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Lung cancer mortality among workers in the European production of man-made mineral fibers — a Poisson regression analysis

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BOFFETTA P, SARACCI R, ANDERSEN A, BERTAZZI PA, CHANG-CLAUDE J, FERRO G, FLETCHER AC, FRENTZEL-BEYME R, GARDNER MJ, OLSEN JH, SIMONATO L, TEPPLO L, WESTERHOLM P, WINTER P, ZOCCHETTI C. Lung cancer mortality among workers in the European production of man-made mineral fibers — a Poisson regression analysis. *Scand J Work Environ Health* 1992;18:279-86. One hundred and eighty-one lung cancer deaths among workers during 301 085 person-years in European man-made mineral fiber production between 1930-1955 and 1982 were analyzed according to Poisson regression models including age, calendar period, country, and exposure variables. Time since first employment was the variable most strongly associated with lung cancer risk in both the rock-slag wool and glass wool subcohorts. Workers in the early technological phase were at higher risk than those in other categories, particularly in rock-slag wool production. No clear trend with duration of employment was suggested. No major changes occurred in the interpretation of the results when workers with less than one year of employment or less than 20 years since first exposure were excluded. The original results, based on analyses for standardized mortality ratios, were confirmed, and workers with a short duration of employment or a short time since first employment did not need to be excluded from the analysis.

Key terms: epidemiology, glass wool, rock wool, slag wool.

Since 1976, the International Agency for Research on Cancer (IARC) has coordinated an epidemiologic study on the mortality and cancer incidence of workers of 13 man-made mineral fiber (MMMF) plants in seven European countries (1). Results of follow-up to 1977 and 1982 have been published (2, 3), as well as results of specific analyses based on national cohort components (4-11). The combined analysis was based on the determination of standardized mortality ratio (SMR) values, and the expected numbers of deaths were cal-

culated on the basis of national reference rates with the use of regional correction factors. The SMR analysis showed an excess mortality from lung cancer (189 observed and 151.2 expected deaths). There was an increase in lung cancer risk with time since first employment but not with duration of employment. The excess of lung cancer was concentrated among rock-slag wool workers, but not glass wool workers, employed in the "early technological phase" (12).

Among the problems arising in the interpretation of these results was the difficulty in disentangling the effect of the different exposure variables, given the small number of deaths in the groups with the highest exposure. Moreover, analyses of trend on the basis of SMR values involve a lack of mutual comparability between the ratios (13, 14). An alternative approach to the calculation of SMR values is multivariate modeling on the basis of a Poisson regression, in which the number of deaths occurring in different cells of exposure variables and covariates such as age and calendar period are regarded as random Poisson variables and fitted to a multiplicative model (15). This approach allows the reciprocal confounding effect of exposure variables to be investigated and also allows the problem of comparability among SMR values based on subgroups of the cohort and between the cohort and the reference populations to be overcome. On the other hand, this approach is relatively unin-

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formative if the variability of exposure within the cohort is small. The present paper presents the results of a Poisson regression analysis based on the data of the last follow-up of the IARC MMMF study.

Subjects and methods

Subjects

The base of the study was the experience of workers ever employed (with at least one year of employment in England and Sweden) in the 13 factories enrolled in the study (table 1). Individuals were identified from factory records and were followed for mortality from the year work in production began (ranged between 1933 and 1950) to 1982–1983 (table 1). Cancer incidence data were collected for individuals from the countries covered by a national cancer register. However, they were not used in this analysis. The original cohort included 24 609 individuals. After women and office workers, which represented 17.4 and 10.7% of the overall cohort, respectively, were excluded, there were 18 753 male production workers left, who provided 301 085 person-years of observation.

The factories were divided according to production process into rock-slag wool, glass wool, and continuous filament (table 1). Factory 14 changed type of production during the study period, and its population was divided into two subcohorts of workers employed respectively during the production of continuous filament only and of glass wool and continuous filament, the latter group being analyzed together with the remaining glass wool factories. Six individuals were employed in factory 14 as office workers during the period of glass wool production and moved subsequently to continuous filament production. They were excluded from this analysis.

