Assessment of Disease Activity in Juvenile Idiopathic Arthritis. The Number and the Size of Joints Matter

LILLEMOR BERNTSON, LISA WERNROTH, ANDERS FASTH, KRISTIINA AALTO, TROELS HERLIN, SUSAN NIELSEN, ELLEN NORDAL, MARITE RYGG, and MAREK ZAK, for the Nordic Paediatric Rheumatology Study Group

ABSTRACT. ***Objective.*** Variables for assessment of disease activity of juvenile idiopathic arthritis (JIA) were studied, in order to develop a disease activity score for children with JIA.

Methods. One randomly chosen hospital visit was studied for each of 312 patients with JIA, with regard to disease activity variables. The physician global assessment score visual analog scale (physician GA) was used as a dependent variable in comparisons between potential disease activity variables. Previous studies have shown this variable to be the most sensitive to changes in JIA disease activity and to be comparable between patients.

Results. Based on Spearman's rank order correlation the number of active joints had a strong association with the physician GA. The median physician GA score rose markedly for each active large joint, but less for small joints, although small joints were also statistically important in assessing disease activity. Among the laboratory data, the erythrocyte sedimentation rate, C-reactive protein level, and platelet count showed weak correlations to the physician GA.

Conclusion. In preparation of a disease activity score for children with JIA the importance of both the number and size of joints involved needs further evaluation. (First Release Sept 15 2007; J Rheumatol 2007;34:2106–11)

Key Indexing Terms:
ARTHRITIS JUVENILE RHEUMATOID DISEASE ACTIVITY CHILD JOINTS

From the Department of Women's and Children's Health, Uppsala University Children's Hospital, Uppsala, Sweden; Uppsala Clinical Research Center, Uppsala University Hospital, Uppsala, Sweden; Department of Paediatrics, Göteborg University, Göteborg, Sweden; Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; Department of Paediatrics, Århus University Hospital, Skejby, Denmark; University Clinic of Paediatrics II, Rigshospitalet, Copenhagen, Denmark; Department of Paediatrics, University Hospital of North Norway, Tromsø, Norway; Institute of Laboratory Medicine, Children's and Women's Health, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway; and Department of Paediatrics, St. Olavs Hospital, Trondheim, Norway.

Dr. Berntson is the senior author of this report.

Supported by grants from the Department of Women's and Children's Health, Uppsala University Children's Hospital, Uppsala; The Queen Silvia Children's University Hospital, Göteborg; the Dalarna Clinical Research Institute, Falun, Sweden; and the Swedish Rheumatism Association and the King Gustaf V 80th Jubilee Fund.

L. Berntson, MD, PhD, Department of Women's and Children's Health, Uppsala University Children's Hospital; L. Wernroth, Biostatistician, Uppsala Clinical Research Center; A. Fasth, MD, PhD, Professor of Paediatric Immunology, Department of Paediatrics, Göteborg University; K. Aalto, MD, PhD, Hospital for Children and Adolescents, University of Helsinki; T. Herlin, MD, PhD, Århus University Hospital; S. Nielsen, MD, University Clinic of Paediatrics II, Rigshospitalet, Copenhagen; E. Nordal, MD, Department of Paediatrics, University Hospital of North Norway; M. Rygg, MD, PhD, Institute of Laboratory Medicine, Children's and Women's Health, Faculty of Medicine, Norwegian University of Science and Technology and Department of Paediatrics, St. Olavs Hospital; M. Zak, MD, University Clinic of Paediatrics II, Rigshospitalet, Copenhagen.

Address reprint requests to Dr. L. Berntson, Department of Paediatrics, Akademiska University Hospital, SE-75185 Uppsala, Sweden. E-mail: lillemor.berntson@telia.com

Accepted for publication June 20, 2007.

Juvenile idiopathic arthritis (JIA) is a heterogeneous disease with an onset at any time before the age of 16 years. Assessment of disease activity is complex, and patients are often too young to actively contribute. No validated disease activity score, such as the Disease Activity Score 28 (DAS28) for adults, is available for JIA[1]. A numerical score representing disease activity in children with JIA would be an important tool for both research and clinical practice. To advance development of such a score, studies of different variables considered important for disease activity assessment have been performed.

