Scand J Work Environ Health 1986;12(1):65-71
Issue date: 1986

Cancer mortality of an Italian cohort of workers in man-made glass-fiber production.

by Bertazzi PA, Zocchetti C, Riboldi L, Pesatori A, Radice L, Latocca R

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/3798057

Print ISSN: 0355-3140 Electronic ISSN: 1795-990X

Scand J Work Environ Health 12 (1986): suppl 1, 65—71

Cancer mortality of an Italian cohort of workers in man-made glass-fiber production

by Pier A Bertazzi, MD, Carlo Zocchetti, ScD, Luciano Riboldi, MD, Angela Pesatori, MD, Laura Radice, MD, Raffaele Latocca, MD[1]

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* 12 (1986): suppl 1, 65—71. This study was undertaken in order to examine possible long-term effects, particularly cancer, associated with working in the man-made glass-fiber production industry in Italy (glass wool and continuous filament). All male production workers employed for a minimum of one year between 1944 and 1974 were admitted to the study (1 098 subjects), and their mortality was examined in the period 1944—1983 (21 325 person-years). The vital status ascertainment was successful for 98.9 %, of the cohort members. An increased risk of cancer of the larynx was noted based, however, on only four deaths. When contrasted with the values of the local population, the increase proved to be statistically significant after 25 years since first exposure. The higher than expected larynx cancer mortality was confined to workers hired before the age of 25 years, exposed for at least 15 years, who started exposure before 1960 (main production: glass wool), and who belonged to the highest cumulative exposure categories. Known confounding factors could not completely account for the excess observed. Among the numerous studies carried out on man-made glass-fiber workers, only one incidence study in France support our findings. No other increased cancer risks have been suggested by the present study.

Key terms: cumulative exposure, expected numbers, larynx cancer.

Industrial production of man-made mineral vitreous fiber (MMMF) began to develop in the 1920s. The first reports of harmful effects in exposed workers were published in the 1940s in France, Italy, and the United States, and they concerned irritating effects on the skin, ocular mucosae, and the upper airways (2, 15). Similar effects were coherent with the definition of "nuisance particulates" attributed to MMMF. More recently, results of experimental, as well as human, studies prompted the reconsideration of the alleged biologically "inert" character of this material in that fibers of appropriate dimensions exerted a carcinogenic action in particular experimental systems (9) and several independent epidemiologic studies thereafter conducted did not allow excluding a possible analogous risk to man under certain exposure conditions (29). In Italy, in particular, repeated observations were made of cases of interstitial lung disease with characteristics similar to asbestosis in workers exposed purely to man-made glass fibers (6, 7, 21).

This mortality study was carried out within the framework of an international European research project that was started in 1977, has been coordinated by the International Agency for Research on Cancer (IARC) (5), and was designed in order to examine any possible long-term effect (especially respiratory cancer) associated with working in the man-made glass-fiber industry in Italy.

Subjects and methods

Plant

The plant studied has been manufacturing glass fibers since 1944. The active workforce at the time the study was started included about 650 persons. Until 1960 the great majority of the production was glass wool (around 70 % of the total), and after, the entire production was, and still is, continuous filament, a process known to produce concentrations of respirable fibers much lower than other types of MMMF production (25). In this plant, resin binder has been used since the beginning, and general ventilation systems have been operating since those days. No use of asbestos has been reported.

Exposure assessment

Nearly 200 different jobs were identified inside the plant. They were grouped into 20 exposure categories, each including similar jobs as far as type of operation performed, location within the plant, and similarity in dust-exposure levels. The level of exposure and the characteristics of the airborne fibers were determined in 1980 by the Edinburgh Institute of Industrial Medicine (25). Personal samples were taken from a random sample of 166 workers, representative of those working under typical exposure conditions. The group mean

[1] Institute of Occupational Health "Clinica del Lavoro Luigi Devoto," University of Milan, Milan, Italy.

Reprint requests to: Dr PA Bertazzi, "Clinica del Lavoro L. Devoto," dell'Università di Milano, Via San Barnaba, 8, I-20122 Milano, Italy.

concentrations of the fibers of respirable size ranged in different categories from 0.005 to 0.027 fibers/ml (membrane filters) and from 0.007 to 0.048 fibers/ml (nucleopore filters); the nonrespirable fraction showed even lower concentrations. The median length varied across the categories from 3.7 to 7.5 μm (scanning electron microscopy) or from 13.4 to 47.5 μm (optical microscopy). Despite the nominal diameter of the continuous filament (greater than 6 μm), the median group diameters of the airborne fibers ranged from 0.30 to 0.70 μm (scanning electron microscopy). Asbestos fibers were not found to be present in any of the samples. Each exposure category was then attributed a fiber concentration value corresponding to the relevant group mean of the respirable fraction.

