

The man-made mineral fiber European historical cohort study

Extension of the follow-up

by Lorenzo Simonato, MD,¹ Antony C Fletcher, MSc,¹ John Cherrie, BSc,² Aage Andersen,³ Pier A Bertazzi, MD,⁴ Nadette Charnay, BSc,¹ Jenny Claude, MHS,⁵ Jim Dodgson, BSc, FIOH,² Jacques Estève, DSc,¹ Rainer Frentzel-Beyme, MD, MHS,⁵ Martin J Gardner, PhD,⁶ Ole M Jensen, MD,⁷ Jørgen H Olsen MD,⁷ Rodolfo Saracci, MD,¹ Lyly Teppo, MD,⁸ Regina Winkelmann,¹ Peter Westerholm, MD,⁹ Paul D Winter, MSc,⁶ Carlo Zocchetti, ScD⁴

SIMONATO L, FLETCHER AC, CHERRIE J, ANDERSEN A, BERTAZZI PA, CHARNAY N, CLAUDE J, DODGSON J, ESTÈVE J, FRENTZEL-BEYME R, GARDNER MJ, JENSEN OM, OLSEN JH, SARACCI R, TEPPLO L, WINKELMANN R, WESTERHOLM P, WINTER PD, ZOCCHETTI C. The man-made mineral fiber European historical cohort study: Extension of the follow-up. *Scand J Work Environ Health* 12 (1986): suppl 1, 34–47. The study concentrated on 21 967 workers producing rock wool/slag wool, glass wool or continuous filament in 13 European factories. The expected deaths and incident cancer cases were derived from multiplying the accumulated person-years by national reference rates across sex, age, and calendar-year strata, correction factors for regional lung cancer mortality also being used. Exposure assessment was based on the results of a historical environmental investigation reported elsewhere. There were 189 deaths (151.2 expected), and for rock-wool/slag-wool and glass-wool workers the standardized mortality ratios for lung cancer showed a pattern of increasing mortality with time since first exposure but not duration of employment. There was an excess of lung cancer among rock-wool/slag-wool workers employed during an early technological phase before the introduction of dust-suppressing agents, and fiber exposure, either alone or in combination with other exposures, may have contributed to the elevated risk. No excess of the same magnitude was evident for glass-wool production, and the follow-up of the continuous filament cohort was too short to allow for an evaluation of possible long-term effects. There was no evidence of an increased risk for pleural tumors or nonmalignant respiratory diseases.

Key terms: cancer incidence, continuous filament, glass wool, lung cancer, mesothelioma, mortality, respiratory disease, rock wool, slag wool.

In this paper we present the results of the extension of the follow-up of a historical cohort of European man-made mineral fiber (MMMF) production workers carried out through international collaboration between the International Agency for Research on Cancer (IARC) and a number of scientific institutions in seven European countries. The preliminary results of the study have been published in *Cancer Letters* (25). The epidemiologic and animal evidence on the car-

cinogenicity of MMMF is reviewed elsewhere in this same supplement (6, 21).

Material and methods

The population under study, as in the previous follow-up, was the workforce ever employed (with at least one year of employment in England and Sweden) in the 13 factories already enrolled in the study (22, 23). These factories are listed in table 1 along with their date of starting MMMF production and the country in which each is located. More information on the factories and their workforces may be found in this supplement in the papers specific to each country.

The current total size of the cohort (24 609 persons) was smaller than in the previous report (22, 23). Some individuals had been removed from the cohort, almost entirely due to two reasons. First, a group of workers had been found in factory 8 to have been employed in a different production area, away from MMMF production. Second, in factories 7, 8, and 9, the population of individuals employed less than one year was incomplete at the factory level or the quality of the data was inadequate for tracing vital status, and so, to minimize the potential for bias, they were excluded from the cohort. The total of 24 609 persons remained

¹ Unit of Analytical Epidemiology, International Agency for Research on Cancer, Lyon, France.

² Institute of Occupational Medicine, Edinburgh, United Kingdom.

³ Institute for Epidemiological Research, The Norwegian Cancer Registry, Oslo, Norway.

⁴ Institute of Occupational Health Clinica del Lavoro "Luigi Devoto," University of Milan, Milan, Italy.

⁵ Institute of Documentation, Information and Statistics, German Cancer Research Center, Heidelberg, Federal Republic of Germany.

⁶ MRC Environmental Epidemiology Unit, Southampton, United Kingdom.

⁷ Danish Cancer Registry, Copenhagen, Denmark.

⁸ Finnish Cancer Registry, The Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland.

⁹ Swedish Trade Union Confederation, Stockholm, Sweden.

Reprint requests to: Dr L. Simonato, Unit of Analytical Epidemiology, International Agency for Research on Cancer, 150 Cours Albert-Thomas, F-69372 Lyon Cédex 08, France.

after these changes. After separation of the office workers most of the analysis concentrated on 21 967 MMMF production workers.

In at least two of the factories (factories 1 and 6) the factory records available at the time of cohort definition were incomplete for the early years. For a number of workers who had worked in MMMF production for relatively short periods and then left, the records had not been kept.

Age- and sex-specific national mortality reference rates were computed at IARC for the study extension period with the use of the mortality data bank of the World Health Organization (WHO). A conversion table was prepared at IARC to allow the pooling of the results over different revisions (26, 27, 28) of the International Classification of Diseases (ICD). National mortality reference rates were extrapolated back to the date of starting MMMF production when this date was prior to the availability of the rates. National reference rates for cancer incidence, all according to the seventh ICD revision, were supplied by the national investigators and used for calculating expected incident cancer cases. This procedure applied to factories 1 to 9 located in four countries providing nationwide cancer registration.

The data processing and analysis were centrally performed at IARC in close collaboration with the national investigators. The expected deaths or incident cancer cases were derived from multiplying the accumulated person-years by the national reference rates across sex, age, and calendar-year strata, and ratios [standardized mortality ratio (SMR) or standardized incidence ratio (SIR)] between observed deaths (or cancer cases) and expected values, multiplied by 100 (4) were calculated. The 95 % confidence intervals for the two types of ratio were computed on the basis of the Poisson distribution. Ratios with confidence intervals excluding 100 were considered significant at the 5 % level.

As it has been suggested that local reference populations may be more comparable to a study popula-

tion in terms of exposure to general pollution, social class composition, or cultural habits (for example cigarette smoking), locally adjusted standardized mortality ratio (SMR) values for cancers of the trachea, bronchus, and lung (referred to as "lung cancer") were estimated from multiplying the expected deaths by a locally derived SMR (16). In the choice of the most appropriate SMR, the following factors have been taken into account: the area should be representative of the area from which the employees are drawn; the size of the reference population should not be too small, and the period for which the SMR was available should not have been too short. For factories 2 and 11, no adjustment was made because the national populations were already quite small. SMR values for the immediate local areas were used for factories 1 and 10, and for the remainder SMR values were calculated at the regional or county level.

All but one of the factories could be uniquely assigned to one of the three production processes, rock wool/slag wool, glass wool, or continuous filament. Factory 14, currently a continuous-filament production plant, was also a glass wool producer during 1946–1960. The results of the hygiene measurements summarized in the previous report (18) indicate that respirable fiber levels are (and presumably have been) higher in glass-wool than in continuous-filament plants. Therefore during 1946 to 1960 the factory was categorized as a glass-wool factory, and the factory cohort has been subdivided into two, those only employed in continuous-filament production (all of whom started in 1961 or later) and those ever employed during the period of glass-wool production. The results by production process or for the total have been generated from the summing of the observed and expected deaths over the relevant factories.