The "core set of outcomes" validated and used in outcome studies[2] was introduced in 1997. This is a useful instrument for evaluating improvement following a given treatment, but the core set has not been validated as an instrument for performing comparisons between patients, and thus it does not provide a complete disease activity score. Variables included in the core set of outcomes are the number of active joints, the number of joints with limited range of movement, the erythrocyte sedimentation rate (ESR), the Childhood Health Assessment Questionnaire (CHAQ), the physician global assessment visual analog scale (VAS) (here denoted the physician GA), and the child/parent global assessment VAS (here denoted child/parent GA).

The separate variables involved in the core set of outcomes are also important in comparing patients to one another[3]. According to Ravelli and colleagues[4], it is necessary to

include variables from all the following 4 categories in disease activity measurements: subjective variables, functional capacity measurements, articular variables, and biochemical variables. In the latter study[4], variables within a given category correlated with each other; however, there was no correlation between the categories.

The DAS28 was constructed based on studies of variables that were important in the improvement of patients with adult rheumatoid arthritis (RA). The DAS is now validated and has become a useful tool in clinical practice. The variables included are the number of swollen joints, number of tender joints, ESR, and the global assessment VAS. The 28 joints evaluated as part of the index are considered representative in discriminating between high and low disease activity[1]. The index has not been evaluated for children.

Studies conducted in children with JIA before and after intraarticular corticosteroid injection have shown that the physician GA is the best variable for predicting disease activity[5]. In a study investigating the efficacy of methotrexate in children with JIA, the physician and parent global assessments were found to be the most responsive measuring factors of disease activity[3]. An Italian study has recently shown that the physician GA is the most sensitive discriminator between high and low disease activity in JIA[6]. The physician GA seems to be the best indicator of disease flare[7] and also a variable with high interobserver agreement[8]. The physician GA is therefore potentially suitable as a dependent variable in studies of other core set variables.

The number of active joints is also important in any assessment of disease activity[6,7]. The issue of joint size in disease activity evaluation has barely been studied.

Our aim was to study the relation between the physician GA and the different variables in the core set of outcomes, and to evaluate the relative influence of large and small joint activity on the physician's assessment, in setting up a disease activity index in children with JIA.

MATERIALS AND METHODS

Patients. Patients were recruited from the database of the Nordic Paediatric Rheumatology Study Group. This patient group initially consisted of 331 patients with visits from the time of onset through the following 8 years of disease. Data for the great majority of visits were collected during the first 3 years of disease. Nineteen patients with systemic JIA were excluded. A total of 691 visits had all variables recorded, and among these, one randomly chosen visit for each of the 279 patients was used for the analyses. The selection was performed using the statistics program SPSS. From among the remaining 33 patients the data from the only recorded visit were used. Data collected for each occasion consisted of the physician GA, the child/parent GA, the CHAQ[9], ESR, C-reactive protein (CRP), platelet count, the number of active joints, and the number of joints with limited range of movement. The physician and child/parent GA are given as a numerical score on a VAS of 0–100 mm, for assessment of the effect of the disease on the overall well-being of the child. For the physician GA, the scale 0 = no disease activity, 100 = maximum disease activity was used, while for the child/parent GA a scale of 0 = very good, 100 = very poor was used. The CHAQ was used for measuring physical functions. The CHAQ was filled out by the patient if the child was 9 years of age or older, otherwise by one of the parents. Joint examination was performed by a group of pediatricians skilled in pediatric rheumatology, according to a study protocol including 74 joints. An active joint was defined as a swollen joint or a joint with 2 of the following 3 signs: limited range of movement, pain on movement, and increased temperature. Data were supplemented with information about small and/or large-joint involvement. The ankle joints, knees, hips, sacroiliac joints, shoulders, elbows, wrists and neck were considered large joints, and the metacarpophalangeal (MCP), proximal interphalangeal (PIP), distal interphalangeal (DIP), metatarsophalangeal (MTP), toe, acromioclavicular, sternoclavicular, mandibular, costal, subtalar, and tarsal joints small joints.