Other measurements had been taken in 1977. The techniques and methodologies used were not comparable; no doubt, however, even in 1977, the concentrations of glass fibers were found to be very low (19).

Population and follow-up

A total of 2 429 workers (2 096 males and 333 females) had been hired by the plant between the commencement of production and 1980. The enumeration of the cohort was ascertained from a check of the progressive counting of the employees registered by law in the personnel files. Only a portion of these subjects have been examined in this report, ie, only that fraction we considered a priori as the most relevant for the hypothesis to be tested: male production workers, with a minimum length of exposure of one year, hired up to 10 years before the conclusion of the follow-up. In all, 1 098 workers met the criteria. Their mortality was studied in the period 1944—1983.

The personnel office was able to supply the following information for each subject: surname, first name, sex, place and date of birth, residence and/or last address, complete work history including the different jobs held (in chronological order), and, for each job, the date in and date out. The vital status of former workers was ascertained at the Population Statistics Office of the municipality they lived in, or else in the municipality where the subject was born if the address registered on the plant file proved to be unknown or incorrect. In case of changes of residence, the request was sent to subsequent municipalities where the subject was resident, until the official notice of the subject's vital status at the closing date of the study was received. Should the subject have died in the meanwhile, the Population Statistics Office of the relevant municipality supplied the cause of death.

Analysis

The calculation of person-years of observation and of expected deaths was carried out by a computer program developed for these types of studies (36). Expected deaths were calculated on the basis of the following two different reference mortalities divided by cause, sex, and five-year calendar time and age groups: the death rates of the Italian population in 1944—1979 and the death rates (1951—1981) of the population of the largest city close to the area where the plant is located (approximately 100 000 inhabitants). Local rates for 1951 were extrapolated back to 1944.

The separation of technological phases, as adopted at the overall European level (31), was not applicable to this particular plant, and, thus, in order to explore a possible dose-response relationship, a different approach was attempted.

Each worker had belonged to one or more of the exposure categories and hence had been exposed to certain estimated fiber concentrations for known numbers of months. Each concentration was attributed a weight depending on the period of exposure: the earlier in time the exposure, the higher the weight. This assignment was made in order to take into account a number of factors, ie, the fiber concentrations in the past (certainly higher than those measured in 1980), the greater importance of past exposure in causation of possibly associated long-term effect, and the possible role played by the retention period of the fibers in the body in producing a pathological response. The weights attributed corresponded to the number of months leading from the time of exposure to the end of the study. Thus, for instance, an exposure experienced the last month of study had a weight of 1; one experienced exactly ten years earlier had a weight of 120, and so on. Finally, the simple products (fiber concentration × weight) calculated for any single month of exposure were summed up. Each worker was thus assigned a "score" of weighted cumulative exposure depending on the level, calendar time, and duration of his individual exposure history. The resulting distribution of scores was then broken down into quartiles, so as to obtain categories of cumulative exposure of comparable size and increasing severity, which have been simply referred to as categories 1 to 4.

The adopted scoring system did not allow for distinguishing between different production processes, ie, glass wool or continuous filament, but we thought it best, other than simplest, to try to separate glass-wool exposure from continuous-filament exposure merely by analyzing the data according to the year of employment in the factory. The mortality experience of the cohort was also analyzed in terms of years since first exposure and total length of exposure.

Hypothesis testing of the observed/expected ratios was performed on the assumption of a Poisson distribution of the events in the numerator. Confidence limits were calculated according to Miettinen's method, using available desk calculator programs (26).

Results

The results of the follow-up of the cohort are presented in table 1. Death certificates were obtained for all 130 deceased subjects.

The number of person-years accumulated and their distribution according to attained age and years since first exposure is given in table 2.

