ORIGINAL ARTICLE

Occupations and exposures in the work environment as determinants for rheumatoid arthritis

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Background and Aims: Several occupational categories have been associated with rheumatoid arthritis (RA); this study was conducted to further evaluate these associations.
Methods: Lifelong occupational history together with exposure experiences were collected through a postal questionnaire answered by 293 incident cases and 1346 population based referents. Occupational determinants were evaluated through stratified and multivariate analyses; pooled analyses with previously gathered data on 422 prevalent cases and 858 referents were also performed.
Results: In both materials, significantly increased logistic odds ratios (LORs) were seen for male conductors, freight and transport workers (LOR 17.8, 95% CI 1.5 to 207.8 and LOR 4.7, 95% CI 1.4 to 16.3, respectively), and farmers and farm workers (LOR 2.4, 95% CI 1.1 to 5.2, and LOR 2.2, 95% CI 1.3 to 3.5, respectively). Among women, increased LORs were seen in the separate and the pooled material for printmakers and process engravers (LOR 5.5, 95% CI 0.9 to 32.6, and LOR 3.0, 95% CI 0.9 to 10.3, respectively). Increased risks were seen in both materials for men exposed to asbestos (LOR 2.5, 95% CI 1.0 to 6.8, and LOR 1.6, 95% CI 0.8 to 3.3, respectively), and vibrations (LOR 2.0, 95% CI 0.9 to 4.4, and LOR 2.2, 95% CI 1.3 to 3.8, respectively). The risk for RA increased with increasing duration of exposure to vibrations and mineral dust, respectively.
Conclusions: There was evidence of a causal relation between exposures to vibrations and mineral dust and development of RA among men. Occupational factors seem to be aetiologically more important for men, and most occupations at risk involve multiple exposures. Several exposures associated with an increased risk for RA are frequent among farmers, and some of the occupations at risk include exposure to organic dust.

Rheumatoid arthritis (RA) is a chronic inflammatory disease, which demands early potent treatment in order to prevent severe impairment and work disability.[1] No primary prevention is available, as the aetiology of RA is not fully understood, although some susceptibility factors and several genes seem to be of importance for disease development.[2] Recent research has also shed light on the pathogenic mechanisms once the disease is initiated.[3–4]

The relevance of exploring external exposures in search for aetiological factors is evident in view of the low genetic penetrance of RA[5] as indicated by a relatively low disease concordance of approximately 15% among monozygotic twins.[6] Some studies have evaluated the importance of occupational determinants; an increased frequency of RA has been observed in several occupational categories.[7–14]

The occupations at risk include both indoor and outdoor work, with or without physical strain or recognised hazardous exposures. Many of the occupations involve multiple exposures but few causative agents have been suggested. The most consistently reported exposure associated with RA is silica.[10 12 15 16] Exposure to organic solvents[8] and mineral oil[17] have also been suggested as risk factors. Experimental studies have shown that mineral oils can induce arthritis in animals,[18–20] and it has been suggested that they may act as so called adjuvants enhancing immune reactions. A similar mode of action has been suggested for silica.[21]

In a previous publication, we presented results from a case-referent study of occupational determinants which both corroborated previous reports and indicated new relationships.[14] In order to further explore the impact of occupational exposures, a second case-referent study with prospective inclusion of cases has now been performed.

MATERIALS AND METHODS

Recruitment of subjects

Incident cases were recruited from the regional project "TIRA" (Swedish acronym for "early intervention in rheumatoid arthritis"). Ten Swedish rheumatology units participated, and 322 patients with recent onset RA were included during a 27 month period (1996–98). All patients fulfilled at least four of the American Rheumatism Association (ARA) 1987 revised classification criteria for RA,[22] *or* suffered from morning stiffness (60 minutes or more as judged by the patients) as well as symmetrical arthritis and arthritis in small joints (fingers/hands/wrists/feet/toes). Approximately 95% of the patients fulfilled at least four of the ARA criteria. The first symptoms and/or signs of arthritis had occurred at least six weeks, but not more than 12 months, before inclusion.

For each case, four referents were chosen at random from the population register of the catchment areas of the rheumatology units at the time when the case was reported. The referents were given a calendar year of enrolment corresponding to the year of diagnosis of the case. Only exposures occurring before the year of diagnosis or enrolment were recorded. For inclusion in the case-referent analyses, cases and references were required to be diagnosed or enrolled, respectively, at age 16–75 years, and all subjects should be born in the Nordic countries. The study finally comprised 293 cases and 1346 referents.