Research ethical committees in each of the participant countries approved the study. Informed consent was obtained from both parents and, depending on age, assent or consent from the children.

Analytical procedures and statistical methods. Nonparametric tests were used, since the CHAQ and VAS are not normally distributed.

Spearman's rank-order correlation rho was used to evaluate the relationship between the physician GA and other variables of disease activity. We defined a value > 0.7 as high, 0.4 to 0.7 moderate, and < 0.4 low. Partial rank-order correlation was calculated to assess the relationship between the physician GA and other disease activity variables after adjusting it to the number of large or large and small active joints. Differences between correlations were tested for statistical significance using the method described by Morrison[10]. A box plot was used to illustrate the relationship between the physician GA and the number of active joints. The Mann-Whitney U test was applied to compare patients with no active joint involvement to patients with at least one active joint, with respect to their median value for the core set variables. To further evaluate the association between the risk of having at least one active joint (response variable) and the core set variables (explanatory variables), logistic regression was used. Simple logistic regression models and one multiple model including all the explanatory variables were estimated. Results are expressed as odds ratios (OR) with 95% confidence intervals (95% CI).

In all statistical analyses a p value < 0.05 (2-sided test) was considered significant.

Statistical analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC, USA) and SPSS version 14.0 software (SPSS Inc.).

RESULTS

The cohort of patients included 226 girls and 86 boys with a median age of 6.8 years (range 0.3–15.5) at disease onset. The randomly chosen visit for collection of disease activity variables was somewhere between the onset of disease and 8 years of disease duration. A total of 138 children were included from Denmark, 87 from Norway, 85 from Sweden, and 2 from Finland. The International League of Associations for Rheumatology (ILAR) classification of patients, during the first year of disease, is presented in Table 1.

We found the physician GA held the strongest correlation with the number of active joints, and a moderate correlation with the child/parent GA, the CHAQ, and the number of joints with limited range of movement; while the ESR, CRP, and platelet count showed a weak correlation with the physician GA (Table 2). The number of active joints seems to be more important to the physician as compared to its significance to the child/parent (rho = 0.686 vs rho = 0.409, respectively, p < 0.001).

The core set variables for patients with no active joint or at least one active joint are presented in Table 3. There was a statistically significant difference between patients with no active joint and those with one or more large active joints for all the other variables (physician GA, child/parent GA, CHAQ, ESR, CRP, and platelet count).

Table 1. ILAR classification performed at 1 year of disease in 312 children with juvenile idiopathic arthritis. The majority of children in the subgroup of "unclassifiable" fulfil criteria for 2 categories.

Subgroup at Onset (ILAR)	No. of Children
Oligoarticular persistent	151
Oligoarticular extended	21
Polyarticular RF-positive	6
Polyarticular RF-negative	78
Enthesitis-related arthritis	12
Psoriatic arthritis	7
Unclassifiable	37
Total	312

ILAR: International League of Associations for Rheumatology, RF: rheumatoid factor.

Table 3. Median (range) of the core set variables for patients with no active joint and patients with at least one active joint.

	No Active Joint, n = 125	At Least One Active Joint n = 187	p*
Physician GA	4.0 (0.0–47.0)	20.0 (0.0–75.1)	< 0.001
Child/parent GA	0.0 (0.0–74.1)	15.0 (0.0–98.1)	< 0.001
CHAQ	0.0 (0.0–1.8)	0.4 (0.0–2.9)	< 0.001
CRP	4.0 (0.0–25.0)	5.0 (0.0–220.0)	0.021
Platelet count	304 (150–752)	322 (164–836)	0.036
ESR	8.0 (0.0–40.0)	10.0 (0.0–125.0)	0.040

* p Value from Mann-Whitney U test to study differences, with respect to the core set variables, between patients with no active joint and patients with at least one active joint. CHAQ: Childhood Health Assessment Questionnaire (0–4), CRP: C-reactive protein (mg/l), platelet count ($\times 10^9$/l), ESR: erythrocyte sedimentation rate (mm/h), GA: global assessment (0–100 mm VAS).