Table 3 shows the observed number of deaths for broad groups of causes in comparison with the number of deaths expected from the national and local rates. The standardized mortality ratio (SMR) values were not consistent between the two choices of reference populations; they were generally higher by a large extent when expected deaths were calculated from the national rates. The significant increase in mortality from all causes and the almost significant excess of deaths from all cancers obtained in comparison with the national rates disappeared when the death rates of the local population were used. Deaths due to cancer of the digestive tract were uniformly lower than expected. The four deaths from larynx cancer made up a remarkable but not significant excess when compared with the national expected figures and an almost twofold nonsignificant increase above the expected figures from the local population. Twelve lung cancer deaths were observed, slightly in excess of the national expected figures but less than expected from the local rates. Cardiovascular deaths were significantly decreased below expectations. Other nonmalignant diseases were increased above expectations, but not significantly so. There was a slightly elevated mortality from chronic respiratory disease, and the excess mortality from diseases of the digestive tract was mainly due to cirrhosis (11 out of 16 deaths). Deaths due to external causes were higher than expected from either reference population.

Given this overall picture, only expected deaths calculated on the basis of the mortality rates of the local population have been shown in tables 4—7. In table 4 analysis by years since first exposure is presented. The general pattern of mortality did not appear to be in relation to the length of this period. A statistically nonsignificant increase in all cancer deaths took place after a period of 20 or more years. Deaths due to cancer of the digestive tract and lung cancer failed to exhibit any definite trend. Of the four deaths due to laryngeal cancer, three had occurred after at least 25 years since first exposure; the observed : expected ratio turned out to be statistically significant.

Analysis by length of exposure yielded the results given in table 5. No clear-cut patterns or trends were appreciable, however, with an apparent exception, ie, larynx cancer. All cases of larynx cancer had occurred after a period of exposure of at least 15 years, and they represented a fivefold increase above expectation.

Table 1. Status of the study population at the end of the follow-up (31 December 1983)

	Number	Percentage
Alive	956	87.1
Dead	130	11.8
Lost to follow-up	12	1.1
Total	1 098	100.0

Table 2. Person-years of observation accumulated during the study period (1944—1983) broken down by years since first exposure (latency) and attained age.

Age (years)	Years since first exposure					
	≤4	5—9	10—14	15—19	20—24	≥25
≥24	1 360	314	4	—	—	—
25—34	2 350	2 380	1 206	274	4	—
35—44	1 271	1 666	1 786	1 270	662	197
45—54	413	798	946	789	698	875
55—64	60	173	292	391	305	407
65—74	3	13	25	63	92	178
>74	—	—	—	—	3	57

Table 3. Mortality from selected causes in 1944—1983. Two sets of expected deaths are shown, calculated, respectively, from the death rates of the national and local population. (SMR = standardized mortality ratio, standardized by age and calendar period; 95 % CI = 95 % confidence interval)

Cause of death[a]	Observed	National reference group			Local reference group		
		Expected	SMR	95 % CI	Expected	SMR	95 % CI
All causes	130	106.4	122	102—145	126.1	103	86—122
All cancers (140—209)	39	28.1	139	99—190	39.1	100	71—136
Cancer of the digestive tract (150—159)	8	9.2	87	38—171	12.3	65	28—128
Cancer of the larynx (161)	4	1.2	337	91—853	2.1	188	52—488
Cancer of the lung (162)	12	8.0	149	77—262	12.5	96	50—168
Cardiovascular disease (390—458)	21	35.0	60	37—92	42.1	50	31—76
Respiratory disease (460—519)	8	6.1	130	57—258	6.0	133	57—263
Alimentary tract disease (520—579)	16	11.2	143	62—199	11.7	137	78—222
External causes (800—999)	20	14.9	135	82—207	13.1	153	93—236

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

Table 4. Mortality from selected causes according to years since first exposure (expected deaths based on local rates). (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death[a]	Years since first exposure														
	≤9			10—14			15—19			20—24			≥25		
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR
All causes	31	33.7	92	20	20.5	97	25	21.0	119	17	17.6	96	37	33.3	111
All cancers (140—209)	5	8.8	57	7	6.8	103	5	7.1	70	8	6.1	131	14	10.3	135
Cancer of the digestive tract (150—159)	1	2.8	36	1	2.1	48	1	2.2	44	3	1.9	154	2	3.2	62
Cancer of the larynx (161)	—	0.5	0	—	0.4	0	—	0.4	0	1	0.3	299	3	0.5	591[b]
Cancer of the lung (162)	3	2.3	131	1	2.2	45	2	2.3	87	2	2.1	94	4	3.5	115

[a] Code of the International Classification of Diseases, eighth revision, in parentheses.
[b] 95 % confidence interval = 150—1 608.