Of the 24 609 members of the cohort, 2 642 (11 %) had only worked in office jobs, and they were considered unexposed to the production environment. The proportion of office workers varied by factory between 0 and 29.5 %.

Table 1. Factories included in the study by country, type of process, and dates of follow-up.

Factory ^a	Year production started	Country	Type of process	Final year of follow-up	
				Mortality	Incidence
01 (C)	1937	Denmark	Rock wool/slag wool	1982	1982
02 (F)	1941	Finland	Glass wool	1981	1981
03 (I)	1950	Norway	Rock wool/slag wool	1982	1983
04 (H)	1940	Norway	Rock wool/slag wool	1982	1983
05 (G)	1948	Norway	Rock wool/slag wool	1982	1983
06 (L)	1935	Norway	Glass wool	1982	1983
07 (D)	1933	Sweden	Glass wool	1982	1982
08 (K)	1943	Sweden	Rock wool/slag wool	1982	1982
09 (M)	1938	Sweden	Rock wool/slag wool	1982	1982
10 (E)	1943	United Kingdom	Glass wool	1983	..
11 (J)	1946	United Kingdom	Continuous filament	1983	..
12 (O)	1941	Germany	Rock wool/slag wool	1982	..
14 (N)	1961	Italy	Continuous filament	1983	..
14 (N)	1946	Italy	Glass wool	1983	..

^a The alphabetic code used in previous publications is given in parentheses.

For most of the factories in the cohort, workers could not be assigned to detailed occupational categories; thus the analysis was carried out using fairly broad occupational categories. Each individual was allocated to one category as follows: (i) employed in the production and preproduction areas only, (ii) employed in secondary processes only, (iii) employed in maintenance occupations only, (iv) employed in other jobs (eg, internal transport drivers, storemen) only, (v) manual worker, unspecified job title or mixed exposure having been employed in more than one of the previously mentioned job categories, (vi) job category unknown, or (vii) mixed exposed and unexposed, having worked some time both in one of the preceding categories and also in office employment.

For analysis by length of exposure, the duration of employment of most of the population was known. However there were 320 individuals who had at least one period of employment of unknown duration, and these plus 372 individuals in the mixed exposed and unexposed category were assigned to the unknown length category.

A historical environmental investigation was carried out which involved a team from the Edinburgh Institute of Occupational Medicine and IARC visiting the 13 factories included in the study and collecting detailed information on the production processes operating in each factory since the start of activity, the raw materials used, the use and type of dust-suppressing agents (mineral oil, resin/binders, pitch) in the different periods of industrial activity, any presence of other contaminants, asbestos in particular, and the

general and local ventilation systems in use since production started (3). All the information was collected from the factory files, management, and personnel presently or previously employed at the factory, and a summary was agreed upon by the factory personnel involved in the survey. No hygiene measurements from the past were available, but the aforementioned information was used to discriminate periods in each factory when the potential for respirable fiber exposure was higher than at present.

An important change from the previous follow-up derived from information newly acquired through the historical environmental investigation. Because of it, workers could be entered into the cohort from the date of their first exposure to MMMF, rather than (as previously) from the date of their first employment at the plant.

The type of process operating and the use and types of dust-suppressing agents having been taken into account, the "technological phases" judged to involve different and decreasing levels of exposure to fibers were defined in advance of the statistical analysis. The similarity of the technology used in the different factories, although at quite different dates, implied sufficient homogeneity in fiber exposure to justify pooling the workers employed within each of the phases for the analysis of mortality.

Airborne levels of MMMF in the factories were estimated to be the highest when no dust-suppressing agent (mainly mineral oil) was used and/or a batch process involving labor intensive and hand-operated production methods were in operation. These conditions were called the *early technological phase*; the lung cancer mortality experience of the part of the cohort employed during this period has been presented for comparison with the part of the cohort employed during periods when oil and resin binder were in use with modern mechanized production methods (*late technological phase*). The intermediate phase with exposure during the use of processes both with and without dust suppressors was called the *intermediate technological phase*.

For the analysis by technological phase, individuals were allocated into the group within which their date of first exposure fell. Thus individuals who were employed for long periods covering, for example, two or three technological phases only contribute to the first subgroup they entered.

The person-years at risk subdivided by length of employment and follow-up are presented in table 2. The contribution to person-years of the longer observation periods (ie, 20—29 and ≥ 30 years since first exposure) was, respectively, 12.4 and 3.7 % of the entire total. The total number of deaths, lost to follow-up, and emigration are presented in table 3. Complete follow-up was successful for 95 % of the cohort.

Due to the exclusion of some individuals and the improved estimates of dates of first exposure, the presented results are not directly comparable with the

Table 2. Person-years for mortality among both sexes by length of employment and follow-up

Length of employment (years)	Years since first exposure				Total
	≤ 9	10—19	20—29	≥ 30	
<1	72 474	30 171	7 002	1 276	110 923
1—4	85 690	35 627	14 275	4 671	140 264
5—9	27 904	16 810	6 842	2 219	53 775
10—19	—	26 222	7 483	2 021	35 726
≥ 20	—	—	7 095	2 587	9 682
Unknown	5 797	5 204	2 658	573	14 232
Total	191 866	114 034	45 355	13 347	364 601

Table 3. Study population by vital status.

	Males		Females		Total	
	N	%	N	%	N	%
Alive at end of follow-up	16 777	82.5	3 725	87.1	20 502	83.3
Dead	2 540	12.5	296	6.9	2 836	11.5
Emigrated	624	3.1	102	2.4	726	3.0
Lost to follow-up	389	1.9	156	3.7	545	2.2
Total	20 330	100	4 279	100	24 609	100
Exposed cohort	18 753	92.2	3 214	75.1	21 967	89.3
Unexposed cohort	1 577	7.8	1 065	24.9	2 642	10.7

previously published findings (23). In addition, other deaths which occurred prior to 1977 have since been identified. To allow a direct comparison of the results with the earlier follow-up, the current cohort was also analyzed up to the date of the end of the previous follow-up (1977 for most factories), the results of which were found to differ only slightly from those previously published (25).

Results

Mortality

As previously stated, the analysis focused on the exposed part of the cohort. However the SMR values for a selected number of causes of death among office workers are presented in table 4. There was a consistent mortality deficit by cause apart from an elevated SMR for bladder cancer.

Observed and expected deaths from selected causes for the entire exposed cohort are presented by sex and for both sexes combined in table 5. All the subsequent results are presented for both sexes combined. A total of 2 719 deaths occurred during the study period versus 2 457 expected, yielding a SMR of 111, which is

statistically significant ($p < 0.05$). For 46 deaths the cause of death was not available. The major contribution to the excess came from mortality from violent causes of death, which was concentrated among workers with less than one year of employment, for whom the SMR was 242 (table 6). This group of workers with short-term employment also had an increased mortality in the categories "diseases of the respiratory system," "diseases of the nervous system," and "diseases of the digestive system." Within this last category deaths from liver cirrhosis were about four times more frequent than for longer term employees. Lung cancer mortality was not however significantly raised, the SMR being 116. For only 9 out of the 13 factories, workers with less than one year's employment were included, and they altogether comprised about one-third of the cohort. Within the cohort employed for at least one year, the overall SMR was 102, that for violent causes fell to 117, and those for most specific causes, except lung cancer, were close to 100.

