Development and Testing of Reduced Joint Counts in Juvenile Idiopathic Arthritis

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ABSTRACT. ***Objective.*** To develop and test reduced joint counts in children with juvenile idiopathic arthritis (JIA).

Methods. Four reduced joint counts including 45, 35, 27, and 10 joints were devised by a panel of experienced pediatric rheumatologists, who selected the joints to be included based on the ease of technical assessment, functional relevance, and frequency of involvement. Three large samples of patients with JIA (total n = 4353) who had a detailed joint assessment available were used to develop and test reduced joint counts. Performance of reduced counts was examined by comparing their Spearman correlation with the standard (i.e., complete) joint count. Construct validity was evaluated by calculating Spearman correlation with other JIA outcome measures. Responsiveness to clinical change was determined through the standardized response mean (SRM).

Results. Spearman correlations of reduced joint counts with the whole joint count and with the other JIA outcome measures were comparable, revealing that they had similar ability to serve as surrogate for the whole joint count and construct validity. Responsiveness to clinical change was also comparable across reduced counts (SRM 0.83–1.09 for active joint counts and 0.63–0.81 for restricted joint counts). Based on these results and considering the relative feasibility of the different counts, the 27-joint reduced count is proposed for use in JIA. This joint count includes the cervical spine and the elbow, wrist, metacarpophalangeal (from first to third), proximal interphalangeal, hip, knee, and ankle joints.

Conclusion. Reduced joint counts appear to be as reliable as standard joint counts in assessment of the severity of joint disease and its change over time in children with JIA. (First Release Oct 1 2008; J Rheumatol 2009;36:183–90; doi:10.3899/jrheum.080432)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS ARTICULAR EXAMINATION JOINT COUNTS
REDUCED JOINT COUNT DISEASE ACTIVITY SCORE

Articular examination has a central role in the clinical assessment of children with juvenile idiopathic arthritis (JIA), in standard clinical care, in observational studies, and in clinical trials. In current recommendations, in each joint the observer is asked to record swelling, tenderness/pain on motion, and restricted motion as present/absent[1,2]. The extension and severity of joint disease is quantified by counting the number of joints with swelling, tenderness/pain on motion, and restricted motion. The count of joints with active disease is calculated by computing the number of joints with swelling or, if swelling is not present or detectable, with tenderness/pain on motion and restricted motion. The counts of joints with active disease and restricted motion are part of the 6 core-set variables of the American College of Rheumatology (ACR) pediatric response criteria[3]. Both these indices have been shown to be responsive to clinically important change[4-6], although it has been suggested that the swollen and tender joint counts are better suited than the count of joints with restricted motion for the assessment of disease flare[7].

Although evaluation of all joints is clearly required in each patient in daily clinical care, recording scores for all joints is tedious and time-consuming. Further, some joints are technically difficult to evaluate, are not likely to exhibit change over time, or are rarely involved in children with JIA. In adult patients with rheumatoid arthritis (RA), a 28-joint reduced count has been shown to be as effective as the indices that include all joints, in both cross-sectional (i.e., at

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Dr. Bazso is a recipient of a scientific training bursary from the European League Against Rheumatism.

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Accepted for publication July 4, 2008.

a single point in time) and longitudinal studies[8,9]. As a result, the 28-joint count has been included as surrogate of the whole joint count in the most recent composite disease activity scores for RA[10,11]. The development of a reduced joint count has never been attempted in JIA. However, it would represent a fundamental step in preparation of a composite disease activity score for JIA, a measure that at present does not exist.

Our purpose was to devise and test several reduced joint counts to select the one that represents the best surrogate for the whole joint count in children with JIA. The study hypothesis was that use of a reduced joint count instead of the full joint count does not lead to loss of relevant information on the severity of arthritis and its influence on patients' well-being, and does not significantly affect the assessment of the therapeutic response in clinical trials.

