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Outcome following onset of juvenile idiopathic inflammatory arthritis: I. Frequency of different outcomes

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***Objective*. To determine the outcome, following the onset of juvenile idiopathic inflammatory arthritis, in terms of remission of disease activity, loss of function and structural damage based on a review of the available published data.**

***Methods*. Electronic databases were searched for major studies publishing outcome data in the past 10 yr in juvenile idiopathic arthritis, juvenile rheumatoid arthritis and juvenile chronic arthritis, and 21 studies were selected. The proportions of children in the different categories of the outcomes of interest are described. Data were stratified where possible by disease subtype.**

***Results*. There were major differences between the studies reviewed in terms of study design, case selection and the results obtained. In general, children with systemic- or polyarticular-onset disease were much less likely to go into remission than those with oligoarticular onset, although the remission rates in the latter group ranged from 36 to 84%. Several different approaches were used to assess functional outcome but the pattern of results between the different subgroups was the same as with remission. Similarly, children with polyarticular disease in all the cohorts reviewed were substantially more likely to have erosive radiological damage on follow-up. The rates of individual outcomes, even within a subgroup, varied considerably between studies and this does not appear to be explained solely by differences in methodology.**

***Conclusions*. There remains a considerable lack of clarity in the prognosis following onset of juvenile idiopathic arthritis for the major outcomes considered, although those with oligoarthritis at presentation have the best outcome. The ability to offer accurate prognosis is particularly important to both reassure parents and guide treatment at disease onset. To achieve this, large definitive prospective studies will be required.**

KEY WORDS: Juvenile arthritis, Outcome, Remission, Function, Bone erosion.

Juvenile idiopathic arthritis (JIA), also known as juvenile chronic arthritis (JCA) (in Europe) and juvenile rheumatoid arthritis (JRA) (in North America), is a chronic inflammatory disease of the joints and extra-articular tissue. This is a heterogeneous group of disorders with an approximate prevalence in the UK of 65/100 000 and approximate annual incidence rate of 10/100 000 children [1, 2]. In North America the reported prevalence ranges between 16 and 113/100 000, with annual incidence rates ranging from 4 to 14 per 100 000 per year [3].

Outcome following arthritis onset is multidimensional as the disease can not only cause joint damage but can also affect extra-articular structures, such as the eyes and viscera. In relation to structural damage, there is a significant detrimental effect on function. The above factors and the associated psychological aspects of chronic disease will have generalized consequences on all aspects of quality of life.

There have been several studies assessing outcome but comparison between studies has been hindered by the lack, until recently, of a universally accepted classification method, given the differences in inclusion and exclusion criteria for the two previous widely used classification systems: EULAR (European League Against Rheumatism) and ACR (American College of Rheumatologists) [4, 5]. Most outcome studies therefore did not use the recently agreed ILAR (International League of Associations for Rheumatology) classification criteria [6] and its subsequent revisions [7–9]. Furthermore, older studies may be no longer relevant, given the shift towards earlier use of disease-modifying anti-rheumatic drugs and modulators of cytokines (biological agents), with a view to controlling disease activity, before the joint pathology becomes permanent [10–17]. Accurate estimation of outcome is of value not only for individual patient prognosis but also for rational service planning, as well as for providing a guide for those designing studies evaluating potential new interventions.

We have therefore reviewed the major published outcome studies in juvenile arthritis over the past 10 yr with the aim of providing the best estimates of the proportion of children achieving (i) disease remission, (ii) functional impairment and (iii) structural damage, after stratification into the main disease subtypes. With regard to variation in results, we have attempted to consider the impact of different methodological approaches, the magnitude of the latter precluding formal meta-analysis.

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Methods

Search strategy

Electronic databases (PubMed and Web of Science) were searched for the following keywords: juvenile arthritis (JIA, JCA, JRA), outcome, remission, prognosis, function, bone erosion, and the reference list of any relevant publication was further scrutinized.

