td>
<td>509.8 (220.6)</td>
<td>0.079</td>
</tr>
<tr>
<td>No. of joints with limited range of motion</td>
<td>361.7 (402.4)</td>
<td>0.030</td>
</tr>
<tr>
<td>No. of active joints</td>
<td>459.1 (503.4)</td>
<td>0.120</td>
</tr>
<tr>
<td>ESR</td>
<td>3842.9 (3005.0)</td>
<td>0.185</td>
</tr>
</tbody>
</table>

* For the measurements y1 and y2 at times t1 and t2, the AUC between these 2 times is calculated as the product of the time difference and the average of the 2 measurements (t2−t1) × (y1 + y2)/2. † Pain correlated with the CHAQ after 3 years in the univariate analysis, but was not analyzed in the final model because of a high correlation with well-being. ‡ Results of the final model of multiple linear regression analysis with the CHAQ score at 3 year followup as the dependent variable. Adjusted R² = 25.1%.
were the CHAQ score and parent’s global assessment of the child’s well-being during the first 6 months.

During the first year of followup, physical function, physician’s assessment of disease activity, and ESR all improved significantly for the patient group as a whole and for the major subgroups. About 60% of our patients started DMARD at baseline, and it is difficult to know whether the improvement over time is due to the natural course of the disease or whether the changes reflect the effect of starting treatment.

Most studies of disease outcome have one endpoint, and the value of comparing these outcomes with our disease levels for oligoarthritis and polyarthritis, but over time they tended to move towards the same or higher levels than the polyarticular onset types. The finding that the persistent oligoarthritis group was the one with least disease activity is in accordance with the findings of several other studies of longer disease duration. However, as far as we can see, ours is the first study that has followed a patient group prospectively using repeated measurements of disease variables. Most studies of disease outcome have one endpoint, and the value of comparing these outcomes with our disease levels over 3 years is limited. Bowyer, et al found no patients with pauciarticular onset JRA who had significant limitations in physical function as measured by the Steinbrocker functional class, either one or 5 years after onset. In contrast, 12% of the patients with polyarticular onset and 30% of those with systemic onset did not require medication 1 year after onset. This could indicate an improvement during the first year, and our results support this.

Our patients with RF negative and RF positive polyarticular JRA had higher levels of disease activity and severity than those with persistently oligoarticular JRA throughout the study. For patients with systemic arthritis, the level of disease activity fluctuated mainly between the disease activity levels for oligoarthritis and polyarthritis, but over time they tended to move towards the same or higher levels than the polyarticular onset types. The finding that the persistent oligoarthritis group was the one with least disease activity is in accordance with the findings of several other studies of longer disease duration. However, as far as we can see, ours is the first study that has followed a patient group prospectively using repeated measurements of disease variables. Most studies of disease outcome have one endpoint, and the value of comparing these outcomes with our disease levels over 3 years is limited. Bowyer, et al found no patients with pauciarticular onset JRA who had significant limitations in physical function as measured by the Steinbrocker functional class, either one or 5 years after onset. In contrast, 12% of the patients with polyarticular onset and 30% of those with systemic onset were in class 3 or 4 after 5 years. Andersson Gäre, et al found after 7 years that CHAQ showed significant differences in physical functioning in girls, where patients with polyarticular disease had higher scores than those with monoarticular, pauciarticular, or sys-
temic disease. In the study of Flatø, et al the patients with polyarticular course had significantly more disability than those with persistently pauciarticular JRA after 10 years of disease duration. This was also found by Oen, et al. Ruperto, et al found the best CHAQ/HAQ scores in patients with pauciarticular JRA and the worst in patients with polyarticular and systemic JRA after 15 years of disease duration. Minden, et al compared the HAQ scores for juvenile idiopathic arthritis (JIA) subgroups after 16.5 years of disease duration and found a tendency towards worse functional status in patients with polyarthritis than in those with systemic and oligo/enthesitis-related JIA.