MATERIALS AND METHODS

Study data sets. Three samples of patients who fulfilled the International League of Associations for Rheumatology (ILAR) criteria for JIA[12] and had a detailed joint assessment available for review were used to develop and test the reduced joint counts: the first consisted of 434 patients seen at the study units (Istituto di Ricovero e Cura a Carattere Scientifico G. Gaslini, Genova, and Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Policlinico S. Matteo, Pavia, Italy) between January 2002 and March 2007; the second comprised 3324 patients included in a study of health related quality of life (HRQOL) performed by the Pediatric Rheumatology International Trials Organization (PRINTO)[13]; the third comprised 595 patients enrolled in a trial conducted by the PRINTO to compare intermediate versus higher doses of methotrexate (MTX)[14]. The first 2 data sets were based on a cross-sectional assessment, whereas the third data set included 2 evaluations: one at treatment baseline and one after 6 months. The main demographic and clinical features of the 3 patient samples are presented in Table 1. Together, these samples are likely representative of the patients seen in most tertiary pediatric rheumatology centers worldwide and cover the entire spectrum of JIA severity. However, there were some demographic differences between the 3 samples: clinic patients had a younger age at disease onset; patients in the HRQOL study were older at study visit; and patients enrolled in the MTX trial had a shorter disease duration. Further, the unselected clinic patients included patients with all JIA subtypes, whereas patients with rheumatoid factor-positive polyarthritis were excluded from the MTX trial, and patients with psoriatic arthritis and enthesitis-related arthritis were excluded from the HRQOL study and the MTX trial.

Development of reduced joint counts. Eight experienced pediatric rheumatologists (AR, NR, SV, SMM, CM, AB, AL, AM) working at the study units were asked to select the joints to be included in a reduced joint count in JIA. Investigators were instructed to consider for each joint, based on their clinical experience, the ease of technical assessment, the functional relevance to children's physical and daily activities, and the frequency of involvement. To facilitate the latter evaluation, investigators were provided with the percentage of patients with active disease in each joint seen in the 3 study samples (Table 2). It was agreed that the joints involved in more than 5% of the patients in all samples should be given the greatest value. After extensive discussion regarding the number and combination of joints required to adequately sample a population of JIA patients having a broad spectrum of disease severity, a consensus was reached among the members of the panel about 3 reduced joint counts, which included 45, 35, and 27 joints, respectively. The joints included in these reduced counts are listed, together with the joints included in the whole 71-joint count, in Table 3. In addition to these joint counts, it was decided to include in the analyses a simple 10-joint count, based on the count of any involved joint, irrespective of its type, to a maximum of 10 joints. This count was chosen to facilitate application of reduced joint counts to retrospective data collections in which the total number of affected joints is known, but no information is available on the type of involved joints.

Additional clinical assessments. Besides joint counts, the following JIA outcome measures were recorded in each patient: physician's global assessment of overall disease activity on a 10-cm visual analog scale (VAS) (0 = no activity; 10 = maximum activity); parent's global assessment of child's well-being on a 10-cm VAS (0 = very good; 10 = very poor); parent's rating of intensity of child's pain on a 10-cm VAS (0 = no pain; 10 = very

Table 1. Main demographic and clinical features of the 3 patient samples. Values are medians (interquartile range), unless otherwise indicated.