Abbreviations: ARA, American Rheumatism Association; CI, confidence interval; LOR, logistic odds ratio; RA, rheumatoid arthritis

Main messages

- External exposures are of significant importance for the development of RA.
- Results further support the previously suggested association between RA and mineral dust.
- Support for a causal relation with other exposures previously not mentioned in the context of RA has also been found. An example is the dose-response relation between RA and vibrations.
- Several exposures associated with RA involve a route of exposure through inhalation.
- Occupational determinants seem to be more important for the development of RA in men than in women. However, as many occupational categories consist almost solely of individuals of the same sex, few exposures can be evaluated for both sexes.

Policy implications

- Results, especially the reproductions of earlier findings in the literature, suggest the importance of occupational risk factors in the pathogenesis of RA, and makes the need for further analytical epidemiological studies in the field clear.

Exposure assessment

Information on lifelong occupational history and certain specified occupational exposures, as well as on other possible aetiological factors, was collected through a postal questionnaire. The subjects were asked to state all previous occupational belongings, and the duration of the employment. Concerning specific exposures, subjects were asked whether or not they had been exposed to specific agents, and if so, for what period of time. The questionnaire was mailed to cases and referents consecutively during the inclusion period. Postal reminders were sent twice, and those still not responding were contacted by telephone. The questionnaire was used in our previous case-referent study.[14] As the response rate in this study was lower than expected, the questionnaire was however slightly modified and shortened.

The subjects' occupations were classified according to the Nordic classification of occupations (Swedish acronym: NYK).[23]

The results from analyses considering occupational categories in both the previous and the present case-referent study indicated the importance of certain exposures not explicitly asked for in the questionnaire. These exposures were organic dust, engine exhaust, and physically strenuous work. A specialist in occupational medicine and an occupational hygienist therefore separately performed additional classification of the occupational categories with regard to exposure to these factors. An occupational group was regarded as exposed when classified as such by both experts, who were uninformed regarding case or referent status of the subjects.

Due to low response rates, information on socioeconomic status for both responders and non-responders was gathered through the local tax authorities to facilitate an evaluation of a possible non-response bias. This information was gathered for the fiscal year of 1997.

The study was approved by the ethics committee at Linköping University Hospital.

Analyses

Based on the age distribution among the referents, the data were stratified on three age categories: 16–37, 38–57, and 58–75 years of age. Since smoking is a risk factor for RA[24–26] and could be suspected to vary between occupations, the data were further stratified on three smoking categories: non-smokers, occasional smokers, and previous or current smokers. Stratified analyses were performed using the computer program EPIINFO (EPIINFO 6.04, Center for Disease Control and Prevention (CDC), USA). Separate analyses were performed for men and women.

To facilitate comparisons with previously published studies, a latency requirement of 20 years between exposure and year of diagnosis, or enrolment, was chosen. Analyses were also performed without a latency requirement, since the induction of arthritis in experimental animal models[18–20] indicates a fairly short latency period.

Occupational determinants with at least five exposed subjects and ORs either $\leqslant 0.5$ or $\geqslant 1.5$, or with results significantly differing from unity in the stratified analyses, were included in the logistic regression analyses (SPSS Inc., Chicago, IL, USA). Occupations and specific occupational exposures were evaluated in separate multivariate analyses, including age and smoking as categorical variables. In the tables, results are presented for determinants with logistic odds ratios (LORs) either $\leqslant 0.5$ or $\geqslant 1.5$.

In order to produce results with higher precision, the subjects were also analysed together with those included in our previous case-referent study.[14] The number of subjects in that study comprised 422 cases and 858 referents. The classification of occupations and exposures was the same as described for the study with incident cases.

After merging data from the two case-referent studies, the pooled material encompassed 715 cases and 2204 referents. The two case-referent data sets are displayed in table 1. Stratified analyses were performed using three age categories: 16–39, 40–57, and 58–75 years of age, respectively, based on the frequency distribution of ages among the referents of the pooled material. The data were also stratified on smoking categories.

Multivariate analyses of the pooled material were performed including the same determinants as in the logistic regression analyses of the material with incident cases, to allow comparison. The models included at most 26 occupational determinants when occupations were analysed among men.

