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Abbreviations: OR, odds ratio; CI, confidence interval; GF, glass fibres; MF, mineral wool fibres; CF, ceramic fibres; MMVF, man made vitreous fibres; PAHs, polycyclic aromatic hydrocarbons; ISCO, International Standard Classification of Occupations (ILO); IARC, International Agency for Research on Cancer; UK, United Kingdom; SIR, standardised incidence ratios

ABSTRACT

Objectives: To investigate the contribution of occupational exposure to asbestos and man-made vitreous fibres (MMVF) to lung cancer in high-risk populations in Europe.

Methods: A multi-center case-control study was conducted in six Central and Eastern European countries and the UK, during the period 1998-2002. Comprehensive occupational and socio-demographic information was collected from 2205 newly diagnosed male lung cancer cases and 2305 frequency matched controls. Odds ratios (OR) of lung cancer were calculated after adjusting for other relevant occupational exposures and tobacco smoking.

Results: The OR for asbestos exposure was 0.92 (95% confidence interval (CI) 0.73-1.15) in Central and Eastern Europe and 1.85 (95%CI 1.07-3.21) in the UK. Similar OR were found for exposure to amphibole asbestos. The OR for MMVF exposure was 1.23 (95%CI 0.88-1.71) with no evidence of heterogeneity by country. No synergistic effect either between asbestos and MMVF or between any of them and smoking was found.

Conclusion: In this large community–based study occupational exposure to asbestos and MMVF does not appear to contribute to the lung cancer burden in men in Central and Eastern Europe. In contrast, in the UK we found an increased risk of lung cancer following exposure to asbestos. Differences in fibre type and circumstances of exposure may explain our results.

INTRODUCTION

Lung cancer is the most common tumour worldwide, apart from non-melanoma skin cancer, and remains one of the most fatal cancer types.[1] The causal relationship between cigarette smoking and lung cancer is well established and in most populations over 90% of all male patients develop their disease following tobacco smoking.[2][3][4] A change in smoking habits in recent decades has resulted in a decline of lung cancer mortality in men in most European countries including Central and Eastern Europe and the UK.[5] Nevertheless, Hungary and Poland are among the countries with the highest lung cancer mortality in the world.[6] Environmental and occupational lung carcinogens also contribute to the global burden of lung cancer, but the quantification of their role is complex.

Asbestos has been recognized as a human carcinogen for many years.[7][8] Consequently, mining and utilization of asbestos have markedly been reduced since 1990 and banned in most European countries. Even so, high levels of exposure to asbestos are still found in Central Europe and the former Soviet Union.[9] Due to their persistence in the environment, asbestos fibres also remain in many work sites as well as in neighbouring areas where asbestos was introduced in the past.[10][11] All commercial brands of asbestos, regardless of fibre type, are considered carcinogenic, but amphiboles (amosite, anthophyllite, crocidolite and tremolite) show greater carcinogenic potency than chrysotile.[12][13] Chrysotile is by far the most common type worldwide and the only asbestos type mined in Europe today, mainly in Russia. In the 1970s amphibole asbestos from South Africa and other countries, was used in over 50 countries, including UK, Italy, the Netherlands, France and the United States.[14]

Asbestos has to some extent been replaced by man-made vitreous fibres (MMVF) in the insulation and construction industry. Therefore, the carcinogenic role of MMVF in humans has been widely studied in recent years.[15][16][17] In 2002 glass wool, rock wool and slag wool were categorized by IARC in Group 3 (unclassifiable as carcinogens) and ceramic fibres were classified in Group 2B (possible human carcinogens) due to sufficient evidence in experimental animals.[18]

Both community-based and industry based studies can contribute to our understanding of occupational carcinogenesis, but both have limitations. Valid and precise exposure information is seldom available in community-based studies while industry-based studies frequently cannot take into account individual smoking patterns and the complete work histories of the subjects. In addition, the exposure assessment in industry-based studies is often based on job titles and employment time only, which limits the possibility to control for confounders.[19][20][21]

The current study provides an opportunity to overcome the above mentioned shortcomings. By analyzing data from a large, multicenter lung cancer case-control study in Europe, with extensive estimations of past occupational exposures and life-style characteristics, we aim to elucidate the extent to which lung cancer burden in men in this region is driven by asbestos and man-made vitreous fibres while controlling for potential confounders.

