Incidence and Prevalence of Rheumatoid Arthritis, Based on the 1987 American College of Rheumatology Criteria: A Systematic Review

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Objectives: To conduct a systematic review of incidence and prevalence studies of rheumatoid arthritis (RA), based on the 1987 revised American College of Rheumatology (ACR) criteria, to compare their methodologies and summarize their results, and to investigate the possible geographic variations and changes over time in the frequency of the disease.

Methods: We conducted a Medline search between January 1988 and December 2005. Studies reporting the incidence and prevalence of RA in adult populations (16 to 20 years and over), based on 1987 ACR criteria, were eligible for inclusion. From each study included, we extracted the country, year of publication, type of study (retrospective, prospective, or cross-sectional), and incidence or prevalence rates. The study areas were grouped into (a) North American countries; (b) north European countries; (c) south European countries; and (d) developing countries. We examined the geographical differences of prevalence and incidence rates using the Mann–Whitney and the Kruskall–Wallis tests.

Results: A total of 28 studies were identified meeting the inclusion criteria. Nine were incidence studies, 17 were prevalence studies, and 2 estimated both prevalence and incidence rates. Incidence studies were not available from developing countries. There is a significant difference of prevalence estimates between northern European and American countries and developing countries. South European countries have lower median incidence rates than North American and north European countries. As concerning the time trends of RA occurrence, only 3 incidence studies provided secular data from the same study area, based on ACR criteria, using the same methods of case ascertainment. Two of these studies indicate a decreasing incidence of RA in Finland and United States of America.

Conclusions: The occurrence of RA varies among countries and areas of the world. A decreasing trend has been observed in countries characterized by high rates of RA incidence and prevalence. However, the relatively small number of studies for most areas of the world and the lack of incidence studies for the developing countries limits the understanding of worldwide RA epidemiology.

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Several incidence and prevalence studies of rheumatoid arthritis (RA) have been reported during the last 2 decades, suggesting a considerable variation of the disease frequency among different populations. Some ethnic and racial groups have an increased occurrence of the disease (1,2). The prevalence of the disease appears to be lower in developing countries. Studies from south European countries also suggest a relative lower occurrence of RA when compared with north European and North American countries (3). Recent studies indicate a decreasing trend in the occurrence of the disease, although it is difficult to confirm this trend (4). Studies of the epidemiology of RA have methodological differences. The 1987 revised American College of Rheumatology (ACR) criteria, the currently accepted criteria for RA diagnosis and classification (5), replaced the earlier existing criteria (1958,

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New York classification criteria), which defined RA as classic, definite, probable, and possible disease (6).

These methodological issues may affect the results of studies comparing the occurrence of the disease among different countries and areas, or investigating the time trends of the disease. As a consequence, it is important to compare data from studies using similar methods based on the same case-identification criteria to create a valid picture of RA epidemiology worldwide.

METHODS

We conducted a Medline search from January 1988 to December 2005 (key words: RA AND incidence and prevalence). The search strategy is presented in Table 1. Additional relevant articles were identified using the option "related articles" in the Medline database, for the articles meeting the inclusion criteria. Articles published before 1987 were not considered, as we included only studies based on the 1987 ACR revised criteria. Studies published in any language and reporting the incidence and prevalence of RA in the general adult populations were considered eligible for inclusion. Studies performed in selected populations, such as specific ethnic or racial groups, and age groups, were excluded. When 2 publications reported results from the same study area using the same sources of case ascertainment, only the more recent was considered.

From each study included, we extracted the country, the year of publication, the type of study (retrospective, prospective, or cross-sectional), and the incidence or prevalence rates. Mean annual incidence rates were considered when an incidence study included an observation period longer than 1 year. When a study provided the crude and the adjusted incidence and prevalence rates, we considered the age-adjusted rates. When a study indicated only the crude rates, we considered these rates. The study areas were grouped into (a) North American countries; (b) north European countries; (c) south European countries; and (d) developing countries. Developing countries included those outside Europe having a per capita income less than $5000. For the comparison of incidence and prevalence rates among geographical areas, North American and north European countries were combined together because of their similar results, and the small number of American studies included (2 incidence studies and 1 prevalence study). The median and ranges of the incidence and prevalence rates of RA were estimated by gender and for the total populations for each group of countries. We examined geographical differences of prevalence and incidence rates using the Mann–Whitney and the Kruskall–Wallis tests (exact probabilities), using as a statistical unit the results of any single study.

