

# Worldwide Prevalence of Juvenile Arthritis — Why Does It Vary So Much?

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**ABSTRACT. Objective.** To review epidemiological studies of childhood arthritis from 1966, and to identify possible reasons for the wide-ranging results for both prevalence and incidence of juvenile arthritis (JA). JA is the term used here collectively for juvenile rheumatoid arthritis, juvenile chronic arthritis, or juvenile idiopathic arthritis as defined in the respective published studies.

**Methods.** A review of 34 epidemiological studies of JA since 1966 was undertaken.

**Results.** Prevalence of JA is reported as 0.07 to 4.01 per 1000 children. Annual incidence is reported as 0.008 to 0.226 per 1000 children. The major factors contributing to differences in estimates include (1) factors due to diagnostic difficulties, to the development of new diagnostic criteria, and to the differing definitions of clinical cases; (2) differences in case ascertainment (community based versus clinical case studies, qualification and experience of study clinicians, definition of study population); (3) factors occurring with the passage of time, i.e., standard of living, health care resources, and increasing knowledge; and (4) small studies and hence more chance fluctuation. The major variation in reported prevalence was due to the difference between true community based studies involving children from within classrooms or homes (and not necessarily previously diagnosed with JA) compared with clinical case studies of children who (by definition) had been previously diagnosed. The highest prevalence was reported for true community based studies.

**Conclusion.** Many factors contribute to the discrepancies between reported prevalence and incidence for JA. Studies based truly in the community reported the highest prevalence, as previously undiagnosed cases were included. Future studies involving standardized criteria and standardized case ascertainment done by fully trained clinicians should show greater consistency of results. (J Rheumatol 2002;29:1520–30)

Key Indexing Terms:

JUVENILE ARTHRITIS      EPIDEMIOLOGY      PREVALENCE      INCIDENCE

The epidemiology of chronic diseases becomes increasingly important with the intense competition for health care resources allocated on the basis of perceived need. There has been considerable interest in the epidemiology of rheumatic diseases of children recently, and many epidemiological studies have been performed particularly in juvenile arthritis (JA), the most common rheumatological disease in children.

The range of results of these studies is too wide to be due solely to true differences between various populations throughout the world, and from true changes over time. Of the many epidemiological studies of JA reported, there was found to be great diversity in the design and methods used in the studies and also in the living conditions and expecta-

tions of health of the times. So great was this diversity that comparisons between studies could only be made in a limited way.

## MATERIALS AND METHODS

Medline and Excerpta Medica were searched under the terms of epidemiology, incidence, prevalence, juvenile rheumatoid arthritis (JRA), juvenile chronic arthritis (JCA), and juvenile idiopathic arthritis (JIA) with articles written in English or at least with abstracts written in English. Further, articles were sought, where reference was made in electronically listed articles, to additional articles not found through electronic searches.

## RESULTS

The results from 34 epidemiological studies cover a wide range for both prevalence and incidence. The reported prevalence of JA was from 0.07 to 4.01 per 1000 children, a greater than 50-fold difference between the extremes<sup>1-25</sup>. Incidence was reported from 0.008 to 0.226 per 1000 children per year<sup>8,10-13,15,16,18,21-23,25-34</sup>, a factor of 28 between the lowest and highest estimate (Table 1).

The major factors found to be causing the wide-ranging results fell into 4 categories: (1) factors due to diagnostic difficulties, to the development of new diagnostic criteria, and to the differing definitions of clinical cases; (2) differing means of case ascertainment (community based versus clinical case studies, qualification and experience of the clini-

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Table 1. Epidemiological studies of juvenile arthritis 1966-98.