Table 5. Mortality from selected causes according to length of exposure (expected deaths based on local rates). (O = observed number of deaths, E = expected number of cases, SMR = standardized mortality ratio)

Cause of death[a]	Length of exposure (years)											
	≤9			10—14			15—19			≥20		
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR
All causes	72	59.9	120	18	27.3	66	20	21.8	92	20	17.2	117
All cancers (140—209)	20	17.9	112	3	7.7	39	6	7.1	85	10	6.4	156
Cancer of the digestive tract (150—159)	4	5.4	74	—	2.7	0	2	2.2	89	2	1.9	103
Cancer of the larynx (161)	—	1.0	0	—	0.4	0	2	0.4	503	2	0.4	553
Cancer of the lung (162)	7	5.6	124	1	2.3	44	2	2.3	88	2	2.3	88

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

Table 6. Mortality from selected causes according to calendar period in which exposure began (expected deaths based on local rates). (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death[a]	Period of first exposure														
	≤1949			1950—1954			1955—1959			1960—1964			≥1965		
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR
All causes	44	49.5	89	17	12.9	132	17	17.9	95	25	25.1	99	27	20.7	130
All cancers (140—209)	17	13.4	127	3	3.6	83	6	6.1	99	4	8.8	45	9	7.3	124
Cancer of the digestive tract (150—159)	4	4.8	84	1	1.2	82	—	1.8	0	1	2.5	40	2	1.9	103
Cancer of the larynx (161)	2	0.7	282	1	0.2	557	1	0.3	294	—	0.5	0	—	0.4	0
Cancer of the lung (162)	6	3.7	163	—	1.0	0	1	2.0	51	—	3.0	0	5	2.7	184

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

Table 7. Mortality from selected causes according to time-weighted cumulative exposure scores. Categories from 1 to 4 in order of increasing severity (expected deaths based on local rates). (O = observed number of deaths, E = expected number of deaths, SMR = standardized mortality ratio)

Cause of death[a]	Cumulative exposure category											
	1			2			3			4		
	O	E	SMR	O	E	SMR	O	E	SMR	O	E	SMR
All causes	34	26.5	129	18	15.9	113	29	29.5	98	49	54.2	90
All cancers (140—209)	12	8.4	144	2	5.3	38	8	9.4	85	17	16.0	106
Cancer of the digestive tract (150—159)	2	2.3	86	—	1.6	0	1	2.9	34	5	5.5	91
Cancer of the larynx (161)	—	0.4	0	—	0.3	0	1	0.5	190	3	0.8	355
Cancer of the lung (162)	4	2.9	139	1	1.8	57	2	3.0	66	5	4.8	105

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

Similar considerations apply to the results presented in table 6, where mortality is presented according to year of first exposure. The year 1960 was the date of cessation of glass-wool production, but the patterns of the SMR values before or after that date do not indicate an ostensibly different mortality between the workers whose exposure started during the glass-wool production period or later when only continuous filament was manufactured. However, if one looks at larynx cancer, it can be noted that all cases had occurred in workers first employed in the plant before 1960; the number of observed deaths (although very low) was well above the expected figures.

Analysis by weighted cumulative exposure (table 7) showed a slightly increased overall mortality among workers in the categories of lowest exposure. For all cancer and lung cancer, a modest increase in the observed:expected ratios was only obtained in category 1 (lowest exposure). Instead, and not unexpected at this step of the analysis, a clear, but still not significant, larynx cancer excess mortality was noted among the workers in category 4, the one of highest exposure.

Discussion

This cohort of workers in man-made glass-fiber production exhibited a mortality from all causes significantly higher than expected from the mortality rates of the national population of the same sex and birth cohort. Also mortality from all cancers showed an increase of borderline significance; with reference to specific sites, larynx cancer and lung cancer deaths were in excess, but not significantly so. In Italy, marked differences in cancer mortality across different regions have been documented (8). Therefore, the use of local rates seemed appropriate, and resulted in a conspicuous change of the SMR values. The overall mortality failed to show any appreciable increase above expectation, and for no type of cancer did the observed deaths result in values higher than expected, with the expection of larynx cancer, for which an almost twofold, but not significant, increase was obtained.