Table 1 Results of Medline Search and Inclusion Criteria for RA

Steps of Searching	Number of Publications
RA and incidence and prevalence publication year 1988–2005	3232
Descriptive epidemiological studies of RA incidence and prevalence in the adult population	51
ACR criteria	46
General population 16–20 years and over	28

The pooling process was repeated after the removal of prospective or retrospective studies, considering this issue as the most important difference in the quality of the studies. For the prevalence studies the same procedure was followed, dividing the studies into retrospective or cross-sectional studies. We also compared the crude rates to the adjusted rates in the analysis. We used these comparisons as a measure of the heterogeneity of data included in this study.

All statistical tests were two-sided, with a P value <0.05 of statistical significance. We also considered P values <0.10 as indicating a trend, but not statistically significant.

RESULTS

Twenty-eight studies were identified from the literature search meeting our inclusion criteria. Nine were incidence studies; 17 were prevalence studies, and 2 estimated both prevalence and incidence rates. All studies that finally met the inclusion criteria were English publications, although there were 2 French and 1 German publication resulting from the initial search. Table 1 summarizes the results of the Medline search (7-34).

Tables 2 and 3 present the results of incidence and prevalence studies for several areas of the world and several countries. Most of the incidence studies were performed in north European countries. There were no incidence studies from developing countries. Prevalence studies were performed in many countries and several areas of the world.

Figure 1 shows the distribution of incidence rates reported by several studies, from different areas of the world. South European countries had a lower incidence of RA. The median annual incidence for the total population observed in south European countries is 16.5 (range 9 to 24) cases per 10^5. For north European countries the median annual incidence observed was 29 (range 24 to 36), and for North American countries 38 (range 31 to 45). The overall distribution of incidence rates does not differ significantly among different areas of the world according to the Kruskall–Wallis test ($P = 0.09$). There is a statistically significant difference observed between north and south European countries for the male population only ($8.5/10^5$ versus $21/10^5$, $P = 0.05$). When considering North American and north European countries as 1 group, the differences between this group and the south European countries had a level of significance of $P = 0.07$

Table 2 Incidence Rates of RA Worldwide in Studies Based on ACR Criteria

Publication	Country	Type of Study	Incidence (cases/10^3 inhabitants)			Population Age (y)
			Total	Male	Female	
Doran 2002 (9)	USA	Retrospective	0.5	0.3	0.6	≥18
Savolainen 2003 (20)	Finland	Prospective	0.4*	0.3	0.5	≥16
Chan 1993 (8)	USA	Retrospective	0.3	0.2	0.5	≥18
Kaipiainen-Seppanen 2000 (19)	Finland	Retrospective	0.3*	0.2	0.4	≥16
Riise 2000 (10)	Norway	Retrospective	0.3*	0.2	0.4	≥20
Uhlig 1998 (12)	Norway	Retrospective	0.3	0.1	0.4	20–79
Kaipiainen-Seppanen 2001 (21)	Finland	Retrospective	0.3	0.2	0.4	≥16
Drosos 1997 (27)	Greece	Retrospective	0.2	0.1	0.4	≥16
Symmons 1994 (14)	England	Prospective	0.2	0.1	0.3	≥16
Soderlin 2002 (16)	Sweden	Prospective	0.2	0.2	0.3	≥16
Guillemin 1994 (23)	France	Retrospective	0.1	0.1	0.1	20–70

*Crude rates.

for the total and 0.04 for the male population. The incidence rates did not differ significantly for the female population ($24.5/10^5$ versus $40/10^5$, $P = 0.11$).