While in the univariate logistic regression, ESR (OR 1.93, 95% CI 1.14–3.28, for ESR ≥ 14 vs ESR < 14) was significantly associated with the risk of having at least one active joint, associations were not statistically significant for CRP and platelet count. The physician GA, child/parent GA, and CHAQ were significantly and positively linked with the risk of having at least one active joint. A physician GA or child/parent GA below 10 was associated with more than a 3-fold increase in risk, compared with a global assessment of zero. In a multiple logistic regression model only the physician GA was found to be significantly associated with the risk of having one or more active joints (Table 4). In a logistic regression model with ESR, CRP, and platelet count included as continuous variables, no significance could be found (results not shown).

The physician GA showed a stronger correlation with the number of large active joints than with the number of small active joints (rho = 0.628 vs rho = 0.410, p < 0.001; Table 2). Children having one (7 patients) or 2 (6 patients) small active joints (no large joint) or one large active joint (no small joint) had the same median physician GA (VAS: 10 mm; Figure 1). The median value of the physician GA rose markedly with each large joint added, and there was a smaller increase with the addition of each small joint as well (Figure 1). A partial-rank correlation revealed a statistically significant additive effect of small joints in the assessment (physician GA: partial rho = 0.281, p < 0.001), but the large joints were the most important factors.

DISCUSSION

Based on previous studies, we chose to use the physician GA as the gold standard for assessing disease activity. The number of active joints, previously known to be an important discriminator between high and low disease activity[6,7], correlated strongly with the physician GA. The size of the joint seemed to play an important role in disease activity assess-

Table 2. Spearman's rank-order correlation between physician global assessment (GA) and the other variables for disease activity in 312 children with juvenile idiopathic arthritis on one randomly chosen visit.

	Spearman's Correlation (95% CI) Physician GA	Spearman's Partial Correlation (95% CI)* Physician GA	Spearman's Partial Correlation (95% CI)** Physician GA
No. of active joints, large and small	0.686 (0.621 to 0.740)		
No. of large active joints	0.628 (0.554 to 0.690)		
CHAQ	0.618 (0.544 to 0.682)	0.477 (0.385 to 0.558)	0.450 (0.357 to 0.535)
Child/parent GA	0.602 (0.525 to 0.668)	0.486 (0.396 to 0.566)	0.483 (0.393 to 0.564)
No. of joints with limited range of movement	0.547 (0.464 to 0.620)	0.234 (0.125 to 0.336)	0.166 (0.056 to 0.273)
No. of small active joints	0.410 (0.313 to 0.489)	0.281 (0.175 to 0.380)	
CRP	0.194 (0.084 to 0.298)	0.131 (0.020 to 0.239)	0.126 (0.015 to 0.234)
ESR	0.158 (0.038 to 0.255)	–0.007 (–0.118 to 0.104)	0.018 (–0.094 to 0.129)
Platelet count	0.132 (0.021 to 0.240)	0.040 (–0.071 to 0.151)	0.086 (–0.033 to 0.188)

* Adjusted for number of large active joints. ** Adjusted for number of large active joints and number of small active joints. CHAQ: Childhood Health Assessment Questionnaire, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate.

Table 4. Logistic regression of at least one active joint versus no active joint in 312 children with juvenile idiopathic arthritis on one randomly chosen visit.