Mortality from all malignant neoplasms in the total exposed cohort was statistically significantly elevated, the excess mainly (but not exclusively) being due to lung cancer. For no site other than lung cancer did the overall SMR values present a statistically significant departure from 100. Moderate excesses were however

Table 4. Mortality of the office workers by detailed cause, both sexes included.

Cause of death ^a	Observed	Expected ^a	Standardized mortality ratio	95 % confidence interval
All malignant neoplasms (140—209)	35	40.7	86	60—120
Buccal cavity & pharynx (140—149)	1	0.7	147	4—819
Esophagus (150)	—	0.8	0	0—465
Stomach (151)	3	3.7	82	17—240
Intestine, except rectum (152—153)	2	2.7	75	9—270
Rectum (154)	1	1.6	61	2—339
Larynx (161)	—	0.4	0	0—1 045
Trachea, bronchus and lung (162)	7	9.6	73	29—151
Bone (170)	—	0.3	0	0—1 263
Prostate (185)	1	1.5	68	2—381
Bladder (188)	4	1.0	396	108—1 014
Leukemia (204—207)	2	1.7	121	15—438
Other lymphatic and hematopoietic neoplasms (200—203, 208—209)	1	2.2	45	1—251
Other malignant neoplasms	13	14.8	88	47—151
Benign and unspecified neoplasms (210—239)	1	0.8	125	3—698
Diseases of the circulatory system (390—458)	46	59.8	77	56—103
Ischemic heart disease (410—414)	35	40.4	87	60—121
Cerebrovascular disease (430—438)	6	10.9	55	20—120
Diseases of the respiratory system (460—519)	5	9.9	51	16—119
Acute infections (460—466)	—	0.2	0	0—2 277
Influenza (470—474)	—	0.4	0	0—997
Pneumonia (480—486)	3	4.0	74	15—217
Bronchitis, emphysema and asthma (490—493)	1	4.5	22	1—124
Diseases of the digestive system (520—577)	2	6.8	29	4—106
Accidents, poisoning and violence (E800—E999)	13	23.9	54	29—93
Suicide (E950—E959)	4	9.0	45	12—114
Other known causes	12	16.8	72	37—125
Cause of death unknown	3	..	..	..
All causes (000—999)	117	158.6	74	61—88

^a The code of the International Classification of Diseases, eighth revision, in parentheses.

^b Based on national age-, sex-, cause-, and calendar-year-specific death rates.

Table 5. Mortality by detailed cause and sex, the total exposed cohort included. (O = observed number of deaths, E = expected number of deaths based on national age-, sex-, cause-, and calendar-year-specific death rates, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval)

Cause of death ^a	Males		Females		Both sexes		SMR	95 % CI
	O	E	O	E	O	E		
All malignant neoplasms (140—209)	564	509.4	97	88.4	661	597.7	111	102—119
Buccal cavity & pharynx (140—149)	10	9.7	3	0.9	13	10.6	123	65—210
Esophagus (150)	14	11.7	—	1.3	14	13.0	108	59—181
Stomach (151)	55	61.7	9	6.8	64	68.5	93	72—119
Intestine, except rectum (152—153)	35	33.7	2	6.8	37	40.5	91	64—126
Rectum (154)	29	23.9	4	3.2	33	27.0	122	84—172
Larynx (161)	9	6.1	—	0.2	9	6.3	143	66—272
Trachea, bronchus and lung (162)	181	143.8	8	7.4	189	151.2	125	108—144
Bone (170)	6	3.4	—	0.5	6	3.9	153	56—332
Prostate (185)	31	33.4	—	—	31	33.4	93	53—132
Bladder (188)	22	16.9	2	1.0	24	17.9	134	86—199
Leukemia (204—207)	15	18.5	2	2.8	17	21.3	80	47—128
Other lymphatic and hematopoietic neoplasms (200—203, 208—209)	25	25.9	8	3.7	33	29.6	112	77—157
Other malignant neoplasms	132	120.8	59	53.8	191	174.6	109	94—126
Benign and unspecified neoplasms (210—239)	17	11.2	1	2.0	18	13.2	136	81—216
Diseases of the circulatory system (390—458)	951	933.5	92	105.8	1 043	1 039.3	100	94—107
Ischemic heart disease (410—414)	669	644.7	53	54.4	722	699.0	103	96—111
Cerebrovascular disease (430—438)	156	170.2	22	32.5	178	202.8	88	75—102
Diseases of the respiratory system (460—519)	152	146.9	13	18.0	165	164.9	100	85—117
Acute infections (460—466)	—	2.1	2	0.4	2	2.5	79	10—287
Influenza (470—474)	8	5.5	—	1.0	8	6.5	124	53—244
Pneumonia (480—486)	58	58.6	7	9.8	65	68.4	95	73—121
Bronchitis, emphysema and asthma (490—493)	64	68.1	2	5.3	66	73.4	90	70—114
Diseases of the digestive system (520—577)	112	97.3	11	10.5	123	107.8	114	95—136
Accidents, poisoning and violence (E800—E999)	384	247.7	22	17.1	406	264.8	153	139—169
Suicide (E950—E959)	102	78.4	8	6.2	110	84.6	130	107—157
Other known causes	226	229.8	31	39.6	257	269.4	95	84—108
Cause of death unknown	43	..	3	..	46	..	..	..
All causes (000—999)	2 449	2 175.7	270	281.3	2 719	2 457.0	111	107—115

^a Code of the International Classification of Diseases, eighth revision, in parentheses.

Table 6. Mortality from selected causes subdivided by duration of employment of less than and more than one year, both sexes included. (SMR = standardized mortality ratio)

Cause of death ^a	Less than one year		More than one year	
	Observed	SMR	Observed	SMR
All causes (000—999)	741	147*	1 978	102
Malignant neoplasms (140—209)	143	119*	518	109*
Lung Cancer (162)	35	116	154	128*
Circulatory diseases (390—458)	216	113	827	98
Respiratory diseases (460—519)	39	150*	126	91
Digestive diseases (520—577)	40	171*	83	99
Violent deaths (E800—E999)	200	242*	206	117*
Other known causes	80	133*	195	89

^a Code of the International Classification of Diseases, eighth revision, in parentheses.

* $p < 0.05$.

present for death from cancers of the buccal cavity and pharynx, rectum, larynx, and bladder. As shown in table 7 for all malignant neoplasms, there was no relationship between the SMR values and time since first exposure, but for lung cancer an increasing pattern was apparent, a statistically significant SMR of 173 appearing for the category ≥ 30 years since first exposure.

The lung cancer findings are presented separately for the three production processes in table 8. The overall SMR values for lung cancer were elevated for each of the three processes when compared to national rates. For each of the rock-wool/slag-wool and glass-wool subcohorts statistically nonsignificant increasing trends for the SMR values were present for time since first exposure (χ^2 1.7 and 2.9, respectively, 1 degree of freedom (df), for national figures). No such pattern was apparent for the continuous-filament subcohort, for which, however, the number of expected deaths more than 20 years after first exposure were very small. Except for continuous filament, the highest SMR values were found for the period ≥ 30 years from first exposure. However, when adjustment factors based on

local lung cancer mortality are applied the results are modified. The SMR values for glass wool and continuous filament are no longer raised, but that for rock wool/slag wool remains almost unchanged, similar trends remaining.

The lung cancer mortality by individual factory is reported in table 9, showing the effect of regional correction for each factory. For rock wool/slag wool, the largest excess was evident for factory 4, although an excess was also present for four other factories. (Factories 1, 4, and 9 contribute most of the excess in the long follow-up periods.) For glass wool, the excess was mainly in factories 7, 10, and 14, reaching statistical significance for the largest (ie, factory 10). The excess mortality was substantially reduced by regional correction for factories 10 and 14.