Inclusion criteria and subgroup classification

Consideration was restricted to studies of outcome in childhood inflammatory arthritis, published in the last 10 yr. This interval was selected to restrict inclusion to those studies which observed children exposed to current therapeutic practices.

We also restricted inclusion only to those studies which provided data on disease subtype according to one of the recognized classification schemes. Thus, studies using ILAR, ACR and EULAR criteria were included. (It should be noted that the EULAR criteria stipulate persistence for 3 months whereas the first two require only 6 weeks.) In order to make the available results from different studies more comparable, we limited analysis to data from the following subtypes, which are common to all three classification systems:

(a) *Systemic*: those with systemic disease.
(b) *Persistent oligoarthritis*: patients who presented with fewer than five active joints which did not extend beyond four affected joints.
(c) *Extended oligoarthritis*: patients who had fewer than five active joints in the first 6 months since disease onset, which later spread to involve a greater number. (Many of the earlier studies grouped b and c collectively as 'pauciarticular'.)
(d) *Polyarthritis, rheumatoid factor-negative*: patients who had five or more active joints in the first six months since disease onset, and are persistently negative for rheumatoid factor (RF).
(e) *Polyarthritis, rheumatoid factor-positive*: similar criteria to d, but positive for RF.

Methodological description

We distinguished three types of studies: (i) true prospective cohort studies, which were designed *ab initio* to follow up all diagnosed children from disease presentation; (ii) retrospective cohort studies, which were able to identify an inception cohort of children from past records and assessed their current status but relied on standard medical records as opposed to standardized information on their status at presentation; and (iii) cross-sectional studies, which captured information only on those currently attending or known to the investigators. The majority of the studies reviewed fell into the last two categories, and by restricting their attention to those children under current follow-up, or a previous period of hospital attendance, would be biased towards those with more severe disease.

Outcome measures assessed

We identified data for three major outcomes: remission, function and structural damage. There was considerable heterogeneity in the approaches used to define all these, particularly for remission and functional loss. Remission was defined using a variety of criteria (e.g. ACR, EULAR, self-report). The proportion in remission for the chosen criteria was used. Health status, including measurements of quality of life, was not dealt with in great detail by most of the studies. Function, however, as one of its many facets, was reported more frequently. Functional limitation was derived from the inability of the patient to carry out activities of daily living, and vocational or educational tasks, as appropriate. Most of the studies used specific tools, such as the health assessment questionnaire (HAQ), the childhood HAQ (CHAQ) or Steinbrocker functional class. Given the variability in the approach to data presentation, we identified for each study the proportion with a disability index below a specific threshold or functional class. The major measures of structural outcomes were the presence of radiological damage and joint deformity, but other structural outcomes reported included joint surgery/replacement, uveitis and linear growth retardation. For the purposes of comparison all these features were also expressed dichotomously, based on their presence or absence at follow-up.

In addition to the variation in definitions used, for both cases and outcomes, there was also variability in the duration of follow-up from 4 to over 25 yr. These differences in the observation period added to the above-mentioned methodological differences between studies, making meta-analysis of their results very difficult.

Results

Overview of studies included

Table 1 shows the summary of 21 outcome studies published between 1995 and 2003. With the exception of five studies [18–22], in which two measurements were conducted, all the remaining studies provided only a single assessment of outcome and thus record state rather than change. The majority of the studies was small, with the number of children in each subgroup typically being below 50. One study [23] (and that only in part) was restricted to evaluation of new-onset cases (inception cohort) and only one other study [24] collected data prospectively. Sixteen studies were hospital-based, whilst prior population surveys provided the cases for the remaining five. Nine studies used the EULAR classification system, with the ACR and ILAR systems used in 10 and two reports, respectively. Patients were divided by subtype in 20 studies, though four were restricted to only one subtype. The remaining study did not provide information regarding patient subtype, although most (80%) patients had polyarticular disease. Seventeen publications measured function as outcome, with persistent disease activity/remission and structural damage reported in 15 and 11 studies, respectively. The follow-up period varied widely between studies, with short-term outcomes (<5 yr) reported in four, medium term (5–10 yr) in three and long term (>10 yr) outcomes in 14 studies.