As regards nonmalignant diseases, deaths due to cardiovascular diseases were consistently and significantly fewer than expected, no matter which set of reference rates was used. Deaths from nonmalignant diseases of the respiratory and digestive tract resulted in a slight excess. This result was somehow in contrast to what was expected after a comparison of an industrial cohort with a geographically defined population. The selection bias affecting such a comparison usually produces a lowered mortality from these causes in the cohort of workers. As mentioned, the excess mortality from diseases of the digestive tract was mainly due to cirrhosis. This occurrence could be an indication of an alcohol consumption much higher on the average among the workers than among the reference population. The slight excess of deaths due to respiratory causes, instead, did not seem to be applicable to vastly different smoking habits between the compared populations, since such a difference would have also been reflected by the results of mortality from cardiovascular causes. The elevated risk of death from external and violent causes was not accounted for by accidents at work.

The possible cancer risk associated with working in this plant was further analyzed. High values of the observed:expected ratio for all cancers were found among workers who had been exposed for at least 20 years and after a latency period exceeding 20 years. This suggestion, however, was not confirmed after analysis by cumulative exposure. On the contrary, when level, calendar time, and duration of exposure were taken altogether into consideration, the only elevated SMR was observed in the category of lowest exposure.

No suggestions of an increased risk of cancer of the digestive tract were provided by any of the analyses performed.

Deaths due to lung cancer showed a slight increase above expectation only in comparison with the national population. Analysis by latency, duration of exposure, period of exposure, and cumulative exposure failed to confirm the hypothesis of an association between lung cancer deaths and man-made glass-fiber exposure in this particular study.

Four malignant tumors of the larynx were observed, a number which in itself calls for caution in interpretation. They were well above the expected figures from the local population, which, in point of fact, was drawn from an area where quite a high background risk from laryngeal cancer had been documented (1). The increase was statistically significant after a latency period longer than 25 years and was confined to the subcohort of workers with a length of exposure of 15 years or more, hired before the age of 25 (table not shown in this paper), and belonging to the category of highest cumulative exposure. The cases were all workers hired in the late 1940s and in the 1950s. These data are relevant, since it can be reasonably assumed that in those days the airborne concentration of fibers was definitely higher in comparison to the measurement carried out in 1980. In addition glass wool was manufactured in those days, a production which, as mentioned, implies a dispersion of fibers in the atmosphere higher than in the production of continuous filament.

The possibly increased risk of laryngeal cancer is the most consistent piece of data yielded by the study. Such a suggestion was put forward even in a previous environmental and morbidity study carried out in 1979 in this same plant on a group of 467 active workers from the main production areas (19) and was also present in the preceding phase of the mortality study of this cohort (3).

The exogenous risk factors of laryngeal cancer have been thoroughly investigated, and the ones almost uni-

versally accepted are tobacco smoking, alcohol, and asbestos. In addition an increased laryngeal cancer risk has been described in association with exposure to a number of substances and/or occupations, as, for instance, nickel, wood dust, mineral oils, mustard gas production, isopropyl alcohol, and ethanol production with the strong acid method (diethyl sulfate being the suspected compound), paper and leather works, textile manufacture, various chemical processes, a series of metal works, and exposure to sulfuric acid (11, 18, 27, 32, 34, 35).

Asbestos is considered a certified risk factor, despite the limited knowledge on the possible concomitant role of tobacco smoking (4, 14, 22, 24, 28, 30, 33). The behavior of glass fibers in the respiratory system differs from asbestos fibers in several critical ways. Asbestos contains, in general, a larger fraction of fibers of respirable size. Asbestos fibers can split longitudinally into fibrils, while glass fibers tend to break transversely with a reduction of their length but not of their diameter. Asbestos fibers (at least the amphiboles) are almost insoluble in the lungs, while the persistence of MMMF is shorter. They are, in fact, according to experimental data, relatively soluble and undergo dissolving and disintegrating processes which in an initial stage cause a reduction of their diameter but, as time proceeds, also their disappearance from the lung (13, 16, 17). These differences may account for a lower deposition, and a quicker elimination from the lung, of the inhaled portion of glass fibers than of asbestos fibers. These differences, however, are less important with regard to other portions of the respiratory tract. The larynx, for instance, can be reached also by "large," nonrespirable fibers (diameter $\geq 3\ \mu m$), and its anatomical structure is such as to favor the impact and the permanence of these fibers. In addition, besides the ciliary escalator mechanism (which can be impaired by smoking), no further clearance mechanisms are known to be acting, contrary to what happens in the lung. Thus the hypothesis of an excess of laryngeal cancer apparent from this study could find a biologically plausible explanation in a direct, continuing, and/or repeated action of the fibers on the laryngeal mucosa.

