

## Occupational exposure and lung cancer risk in a coastal area of Northeastern Italy

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**Summary.** A case-control study of lung cancer and occupational exposure was conducted in a coastal area of Northeastern Italy where metallurgical and mechanical industries, docks and shipyards are located. Cases comprised 756 men who died of primary lung cancer in a 5-year period. Controls comprised 756 male subjects dying from other causes during the same period. Occupational exposures to lung carcinogens were assessed according to a job title-based approach, using two separate lists of industries/occupations recognized as being causally associated (list A) or suspected of being causally associated (list B) with lung cancer in humans. Exposure to asbestos was classified as absent, possible, or definite. After adjustment for cigarette smoking and place of residence, a significant association was found between lung cancer and occupations in both list A [relative risk (RR) = 2.25, 95% confidence interval (CI) = 1.68–3.03] and list B (RR = 1.33, 95% CI = 1.03–1.71). A significant excess risk was found for workers with definite exposure to asbestos as compared to those with no exposure to lung carcinogens (RR = 1.98, 95% CI = 1.42–2.75). Among occupations with recognized exposure to lung carcinogens other than asbestos, a significant excess risk for lung cancer was observed in iron and metalware workers. In occupational groups with definite exposure to asbestos, elevated risk estimates were found for shipyard workers, dockworkers, carpenters, and electricians. The combined effect of smoking and asbestos was found to be compatible with that expected under a multiplicative model. The overall population-attributable risk (ARp) for cigarette smoking was found to be 87.5%. The ARp estimate for occupations in list A was 16.0%. The estimate increased to 25.3% (95% CI = 16.2–34.4) when occupations in list B were included. The ARp estimate for possible or definite exposure to asbestos was 20.0% (95% CI = 11.5–28.5). With regard to the histologic types of lung cancer, significant associations were found between definite exposure to asbestos and squa-

mous cell carcinoma (RR = 2.00, 95% CI = 1.28–3.11), small cell carcinoma (RR = 2.11, 95% CI = 1.31–3.39), and adenocarcinoma (RR = 2.16, 95% CI = 1.32–3.53).

**Key words:** Asbestos – Case-control study – Histology – Lung carcinogens – Smoking

### Introduction

Several studies published over the last decade have given estimates of the proportion of lung cancers attributable to occupational exposure [10, 13, 15, 21, 24]. In 1981 Doll and Peto [8] estimated that about 15% of all lung cancers occurring in the male population of the United States could be due to exposure to occupational carcinogens. This overall estimate is consistent with those reported in a review of five case-control studies of lung cancer carried out in the United States [23], where the percentage of lung cancers attributable to occupational exposure was found to range between 3% and 17%. Reviewing 16 American and European epidemiologic studies in which the confounding effect of smoking was controlled for, Simonato et al. [21] observed that the proportion of lung cancers due to occupational exposure varied from 0% to 40%. The wide variability of attributable risk estimates has been ascribed to differences in the study design and in the degree of industrialization in the geographic areas where the studies were conducted. The present paper reports the results of a case-control study designed to assess the risk of lung cancer due to occupation in a coastal area of Northeastern Italy (Trieste) where small and medium-size metallurgical and mechanical industries, docks, and shipyards are located. The predominance of shipbuilding and ship repairing in this geographic area suggests that several occupational groups have been exposed to asbestos, especially in the past. The province of Trieste has a higher lung cancer mortality than Italy as a whole. In particular, the crude

mortality rate for lung cancer among male residents is 150 per 10<sup>5</sup> person-years (average for the years 1980–1983) and the standardized mortality ratio is 141 (95% confidence interval: 131–151) (standard: age-specific rates for the Italian population).

## Materials and methods

The study is based on the autopsy records of 938 men who died of primary lung cancer (International Classification of Diseases, ninth revision, code 162) in the province of Trieste during a 5-year period (1979–1981, 1985–1986). The study was performed in two different periods because of administrative problems related to the availability of personnel and funds. Information on the deceased subjects, autopsy reports, and histologic types of lung cancer [27] were obtained from the records of the local Cancer Registry, which represents the reference center for all cancers occurring in the province of Trieste. For 182 cases information on next-of-kin was missing or inadequate, so that interviews could not be carried out.