Some occupational categories of interest according to a priori hypotheses included very few subjects in the separate material with incident cases, and were thus not included in the previously described logistic regression analyses according to the inclusion criteria used. These categories were male textile workers, millers and bakers, metal, foundry, and hardware workers, and asphalt layers, of which the latter group was very small but significantly associated with RA in the stratified analyses of the pooled material. To evaluate the importance of these categories, multivariate analyses were also performed on the pooled material including all determinants with at least 10 exposed subjects and ORs either $\leqslant 0.5$ or $\geqslant 1.5$, or with results significantly differing from unity in the stratified analyses. Using these criteria, some determinants were excluded which were included in the previous multivariate analyses.

To evaluate any possible dose-response relation, specific occupational exposures with at least 50 exposed subjects in the pooled material were divided into three categories of duration: $\leqslant 10$ years, 11–20 years, and $\geqslant 20$ years. Stratified analyses were then performed with adjustment for age and

Table 1 A comparison of the two case-referent studies included in the pooled analysis

	Study of incident cases of RA	Study of prevalent cases of RA
Exposure assessment	Questionnaire based	Questionnaire based
Occupational history	Lifelong	Lifelong
Cases		
Inclusion criteria		
ARA criteria* (n)	⩾4 or 3 specific†	⩾4
Age at diagnosis, range (years)	16–75	25–75
Year of diagnosis, range	1996–98	1980–95
Residency	Southeastern Sweden‡	Southeastern Sweden‡
Ethnicity	Nordic	Nordic
Origin of cases	Hospital based	Hospital based
No. included (n)	298	422
Age at diagnosis, mean (years)	55	54
Age at participation§, mean (years)	55	62
Referents		
Inclusion criteria		
Age at enrolment, range (years)	16–75	25–75
Year of enrolment, range	1996–1998	1980–1995
Residency	Southeastern Sweden‡	Southeastern Sweden‡
Ethnicity	Nordic	Nordic
Origin of referents	Population based	Population based
No. included (n)	Cases ×4	Cases ×2
Age at enrolment, mean (years)	47	50
Age at participation§, mean (years)	47	58

*American Rheumatism Association (ARA) 1987 Revised Criteria for Rheumatoid Arthritis.[22]
†Morning stiffness >60 minutes *and* symmetrical arthritis *and* arthritis of small joints.
‡Cases and referents in the study using prevalent cases were recruited from the catchment area of the University Hospital in Linköping, situated in southeastern Sweden. Cases and referents in the study using incident cases were recruited from this area as well as from the catchment areas of nine other rheumatology units located in Southeastern Sweden.
§Age when responding to the postal questionnaire.

smoking. An evaluation of the possible presence of a non-response bias was also performed in the pooled material.

RESULTS

In the study using incident cases, responded questionnaires were received from 80% (n = 235) of the cases and 56% (n = 752) of the referents. Sixty eight per cent of the responding cases and 49% of the responding referents were women.

Most differences between responders and non-responders affected cases and referents equally, therefore were unlikely to have resulted in any non-response bias. However, in the study with incident cases, there was a selective loss of male referents with a lower socioeconomic status, while in the pooled material there seemed to be a loss of both male and female cases with a lower socioeconomic status. This indicates a loss of subjects with an occupational history presumably involving more hazardous exposures.

For men, results from the logistic regression analyses of occupations in the incident and the pooled materials are shown in table 2, while results from the analyses of specified occupational exposures, including the classification of work groups with common exposures to additional agents, appear in table 3. Similarly, results for women are shown in tables 4 and 5. The results from the study with prevalent cases have been presented in a separate paper.[14]

When the smaller occupational categories, of interest according to a priori hypotheses, were included in the multivariate analyses of the pooled material, increased risks were also seen for male asphalt layers (exposed cases/referents 5/1, LOR 7.2, 95% CI 0.6 to 80.2), millers and bakers (exposed cases/referents 4/8, LOR 1.8, 95% CI 0.5 to 6.6), and textile workers (exposed cases/referents 4/6, LOR 3.3, 95% CI 0.9 to 12.4). Similarly, increased risks were seen among men for exposure to asphalt (exposed cases/referents 9/4, LOR 3.5, 95% CI 0.4 to 28.9) and flour (exposed cases/referents 13/20, LOR 2.0, 95% CI 0.7 to 5.4) (data not shown in tables).

For most exposures, the use of a latency period resulted in more polarised risk estimates. The opposite was however seen for male mechanics, repairers, sheet metal workers, and welders in the separate material, secretaries, typists, and office cashiers in both the separate material and the pooled material, and millers and bakers in the pooled material, as well as for men exposed to mineral oil in the separate material using incident cases.