METHODS

This multicenter case-control study on lung cancer was conducted during the period 1998-2002 in seven European countries. Sixteen centers were included : Borsod, Heves, Szabolcs, Szolnok, Budapest (Hungary), Lodz, Warsaw (Poland), Banska Bystrica, Bratislava, Nitra (Slovakia), Brno, Olomouc, Prague (Czech Republic), Bucharest (Romania), Moscow (Russia), and Liverpool (UK). Approvals were obtained from local as well as from the IARC ethical review committees. The study population comprised all incident lung cancer cases (age <75 years) diagnosed in the participating centers. The response rate in the overall study was 84% among cases and 85% among controls. A small proportion of women was ever exposed to asbestos or synthetic fibres, 2.2% and 0.9%, and were not further analysed. Thus, 2205 male lung cancer cases and 2305 controls who were frequency matched to cases on age (±3 years) and sex were included in the analysis. Population controls were selected from the electronic register of residents in Warsaw and from the general practitioner registry in Liverpool. In the other centers, controls were selected among patients admitted to the same hospitals as the cases or from general hospitals serving the same population. Patients suffering from smoking-related conditions were not considered eligible. No single disease represented more than 10% of the diagnoses of controls. Detailed occupational history was obtained from each participant by a face-to-face interview conducted by a trained interviewer. The questionnaire covered lifestyle factors, smoking habits and all jobs held for more than one year. For 18 specific occupations or industries, specialized questionnaires were designed and used. Detailed information on study design and methodology has been presented previously.[22] Assessment of exposure to 70 agents including chrysotile and amphibole asbestos, glass fibres, mineral wool and ceramic fibres was conducted by a group of local trained experts who were blinded to the case-referent status of the study subjects. A variable “asbestos” was created encompassing all fibre types. In addition, experts specified if subjects were exposed to amphiboles and/or chrysotile when there was enough confidence regarding the specific circumstances of exposure. For synthetic fibres the categories were glass fibres (GF), mineral wool fibres (MF), or ceramic fibres (CF), whereupon we created the variable “MMVF” encompassing GF and MF. Based on data in the general and specialized (when applicable) questionnaires, the experts assessed each job held by a concerned subject and indicated their confidence in the presence of specific exposures expressed in the following categories: possible, probable or certain. Exposures were further assessed by frequency and intensity. Frequency of exposure was defined as the percentage of working time the person was assumed to be exposed to the agent, with the categories 1-5%, 5-30% and over 30% of the working time. Each year was considered to represent 2000 working hours. Regarding intensity of exposure the cut-points used for asbestos and MMVF were <0.1 fibres/ml for low, 0.1-1 fibres/ml for medium, and >1 fibres/ml for high exposure.

Statistical analyses were done using SAS and STATA packages. Odds ratios (OR) of lung cancer and 95% confidence interval (CI) were calculated by applying unconditional logistic regression modelling, adjusted for age, center, smoking (cumulative consumption), as well as for occupational exposures to silica, PAH, arsenic, cadmium and chromium. ORs for asbestos were then also adjusted for MMVF and vice versa.