The subjects were classified into the following occupational groups: (i) production and preproduction, (ii) secondary processes, (iii) maintenance occupations, (iv) other jobs, such as internal transport driver, storeman, (v) unspecified or mixed manual job, and (vi) unknown job. The 329 individuals employed in both manual and office jobs were excluded from this analysis.

Individuals contributed to the person-years between the beginning of employment and the end of follow-up or exit (death, emigration, or last date of employment, for subjects lost to follow up). This time period was also used to classify subjects according to time since first employment, divided into four levels (≤ 9 , 10–19, 20–29, and ≥ 30 years). For the analysis by duration of employment, only employment in the aforementioned production processes was taken into account. There were 219 individuals who had at least one period of employment of unknown duration. They were excluded from the analysis by duration of employment, which was based on five levels (< 1 , 1–4, 5–9, 10–19, and ≥ 20 years).

All of the analyses were repeated after all of the subjects with less than one year of employment were excluded, as well as after the subjects with less than 20 years since first employment were excluded. A third approach was a lag-time analysis, in which the person-years and the mortality experience were referred to the exposure experience that took place 5 or 20 years earlier, respectively (16, pp 153–155).

The cohort was analyzed as a whole, and most of the analyses were repeated for the rock-slag wool and glass wool subcohorts separately. The continuous filament subcohort was too small to allow a separate analysis. The outcome of interest was death from cancer of the trachea, bronchus, and lung [referred to as lung cancer, International Classification of Diseases (ICD), 7th revision, 162–163, and ICD 8th and 9th revisions, 162] (17).

Estimation of exposure to man-made mineral fibers

The period of MMMF production in each factory was divided into an early, intermediate, and late technological phase (12). Airborne levels of MMMF were estimated to be highest when no dust-suppressing agents were used or a batch process involving labor intensive and hand-operated production methods was in operation. These aspects characterized the early technological phase. The late technological phase corresponded to the periods when oil and resin binders were in use with modern mechanized production methods. The periods in between were classified as intermediate phases. However, such a classification was not applied to two factories, and for five other factories only two phases were identified (12). The workers were allocated according to the phase within which their date of first exposure fell.

Statistical analysis

Relative risks (RR) and confidence intervals were estimated by fitting Poisson regression models to country-, age-, time-, and exposure-specific rates according to a multiplicative model (15). No external mortality rates were used. All of the regression models included age (usually on eight levels), calendar period (six levels), and country. Different combinations of the exposure variables were tested, along with the first-level interaction terms. The results presented in the tables were generally based on models including all of the relevant exposure variables and no interaction terms. The tests for linear trend were performed by introducing a single exposure term to the model as a continuous variable with values corresponding to the mid point of each interval or to a unitary scale. The program PERSON-YEARS was used to estimate the individual contribution to each stratum (18), and the GLIM (general linear interactive modeling) statistical package was used for the multivariate analysis (19).

Results

During the study period there were 181 lung cancer deaths. Nine of them occurred among the subjects excluded from the analysis for the aforementioned reasons, and 172 deaths were left for the analysis. There were 79 lung cancer deaths in both the rock-slag wool and the glass wool subcohorts, the remaining 14 deaths having occurred among continuous filament workers. When the analysis was restricted to individuals with at least one year of employment, the number of lung cancer deaths fell to 131. After the subjects with less

than 20 years since first employment were excluded also, there were 61 lung cancer deaths left, of which 26 had occurred in the rock-slag wool subcohort and 35 in the glass wool subcohort. There were no continuous filament workers with more than 20 years since first employment. Table 2 shows the results according to time since first employment, duration of employment, technological phase, and type of production for the rock-slag wool and glass wool cohorts combined. The results specific for type of production are presented in table 3. Workers in continuous filament production were excluded from table 2 since they were

Table 1. Characteristics of the factories included in the study. (MMM = man-made mineral fibers)