	Clinic Patients		HRQOL Study		MTX Trial at Baseline	
	N	(N = 434)	N	(N = 3324)	N	(N = 595)
Age at disease onset, yrs	434	3.4 (1.9; 6.0)	3114	5.2 (2.6; 8.7)	592	4.4 (2.0; 8.5)
Age at study visit, yrs	434	7.2 (3.9; 11.2)	3141	10.6 (7.2; 14)	595	7.8 (4.2; 11.3)
Disease duration, yrs	434	2 (0.8; 5.4)	3115	3.8 (1.6; 6.7)	592	1.1 (0.4; 3.4)
Swollen joint count	425	2 (0; 3)	2768	1 (0; 4)	594	7 (4; 13)
Tender joint count	425	1 (0; 3)	2768	1 (0; 3)	594	7 (4; 14)
Restricted joint count	425	1 (0; 3)	2768	2 (0; 7)	594	8 (5; 14)
Active joint count	425	2 (0; 4)	2768	2 (0; 5)	594	9 (6; 16)
Physician's global assessment*	400	3.4 (0.0; 7.3)	2758	1.8 (0.4; 3.9)	590	5.1 (3.7; 6.6)
Parent's global assessment*	225	1 (0.0; 3.7)	2853	1.3 (0.1; 4.1)	591	4.5 (2.2; 6.3)
Parent's pain assessment*	225	1 (0.0; 3.7)	2849	1.3 (0.1; 4.0)	589	4.5 (2.4; 6.9)
C-HAQ score**	232	0.1 (0.0; 0.3)	2857	0.4 (0.0; 1.1)	592	1.2 (0.6; 1.7)
ESR, mm/h†	306	15 (9; 38)	2450	20 (10; 38)	581	40 (22; 62)
Patients with ≤ 10 active joints (%)	425	396 (93.2)	2768	2444 (88.3)	594	351 (59.1)

* Range 0 (best) to 10 (worst); ** range 0 (best) to 3 (worst); † normal < 20 mm/h. HRQOL: health-related quality of life; MTX: methotrexate; C-HAQ: Childhood Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate.

Table 2. Patients with active disease (%) in each joint in the 3 patient samples.

Joint	Clinic Patients (N = 434) R/L	HRQOL Study (N = 3324) R/L	MTX Trial at Baseline (N = 595) R/L
Cervical spine	5.5	7.2	20.6
Temporomandibular	1.5/1.2	1.9/1.9	7.4/6.2
Sternoclavicular	0.3/0.3	0.3/0.3	1.3/1.3
Acromioclavicular	0.6/0.6	1.4/1.2	1.7/1.1
Shoulder	4.9/4.9	5.3/5.1	7.9/8.5
Elbow	9.5/10.4	11.3/11.1	31.5/32.0
Wrist	21.8/18.7	28.7/27.1	59.5/59.0
Metacarpophalangeal			
1	6.1/6.4	9.1/8.5	19.3/19.9
2	8.0/7.7	11.5/10.5	32.8/30.9
3	7.7/6.1	10.9/9.9	30.7/25.6
4	3.4/4.3	6.5/6.5	17.6/16.8
5	2.1/3.1	5.1/5.3	12.8/13.1
Proximal interphalangeal			
1	6.1/5.5	9.6/8.7	22.5/20.4
2	13.2/12.3	15.3/14.5	35.9/33.9
3	13.5/9.5	14.5/14.1	35.3/35.4
4	8.0/8.6	12.6/11.8	28.2/27.4
5	5.5/5.5	9.0/8.7	18.2/19.8
Distal interphalangeal			
2	2.5/2.1	2.6/2.5	4.7/3.6
3	2.5/2.5	3.0/2.5	4.1/4.1
4	1.5/1.5	2.1/1.8	3.2/2.2
5	1.5/1.2	2.0/1.7	2.8/1.4
Hip	7.4/5.5	9.1/9.5	19.5/18.2
Knee	48.8/42.9	39.7/35.4	66.9/66.6
Ankle	29.8/32.8	27.0/28.2	59.5/60.3
Subtalar	7.7/9.8	2.9/2.9	13.9/12.8
Tarsometatarsal	2.5/1.8	3.7/4.1	11.4/10.9
Metatarsophalangeal			
1	4.0/3.7	5.3/5.2	14.1/13.6
2	2.1/3.4	3.4/3.5	8.2/7.3
3	1.5/1.8	3.0/3.2	7.0/6.5
4	0.9/2.5	2.3/2.5	6.0/5.4
5	1.8/0.6	1.9/1.9	5.2/5.4
Foot interphalangeal			
1	3.4/3.4	2.2/2.1	4.4/3.6
2	1.8/3.4	1.9/2.1	4.6/4.0
3	0.6/0.6	1.5/1.5	2.7/2.5
4	0.3/1.5	1.2/1.3	2.4/2.4
5	0.3/0.3	1.0/0.8	1.6/1.7

HRQOL: health-related quality of life; MTX: methotrexate; R: right; L: left.

severe pain); parent's assessment of child's functional ability through the national language version of the Childhood Health Assessment Questionnaire (C-HAQ)[15]. Laboratory assessments included erythrocyte sedimentation rate (ESR; Westergren method).