The role of alcohol consumption and tobacco smoking in the causation of larynx cancer has been thoroughly investigated (12, 27), and plausible explanations of their joint biological actions have been proposed (20). In our study, it is unlikely that the smoking habits of the workers and the local population differed to such an extent as to justify completely the excess mortality observed, also in the view of the not higher than expected mortality from lung cancer, whereas a suggestion of a greater alcohol consumption among the workers comes from the higher than expected mortality from cirrhosis, even in comparison with the local population (11 observed versus 8.4 expected).

Our finding of an elevated mortality from cancer of the larynx was not corroborated by the results of the studies carried out concurrently in other countries and presented in this same supplement. Nor was such an excess mortality noted in the pooled analysis of the European study (31) and in the largest study conducted in the United States (10). Such a discrepancy could also possibly stem from different attitudes, from country to country, in certifying this cancer as cause of death, given the long survival of patients suitably treated and the consequent possibility of intervening disease leading to death. Instead, some incidence data tend to support our finding. Suggestions of an increased cancer incidence in the upper respiratory tract came from the European study (31), and, quite recently, a study in a French glass-wool plant (23) disclosed a significantly elevated incidence of cancers of the upper respiratory and alimentary tract, and a clearly higher than expected incidence of larynx cancer (5 observed versus 2.2 expected).

In our interpretation, the preceding discussion enhances the credibility of the hypothesis generated by this study of a possible association between exposure to man-made glass fibers under certain circumstances and an increased risk of laryngeal cancer. However the following three factors stand against this hypothesis: (i) the small number of cases on which the excess was based, (ii) the lack of an accurate histological characterization of the cases, and (iii) the lack of individual information on other possible risk factors. (In conjunction with factor i it is worth mentioning in this respect that two additional deaths from larynx cancer were known, but according to the admission criteria adopted, they were considered a priori not related to occupational exposure — one occurred in a worker exposed for less than one year and the other in a worker hired after 1974.)

References

1. Assi A, Turolla E, Berrino F. Epidemiologia del carcinoma laringeo nell'alto milanese. Epidemiolog Prevenzione 2 (1977) 43—50.
2. Bertazzi PA. Fibre di vetro. Esposizione e rischio per l'uomo. Med Lav 67 (1976) 535—550.
3. Bertazzi PA, Zocchetti C, Pesatori A, Radice L, Riboldi L. Mortalita' per tumori in una coorte di produttori di fibre vetrose. Med Lav 75 (1984) 339—350.
4. Bianchi C, Di Bonito L, Castelli M, Brollo A. Exposition a l'amiante dans le cancer du larynx. Pathologica 70 (1978) 403—408.
5. Cameron JD. Coordinated research into the biological effects of MMMF — Its origin and development in Europe. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of a WHO/IARC conference in association with JEMRB and TIMA. Copenaghen 20—22 April 1982. Volume 1. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 5—11.
6. Chiappino G, Scotti PG, Anselmino A. Broncopneumopatie professionali da fibre vetrose: Osservazioni cliniche. Med Lav 72 (1981) 96—101.