Author	District	Case Ascertainment	JRA/JCA	Maximum Age, yrs	Number of Prevalent Cases	Prevalence Per 1000	Prevalence 95% CI	AI per 1000
Laaksonen, 1966 <sup>26</sup>	Finland	Hospital attendance	JRA	15				0.06-0.08
Bywaters, 1968 <sup>1</sup>	Taplow, UK	Hospital attendance	JCA	15	43	0.65	0.42-0.88	
Sullivan, 1975 <sup>2</sup>	Michigan	Hospital attendance	JRA	15		0.092		
Rodary, 1977 <sup>3</sup>	France	Hospital attendance	JCA	15		0.08		
Hicks, 1977 <sup>4</sup>	Hawaii	Clinic attendance	JRA		58	0.21	0.16-0.27	
Arendarczyk, 1977 <sup>5</sup>	Poland	Records	JRA			0.07		
Pless, 1977 <sup>6</sup>	Genesee, NY	Pediatrician questionnaire	Arth* (JRA)			1.10 <sup>†</sup> (0.55)		
Rosenberg, 1982 <sup>7</sup>	Western Canada	Clinic attendance	JRA	16	17 75	(i) 0.36, (ii) 0.20	(i) 0.21-0.58, (ii) 0.16-0.25	
Towner, 1983 <sup>8</sup>	Rochester, MN (i) 1970, (ii) 1980	Hospital attendance	JRA	18	(i) 16, (ii) 15	(i) 0.96, (ii) 1.13	(i) 0.55-1.55, (ii) 0.69-1.96	0.139
Towner, 1983 <sup>8</sup>	Rochester MN (i) 1970, (ii) 1980	Hospital attendance	JCA	18	(i) 14, (ii) 11	(i) 0.86, (ii) 0.84	(i) 0.46-1.50, (ii) 0.46-1.40	0.108
Gewanter, 1983 <sup>9</sup>	Monroe County, NY	(i) National Center Health Statistics, (ii) practitioner survey, (iii) hospital attendance	JRA	16	2 3 55	(i) 0.21, (ii) 0.16, (iii) 0.27	(i) 0.0-0.36, (ii) 0.0-0.35, (iii) 0.2-0.34	
Hochberg, 1983 <sup>10</sup>	Baltimore (Black)	Hospital attendance	JRA	17	4	0.26	0.07-0.63	0.066
Kunnamo, 1986 <sup>11</sup>	Helsinki	Primary care physician, specialist attendance	JRA	15				0.196
Prieur, 1987 <sup>12</sup>	(i) Western Paris, (ii) Brittany	Hospital and specialist attendance	JCA	15	74 62	(i) 0.077, (ii) 0.100	(i) 0.061-0.096, (ii) 0.077-0.13	(i) 0.019, (ii) 0.013
Andersson Gare, 1987 <sup>13</sup>	Western Sweden	Hospital and specialist attendance	JCA	15	223	0.56	0.49-0.63	0.12
Boyer, 1988 <sup>34</sup>	Alaska (Inupiat Eskimo)	Hospital records	Arth**	15				0.28
Boyer 1990 <sup>14</sup>	Alaska (Yupik Eskimo)	Hospital records	JRA Arth**	15 15				0.0531 0.425
Khuffash, 1990 <sup>15</sup>	Kuwait	Hospital attendance	JCA	12	108	0.187	0.153-0.226	0.0284
Boyer, 1991 <sup>25</sup>	Alaska (Southeast Indian)	Hospital records	Arth**	16	5	1.38	0.45-3.14	0.386
Steven, 1992 <sup>24</sup>	Scotland	Practitioner attendance & records	JCA	15	16	2.0	1.14-3.23	

Table 1. continued

Author	District	Case Ascertainment	JRA/JCA	Maximum Age, yrs	Number of Prevalent Cases	Prevalence Per 1000	Prevalence 95% CI	AI per 1000
Andersson Gare, 1992 <sup>16</sup>	Southwest Sweden	Hospital & specialist attendance	JCA	15	334	0.863	0.77–0.96	0.109
Mielants, 1993 <sup>17</sup>	Belgium	Parent questionnaire, clinical exam in schools	JCA	18	5	1.67	0.54–3.81	
Oen, 1995 <sup>27</sup>	Manitoba, Canada	Hospital attendance	JRA	15				0.0534
Arguedas, 1995 <sup>28</sup>	Costa Rica	Referral from physicians to study	JCA	15				0.054
Malleison, 1996 <sup>29</sup>	Canada	Attendance at 13 centers	JRA	16				0.0239
Symmons, 1996 <sup>30</sup>	UK	Attendance at 2 centers	JCA	15				0.10
Peterson, 1996 <sup>18</sup>	Rochester, MN	Hospital records	JCA	15	65	1980: (i) 0.943, 1990: (ii) 0.861	(i) 0.41–1.48, (ii) 0.37–1.35	1960–69: 0.150, 1970–79: 0.141, 1980–93: 0.078, 0.14
Kaipiainen-Seppanen, 1996 <sup>31</sup>	Finland	Sickness Insurance records	JRA	15				
Manners, 1996 <sup>19</sup>	Australia	Community	JCA	12	9	4.01	1.84–7.53	
Fujikawa, 1997 <sup>33</sup>	Japan	Questionnaire to hospitals	JRA	15				0.0083
Ozen, 1998 <sup>20</sup>	Turkey	Parent questionnaire, clinical exam in homes	JCA	15	30	0.64	0.43–0.91	
Moe, 1998 <sup>21</sup>	Norway	Disease registry records	JCA	15	71	1.481	1.15–1.87	0.226
Kiessling, 1998 <sup>22</sup>	Germany	Hospital records	JCA	15	50.2 (mean over 9 years)	0.20	1.66–2.47	0.035
Arguedas, 1998 <sup>23</sup>	Costa Rica	Referral from physicians to study	JCA	15	122	0.349	0.289–0.416	0.068

AI: Annual Incidence. \* Unspecified arthritis in children. \*\* JRA and spondyloarthritis. † Corrected approximate estimate of prevalence for JRA was 0.55 per 1000.

cians involved, definition of study population); (3) factors occurring with the passage of time, i.e., standard of living, health care resources, and increasing knowledge; and (4) small studies leading to chance variation in rates.

*Factors due to diagnostic difficulties, to development of new diagnostic criteria, and to the differing definition of clinical cases.* A basic requirement for good epidemiological studies is a clear, consistent, and reproducible definition of a case. This proves to be difficult for JA for a number of reasons.