Variable	No Active Joint, n = 125 n	%	At Least One Active Joint, n = 187 n	%	Univariate OR (95% CI)	Multiple* OR (95% CI)
Physician GA = 0	49	39.2	7	3.7	1.00	1.00
0 < physician GA < 10	35	28.0	18	9.6	3.60 (1.36 to 9.54)†	2.64 (0.90 to 7.70)
10 ≤ physician GA < 20	32	25.6	60	32.1	13.12 (5.33 to 32.30)†	10.27 (3.80 to 27.79)†
≥ 20	9	7.2	102	54.5	79.33 (27.90 to 225.53)†	47.33 (14.67 to 152.75)†
Child/parent GA = 0	64	51.2	35	18.7	1.00	1.00
0 < child/parent GA < 10	19	15.2	34	18.2	3.27 (1.63 to 6.57)†	2.99 (1.20 to 7.44)†
10 ≤ child/parent GA< 20	24	19.2	36	19.3	2.74 (1.42 to 5.31)†	0.85 (0.34 to 2.11)
≥ 20	18	14.4	82	43.9	8.33 (4.32 to 16.05)†	1.48 (0.57 to 3.85)
CHAQ = 0	79	63.2	41	21.9	1.00	1.00
0 < CHAQ ≤ 0.2	13	10.4	23	12.3	3.41 (1.57 to 7.42)†	1.54 (0.60 to 3.96)
0.3 ≤ CHAQ ≤ 0.5	15	12.0	40	21.4	5.14 (2.54 to 10.38)†	2.35 (0.97 to 5.67)
≥ 0.6	18	14.4	83	44.4	8.88 (4.71 to 16.75)†	2.13 (0.86 to 5.29)
CRP < 5	65	52.0	92	49.2	1.00	1.00
CRP ≥ 5	60	48.0	95	50.8	1.12 (0.71 to 1.76)	0.75 (0.40 to 1.42)
Platelet count < 350	86	68.8	114	61.0	1.00	1.00
Platelet count ≥ 350	39	31.2	73	39.0	1.41 (0.87 to 2.28)	1.10 (0.57 to 2.15)
ESR < 14	99	79.2	124	66.3	1.00	1.00
ESR ≥ 14	26	20.8	63	33.7	1.93 (1.14 to 3.28)†	1.69 (0.79 to 3.61)

* All explanatory variables are included in the model. † Significant values. CHAQ: Childhood Health Assessment Questionnaire, Physician GA: physician global assessment visual analog scale, child/parent GA: child/parent global assessment VAS, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate.

ment, since the physician GA showed a more significant correlation with the number of large active joints than with the number of small active joints.

The number of large joints was more important to the physician than the number of small joints, but the small joints also played a statistically significant role in disease activity. In our study, children having 1–2 small active joints (no large active joint) or one large active joint (no small active joint) had the same median physician GA. However, this finding was based on only 13 observations and needs to be confirmed in further studies.

The importance of joint size has been evaluated in an Italian study[11]. In a study conducted on 121 children with JIA, 6 skilled pediatric rheumatologists estimated how much the specific arthritic joint affected the given child. Activity in a large joint affected the child more than activity in a small joint, and weighting the joint count improved correlation between swollen or active joints and the physician GA. This is in accord with our results, although our study was not designed for specific weighting of the different small and large joints.

What is to be considered a large or a small joint may not be obvious. Our choice of ankles, knees, hips, sacroiliac joints, shoulders, elbows, wrists, and neck as large joints, and the MCP, PIP, DIP, MTP, toe, acromioclavicular, sternoclavicular, mandibular, costal, subtalar, and tarsal joints as small joints was partly based on the weighting of joints presented in the Italian study[11].

Another finding was a moderate correlation between the child/parent GA and the physician GA. In an earlier study the physician GA or parent GA was considered the most sensitive factor for responsiveness, but others later found only a weak correlation between the parent GA and the physician GA[3,12]. In reports of pain and disability, the children's own ratings are in only moderate agreement with parents' and physicians' ratings[13,14]. One implication is the difficulty even for older children to reliably transform and interpret their experience, pain, for example, into an assessment on an analog scale[15]. Assessment of disease activity using a VAS is likely to face the same problem. Physicians are probably more accustomed to the VAS, but categorical scales for subjective variables of disease activity might still be preferable.

In concurrence with other studies[6,7], there was a weak correlation between laboratory variables and the physician GA. In contrast, there was a significant difference between the physician GA results in the case of one or more active joints as compared to no active joint. This could indicate that the laboratory tests used today are not sufficiently sensitive.

The physician GA was the only variable having enough statistical strength to predict activity in one or more joints, when all core set variables were studied together. Although we could demonstrate that the number of active joints is important to the physician, it was not possible to clarify statistically what the physician's assessment was based on, since the CHAQ and the visual analog scales did not allow the use of a parametric method.

