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Individual asbestos exposure: smoking and mortality — a cohort study in the asbestos cement industry

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Abstract

A historical prospective cohort study comprised all persons employed from 1950 to 1981 for at least three years in the oldest asbestos cement factory in the world. From 2816 persons eligible for the study, record based estimates and measurements of dust and fibres and histories of smoking based on interviews were used to calculate individual exposures over time. After observation of 51 218 person-years and registration of 540 deaths, underlying causes of death for this cohort were compared with those for the regional population on the basis of death certificates. Deaths from lung cancer in asbestos cement workers were higher (standard mortality ratio (SMR) 1·7), but after adjustment for age and sex specific smoking habits this was not significant (SMR 1·04). The study had a probability of greater than 92% of detecting a smoking adjusted SMR of 1·5 or more. Using the best available evidence (including necropsy records) 52 deaths were assigned to lung cancer and five to mesothelioma. Life table analyses confirmed the predominant influence of smoking on lung cancer. Mesothelioma was associated with the use of crocidolite in pipe production. From present working conditions with much lower concentrations of chrysotile and no crocidolite no more occupational cancers are expected in the asbestos cement industry.

This paper presents results of a historical prospective cohort study conducted in the oldest asbestos cement factory in the world, in a region in which the diagnoses on death certificates are made on the basis of necropsy in every third case of death (Vöcklabruck, upper Austria). The cohort and reference population have been described earlier.[1–3]

In Austria asbestos consumption relies on imports, which (after exhaustion during the second world war) increased to 39 583 tonnes in 1973 when 28 063 tonnes (70%) were used by the company investigated.[4] In 1985 about 18 000 tonnes (90%) of imported asbestos were used by this factory.

In Vöcklabruck chrysotile was used predominantly (from 1895). From 1920 to 1977 crocidolite was also used in the pipe factory. Amosite (utilised for certain products from 1970 to 1986) played no part in the exposure of employees. The supply of asbestos as dust in jute sacks was stopped during 1960–70. Open edge mills (kollergangs) were still a major source of exposure up to 1965. Most persons exposed to high concentrations were from the period of increased production after 1945 when work was carried out until the mid 1960s without appropriate removal of dust, and high speed machines had been introduced into the finishing area. Extraction of respirable dust has been considered satisfactory since 1969 and in 1975 a new high performance system for removing dust was put into operation.

Methods

From 1950 onwards the workforce was stable, and records existed for classification of individual exposures. The cohort consisted of all persons employed (for at least three years) in the asbestos cement plant at Vöcklabruck from 1950 to 1981 and comprised 2816 persons from the employment lists, 82% of whom had been employed before 1969 (the decisive year in improving the dust situation). Most of our cohort members started work in asbestos cement production around 20 years of age, but older persons were also taken on the workforce especially in the period of full employment. Details of exposure and age distributions have been reported.[3] Individual exposures were estimated (from 1973) from personal records on duration of exposure at different workplaces, estimations of dust concentration until 1965, dust measurements mainly by a conimeter method until 1975, and by personal air samplers and membrane filter methods[5] subsequently. Independently of the exposure study of the factory carried out by the safety engineers in cooperation with the Austrian Dust and Silicosis Control Office, we sent trained interviewers to all cohort members who had left the plant after 1950 and were still alive in 1982 to obtain data by standardised questionnaire on occupational exposures and smoking. This investigation produced

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complete smoking histories for 2095 workers. The coding of exposure to tobacco was carried out according to time, changing number of cigarettes smoked, and tar content. As a minimum the information "smoker, non-smoker, or ex-smoker" was obtained for 433 deceased persons from relatives and (independently of this) from four workmates. Of these subjects, 318 could also be categorised by average number of cigarettes smoked.

The follow up investigation with the government registration offices and the determination of the cause of death with the aid of the death registries, physicians, and pathologists was separate from the enquiries about exposure. Standardised mortality ratios (SMRs) were computed from diagnoses on official death certificates for comparison with the general population. For comparison within the cohort (smokers and non-smokers and groups with different cumulative asbestos exposure) we used the best available information on cause of death and life table analyses.