The lung cancer mortality among workers with at least 20 years of follow-up is presented by occupational category in table 10. For rock-wool/slag-wool workers the excess is evident among the production/preproduction, maintenance, and unknown groups. The unknown category dates from early in the history of MMMF production when most of the workforce was engaged directly in production work. For glass wool the lung cancer excess was distributed over production-

preproduction, maintenance, and unspecified and mixed production workers.

In table 11, lung cancer mortality 20 years or more since first exposure in the rock-wool/slag-wool sub-cohort is presented by duration of employment. The total length of employment and employment during the early and intermediate technological phases only are presented before and after correction for regional mortality rates. The total employment showed no pattern, with a high SMR for the one to four years' employment group. When only the employment in the first two technological phases is considered, the SMR is consistently high up to 20 years, after which both observed and expected deaths are truncated by the restricted length of the two technological phases. Within the early phase, the number of expected deaths was rather small for carrying out an analysis by duration of employment. For the ten cases in the early phase, the average duration of employment was 9.8 years, with 2.5 years within the early-phase period, compared with 12.5 years (2.7 within the early phase) for the whole early-phase subcohort (331 individuals). These figures compare to an average duration of employment of 3.8 years for the whole rock-wool/slag-wool sub-cohort.

Table 7. Mortality of the total exposed cohort (both sexes included) from selected causes by time since first exposure to man-made mineral fibers. (O = observed number of deaths, E = expected number of deaths based on national age, sex-, cause-, and calendar-year-specific death rates, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Cause of death ^a															
	All causes (000—999)				All malignant neoplasms (140—209)				Cancer of trachea, bronchus and lung (162)				All nonmalignant respiratory diseases (460—519)			
	O	E	SMR	95 % CI	O	E	SMR	95 % CI	O	E	SMR	95 % CI	O	E	SMR	95 % CI
≤9	721	654.7	110	102—118	146	149.4	98	83—115	39	36.3	107	76—147	24	34.7	69	44—103
10—19	936	835.8	112	105—119	237	207.9	114	110—129	70	55.3	127	99—160	61	55.7	110	84—141
20—29	724	655.9	110	102—119	196	163.7	120	104—138	51	42.8	119	89—157	51	50.6	101	75—133
≥30	338	310.7	109	97—121	82	76.7	107	85—133	29	16.8	173	116—248	29	23.9	122	81—175
Total	2 719	2 457.0	111	107—115	661	597.7	111	102—119	189	151.2	125	108—144	165	164.9	100	85—117

^a Code of the International Classification of Diseases, eighth revision, in parentheses.

Table 8. Lung cancer mortality by time since first exposure and by process, both sexes included. The expected number of deaths (E) and standardized mortality ratio (SMR) are shown according to both the national and local reference populations. (O = observed number of deaths)

Years since first exposure	Rock-wool/slag-wool subcohort				Glass-wool subcohort				Continuous-filament subcohort				Total cohort			
	Reference population				Reference population				Reference population				Reference population			
	National		Local		National		Local		National		Local		National		Local	
	O	E	SMR	E	SMR	O	E	SMR	O	E	SMR	E	O	E	SMR	E
≤9	17	16.5	103	16.4	104	13	15.8	82	19.3	68	9	4.0	224*	5.1	176	39
10—19	30	24.6	122	24.7	122	34	24.5	139	30.0	113	6	6.3	96	7.9	76	70
20—29	22	17.6	125	17.8	124	29	23.3	125	28.9	100	—	2.0	0	2.1	0	51
≥30	12	6.7	178	6.5	185	17	9.8	173*	12.4	138	—	0.3	0	0.3	0	29
Total	81	65.4	124	65.3	124	93	73.3	127*	90.5	103	15	12.5	120	15.4	97	189

* p<0.05.

In table 12, the equivalent data are presented for glass wool. Whether the total employment or only that in the early and intermediate technological phases is considered, the risk appears to be unrelated to length — high for the second- and fourth-duration categories,

Table 9. Lung cancer mortality (both sexes included) by factory and process according to both the national and local reference populations. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Factory	O	Reference population			
		National		Local	
		E	SMR	E	SMR
<i>Rock-wool/slag-wool process</i>					
Factory 1	39	32.0	122	32.3	121
Factory 3	—	1.3	0	1.2	0
Factory 4	7	1.9	360*	2.3	300*
Factory 5	6	5.1	119	5.1	119
Factory 8	—	2.4	0	2.1	0
Factory 9	8	5.2	153	2.9	275*
Factory 12	21	17.5	120	19.4	108
Total	81	65.4	124	65.3	124
<i>Glass-wool process</i>					
Factory 2	4	5.9	68	5.9	68
Factory 6	1	2.5	40	2.5	40
Factory 7	10	8.8	114	11.5	87
Factory 10	71	50.6	140*	61.7	115
Factory 14 ^a	7	5.6	125	9.0	78
Total	93	73.3	127	90.5	103
<i>Continuous-filament process</i>					
Factory 11	8	7.8	103	7.8	103
Factory 14 ^a	7	4.7	148	7.7	91
Total	15	12.5	120	15.4	97

^a Glass-wool producer from 1946 to 1960, continuous-filament producer from 1961 on.

* $p < 0.05$.

low for the others. By average length of employment, the 16 early-phase lung cancer deaths were employed for 8.5 years (3.8 within the early phase) compared to an average of 7.2 years (4.4 within the early phase) for the 1 182 early-phase individuals. The average duration of employment was 5.6 years for the whole glass-wool cohort.

The SMR values for lung cancer classified by the technological phase during which workers first entered a plant are shown in table 13. For rock wool/slag wool the results for the periods 20–29 years and ≥ 30 years since first exposure in the early technological phase showed the highest values. They ranged from 244 to 317, depending on the reference population used. Somewhat lower values, ranging from 161 to 217, were found for the intermediate technological phase, but all the latter ones have wide confidence limits, and none is statistically significant. For the late technological phase the corresponding SMR values ranged from 77 to 93. For 20 or more years since first exposure the decreasing trend for lung cancer from the early to the late technological phase was statistically significant ($\chi^2 = 6.5$ or 9.8 for national or local, respectively). For the same time intervals since first exposure, the SMR values for glass wool were much lower in the early technological phase (SMR 80 to 145), but slightly elevated in the intermediate technological phase (SMR 106 to 194).

Only one case of mesothelioma was found out of 364 601 person-years at risk. The person involved was employed for less than one year and died 13 years after first exposure. Reference rates were not available for pleural mesothelioma; however a reasonable expectation of the number of cases from a male population of that size would probably lie in the range of 1 to 3.

Table 10. Lung cancer mortality (both sexes included) by occupational category ≥ 20 years since first exposure to man-made mineral fibers according to both the national and local reference populations.

Job category	Observed	Rock-wool/slag-wool production				Glass-wool production			
		Reference population				Reference population			
		National		Local		National		Local	
		Expected	Standardized mortality ratio	Expected	Standardized mortality ratio	Expected	Standardized mortality ratio	Expected	Standardized mortality ratio
Production/pre-production	11	6.1	181	5.3	209*	13	7.2	180	144
Secondary process	1	0.2	455	0.2	455	5	6.5	77	65
Maintenance	7	4.1	169	4.3	161	9	4.6	196	152
Others	—	0.5	0	0.4	0	2	3.0	67	53
Unspecified and mixed production	7	9.4	75	10.0	70	15	8.7	173	134
Unknown	8	3.6	222	3.6	220	—	2.0	0	0
Mixed exposed and unexposed	—	0.4	0	0.3	0	2	1.1	190	154
Total	34	24.4	140	24.2	140	46	33.1	139*	111

* $p < 0.05$.