Results from evaluations of dose-response relations among men can be seen in table 6. Mineral dust exposure denotes exposure to mineral dust both with and without known silica content, but does not include exposure to asbestos or man made mineral fibres (MMMF). When exposure to vibrations was classified as either exposure to vibrating tools or whole body vibrations, the ORs were 2.3 (exposed cases/referents 45/66, 95% CI 1.4 to 3.7) and 1.6 (exposed cases/referents 23/43, 95% CI 0.9 to 3.0), respectively.

DISCUSSION

For incident cases, the time span from diagnosis to participation was short, probably improving the accuracy of the exposure information and preventing a change in lifestyle due to the disease. However, they were aware of their case status, which is why there is a possibility for recall bias, although occupations are fairly clear, and hard facts and the reporting therefore less likely to be affected by the mechanisms underlying such a bias. This consciousness may also have contributed to their high response rate.

The selective loss of male referents with a lower socioeconomic status in the study of incident cases may result in an overestimation of risks for RA among blue collar workers. In the pooled analyses, the selective loss of both male and female cases with a lower socioeconomic status on the contrary could imply an underestimation of risks for these

Table 2 Multivariate analysis of occupational categories among men with adjustment for age and smoking; analysis of: 74 incident cases and 382 referents; and 176 cases and 630 referents in the pooled material

	Incident cases			Pooled material		
Occupation (NYK codes)	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Conductors, freight, and transport workers (651–659)	3/2	17.8	1.5 to 207.8	7/6	4.7	1.4 to 16.3
ADP workers (251–259)	2/3	10.2	1.2 to 86.5	3/4	3.5	0.6 to 19.5
Electricians, electromechanical workers, and service personnel (761–769)	9/18	3.4	1.2 to 9.4	15/29	1.8	0.8 to 3.6
Chemical, rubber, and plastic industry workers (831–839)	4/5	2.7	0.6 to 11.3	4/7	1.4	0.4 to 5.3
Cleaners and caretakers (931–939)	1/4	2.7	0.2 to 45.4	2/7	0.7	0.1 to 4.1
Farmers and farm workers (400, 402, 411, 412)	20/41	2.4	1.1 to 5.2	49/77	2.2	1.3 to 3.5
Pulp and paper workers (841–849)	5/4	2.4	0.5 to 12.2	7/5	3.1	0.9 to 11.4
Gardeners (401, 403, 413)	4/6	2.1	0.5 to 9.5	5/13	0.6	0.2 to 1.8
Goods handling workers, machine men, transport workers (871–879)	4/10	2.1	0.5 to 8.2	7/14	1.5	0.6 to 4.2
Post and telegraph personnel (671–689)	5/13	2.0	0.5 to 7.3	8/21	1.5	0.6 to 3.7
Mechanics, repairers, sheet metal workers, and welders (751–759)	29/75	1.8	1.0 to 3.4	54/126	1.4	0.9 to 2.1
Building and construction workers, except asphalt layers (791–799)	8/23	1.7	0.5 to 5.4	21/42	1.1	0.5 to 2.3
Painters, lacquers, and floor layers (781–789)	3/7	1.6	0.3 to 7.8	6/11	1.3	0.4 to 3.8
Secretaries, typists, and office cashiers (241–249)	2/9	1.2	0.2 to 7.0	6/12	2.1	0.7 to 6.5
Administrators and managers in society or companies (201–219)	1/13	0.7	0.1 to 6.0	3/22	0.5	0.1 to 1.9
Packers and warehouse workers (881–889)	3/10	0.7	0.1 to 3.4	10/18	1.5	0.6 to 3.6
Engineers and technicians (001–009)	8/39	0.6	0.2 to 1.6	13/64	0.5	0.3 to 1.0
Printmakers, process engravers, etc (801–809)	1/10	0.5	0.1 to 5.2	2/13	0.4	0.1 to 2.2
Hotel and restaurant workers (911–919)	1/10	0.3	0.0 to 2.8	2/13	0.4	0.1 to 1.8
Accountants, personnel management, and other administrative workers (221–239, 261–299)	1/21	0.2	0.0 to 1.3	5/41	0.4	0.1 to 1.0
Ship officers, pilots, and other seamen (601–619)	1/9	0.1	0.0 to 1.3	3/12	0.5	0.1 to 2.1

Logistic odds ratios (LORs) along with confidence intervals (CI) are shown. Latency requirement is 20 years. Results are presented when LORs $\leqslant 0.5$ or $\geqslant 1.5$.
ADP, automatic data processing.

occupations. Especially among men, several associations between RA and blue collar occupations are in fact stronger in the incident material compared with the pooled material, indicating a possible effect from a bias, but few results are divergent between the two materials.