Figure 2 shows the distribution of prevalence estimates from different areas of the world. The median prevalence estimate for the total population in south European countries is 3.3 (range 3.1 to 5.0) cases per 10^3, for north European countries 5.0 (range 4.4 to 8.0), and for developing countries 3.5 (range 2.4 to 3.6). A study from North America showed a prevalence estimate of 10.7 cases per 10^3. The overall distribution of prevalence for the total and the male population differs significantly among different areas of the world according to the Kruskall–Wallis test ($P = 0.02$). The difference observed is marginally significant for the female population ($P = 0.11$).

The prevalence rates between northern European and American countries (considered as 1 group) and the south European countries for the female ($P = 0.05$) and for male populations ($P = 0.02$) are significantly different and marginally significant for the total population ($P = 0.07$). The prevalence rates are significantly different between north European and American countries (considered as 1 group) and developing countries, for the total population ($P = 0.003$), and for men ($P = 0.04$) but not for south European countries and developing countries.

Table 3 Prevalence Estimates of RA Worldwide in Studies Based on ACR Criteria

Publication	Country	Type of Study	Prevalence (cases/10^3 inhabitants)			Population Age (y)
			Total	Male	Female	
Gabriel 1999 (7)	USA	Retrospective	10.7	7.4	13.7	≥35
Symmons 2002 (13)	England	Cross-sectional	8.5*	4.4	11.2	≥16
Hakala 1993 (18)	Finland	Retrospective	8.0*	6.1	10.0	≥16
Andrianakos 2003 (28)	Greece	Cross-sectional	7*		19	
Simmonson 1999 (17)	Sweden	Cross-sectional	5.1*		20–74	
Saraux 1999 (24)	France	Cross-sectional	5.0	2.4	7.6	≥18
Carmona 2002 (22)	Spain	Cross-sectional	5*	2	8	≥20
Power 1999 (15)	Ireland	Cross-sectional	5*			
Akar 2004 (34)	Turkey	Cross-sectional	3.6*	1.5	7.7	≥20
Kvien 1997 (11)	Norway	Cross-sectional	4.4*	1.9	6.7	20–79
Riise 2000 (10)	Norway	Retrospective	4.3*	2.7	5.8	≥20
Pountain 1991 (33)	Oman	Cross-sectional	3.6*	16		
Drosos 1997 (27)	Greece	Retrospective	3.5	1.9	4.5	≥16
Lau 1993 (31)	China	Cross-sectional	3.5*			≥16
Cimmino 1998 (26)	Italy	Cross-sectional	3.3*	1.3	5.1	≥16
Guillemin 2005 (25)	France	Cross-sectional	3.1	0.9	5.1	≥18
Dai 2003 (32)	China	Cross-sectional	2.8	1.4	4.1	≥16
Spindler 2002 (30)	Argentina	Retrospective	2.0*	0.6	3.2	≥16
Stojacovic 1998 (29)	Yugoslavia	Cross-sectional	1.8*	0.9	2.9	≥20

*Crude rates.

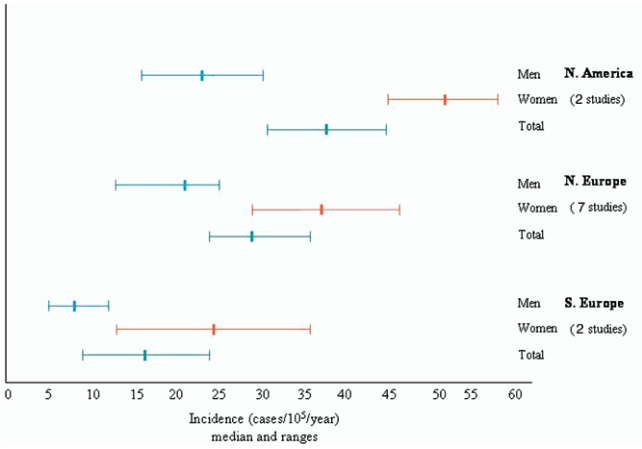

Figure 1 Incidence of RA in different areas of the world (medians and ranges of observed incidence rates in groups of countries). (Color version of figure is available online.)