Table 11. Lung cancer mortality (both sexes included) for the rock-wool/slag-wool production subcohort ≥ 20 years since first exposure to man-made mineral fibers by duration of employment according to both the national and local reference population.

Duration of employment (years)	Total employment					Employment in early and intermediate phases				
	Observed	Reference population				Observed	Reference population			
		National		Local			National		Local	
		Ex-pected	Stan-dardized mortality ratio	Ex-pected	Stan-dardized mortality ratio		Ex-pected	Stan-dardized mortality ratio	Ex-pected	Stan-dardized mortality ratio
< 1	8	5.7	141	5.9	136	8	3.8	210	3.8	211
1—4	9	4.9	185	4.5	200	7	3.1	225	2.7	257*
5—9	3	2.2	138	2.1	140	4	1.9	209	1.7	236
10—19	5	4.9	102	5.0	100	2	1.0	195	0.9	214
≥ 20	9	6.3	142	6.4	141	—	0	0	0	0
Unknown	—	0.4	0	0.3	0	—	0.3	0	0.3	0
Total	34	24.4	140	24.2	140	21	10.2	206*	9.4	223*

* $p < 0.05$.

Table 12. Lung cancer mortality (both sexes included) for the glass-wool production subcohort ≥ 20 years since first exposure to man-made mineral fibers by duration of employment according to both the national and local reference population.

Duration of employment (years)	Total employment					Employment in early and intermediate phases				
	Observed	Reference population				Observed	Reference population			
		National		Local			National		Local	
		Ex-pected	Stan-dardized mortality ratio	Ex-pected	Stan-dardized mortality ratio		Ex-pected	Stan-dardized mortality ratio	Ex-pected	Stan-dardized mortality ratio
< 1	1	1.6	63	1.9	53	1	1.6	62	1.9	52
1—4	19	9.7	197*	12.0	158	19	10.0	191*	12.4	154
5—9	1	5.1	20	6.4	16*	2	5.7	35	7.1	28
10—19	15	7.9	190*	10.2	146	17	10.5	163	13.4	127
≥ 20	5	6.9	73	8.3	60	2	3.2	62	3.9	51
Unknown	5	2.0	249	2.5	202	5	2.0	249	2.5	202
Total	46	33.1	139*	41.3	111	46	33.0	139*	41.2	112

* $p < 0.05$.

The only other cause of death showing an increasing pattern with time since first exposure was bladder cancer (table 14). When broken down by type of process, no excess was discernible in the continuous-filament subcohort, while an elevated SMR was present in both the rock-wool/slag-wool and glass-wool groups. Analysis by time since first exposure showed no trend for glass wool, while an increasing trend ($p < 0.05$) was evident for rock-wool/slag-wool production. The bladder cancer mortality was also analyzed by technological phase and did not show the same pattern as the lung cancer results, but after subdivision the numbers were very small.

The extension of the follow-up confirmed the previous finding of an elevated mortality from larynx cancer in factory 14; this finding is discussed in detail in another paper in this issue (2). In the rest of the study population three deaths were observed versus 4.78 expected.

No overall death excess from nonmalignant respiratory diseases was present for the total cohort (ta-

ble 5). Workers with less than one year of exposure showed however an elevated SMR which was statistically significant (table 6). Aside from these short-term workers, when mortality from this group of causes was analyzed by process, by time since first exposure, and by length of employment, no excess was discernible in any of the industrial processes. The analysis by technological phase did not show any pattern either in the glass-wool or in the rock-wool/slag-wool production subcohorts. These results are not presented in the tables.

Incidence (factories 1–9)

The SIR for the total cohort did not indicate an overall cancer excess (table 15). The overall lung cancer incidence was increased in the rock-wool/slag-wool subcohort but not in the glass-wool one, for which however the results were less informative due to the exclusion of two large factories for which incidence data were not available. In both processes the lung cancer

Table 13. Lung cancer mortality (both sexes included) by time since first exposure to man-made mineral fibers and by technological phase and as determined according to both the national and local reference populations. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Rock-wool/slag-wool technological phase																						
	Early						Intermediate				Late				Early								
	National			Local			National			Local	National			Local	National			Local					
	O	E	SMR	E	SMR		O	E	SMR	E	SMR	O	E	SMR	E	SMR	O	E	SMR	E	SMR		
≤9	—	0.2	0	0.1	0		—	1.0	0	1.0	0		17	15.3	111	15.2	112		2	1.6	123	1.9	10
10—19	—	0.6	0	0.5	0		3	2.8	106	2.8	107		27	21.2	127	21.4	126		3	3.8	80	4.3	7
20—29	4	1.5	270	1.3	317		7	4.3	161	4.3	164		11	11.8	93	12.2	90		5	5.4	93	6.3	8
≥30	6	2.5	244	2.0	295*		4	1.9	211	1.8	217		2	2.4	84	2.6	77		6	4.1	145	5.0	12
Total	10	4.7	214*	3.9	257*		14	10.1	139	9.9	141		57	50.7	113	51.5	111		16	14.9	107	17.4	9

Table 14. Bladder cancer mortality (both sexes included) by the time since first exposure and by process. (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Rock-wool/slag-wool process				Glass-wool process				Continuous-filament process				Total			
	O	E	SMR	95 % CI	O	E	SMR	95 % CI	O	E	SMR	95 % CI	O	E	SMR	95 % CI
≤9	1	2.1	48	1—267	2	1.3	157	19—564	—	0.3	0	0—1 476	3	3.6	83	17—242
10—19	3	3.5	87	18—254	3	2.4	127	26—372	—	0.5	0	0—802	6	6.3	96	35—208
20—29	6	2.7	221	81—480	4	2.6	156	43—400	—	0.2	0	0—2 459	10	5.4	184	88—339
≥30	3	1.2	249	51—725	2	1.4	147	18—527	—	0.0	0	0—1 844	5	2.6	193	63—451
Total	13	9.5	137	73—235	11	7.6	145	73—260	—	0.9	0	0—373	24	17.9	134	86—199

Table 15. Cancer incidence of the total exposed cohort (both sexes included) by site.

Cancer site ^a	Observed	Expected	Standardized incidence ratio	95 % confidence interval
Buccal cavity and pharynx (140—148)	28	17.0	164	109—238
Esophagus (150)	8	6.0	133	57—262
Stomach (151)	46	40.1	115	84—153
Intestine, except rectum (152—153)	36	36.8	98	69—136
Rectum (154)	28	26.1	107	71—155
Larynx (161)	6	7.3	82	30—179
Trachea, bronchus and lung (162—163)	87	75.1	116	93—143
Breast (170)	16	20.7	77	44—125
Cervix uteri (171)	4	6.0	67	18—172
Uterus (172—174)	9	5.7	157	72—299
Prostate (177)	45	54.7	82	60—110
Bladder (181)	35	32.2	109	76—151
Melanoma of skin (190)	12	13.8	87	45—152
Bone (196)	3	1.6	184	38—537
Leukemia (204)	15	15.3	98	55—162
Other lymphatic and hematopoietic neoplasms (200—203, 205)	22	22.7	86	54—130
Other malignant neoplasms	137	146.33	94	79—111
All malignant neoplasms (140—205)	537	530.6	101	93—110

^a Code of the International Classification of Diseases, seventh revision, in parentheses.

incidence tended to increase with the time since first exposure, as shown in table 16. The analysis by technological phase (table 17) tended to confirm the lung cancer mortality patterns with slightly lower ratios. For glass wool the intermediate technological phase was not informative due to the exclusion of factories 10 and 14, the results from which contributed almost

entirely to the observed and expected values in the mortality analysis.