Frequency of remission

Table 2 summarizes the results of the 13 studies which reported on remission rates. There are no agreed validated remission criteria for use in the paediatric rheumatology cohorts and the published reports relied on either ACR or EULAR criteria that had been designed for use in adult patient populations. Such criteria were used in five and three studies, respectively, whilst three studies used study-specific criteria, defined as absence of active joints, normal ESR, and not taking anti-rheumatic medications ($\geq$6 months [25] and $\geq$2 yr [26, 27]) as minimum requirements for remission. Two studies [26, 28] also required absence of uveitis in the same period. Table 2 includes remission rates from two studies combining all subtypes, one reporting a two-thirds higher rate than the other (56 *vs* 33%).

There is a very clear difference in remission rate between the different subgroups analysed within studies. There was a consistently reported higher remission rate in those with oligoarticular disease than in the other groups. The exception was one study [29], in which systemic and oligoarticular onset

TABLE 1. Key characteristics of outcome studies in childhood inflammatory arthritis

Reference	Design and classification	Recruitment period	Number in subtype: Oligoarthritis Persistent	Oligoarthritis Extended	Poly	Systemic	Total	Outcome recorded: Remission	Function	Structure	Follow-up Mean (range), yr
32, 37	Retrospective JCA	1986–1992	40	32	36	3	124	✓	✓	✓	7.1[b] (1.5–21.9)
38	Retrospective JRA	1960–1993	32[a]		8	4	44	×	✓	×	24.5[c] (7–38)
34, 39	Cross-sectional JRA	1958–1990	127[a]		55	45	227	×	✓	×	12.4[b] (5.3–36.1)
18	Retrospective JRA[1]	1985–1995	25	7	17	4	72	✓	✓	✓	9.7[b] (7.9–11.5)
33	Cross-sectional JRA	1995	45[a]		28	15	88	×	✓	×	N/A[b] (2.2–3.6)
27	Cross-sectional JCA	1996–1997	21	22	17	5	65	✓	✓	×	26.4[b] (N/A)
40	Cross-sectional JCA	Not stated					161	✓	✓	×	N/A
29	Retrospective JCA[2]	1980–1988	96	5	24	11	171	✓	✓	✓	7.4[c] (1–15)
26	Retrospective JIA	1988–1998	207[a]		N/A	N/A	207	✓	×	✓	4.2[c] (0.5–10)
36	Retrospective JRA	1980–1994	N/A	N/A	N/A	111	111	×	✓	×	7.7[c] (6.4–8)
35	Retrospective JRA	Since 1971	N/A	N/A	N/A	80	80	✓	✓	✓	10.7[c] (3–33)
19	Retrospective JCA	Not stated	N/A	N/A	N/A	91	91	✓	×	×	8.57[c] (3–23.9)
24	Prospective JCA[3]	1998	606[a]		216	108	1082	✓	✓	×	4[b] (N/A)
23	Prospective	1993–1995	24	4	10	2	47	✓	×	✓	4.1[b] (2.9–4.9)
	Cross-sectional JCA[4]		36	1	8	0	49				6.0[b] (3–12)
31	Retrospective JIA[5]	2001	15	55	78	2	246	✓	✓	✓	28.3[b] (8–73)
28	Prospective Cross-sectional JIA[6]	1978–1988	59	26	30	30	215	✓	✓	×	16.5[b] (10–30)
30	Retrospective Cross-sectional JRA	1974–1994	185	39	120	48	392	✓	✓	✓	10.5[b] (4.8–23.1)
20	Retrospective JRA	1980–1985	106	57	76	29	268	✓	✓	✓	14.9[b] (11.7–25.1)
21	Retrospective 2 measurements JRA	1992–1997	328	48	232	95	703	×	✓	✓	1 and 5
22	Retrospective Cross-sectional JRA	Not stated	97[a]		89	30	216	×	✓	✓	8.6[b] (1.9–19.2)
25	Retrospective Cross-sectional JCA[7]	1970–1998	420[a]		108	88	683	✓	×	×	10[b] (9.3–11.1)

