Socioeconomic Status and Risk of Rheumatoid Arthritis: A Danish Case-Control Study

MERETE PEDERSEN, SØREN JACOBSEN, METTE KLARLUND, and MORTEN FRISCH

ABSTRACT. ***Objective***. To examine whether markers of socioeconomic status (SES) are associated with risk of rheumatoid arthritis (RA), and if so, whether selected lifestyle-related factors could explain this association.

Methods. We conducted a frequency matched case-control study; subjects comprised 515 patients (participation rate 83%) attending rheumatology and internal medicine departments in Denmark, with recently diagnosed RA according to the American College of Rheumatology (ACR) 1987 classification criteria for RA (mean disease duration 2.3 yrs), and 769 frequency-matched population controls (participation rate 64%). Information about SES and environmental exposure was obtained by structured telephone interview. Logistic regression analyses evaluated the role of markers of SES.

Results. Level of education was significantly inversely associated with risk of RA, with a 2-fold lower risk of RA among those with the longest formal education compared with those having the lowest level of education (multivariate odds ratio = 0.43, 95% confidence interval 0.24–0.76, p trend = 0.001). None of a series of studied lifestyle factors could explain this finding in multivariate logistic regression analyses. When dividing the RA cases into clinical subgroups, the inverse association with level of education was found to apply predominantly to rheumatoid factor (RF)-positive RA.

Conclusion. The inverse association between level of education and risk of RF-positive RA was not explained by any of the examined lifestyle factors. RF-positive and RF-negative RA may be 2 distinct diseases with different etiologies, with unmeasured factors related to educational level predominantly associated with the risk of RF-positive RA. However, because mechanisms underlying referral to a hospital might be linked to educational level, our observation based on hospital–referred RA patients should be evaluated cautiously. The study stresses the importance of taking SES measures into account in studies that aim at identifying environmental risk factors for RA. (First Release April 15 2006; J Rheumatol 2006;33:1069–74)

Key Indexing Terms:
RHEUMATOID ARTHRITIS EDUCATION SOCIOECONOMIC STATUS
ETIOLOGY RHEUMATOID FACTOR

Rheumatoid arthritis (RA) is the most common autoimmune rheumatic joint disease, with a prevalence of about 0.5–1.0% and an annual incidence rate between 25 and 50 per 100,000 individuals[1]. A range of both inherited and environmental factors have been suggested as causal factors in RA[2].

From the Department of Epidemiology Research, Danish Epidemiology Science Centre, Statens Serum Institut; and Department of Rheumatology, University Hospital of Copenhagen, Copenhagen, Denmark.

Supported by grants from The Danish Rheumatism Association, Aase and Ejnar Danielsen's Foundation, The Gangsted Foundation, Dagmar Marshall's Foundation, Krista and Viggo Petersen's Foundation, Frederik Leth Christiansen's Foundation, Lily Benthine Lund's Foundation, Kurt Bønnelycke and Mrs. Grethe Bønnelycke's Foundation, Hede Nielsen's Foundation, Poul Martin Christiansen's Foundation, The Linex Foundation, Apoteker-fonden, the Frimodt-Heineke Foundation, Director Ib Henriksen's Foundation, Henny and Helge Holgersen's Memorial Fund, Torben and Alice Frimodt's Foundation, Max Fodgaard's Foundation, Niels Hansen and Wife's Foundation, and Frode V Nyegaard and Wife's Foundation.

M. Pedersen, MSc, Department of Epidemiology Research, Danish Epidemiology Science Centre; S. Jacobsen, MD, PhD; M. Klarlund, MD, PhD, Department of Rheumatology, University Hospital of Copenhagen; M. Frisch, MD, PhD, Department of Epidemiology Research, Danish Epidemiology Science Centre.

Address reprint requests to M. Pedersen, Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, DK-2300 København S, Denmark. E-mail: mtb@ssi.dk

Accepted for publication January 26, 2006.