First, there are no laboratory tests to confirm a diagnosis of JA. There remains a widespread mistaken perception that the presence of rheumatoid factor is a useful diagnostic marker for JA<sup>35</sup>, even though it occurs in less than 10% of children with JA<sup>36–38</sup>. JA is a diagnosis of exclusion and thus

a multitude of other conditions must first be considered and excluded. The more common of these include osteomyelitis, septic arthritis, leukemia, other malignancies, viral arthritis, trauma, other autoimmune diseases, hemarthroses, rheumatic fever, Henoch-Schönlein purpura, irritable hip, “growing pains,” mechanical joint problems, Perthes’ disease, and psychosomatic illness. There is often an insidious onset of JA, which may cause children little pain and contribute to delay in diagnosis or to a completely missed diagnosis<sup>23,39</sup>. Disease expression is diverse, and at times the clinical signs of the condition, such as swelling, may be subtle and difficult to diagnose.

Second, the changing definition of diagnostic criteria for JRA, JCA, and more recently JIA made study results diffi-

cult to compare with any accuracy. Studies that investigated the effect of differing diagnostic criteria for the study cohort include that of Rosenberg, *et al* in 1982<sup>7</sup> and Towner, *et al* in 1983<sup>8</sup>. Prior to 1977 there had been few formal recommendations for diagnostic criteria and there was a tendency for different diagnostic criteria to be formulated for each individual study. In 1977, 2 sets of criteria were formulated, the European criteria (European League Against Rheumatism, EULAR) for JCA<sup>40</sup> and the North American criteria (American College of Rheumatology, ACR) for JRA<sup>41</sup>. There were some similarities and each defined the 16th birthday as the upper age limit at onset. The EULAR criteria for JCA included the spondyloarthropathies and required disease to have been present for 12 weeks. The ACR criteria for JRA excluded the spondyloarthropathies, and required only 6 weeks of joint inflammation for a diagnosis. Following 1977, many studies would use either JRA or JCA as defined, but some studies continued to use a mixture of both or some other set of criteria. In 1995, an international committee with representatives from Europe, Africa, America, and Asia was constituted to review the classification and diagnostic features of childhood arthritis and a new uniform set of criteria was proposed<sup>42</sup>. These were later modified and published in 1997<sup>43</sup>. These criteria have provided some uniformity for future studies, but may need modification as understanding of the disease increases.

Third, for some studies, precision and standardization of the clinical case definition for inclusion were lacking, which compounded the problem of comparability of studies. For example, some studies included only active cases of JA; some failed to define whether inactive cases were included or not. This issue was addressed in the studies of Towner, *et al* in 1983<sup>8</sup>, Andersson Gare and Fasth in 1992<sup>16</sup>, and Mielants, *et al* in 1993<sup>17</sup>. It is sometimes difficult to know whether a particular child's JA has become inactive and experienced clinical judgment is often needed to differentiate between active and inactive disease.

Finally, the upper age limit of children in past studies varied between 12 and 18 years (Table 1). Since many children first manifest JA between the ages of 12 and 16 years, prevalence will be underestimated where the upper limit is 12 years. JA by current definition begins before the 16th birthday. Where studies have included children to the age of 18 years, there may be an overestimation of prevalence if onset of arthritis occurred after the 16th birthday, and additionally a higher proportion of the population will be included in the estimates. Thus, upper age limit for studies may have a major effect on results and further compromise comparability between studies.

*Differences in case ascertainment.* Case ascertainment varies with the type of study and with the level of skill and experience of the clinicians, since diagnosis is clinical, and is not based on laboratory tests. The precision with which a study population is defined also affects case ascertainment.

Community studies (i.e., of children in classrooms or homes) will include children who have not been previously diagnosed. There is evidence that the number of undiagnosed children in a community may be considerable<sup>17,19,39</sup>. It is therefore not unexpected that community based studies show significantly higher prevalence rates than clinical case studies, as in the studies of Mielants, *et al*<sup>17</sup> and Manners and Diepeveen<sup>19</sup>. However, if studies are conducted in classrooms, due consideration must be given to the potential for bias. For example, school attendance may not be compulsory for all children in some populations and certain sectors are at risk for being excluded, e.g., female children or children from economically disadvantaged families. However, clinical case studies have the potential for similar bias, where, for example, medical help may not be sought equally for male and female children, where resources of a family may be limited. This may possibly have been a factor in the study of Khuffash, *et al*<sup>15</sup>, where female children seemed to be significantly underrepresented in the cohort with disease compared with most other studies.

Studies depending on surveys of children, or their parents, or of hospital or practitioners' notes may introduce certain biases such as the ability of the parents to answer questionnaires, language barriers, lack of complaint of symptoms in the child, and quality of note keeping within medical filing systems. Surveys have many different forms, and may consist of questionnaire surveys, medical record surveys, phone interview surveys, or surveys of samples of each of these. The accuracy and quality of a survey can only reflect the accuracy and quality of the notes, the questionnaires, or the memories of those surveyed. Comparing such studies with each other is therefore fraught with many difficulties and potential inaccuracies. In addition, in such studies, undiagnosed children are not included (by definition) and thus the results will be less than for true community based studies.