Another question concerning the accuracy of the study

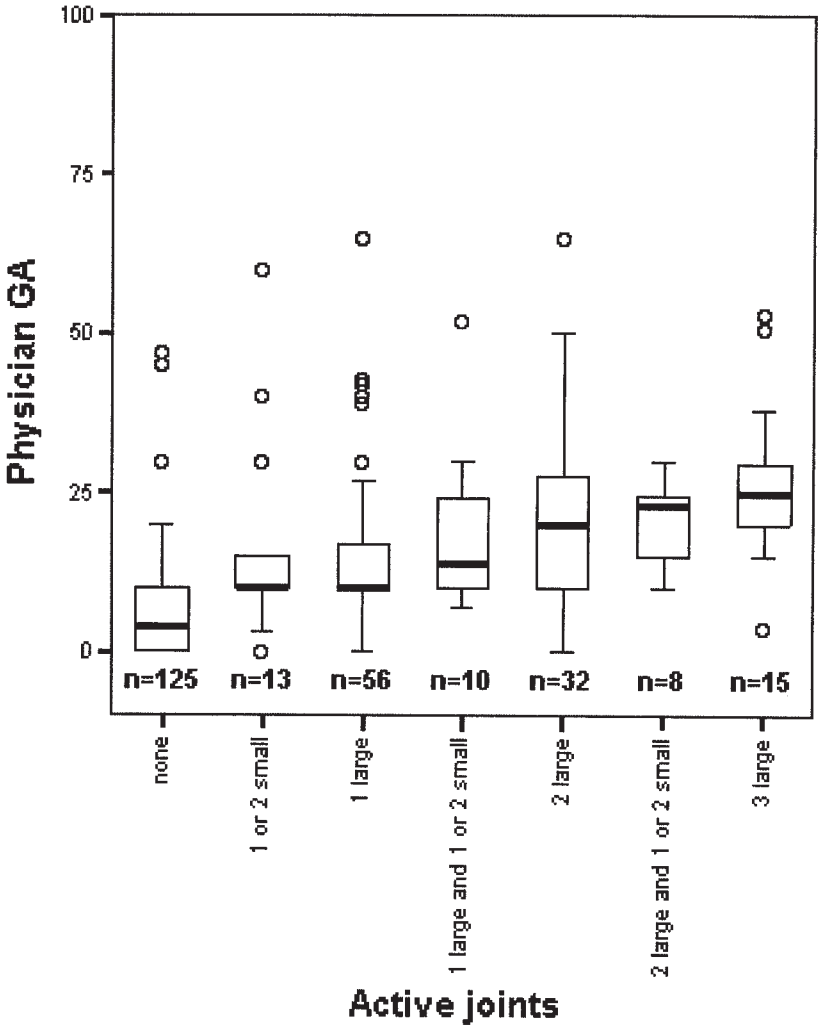

Figure 1. The physician global assessment (physician GA) for subgroups of children included from a cohort of 312 children with JIA. Each subgroup consists of all children with a specified number of active joints, large or small. The physician GA for each subgroup is presented in a box plot, and the median value is marked.

could be raised because of the exclusion of 19 patients with systemic JIA. A Canadian group presented the most important clinical variables for disease activity in the systemic subgroup of JIA. Systemic symptoms like fever, rash, splenomegaly, and lymphadenopathy are important and common features of disease activity. The group's results showed that the systemic disease subgroup needs a disease activity score of its own, especially regarding the initial time after the onset of disease[16]. The core set of outcomes is, however, considered accurate for all subtypes of JIA, including the systemic subtype[2].

In our study of disease activity variables in JIA, the significance of the number of active joints is demonstrated. In addition, the study suggests that the size of the joint is also of importance. The influence of large and small joints, as well as the other variables in the core set of outcome, needs further evaluation before a disease activity index for JIA is proposed.