A number of chronic diseases occur more frequently in individuals with limited formal education[3,4]. For RA, an inverse association between educational level and clinical symptoms has been described in several studies[5-7]. However, from an etiological viewpoint the association between educational level and risk of developing RA has not been thoroughly investigated. An inverse association between educational level and risk of RA was found in a Swedish hospital-based case-control study[8]. Whether this association is related to differences in lifestyle or socioeconomic status (SES) differences in access to healthcare is unknown. A recent population-based case-control study, also from Sweden, found that individuals without a university degree had significantly higher risk of RA compared to individuals with a university degree. This association was seen only for rheumatoid factor (RF)-positive cases. Further, the combined group of manual laborers, and assistant and intermediate nonmanual workers had significantly higher risk of RF-positive RA, but not RF-negative RA, compared to higher nonmanual workers[9]. A population-based study in Norway found a negative association between years of education and risk of RA, but this association was not statistically significant after adjustment for age, sex, marital status, body mass index, employment status, and current

smoking[10]. Another population-based study in the United Kingdom found no association between social class, based on occupational status, and incidence of RA[11].

The overall aim of our study was to examine a large number of hypothesized risk factors for RA in order to identify possible interactions between the studied factors. For that purpose we collected information from study participants about a wide range of background variables and exposures in order to investigate them in detail in subsequent reports. An association between markers of SES and risk of RA might lead to new hypotheses about the role of environmental and lifestyle-related factors in the etiology of RA. In this report, therefore, we examined whether markers of SES including schooling, level of education, economic status in childhood, and economic status in adulthood are associated with risk of RA. Further, if measures of SES were found to be associated with risk of RA, we examined whether a series of selected lifestyle-related factors could explain the association.

MATERIALS AND METHODS

Identification of cases and controls. We conducted a frequency matched case-control study consisting of cases identified among inpatients and outpatients from hospital based rheumatology and internal medicine departments throughout Denmark. To be included, cases had to be diagnosed between ages 18 and 65 years with RA according to the American College of Rheumatology (ACR) 1987 classification criteria for RA[12] between August 1998 and July 2003. Information about date of diagnosis, defined as the date where the RA diagnosis was clinically confirmed by an experienced rheumatologist, cumulative fulfilment of the ACR 1987 classification criteria for RA, RF status, and erosions was obtained from medical records by a rheumatologist at each department or by the project coordinator (MP) and a rheumatologist (MK) from the study team. RF tests performed as part of the diagnostic process had been analyzed for IgM RF using the lower 5th percentile of healthy individuals as cutoff level, and radiographic characteristics were obtained from descriptions of routine radiographs performed by various examiners who had no knowledge of the current study. Radiographic changes in hand radiographs had to include at least bony decalcification localized to or most marked adjacent to the involved joints to qualify as meeting the classification criterion. Radiographic changes had to clearly show marginal bony defects to be classified as erosive, i.e., joint space narrowing or juxtaarticular bony decalcification alone were not termed as erosive changes.

Controls, frequency-matched for sex and year of birth, were randomly selected from the Danish population by use of the Danish Civil Registration System. Using identical invitation letters to cases and controls, we aimed at a 1:1 control-case ratio for women and a 2:1 control-case ratio for men, but all invited subjects who were willing to participate were included in the study.

Data collection. The procedure for the data collection was tested in a pilot experiment to which 100 individuals (50 cases and 50 controls) were invited. On positive response these individuals were interviewed and blood samples were collected. Minor adjustments were made in the study procedures after the pilot phase. Information from participants in the pilot experiment is not included in our present report.