An exploratory data analysis did not evince any significant difference in the distribution of age and histologic types of lung cancer between the initial case sample and the remaining 756 cases (80.6%). For each subject of the final case sample, one male control of similar age ( $\pm 2$  years), deceased within the same 6-month period, was randomly selected from the registry of the Department of Pathology, in which the autopsy records of 70% of all subjects deceased in the province of Trieste during the last two decades are reported. The controls had died of causes other than chronic lung diseases or cancers of the upper aerodigestive tract, urinary tract, pancreas, liver, and gastrointestinal system. The diagnoses of death for the controls were ischemic heart disease (29.9%), cerebrovascular disease (18.9%), other cardiovascular disease (16.1%), gastrointestinal disease (18.8%), respiratory disease (9.1%), urologic disease (3.2%), infectious disease (2.8%), other malignant neoplasms (1%), metabolic disease (0.1%), and traumas (0.1%).

Interviews of the next-of-kin were carried out by telephone for both cases and controls after at least 1 year from the death of the subjects. The interviewers were trained physicians who were not aware of the case/control status of the study subject. The next-of-kin were informed that the aim of the interview was to collect material for medical research. During the interview, the cause of the subject's death was never mentioned. By means of a standardized questionnaire, information was collected about smoking habit, place of residence, and occupational history with particular reference to job titles, industries, place of work and/or employer's name, and duration of employment for each job title. The main source of information on occupational histories was the subject's employment card, which is carefully kept by families in Trieste because of a traditional attention to social security problems. No next-of-kin refused the interview for either cases or controls.

Smoking habit was quantified as average number of cigarettes smoked per day, dividing the lifetime cigarette consumption by the mean duration of smoking among the present and former smokers in the study. For a few cigar or pipe smokers ( $n = 15$ ), 1 g of tobacco was considered to be equivalent to one cigarette.

Place of residence was classified as urban or rural. The province of Trieste was divided into three areas: (1) urban area A (population density: 5421 inhabitants/km<sup>2</sup>) with high levels of air pollution as evidenced by a previous survey [16]; in this area the main sources of air pollutants are road traffic and emissions from a shipyard, an iron foundry, and a waste incinerator; (2) urban area B (population density: 4879 inhabitants/km<sup>2</sup>) with moderate levels of ambient air pollution, mainly due to motor vehicle emissions; (3) rural area C, which consisted of the rural districts surrounding the city (population density: 192 inhabitants/km<sup>2</sup>), where low-level air pollution was observed [16].

Work histories were assessed in terms of occupational exposure to lung carcinogens by an occupational physician (M.B.) and a team of industrial hygienists who were not informed of the case/control status of the subjects. Job titles and occupations were classified according to two separate lists, A and B, as defined in a review based on the IARC Monographs Programme [20]. List A includes industries/occupations recognized as being causally associated with lung cancer in humans. List B contains occupations suspected of being related to an increased lung cancer risk. Asbestos exposure was classified as absent, possible, or definite on the basis of an exhaustive knowledge of both the use of asbestos in the local industries and the links between job titles and asbestos exposure in the industries at risk. Information on asbestos exposure was also obtained by consulting the historical archives of some industries and by contacting employers and retired workers who had been engaged in specific jobs at risk. The following occupations were considered to be associated with definite exposure to asbestos: asbestos production workers, shipyard and dockyard workers, ship engine maintenance workers, smelting/foundry workers, insulators and pipe coverers working in the construction industry, and carpenters and electricians employed in shipbuilding-related industries. Occupational groups with possible exposure to asbestos included: boilermakers, carpenters, electricians, plumbers, pipe-

**Table 1.** Distribution of cases and controls by age, cigarette smoking, occupations causally associated (list A) or suspected of being causally associated (list B) with lung cancer, and place of residence. The distribution of the histologic types of lung cancer among the cases is also reported