In table 18 the pattern of the 87 incident respiratory cancer cases is shown subdivided by histological type and country. The 10 cases occurring among those employed during the early phase comprised three squamous cell, two small cell, three “others,” and two with

exposure as identified in the historical environmental investigation of deaths, SMR = standardized mortality ratio)

s-wool technological phase							
Intermediate				Late			
National		Local		National		Local	
O	SMR	E	SMR	O	SMR	E	SMR
7.7	52	9.5	42	7	6.6	107	7.9
7.7	164*	22.0	132	2	3.1	66	3.6
7.8	135	22.6	106	—	0.1	0	0.1
5.7	194	7.4	149	—	0.0	0	0.0
8.8	139*	61.4	111	9	9.7	93	11.7

no histological confirmation.

The histological breakdown was not available for all the Nordic countries for comparison, but recent data from Norway (12) and Finland (all lung cancers 1974–1978) suggest that our reported patterns are not unusual. In Norway, for squamous, small cell, and adenocarcinoma, there were 34, 9, and 11 %, respectively. In Finland there were 28, 13, and 7 %, respectively. The proportion of adenocarcinoma appeared to be higher than is normally expected. However the interpretation of this finding is limited by the small numbers involved and because reference proportions

Table 16. Lung cancer incidence of the total cohort (both sexes included) by process and time since first exposure. (O = observed number of cases, E = expected number of cases, SIR = standardized incidence ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Rock-wool/slag-wool process				Glass-wool process				Total			
	O	E	SIR	95 % CI	O	E	SIR	95 % CI	O	E	SIR	95 % CI
≤9	15	16.9	89	50–147	1	3.8	26	1–146	16	20.7	77	44–126
10–19	31	22.0	141	96–200	4	6.0	67	18–172	35	28.0	125	87–174
20–29	18	12.3	146	87–231	6	5.5	110	40–240	24	17.8	135	87–201
≥30	8	5.1	158	68–311	4	3.6	111	30–285	12	8.7	139	72–242
Total	72	56.3	128	100–161	15	18.8	80	45–132	87	75.1	116	93–143

Table 17. Lung cancer incidence by time since first exposure and by technological phase at first exposure as identified in the historical environmental investigation, both sexes included. (O = observed number of deaths, E = expected number of deaths, SIR = standardized incidence ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Rock-wool/slag-wool technological phase												Glass-wool technological phase											
	Early				Intermediate				Late				Early				Intermediate				Late			
	O	E	SIR	95 % CI	O	E	SIR	95 % CI	O	E	SIR	95 % CI	O	E	SIR	95 % CI	O	E	SIR	95 % CI	O	E	SIR	95 % CI
≤9	—	0.1	0	0–7233	—	1.1	0	0–335	15	15.7	95	53–157	1	1.2	83	2–460	—	0.3	0	0–1146	—	2.3	0	0–162
10–19	—	0.5	0	0–716	4	3.3	120	33–308	27	18.2	148	98–216	3	3.7	82	17–239	—	0.5	0	0–700	1	1.8	57	1–315
20–29	4	1.7	232	63–593	10	5.3	190	91–350	4	5.3	75	21–193	6	5.4	112	41–244	—	0.1	0	0–7094	—	0.0	0	0–9222
≥30	6	2.8	214	78–465	2	2.2	93	11–334	—	0.1	0	0–3581	4	3.6	111	30–285	—	0.0	0	—	—	0.0	0	—
Total	10	5.1	196	94–360	16	11.8	135	77–219	46	39.3	117	86–156	14	13.8	101	55–170	—	0.9	0	0–409	1	4.1	25	1–137

Table 18. Respiratory cancer cases by histological type and country.

Type of cancer	Denmark	Finland	Norway	Sweden	Total	Percentage of the total of all countries together
Squamous cell carcinoma	14	1	4	6	25	29
Small cell carcinoma	11	2	—	—	13	15
Adenocarcinoma	5	—	5	3	13	15
Others	2	1	5	9	18	21
No histology	13	—	5	1	19	22
Total	45	4	19	19	87	100

Table 19. Incidence of cancer of the buccal cavity and pharynx^a by follow-up and process, both sexes included. (O = observed number of cases, E = expected number of cases, SMR = standardized mortality ratio, 95 % CI = 95 % confidence interval)

Years since first exposure	Rock-wool/slag-wool subcohort				Glass-wool subcohort				Total cohort			
	O	E	SMR	95 % CI	O	E	SMR	95 % CI	O	E	SMR	95 % CI
≤9	5	4.0	125	40–290	—	1.1	0	0–326	5	5.1	97	32–227
10–19	11	4.6	238	119–426	—	1.5	0	0–249	11	6.1	180	90–323
20–29	7	2.6	272	109–559	3	1.3	231	48–674	10	3.9	258	124–475
≥30	1	1.0	102	3–569	1	1.0	105	3–587	2	1.9	104	13–376
Total	24	12.2	197	126–293	4	4.9	83	23–211	28	17.0	164	109–238

^a Code 140–148 in the International Classification of Diseases, seventh revision.

of histological type were not available for Denmark, which alone contributed more than half of the cases.

For cancer of the buccal cavity and pharynx there was a statistically significant excess (table 19). The incidence for these sites increased with time since first exposure till the 20- to 29-year group (10 observed versus 3.9 expected) and then fell in the group ≥ 30 years since first exposure (2 observed versus 1.9 expected).

No other cancer site showed a relationship between SIR and time since first exposure.

Discussion

For a number of cancer sites (buccal cavity and pharynx, larynx, bladder, rectum) increases in mortality and/or cancer incidence have been observed which, however, are not large, are not consistently related to time since first exposure, nor appear to be consistent across factories within a given production process. In addition, for these sites, there were no suspicions emerging from a priori evidence derived from animal experiments or previous epidemiologic findings. Such evidence, on the other hand, makes two malignancies, mesotheliomas and lung cancer, as well as nonmalignant respiratory disease worth special attention. For mesothelioma and nonmalignant respiratory disease no excesses were found in the present study. In none of the other published studies of MMMF-exposed populations has any case of mesothelioma been reported (9, 21). For nonmalignant respiratory disease an increased risk was reported in the large cohort study of MMMF workers in the United States (8). For lung cancer an elevation in mortality (paralleled, to a less extent, by an elevation in incidence) was found among workers with a long period of observation (at least 20 years since first exposure) and was particularly marked within the early technological phase of rock-wool/slag-wool production.

In assessments of the validity of death certificate data cancer registration data can be used. In the four Scandinavian countries where cancer incidence data were available, 75 deaths from lung cancer occurred. Sixty-eight of these cases were also registered as incident cases of lung cancer. Of the remaining seven deaths, one took place in 1948 (before the cancer register was established), one had been registered as a stomach cancer, one had not been registered, and four were coded as secondary and unspecified cancers. The stomach cancer and one secondary and unspecified cancer occurred during the early technological phase in a glass-wool worker. The other three secondary and unspecified cases occurred in rock-wool workers, one each in the early, intermediate, and late phases. On the other hand 9 of the 87 persons with registered cases of respiratory cancer were certified as having died from some other cause.