Statistical analyses. Descriptive statistics are reported in terms of medians and interquartile ranges for continuous variables and absolute frequencies and percentages for categorical variables. In all analyses, nonparametric statistics were used to account for the non-normal distribution of the articular indices and most of the other outcome variables. For each joint count, either complete or reduced, the respective number of joints with active disease and restricted motion, which are the 2 articular indices included in the ACR pediatric response criteria, was computed. The performance of the different reduced joint counts was first assessed by examining their ability to serve as a surrogate measure for the whole joint count. This analysis was conducted by comparing the Spearman correlation of each reduced joint count with the whole joint count. Second, the construct validity of reduced joint counts was compared by calculating their Spearman correlations with the other JIA outcome measures. Because active and restricted joint counts are thought to reflect, for the most part, disease activity and damage, respectively, the former counts were correlated with 2 other measures of disease activity (the physician's global assessment and the ESR), whereas the latter counts were correlated with a measure of (functional) damage (the C-HAQ score). Because the parent's global assessment was previously found to reflect both disease activity and damage in JIA[16], it was correlated with both active and restricted joint counts. Correlations between variables were assessed on cross-sectional values (i.e., on values obtained in a single visit) in the clinic-patient and HRQOL study samples and on the baseline to 6-month change in the MTX trial. Correlations > 0.7 were considered high, correlations from 0.4 to 0.7 moderate, and correlations < 0.4 were considered low[17]. In all analyses, the higher the correlation, the better

Table 3. Joints included (+) or not included (–) in 4 joint indices for the evaluation of JIA. The 28-joint reduced count used in adult patients with rheumatoid arthritis (RA) is shown for comparison in the last column.

Joint	Index				
	71-joint	45-joint	35-joint	27-joint	RA 28-joint
Cervical spine	+	+	+	+	–
Temporomandibular	+	+	–	–	–
Sternoclavicular	+	–	–	–	–
Acromioclavicular	+	–	–	–	–
Shoulder	+	+	+	–	+
Elbow	+	+	+	+	+
Wrist	+	+	+	+	+
Metacarpophalangeal					
1	+	+	+	+	+
2	+	+	+	+	+
3	+	+	+	+	+
4	+	+	+	–	+
5	+	+	+	–	+
Proximal interphalangeal					
1	+	+	+	+	+
2	+	+	+	+	+
3	+	+	+	+	+
4	+	+	+	+	+
5	+	+	+	+	+
Distal interphalangeal					
2	+	–	–	–	–
3	+	–	–	–	–
4	+	–	–	–	–
5	+	–	–	–	–
Hip	+	+	+	+	–
Knee	+	+	+	+	+
Ankle	+	+	+	+	–
Subtalar	+	–	–	–	–
Tarsometatarsal	+	–	–	–	–
Metatarsophalangeal					
1	+	+	+	–	–
2	+	+	–	–	–
3	+	+	–	–	–
4	+	+	–	–	–
5	+	+	–	–	–
Foot interphalangeal					
1	+	–	–	–	–
2	+	–	–	–	–
3	+	–	–	–	–
4	+	–	–	–	–
5	+	–	–	–	–

was the construct validity. Differences in the magnitude of correlation for each reduced joint count were interpreted qualitatively. The responsiveness of joint counts to clinical change was determined by calculating the standardized response mean (SRM) in the MTX trial. The SRM was calculated as the mean absolute change in joint count between the baseline and the 6-month visit divided by the standard deviation (SD) of individuals' change in joint count[18]. According to Cohen[19], the threshold levels for SRM were defined as follows: ≥ 0.20 = small, ≥ 0.50 = moderate, and ≥ 0.80 = good. The statistical package used was Statistica (StatSoft Corp., Tulsa, OK, USA).

