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Editorial comment in the form of a Letter to the Editor is invited; however, it should not exceed 800 words, with a maximum of 10 references and no more than 2 figures (submitted as camera ready hard copy per Journal Guidelines) or tables and no subdivision for an Abstract, Methods, or Results. Letters should have no more than 4 authors. Full name(s) and address of the author(s) should accompany the letter as well as the telephone number, fax number, or E-mail address.

Contact. **The Managing Editor, The Journal of Rheumatology, 365 Bloor Street East, Suite 901, Toronto, ON CANADA M4W 3L4. Tel: 416-967-5155; Fax: 416-967-7556; E-mail: jrheum@jrheum.com Financial associations or other possible conflicts of interest should always be disclosed.**

Epidemiology of Rheumatic Diseases in Greece

To the Editor:

We read with interest the recent article by Dr. Andrianakos and colleagues, concerning the prevalence of rheumatic diseases in Greece. The study of the descriptive epidemiology of rheumatic diseases in several countries and areas of the world is of interest, as the occurrence of these diseases seems to present significant variations among different populations. Ethnic, racial, and geographic factors have been associated with the frequency and expression of several rheumatic diseases. However, the role of possibly related environmental and genetic factors remains uncertain. There is scarce information on the incidence and prevalence of rheumatic diseases in Southern European and Mediterranean countries. The investigation of the epidemiological profile of rheumatic diseases in these countries would be of interest because of the possible role of environmental and lifestyle factors characterizing their populations.

From this point of view the article by Andrianakos, *et al* offers interesting data concerning the prevalence of rheumatic diseases in the Greek population[1]. The study was carried out in a sample of 8740 Greek adults, and was based on a standardized questionnaire as well as clinical and laboratory evaluation of participants (ESORDIG Study).

Our study group has implemented a systemic recording system of autoimmune rheumatic diseases in a defined area of northwest Greece with a population of about 500,000 inhabitants, in order to study the epidemiological profile of these diseases in the area. Thus we compared our data to the results of the ESORDIG Study. The prevalence rates we estimated in northwest Greece are similar to those of the ESORDIG study for some autoimmune rheumatic diseases, but differ significantly for some others.

Specifically, the age-adjusted prevalence rate for systemic lupus erythematosus (SLE) was found to be 0.04% in northwest Greece[2] and 0.05% in the sample of the ESORDIG study. However, for rheumatoid arthritis (RA) the prevalence rates estimated in the 2 studies were 0.33%[3] and 0.67%, respectively. For psoriatic arthritis (PsA) the respective prevalence rates were 0.06%[4] and 0.17%, and for ankylosing spondylitis (AS) 0.03% and 0.24% (unpublished data). It is impressive that the 2 studies found very similar rates for SLE, but for the other autoimmune rheumatic diseases the prevalence estimated by the ESORDIG study is 2 to 8-fold higher than the prevalence estimated in northwest Greece. The differences observed are statistically significant, and this is obvious considering the 95% CI presented by the authors. What could be the possible explanations for these differences?

The Greek population is a relatively homogeneous Caucasian population. There are no important ethnic, racial, or socioeconomic differences between the population of northwest Greece and the areas included in the ESORDIG study. Environmental factors such as climate or nutrition are not likely to differ significantly among the areas studied.

The differences observed could represent a possible overestimation by the ESORDIG study or underestimation of the prevalence in northwest Greece studies. Considering the first possibility: (1) The sampling method in the ESORDIG study could be related to a possible selection bias. From an initial target population of 14,233 individuals invited to participate, a total of 8740 were finally examined (total response rate 61.4%). It is possible that subjects with rheumatic disorders or symptoms had an increased probability to respond to the study. However, the authors state that analysis of data of a random sample of nonresponders showed no significant difference from responders with respect to age, sex, and prevalence of rheumatic symptoms or diseases. In any case a possible selection bias cannot explain a 2 to 8-fold higher prevalence of autoimmune rheumatic diseases. (2) Another possible explanation could be related to different application of diagnostic criteria. This is more probable for PsA and AS, as definition criteria are not clear enough for these diseases. Misclassification of cases could partly explain the differences observed. (3) The sample investigated in the ESORDIG study could not be considered as representative of the general Greek population, since it does not include any area of northwest Greece or other departments of Greece (central midland area or the islands area). However, it is unlikely that the areas included in this study represent a population characterized by such a higher prevalence of rheumatic disease.