Concerning the time trends of RA occurrence, only 3 incidence studies provided secular data from the same study area, based on ACR criteria, using the same methods of case ascertainment. Doran and coworkers (9) estimated the trends of RA incidence in Rochester, Minnesota, over a 40-year period. The incidence rate in the adult population fell progressively over the 4 decades of study, from 61.2/10^5 in 1955 to 1964 to 32.7/10^5 in 1985 to 1994. In the study of Kaipiainen-Seppanen and coworkers (19) performed in 5 districts in Finland, the annual incidence of RA in the adult population was estimated over 3 years: 1980, 1985, and 1990. In 1990 a decline in incidence of about 15% compared with previous study years was observed, affecting mainly rheumatoid factor-negative disease. A study performed in a defined area of Greece by our group (27) estimated the annual incidence rates over the period 1987 to 1995. Annual incidence rates fluctuated between 15 and 36/10^5 inhabitants, but no significant trend in the disease occurrence was observed. All these studies were retrospective, based on medical records.

Prospective incidence studies did not have significantly lower incidence rates than retrospective studies. The median incidence for the total adult population increased from 29 (cases/10^5) to 30, after the removal of prospective studies. The median gender-specific incidence rates increased from 18 to 18.5 for males and from 37 to 38.5 for females. The prevalence estimates did not change significantly after removing retrospective or cross-sectional studies. The median prevalence for the total adult population increased from 4.9 (cases/10^3) to 5.0, when considering only cross-sectional studies. The respective changes for gender-specific rates were from 2.2 to 2.0 for men and from 6.6 to 7.7 for women. Three of 11 incidence studies (27%) and 14 of 19 (74%) prevalence studies presented only crude rates in the original articles. When removing the crude rates or the adjusted rates included in the analysis, there were no statistically significant changes for the incidence or for the prevalence studies.

DISCUSSION

According to the results of this systematic review, the incidence and prevalence studies of RA based on 1987 ACR criteria differ considerably in their methods and result in a wide variation of the incidence and prevalence estimates.

Methodological differences include the methods of case identification and case recording, as well as the type of incidence and prevalence rates. Some studies do not present age-adjusted rates. In addition, adjusting methods for age differ among studies or are not described in the articles. However, the methodological differences of the studies could only partly explain the differences in RA occurrence observed across areas. These differences could also be related to medical practice, access to care, and variability in prevalence of environmental and genetic risk factors.

South European countries have lower median incidence and prevalence rates than north European and North American countries, although these differences were not statistically significant for the female population. However, the lack of statistical significance could be related to the small number of studies from southern Europe. In addition, some of these studies are based on relatively small sample sizes. It has been suggested that RA in southern Europe has a particular genetic, epidemiological, and clinical profile (35-39). Some studies indicate that RA is milder, with less extra-articular and radiological manifestations in south European populations. Environmental and lifestyle factors may contribute to this different profile. Dietary factors such as olive oil and fish consumption, as well as the Mediterranean diet, may offer a protective effect for disease development and disease se-

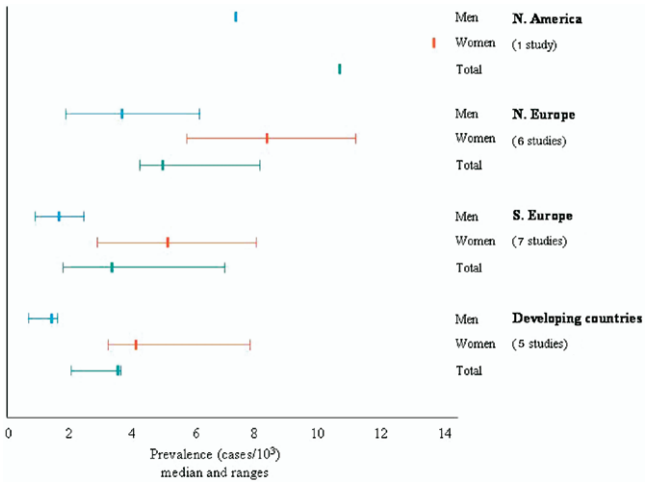

Figure 2 Prevalence of RA in different areas of the world (medians and ranges of prevalence estimates in groups of countries). (Color version of figure is available online.)

verity (40-43). The genetic associations of RA are likely to be different in south European populations than in northern Europe and the USA. The "shared epitope" alleles are observed in about three-quarters of northern Europeans, whereas these alleles are observed in about half of southern European patients. In addition, these alleles do not seem to be risk factors for disease severity to the same extent in all populations studied (37-39).