RESULTS

Table 2 shows the percentage of patients with active disease in each specific joint in the 3 study samples. Overall, the joints most frequently affected were the knee, ankle, wrist, elbow, proximal interphalangeal joints, metacarpophalangeal (MCP) joints, cervical spine, hip, subtalar, and first metatarsophalangeal (MTP) joints. As expected, patients in the MTX trial, all of whom had active polyarthritis as per inclusion criteria, had a greater frequency of active disease in all joints compared with patients in the other samples. Compared to the Italian clinic patients, patients in the HRQOL study had a greater frequency of involvement of cervical spine, wrist, hand, hip, and foot joints and a lower frequency of involvement of knee, ankle, and subtalar joints. The latter phenomenon may reflect the high prevalence in Italy of the antinuclear antibody-positive subset of JIA, which is characterized by preferential involvement of the large joints in the lower limbs[20,21].

The joints included in the complete and reduced joint counts are listed in Table 3. Sternoclavicular, acromioclavicular, distal interphalangeal, subtalar, tarsometatarsal, and foot interphalangeal joints were excluded from the least reduced joint count (i.e., the 45-joint reduced count). In addition to the above joints, temporomandibular and MTP joints from the second to the fifth were excluded from the 35-joint reduced count. In the 27-joint reduced count, shoulder, fourth and fifth MCP, and first MTP joints were also excluded. The thoracic and lumbar spine and the sacro-iliac joints were not included in any joint count because they are rarely involved in JIA, whereas they are typically affected in juvenile spondyloarthropathies.

Reduced joint counts were first tested on cross-sectional data. Table 4 shows the Spearman correlations of reduced count of joints with active disease and restricted motion with their respective whole joint count and with other JIA outcome measures in the Italian clinic patients, in the HRQOL study sample, and in the MTX trial. All correlations between complete and reduced joint counts were almost perfect (i.e., close to 1), with the exception of the poorer correlations between changes in the complete and 10-joint reduced counts in the MTX trial. Correlations for the physician's global assessment were in the moderate to high range, whereas correlations for the parent's global assessment and the C-HAQ were poor to moderate. Overall, correlations were comparable for all reduced joint counts, revealing that they had similar construct validity. Notably, correlations of reduced joint counts with JIA outcome variables were lower in the MTX trial than in the other 2 patient samples.

To obtain further insights on the relative performance of reduced joint counts, we reexamined the above correlations in the extreme phenotypes of JIA, that is, in patients with a high number (≥ 28) or a low number (≤ 10) of affected joints. This assessment was made on the baseline to 6-month changes in the MTX trial. In the former sample (Table 5), there was a minor drop in the correlations for the 27-joint reduced count relative to the 45 and 35-joint reduced counts, whereas the decrease was much more pronounced for the 10-joint reduced count. In the latter sample (Table 6), correlations remained similar for all reduced counts. We also investigated whether the substitution of the complete joint counts with the reduced joint counts in the ACR pediatric core set led

Table 4. Spearman correlations between complete and reduced active (AJC) and restricted (RJC) joint counts and physician's global assessment, parent's global assessment, C-HAQ score, and erythrocyte sedimentation rate (ESR) in cross-sectional patient samples and in the methotrexate (MTX) trial.