Originally it was intended to use cement factory workers from the neighbouring town, Gmunden, without history of occupational exposure to asbestos, as a control group.[6] This group, consisting of 252 employees was, however, too small to give reliable results in the available period of observation. We decided, therefore, to take the total Upper Austrian population as local reference.

Calculation of SMRs for the total group was by the usual method. Four census results and migration corrected interpolations from births and deaths in the years between censuses were used for calculation of expected ratios. Adjustments for smoking were

Table 1 Causes of death (International Classification of Diseases (ICD) 9th revision) 1950–87. Number of deaths by underlying cause according to death certificate (and according to best available information)

	Official diagnosis (best information)	*Additional diagnoses**
Malignant neoplasias:	153 (155)	
Respiratory organs, intrathoracic organs (160–165)	59 (58)	
Lungs (162)	50 (52)	
Pleura (163)	7 (4)	
Larynx (161)	1 (1)	
Other (nose)	1 (1)	
Organs of digestion, peritoneum (140–159)	58 (59)	
Stomach (151)	34 (35)	1
Intestine (152, 153)	3 (4)	
Rectum (154)	4 (4)	
Oesophagus (150)	2 (2)	
Liver (155)	1 (1)	
Gall bladder (156)	3 (3)	
Pancreas (157)	4 (5)	1
Oral cavity and pharynx (140–149)	4 (4)	
Peritoneum (158)	3 (1)	
Other	31 (33)	
Urinogenital organs (179–189)	14 (14)	1
Other locations	17 (19)	
Primary location poorly designated	4 (5)	
Neoplasias of unknown character (239)	1 (0)	
Diseases of the respiratory organs (460–519):	32 (33)	
Chronic bronchitis (491)	4 (5)	3
Emphysema (492)	6 (6)	4
Asthma (493)	8 (9)	2
Tuberculosis (011, 012)	6 (5)	—
Pneumoconiosis (500–505)	1 (2)	8
Other chronic diseases	0 (0)	2
Pneumonia (480–486)	4 (4)	11
Other acute (infectious) diseases	3 (3)	—
Diseases of the circulatory system (390–459):	203 (201)	
Myocardial infarction (410)	61 (62)	2
Other ischaemic heart diseases	31 (31)	9
Cor pulmonale	7 (6)	3
Other cardiac diseases	39 (37)	13
Diseases of cerebral vessels (430–438)	40 (40)	6
Other circulatory diseases	25 (25)	25
Diseases of the organs of digestion (520–579):	47 (47)	
Gastric and duodenal ulcer (531–534)	7 (7)	6
Hepatic cirrhosis (571)	29 (29)	1
Other	11 (11)	—
Other diseases	27 (25)	11
Accidents (800–949)	54 (55)	2
Suicide and violent cause of death (E 950–999)	19 (19)	—
Unknown causes of death	5 (5)	

*Important additional diagnoses not considered to be the underlying cause of death.

carried out in two different ways. Based on an Austrian microcensus on smoking habits, age and sex specific incidence for upper Austria was computed assuming a risk for lung cancer for smokers eight times greater than that for non-smokers; the incidence was then related to the data of our cohort stratified into smokers and non-smokers (ex-smokers were treated as non-smokers, giving bias in the direction of higher risk for the exposed workers. For subjects with unknown smoking history the rates of the total Upper Austrian population were applied).

The second method of adjustment was applied in the subgroup of 2413 workers for which the average number of cigarettes smoked each day was known. From the results of four studies[7-10] the relation between the number of cigarettes smoked and incidence of lung cancer was analysed. We found an almost perfect linear relation (r = 0·97) between the logarithm of the number of cigarettes smoked each day (plus one) and the logarithm of the deaths from lung cancer per 100 000 person-years.[11] This relation served as the basis for the computation of expected incidence of lung cancer adjusted for smoking.