N/A, not applicable. [1]Included 19 spondyloarthritis cases. [2]Included 18 spondyloarthritis, 1 psoriatic arthritis and 3 inflammatory bowel disease cases. [3]Included 87 spondyloarthritis and 65 psoriatic arthritis cases. [4]Included 7 and 4 spondyloarthritis cases in the 2 cohorts. [5]Included 32 early rheumatoid arthritis and 13 psoriatic arthritis cases. [6]Included 3 psoriatic arthritis, 33 enthesitis related arthritis and 34 other arthritis. [7]Included 67 spondyloarthritis. [a]Only onset subtypes reported. [b]Since disease onset. [c]Since presentation.

TABLE 2. Frequency of remission in reported studies

Reference	Remission criteria	Proportion in remission (%): Oligoarthritis Persistent	Oligoarthritis Extended	Polyarthritis RF$^+$	Polyarthritis RF$^-$	Systemic	Total
37	EULAR	51.5 (71.4[a])		20[b]			
18	ACR	84	28	65		0	
27	Study-defined	81	50	53		20	
40	N/A						56.3
29	ACR	47[c]		13		47	
26	Study-defined	36[c]					
35	EULAR					36	
24	NRS-11 (score 0)						33
23	EULAR						
	Incident cohort	66[c]		30			
	Cross-sectional group	53		33			
30	ACR	47[c]		6	23	37	39
28	ACR	73	12	0	30	47	40
	No drugs 2 months						
	No uveitis						
20	ACR	57	35	46	15	76	
25	Study-defined	43	13	18		33	33

[a]Subgroup with monoarticular-only disease. [b]Polyarticular course here includes extended oligoarticular subtype. [c]Oligoarticular onset.

had equal remission rates. There was, however, considerable variation across the studies in their reported remission rate for the oligoarticular subtype, which ranged from 36 to 84%. The oligoarticular group was stratified into persistent and extended subtypes in five studies. In each of these studies the remission rates were, not surprisingly perhaps, lower in the extended group, with a sixfold lower remission rate seen in one [28]. Given this difference, in the absence of this further subtyping in the other studies, the remission rate in the oligoarticular subtype remains unclear.

As stated, remission rates in the other subgroups were lower but the variation in remission rates was even greater in both the polyarticular (12.5–65%) and systemic (0–76%) subtypes. These two subgroups are more infrequent than the oligoarticular group and hence some of this variation will be random. In several of these studies, despite the small sample sizes, the differences between subgroups were statistically significant [18, 20, 29, 30].

There were, of course, other approaches adopted for measuring disease activity amongst the above studies, which included individual clinical and laboratory indices of disease activity. There was no consistency, amongst studies, in the markers used and hence comparisons are impossible.

Functional outcome

Table 3 summarizes the findings of 16 studies which reported on functional outcomes or disability indices (DI). There was variation in how function was measured, 11 studies using CHAQ or the adult HAQ and eight (including four that also used the HAQ/CHAQ) using Steinbrocker functional classification. The remaining study [24] used the Numeric Rating Scale (NRS-11), a patient/parent self-reported tool for measuring function and pain, based on using a discrete numerical scale (0 = very good, 10 = very bad). Not surprisingly, there were correlations between the scores between the Steinbrocker classification and the more discriminatory HAQ/CHAQ when both were evaluated [27, 28, 31, 32].

In interpreting the relative findings from these studies, the small numbers, as discussed above, will clearly impact on the robustness of the estimates obtained. There was a wide variation in terms of reported disability index/functional class and their relationship to the subtype onset or course. In general, the functional loss was lower in the oligoarticular subtype in 11 studies, which was statistically significant in seven, when compared with the other subtypes. Indeed, the frequency of severe disability was low in all studies in this subtype. By contrast, all nine studies reporting on functional outcome in the systemic subtype showed functional impairment in an important proportion of children. In one of the largest studies the proportion with severe disability (DI 1.5–3.0) was very high [31]. Further, the mean or median for disability score in the systemic subtype in seven studies was also high compared with all other groups [18, 21, 24, 30, 31, 33, 34], reaching statistical significance in three [18, 31, 34]. By contrast, one study reported lower CHAQ DI in females with systemic disease compared with polyarticular disease [32], although there was only one female with systemic disease in this cohort.