Ultimately in all studies of JA, a clinician's decision is required to make a diagnosis. The range of clinicians who are responsible for diagnosing children in various studies include nurses, medical students, family doctors, pediatricians, pediatric rheumatologists, and other specialists. Differing levels of skill and experience in these groups of people will affect the accuracy of the diagnoses, and will be reflected in the results reported in the various studies. This issue was investigated in the studies of Arguedas, *et al* in 1998<sup>23</sup> and Kiessling, *et al* in 1998<sup>22</sup>, where the effect of differing qualifications of types of clinicians involved in case ascertainment was assessed.

Clear definition of a study population is a prerequisite for precise case ascertainment. Where a population is mobile, and has several possible facilities at different locations for the provision of medical attention, there will be difficulty in defining the true numbers within the study population, particularly for clinical case studies. This issue was

addressed in the study of Oen, *et al* in 1995<sup>27</sup>, where it was postulated that some children may have presented to medical centers in neighboring provinces, contributing to underestimation of clinical cases. Studies such as that of Hicks<sup>4</sup>, of a relatively isolated population of children in Hawaii, allow better definition of a study population. The problem of defining a constant study population increases with time, as there are increasing tendencies for families to travel. The isolated well defined study population is becoming increasingly hard to find.

*Factors occurring with the passage of time.* Over time, there have been changes in standards of living and an increased expectation of good health, particularly for children. It is likely, though difficult to prove, that musculoskeletal problems of children in times past were not necessarily brought to medical attention as readily as in current times, as there was little knowledge within the medical profession regarding childhood arthritis, and even less knowledge within the lay community. Parents may have been unaware of a possible diagnosis of childhood arthritis, particularly where symptoms were minimal, as has been documented for some children with arthritis<sup>39</sup>. Medical services were less accessible to ordinary people and parents less likely to seek medical advice for their child, particularly where there were few systemic symptoms. For these reasons, it could be argued that the level of undiagnosed arthritis is likely to have been higher in children in former times. In addition, chronic illness did not have a high priority with regard to allocation of health care resources. Previously, it was only possible to attend to seriously ill children with acute illnesses such as gastroenteritis and pneumonia from which they were likely to die. This situation still exists in some developing countries. Further, there was little knowledge or awareness of childhood arthritis in earlier times. As knowledge, awareness, and medical resources have increased, childhood arthritis is diagnosed more frequently and an apparent increase in prevalence and incidence is likely to be due, at least in part, to these factors.

*Small studies.* Many of the studies are based on small study populations and small numbers of cases, and hence the calculated incidence and/or prevalence are subject to considerable random fluctuation. For each of the studies reviewed, 95% confidence intervals have been calculated (based on a Poisson distribution), where the relevant data were available.

The 34 studies identified for this review are summarized in Table 1 and discussed individually in more detail below.

In 1966, Laaksonen<sup>26</sup> reported an annual incidence of 0.06–0.08 per 1000 for JRA in Finland based on 544 cases identified from hospital records. The author had personally examined 372 of these cases.

Case ascertainment: Attendance at specialist clinic.

Prospective study.

Special features: Longterm followup study and first significant epidemiological study of JRA.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community.

In 1968, Bywaters and Ansell<sup>1</sup> reported a prevalence of 0.65 per 1000 for JCA at the Taplow Canadian Red Cross Memorial Hospital, this being a referral center and inpatient facility at the time, for all British children with rheumatic disorders. Prevalence was estimated on local children, with 66,000 children living within a 6 mile radius of the hospital, of whom 43 had presented to Taplow with JCA.

Case ascertainment: Clinical cases, referral to specialist hospital center. Retrospective study.

Special features: First study of children with arthritis from a unit dedicated to the care of children with arthritis.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral from primary care practitioners.

In 1975, Sullivan, *et al*<sup>2</sup> reported an incidence of 0.092 per 1000 in Michigan, based on numbers of children seen in a clinic for children with arthritis. It was noted that the further children came to attend the specialist clinic, the more serious was the disease. Children with less serious disease may have been less likely to travel greater distances for medical attention.

Case ascertainment: Clinical cases referred to specialist clinic. Prospective study.

Special features: Analysis of subgroups in relation to proximity to specialist referral center. Analysis of age of onset and other variables.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral from primary care practitioners.

In 1977, Rodary, *et al*<sup>3</sup> reported a prevalence of JA in France of 0.08 per 1000 children on a sample survey from hospital patients that was restricted to hospital inpatients.

Case ascertainment: Sample survey. Retrospective study.

Special features: First study of French children.

Potential weakness: Possible incomplete case ascertainment due to undiagnosed cases in the community and cases not requiring inpatient hospital care.

In 1977, Hicks<sup>4</sup> reported a prevalence of 0.21 per 1000 based on 58 children she reviewed with JRA from a childhood population of 282,000 in Hawaii.

Case ascertainment: Clinical cases seen by single observer.