Results

Of the 2816 persons eligible for the study 2155 were alive and 540 were dead in 1987. One hundred and twenty one persons (4·3%) had been lost at different dates, mainly by emigration. Altogether, 51 218 person-years were available for analysis. These included 24 897 observation-years after the 40th year of life, which are relevant for the assessment of the risk of lung cancer. Table 1 shows the official diagnoses of underlying cause of death taken from 535 death certificates. The best available information on the main cause of death obtained from enquiries in hospitals, pathological institutes, and social insurance is also given. Subsidiary causes of death or other important diseases which were diagnosed besides the main disease leading to death are listed under additional diagnoses.

Malignant neoplasias accounted for 10·9% of all underlying causes of death. Of these, lung cancer (SMR 1·7) and stomach cancer (SMR 1·5) were significantly more frequent than in the upper Austrian general population of corresponding age and sex. Within the follow up period 50 deaths from lung cancer (49 up to the end of 1986) and 34 deaths from stomach cancer were found from death certificates. Pleural and peritoneal cancer were also significantly more frequent; even taking into consideration the fact that, after enquiries, some of these cases turned out not to be mesotheliomas. Misdiagnosed conditions included pleuritis carcinomatosis secondary to adenocarcinoma of the lung and carcinosis peritonei from pancreatic carcinomas. On the other hand, no additional case of mesothelioma could be discovered after re-examination of diagnoses that it was considered may have concealed one. An exceedingly high relative risk of mesothelioma could nevertheless be inferred from the five confirmed cases of mesothelioma according to the best available information, four of them verified by necropsy and histology; the corresponding rates of histologically verified mesothelioma cases in the general Austrian population were orders of magnitude lower.[12 13]

Diseases of the respiratory organs accounted for 5·9% of the causes of death. Pneumoconioses appeared mainly as subsidiary causes of death or were registered as additional diagnoses. For diseases of the circulatory system, which accounted for 37·6% of all causes of death, only the deaths with cor pulmonale (without more detailed specification) were of interest in this connection. For diseases of the digestive organs (8·7%), ulcers and liver cirrhosis are listed separately, because of interest in the risk for dust workers in general, asbestos cement workers, and certain other subgroups for cancer of the stomach, possibly characterised by nutritional and drinking habits, shift work, and other related factors.[13] The remaining causes of death were other diseases (5%), accidents (10%), and suicide (3·5%). The cause of death could not be determined in five cases (0·9%). The overall mortality was not significantly higher than in the corresponding general population of Upper Austria (SMR 1·04).

Table 2 shows the increase in lung cancer in comparison to the age and sex matched reference population. Considering the observed number of deaths as a Poisson variable the increase in SMR for lung cancer was statistically significant. If smoking habits were taken into account in the calculation of

Table 2 Mortality from lung cancer for Austrian asbestos cement workers, 1950–1986

Lung cancer (ICD 162)	*O*	*E*	*SMR*	*(95% CI)*	*p Values*
Total	49	28·50	1·72	(1·21–2·57)	<0·01
Total smoker adjusted	49	47·04	1·04	(0·79–1·41)	NS
⩽25 Fibres/ml-year	25	12·80	1·95	(1·17–3·74)	<0·01
⩽25 Fibres/ml-year, smoker adjusted	25	19·91	1·26	(0·83–1·95)	NS
>25 Fibres/ml-year	24	15·04	1·60	(1·01–2·96)	<0·05
>25 Fibres/ml-year smoker adjusted	24	26·16	0·96	(0·64–1·43)	NS

O = Number of observed cases; E = number of expected cases. NS = p > 0·05.