Odds ratios were calculated for ever exposure, defined as exposure for at least one year during the working life to the agent of interest. To model level of exposure to asbestos or MMVF, two indices were built: (i) duration of exposure – and (ii) cumulative exposure – based on the total number of hours effectively exposed, multiplied by the intensity level assessed for each exposed year. The frequency and intensity values were based on assigning mid-interval weighting for each interval, while duration was expressed in years. Analysis were repeated with a 20 and a 30 year lag, in which all jobs held within 20 (or 30) years before year of interview were considered not exposed. ISCO-68 was used for the classification of occupations.[23]

RESULTS

There were 2205 male cases and 2305 controls recruited from the 7 participating countries. The mean age of the cases was 60.8 (s.d. 8.8) years and for the matched controls 60.6 (s.d. 8.5) years. Table 1 shows the distribution of the study group by country, age group and tobacco smoking. As expected, we found a marked difference between cases and controls with respect to smoking habits.

Among cases 14.4% were classified as ever exposed to asbestos and in the control group the prevalence of ever exposure to asbestos was 13.1%. For MMVF (glass and mineral wool), these proportions were 5.2% and 3.9%, respectively. The proportion of exposure to asbestos among controls was 8.1% in Poland, 8.3% in Romania, 9.4% Russia, 9.8% Hungary, 15.6 in Slovakia, 19.8 % in the Czech Republic and 37.1% in the UK. The proportion of ever exposed and highly exposed to asbestos and synthetic fibres was considerably higher in the UK, while high frequency of exposure was more often reported among subjects in Central and Eastern Europe (see table 2).

Lung cancer risk following ever exposure to asbestos differed between countries (p-value 0.01), UK showed an elevated OR of 1.85 (95%CI 1.07-3.21) and Romania 2.08 (95%CI 0.82-5.27) while ORs for the rest of the countries ranged between 0.64-1.02. When testing the heterogeneity in Central and Eastern Europe there was no significant difference between the countries (p-value 0.39). Thus, in the subsequent analysis on asbestos we decided to keep the countries from Central and Eastern Europe separated from the UK. With regard to MMVF, there was no significant difference between the countries, including the UK (p-value 0.18).

The prevalence of asbestos exposure among all subjects in Central and Eastern Europe was 11.4%, while in the UK the corresponding proportion was 46.8%. In Central and Eastern Europe 2.9% had been exposed to amphiboles (along with chrysotile), 5.2% to chrysotile but not amphiboles and 3.3% to unknown type of asbestos. In the UK 36.8% had experienced exposure to amphiboles (along with chrysotile), and 10% to chrysotile but not amphiboles. No subjects were assigned “unknown” fibre type in the UK. No elevated risk of lung cancer following exposure to asbestos was observed in Central and Eastern Europe (see table 3), nor was there evidence of a trend with intensity of exposure (p-value 0.46), cumulative exposure (p-value 0.60) or year of first exposure (p-value 0.35). Similarly, analyses based on a lag of 20 and 30 years or restricted to individuals with the highest confidence level, did not show any association.

In contrast, an increased risk of lung cancer was found in the UK (OR 1.85, 95%CI 1.07-3.21), in particular in workers exposed to amphiboles (OR 1.91, 95%CI 1.06-3.45). However, we found no trend of increased risk with rising cumulative exposure (p-value 0.95) and no trend with regard to latency (p-value 0.20). Analysis including only subjects with the highest confidence level or applying a lag of 20 and 30 years gave similar results.

There was no detectable modification of the effect of asbestos between smokers and non-smokers, in either Central and Eastern Europe (p-value 0.37) or in the UK (p-value 0.62).

Table 4 describes lung cancer risk following exposure to MMVF and ceramic fibres. Forty-nine percent of exposed subjects were exposed to only glass fibres, 24% to only mineral wool fibres and 27% to both glass and mineral wool fibres. Eight of the 115 exposed cases and 6 of the 89 exposed controls had experienced high levels of MMVF exposure. Twelve cases and 12 controls had been exposed to ceramic fibres, 12 of them (7 cases, 5 controls) to ceramic fibres but not MMVF and the remaining 12 (5 cases, 7 controls) to ceramic fibres and MMVF. None of the subjects was exposed to high levels of ceramic fibres.