Factory	Country	Type of production	Number of subjects	Year MMMF production started	End of follow-up
1	Denmark	Rock wool	4431	1937	1982
2	Finland	Glass wool	603	1941	1982
3	Norway	Rock wool	470	1950	1982
4	Norway	Rock wool	436	1940	1982
5	Norway	Rock wool	862	1948	1982
6	Norway	Glass wool	525	1935	1982
7	Sweden	Glass wool	1480	1933	1982
8	Sweden	Rock wool	300	1943	1982
9	Sweden	Rock wool	1103	1938	1982
10	United Kingdom	Glass wool	3253	1943	1983
11	United Kingdom	Continuous filament	1169	1946	1983
12	Germany	Rock wool	2092	1941	1983
14	Italy	Continuous filament	1612	1944	1983
14	Italy	Glass wool	417	1944	1983

Table 2. Relative risks (RR) and 95% confidence intervals (95% CI) of lung cancer deaths for duration of employment, time since first employment, technological phase, and type of production in the MMMF industry — results of a Poisson regression analysis.^a (MMM = man-made mineral fiber)

	All individuals			Duration of employment ≥ 1 year and time since first employment ≥ 20 years		
	N ^b	RR	95% CI	N ^b	RR	95% CI
Time since first employment (years)						
≤ 9	30	1.00 ^c	—	—	—	—
10–19	59	1.32	0.78–2.21	—	—	—
20–29	44	1.32	0.68–2.56	38	1.00 ^c	—
≥ 30	25	2.14	0.92–5.00	23	1.76	0.93–3.33
Test for linear trend ^d		0.13				
Duration of employment (years)						
< 1	27	1.00 ^c	—	—	—	—
1–4	45	1.17	0.68–2.01	24	1.00 ^c	—
5–9	27	1.22	0.67–2.22	4	0.33	0.11–0.96
10–19	45	1.51	0.85–2.69	19	0.75	0.38–1.46
≥ 20	14	0.78	0.36–1.70	14	0.51	0.25–1.04
Test for linear trend ^d		0.75			0.11	
Technological phase						
Late ^c	65	1.00	—	12	1.00	—
Intermediate	69	1.01	0.55–1.86	32	1.50	0.37–6.09
Early	24	1.56	0.70–3.48	17	1.70	0.38–7.58
Type of production						
Rock wool ^c	79	1.00	—	26	1.00	—
Glass wool	79	0.56	0.24–1.30	35	0.76	0.27–2.16

^a The regression models included country, age, calendar period, and exposure variables (time since first exposure, duration of employment, technological phase, type of production).

^b Number of lung cancer deaths.

^c Reference category.

^d P-value.

Table 3. Relative risks (RR) and 95% confidence intervals (95% CI) of lung cancer deaths for duration of employment, time since first employment, and technological phase by type of production — results of a Poisson regression analysis.^a

	All individuals			Duration of employment ≥ 1 year and time since first employment ≥ 20 years		
	N ^b	RR	95% CI	N ^b	RR	95% CI
<i>Rock wool — slag wool</i>						
Time since first employment (years)						
≤ 9 ^c	17	1.00	—	—	—	—
10—19	29	1.29	0.64—2.57	—	—	—
20—29	22	1.38	0.55—3.46	17	1.00	—
≥ 30	11	1.87	0.52—6.74	9	1.35	0.45—4.04
Test for linear trend ^d		0.38				
Duration of employment (years)						
< 1 ^c	24	1.00	—	—	—	—
1—4	17	1.11	0.58—2.11	9	1.00	—
5—9	15	1.90	0.97—3.72	3	0.69	0.18—2.63
10—19	14	1.24	0.59—2.62	5	0.48	0.15—1.59
≥ 20	9	1.17	0.46—2.94	9	0.71	0.26—1.94
Test for linear trend ^d		0.41			0.44	
Technological phase						
Late ^c	56	1.00	—	12	1.00	—
Intermediate	14	0.99	0.44—2.23	6	1.27	0.27—6.03
Early	9	1.53	0.52—4.47	8	1.73	0.30—9.87
<i>Glass wool</i>						
Time since first employment (years)						
≤ 9 ^c	13	1.00	—	—	—	—
10—19	30	1.53	0.65—3.59	—	—	—
20—29	22	1.36	0.49—3.80	21	1.00	—
≥ 30	14	2.59	0.77—8.64	14	2.01	0.90—4.48
Test for linear trend ^d		0.21				
Duration of employment (years)						
< 1 ^c	3	1.00	—	—	—	—
1—4	28	0.74	0.17—3.18	15	1.00	—
5—9	12	0.53	0.12—2.37	1	0.12	0.02—0.91
10—19	31	1.04	0.24—4.48	14	0.92	0.41—2.07
≥ 20	5	0.30	0.05—1.76	5	0.36	0.12—1.11
Test for linear trend ^d		0.70			0.20	
Technological phase						
Late ^c	9	1.00	—	—	—	—
Intermediate	55	0.88	0.32—2.37	26 ^e	1.00 ^c	—
Early	15	1.64	0.43—6.25	9	0.87	0.10—7.36