The JAS/SEA patients seemed to have poor health status in our study. Their physical function, well-being, and pain were markedly worse than that of the other disease subtypes throughout the study, except for the levels of RF positive polyarthritis. Due to the small number of patients in the JAS/SEA group, these results should be interpreted with caution. The JAS patients represent those with the most severe spondyloarthropathies. All the patients with SEA syndrome had arthritis. Thus our JAS/SEA patient group have a bias towards more severe forms of disease. However, the poor health in the JAS/SEA group compared with the other onset groups is in accordance with findings in other studies. Burgos-Vargas, et al reported that peripheral joint disease became polyarticular in most patients with JAS. Pain is the most frequent symptom in JSpA. Andersson Gäre, et al found that girls with JAS had higher CHAQ scores than those with monoarticular, pauciarticular, or systemic disease after 7 years. Flato, et al found that radiographic changes in the hips, and erosion of a peripheral joint were more frequent in juvenile arthritis patients with sacroiliitis than in those without. On the other hand, Flato, et al did not find a statistically significant difference in the median disability index between JRA and JSpA after 10 years of followup. More prospective studies are needed to settle this issue.

Health status and disease activity generally improved in the patient group after 3 years except for pain and fatigue, which remained mainly unchanged. According to Dempster, et al an improvement in disability index of more than 0.13 is of clinical importance, and the change in disability index for our patients was higher than this. In our study, patients with active disease had worse physical function, pain, and general health than the control group at followup. The patients in remission had pain and physical function comparable to those of the controls, indicating that these variables are reversible in most patients during early disease. However, the patients in remission considered their general health to be inferior to that of the controls. This is in accordance with other studies of longer disease duration.

In our study we saw that the level of pain had not significantly improved after 3 years in spite of the significant reduction in most other disease activity variables. Our data support the view that pain is an important dimension in the burden of disease in JRA and JSpA.

There was a minor change over time in psychosocial function for the patient group as a whole, but this was not considered to be clinically relevant since it was within the normal range.

Physical function and well-being during the first 6 months were of importance for predicting physical function at 3 years in our study. Disability index at disease onset has not previously been assessed as a possible predictor in JRA and JSpA, but has been shown to be important in RA. Our results are in accordance with those of Ruperto, et al, indicating that parent’s global assessment is a sensitive instrument. Our finding that disability and well-being at baseline are important and sensitive predictors of functional disability over time suggests that these variables might be of value in clinical practice. However these variables explained only 25% of the variance in our analysis, implying that factors other than disease variables and patient characteristics influence the level of disability.

Our patient group is a referral-based cohort, which probably represents about half of the estimated JRA and JSpA patients in Norway. These patients probably have more severe disease than cohorts selected from the general population. However, our patient group is comparable to the JRA/juvenile chronic arthritis patients in a number of epidemiological studies as regards age, gender, and distribution of onset type. The JAS/SEA patients seemed to have poor health status in our study, their physical function, well-being, and pain were markedly worse than that of the other disease subtypes throughout the study, except for the levels of RF positive polyarthritis. Due to the small number of patients in the JAS/SEA group, these results should be interpreted with caution. The JAS patients represent those with the most severe spondyloarthropathies. All the patients with SEA syndrome had arthritis. Thus our JAS/SEA patient group have a bias towards more severe forms of disease. However, the poor health in the JAS/SEA group compared with the other onset groups is in accordance with findings in other studies. Burgos-Vargas, et al reported that peripheral joint disease became polyarticular in most patients with JAS. Pain is the most frequent symptom in JSpA. Andersson Gäre, et al found that girls with JAS had higher CHAQ scores than those with monoarticular, pauciarticular, or systemic disease after 7 years. Flato, et al found that radiographic changes in the hips, and erosion of a peripheral joint were more frequent in juvenile arthritis patients with sacroiliitis than in those without. On the other hand, Flato, et al did not find a statistically significant difference in the median disability index between JRA and JSpA after 10 years of followup. More prospective studies are needed to settle this issue.

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