In order to explain the lung cancer excess, on which the discussion is centered, several possible causes have to be considered.

Tobacco is the most important single cause of lung cancer, and the absence of information on smoking habits of the population under study is certainly a limitation, as it is in most historical cohort studies. However for the following reasons smoking is unlikely to explain the entire excess: (i) the magnitude of the risk in the rock-wool/slag-wool early group was larger than can be plausibly explained by differences in smoking habits between the study population and the general population (1, 5, 16) and (ii) the use of local reference populations should have, at least partially, taken into account the effect of different smoking habits within the countries where such differences may exist.

No information was available on other occupational exposures experienced before or after employment in MMMF production. In order to have a confounding effect, however, the other occupational exposures should both carry a carcinogenic risk for the lungs and be associated with the part of the workforce (ie, employed in rock-wool/slag-wool production, early technological phase) estimated to be at risk of higher exposure to MMMF. Such a situation, although it cannot be excluded, appears to be a rather remote possibility. In addition, the group estimated to be at high risk of exposure to MMMF started to show an excess 20 years after first exposure, which is the lag-time usually needed for a display of effect, for example, for asbestos fibers.

As part of the historical environmental investigation, occupational exposures were identified which could conceivably be associated with an excess lung cancer risk. Of particular concern was asbestos. While major amounts of asbestos usage disqualified factories from being included in the study, some minor uses were identified. Some use of asbestos insulation for furnaces or asbestos gloves and aprons were reported, as is to be expected in an industry involving hot processes. Some limited use of asbestos, such as stitching yarn, was identified in factories 1, 2, 10, and 12. Analysis of the mortality of those workers employed during these periods of asbestos use did not show any excess for lung cancer. In factory 1, there was one lung cancer death (0.2 expected) with less than 10 years since first exposure. Factory 2 showed a slight deficit for lung cancer, and none of the four who died from lung cancer was employed during the relevant years. In both factory 10 and factory 12, most of the cohort was employed for some time during the reported use of asbestos. Factory 10 was one of the three glass-wool factories contributing to the excess in 30 or more years since first exposure. Factory 12 did not contribute to the excess of lung cancer deaths in the long observation period in rock-wool production.

Bitumen and pitch have both been used to varying extents as dust suppressive agents early in the history

of MMMF production, and they can contain carcinogenic polycyclic aromatic hydrocarbons. Within the rock-wool category the following four factories had used bitumen or pitch binders: factory 1 (1950–1954), 4 (1942–1955), 5 (1948–1960), and 9 (1946–1949). Within the glass-wool production only factory 10 used bitumen during 1945–1962. Within the rock-wool category mortality of the group employed during periods of bitumen use accounted for some of the excess in the 20- to 29-year follow-up (7 observed versus 4.6 expected) but none of the excess in the group with 30 or more years since first exposure (1 observed versus 1.2 expected).

The industrial hygiene measurements previously carried out in these factories indicated that respirable fiber levels tended to be higher for rock wool/slag wool than for glass wool and higher in secondary processes than in production areas (18). However the relative position of respirable dust levels between production and secondary processes may not have been the same in the past, especially when the production methods were less automated and less enclosed. The lung cancer mortality analyzed by occupational category did not appear to be concentrated in any particular group. For the rock-wool/slag-wool subcohort the SMR in the secondary process is hard to interpret given the small number of exposed persons in the group.

The most convincing evidence of a causal association would derive from a relationship of increasing lung cancer risk with increasing dose. Taking length of employment instead of dose gives no evidence in this study of such a relationship for the total cohort or single process. For none of the three processes was there any association between lung cancer mortality and length of employment, whether for the complete follow-up or for the observed and expected deaths more than 20 years since first exposure. However length of employment is not necessarily a reliable estimate of the true cumulative dose. The MMMF industry has, since its inception, undergone improvements in industrial hygiene with a reduction in respirable fibers. Short periods during the dustier exposures could lead to cumulative doses as high or higher than long periods of exposure to low dust levels. Quantitative estimates of exposure levels in the early technological phase were not available for any of the factories under study, although the respirable fiber levels are generally thought to have been higher than today (3, 10, 24). Airborne levels have recently been measured in a rock-wool factory during the manufacture of a product without any use of oil or binder, giving results ranging from 9.8 to 25.6 fibers/ml (17). The line was completely mechanized, and no worker exposure occurred in the area.

Using these latter results and the average duration of exposure in the rock-wool early phase (2.7 years) to estimate the highest cumulative exposure, we obtain a cumulative dose in the range of 25–70 fibers-years/ml. Such cumulative fiber dose and the SMR

values observed in the early phase group are compatible with the dose-response estimates from other studies on workers exposed to chrysotile asbestos (7, 14, 15, 19, 20). However the preceding exposure estimates are highly imprecise, and the dose estimates in the asbestos studies themselves suffer from errors related to the conversion of limited particle count data into fiber levels.

Quantitative measures of present airborne fiber levels (18) have not been used for constructing a cumulative dose because of the uncertainty of extrapolating present levels back to the past MMMF exposure. A qualitative approach has been chosen that takes into account the type of process operating, the use of binders, and the types of binder so as to identify a priori the groups with highest exposure. As previously mentioned, during the early technological phase in rock-wool/slag-wool production, mainly because of the absence of oil, higher concentrations of airborne fibers were very probably present (no direct measurements were available) than in the intermediate and late technological phases. This situation contrasts with that in glass-wool production where two changes (introduction of oil binders but also a reduction in nominal diameter of the fibers produced) took place between the early and the subsequent technological phases, the effects of which act in opposite directions on airborne fiber levels. As a result changes in airborne fiber exposure between the early and intermediate technological phases were likely to have been less conspicuous than in rock-wool/slag-wool production.

The results of the lung cancer analysis indicated that the lung cancer excess was associated with the early technological phase in the rock-wool/slag-wool subcohort. The SMR values are still raised, but lower, in the intermediate technological phase. Restricting the analysis by duration of exposure to the technological phases (early and intermediate) which show elevated SMR values revealed no clear association although the pattern was less irregular than in the analysis by overall duration of employment. No risk excess was detected in the late technological phase. This finding, which certainly requires further confirmation, is however suggestive of a decrease or absence of risk among workers entering work during more recent MMMF production.

The historical environmental investigation identified some use of slag in the rock-wool/slag-wool plants during their early history. This use was on a limited or experimental basis in factories 4 and 5 but was a large component of the material in factories 1, 8, and 9 (for the first 8, 25, and 16 years, respectively). For a short period in factory 1, copper slag was used, which would therefore have been contaminated with arsenic, an element which has been shown to be carcinogenic in some compounds (11).

The industry has reported that during the early years of production and thus the early technological phase, environmental conditions were affected by poor ventilation which might have also resulted in a potential

exposure to polycyclic aromatic hydrocarbons from furnace fumes. Possible effects of such exposure, either alone or in combination with fiber exposures, cannot be excluded.

For glass wool, after adjustment for local populations' mortality, no clear excess or pattern was discernible, apart from a slight increase in the SMR for the middle technological phase, which was dominated by the presence of factory 10. This factory was characterized by different production lines which used bitumen, oil binder, and no binder at all and which had been operating at the same time, as well as a line producing microfibers, some continuous-filament production, and some reported asbestos use. This excess might be related to one or more of these specific processes, but the currently available occupational histories do not allow allocation of individuals according to the different processes or exposures. A more-detailed analysis is underway.