^a The regression models included country, age, calendar period, and exposure variables (time since first exposure, duration of employment, technological phase). The continuous filament subcohort was excluded from this analysis.

^b Number of lung cancer deaths.

^c Reference category.

^d P-value.

^e Includes the late phase (no deaths).

not classified as for technological phase. When the latter variable was not included in the regression model and the entire cohort was retained in the analysis, the relative risks for time since first employment were 1.18 [95% confidence interval (95% CI) 0.76—1.84], 1.18 (95% CI 0.69—2.00), and 2.03 (95% CI 1.06—3.89) for 10—19, 20—29 and ≥ 30 years, respectively, and those for duration of employment were 1.04 (95% CI 0.63—1.72), 1.13 (95% CI 0.65—1.95), 1.31 (95% CI 0.76—2.25), and 0.78 (95% CI 0.37—1.63) for 1—4, 5—9, 10—19, and ≥ 20 years of employment, respectively.

Albeit the relative risks of lung cancer increased in subsequent categories of time since first employment, as shown in tables 2 and 3, the slope of the regression

line fitted to a multiplicative model (ie, on the assumption of an exponential increase in relative risk) did not reach the conventional level of statistical significance. Duration of employment was not associated with lung cancer risk when the other variables, and specifically time since first employment, were included in the model. The relative risks of lung cancer for duration of employment, not controlled for time since first employment (all individuals, all subcohorts), were 1.05 (95% CI 0.64—1.73), 1.13 (95% CI 0.65—1.96), 1.40 (95% CI 0.82—2.37), and 0.96 (95% CI 0.49—1.95) for 1—4, 5—9, 10—19, and ≥ 20 years of employment, respectively.

The risk of lung cancer in the glass wool subcohort was 0.56 that of the rock-slag wool subcohort when

the other variables were controlled (table 2). After workers with less than 20 years since first employment were excluded, this difference was smaller. The relative risk of the continuous filament workers, as compared with the rock-slag wool workers, was 0.64 (95% CI 0.24–1.73) for all durations of employment and 0.44 (95% CI 0.15–1.30) for one or more years of employment.

In the analysis for all individuals (table 3), workers first employed in the early technological phase in both the rock-slag wool and glass wool subcohorts showed a higher lung cancer risk than individuals employed later. However, when the analysis was restricted to workers with at least 20 years since first employment (and at least one year of employment), only the rock-slag wool subcohort showed higher lung cancer risks in the early phase, as compared with the late phase.

The reciprocal confounding effect of the exposure variables was investigated by fitting regression models including different combinations of covariates. There

was no evidence of strong confounding effects, not even in the case of variables with some degree of colinearity, such as time since first employment and technological phase at first employment.

Table 4 presents the results for time since first employment and duration of employment for the rock-slag wool workers who were first employed in the early technological phase. These are the workers most likely to have been exposed to high levels of MMMF. The power of this analysis was strongly limited by the small number of lung cancer deaths (nine deaths overall and only six among the workers employed for ≥ 1 years), and the variables had to be categorized into few levels. However, there was a suggestion of an association between lung cancer risk and both time since first employment and duration of employment.