The OR for lung cancer among men ever exposed to MMVF was 1.23 (95%CI 0.88-1.71). The OR for lung cancer following exposure to ceramic fibres but not MMVF was similar 1.25 (95%CI 0.33-4.74) but the number of exposed subjects was very small. With regard to intensity, latency, duration and cumulative exposure to MMVF, some ORs were elevated but there was no consistent pattern, the p-values for trend were 0.87, 0.72, 0.10 and 0.62 respectively. In none of the countries was there a significantly increased OR for MMVF exposure. Similarly, there was no significant modification of the effect of MMVF exposure in stratified analysis for smoking or occupational exposure to asbestos.

DISCUSSION

Asbestos and MMVF did not appear to exert an effect on lung cancer risk in our study population in Central and Eastern Europe, while in the UK we found an increased lung cancer risk following occupational exposure to asbestos. These results may be due to differences in fibre type or circumstances of exposure or could be due to a difference in degree of misclassification in the UK versus Central and Eastern Europe, i.e. if experts systematically overestimated asbestos exposure in the UK while experts in Central and Eastern Europe underestimated exposure. However, simulations assuming that the exposure assessment method has a sensitivity of 0.4 and a specificity of 0.9 in our study have suggested that differences in exposure misclassification are not likely to explain such a big difference in observed ORs: exposure prevalence has a strong effect on OR attenuation in the presence of misclassification. The lower prevalence of exposure to asbestos in Central and Eastern European countries as compared to UK might therefore explain a stronger attenuation in the OR in the former countries.[22]

The prevalence of occupational asbestos exposure in the present study, 11.4% in Central and Eastern, is comparable to what could be expected in a community based study in Europe but was lower than that of lung cancer patients classified as exposed to 5 or more fibre-years in a series of 297 lung cancer cases from Hungary (18.7%).[24]

The prevalence of occupational asbestos exposure among controls from the UK appears to be high (37.1%) compared to previous population or hospital based case-control studies in this country (11-26%).[9] Part of the explanation could be that the UK part of the study represents only the Liverpool area, which is a highly industrialized city including shipyards, and therefore may show a higher prevalence of exposure than the country overall. Exposure to asbestos clusters in certain occupations, e.g. workers at extraction facilities, asbestos-cement workers, insulation workers and ship-yard workers.[25] In our data few of the exposed men (0.2%) in Central and Eastern Europe had worked as dockers and freight handlers as compared to 13% in the UK. A majority of UK dockworkers reported handling asbestos in loose bags, sacks or boxes up to the early 1970's. Such exposure circumstances were also similar there for insulators. In Central and Eastern Europe exposed men were more often employed as motor-vehicle mechanics, where asbestos exposure may originate from the brakes and clutches and usually occurs at low levels. Other relevant differences in occupations held by exposed men in the UK and Central and Eastern Europe are listed in Table 5.

The fibre lung burden analysis of 25 Hungarian lung cancer cases belonging to the series mentioned above and compared to 66 cases from Germany showed comparable level of chrysotile fibres but lower level of amphibole fibres.[26] Our study showed similar results where 2.9 % of the subjects in Central and Eastern Europe had been exposed to amphibole fibres and chrysotile, 5.2% to only chrysotile and 3.3% to unknown type of asbestos.

Stayner *et al.* argue that the potency of amphiboles with respect to lung cancer is not different from that of chrysotile and that variations in risk depends more on fibre characteristics such as length and diameter than on type.[27] Others state that chrysotile is less carcinogenic.[12][13] Asbestos production in the former Soviet Union was estimated to 2 500 000 tons in 1986, which represented more than half of the world production at the time .[9] Most of the asbestos used in Central and Eastern Europe was chrysotile imported from Russia, of which there are few epidemiological studies available. The largest part of data on carcinogenicity concerning chrysotile is based on minerals from Canada, USA and South Africa.[28][29] A study on fibres obtained from the lung tissue of workers and residents in a Russian chrysotile industry area concluded that the mean size of chrysotile fibres in Russia was about the same as in Canada, but that mean concentration of tremolite in the Russian samples were at least one order of magnitude lower compared to Canada. Moreover, no amosite or crocidolite fibres could be detected in the Russian samples while low levels were detected in the Canadian samples.[30] However, experimental data have shown that Russian chrysotile has a mutagenic effect on human lymphocytes and that intratracheal injection into hamsters resulted in tumours in 63% of the animals, whereof 41% were