Many occupational categories almost solely consist of individuals of the same sex, explaining why few common determinants of risk were found in both sexes. Post and telegraph personnel, automatic data processing (ADP) workers, and those exposed to vibrations had increased risks for RA among both men and women. In many instances the individual work tasks may, even in the same occupational category, not be the same for men and women, which might explain some of the divergent results between sexes.

The polarisation of risk estimates when a latency period was used, indicates a long induction period between exposure and the development of RA. There were however some exceptions. The risk associated with exposure to mineral oil was higher without a latency period, which could be due to a shorter induction period, in agreement with results from experimental animal models.[18–20] In both materials, male secretaries, typists, and office cashiers had a significantly increased risk of RA solely when no latency requirement was used. These results could reflect that those with symptoms of yet undiagnosed RA choose less strenuous work tasks. However, when evaluated in our previous study,[14] there was no indication of cases choosing such occupations due to early RA symptoms.

Table 3 Multivariate analysis of certain specified occupational exposures among men with adjustment for age and smoking; analysis of: 74 incident cases and 382 referents; and 176 cases and 630 referents in the pooled material

	Incident cases			Pooled material		
Exposure	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Asphalt	2/3	6.4	0.4 to 109.2	9/4	4.0	0.5 to 31.2
Asbestos	12/19	2.5	1.0 to 6.8	24/33	1.6	0.8 to 3.3
Organic dust	31/80	2.1	0.9 to 4.9	63/140	1.4	0.8 to 2.5
Vibrations	27/47	2.0	0.9 to 4.4	59/98	2.2	1.3 to 3.8
Mineral dust*	11/20	1.8	0.6 to 5.5	25/41	1.9	0.8 to 4.2
Crops and/or forage	22/60	1.6	0.2 to 10.7	65/122	3.2	0.9 to 11.8
Mineral oils	26/52	1.6	0.7 to 3.4	44/87	1.2	0.7 to 2.1
MMMF	9/20	1.5	0.4 to 4.9	13/37	0.7	0.3 to 1.9
Fertilisers	17/40	1.4	0.3 to 7.4	47/79	1.7	0.6 to 4.8
Grain	5/11	0.9	0.1 to 5.2	16/29	1.5	0.6 to 3.6
Farm animals	24/61	0.5	0.1 to 3.4	65/120	0.4	0.1 to 1.6
Pesticides	5/22	0.3	0.1 to 1.5	16/34	0.4	0.1 to 1.2

Logistic odds ratios (LORs) along with confidence intervals (CI) are shown. Latency requirement is 20 years. Results are presented when LORs $\leqslant 0.5$ or $\geqslant 1.5$.
*Defined as stone and/or silica dust.
MMMF, man made mineral fibres.

Table 4 Multivariate analysis of occupational categories among women with adjustment for age and smoking; analysis of: 160 incident cases and 368 referents; and 339 cases and 627 referents in the pooled material

	Incident cases			Pooled material		
Occupation (NYK codes)	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Printmakers, process engravers, etc (801–809)	4/2	5.5	0.9 to 32.6	8/4	3.0	0.9 to 10.3
ADP workers (251–259)	4/4	3.0	0.7 to 12.5	5/5	2.1	0.6 to 7.3
Post and telegraph personnel (671–689)	11/11	2.0	0.8 to 4.9	23/21	1.7	0.9 to 3.3
Millers and bakers (821–822)	3/3	1.5	0.3 to 7.9	6/6	1.5	0.5 to 4.8
Packers and warehouse workers (881–889)	4/4	1.5	0.3 to 6.1	9/10	1.2	0.5 to 3.1
Hairdressers and beauticians (941–949)	4/5	1.4	0.4 to 5.6	11/10	1.8	0.7 to 4.3
Engineers and technicians (001–009)	2/4	1.2	0.2 to 6.7	2/8	0.4	0.1 to 2.1
Electricians, electromechanical workers, and service personnel (761–769)	2/7	0.4	0.1 to 2.2	5/10	0.7	0.2 to 2.1

Logistic odds ratios (LORs) along with confidence intervals (CI) are shown. Latency requirement is 20 years. Results are presented when LORs $\leqslant 0.5$ or $\geqslant 1.5$.
ADP, automatic data processing.