The results of the analysis by department of employment for the workers having at least 20 years since first employment are shown in figure 1. In most cases, the small number of lung cancer deaths caused impre-

Table 4. Relative risks (RR) and 95% confidence intervals (95% CI) of lung cancer deaths for duration of employment and time since first employment in the rock-slag wool industry. Only individuals who started in the early technological phase are included — results of a Poisson regression analysis.^a

	All individuals			Duration of employment ≥ 1 year and time since first employment ≥ 20 years		
	N ^b	RR	95% CI	N ^b	RR	95% CI
Time since first employment (years)						
$\leq 29^c$	4	1.00	—	3	1.00	—
≥ 30	5	1.42	0.22–9.38	3	1.30	0.17–9.82
Duration of employment (years)						
< 1	3	1.00 ^c	—	—	—	—
1–4	3	0.92	0.12–6.84	3	1.00 ^c	—
≥ 5	3	1.74	0.22–13.93	3	1.48	0.26–8.39

^a Regression models included country, age, calendar period, and the exposure variables (time since first exposure, duration of employment).

^b Number of lung cancer deaths.

^c Reference category.

Figure 1. Relative risk and number of lung cancer deaths by department of employment. (Note: the regression models included country, age, calendar period, time since first exposure, duration of employment, type of production and technological phase.) (prod = production, preprod = preproduction, proc = processes, unspecif = unspecified)

Figure 2. Comparison of standardized mortality ratios (SMR) and relative risks (RR) by time since first employment. (Note: the regression models included country, age, and calendar period.) (A = 10–19 years since first employment, B = 20–29 years since first employment, C = ≥30 years since first employment, reference category = 0–9 years since first employment)

Table 5. Relative risks (RR) and 95% confidence intervals (95% CI) of lung cancer deaths for duration of employment, time since first exposure, technological phase, and type of production in the MMMF industry, applying a 20-year lag — results of a Poisson regression analysis.^a (MMMF = man-made mineral fibers)

	All types of production			Rock wool			Glass wool		
	N ^b	RR	95% CI	N ^b	RR	95% CI	N ^b	RR	95% CI
Time since first employment (years)									
20–29 ^c	36	1.00	—	16	1.00	—	20	1.00	—
≥30	23	1.93	0.99–3.76	9	1.51	0.49–4.66	14	2.43	1.04–5.66
Duration of employment (years)									
1–4 ^c	36	1.00	—	13	1.00	—	23	1.00	—
≥5	23	0.58	0.32–1.06	12	0.80	0.32–2.01	11	0.43	0.19–0.96
Technological phase									
Late ^c	12	1.00	—	12	1.00	—	—	—	—
Intermediate	30	1.20	0.29–4.97	5	0.97	0.19–4.82	25 ^d	1.00 ^c	—
Early	17	1.24	0.27–5.57	8	1.36	0.23–8.05	9	0.64	0.08–5.16
Type of production									
Rock wool ^c	25	1.00	—	—	—	—	—	—	—
Glass wool	34	0.80	0.28–2.28	—	—	—	—	—	—

^a The regression models included country, age, calendar period, and exposure variables (time since first exposure, duration of employment, technological phase, type of production).

^b Number of lung cancer deaths.

^c Reference category.

^d Includes the late phase (no deaths).

cise risk estimates. No department was consistently at higher risk than the remaining ones. The relative risk for all other specified jobs (ie, secondary processes, maintenance, and other jobs) combined, as compared with primary production, was 0.70 (95% CI 0.43–1.13) for all of the workers. The analysis by department was repeated including also workers with less than 20 years since first employment (figure 2), and the results were very similar to those shown in figure 1. The results of the 20-year lag analyses are shown in table 5. They were based on workers with 20 or more years since first employment, and it should be noted that the classification of the subjects according to duration of employment was different from that shown in tables 2 and 3. The five-year lag analysis (not shown)

provided results very similar to those based on workers with at least 20 years since first employment (tables 2 and 3), and the 20-year lag-time analysis of table 5 suggests an even stronger effect of time since first employment.