Three trained female medical students carried out all interviews between September 2002 and February 2004, and bimonthly meetings were held to ensure that all interviews were done in a uniform manner. The telephone questionnaire was developed by the research group based on new and previously hypothesized risk factors for RA. Interviews were conducted as computer assisted telephone interviews, and answers were entered directly into a database. Logical tests were built into the program, and data entry mistakes were therefore kept at a minimum. Each telephone interview required about half an hour. Interviews included, among a long list of variables, information about markers of SES: schooling (≤ 7 yrs, 8–9 yrs, 10 yrs, and > 10 yrs of schooling), level of education [no education (including current students); semi-skilled worker, short education (< 1 yr), or apprentice; advanced studies of short or medium length (1–4 yrs); longer-term advanced studies (> 4 yrs)], economic status in childhood, and economic status in adulthood (participants were asked to classify themselves as belonging to the least affluent third, the middle third, or the most affluent third of the population). As mentioned, detailed information about a large number of hypothesized lifestyle-related risk factors for RA, including smoking, body mass index, physical activity, marital status, number of children, and coffee and alcohol intake will be presented separately.

Data analysis. Only exposures before clinical diagnosis of RA were considered in the analyses. An arbitrary pseudo-year of diagnosis was attributed to our population controls according to the frequency distribution of year of RA diagnoses in cases of the same sex. All information about exposures after the year or pseudo-year of diagnosis was omitted from analyses.

Logistic regression analyses (PROC LOGISTIC procedure, SAS Version 9.1) with adjustment only for sex, year of birth, year or pseudo-year of diagnosis, and place of residence (Copenhagen, suburbs of Copenhagen, other towns with ≥ 100,000 inhabitants, towns with 10,000–99,999 inhabitants, and rural areas/towns with < 10,000 inhabitants) were performed as the initial investigation into the role of the 4 markers of SES (schooling, education level, economy in childhood, and economy as adult) and for a set of hypothesized risk factors for RA, which might be related to SES (see below). We refer to these analyses as univariate analyses to indicate that only basic demographic confounders were taken into account. Tests for homogeneity were performed in order to identify statistically significant differences between groups, and simple qualitative trend tests were performed by enumerating classes by consecutive numbers starting with 1.

To examine which of the 4 markers of SES best revealed socioeconomic differences in our study, a multivariate logistic regression analysis was performed, which included all 4 markers of SES in addition to sex, year of birth, year or pseudo-year of diagnosis, and place of residence.

Assuming that the observed association between level of education and risk of RA is explained by differences in lifestyle between different socioeconomic groups, we examined whether any of a range of lifestyle-related factors for which we had interview information could explain this association. The factors in this multivariate logistic regression model were in addition to sex, year of birth, year or pseudo-year of diagnosis, and place of residence, and included: tobacco smoking (cumulative exposure expressed as pack-years, one pack-year equivalent to 20 cigarettes smoked per day for one year. One cigarette was taken as equivalent to 1 g, one cheroot to 3 g, and one cigar to 4 g tobacco), body mass index at 20 years of age, physical activity at work and during leisure time (heavy, moderate, light, no physical activity), marital status (married or cohabiting with partner; widowed, divorced, or separated; unmarried), number of live-born children, coffee intake, and alcohol consumption. All of these had p values below 0.20 in univariate logistic regression analyses (tests for homogeneity) of their association with risk of RA. These variables were chosen among a larger list of variables under the assumption that they might be associated with differences in lifestyle. The multivariate analysis was repeated in subgroups of cases (RF-positive/negative cases and erosive/non-erosive cases) versus all controls.

Our study was approved by the Scientific Ethical Committees for Copenhagen and Frederiksberg (J. no. KF 01-039/01) and the Danish Data Protection Agency (2001-41-0658).

RESULTS

The study population consisted of 515 cases with recently diagnosed RA and 769 frequency-matched controls. This corresponds to participation of 83% of 619 invited cases and 64% of 1207 invited controls. Selected characteristics of the study population are shown in Table 1. Mean disease duration at the time of interview was 2.3 years (range 0–5).

Table 1. Selected characteristics of the study population.