On the other hand, the systematic recording system implemented in northwest Greece could partly underestimate the prevalence of these diseases, as it is based on diagnosed cases. In our studies on the epidemiology of autoimmune rheumatic diseases in this area we estimated that only a small number of mild cases could escape the recording system, as it is relatively complete, using multiple sources of retrieval[2,4].

Comparing the findings of the Greek studies to international data, we could say that the ESORDIG study estimated a prevalence rate of RA higher than those found in other southern European countries, and prevalence rates for PsA and AS higher than those found even in northern European countries or in the United States. In contrast, the prevalence estimated for SLE was lower than in other countries. The prevalence rates estimated by our group were about half those found in northern European countries or areas of the USA, for all these diseases. We also found a milder expression of the diseases in our study population. Studies from other southern European countries also indicated a relatively low frequency and milder expression for autoimmune rheumatic diseases, and these findings may be related to environmental and lifestyle factors characterizing these areas[5,6].

We consider that the ESORDIG study overestimates the prevalence of autoimmune rheumatic diseases in the Greek population, especially the prevalence of AS. A more complete investigation is needed in order to describe the epidemiological profile of these diseases in the whole country. This includes a representative sample of the general population, and study of the incidence and severity (and not only the prevalence) of cases for each disease, as well as their distribution by sex, age, and socioeconomic groups.

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Dr. Andrianakos, *et al* reply

To the Editor:

We thank Dr. Alamanos and coworkers for their comments and their interest in our article[1]. In comparing the results of our cross-sectional population based epidemiological study of rheumatic diseases in Greece (ESORDIG study)[1] to the results of their studies[2,3] based on diagnosed cases in 2 hospitals and private rheumatologists' offices in northwest Greece, Alamanos, *et al* comment on the prevalence rates of some inflammatory rheumatic diseases. Their estimated prevalence rates for rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) at 0.33%, 0.06%, and 0.03% respectively, were indeed very low, compared to those we found (0.67%, 0.17%, and 0.24%). We agree that differences in the prevalence rates could be attributed either to a possible overestimation in our study or to underestimation in the northwest Greece studies.

Regarding an overestimation on our part: In stating that the participation rate in our study was 61.4%, leading to a possible selection bias effect, Dr. Alamanos and coworkers are mistaken: the participation rate was 82.1%, as we reported. A more cautious reading of our article reveals that the ESORDIG study population consisted of the total, nonselected adult population (≥ 19 years old) of 2 urban, one suburban, and 4 rural areas located throughout mainland Greece (8547 subjects), as well as 2100 out of 5686 randomly selected subjects in one additional rural and one suburban community in which every second and third household, respectively, was selected from a randomly chosen starting point (systematic sampling). Thus, the total (before selection) and the final (after selection) target population of the study was 14,233 and 10,647 adults, respectively. Of the final target population of 10,647 subjects who were visited at their homes by the participating rheumatologists, 8740 took part in the study. Therefore the participation rate in our study was 82.1%, not 61.4%, as mistakenly perceived by Dr. Alamanos, *et al.* It follows that with such a high participation rate in a population based study, a selection bias is indeed only a very remote possibility. Moreover, analysis of the data of a random sample of nonresponders showed no significant difference from that of responders with respect to age, sex, and prevalence of rheumatic symptoms or diseases. It is also of interest that logistic regression analysis showed that there was no population selection or nonselection effect on the prevalence rates of the rheumatic diseases in general, and of RA, PsA, and AS in particular.

Further, as we clearly stated, the diagnosis of RA was based on the American College of Rheumatology (formerly the American Rheumatism Association) criteria, while that of seronegative spondyloarthropathies was based on the European Spondylarthropathy Study Group criteria. More specifically, the diagnosis of AS was made on the basis of the modified New York criteria. Moreover, in every single case, the diagnosis of rheumatic diseases was made by an experienced rheumatologist who, prior to the start of the study, had attended a training course on standardizing the use of the rheumatic disease classification criteria. As shown by logistic regression, it is noteworthy that in diagnosing rheumatic diseases, there was no significant variation among the participating rheumatologists.