Even within the systemic group there may be differences in outcome. Thus, in a small study of 90 children Lomater *et al.* [35] separated three types of systemic disease according to severity at baseline: (i) single-episode disease ($n = 9$)

Table 3. Frequency of functional outcomes in reported studies

			Oligoarthritis		Polyarthritis			
Reference	Measure used	Category	Persistent	Extended	RF^+	RF^-	Systemic	Total
32	CHAQ DI							
		0						40%
		<0.5						32%
		0.5–1.5						22%
		>1.5						7%
	Steinbrocker class	I/II		100%[a]		95%	100%	97%
	Steinbrocker class	III/IV		0%		5%	0%	3%
38	HAQ DI							39%
	>0							
34	CHAQ/HAQ: mean			0.2[a]		0.4	0.4	0.3
18	CHAQ: median		0.0	0.6		0.0	0.6	
33	CHAQ: mean			0.30[a]		0.54	0.56	
27	HAQ DI	0		90%				36%[b]
		>0		10%				64%
	Steinbrocker class	I		100%				52%
	Steinbrocker class	II–IV		0%				48%
40	Steinbrocker class	III/IV						6.5%
29	Steinbrocker class	III/IV		7%		27%	19%	12%
36	CHAQ DI							
		<0.75					77%	
		≥0.75					23%	
35	Steinbrocker class	I					54%	
		II					18%	
		III					25%	
		IV					4%	
24	NRS-11: mean		1.1[c]			1.8	1.5	1.4
31	HAQ DI	<1.5	100%	58%	47%	50%	37.5%	
		1.5–3.0	0%	42%	53%	47%	62.5%	
20	HAQ DI	>0	22%	47%	46%	47%	Not shown	36%
21	Steinbrocker class	III and IV		0%[a]		12%	30%	
28	HAQ	DI	0.18	Not shown	0.54	0.39	0.27	0.22
	Steinbrocker class	III/IV						10%
	Steinbrocker class	I/II						35%
30	CHAQ DI	>1.5		1%	18%	8%	15%	Not shown
	Steinbrocker class	III/IV		0.5%	5%	3%	7%	Not shown

[a]Oligoarticular onset. [b]All other types combined. [c]Pauciarticular course. [d]Early-onset pauciarticular. [e]Late-onset pauciarticular.

(ii) intermittent fevers and arthritis interspersed with periods of remission ($n=27$); and (iii) persistent disease activity ($n=44$). These groups also differed in their outcomes at follow-up. Thus, all nine patients with subtype I disease were in functional class I compared with 78 and 61% in subtype II and III cases, respectively. Similar findings were observed by Spiegel *et al*. [36], who reported 85% of their 'low risk' and 50% of their 'high risk' systemic patients to have DI < 0.75. Eleven studies reported function in the polyarticular subtype. In two studies polyarticular onset had significantly worse functional outcome than oligoarticular course [20, 31]. This observation included both RF^+ and RF^- polyarticular subtypes in the former, a large Norwegian study, though the difference in the latter study was limited to the RF^- subgroup. This was probably due to lack of power rather than any obvious difference between these two RF-derived subgroups. In another study [32] polyarticular onset was also associated with an increased likelihood of a worse function; however, this was only observed in the female cases.