	Cases		Controls	
	No.	%	No.	%
<b>Age group (years)</b>				
40–54	61	8.1	55	7.3
55–59	70	9.3	72	9.5
60–64	78	10.3	74	9.8
65–69	131	17.3	110	14.6
70–74	169	22.4	156	20.6
75–79	147	19.4	160	21.2
≥80	100	13.2	129	17.1
<b>Smoking (cigarettes/day)</b>				
0 (Nonsmokers)	22	2.9	188	24.9
1–19	214	28.3	278	36.8
20–39	305	40.3	200	26.4
≥40	215	28.4	90	11.9
<b>Occupational exposure to lung carcinogens</b>				
None	255	33.7	352	46.6
List B	283	37.4	279	36.9
List A	218	28.8	125	16.5
<b>Place of residence</b>				
Urban area A	260	34.4	221	29.2
Urban area B	444	58.7	450	59.5
Rural area C	52	6.9	85	11.2
<b>Histologic type of lung cancer</b>				
Squamous cell carcinoma	268	35.4	–	–
Small cell carcinoma	218	28.8	–	–
Large cell carcinoma	90	11.9	–	–
Adenocarcinoma	158	20.9	–	–
Other histologic types	22	2.9	–	–

fitters, and steamfitters employed in industries other than shipbuilding and ship repairing; electrochemical workers; machinists and machine operators; mariners; mechanics; naval officers; railway workers; and textile workers.

Data analysis was performed by unconditional logistic regression technique [7], and odds ratios were obtained by taking the antilog of the estimates of the logistic regression coefficients [ $\exp(b_1)$ ]. Odds ratios, adjusted for smoking (four levels: non-smokers, 1–19, 20–39,  $\geq 40$  cigarettes/day) and place of residence (three residential areas), were used as estimators of the relative risk (RR), assuming the subjects not included in list A or B as the reference category. Ninety-five percent confidence intervals (95% CI) were calculated by using the estimated coefficients and the standard errors from the logistic regression. The goodness of fit of the logistic models was assessed by the log likelihood statistic (G) [3]. The significance of additional parameters in the model was tested by the likelihood ratio statistic. The attributable risk in the population (ARp in %) was calculated as  $\Sigma (ARe \cdot Pec)$ , where Pec is the proportion of exposed cases in each exposure category and ARe is the attributable risk among the exposed. ARe was calculated as  $(RR_i - 1)/RR_i$ , where  $RR_i$  is the adjusted odds ratio in the  $i$ th exposure category from the logistic regression analysis. The 95% CI estimates for ARp were obtained by computing the standard error with the formula given by Walter [25].

## Results

Table 1 reports the characteristics of cases and controls and the distribution of the histologic types of lung cancer among the cases [27]. Preliminary data analysis showed no difference in the age distribution of cases and controls within each category of smoking, occupational exposure, and place of residence. The proportion of cases and controls included in list B was 37.4% and 36.9%, respectively. The corresponding figures for occupations in list A were 28.8% and 16.5%. Definite exposure to asbestos was observed in 19.4% of cases ( $n = 147$ ) and 12.4% of controls ( $n = 94$ ). Among the 343 subjects included in

list A, 70.3% showed definite asbestos exposure, whereas the remaining 29.7% had job titles related to exposure to other occupational lung carcinogens (mainly polycyclic aromatic hydrocarbons).

Table 2 gives the distribution of cases and controls by smoking and occupational exposure. After adjustment for smoking and place of residence, a significant association was found between lung cancer and occupations in list A ( $RR = 2.25$ , 95% CI = 1.68–3.03) and in list B ( $RR = 1.33$ , 95% CI = 1.03–1.71). The ARe for the subjects included in list A occupations was 55.5%. The corresponding figure for ARp was found to be 16.0%. Combining lists A and B increased the ARp estimate to 25.3% (95% CI = 16.2%–34.4%). The logistic regression model with three independent variables (smoking, occupational exposure, and place of residence) was satisfactory, as indicated by the goodness of fit chi-square statistic [ $G = 13.2$ , 28 degrees of freedom ( $df$ ),  $P = 0.992$ ]. Since the independent variables were not correlated, the adjusted relative risks were only slightly smaller than the crude estimates. Among occupations with recognized exposure to lung carcinogens other than asbestos, increased relative risks were observed for gas workers, asphalt workers, and iron and metalware workers (Table 3), but only for this latter occupational group was the excess risk for lung cancer significant ( $RR = 3.25$ , 95% CI = 1.39–7.60).