malignant lung tumours.[31][32] Pylev *et al.* have also shown that the carcinogenicity of chrysotile varies between deposits within Russia.[33]
Several epidemiological studies involving small portions of amphibole asbestos, sometimes only in terms of a tremolite contamination, have shown an increased risk of lung cancer.[21][34][35][36] Whereas studies based on amphibole-free exposure circumstances have not produced consistent evidence of an effect.[37] A few epidemiological studies have been conducted on lung-cancer risk among asbestos-exposed workers in Central and Eastern Europe. Smailyte *et al.* studied morbidity in two Lithuanian asbestos-cement producing plants using only chrysotile asbestos and showed no increased risk of lung cancer (SIR 0.90, 95%CI 0.70-1.30).[19] Likewise, a cohort from two asbestos cement plants in Poland using only chrysotile until 1985 failed to detect an increased risk of lung cancer in men (SMR 0.84, 95%CI 0.56-1.21).[20] In the present study the OR for lung cancer after exposure to chrysotile only was lower than the OR for combined exposure to chrysotile and amphiboles in the UK. (see table 3). Thus, our results are in line with previous studies. We did not detect an increased risk of lung cancer following exposure to amphiboles in Central and Eastern Europe. Possible reasons are low exposure levels, misclassification of exposure and different characteristics of fibres used in Central and Eastern Europe as compared to those used in the UK and elsewhere. It is also worth to consider that the asbestos consumption in the UK peaked early, in the 1960s and declined significantly thereafter.[38] In Central and Eastern Europe asbestos consumption peaked later, in the 1970s and 1980s, and still continue so lung cancer burden from asbestos in Central and Eastern Europe may not yet have reached a sufficient level to show in our study.[9]
Recall bias must be considered as cases suffering from a chronic disease may ponder the possible causes of their disease, and therefore be more likely to recall some past exposures than would healthy controls. Nevertheless, our study was investigating a wide range of occupational, environmental and lifestyle factors so the subjects could not reveal any particular hypothesis with regard to specific exposures. The subjects were also not confronted with questions about agents but were asked about job titles and job activities and first thereafter local experts designated corresponding exposures and levels.
Another concern is the possibility of misclassification of exposure. In our study the experts (e.g. industrial hygienists) were trained together but worked in respective country where they were familiar with materials and processes in the different time periods. A validation study on the occupational exposure assessment showed that inter-team agreement was poor with regard to asbestos and man-made fibres and this was partly due to true differences in technology and use of materials between the countries.[22] The same study suggested that misclassification was non-differential between cases and controls and that the likely effects of misclassification on risk estimates were an attenuation towards the null, in particular for agents with poor agreement and with low prevalence in the study population. High exposure prevalence (such as observed in the UK) makes the attenuation effect of non-differential exposure misclassification less severe. Thus, high prevalence of exposure alone makes it more likely to detect an association in the UK population and observe a higher OR, even if the true ORs would be comparable in both populations.
We did not find a carcinogenic effect of exposure to MMVF or for CF. Also, no synergistic effect, i.e. departure from a multiplicative joint effect, of simultaneous exposure to asbestos and MMVF could be shown. The number of exposed subjects in our study is limited (5.2% to MMVF, even lower to CF) and most exposed subjects are exposed to low levels, which reduces the power to detect an excess risk.