Structural outcomes

Table 4 presents the proportions with radiological erosion reported in the small number of the above studies with available data. Given the paediatric nature of the population, it was not surprising that radiological examination was not carried out routinely in any study, but only when clinically indicated or before intra-articular corticosteroid injection [26]. There was a variation in the radiographic classification systems used: the Dale was adopted in three reports [18, 20, 26], whilst Steinbrocker was used in one [29]. One of the remaining studies employed a two-class system based on the early (class I) or late (class II) radiological changes [23], whilst the remaining study did not use a predefined system. As with the other outcomes, oligoarticular disease was consistently found to have a lower risk of erosions, this difference being highly significant in three studies [18, 20, 22]. The prevalence of erosions in the oligoarticular group was very low in most, but not all, of the studies. By contrast, the RF^+ polyarticular group was associated with high prevalence of erosive disease, which was 100% in the admittedly small Norwegian study [18]. The cumulative prevalence of erosive disease in systemic onset is unclear, with substantial variation amongst predominantly small sample sizes, precluding useful comment.

Other structural outcomes were reported in some studies. Linear growth was found to be retarded in the patient cohort studied by Packham and Hall [31] when compared with the normal population, whilst another study [32] reported normal values. Two other studies [18, 29] reported relatively high percentages (9 and 6%, respectively) of short stature in their patients. The influence of subgroup on this is, however, unclear. Uveitis was more frequent in oligoarticular ($P<0.05$) and extended oligoarticular ($P<0.001$) subtypes, and lower in systemic and (RF^+) polyarticular subtypes ($P<0.005$), when compared against the rest of the cohort [31]. Other studies did not provide statistically significant results, although the rate of uveitis in one study was very similar between subgroups [37]. One study found similar rates of uveitis between oligoarticular and extended oligoarticular JIA, with an overall risk of 30% after 4 yr disease [26].

Discussion

Our aim was to determine whether the currently available data were sufficiently robust to provide a guide as to outcome following the onset of JIA. A separate objective was to evaluate whether the disease subtype as defined in standard classification systems had a major influence on outcome. The most consistent conclusion was that those with an oligoarticular course have a better prognosis in terms of higher remission rates, better functional outcome and lower rate of erosive damage in most of the studies.

The available data vary widely and this variation is likely to be explained, perhaps not surprisingly, by differences in case definition, method of outcome assessment and duration of follow-up. In addition there are likely to be differences in patient selection, especially within subgroups, and in therapy and management policies, all of which could have influenced outcome.

The absence of universal remission criteria suitable for use in a paediatric population makes comparison between studies very difficult. The two remission criteria more commonly used amongst the studies reviewed were those formulated by EULAR and ACR. The ACR criteria, if strictly applied, can be more difficult to meet. Remission is defined by the presence of subjective reports, such as less than 15 min early morning stiffness, no fatigue, no joint pain, and no joint tenderness, but it does not take into account the presence or absence of drug treatment. The presence of remission using the EULAR criteria is determined from the active joint count, the presence of extra-articular manifestations of arthritis, and the nature of drug

Table 4. Frequency of erosions in reported studies

	Prevalence of erosions (%)					
	Oligoarticular		Polyarticular			
Reference	Persistent	Extended	RF^-	RF^+	Systemic	Total
18	4	43	100	7	100	23
29	15.5[a,b]		57.1[b]		45.5[b]	
26	35					
23						
Incidence cohort						4[c]
Cross-sectional cohort						2[c]
22						
Within 2 yr of onset	9		56	16	35	
>2 yr since onset	26		75	39	63	
20	5	33	40	77	14	24

[a]Oligoarticular onset. [b]Steinbrocker radiological classes 3 and 4 (erosions exceeding 2/3 joint-area, joint destruction, bony ankylosis). [c]Class II radiological changes (cartilage destruction, bone destruction, bony ankylosis, large joint subluxation, epiphyseal fracture, vertebral compression fracture).

treatment. These latter criteria, therefore, use more objective information.