	Cases	Controls
Participants, n	515	769
Women (participation rate)	366 (84% of 436 invited)	478 (65% of 730 invited)
Men (participation rate)	149 (81% of 183 invited)	291 (61% of 477 invited)
Mean age at diagnosis, yrs (range)[a]	49 (18–65)	48 (16–68)
Birth year, no. (%)		
< 1940	71 (13.8)	98 (12.7)
1940–49	171 (33.2)	250 (32.5)
1950–59	145 (28.2)	223 (29.0)
1960–69	77 (15.0)	129 (16.8)
≥ 1970	51 (9.9)	69 (9.0)
Place of residence, no. (%)		
Copenhagen	86 (16.7)	102 (13.3)
Suburbs of Copenhagen	90 (17.5)	137 (17.8)
Other towns with ≥ 100,000 inhabitants	78 (15.2)	77 (10.0)
Towns with 10,000–99,999 inhabitants	93 (18.1)	197 (25.6)
Rural areas/towns with < 10,000 inhabitants	168 (32.6)	256 (33.3)
Marital status, no. (%)		
Married or cohabiting with partner	383 (74)	581 (76)
Widowed, divorced, separated	66 (13)	123 (16)
Unmarried	66 (13)	65 (8)
Cigarette smoking, pack-years[b], (%)		
0	154 (30)	298 (39)
> 0 ≤ 10	98 (19)	142 (19)
> 10 ≤ 20	103 (20)	125 (16)
> 20	154 (30)	196 (26)

[a] Age in controls calculated as pseudo-year of diagnosis minus birth year. [b] Insufficient information to calculate pack-years for 6 cases and 8 controls.

In univariate analyses, years of schooling (test for homogeneity, $p = 0.002$) and educational level (test for homogeneity, $p < 0.001$) were both significantly and inversely associated with risk of RA (Table 2). The association between level of education and risk of RA was found in univariate analyses of both males and females and in analyses of individuals below and above the median age at invitation (52 yrs; data not shown). Individuals who categorized themselves as belonging to the most affluent third of the population in childhood and/or in adulthood tended to be at lower risk than those who classified themselves as belonging to the least affluent third. However, the 3 economic categories did not differ significantly ($p > 0.05$).

In the multivariate logistic regression model including all 4 markers of SES, only educational level remained significant at the 5% level (Table 2). The association of level of education with risk of RA could not be explained by underlying differences in lifestyle-related factors, including measures of tobacco smoking, body mass index, physical activity, marital status, parity, and intake of coffee and alcohol (Table 3, "All RA cases"). However, when dividing the cases into serological subgroups, the association between educational level and RA was seen predominantly among RF-positive cases (Table 3).

DISCUSSION

Among our measures of socioeconomic factors we found a significant inverse association between level of education and risk of RA. In order to examine whether this association could be explained by differences in lifestyle, we developed a multivariate logistic regression model including in addition to level of education a range of lifestyle-related factors. We found that the significant inverse association between educational level and risk of RA was not explained by differences in these lifestyle variables. Pincus, *et al* discuss how measures of SES often explain health status more effectively than biomedical risk factors[13]. We agree that unmeasured lifestyle or behavioral conditions may explain the observed association between educational level and RA risk in our study.

The observed inverse association between level of education and risk of RA should be viewed in light of the fact that it was estimated that two-thirds of Danish patients who meet ACR 1987 criteria for RA are not referred to hospital[14]. The Danish healthcare system provides free access to medical care, and economic differences among socioeconomic groups are therefore unlikely to result in differences in use of the healthcare system. However, if patients from lower socioeconomic groups are more likely to have clinically severe RA, as suggested by prior studies[1-3], they may be overrepresented among RA patients recruited from hospital departments as in our current study. Such a potential bias would be compatible with prior reports of no link between SES and risk of RA in population-based studies[10,11], whereas an inverse association

Table 2. Univariate and multivariate logistic regression analyses of the association of markers of socioeconomic status with risk of RA.