CONCLUSION

According to our data, asbestos does not contribute to the high burden of lung cancer in Central and Eastern Europe, but due to increasing trends in asbestos consumption, the full extent of lung cancer burden in Central and Eastern European countries may not yet be realized. In the UK men exposed to asbestos, in particular to amphiboles, experienced an increased risk of lung cancer. It is not clear to what extent this result is due to differences in

fibre type, exposure conditions or degree of exposure misclassification but the most plausible explanation appears to be a true difference in exposure prevalence.

With regard to man-made vitreous fibres and ceramic fibres, we did not observe an overall significant increased risk of lung cancer, but the power of our study to detect a small increased risk was low.

Table 1 Description of the study population, men only

Study population characteristic	Cases		Controls	
	n= 2205	%	n=2305	%
Country				
Czech Republic	235	10.7	323	14.0
Hungary	315	14.3	266	11.5
Poland	557	25.3	581	25.2
Romania	141	6.4	169	7.3
Russia	521	23.6	521	22.6
Slovakia	288	13.1	294	12.8
United Kingdom	148	6.7	151	6.6
Age (years)				
<45	94	4.3	119	5.2
45-54	455	20.6	510	22.1
55-64	829	37.6	777	33.7
65-74	762	34.6	799	34.7
> 75	65	3.0	100	4.3
Tobacco consumption				
Never smoker	48	2.2	534	23.2
Ex-smoker	494	22.4	842	36.5
Current smoker <20 pack-years	132	5.6	196	8.5
Current smoker 20-39 pack-years	758	34.4	450	19.3
Current smoker >40 pack-years	773	35.4	283	12.5

Table 2 Exposure to asbestos and MMVF among cases and controls in Central and Eastern Europe (CEE) and the United Kingdom (UK) respectively