As well, the ESORDIG study was conducted in urban, suburban, and rural areas located in northern, central, and southern mainland Greece as shown in Figure 1 in our article[1]. Using Pearson correlation coefficients, we found a significant similarity in the age distribution between the study participants, the total target adult population, and the total adult population of Greece, even when the data were analyzed separately for each sex in the participating urban, suburban, and rural populations and compared to the respective analysis by sex of the total adult Greek urban, suburban, and rural populations. It follows, therefore, that the ESORDIG study population was representative of the total Greek general adult population in terms of age and sex distribution. It is true that areas from northwest Greece or the islands were not included in our study, although 4% of the study participants were of island descent. However, as Dr. Alamanos and colleagues also state, the population of Greece is a relatively homogeneous Caucasian one without important socioeconomic, environmental, or other differences between the geographic departments of the country. In this respect, it should be emphasized that there were no significant differences in the prevalence of rheumatic diseases, including RA, PsA, and AS, between the studied northern, central, and southern areas of the country.

Based on the above findings, it does appear to be unlikely that the northwest region of Greece could be characterized by a lower prevalence of RA, PsA, and AS than that found by the ESORDIG study in so many other areas of the country.

Regarding an underestimation on the part of Alamanos, *et al*, the prevalence rates of RA[2], PsA[3], and AS in the northwest Greece studies may be underestimated due to the methodology used. The National Health System of Greece is characterized by the absence of systematic patient referral to specialized centers: patients have the freedom to choose their personal physician and can move from one area to another seeking what is, in their opinion, better health care. Therefore, patients with severe forms of RA, PsA, or AS could feasibly have moved and sought health care in areas outside northwest Greece, and mild cases may have been under the care of other medical specialties and thus not recorded. In connection with the latter, it should be taken into account that in our ESORDIG study findings, only 10.5% of AS patients had visited a rheumatologist as a first visit, while during the course of their disease (mean disease duration ± SD 18.03 ± 10.93 years) 32% of AS patients had never visited a rheumatologist (unpublished data).

In referring to international data, most of the prevalence studies for RA, PsA, and AS, in other European countries, have reported prevalence rates for these diseases which are very close to or even higher than those found in the ESORDIG study. Saraux, *et al*[4] from France have recently reported prevalence rates for RA and seronegative spondyloarthropathies at the level of 0.62% and 0.47% of adults, respectively, which are almost identical to those of the ESORDIG study (0.67% and 0.49%, respectively). In a study from Spain, Carmona, *et al*[5] found an RA prevalence of 0.5%. The prevalence rates for AS and PsA estimated by Braun, *et al*[6] in Berlin were at the level of 0.86% and 0.29%, respectively. On the other hand, studies in the USA have reported a prevalence rate for RA of approximately 1%[7] and for PsA of 0.1%[8], although the latter has been considered to be underestimated[9].

It is quite clear that methodological differences exist between our population based cross-sectional epidemiological study and the studies by Drs. Alamanos and Drosos and coworkers[2,3], which were based on diagnosed cases in 2 hospitals and private rheumatologists' offices and then extrapolated to the population of northwestern Greece. It is our strong belief that methodological differences are the most likely explanation for discrepancies in RA, PsA, and AS prevalences between the northwest Greece studies and our ESORDIG study.

To our knowledge, the ESORDIG study is the first population based, cross-sectional epidemiological study that has simultaneously assessed the prevalence of all rheumatic diseases in the general adult population. The

study, based on a standardized questionnaire as well as on clinical evaluation and laboratory investigation of the participants, was carried out in both phases exclusively by experienced rheumatologists who visited a representative sample of the Greek general adult population at their homes. Therefore, the estimated age and sex adjusted prevalence of all rheumatic diseases, including RA, PsA, and AS, can be considered to be representative of the prevalence of these diseases in the general adult population of Greece.

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Correction

Saunders D. Coping with chronic pain: what can we learn from pain self-efficacy beliefs. J Rheumatol 2004;31:1032-4. The author's correct E-mail address is "douglas.saunders @utoronto.ca" We regret the error.