Table 4 reports the distribution of cases and controls by smoking and asbestos exposure. Definite exposure to asbestos was graded according to the duration of employment (1–5, 6–40, or  $> 40$  years). A significant excess risk was found for workers with definite exposure to asbestos when compared to those with no exposure to lung carcinogens ( $RR = 1.98$ , 95% CI = 1.42–2.75). The risk for lung cancer increased with increasing asbestos exposure and a relative risk of 2.31 (95% CI = 1.23–4.32)

**Table 2.** Distribution of cases and controls by cigarette smoking and occupations causally associated (list A) or suspected of being causally associated (list B) with lung cancer. Crude and adjusted relative risks (RR), attributable risks among the exposed (ARe), attributable risks in the population (ARp), and 95% confidence interval (95% CI) are reported

Smoking (cigarettes/day)	Occupational exposure to lung carcinogens	None	List B	List A	Lists A and B	RR <sub>2</sub>	ARp (%)
0	Cases	10	6	6	12	1.0	0
	Controls	103	61	24	85		
1–19	Cases	66	86	62	148	6.15	23.7
	Controls	122	108	48	156		
20–39	Cases	99	109	97	206	12.0	36.9
	Controls	88	73	39	112		
$\geq 40$	Cases	80	82	53	135	19.3	26.9
	Controls	39	37	14	51		
RR <sub>0</sub>		1.0	1.40	2.41	1.71		
RR <sub>1</sub>		1.0	1.33	2.25	1.62		
95% CI	Lower limit	–	1.03	1.68	1.29		
	Upper limit	–	1.71	3.03	2.03		
ARe (%)		0	24.8	55.5	38.3		
ARp (%)		0	9.29	16.0	25.3		
95% CI		–	–	–	16.2–34.4		

RR<sub>0</sub>, With reference to nonexposed, crude estimate

RR<sub>1</sub>, With reference to nonexposed, adjusted for smoking and place of residence

RR<sub>2</sub>, With reference to nonsmokers, adjusted for occupational exposure and place of residence

**Table 3.** Distribution of cases and controls according to selected occupations or job titles with definite exposure to lung carcinogens other than asbestos. Relative risks (RR) and 95% confidence intervals (95% CI) are reported. Reference category: subjects unexposed to lung carcinogens

Occupation/job title	Cases (n)	Controls (n)	RR <sup>a</sup>	95% CI
Mining and quarrying work	8	11	0.80	0.30–2.07
Iron and metalware work	21	9	3.25	1.39–7.60
Gas workers	7	6	1.43	0.45–4.47
Asphalt workers	7	3	2.27	0.50–10.3

<sup>a</sup> Adjusted for smoking (0, 1–19, 20–39, ≥40 cigarettes/day)

**Table 4.** Distribution of cases and controls by cigarette smoking and asbestos exposure. Crude and adjusted relative risks (RR), attributable risks among the exposed (AR<sub>e</sub>), attributable risks in the population (AR<sub>p</sub>), and 95% confidence interval (95% CI) are reported