There was a wide range in the reported remission rates within the oligoarticular subtype, although the numbers studied in all of the above reports were very small. The two lowest reported rates (36 and 47%) were those from studies [26, 29] using onset subtypes to categorize their patients, their groups almost certainly containing mixed cases of persistent and extended oligoarticular disease. In those studies restricted to persistent oligoarticular cases, the lowest remission rate (43%) was observed in the only study using self-defined remission criteria [25]. Interestingly the latter were less stringent, requiring duration of remission of only 6 months compared with the 2 yr used in the other reports. The two highest remission rates (84 and 81%) were reported by studies [18, 27] with relatively long follow-up periods (10 and 26 yr, respectively). This was not a universal observation as one study with 15 yr of follow-up [20] reported a lower (57%) remission rate. The differences between the four studies reporting remission rates amongst the extended oligoarticular cases could not be explained by the remission criteria used, as the highest rate corresponded to the study with the most restrictive criteria. It is possible that the relatively high loss to follow-up rate in the study with higher remission rate [27] may be responsible. Indeed, in another study there was a significantly lower remission rate in their study cases compared with those lost to follow-up [25].

Wide variation in the reported remission rates was not limited to the oligoarticular onset subtype, and was seen in both the polyarticular and systemic onset subgroups. The lowest remission rates in systemic disease (0%, 20%) were also only reported in the two studies [18, 27] with tiny numbers of cases: four and five, respectively. Small case number may not be the only reason for the inconsistency, as the two studies [20, 35] with the largest numbers (29 and 80) also showed a substantial variation in their remission rates (36 and 76%). One possible explanation for this is the difference in the definitions used for remission, the former study using ACR and the latter using EULAR remission criteria.

The majority of the studies used CHAQ or HAQ to assess functional outcome, with the Steinbrocker functional classification system used in only a few studies. This latter system clearly lacks discrimination in terms of both the type of functional impairment and identifying small changes in disability, making comparisons with other studies or even within the same study speculative at best. The systemic disease subgroup had significantly greater impaired function [18, 31, 34], although, the actual disability levels varied substantially between studies. The highest rate of disability reported [31] is probably attributed to a high selection bias, that study being based upon prevalent cases; hence patients with more severe disease were more likely to continue to have been seen at the hospital. In only one study was polyarticular onset found [18] to have significantly better function than extended oligoarticular and systemic subtypes.

Variability was also observed in the reported erosion rates in the studies examined. The highest overall rate of erosive disease in one study [26] is probably the result of including a disproportionately high number of extended oligoarticular cases (50%). This is in contrast to the study with the lowest erosion rate, which included only 5% with polyarticular disease [29]. Subtype distribution alone could not explain the disparity in results, given the wide variation observed when the rates of erosive disease were compared within subtype between studies [18, 20]. Thus the erosion rate in one study [20] was considerably lower in the systemic compared with the polyarticular subgroups, whereas no difference was observed between these same two groups in another study.

Some of the variability observed between studies may, of course, be real, reflecting true differences in genetic and environmental factors between the cohorts studied. Furthermore, the influence of therapy was not assessed in these observational studies but is likely to have had some influence on the outcomes measured. There remains, therefore, a considerable lack of clarity about the prognosis following the onset of JIA, both in total and by subgroup.

We deliberately restricted our consideration to publications from the past 10 yr in an attempt to make the conclusions relevant to modern therapeutic regimes. However, there has been a recent proliferation in the use of new biological agents, such as tumour necrosis factor α (TNF-α) inhibitors, which might be expected to influence the outcome in children in those subtypes with poor prognosis. Thus, further studies are required to consider the impact of such regimes on disease outcome.

In summary, for all the reasons stated above there is a need for studies that are (i) prospectively designed, with cases ascertained soon after disease onset to enhance data quality in terms of standardization and completeness of both predictors and outcomes; ideally, such studies should aim to capture all incident cases within a target geographical population; (ii) of appropriately large size to provide numbers in each of the subtypes of interest to provide sufficient statistical power; this will probably require multicentre recruitment; (iii) use standardized classification schemes to ensure homogeneity of the selected cases and allow comparison with other studies; and (iv) use well-validated instruments and universally accepted criteria to measure remission, radiological damage and health status outcomes, including function and quality of life.

The onset of inflammatory arthritis is a major source of anxiety for the affected child and the family and it is particularly important to be able to give accurate information, both to provide reassurance where appropriate and guide the targeted use of effective but potentially toxic therapies to those most at risk.

The authors have declared no conflicts of interest.

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