	Cases, no. (%)	Controls, no. (%)	Univariate OR (95% CI)[a]	Multivariate OR (95% CI)[b]
Schooling, yrs				
≤ 7	106 (20.6)	127 (16.5)	1 (ref)	1 (ref)
8–9	118 (22.9)	145 (18.9)	0.94 (0.64–1.40)	1.03 (0.69–1.55)
10	123 (23.9)	201 (26.2)	0.64 (0.43–0.95)	0.75 (0.50–1.14)
> 10	168 (32.6)	295 (38.4)	0.52 (0.35–0.78)	0.76 (0.48–1.20)
Test for homogeneity			p = 0.002	p = 0.27
Trend test[c]			p < 0.001	p = 0.11
Education				
No education[d]	123 (23.9)	120 (15.6)	1 (ref)	1 (ref)
Semi-skilled worker, short education (< 1 yr) or apprentice	204 (39.6)	293 (38.1)	0.71 (0.51–1.00)	0.76 (0.53–1.07)
Short or medium length advanced studies (1–4 yrs)	156 (30.3)	265 (34.5)	0.52 (0.36–0.73)	0.58 (0.40–0.84)
Longer term advanced studies (> 4 yrs)	32 (6.2)	90 (11.7)	0.30 (0.18–0.51)	0.37 (0.20–0.66)
Test for homogeneity			p < 0.001	p = 0.003
Trend test[c]			p < 0.001	p < 0.001
Economic status as child				
Least affluent third	113 (22.0)	157 (20.5)	1 (ref)	1 (ref)
Middle third	362 (70.4)	528 (69.0)	0.90 (0.67–1.21)	1.01 (0.74–1.36)
Most affluent third	39 (7.6)	80 (10.5)	0.66 (0.41–1.06)	0.86 (0.52–1.40)
Test for homogeneity			p = 0.22	p = 0.77
Trend test[c]			p = 0.11	p = 0.64
Economic status as adult				
Least affluent third	40 (7.8)	44 (5.7)	1 (ref)	1 (ref)
Middle third	374 (72.6)	548 (71.4)	0.78 (0.49–1.25)	0.83 (0.51–1.34)
Most affluent third	101 (19.6)	176 (22.9)	0.64 (0.38–1.07)	0.84 (0.49–1.43)
Test for homogeneity			p = 0.19	p = 0.75
Trend test[c]			p = 0.07	p = 0.60

[a] Univariate analyses adjusted for sex, year of birth, year or pseudo-year of diagnosis, and place of residence. [b] Multivariate model including (in addition to sex, year of birth, year or pseudo-year of diagnosis, and place of residence) all 4 markers of socioeconomic status. [c] Simple qualitative trend test. [d] Including current students (n = 18 cases, n = 16 controls). Numbers do not sum to 515 patients/769 controls because of missing questionnaire information for some individuals. RA: Rheumatoid arthritis, OR: odds ratio, CI: confidence intervals.

similar to ours was reported in another case-control study with RA patients recruited from hospital departments[8]. On the other hand, well educated persons might seek clinical advice from their doctors and contact specialists in hospital departments at an earlier stage of their disease than persons of lesser education. Such a mechanism working in the opposite direction would favor an overrepresentation of well educated persons among hospital-referred RA patients and, consequently, would tend to underestimate any true inverse relationship between educational level and RA risk. If so, the strong inverse link between education and RA risk in our study may even be conservative.

Another potential source of bias to be considered is that a larger proportion of well educated than non-educated control individuals might be willing to participate in the study, whereas RA patients of all educational levels might be more equally motivated to participate. Accordingly, the inverse association between level of education and risk of RA might in part be due to the lower response rate among controls. However, we find it unlikely that the difference of 19% in response rates between cases and controls should alone explain the more than 2-fold difference in risk of RA seen between the most educated and the least educated group. Specifically, to get an odds ratio of 1 between individuals with longterm advanced studies and those without education, it would require that all nonresponding controls, corresponding to the difference of 19% in response rate between cases and controls, belong to the "no education" group.

Further, the above-mentioned potential sources of bias fail to explain that the association with level of education was predominantly seen for RF-positive RA, a finding that is in accord with a recent study in Sweden. That study reported a stronger association between SES, measured by educational status and occupation, and risk of RF-positive RA than between SES and risk of RF-negative RA[9]. These findings suggest that RF-positive and RF-negative RA may be 2 distinct diseases with different etiologies, and that unmeasured factors related to educational level are associated predomi-

Table 3. Multivariate logistic regression analysis of the association between level of education and risk of RA overall and by subgroups of RA.