The results from the extension of this study are consistent with those from other cohort studies reviewed elsewhere in this supplement (21). They show an excess of lung cancer in the long-term follow-up of workers in the MMMF production industry. In particular a large cohort study conducted by Enterline & Marsh in the United States (19) found an excess of lung cancer 30 or more years since first exposure among workers in rock-wool/slag-wool production (14 observed versus 8.1 expected).

Conclusions

No excess mortality from nonmalignant respiratory diseases has been found in the study population in any of the three production processes.

An elevated mortality for lung cancer among *rock-wool/slag-wool* workers was associated with employment during the early technological phase of this process. Exposures such as smoking or previous employment were considered unlikely to provide a sufficient explanation for the excess. The concentration of the lung cancer excess in the group of workers employed during periods identified a priori as having a potential for the highest levels of fibrous dust exposure indicates that the association may be of causal nature. Environmental conditions during the early technological phase of production were also reported to be affected by the use of slag, some of which contained arsenic and, because of poor ventilation, resulted in potential exposure to polycyclic aromatic hydrocarbons from furnace fumes. Possible effects of such exposures either alone or in combination with fiber exposures cannot be excluded on the basis of the information available. Since respirable fibers were a significant component of the ambient pollution, it is plausible that fiber exposure during the early period of rock-wool/slag-wool production — alone or in combination with other factors — may have contributed

to the observed lung cancer excess. No increased risk was found after the full introduction of dust-suppressing agents. No excess of the same magnitude was present in *glass-wool* production, where a lung cancer excess 30 or more years since first exposure was largely reduced by adjustment for local mortality rates. Due to the short follow-up of the *continuous-filament* subcohort, no evaluation of possible long-term effects of occupational exposure could be made.

The data provide no evidence of an increased risk for pleural tumors in the study population.

References

1. Axelson O. Aspects of confounding in occupational health epidemiology. *Scand J Work Environ Health* 4 (1978) 85–89. (Letter to the Editor).
2. Bertazzi PA, Zocchetti C, Riboldi L, Pesatori A, Radice L. Cancer mortality of an Italian cohort of workers in man-made glass fiber production. *Scand J Work Environ Health* 12 (1986): suppl 1, 65–71.
3. 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* 12 (1986): suppl 1, 26–33.
4. Coleman M, Douglas A, Hermon C, Peto J. Cohort study analysis with a fortran computer program. *Int J Epidemiol* 15 (1986) 134–137.
5. Cornfield J, Haenszel W, Hammond EC, Lilienfeld AM, Shimkin MB, Wynder EL. Smoking and lung cancer: Recent evidence and a discussion of some questions. *J Natl Cancer Inst* 22 (1979) 173–203.
6. Davis JMG. A review of the experimental evidence for the carcinogenicity of man-made vitreous fibers. *Scand J Work Environ Health* 12 (1986): suppl 1, 12–17.
7. Dement JM, Harris RL, Symons MJ, Shy C. Estimates of dose-response for respiratory cancer among chrysotile asbestos textile workers. *Ann Occup Hyg* 26 (1982): 1–4, 869–887.
8. Enterline PE, Marsh CM. The health of workers in the MMMF industry. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20–22 April 1982. World Health Organization, Regional Office for Europe, Copenhagen 1984, pp 311–339.
9. Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20–22 April 1982. World Health Organization, Regional Office for Europe, Copenhagen 1984.
10. Hartung WJA. Technical history of MMMF with particular reference to fibre diameter and dustiness. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20–22 April 1982. World Health Organization, Regional Office for Europe, Copenhagen 1984, pp 12–19.
11. International Agency for Research on Cancer. Some metals and metallic compounds. Lyon 1980. (Monographs on the evaluation of the carcinogenic risk of chemical to humans, volume 23).
12. International Agency for Research on Cancer. Final report on mortality and cancer incidence among man-made mineral fibre production workers in thirteen factories. Lyon 1983.
13. Kvale G, Bjelke E, Heuch I. Occupational exposure and lung cancer risk. *Int J Cancer* 37 (1986) 185–193.
14. McDonald AD, Fry JS, Woolley AJ, McDonald J. Dust

- exposure and mortality in an American chrysotile textile plant. *Br J Ind Med* 40 (1983) 361—367.
15. McDonald JC, Liddell FDK, Gibbs GW, Eysen GE, McDonald AD. Dust exposure and mortality in chrysotile mining, 1910—75. *Br J Ind Med* 37 (1980) 11—24.
 16. Medical Research Council. Expected numbers in cohort studies: Proceedings of a meeting held in Southampton, 21 May 1984. Southampton 1984. (Scientific report no 6).
 17. Ottery J. Report on the environmental investigation at Rockwool A/B, Skode, 12—14 May 1981. Institute of Occupational Medicine, Edinburgh 1981. (BP 31075/2/B(4)13.1).
 18. Ottery J, Cherrie JW, Dodgson J, Harrison GE. A summary report on environmental conditions at 13 European MMMF plants. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20—22 April 1982. Volume 1. World Health Organization, Regional Office for Europe, Copenhagen 1984, pp 83—117.
 19. Peto J, Doll R, Hermon C, Binns W, Clayton R, Goffe T. Relationship of mortality to measures of environmental asbestos pollution in an asbestos textile factory. *Ann Occup Hyg* 29 (1985): 3, 305—355.
 20. Rubino GF, Piolatto G, Newhouse ML, Scansetti G, Aresini GA, Murray R. Mortality of chrysotile asbestos workers at the Balangero Mine, Northern Italy. *Br J Ind Med* 36 (1979) 187—194.
 21. Saracci R. Ten years of epidemiologic investigations on man-made mineral fibers and health. *Scand J Work Environ Health* 12 (1986): suppl 1, 5—11.
 22. Saracci R, Simonato L, Acheson ED, Andersen A, Bertazzi PA, Claude J, Charnay N, Estève J, Frentzel-Beyme RR, Gardner MJ, Jensen OM, Maasing R, Olsen JH, Teppo L, Westerholm P, Zocchetti C. The IARC mortality and cancer incidence study of MMMF production workers. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20—22 April 1982. World Health Organization, Regional Office for Europe, Copenhagen 1984, pp 279—310.
 23. Saracci R, Simonato L, Acheson ED, Andersen A, Bertazzi PA, Claude J, Charnay N, Estève J, Frentzel-Beyme RR, Gardner MJ, Jensen OM, Maasing R, Olsen JH, Teppo L, Westerholm P, Zocchetti C. Mortality and incidence of cancer of workers in the man-made vitreous fibres producing industry: An international investigation at 13 European plants. *Br J Ind Med* 41 (1984) 425—436.
 24. Schneider T, Smith ED. Characteristics of dust clouds generated from old MMMF products: Part II Experimental approach. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA Copenhagen, 20—22 April 1982. World Health Organization, Regional Office for Europe, Copenhagen 1984, pp 33—43.
 25. Simonato L, Fletcher AC, Cherrie J, Andersen A, Bertazzi PA, Bolander AM, Charnay N, Claude J, Dodgson J, Estève J, Frentzel-Beyme RR, Gardner MJ, Jensen O, Saracci R, Teppo L, Westerholm P, Winkelmann R, Winter P, Zocchetti C. Updating lung cancer mortality among a cohort of man-made mineral fibre production workers in seven European countries. *Cancer Lett* 30 (1986): 2, 189—200.
 26. World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death. Geneva 1957. (Seventh revision conference).
 27. World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death. Geneva 1967. (Eighth revision conference).
 28. World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death. Geneva 1978. (Ninth revision conference).