Prospective study.

Special features: Isolated community ideal for epidemiological studies. Single clinician as researcher.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community.

In 1977, Arendarczyk<sup>5</sup> reported a prevalence of JRA in Poland to be 0.07 per 1000 estimated from the records of the Central Institute in Warsaw.

Case ascertainment: Clinical case records. Retrospective study.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community, and cases diagnosed elsewhere and possibly omitted from a central disease register.

In 1977, Baum<sup>6</sup> reported a prevalence of all types of childhood arthritis of 1.1 per 1000, these data being obtained from practitioner questionnaires performed in the Genesee region of New York State, with trained interviewers visiting 82 pediatricians (primary care givers) in the area. Practitioner studies reported by Gewanter, *et al*<sup>9</sup> estimated of all childhood arthritis, 50% would be JA. Kunnamo, *et al*<sup>11</sup> found of all childhood arthritis, only 17.5% were JA. Thus the true prevalence of JRA in contrast to childhood arthritis may have been significantly less than 1.1 per 1000.

Case ascertainment: Physician interview by trained interviewers re: past and current patients. Retrospective study.

Special features: 82 primary care practitioners interviewed.

Potential weakness: Inclusion of children with all kinds of arthritis, not just JA, thus overestimation. Dependent on physician recall, with possible incomplete recall. Possible underestimation of numbers due to undiagnosed cases in the community.

In 1982, Rosenberg, *et al*<sup>7</sup> studied the prevalence of JRA in Indian children attending specialist clinics in Winnipeg and Vancouver from a total population of 46,707 Indian children and compared these with Caucasian children attending the same clinics. The prevalence for JRA in the Indian children was estimated to be 0.36 and for Caucasian children 0.20 per 1000, with a higher percentage of Indian children having rheumatoid factor present (35.7% vs 9.1%). Caucasian children had a higher prevalence of spondyloarthritis even though it had been defined that the Indian population had a higher prevalence for the presence of HLA-B27 antigen.

Case ascertainment: Attendance at specialist clinic.

Prospective study.

Special features: Comparison between 2 different racial groups.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community, which may differ between the 2 racial groups.

In 1983, Towner, *et al*<sup>8</sup> reported the prevalence of child-

hood arthritis at 2 different times in the same community, Rochester, Minnesota, USA, 10 years apart and compared the difference between prevalence of JRA and JCA for the same cohort of children. In 1970, the prevalence of JRA and JCA was reported as 0.96 and 0.86, respectively, within a population of 16,749 children. Ten years later the prevalence was reported as 1.13 and 0.84 per 1000 for JRA and JCA, respectively, within a population of 13,234 children. The annual incidence reported for JRA was 0.139 per 1000 and for JCA 0.108 per 1000. There was no inclusion of cases that may have fitted the criteria for JCA but not for JRA, of which there may have been some, since only JCA includes spondyloarthropathies.

Case ascertainment: Clinical case records. Retrospective study.

Special features: Comparison in same cohort between the diagnoses of JCA and JRA. Comparison of same cohort, 10 years apart. Analysis of differences between active and inactive disease.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and cases not clinically confirmed by authors.

In 1983, Gewanter, *et al*<sup>9</sup> reported a prevalence of JRA of between 0.2 and 1.0 per 1000 children based on 3 sets of data from records or from interviews of pediatricians: (1) a national survey using the 1978 National Ambulatory Medical Care Survey data; (2) a survey of 30 pediatricians, randomly chosen, in Monroe County, New York State; and (3) a study of children attending Strong Memorial Hospital Pediatric Arthritis Clinic.

Case ascertainment: Three separate sources: survey data, from physician interviews and from clinic attendance.

Retrospective study.

Special features: Large numbers of children.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community, or nonreferral of mild cases by primary care practitioners.

In 1983, Hochberg, *et al*<sup>10</sup> reported the prevalence (0.26 per 1000) and annual incidence (0.066 per 1000) of JRA in 15,816 urban black children in Baltimore, USA, with the aim of determining whether JRA was increased in this racial group of children. Case ascertainment was based on numbers of children with newly diagnosed JRA admitted to Johns Hopkins Hospital or Baltimore City Hospital, or who attended as outpatients at Johns Hopkins Pediatric Arthritis Clinic or outpatient clinics associated with the East Baltimore Medical Plan for the years 1979 and 1980. They concluded neither prevalence nor incidence was increased for this particular group of children.

Case ascertainment: Hospital case records and attendance.

Prospective study.

Special features: Comparison between racial groups.

Potential weakness: Small numbers. Possible underestimation of numbers due to undiagnosed cases in the community, particularly of poorer black children.

In 1986, Kunnamo, *et al*<sup>11</sup> reported an annual incidence of 1.085 per 1000 for all types of arthritis in children and 0.196 per 1000 for JRA in an area of Finland, in which there was cooperation of colleagues from several medical disciplines with all children who presented with swelling or limitation of one or more joints, with limping or hip pain being referred to the study team immediately, and with 71% of 157 children being seen within one week of the alleged onset of symptoms. Only 16.8% fulfilled the criteria for JRA (with arthritis of at least 6 weeks' duration) and 17.4% had arthritis for more than 3 months' duration.