Table 5 Multivariate analysis of certain specified occupational exposures, respectively, among women with adjustment for age and smoking; analysis of: 160 incident cases and 368 referents; and 339 cases and 627 referents in the pooled material

	Incident cases			Pooled material		
Exposure	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Vibrations	3/3	6.1	0.6 to 61.1	6/7	1.8	0.5 to 6.3
Meat	7/5	2.8	0.6 to 13.0	21/14	2.0	0.9 to 4.4
Pesticides	5/2	1.8	0.2 to 15.3	6/4	0.9	0.2 to 5.7
Engine exhaust	10/12	1.4	0.5 to 3.5	19/17	1.5	0.7 to 3.1
Hairdressing chemicals	2/4	0.0	0.0 to ∞	10/9	1.6	0.1 to 26.6

Logistic odds ratios (LORs) along with confidence intervals (CI) are shown. Latency requirement is 20 years. Results are presented when LORs $\leqslant 0.5$ or $\geqslant 1.5$.

For most of the exposures associated with RA among men, the risk was highest in the category with the longest duration of exposure. There was evidence of a dose-response relation for exposure to vibrations and mineral dust, defined as exposure to stone or silica dust. The possibility of induction of RA, as well as of other systemic inflammatory diseases, through inhalation of mineral dust particles containing silica has previously been suggested,[10 12 15] although another study has not shown any association.[27] In the present study, the actual silica content of the dust is however unknown. Vibrations have previously not been pointed out as a possible risk factor for RA.

Farmers and farm workers and pulp and paper workers, but also other occupations—that is, textile workers and millers and bakers with exposure to respirable organic dust were associated with RA among men in the pooled material when smaller occupational categories also were included. All occupations have also previously been found to have an increased risk of RA.[7 9 14] Systemic inflammatory reactions to organic dust inhalation have previously been observed among several occupational categories. For example, humoral immune responses have been seen among farmers exposed to grain dust contaminated with Gram negative bacteria.[28]

In conclusion, external factors are known to be important for RA development. Several exposures associated with RA in the present study involve respirable particles, and for exposure to mineral dust there was a dose-response relation. It is possible that the inhaled agents are antigenic per se or

Table 6 Stratified analysis of specified occupational exposures with at least 50 exposed subjects among men, 176 cases and 630 referents, in the pooled material with adjustment for age and smoking

	Duration							
	0 years		>0, ⩽10 years		11–20 years		⩾20 years	
Exposure	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Asbestos	1.0	–	2.8	1.3 to 6.2	1.3	0.4 to 4.3	2.4	0.5 to 11.3
Vibrations	1.0	–	1.9 p for trend <0.001	1.1 to 3.3	2.0	1.1 to 3.8	2.5	1.0 to 6.7
Mineral dust†	1.0	–	1.4 p for trend <0.05	0.6 to 2.8	2.3	0.9 to 5.9	2.6	0.4 to 19.5
Crops and/or forage	1.0	–	2.6	1.6 to 4.4	2.1	0.9 to 4.9	3.2	1.6 to 6.7
Mineral oils	1.0	–	1.5	0.8 to 2.6	1.3	0.6 to 2.8	1.6	0.7 to 3.5
MMMF	1.0	–	1.6	0.9 to 3.0	1.0	0.4 to 2.6	1.6	0.5 to 6.0
Fertilisers	1.0	–	1.8	1.0 to 3.2	3.0	1.3 to 6.8	2.0	1.0 to 4.3

The duration of exposures are divided into three categories to evaluate the dose-response relation, with those without exposure to the determinant in question as unexposed. Odds ratios (ORs) along with confidence intervals (CI) are shown. Latency requirement is 20 years. Those never exposed to the respective determinant were taken as referents.
*OR, Mantel-Haenszel odds ratio,[29] CI, confidence interval as outlined by Robins *et al*.[30]
†Defines as stone and/or silica dust.
MMMF, man made mineral fibres.

that they act as immunological adjuvants, enhancing an inflammatory response to other causative factors. Systemic inflammatory responses and associations with other immunologically mediated conditions have been seen for several of the exposures associated with RA in our study. There was also a dose-response relation between RA and vibrations which indicate another possible pathophysiological mechanism.

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