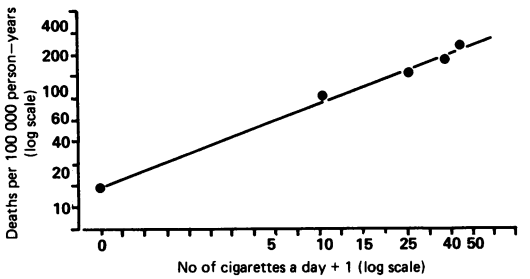

Figure 1 Deaths of Austrian asbestos cement workers from lung cancer per 100 000 person-years as function of number of cigarettes smoked(●) related to expected deaths (solid line).

expected values, however, the adjusted SMR (1·04) was not significantly raised. For this adjustment the age and sex specific results of a microcensus on smoking in upper Austria[14] and a lung cancer risk factor eight times as high as that for non-smokers[15] were used for the smokers as described in the previous section. No higher lung cancer rate was found in workers who accumulated more than 25 fibres per ml-year. Lung cancers found in persons with lower cumulative doses also included two cases who died after only four years of employment.

To investigate the latency of lung cancer induced by asbestos we removed from our cohort all persons who had not been observed for more than 15 years from start of exposure. The result of this additional analysis was 42 observed cases of lung cancer compared with 24·72 expected cases in the Upper Austrian population (SMR 1·70, 95% confidence interval (95% CI) 1·21–2·69). After adjustment for smokers there were 41·82 expected cases of lung cancer (SMR 1·00, 95% CI 0·71–1·59). These results did not differ essentially from that presented for the total cohort (table 2).

The second adjustment utilised the information about average number of cigarettes smoked each day. Figure 1 shows the death rates from lung cancer in five groups, differing in the number of cigarettes smoked each day. The straight line is the regression line, estimated from the studies referred to in the previous section.[7–10] The observed incidences are in good agreement with those expected from smoking habits. The SMR (1·03) obtained after the second adjustment was almost the same as that after the first adjustment. We therefore conclude that the null hypothesis—exposure to chrysotile within the asbestos cement industry does not increase the risk of lung cancer—could not be rejected from our data.

This conclusion is also supported by life table analyses comparing exposure groups differing with respect to duration of exposure, intensity of exposure, or fibre-years, which showed no association between exposure and the probability of death from lung cancer. A life table analysis based on the best available diagnoses showed the expected differences between smokers and non-smokers; the overall probability of survival of smokers was 1·7% at the end of observation and 64·1% (95% CI 59·6–68·2%) at age 65. Survival of those who had never smoked was 7·9% at the end of observation and 67·1% (95% CI 58·9–75·3%) at age 65. Survival from lung cancer was 78·4% for smokers (93·7% (95% CI 91·0–96·4) at age 65) and 96·0% for those who had never smoked (99·2% (95% CI 97·7–100·0) at age 65). These differences were statistically significant (log rank test, $p < 0·01$). The same life table calculation for groups with different levels of exposure to asbestos (according to cumulative doses and to exposure class at start of work) showed no systematic relation to the probability of surviving from lung cancer.

As an example, we show this for the subgroups with up to, and more than 25 fibre-years. Neither for age (fig 2) nor for years since onset of exposure (fig 3) could an association be shown (for years from onset the lower exposure group had a significantly worse prognosis).

Discussion

The excess mortality from lung cancer in asbestos cement workers compared with the general popula-

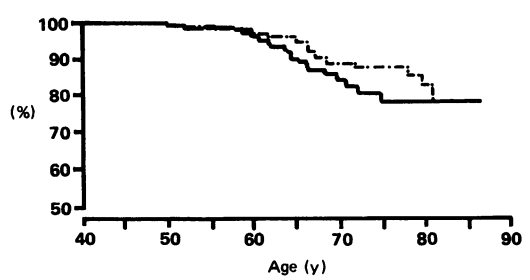

Figure 2 Life table analysis of lung cancer in smokers exposed to up to (full line) or to more than (dashed line) 25 fibres per ml-year, for years of age.

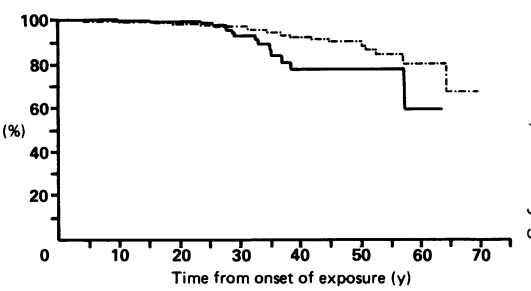

Figure 3 Life table analysis of lung cancer in smokers exposed to up to (full line) or to more than (dashed line) 25 fibres per ml-year, for years from onset of exposure.