Case ascertainment: Clinical cases referred to study.  
Prospective study.

Special features: All incident cases examined by study team at time of onset. All cases of arthritis reviewed by trained practitioners, and those with JRA carefully defined.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community.

In 1987, Prieur, *et al*<sup>12</sup> compared the epidemiology of JCA in 2 districts of France, a section of Paris and an area of Brittany, with letters sent to 2098 doctors in Paris and to 280 in Brittany, followed by second letters and then telephone calls. Physicians completed questionnaires on all children with JCA. The reported prevalence for the 2 districts was 0.077 and 0.100 per 1000 children, respectively, with incidence of 0.019 and 0.013 per 1000 children per year; with 964,284 and 618,136 being the total number of children living in the 2 respective areas.

Case ascertainment: Mail and phone interview of practitioners. Retrospective study.

Special features: Comparison of 2 differing areas of France. Analysis of subgroups. Longterm disability data.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and incomplete physician recall.

In 1987, Andersson Gare, *et al*<sup>13</sup> reported a study performed in Western Sweden with JCA case ascertainment from 8 hospitals and community pediatricians serving an estimated 400,600 children. The prevalence of JCA was reported as 0.56 per 1000. The annual incidence estimated over a 9 month period was found to be 0.12 per 1000.

Case ascertainment: Clinical cases attending 8 hospitals, and case records of community pediatricians. Prospective study.

Special features: Analysis of subgroups.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral by primary care practitioners.

In 1988, 1990, and 1991, Boyer, *et al* in 3 separate studies<sup>14,25,34</sup> reported incidence of JA per 1000 of 0.28 for Inupiat Eskimo children, 0.425 for Yupik Eskimo children, and 0.386 for Southeastern Alaska Indian children. For the latter, there was a total population of 4587 children. Prevalence for this group was estimated to be 1.38 per 1000 children for active and inactive disease. For active disease only, with inactive excluded, prevalence was 0.83 per 1000. For the 3 studies, JA was defined as JRA or spondyloarthropathy beginning in children less than 16 years of age. For the 1990 study of Yupik Eskimo children, there were a total of 24 children with JA, of whom only 3 fulfilled the criteria for JRA, and 21 had spondyloarthropathy, this being a significantly higher proportion than in most populations of children.

Case ascertainment: Clinical case records. Retrospective studies.

Special features: Studies of 3 defined races of Alaskan children. Comparison of data for active and inactive disease.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community. Small population sizes.

In 1990, Khuffash, *et al*<sup>15</sup> reported a prevalence of 0.187 per 1000 for JCA in a study of children in Kuwait conducted in 5 regional government hospitals serving 1.35 million children under the age of 12 years (older children attended adult institutions), and showed a marked increase in the proportion of male children with JCA in comparison to other studies.

Case ascertainment: Clinical case records from 5 hospitals. Retrospective study.

Special features: Large population cohort.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral by primary care practitioners. Children between 12 and 16 years not included. Female children possibly underrepresented.

In 1992, Steven<sup>24</sup> reported a prevalence of JCA of 2.0 per 1000 children cared for by 29 community practitioners for a total population of 35,251 living in 4 relatively isolated areas of the Scottish Highlands.

Case ascertainment: Practitioner questionnaire survey with specialist rheumatologist review of questionnaire results. Retrospective study.

Special features: Study of 4 defined populations of Scottish children. Highest prevalence reported for clinical case study. Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community. Small population size.

In 1992, Andersson Gare and Fasth<sup>16</sup> reported a Swedish study in which figures were collected over 5 years from 8

pediatric departments and local pediatricians in the southwest district of Sweden, an area serving 386,817 children; they provided detailed information on the subgroups of JA at presentation and during the initial course of the illness with detailed serological analysis and ophthalmological review. Active disease was estimated to be 74.3% of the total.

Case ascertainment: Clinical case records from 8 hospitals.

Prospective study.

Special features: Detailed analysis of subgroups, serology, and ophthalmology.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community.

In 1993, Mielants, *et al*<sup>17</sup> reported a study in Belgium in which children in schools were surveyed for arthritis and other rheumatological disorders by questionnaire to 2990 secondary school students and their parents. Of these, 524 children who were considered to have possible rheumatological disease were examined by a rheumatology resident, who then selected 41 children to be examined by the medical staff of a rheumatology department. Five cases of definite JCA and 4 cases of presumptive late pauciarticular onset JCA were defined.

Case ascertainment: Questionnaire screening of school children, with subsequent clinical examination by rheumatologists of 17.5% of children surveyed. Prospective study.

Special features: True community based study with consideration of undiagnosed cases in the classroom. Comparison of data for active and inactive disease. Analysis of the difference between ascertainment from primary care practitioners and from hospital cases.

Potential weakness: Possible underestimation due to exclusion of undiagnosed cases not identifiable from questionnaires.