		N	AJC-71	AJC-47	AJC-35	AJC-27	AJC-10
Clinic patients	AJC-71	425	—	0.99	0.98	0.98	0.99
	Physician global assessment	393	0.70	0.70	0.69	0.69	0.69
	Parent global assessment	225	0.42	0.44	0.42	0.41	0.42
HRQOL study patients	AJC-71	2768	—	0.99	0.98	0.97	0.99
	Physician global assessment	2758	0.66	0.65	0.65	0.64	0.66
	Parent global assessment	2735	0.38	0.38	0.38	0.37	0.38
MTX trial patients							
Baseline data	AJC-71	594	—	0.98	0.96	0.94	0.95
	Physician global assessment	590	0.30	0.30	0.27	0.27	0.24
	Parent global assessment	591	0.11	0.11	0.08	0.08	0.08
Baseline-6 month change	AJC-71	490	—	0.97	0.93	0.91	0.68
	Physician global assessment	490	0.45	0.45	0.41	0.43	0.51
	Parent global assessment	490	0.22	0.21	0.18	0.19	0.29
	ESR	490	0.15	0.16	0.15	0.16	0.23
		N	RJC-67	RJC-45	RJC-35	RJC-27	RJC-10
Clinic patients	RJC-67	425	—	0.99	0.97	0.96	0.99
	Parent global assessment	393	0.47	0.47	0.45	0.45	0.47
	C-HAQ score	232	0.40	0.40	0.37	0.39	0.40
HRQOL study patients	RJC-67	2768	—	0.99	0.98	0.98	0.99
	Parent global assessment	2735	0.36	0.36	0.35	0.35	0.36
	C-HAQ score	2739	0.47	0.47	0.47	0.47	0.47
MTX trial patients							
Baseline data	RJC-67	594	—	0.99	0.97	0.96	0.97
	Physician global assessment	591	0.12	0.13	0.11	0.10	0.10
	Parent global assessment	592	0.28	0.28	0.27	0.26	0.24
Baseline-6 month change	RJC-67	490	—	0.99	0.95	0.93	0.75
	Parent global assessment	490	0.25	0.25	0.24	0.25	0.28
	C-HAQ score	488	0.27	0.27	0.27	0.28	0.26

C-HAQ: Childhood Health Assessment Questionnaire.

to a significant alteration in the percentage of patients classified as improved or not improved in the MTX trial (Table 7). Use of reduced joint counts led to increases of the percentage of nonresponders of 0.4% for the 45-joint reduced count, of 1.7% for the 35-joint reduced count, of 2% for the 27-joint reduced count, and of 4.1% for the 10-joint reduced count. The proportion of patients classified in the different levels of the ACR pediatric response was unchanged.

The SRM (95% confidence interval) of standard joint count and of 47, 35, 27, and 10-joint reduced counts in the MTX trial data was 0.83 (0.73; 0.92), 0.84 (0.74; 0.93), 0.87 (0.77; 0.96), 0.93 (0.83; 1.02), and 1.09 (0.99; 1.18), respectively, for the active joint counts and 0.63 (0.53; 0.73), 0.64 (0.54; 0.73), 0.63 (0.53; 0.73), 0.66 (0.57; 0.76), and 0.81 (0.72; 0.91), respectively, for the restricted joint counts. It is notable that the more reduced the joint count, the better was the responsiveness to clinical change.

Based on these results, the study investigators agreed that the 27-joint reduced count, which performed similarly to the 45 and 35-joint reduced counts, is best suited due to its greater simplicity for inclusion in a disease activity score in JIA. The simplest 10-joint reduced count showed the best responsiveness to clinical change, but yielded lower correlations with the complete joint count in the MTX trial and in patients with a greater number of affected joints, and led to misclassifying as "nonimproved" more than 4% of the patients previously classified as responders in the MTX trial. For these reasons, use of this reduced count was advised only for retrospective studies, when the values of joint counts are known, but no information on the individual involved joints is available.

DISCUSSION

We devised and tested several reduced joint counts with the aim of identifying the one that represented the best surrogate for the standard (i.e., complete) joint count in children with JIA and, at the same time, was simple and feasible enough to reduce the amount of time required to make joint assess-

Table 5. Spearman correlations between changes in complete and reduced active and restricted joint counts and physician's global assessment, parent's global assessment, C-HAQ score, and erythrocyte sedimentation rate (ESR) in cross-sectional patient samples and in the methotrexate trial in patients with active joint count (AJC) ≥ 28 (n = 39) or restricted joint count (RJC) ≥ 28 (n = 32).