Discussion

Theoretically, interpreting trends based on SMR values could lead to erroneous conclusions, given the inherent lack of comparability of risk estimates obtained via indirect standardization with an external population (14, 20). It is well recognized, however, that in most instances the difference in the structure of the populations from which the SMR values were calculated

were not large enough to cause severe problems (16, pp 126–127). The results of the present multivariate analysis agree with this conclusion. In fact, the risk estimates which were derived from the Poisson regression and which were adjusted only for age, calendar period, and country (ie, the variables used in the indirect standardization) were remarkably similar to the ratios of the corresponding SMR values. As an example, figure 2 shows lung cancer risk estimates for time since first employment. (The difference in the risk ratios in figure 2 and those shown in tables 2 and 3 are due to the inclusion of other covariates in the latter models.) All of the major results based on SMR values have been confirmed by the present multivariate analysis. A trend of lung cancer risk is shown for time since first employment, but not for duration of employment, and workers employed in the early technological phase and in the rock-slag wool subcohort had a higher risk of lung cancer than workers in the remaining categories. The application of a 5- or 20-year lag time further added to the consistency of the results according to time since first employment. Moreover, this analysis allowed some insight into the relationship between the exposure variables, and the results suggest that time since first employment is the variable most strongly associated with lung cancer risk, but that an effect of employment during the early technological phase is still suggested after adjustment for time since first employment and duration of employment. The only interaction terms which significantly improved the goodness of fit were age-duration and time since first employment-duration, but their inclusion did not allow any material change in the interpretation of the results.

It has been argued that short-term workers should not be included in epidemiologic studies on occupational cancer since they are likely to be different from workers with longer employment with respect to social or behavioral factors possibly related to cancer risk, such as education or tobacco smoking (21). This criticism has been recently applied to studies on the mortality of MMMF workers (20). When duration of employment was analyzed in this study, workers employed for less than one year in the rock-slag wool subcohort were at lower risk of lung cancer than workers employed for longer periods, whereas the opposite pattern was found for the glass wool cohort (table 3). All of the analyses shown in tables 2–5 have been repeated after workers employed for less than one year were excluded, and the results were not modified. As an example, the relative risks for lung cancer according to time since first employment were (for the categories 10–19, 20–29, and ≥ 30 years, respectively) 1.28, 1.54, and 2.33 for the rock-slag wool cohort and 1.35, 1.21, and 2.33 for the glass wool cohort. Therefore, it does not seem necessary to exclude short-term workers from the analysis of this population. Two further arguments strengthen this conclusion. Employment in MMMF production, especially in the past, did not require high technical skill, and therefore no major

difference in social class may be expected between short- and long-term workers. In addition short-term workers might well have been employed in most dusty jobs, such as the removal of fibers from the blowing chamber when batch production was in use, and, therefore, they might represent a category of particularly high exposure to MMMF.

Some problems, however, remain in the interpretation of the results. In particular, the possible confounding effect of lung carcinogens in the raw material used in the production of MMMF, such as arsenic in slag and asbestos, was not controlled in this analysis. However, previous analyses based on SMR values did not suggest that confounding by arsenic-containing slag, asbestos, or formaldehyde was likely to have played an important role (22). On the other hand, it is unlikely that confounders such as tobacco smoking or socioeconomic status were responsible for the differences in lung cancer risk found in this analysis, which was entirely based on internal comparisons.

Further developments of the IARC study include an updating of the follow-up, which will provide a larger contribution of person-years, in particular in the category of workers with the longest latency, and a pilot phase of a nested case-referent study of lung cancer in the rock-slag wool cohort, aimed to assess the feasibility and reliability of abstracting for selected individuals of the cohort, more detailed job descriptions, and the tracing of next-of-kin to obtain data on smoking and occupational exposures outside the MMMF production industry. Finally, the possibility of applying model-based quantitative estimates of MMMF exposure in the rock-slag wool plants (23) is being currently investigated.