ACKNOWLEDGMENT

The authors are grateful to the local Swedish coordinators for collecting data. They were: Eva Edlund, MD, and Gunilla Petersson, Lund; Karin Mellgren, MD, and Ewa Winsö, RN, Göteborg; Nils Olof Jonsson, MD, Jönköping; Anders Berner, MD, and Hans Ekström, MD, Karlstad; Eric Ronge, MD, Skövde; Agne Lind, MD, and Lars Hammarén, MD, Borås; Johan Robinsson, MD, and Marianne Bjernstrand, RN, Trollhättan; and Anna-Lena Nilsson, MD, Östersund. We are also grateful to Prof. Gudmund Marhaug, Trondheim; Docent Boel Andersson Gäre, Jönköping; Prof. Freddy Karup Pedersen, Copenhagen; Pekka Lahdenne, MD, Helsinki; Ove Ramsgård Hansen, MD, Århus, and Birgitte Möller, RN, Copenhagen; Nils Thomas Songstad, MD, and Anne Elisabeth Ross, MD, Tromsø; Kjell Berntzen, MD, and Nina Moe, MD, Trondheim.

REFERENCES

1. Prevoo MLL, Van't Hof MA, Kuper HH, Van Leeuwen MA, Van de Putte LBA, Van Riel PLC. Modified disease activity scores that include twenty-eight-joint counts. Arthritis Rheum 1995;38:44-8.
2. Giannini EH, Ruperto N, Ravelli A, Lovell DJ, Felson TF, Martini

A. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997;40:1202-9.
3. Ruperto N, Ravelli A, Falcini F, et al. Italian Pediatric Rheumatology Study Group. Responsiveness of outcome measures in juvenile chronic arthritis. Rheumatology Oxford 1999;38:176-80.
4. Ravelli A, Viola S, Ruperto N, Corsi B, Ballardini G, Martini A. Correlation between conventional disease activity measures in juvenile chronic arthritis. Ann Rheum Dis 1997;56:197-200.
5. Moretti C, Viola S, Pistorio A, et al. Relative responsiveness of condition specific and generic health status measures in juvenile idiopathic arthritis. Ann Rheum Dis 2005;64:257-61.
6. Magni-Manzoni S, Solari N, Palmisani E, et al. Toward the development of a disease activity score for juvenile idiopathic arthritis [abstract]. Arthritis Rheum 2005;52 Suppl:(149) S89.
7. Magni-Manzoni S, Garay S, Cugno C, et al. Responsiveness of clinical measures to flare of disease activity in juvenile idiopathic arthritis. Clin Exp Rheumatol 2005;23:421-5.
8. Falcone A, Cassone R, Rossi E, Pistorio A, Martini A, Ravelli A. Inter-observer agreement of the physician's global assessment of disease activity in children with juvenile idiopathic arthritis. Clin Exp Rheumatol 2005;23:113-6.
9. Singh G, Athreya BH, Fries JF, Goldsmith DP. Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum 1994;37:1761-9.
10. Morrison DF. Multivariate statistical methods. New York: McGraw-Hill; 1976.
11. Bandeira M, Falcone A, Pistorio A, et al. Weighting improves the information provided by joint counts on the severity of arthritis and its impact on patients' well-being in juvenile idiopathic arthritis. Rheumatology Oxford 2006;45:343-7.
12. Sztajnbok F, Coronel-Martinez DL, Diaz-Maldonado A, et al. Discordance between physician's and parent's global assessments in juvenile idiopathic arthritis. Rheumatology Oxford 2007; 46:141-5.
13. Garcia-Munitis P, Bandeira M, Pistorio A, et al. Level of agreement between children, parents, and physicians in rating pain intensity in juvenile idiopathic arthritis. Arthritis Rheum 2006;55:177-83.
14. Palermo TM, Zebracki K, Cox S, Newman AJ, Singer N. Juvenile idiopathic arthritis: parent-child discrepancy on reports of pain and disability. J Rheumatol 2004;31:1840-6.
15. Berntson L, Svensson E. Pain assessment in children with juvenile chronic arthritis: a matter of scaling and rater. Acta Paediatr 2001;90:1131-6.
16. Ramanan AV, Schneider R, Batthish M, et al. Developing a disease activity tool for systemic-onset juvenile idiopathic arthritis by international consensus using the Delphi approach. Rheumatology Oxford 2005;44:1574-8.