	AJC-71	AJC-45	AJC-35	AJC-27	AJC-10
AJC-71	—	0.96	0.94	0.87	0.70
Physician global assessment	0.66	0.69	0.60	0.56	0.48
Parent global assessment	0.26	0.27	0.24	0.19	0.15
ESR	0.35	0.32	0.29	0.26	0.29
	RJC-67	RJC-45	RJC-35	RJC-27	RJC-10
RJC-67	—	0.93	0.92	0.87	0.66
Parent global assessment	0.27	0.23	0.20	0.21	0.06
C-HAQ score	0.41	0.38	0.34	0.43	0.35

C-HAQ: Childhood Health Assessment Questionnaire.

Table 6. Spearman correlations between changes in complete and reduced active and restricted joint counts and physician's global assessment, parent's global assessment, C-HAQ score, and erythrocyte sedimentation rate (ESR) in cross-sectional patient samples and in the methotrexate trial in patients with active joint count (AJC) ≤ 10 (n = 286) or restricted joint count (RJC) ≤ 10 (n = 316).

	AJC-71	AJC-45	AJC-35	AJC-27	AJC-10
AJC-71	—	0.98	0.92	0.90	1.00
Physician global assessment	0.50	0.49	0.46	0.47	0.50
Parent global assessment	0.25	0.25	0.22	0.25	0.25
ESR	0.24	0.26	0.26	0.27	0.23
	RJC-67	RJC-45	RJC-35	RJC-27	RJC-10
RJC-67	—	0.99	0.95	0.94	1.00
Parent global assessment	0.29	0.29	0.27	0.28	0.29
C-HAQ score	0.24	0.24	0.25	0.26	0.24

C-HAQ: Childhood Health Assessment Questionnaire.

Table 7. Number (%) of ACR pediatric nonresponders or responders at 30%, 50%, and 70% in the methotrexate trial obtained using the whole or reduced count of joints with active arthritis and restricted motion.

	Whole Joints	45 Joints	35 Joints	27 Joints	10 Joints
Not improved	119 (24.3)	121 (24.7)	126 (25.7)	129 (26.3)	139 (28.4)
ACR Ped 30%	63 (12.9)	60 (12.2)	64 (13.1)	63 (12.9)	62 (12.7)
ACR Ped 50%	115 (23.5)	116 (23.7)	110 (22.4)	111 (22.7)	103 (21.0)
ACR Ped 70%	193 (39.4)	193 (39.4)	190 (38.8)	187 (38.2)	186 (38.0)

ment. This study is preparation for the development of a composite disease activity score for JIA. To ensure the maximum face validity and reliability of the process, selection of reduced joint counts was based on the consensus of 8 experienced pediatric rheumatologists, and on the analysis of 3 JIA patient samples including a total of 4353 patients who were recruited in a large number of countries and were representative of the entire spectrum of disease severity.

Overall, statistical analyses showed that the 45, 35, and 27-joint reduced counts were comparable in terms of ability to serve as surrogate for the whole joint count, construct validity, and responsiveness to clinical change. Based on these results and considering the relative feasibility of the different counts, the study panel decided to recommend the 27-joint reduced count for inclusion in a future composite disease activity score for JIA. It should be kept in mind, however, that investigators can also use the 45 or 35-joint reduced counts as they may deem them appropriate for the main hypothesis that is being tested. The good statistical performance of the simplest 10-joint reduced count in terms of responsiveness to clinical change may be explained by most JIA patients, particularly those seen in standard clinical practice, having few involved joints. Indeed, the median number of joints with active disease in the Italian clinic sample, in the HRQOL study sample, and in the MTX trial was 2, 2, and 9, respectively. Further, the percentage of patients with 10 or fewer active joints in the same samples was 93.2%, 88.3%, and 59.1%, respectively. However, the 10-joint reduced count does not enable a precise assessment of joint disease and may limit the ability to detect new joint involvement over time. As well, it yielded lower correlations with the complete joint count in the MTX trial and in patients with a greater number of affected joints, and led to misclassifying as nonimproved more than 4% of the patients previously classified as responders in the MTX trial. Thus, the study investigators believe that it is best suited for use in retrospective studies, when the values of joint counts are known, but no information on the individual affected joints is available. It has recently been suggested that weighting of joints based on their functional importance to children's physical and daily activities[22] or on their size[23] may better reflect the severity of arthritis and its influence on children's well-being. However, the study panel decided not to incorporate these findings in the analyses to avoid making the calculation of joint scores too complex.