In 1995, Oen, *et al*<sup>27</sup> reported an incidence over the period 1975 to 1992 in Manitoba, Canada, of 0.534 per 1000 per year. A cyclic increase was evident in the years 1979, 1982, 1986, and 1990-91, with peaks correlating with increased incidence of confirmed *Mycoplasma* infections from an analytic study based on data obtained from the disease registry of the Pediatric Rheumatology Clinic, Children's Hospital, Winnipeg, Manitoba.

Case ascertainment: Hospital clinical case records.

Retrospective study.

Special features: Correlation with *Mycoplasma* infection prevalence.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and to nonreferral to a tertiary center.

In 1995, Arguedas, *et al*<sup>28</sup> reported on incidence in Costa Rica. Refer below to reference 23.

In 1996, Malleon, *et al*<sup>29</sup> reported on nationwide data collected over 3 years from 13 pediatric rheumatology specialist centers across Canada with data on 92 separate diagnoses and showed incidence calculated for an 18 month period for JRA to be 0.0284 per 1000.

Case ascertainment: Clinical cases referred to specialist centers. Prospective study.

Special features: Extensive data from 13 specialist centers including 92 separate diagnoses, including both classical rheumatic diseases, various pain syndromes, mechanical and orthopedic problems. Analysis of subgroups of JRA, sex distribution, age of onset, and other variables. Epidemiology data on less common autoimmune diseases of children.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral from primary care practitioners.

In 1996, the British Pediatric Rheumatology Group<sup>30</sup> reported on data collected from 23 centers throughout the United Kingdom with annual incidence of JA determined for 2 centers (Canterbury and Liverpool).

Case ascertainment: Clinical case records from 23 centers with incidence studies from 2 centers. Prospective study.

Special features: Large population cohort from across Britain.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and to nonreferral by primary care practitioners.

In 1996, Peterson, *et al*<sup>18</sup> reported on the trends in incidence and prevalence of JRA in Olmsted County, Minnesota, USA, over 33 years based on information retrieved from the Rochester Epidemiology Project with information on children with a potential diagnosis of JRA over the period 1960 to 1993.

Case ascertainment: Clinical case data from Rochester Epidemiology Project. Retrospective study.

Special features: Data from 33 years. Trends examined.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and to nonreferral by primary care practitioners.

In 1996, Kaipainen-Seppanen and Savolainen<sup>31</sup> reported the annual incidence of JRA in children in Finland during 3 separate years 1980, 1985, and 1990. Case ascertainment was from records of entitlements to reimbursement of payment for medication for juvenile rheumatic diseases in 5 central hospital districts in Finland. An important observation was made that there was no reduction in the annual incidence of JRA after 1982, with the introduction of vaccination against measles, mumps, and rubella for more than 90% of the child population.

Case ascertainment: Clinical case records, where application made for reimbursement for medication for JRA.

Retrospective study.

Special features: Three separate years compared. Observation of effect on disease incidence by vaccination program.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and cases not treated with medications.

In 1996, Manners and Diepeveen<sup>19</sup> reported a prevalence for JCA of 4.01 per 1000 children in a community based study in Western Australia in which 2241 twelve-year-old children were examined by a single rheumatologist after parents and children had returned questionnaires with a 90% return rate. Of the 9 cases defined, 7 had not previously been diagnosed but were found to fulfil the criteria for JCA. If a clinical case study had been performed on the same cohort, the prevalence would have been 0.89 per 1000, similar to results from many other clinical case studies. Before the main study, a pilot study had been completed on 816 ten-year-old children, with each child examined after completion of questionnaires (85.9%), which showed a prevalence of 3.68 per 1000 children, with 2 of the 3 prevalent cases of JCA being previously undiagnosed. This study highlights the importance of community based studies, which will show higher prevalence rates due to the inclusion of previously undiagnosed cases, if each child in the study population is examined rheumatologically by an experienced clinician.

A study of incidence of JCA was performed in the same city, using clinical cases<sup>32</sup>. The incidence was shown to be 0.106 per 1000 children (95% CI 0.076–0.143), which is concordant with many incidence studies done elsewhere. This suggests that the population of Western Australia is similar to other study populations, and that the percentage of undiagnosed cases within the community may be similarly large in other centers around the world.

Case ascertainment: Clinical examination of each child within the population of school children, following completion of questionnaires by parents and children.

Prospective study.

Special features: 2241 children each examined by a single examiner; highest prevalence ever reported.

Potential weakness: The children were on average 12 years old, and since by definition the onset of JCA is before the 16th birthday, the estimated prevalence is likely to be an underestimate. The size of the study population of 2241 is not large, and the confidence interval for the prevalence of 4.01 is wide at 1.84–7.53.

In 1997, Fujikawa and Okuni<sup>33</sup> reported an annual incidence for JRA of 0.0083 per 1000 estimated by hospital attendance of 1606 incident cases during a 10 year period 1984–94. Questionnaires were sent to 1290 hospitals in Japan, which included every hospital in Japan with more

than 100 pediatric beds, with 64.9% of the hospitals responding. Of these, 206 hospitals had no patients with JRA during the surveillance period.