Exposure status	Asbestos (All types)		Asbestos (Chrysotile only)		Man-made vitreous fibers (Glass and Mineral wool)		Ceramic fibers only*	
	Cases (%)	Controls (%)	Cases (%)	Controls (%)	Cases (%)	Controls (%)	Cases (%)	Controls (%)
Never exposed CEE†	**1824 (88.7)**	**1908 (88.6)**	**1824 (94.9)**	**1908 (94.1)**	**1954 (95.6)**	**2070 (96.6)**	**1954 (99.6)**	**2070 (99.8)**
Ever exposed CEE	**233 (11.3)**	**246 (11.4)**	**99 (5.1)**	**120 (5.9)**	**91 (4.4)**	**73 (3.4)**	**7 (0.4)**	**5 (0.2)**
Never exposed UK†	64 (43.2)	95 (62.9)	64 (78.0)	95 (88.8)	124 (83.8)	134 (89.3)	124 (100)	134 (100)
Ever exposed UK	84 (56.8)	56 (37.1)	18 (22.0)	12 (11.2)	24 (16.2)	16 (10.7)	0 (0.0)	0 (0.0)
Intensity of exposure CEE								
Low	**171 (73.4)**	**194 (78.9)**	**76 (76.8)**	**98 (81.7)**	**60 (65.9)**	**54 (74.0)**	**5 (71.4)**	**3 (60.0)**
Medium	**50 (21.5)**	**42 (17.1)**	**18 (18.2)**	**15 (12.5)**	**26 (28.6)**	**15 (20.5)**	**2 (28.6)**	**2 (40.0)**
High	**12 (5.2)**	**10 (4.1)**	**5 (5.1)**	**7 (5.8)**	**5 (5.5)**	**4 (5.5)**		
Intensity of exposure UK								
Low	49 (58.3)	33 (58.9)	12 (66.7)	10 (83.3)	13 (54.2)	7 (43.8)	0 (0.0)	0 (0.0)
Medium	22 (26.2)	15 (26.8)	4 (22.2)	1 (8.3)	8 (33.3)	7 (43.8)	0 (0.0)	0 (0.0)
High	13 (15.5)	8 (14.3)	2 (11.1)	1 (8.3)	3 (12.5)	2 (12.5)	0 (0.0)	0 (0.0)
Frequency of exposure CEE								
1-5%	**122 (48.1)**	**124 (50.4)**	**58 (58.6)**	**64 (53.3)**	**51 (56.0)**	**42 (57.5)**	**1 (14.3)**	**1 (20.0)**
5-30%	**73 (31.3)**	**74 (30.1)**	**26 (26.3)**	**31 (25.8)**	**26 (28.6)**	**20 (27.4)**	**3 (42.9)**	**3 (60.0)**
>30%	**48 (20.6)**	**48 (19.5)**	**15 (15.2)**	**25 (20.8)**	**14 (15.4)**	**11 (15.1)**	**3 (42.9)**	**1 (20.0)**
Frequency of exposure UK								
1-5%	45 (53.6)	41 (73.2)	9 (50.0)	10 (83.3)	12 (50.0)	8 (50.0)	0 (0.0)	0 (0.0)
5-30%	33 (39.3)	12 (21.4)	7 (38.9)	2 (16.7)	10 (41.7)	7 (43.8)	0 (0.0)	0 (0.0)
>30%	6 (7.1)	3 (5.4)	2 (11.1)	0 (0.0)	2 (8.3)	1 (6.3)	0 (0.0)	0 (0.0)
Confidence in assessment CEE								
Possible	**30 (12.9)**	**22 (8.9)**	**11 (11.1)**	**15 (12.5)**	**8 (8.8)**	**10 (13.7)**	0 (0.0)	0 (0.0)
Probable	**80 (34.3)**	**98 (39.8)**	**37 (37.4)**	**49 (40.8)**	**29 (31.9)**	**23 (31.5)**	**1 (14.3)**	**0 (0.0)**
Certain	**123 (52.8)**	**125 (50.8)**	**50 (50.5)**	**56 (46.7)**	**54 (59.3)**	**40 (54.8)**	**6 (85.7)**	**5 (100)**
Confidence in assessment UK								
Possible	0 (0.0)	2 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Probable	24 (28.6)	19 (33.9)	5 (27.8)	4 (33.3)	5 (20.8)	3 (18.8)	0 (0.0)	0 (0.0)
Certain	60 (71.4)	35 (62.5)	13 (72.2)	7 (58.3)	19 (79.2)	13 (81.3)	0 (0.0)	0 (0.0)

* Excludes subjects exposed to mixed synthetic fibres

† Never exposed to any type of asbestos or synthetic fibers, respectively

Table 3 Asbestos exposure and lung cancer risk in Central and Eastern Europe and the UK respectively

		Central and Eastern Europe			UK		
Type of exposure	Exposure Category	Cases/ Controls	OR*	95% CI	Cases/ Controls	OR*	95% CI
Exposure to asbestos	Never	1824/1908	1.00	(reference)	64/95	1.00	(reference)
	Ever	233/246	0.92	0.73-1.15	84/56	1.85	1.07-3.21
Exposure to amphiboles		58/63	0.93	0.60-1.45	66/44	1.91	1.06-3.45
Exposure to chrysotile		99/120†	0.77	0.56-1.05	18/12	1.53	0.61-3.86
Asbestos intensity	Low	171/194	0.88	0.68-1.13	49/33	2.01	1.08-3.76
	Medium	50/42	1.08	0.67-1.73	22/15	1.66	0.71-3.85
	High	12/10	0.95	0.36-2.47	13/8	1.53	0.51-4.54
Test for linear trend, p-value			*0.46*			*0.62*	
Cumulative asbestos	<41.99	64/62	1.05	0.70-1.59	18/14	1.66	0.72-3.85
exposure (fibres/ml-hrs)	<125.98	55/63	0.87	0.57-1.31	19/15	2.03	0.87-4.76
	<699.95	49/68	0.70	0.45-1.09	20/7	2.95	1.05-8.26
	>=699.95	65/53	1.07	0.70-1.63	27/20	1.49	0.67-3.33
Test for linear trend, p-value			*0.60*			*0.95*	
Year of first asbestos	-1960	99/89	1.05	0.74-1.50	57/41	1.77	0.97-3.24
exposure	1961-1970	74/86	0.90	0.62-1.31	18/13	1.48	0.56-3.91
	1971-1980	36/45	0.72	0.44-1.18	7/2	4.51	0.72-28.24
	1981-1990	16/19	0.70	0.33-1.47	2/0		
	1991-	8/7	1.47	0.47-4.60	0/0		
Test for linear trend, p-value			*0.35*			*0.20*	