Education	Cases, no. (%)[a]	Controls, no. (%)[a]	Multivariate OR (95% CI)[b] All RA Cases vs Controls (n = 488 cases)	RF-Positive RA vs Controls (n = 369 cases)	RF-Negative RA vs Controls (n = 119 Cases)	Erosive RA vs Controls (n = 149 cases)[c]	Non-erosive RA vs Controls (n = 313 cases)[c]
No education[d]	112 (23.0)	109 (15.0)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Semi-skilled worker, short education (< 1 yr) or apprentice	198 (40.6)	277 (38.2)	0.84 (0.59–1.22)	0.72 (0.48–1.06)	1.41 (0.71–2.80)	0.55 (0.32–0.95)	0.98 (0.64–1.50)
Short or medium length advanced studies (1–4 yrs)	148 (30.3)	253 (35.0)	0.64 (0.44–0.95)	0.54 (0.36–0.83)	1.07 (0.53–2.16)	0.47 (0.26–0.84)	0.71 (0.45–1.13)
Long advanced studies (> 4 yrs)	30 (6.1)	86 (11.9)	0.43 (0.24–0.76)	0.32 (0.17–0.62)	0.85 (0.32–2.27)	0.35 (0.15–0.84)	0.48 (0.24–0.94)
Test for homogeneity			p = 0.01	p = 0.003	p = 0.52	p = 0.04	p = 0.06
Trend test[e]			p = 0.001	p < 0.001	p = 0.53	p = 0.008	p = 0.01

[a] No. of individuals (all RA cases and controls). [b] Multivariate logistic regression model adjusted for sex, year of birth, year or pseudo-year of RA diagnosis, and place of residence as well as for tobacco smoking (pack-years in 4 categories), body mass index at age 20 yrs (4 categories), physical activity at work and during leisure time (4 categories each), marital status (3 categories), no. of live-born children (continuous variable), intake of coffee (daily consumption 10 yrs prior to interview, continuous variable), and intake of alcohol (weekly consumption 10 yrs prior to interview, 4 groups). [c] Information about erosions not available for 26 cases. [d] Including current students. [e] Simple qualitative trend test. Numbers do not sum to 515 patients/769 controls because of missing questionnaire information for some individuals. RA: Rheumatoid arthritis, OR: odds ratio, CI: confidence intervals, RF: rheumatoid factor.

nantly with the risk of RF-positive RA. Studies of the association between tobacco smoking and risk of RA have shown that smoking is associated with increased risk of RF-positive RA but not with RF-negative RA[15,16]. Also, coffee consumption has been found to be selectively associated with RF-positive RA in a dose-dependent way, supporting the concept of different etiologies for RF-positive and RF-negative RA[17].

In conclusion, level of education was inversely associated with risk of RF-positive RA. This finding could not be explained by any of the examined lifestyle factors, but is likely to be explained by unmeasured risk factors related to low educational level. However, cautious interpretation is warranted because spurious selection mechanisms related to the recruitment of patients with RA from hospital departments and the lower participation rate among controls might have contributed to the observed inverse association between educational level and RA risk. Regardless, our study stresses the importance of taking measures of socioeconomic status into account in studies that aim at identifying environmental risk factors for RA.