Case ascertainment: Questionnaires to 1290 hospitals.

Retrospective study.

Special features: Very large population cohort across Japan.

Potential weakness: Possible underestimation of numbers due to cases not referred to hospital but treated outside hospitals, undiagnosed cases in the community, and cases treated at the hospitals that did not return questionnaires.

In 1998, Ozen, *et al*<sup>20</sup> reported a prevalence of 0.64 per 1000 children for JCA in 5 districts of Turkey with a population of 46,813 children, with a total of 146 practitioners and pediatricians visiting a sample of homes, administering questionnaires to parents, and examining children if the answers to the questionnaires indicated possible rheumatic disease.

Case ascertainment: Questionnaire screening of parents in homes, with subsequent clinical examination by trained practitioners and pediatricians of identified children.

Prospective study.

Special features: True community based study with consideration of undiagnosed cases of children in the homes. Detailed data on familial Mediterranean fever. Investigation of difference in JCA prevalence between urban and rural children.

Potential weakness: Possible underestimation due to exclusion of undiagnosed cases not identifiable from questionnaires.

In 1998, Moe and Rygg<sup>21</sup> reported a point prevalence of 1.481 per 1000 children for JCA in the 2 northernmost counties of Norway, with case ascertainment from medical records at a common disease registry for the University Hospital of Tromsø with a catchment population of children of 47,941.

Case ascertainment: Clinical cases records, disease registry. Retrospective study.

Special features: Highest prevalence reported in clinical case study based on hospital records.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral by primary care practitioners.

In 1998, Kiessling, *et al*<sup>22</sup> reported a prevalence and annual incidence in children of East Berlin for the period 1980–88, where children with the disease were compelled by government ordinance to be treated only at 2nd Children's Hospital at Berlin-Buch, and the authors therefore had an opportunity to review all cases of referred JCA for a population of children whose mean calculated over 9 years was 247,906. Prevalence was estimated for each of 9 successive years, and the mean over the same period was 0.20 per 1000 children.

Case ascertainment: Clinical cases referred to hospital.  
Retrospective study.

Special features: One referral center, designated by government ordinance. Children in the community routinely checked by pediatricians. Accuracy of diagnoses of pediatricians compared with diagnoses of pediatric rheumatologists. Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral by primary care practitioners.

In 1998, Arguedas, *et al*<sup>23</sup> reported an annual incidence of 0.068 and prevalence of 0.349 per 1000 children in urban San Jose, Costa Rica (with catchment of 350,000 children), following a pilot study in 1995<sup>28</sup>, which showed an annual incidence of 0.054 per 1000. An extensive educational program was conducted between the 2 studies, and completed by all physicians in the area to improve expertise in pediatric rheumatology in preparation for the second study. Case ascertainment was by physician referral. In addition, health workers visited homes regularly asking about childhood rheumatological symptoms.

Case ascertainment: Clinical cases referred by practitioners. Prospective and retrospective study.

Special features: Two separate studies, on same cohort, 3 years apart. Educational program conducted prior to second study. Consideration of differences due to tropical climate and therefore different range of infections.

Potential weakness: Possible underestimation of numbers due to undiagnosed cases in the community and nonreferral by primary care practitioners.

## DISCUSSION

It is apparent that as time passes, and awareness of the condition increases, studies show increasing prevalence of JA. As communities become more prosperous, more resources are available for children with chronic illness including JA, and there is an apparent increase in prevalence and incidence. Of the many reasons why results of epidemiological studies differ significantly, the method of case ascertainment is perhaps the most important. Studies done in the community (such as in homes or schools) involving children who have not necessarily sought medical attention for musculoskeletal symptoms will include undiagnosed cases. It can be expected that these studies will yield the higher results for prevalence as in the studies of Mielants, *et al*<sup>17</sup> and Manners and Diepeveen<sup>19</sup>.

The ideal study of prevalence of childhood arthritis would involve large numbers of children in homes or schools in the months before their 16th birthday, with a history taken of possible active or inactive arthritis in the previous 16 years, followed by a clinical examination by experienced pediatric rheumatologists. Standardized diagnostic criteria would be used. Where there was clinical evidence of joint inflammation, in order to fulfil the diag-

nostic criteria for JIA, a second clinical examination would be undertaken to ensure that inflammation remained for at least 6 weeks, and that other conditions were excluded. Such a study would be virtually impossible to perform.

Because annual incidence of JA within a particular community is relatively small, it would not be feasible to estimate annual incidence by community based studies because of the size of the required study cohort. The ideal study of incidence of childhood arthritis would involve at least experienced pediatric rheumatologists using standardized diagnostic criteria.

There are a number of clearly defined reasons, categorized in 4 broad areas, why results for prevalence and incidence for JA differ markedly across a range of studies. Studies undertaken on children within the community show the highest prevalence, with previously undiagnosed cases included. Ideally, the prevalence of JA should be estimated by studies using standardized methods and standardized diagnostic criteria, with case ascertainment within the community, using clinicians trained and experienced in pediatric rheumatology. Only then will differences between studies be able to be compared in a meaningful way.

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