Smoking (cigarettes/day)	Asbestos exposure							RR <sub>2</sub>	AR <sub>p</sub> (%)	
	None	Possible	Definite (years)			Total	Definite and possible			
			1–5	6–40	>40					
0	Cases	10	4	1	1	2	4	8	1.0	0
	Controls	103	26	5	10	4	19	45		
1–19	Cases	66	41	13	20	7	40	81	5.48	23.3
	Controls	122	46	18	17	2	37	83		
20–39	Cases	99	38	12	33	18	63	101	10.4	35.0
	Controls	88	30	2	14	11	27	57		
≥40	Cases	80	31	10	21	9	40	71	18.5	27.7
	Controls	39	13	3	6	2	11	24		
RR <sub>0</sub>		1.0	1.37	1.77	2.20	2.62	2.16	1.72		
RR <sub>1</sub>		1.0	1.36	1.79	1.95	2.31	1.98	1.65		
95% CI	Lower limit	–	0.98	1.02	1.27	1.23	1.42	1.26		
	Upper limit	–	1.90	3.14	2.99	4.32	2.75	2.15		
AR <sub>e</sub> (%)		0	26.5	44.1	48.7	56.7	49.5	39.4		
AR <sub>p</sub> (%)		0	5.85	3.08	7.08	3.96	14.1	20.0		
95% CI		–	–	–	–	–	–	11.5–28.5		

RR<sub>0</sub>, With reference to nonexposed, crude estimate

RR<sub>1</sub>, With reference to nonexposed, adjusted for smoking and place of residence

RR<sub>2</sub>, With reference to nonsmokers, adjusted for asbestos exposure and place of residence

**Table 5.** Stratified analysis to assess the combined effect of cigarette smoking (S) and asbestos exposure (A). Relative risks (RR) and percent of excess risk due to interaction (PERDI) are reported

Asbestos exposure	Cases (n)	Controls (n)	RR	PERDI <sup>b</sup> (%)
None <sup>a</sup>				
Nonsmokers	10	103	1.0	–
1–19 cigarettes/day	66	122	5.57	–
20–39 cigarettes/day	99	88	11.6	–
≥40 cigarettes/day	80	39	21.1	–
Possible				
Nonsmokers	4	26	1.58	–
1–19 cigarettes/day	41	46	9.18	3.70
20–39 cigarettes/day	38	30	13.0	7.35
≥40 cigarettes/day	31	13	24.6	12.1
Definite				
Nonsmokers	4	19	2.17	–
1–19 cigarettes/day	40	37	11.1	43.3
20–39 cigarettes/day	63	27	24.0	48.9
≥40 cigarettes/day	40	11	37.4	41.6

<sup>a</sup> No exposure to lung carcinogens

<sup>b</sup> PERDI =  $[(RR_{SA} - RR_S - RR_A + 1) / ((RR_{SA} - 1))] \cdot 100$

was observed for the subjects exposed for more than 40 years. The trend in log relative risk with increasing asbestos exposure appeared to be linear [test for departure from linearity ( $\Delta G$ ) = 0.51, 3 *df*, *P* = 0.92]. The AR<sub>p</sub> for definite asbestos exposure was 14.1%. The overall AR<sub>p</sub> for possible or definite exposures to asbestos was estimated to be 20.0% (95% CI = 11.5%–28.5%). The AR<sub>p</sub> for cigarette smoking was found to be 86.0%. Assuming the non-occupationally exposed nonsmokers as the reference category, the combined AR<sub>p</sub> for asbestos and/or smoking was estimated to be 89.4%.

A stratified analysis (Table 5) pointed out that the effect of the joint exposure to smoking and asbestos was near multiplicative according to the classification proposed by Saracci [19]. Among the subjects with definite asbestos exposure, the percentage of the excess risk over simple additivity varied from 41.6% to 48.9%. A very high relative risk was observed in heavy smokers (≥40 cigarettes/day) with definite exposure to asbestos (RR = 37.4).