7. Ciaccia A, Pusinanti F, Beltrami A, Fasano E. Pneumoconiosi da fibre di lana di roccia. Riv Patol Clin Tuberc Pneumol 49 (1978) 305—333.
8. Cislaghi C, De Carli A, Morosini PL, Puntoni R. Atlante di mortalita'per tumori in Italia: Triennio 1970—72. Lega italiana per la lotta contro i tumori, Roma 1978.
9. Davis JMG. A review of experimental evidence for the carcinogenicity of man-made vitreous fibers. Scand J Work Environ Health 12 (1986): suppl 1, 12—17.
10. Enterline PE, Marsh GM. The health of workers in the MMMF industry. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of WHO/IARC conference in association with JEMRB and TIMA. Copenaghen, 20—22 April 1982. Volume 1. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 311—339.
11. Flanders WD, Rothman KJ. Occupational risk for laryngeal cancer. Am J Public Health 4 (1982) 369—372.
12. Flanders WD, Rothman KJ. Interaction of alcohol and tobacco in laryngeal cancer. Am J Epidemiol 3 (1982) 371—379.
13. Hammad YY. Deposition and elimination of MMMF. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of WHO/IARC conference in association with JEMRB and TIMA. Copenaghen, 20—22 April 1982. Volume 2. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 126—142.
14. Hammond FC, Selikoff IJ, Seidman H. Multiple interaction effects of cigarette smoking: Extrapulmonary cancer. In: Bucalossi P, Veronesi U, Cascinelli N, ed. Cancer epidemiology, environmental factors. Volume 3. Elsevier, New York, NY 1974, pp 147—150.
15. Hill GW. Fibres, man-made glass and mineral. In: International Labour Office. Encyclopedia of occupational health and safety, Geneva 1983, p 852.
16. Johnson NF, Griffiths DM, Hill RJ. Size distribution following long-term inhalation of MMMF. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of WHO/IARC conference in association with JEMRB and TIMA. Copenaghen, 20—22 April 1982. Volume 2. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 102—125.
17. Leineweber JP. Solubility of fibres in vitro and in vivo. In: Guthe T, ed. Biological effects of man-made mineral fibres: Proceedings of WHO/IARC conference in association with JEMRB and TIMA. Copenaghen, 20—22 April 1982. Volume 2. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 87—101.
18. Lynch J, Hanis NM, Bird MG, Murray KJ, Walsh JP. An association of upper respiratory cancer with exposure to diethyl sulfate. J Occup Med 21 (1979) 333—341.
19. Maggioni A, Meregalli G, Sala C, Riva M. Patologia respiratoria e cutanea negli addetti alla produzione di fibre di vetro (filato). Med Lav 71 (1980) 216—227.
20. McCoy GD, Wynder EL. Etiological and preventive implications in alcohol carcinogenesis. Cancer Res 39 (1979) 2844—2850.
21. Molinini R, Pesola M. Fibrosi polmonare diffusa in soggetto esposto ad inalazione di lana di vetro. Riv Med Lav Ig Ind 3 (1979) 117—126.
22. Morgan RW, Shettigara PT. Occupational asbestos exposure, smoking and laryngeal carcinoma. Ann NY Acad Sci 271 (1976) 308—310.
23. Moulin JJ, Mur JM, Wild P, Perreaux JP, Pham QT. Oral cavity and laryngeal cancers among man-made mineral fiber production workers. Scand J Work Environ Health 12 (1986) 27—31.
24. Newhouse ML, Berry G. Asbestos and laryngeal carcinoma. Lancet 2 (1973) 615.
25. 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 WHO/IARC conference in association with JEMRB and TIMA. Copenaghen, 20—22 April 1982. Volume 1. World Health Organization, Regional Office for Europe, Copenaghen 1984, pp 83—117.
26. Rothman KJ, Boice JD Jr. Epidemiologic analysis with a programmable calculator. Epidemiologic Resources Inc, Boston, MA 1982, pp 30—31.
27. Rothman KJ, Cann CI, Flanders D, Fried MJ. Epidemiology of laryngeal cancer. Epidemiol Rev 2 (1980) 195—209.
28. 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.
29. Saracci R, Simonato L. Man-made vitreous fibers and workers' health: An overview of the epidemiologic evidence. Scand J Work Environ Health 8 (1982) 234—242.
30. Segnan N, Tanturri G. Studio sulla patologia geografica dei tumori laringei, vescicali ed infantili nella provincia di Torino. Tumori 62 (1976) 377—386.
31. 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, Teppo 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—37.
32. Soskolne CL, Zeighami EA, Hanis NM, Kupper LL, Herrmann N, Amsel J, Mausner JS, Stellman JM. Laryngeal cancer and occupational exposure to sulfuric acid. Am J Epidemiol 120 (1984) 358—369.
33. Stell PM, McGill T. Exposure to asbestos and laryngeal carcinoma. Lancet 2 (1973) 416—417.
34. Terracini B, Anglesio E, Panero M, Vineis P. Descriptive epidemiology of cancer of the larynx in the province of Torino, Italy. Tumori 64 (1978) 445—456.
35. Wynder EL, Covey LS, Mabuchi K, Mashinski M. Environmental factors in cancer of the larynx: A second look. Cancer 38 (1976) 1591—1601.
36. Zocchetti C, Bertazzi PA. Un programma computerizzato per l'analisi di studi coorte di mortalita' negli ambienti di lavoro. Med Lav 1 (1982) 9—21.