ACKNOWLEDGMENT

The authors thank members of the CACORA Study Group for providing patients to the study: Jens Kristian Pedersen (Kong Christian X's Gigthospital, Gråsten); Søren Freiesleben-Sørensen (Bispebjerg Hospital); Anne Rødgaard (Roskilde County Hospital Køge); Annette Hansen and Michael Sejer Hansen (Copenhagen County Hospital, Glostrup); Lars Juul (Frederiksberg Hospital); Hans Henrik Mogensen (Hørsholm Hospital); Barbara Unger (Holstebro Hospital); Peter Mosborg Petersen (Randers Hospital); Jan Christensen (Naestved Hospital); Randi Pelck (Roskilde County Hospital, Roskilde); Merete Graakjær Nielsen (Aarhus University Hospital); Nanna Gregersen (Bornholm Hospital); and Jesper Sylvest (Amager Hospital). We also thank rheumatology departments for permission to identify patients for our study: University Hospital of Copenhagen, Hvidovre Hospital, Herlev University Hospital, Esbjerg Hospital, Gentofte Hospital, Odense University Hospital, Slagelse Hospital, and Århus University Hospital. Additional thanks to statisticians Bo V. Pedersen and Jan Wohlfart for discussions of the statistical analyses.

REFERENCES

1. Kaipiainen-Seppanen O, Aho K. Incidence of chronic inflammatory joint diseases in Finland in 1995. J Rheumatol 2000;27:94-100.
2. Symmons D, Harrison B. Early inflammatory polyarthritis: results from the Norfolk Arthritis Register with a review of the literature. I. Risk factors for the development of inflammatory polyarthritis and rheumatoid arthritis. Rheumatology Oxford 2000;39:835-43.
3. Pincus T, Callahan LF, Burkhauser RV. Most chronic diseases are reported more frequently by individuals with fewer than 12 years of formal education in the age 18-64 United States population. J Chronic Dis 1987;40:865-74.
4. Mitchell JM, Burkhauser RV, Pincus T. The importance of age, education, and comorbidity in the substantial earnings losses of individuals with symmetric polyarthritis. Arthritis Rheum 1988;31:348-57.
5. Callahan LF, Pincus T. Formal education level as a significant marker of clinical status in rheumatoid arthritis. Arthritis Rheum 1988;31:1346-57.
6. Pincus T, Callahan LF. Formal education as a marker for increased mortality and morbidity in rheumatoid arthritis. J Chronic Dis 1985;38:973-84.
7. ERAS Study Group. Socioeconomic deprivation and rheumatoid disease: What lessons for the health service? Ann Rheum Dis 2000;59:794-9.
8. Reckner OA, Skogh T, Wingren G. Comorbidity and lifestyle, reproductive factors, and environmental exposures associated with rheumatoid arthritis. Ann Rheum Dis 2001;60:934-9.
9. Bengtsson C, Nordmark B, Klareskog L, Lundberg I, Alfredsson L. Socioeconomic status and the risk of developing rheumatoid arthritis. Results from the Swedish EIRA study. Ann Rheum Dis 2005;64:1588-94.
10. Uhlig T, Hagen KB, Kvien TK. Current tobacco smoking, formal education, and the risk of rheumatoid arthritis. J Rheumatol

1999;26:47-54.
11. Bankhead C, Silman A, Barrett B, Scott D, Symmons D. Incidence of rheumatoid arthritis is not related to indicators of socioeconomic deprivation. J Rheumatol 1996;23:2039-42.
12. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.
13. Pincus T, Esther R, DeWalt DA, Callahan LF. Social conditions and self-management are more powerful determinants of health than access to care. Ann Intern Med 1998;129:406-11.
14. Pedersen M, Klarlund M, Jacobsen S, Svendsen AJ, Frisch M. Validity of rheumatoid arthritis diagnoses in the Danish National Patient Registry. Eur J Epidemiol 2004;19:1097-103.
15. Stolt P, Bengtsson C, Nordmark B, et al. Quantification of the influence of cigarette smoking on rheumatoid arthritis: results from a population based case-control study, using incident cases. Ann Rheum Dis 2003;62:835-41.
16. Padyukov L, Silva C, Stolt P, Alfredsson L, Klareskog L. A gene-environment interaction between smoking and shared epitope genes in HLA-DR provides a high risk of seropositive rheumatoid arthritis. Arthritis Rheum 2004;50:3085-92.
17. Heliovaara M, Aho K, Knekt P, Impivaara O, Reunanen A, Aromaa A. Coffee consumption, rheumatoid factor, and the risk of rheumatoid arthritis. Ann Rheum Dis 2000;59:631-5.