The sternoclavicular, acromioclavicular, distal interphalangeal, and foot interphalangeal joints were excluded from all reduced joint counts because they are rarely affected in children with JIA, are difficult to assess, or have been shown to be relatively insensitive to clinical change in adult RA clinical trials[9]. Subtalar and tarsometatarsal joints were also not included because arthritis in these joints, particularly in the subtalar joint, is generally associated with involvement of the ankle (talocrural) joint. It was felt, therefore, that inclusion of the ankle could be sufficient to represent arthritis in this area. Further exclusion of joints from the different reduced counts was based on the ease of their assessment and the relative frequency of their involvement in the 3 patient samples. The 27-joint reduced count includes the cervical spine and the elbow, wrist, MCP (from the first to the third), interphalangeal, hip, knee, and ankle joints.

There are some differences between the 27-joint reduced count that is proposed for use in JIA and the 28-joint reduced count that is incorporated in most of the composite disease activity scores developed for adult patients with RA[8,10,11]. The 28-joint reduced count includes the shoulder, which is excluded from the 27-joint reduced count, and excludes the cervical spine and the hip, which are included in the 27-joint reduced joint count; further, the fourth and fifth MCP joints are included in the 28-joint reduced count, but are excluded from the 27-joint reduced count. These discrepancies are partly explained by the diversities in the joint indices included in the ACR response criteria for adult RA[24] and in the ACR pediatric response criteria for JIA[3]: the former criteria include the count of joints with swelling and tenderness, whereas the latter criteria include the count of joints with active disease and restricted motion. Because swelling is usually not detectable clinically in the cervical spine and hip, these joints are excluded from the swollen joint count in adult patients with RA. However, in childhood arthritis, if swelling is not present or detectable (as in the cervical spine and hip), the simultaneous presence of tenderness/pain on motion and restricted motion is considered sufficient for a joint to qualify as active. For this reason and because the cervical spine and hip are important and frequently affected joints in children with JIA, the study investigators decided to include both these joints in the 27-joint reduced count. Exclusion of the shoulder from the 27-joint reduced count was mostly based on the relatively low frequency of its involvement in the 3 patient samples, and on

the feeling of study investigators that assessment of swelling in this joint could raise some problems in reliability, particularly in younger children. The fourth and fifth MCP joints were excluded as well, due to the relatively low frequency of their involvement in the 3 patient samples. Further, since involvement of hand joints in children with JIA is often scanty and asymmetric, it was believed that omission of these joints would have little overall effect.

It should be acknowledged that joints that are not included in the reduced joint counts may be very important for individual patients and should be assessed periodically as part of clinical care. For instance, temporomandibular joint involvement may occur in a sizable proportion of patients with JIA, is often asymptomatic, and is an important source of longterm damage[25,26]. However, assessment of these joints will not necessarily improve the ability to accurately assess a change in inflammation over time in the context of a clinical trial. Notably, the study results might not be extrapolated to the categories of psoriatic arthritis and enthesitis-related arthritis, which were not included by the original enrollment criteria in 2 of the 3 patient samples. Application of reduced joint counts to juvenile spondyloarthropathies might also be hampered by the exclusion of the thoracic and lumbar spine and the sacroiliac joints.

Reduced joint counts appear to be as reliable as standard joint counts in assessment of the severity of joint disease and its change over time in children with JIA. Use of reduced joint counts may reduce the burden of joint assessments without requiring larger sample sizes in clinical trials; and may facilitate the use of quantitative assessments in following clinical course and determining response to treatment in routine patient care.

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