Table 3 Crocidolite exposure of four cases of mesothelioma (verified by necropsy) and controls matched for sex, age, time of first employment, and duration of employment

	Exposure estimate				
	High	*High/medium*	*Medium*	*Negligible*	*Unknown*
Mesothelioma	xx	x	x		
Lung cancer (without asbestosis)		x	x	xx	
Non-malignant respiratory disease		x		xx	x
Cardiovascular disease	x		xx	x	
Controls alive in 1987			x	xxx	

tion of corresponding age and sex could be explained by the higher tobacco consumption of the asbestos cement workers (52% of smokers, compared with 39% expected in the general population from the microcensus for Upper Austria), a difference which was even more pronounced in workers older than 40 (below the age of 40 there were 50% of smokers among the asbestos cement workers compared with 47% expected from the microcensus whereas in workers older than 40 the values were 53% compared with only 25% expected). No additional influence of exposure to asbestos could be shown. Our study had a probability of more than 92% of detecting an SMR adjusted for smoking of 1·5 or greater. These results agreed with those from similar factories and industries processing mainly chrysotile without extreme exposures.[16-23]

A possible reason for underestimation of risk for lung cancer can be selection bias through a healthy worker effect,[24] but the total SMR (overall mortality) and the mortality from lung cancer of the low exposure group (table 2) indicates that it did not play an important part in our study. This might be because in the 1950s and 60s production increased so rapidly that all available workers were hired without selection for health.

Furthermore, to determine whether an underestimation of the risk of lung cancer in our cohort was because of the choice of reference population (general population of Upper Austria), we determined a national SMR (0·92) for lung cancer in men for the period 1970–1980 in the political district of Vöcklabruck. This did not differ significantly from the value for the province of Upper Austria (SMR 0·95); neither were significant differences found in women between the district and the province.[2] Hence, we have no reason to believe that the risk of lung cancer in members of the cohort from Vöcklabruck was over or underestimated by comparison with the general Upper Austrian population.

The results are compatible with a threshold for lung cancer of between 25 and 100 fibres per ml-year[25] and a non-genotoxic action of asbestos on the bronchial epithelium. For mesothelioma, however, asbestos could be a complete carcinogen with much lower fibre doses being sufficient to initiate the tumour. The lowest dose we registered was in a woman who was only exposed from 1958 to 1963 to about one fibre per ml-year. This woman was, however, exposed to crocidolite in the production of pipes (crocidolite exposure level classed as "medium"). In a nested case control study the four deaths from mesothelioma verified by necropsy were matched to 16 controls by sex and as close as possible by year of first employment, duration of employment, and year of birth. Exposure to crocidolite (disregarding duration) was classified without knowledge of the diagnosis from existing records. All verified cases of mesothelioma were found to have had medium to high exposure to crocidolite whereas controls alive in 1987 had negligible to medium exposures (table 3). The exposure to crocidolite of the four mesothelioma cases and the 16 matched controls were significantly different (Miettinen χ^2 test $= 2{\cdot}81$, df $= 1$, $p = 0{\cdot}047$ (one sided)). This result is compatible with other studies[16,26] and also with our own experience from a population based case-control study on 120 verified mesothelioma cases in Austria.[12,13] Our results confirm that the absolute risk of mesothelioma in asbestos cement production is low, but that there is a high relative risk probably associated with the use of crocidolite. According to latency we expect more cases of mesothelioma in our cohort and cannot exclude the occurrence of lung cancers induced by asbestos in the near future, because 148 surviving members of our cohort have had exposures of more than 50 fibres per ml-year. From present working conditions at much lower concentrations of chrysotile, however (the use of crocidolite in the production of pipes has been stopped completely), we do not expect any more occupational cancer in the asbestos cement industry.

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