The few prevalence studies performed in developing countries based on ACR criteria indicate a significantly lower frequency of the disease in these countries than in north European and American countries. This lower frequency observed could partly be related to lower occurrence of the disease in developing countries, but may also reflect differences in the age distribution between the populations studied. In addition, cases with mild RA may be less likely to be ascertained, depending on access to medical care. This may lead to a relative underestimation of RA occurrence for the studies based on medical records. The lack of studies performed in other parts of the world such as Africa, Russia, and large parts of Asia may also represent a limitation of our study.

Concerning the changes of RA occurrence over time, the existing data are limited. Only the study by Doran and coworkers (9) examined the evolution of disease occurrence for a long period (4 decades), applying the 1987 ACR criteria retrospectively, based on medical records for a defined area of the USA. This study demonstrates a significant decline of RA incidence over the past decades. The study of Kaipiainen-Seppanen and coworkers (21) also suggests a slight decline of RA incidence in Finland between 1980 and 1990. However, it is difficult to suggest a general trend of decreasing RA incidence for all countries based on the results of these studies. As we have seen, there is a considerable variation of RA incidence and prevalence among countries and areas of the world. Finland and the USA are likely to have higher rates of RA in comparison to many other countries (Table 2). The retrospective character of these studies also place some limitations in the interpretation of their data. As a consequence, more data from several countries are needed, investigating the occurrence of the disease over time in defined populations, based on 1987 ACR criteria and using the same methods and sources of case ascertainment for each time period (44).

The interpretation of summary statistics of incidence and prevalence data presents some limitations related to methodological issues of the studies included. These studies come from different research environments and use different methods of case ascertainment. Most of the incidence studies had a retrospective design based on medical records, and only 3 were prospective. The small number of incidence studies does not allow a comparison between retrospective and prospective studies for the same areas. When considering all studies together, the prospective studies did not have significantly different incidence rates than retrospective studies. However, prospective incidence studies are very few and were performed in areas with relatively low occurrence of RA. Concerning the prevalence studies, most of them were cross-sectional based on a population survey and the examination of a sample of the general population. Four prevalence studies were retrospective based on medical records. The prevalence estimates did not differ significantly between the 2 types of studies.

Another limitation is that both incidence and prevalence studies often used different age-adjustment methods, and some did not provide the adjusted rates. We chose to consider the adjusted incidence and prevalence rates when available. When comparing the crude rates to the adjusted rates included in the analysis, there was no significant difference for incidence or prevalence. Other limitations in data interpretation could be related to the differences of sample sizes, and the differing age distributions of the individual study populations.

Several studies have presented summary statistics in the frame of a systematic review of descriptive epidemiological studies. A few of them use the term "meta-analysis" for this procedure. There are no methodological articles proposing a standard procedure for reporting meta-analysis of descriptive studies. Published proposals for reporting meta-analysis of observational and epidemiological studies suggest specific criteria to evaluate the methodological quality of the studies included. These criteria include case definition, type of study, definition of the study population, and type of rates estimated (45,46). In this study we considered as methodological quality criteria the type of the study (prospective, retrospective, or cross-sectional), and the type of estimated rates (crude or adjusted). We avoided creating a total quality score for each study, as we think that such a procedure could be considered arbitrary. In addition, some of the quality criteria proposed, such as case definition or definition of the study population, were inclusion criteria for the present study. Thus, we conducted a sensitivity analysis based on the type of study and the type of rates only. However, factors influencing RA risks in the included base populations are also important, when comparing RA occurrence between different countries and areas of the world. Those factors are different age and sex distributions, different socioeconomic status and access to medical care, and others.

In conclusion, the occurrence of RA likely has important variations among countries and areas of the world. A decreasing trend has been observed in countries characterized by high rates of RA incidence and prevalence. However, the relatively small number of studies for most areas of the world, as well as their methodological differences and the lack of incidence studies for the developing countries, limits our understanding of worldwide RA epidemiology.

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