Table 6 shows the relative risks for lung cancer in some occupational groups with definite exposure to asbestos. A significant excess risk was found for ship-

**Table 6.** Distribution of cases and controls according to job titles with definite asbestos exposure. Relative risks (RR) and 95% confidence intervals (95% CI) are reported. Reference category: subjects unexposed to lung carcinogens

Job title	Cases (n)	Controls (n)	RR <sup>a</sup>	95% CI
Shipyards workers	74	42	2.40	1.54–3.74
Ship engine maintenance workers	4	1	5.75	0.62–53.4
Dockworkers	32	21	2.13	1.13–4.04
Smelting/foundry workers	9	4	3.69	0.99–13.7
Carpenters	15	1	22.0	2.64–184
Construction workers	2	1	2.97	0.26–34.2
Electricians	9	3	4.23	1.03–17.4

<sup>a</sup> Adjusted for smoking (0, 1–19, 20–39, ≥40 cigarettes/day)

**Table 7.** Relative risks<sup>a</sup> (95% confidence intervals) for histologic types of lung cancer according to asbestos exposure. Reference category: subjects unexposed to lung carcinogens

Histology	Cases (n)	Asbestos exposure		
		None	Possible	Definite
Squamous cell carcinoma	182	1.0	1.52	2.00
		–	(0.96–2.39)	(1.28–3.11)
Small cell carcinoma	146	1.0	1.54	2.11
		–	(0.95–2.50)	(1.31–3.39)
Large cell carcinoma	56	1.0	1.01	1.38
		–	(0.48–2.14)	(0.67–2.85)
Adenocarcinoma	119	1.0	1.15	2.16
		–	(0.66–1.98)	(1.32–3.53)

<sup>a</sup> Adjusted for smoking (0, 1–19, 20–39, ≥40 cigarettes/day) and place of residence (three residential areas)

yard workers, dockworkers, carpenters, and electricians. However, for the latter two categories the 95% CI estimates were wide owing to the small number of subjects. Among dockworkers and shipyard workers, smoking-adjusted RR was more elevated for those who entered the job in the years 1930–44 (RR = 2.71, 95% CI = 1.46–5.02) than for those who began to work before 1930 (RR = 2.13, 95% CI = 1.26–3.61) or after 1944 (RR = 2.14, 95% CI = 0.98–4.67).

With regard to the histologic types of lung cancer (Table 7), significant associations were found between definite exposure to asbestos and squamous cell carcinoma (RR = 2.00), small cell carcinoma (RR = 2.11), and adenocarcinoma (RR = 2.16). Cigarette smoking was strongly associated with all histologic types of lung cancer. After adjustment for asbestos exposure and place of residence, in the heavy smoker category the RR estimate was 25.5 for squamous cell carcinoma, 20.5 for small cell carcinoma, and 48.1 for large cell carcinoma, while the weakest association was found for adenocarcinoma (RR = 10.2).

## Discussion

This case-control study showed a significant excess risk of lung cancer for subjects who had been engaged in selected jobs or activities included in two lists of occupations with recognized (list A) or suspected (list B) carcinogenic exposures for the human lung. The point estimates for the population-attributable risk were 16.0% for occupations in list A and 25.3% for occupations in

list A or B. These estimates are higher than those observed in five industrialized areas of the United States [23], while they are consistent with those reported in some European studies [21]. In this study, occupational exposure to lung carcinogens has been assessed on the basis of a job title approach. It has been noted that studies using job-exposure matrices give higher risk estimates [21, 24], probably because exposure misclassifications occur less frequently. Nevertheless, the ARp estimates from this study are not very dissimilar from those reported in studies based on job-exposure matrices. It is likely that both the good quality information from the employment cards of the deceased subjects and the specific knowledge of the work environment in the industries of the study area have contributed to minimize errors in the exposure ascertainment. However, differences in the methods of exposure classification may explain only partially the wide variability of the ARp estimates reported in various studies (0%–40%). As pointed out by Simonato et al. [21], the different levels of exposure in the geographic areas where the studies were conducted can account for the major part of the interarea variations in the ARp estimates.