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References

1. Saracci R. Ten years of epidemiologic investigations on man-made mineral fibers and health. *Scand J Work Environ Health* 1986;12 suppl 1:5–11.
2. Saracci R, Simonato L, Acheson ED, Andersen A, Bertazzi PA, Claude J, et al. Mortality and incidence of cancer of workers in the man-made vitreous fibers producing industry: an international investigation at 13

- European plants. *Br J Ind Med* 1984;41:425—36.
3. Simonato L, Fletcher AC, Cherrie J, Andersen A, Bertazzi PA, Charnay N, et al. The man-made mineral fiber European historical cohort study: extension of the follow-up. *Scand J Work Environ Health* 1986;12 suppl 1:34—47.
4. Andersen A, Langmark F. Incidence of cancer in the mineral-wool producing industry in Norway. *Scand J Work Environ Health* 1986;12 suppl 1:72—7.
5. Bertazzi PA, Zocchetti C, Riboldi L, Pesatori A, Radice L, Latocca R. Cancer mortality of an Italian cohort of workers in man-made glass-fiber production. *Scand J Work Environ Health* 1986;12 suppl 1:65—71.
6. Claude J, Frentzel-Beyme R. Mortality of workers in a German rock-wool factory — a second look with extended follow-up. *Scand J Work Environ Health* 1986;12 suppl 1:53—60.
7. Gardner MJ, Winter PD, Pannett B, Simpson MJC, Hamilton C, Acheson ED. Mortality study of workers in the man-made mineral fiber production industry in the United Kingdom. *Scand J Work Environ Health* 1986;12 suppl 1:85—93.
8. Gardner MJ, Magnani C, Pannett B, Fletcher AC, Winter PD. Lung cancer among glass fibre production workers: a case-control study. *Br J Ind Med* 1988;45:613—8.
9. Olsen JH, Jensen OM, Kampstrup O. Influence of smoking habits and place of residence on the risk of lung cancer among workers in one rock-wool producing plant in Denmark. *Scand J Work Environ Health* 1986;12 suppl 1:48—52.
10. Teppo L, Kojonen E. Mortality and cancer risk among workers exposed to man-made mineral fibers in Finland. *Scand J Work Environ Health* 1986;12 suppl 1:61—4.
11. Westerholm P, Bolander AM. Mortality and cancer incidence in the man-made mineral fiber industry in Sweden. *Scand J Work Environ Health* 1986;12 suppl 1:78—84.
12. Cherrie J, Dodgson J. Past exposures to airborne fibers and other potential risk factors in the European man-made mineral fiber production industry. *Scand J Work Environ Health* 1986;12 suppl 1:26—33.
13. Yule GU. On some points relating to vital statistics, more especially statistics of occupational mortality. *JR Stat Soc* 1934;97:1—72.
14. Miettinen OS. Standardization of risk ratios. *Am J Epidemiol* 1972;96:383—8.
15. Breslow NE, Day NE. Statistical methods in cancer research; vol II (The design and analysis of cohort studies). International Agency for Research on Cancer, Lyon, 1987:119—76.
16. Checkoway H, Pearce NE, Crawford-Brown DJ. Research methods in occupational epidemiology. New York, NY: Oxford University, 1989.
17. World Health Organization (WHO). Manual of the international statistical classification of diseases, injuries and causes of death. 9th revision. Geneva: WHO, 1977.
18. Coleman M, Douglas A, Hermon C, Peto J. Cohort study analysis with a FORTRAN computer program. *Int J Epidemiol* 1986;15:134—7.
19. Payne CD. The GLIM system: release 3.77. Oxford: Numerical Algorithms Group, 1985.
20. Miettinen OS, Rossiter CE. Man-made mineral fibers and lung cancer: epidemiologic evidence regarding the causal hypothesis. *Scand J Work Environ Health* 1990;16:221—31.
21. Gilbert ES. Some confounding factors in the study of mortality and occupational exposure. *Am J Epidemiol* 1982;116:177—88.
22. Simonato L, Fletcher AC, Cherrie JW, Andersen A, Bertazzi P, Charnay N, et al. The International Agency for Research on Cancer historical cohort study of MMMF production workers in seven European countries: extension of the follow-up. *Ann Occup Hyg* 1987;31(4B):603—623.
23. Krantz S, Cherrie JW, Schneider T, Öhberg I, Kamstrup O. Modelling of past exposure to MMMF in the European rock/slag wool industry. Stockholm: Arbets- och skyddsverket, 1991:1—42. (*Arbete och Hälsa* 1991:1.)

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