*Odds ratio adjusted for center, age, tobacco smoking, silica, PAHs, MMVF, arsenic, chromium and cadmium
† Excludes subjects exposed to unknown type of asbestos or combined exposure to amphiboles

Table 4 MMVF exposure and lung cancer risk in Central/Eastern Europe and the U.K.

		Central/Eastern Europe and the UK		
Type of exposure	Exposure Category	Cases/ Controls	OR*	95% CI
Exposure to MMVF (GF, MF)	Never†	2078/2204	1.00	
	Ever	115/89	1.23	0.88-1.71
Exposure to ceramic fibres only‡		7/5	1.25	0.33-4.74
Exposure intensity to MMVF	Low	73/61	1.23	0.82-1.84
	Medium	34/22	1.28	0.70-2.34
	High	8/6	1.02	0.31-3.33
Test for linear trend, p-value			*0.87*	
Duration of exposure to MMVF	<2 years	7/2	3.81	0.59-24.52
(years)	2-5 years	29/24	1.02	0.55-1.87
	6-10 years	17/9	1.80	0.72-4.52
	11-20 years	26/16	2.02	0.98-4.15
	21-30 years	21/20	0.93	0.47-1.84
	30+ years	15/18	0.77	0.35-1.68
Test for linear trend, p-value			*0.10*	
Cumulative exposure to MMVF	<56.99	34/23	1.60	0.85-3.00
(fibres/ml-hrs)	<180.99	25/25	0.97	0.52-1.80
	<839.97	27/23	1.17	0.63-2.19
	>=839.97	29/18	1.26	0.64-2.47
Test for linear trend, p-value			*0.62*	
Year of first exposure to MMVF	-1960	45/31	1.36	0.80-2.31
	1961-1970	30/29	1.09	0.60-1.97
	1971-1980	25/21	1.05	0.54-2.03
	1981-1990	11/6	1.64	0.54-4.96
	1991-	4/2	1.57	0.25-9.88
Test for linear trend, p-value			*0.72*	

*Odds ratio adjusted for center, age, tobacco smoking, silica, PAHs, asbestos, arsenic, chromium and cadmium
† Never exposed to any kind of synthetic fibres
‡ Excludes 12 subjects exposed to mixed synthetic fibres

Table 5 Proportion of exposed men ever employed in jobs entailing exposure to asbestos in the U.K. and the Central/Eastern European countries respectively

ISCO-68	Occupation	UK (%)	Central/Eastern Europe (%)
581	Fire-fighters	6	0.4
700	Production supervisors and general foremen	9	3
839	Blacksmiths, toolmakers and machine-tool operators not elsewhere classified	1	4
843	Motor-vehicle mechanics	9	22
871	Plumbers and pipe fitters	4	7
872	Welders and flame-cutters	5	6
943	Non-metallic mineral product maker (asbestos cement)	0.7	2
951	Bricklayers, stonemasons and tile setters	0.7	4
953	Roofers	5	2
954	Carpenters, joiners and parquetry workers	6	0.6
956	Insulators	3	1
959	Construction workers not elsewhere classified	2	5
971	Dockers and freight handlers	13	0.2
985	Motor-vehicle drivers	4	9

COMPETING INTERESTS STATEMENT

All authors declare that they have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated.

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