The results of this investigation confirm the prominent role of cigarette smoking in the etiology of lung cancer. The RR and ARp estimates for smoking are consistent with those reported in previous studies [6, 10, 15]. Nevertheless, in the present study an underestimation of the effect of smoking on lung cancer might arise from the inclusion in the control series of individuals who died of smoking-related diseases. When the 306 controls who died of ischemic heart disease (ICD 410–414), stomach

diseases (ICD 531–535), and some respiratory diseases (ICD 485–519) were excluded from the analysis, the RR estimates for smoking showed an increase only for the highest smoking level ( $\geq 40$  cigarettes/day), for which the RR estimate changed from 19.3 to 25.3. No substantial change in the RR estimates for occupational exposure was observed. It is worth noting that smoking had not a strong confounding effect on the association between lung cancer and occupation, as the crude RR estimates for occupational exposure reduced very little after adjustment for smoking (5%–10%).

Among occupations in list A with exposure to non-asbestos carcinogenic substances, this study pointed out an excess risk of lung cancer in iron and metal workers. This occupational group included forge workers, mould makers, ferrous foundry workers, and coke workers of a large iron foundry. This finding is consistent with the results reported by other authors [2], who hypothesized that polycyclic aromatic hydrocarbons, and perhaps chromium and nickel compounds, could be responsible for the increased risk of lung cancer among iron and steel manufacturing workers.

In this study, the ARp for possible or definite exposure to asbestos was estimated to be 20%. This figure is only slightly lower than that observed when occupational exposure was assessed in terms of job titles. This finding may be explained taking into account that more than two-thirds of the subjects included in list A had a definite asbestos exposure. Dockworkers and shipyard workers were the job categories with the greater numbers of lung cancer cases. The excess risk for lung cancer among these workers may be ascribed to the heavy asbestos exposure that occurred prior to and during World War II, when shipbuilding and ship repairing were the predominant industrial activities in this coastal area. The extensive use in the past of insulating panels or boards containing asbestos (marinite) can account for the elevated relative risk discovered among carpenters, even though other potential carcinogens, such as wood dust or chemicals, have been suspected [18]. Our data indicate that the combined effect of smoking and asbestos exposure conforms more closely to a multiplicative model than to an additive one. This is in agreement with the results of a review by Saracci [19], who concluded that for most of the studies of lung cancer the magnitude of the interaction of tobacco smoking with asbestos was in the multiplicative region. In this study, definite asbestos exposure was associated with both Kreyberg type I tumours (squamous cell carcinoma and small cell carcinoma) and type II tumours (adenocarcinoma) [12]. This finding appears to be important from a medicolegal and insurance viewpoint, as it seems that asbestos exposure is not related to a specific histologic cell type of lung cancer. Other studies have shown different associations between asbestos exposure and histologic lung cancer types [1, 9, 22]. Our results suggest that all the three major histologic types of lung cancer can occur in asbestos workers, supporting the opinion that compensation of the affected workers cannot be based on the presence or absence of a specific cell type [5].

The design of this study has some limitations with regard to the choice of the controls who were selected

among deceased individuals. This issue has been discussed by some authors [4, 26], who focused on both the criteria for selection of decedent controls and the potential biases introduced by surrogate respondents. In this study, deceased individuals were used as the control group in order to ensure comparability of the information from next-of-kin for both cases and controls and to keep the interviewers in a blind condition with respect to the case/control status. Obviously, this methodological approach does not exclude misclassifications arising from imprecision of the information provided by the relatives. The results of some validation studies, however, suggest that the interviews with close relatives can provide adequate data on smoking habit and occupations held by the deceased patients [11, 14, 17].

In conclusion, the findings of this case-control study indicate that the proportion of lung cancers due to occupational exposure in the male population of a coastal area of Northeastern Italy can be estimated as between 16% and 25%. Asbestos exposure was found to account for most lung cancers due to occupation. Since 1977–1978 the use of asbestos in shipbuilding and metallurgical industries has been abolished in this geographic area. It should be stressed that this administrative measure does not exempt public health authorities from continuing health surveillance of workers who have been exposed to asbestos in the past, given the long latency between the first occupational exposure and the clinical appearance of the malignant neoplasm. In addition, the evidence of a multiplicative interaction of tobacco smoking with asbestos suggests that antismoking campaigns and smoking cessation programs should be promoted among ex-asbestos workers.

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