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What this paper adds

- Data on long-term mortality of chrysotile miners and millers according to indicators of exposure are limited.
- We identified an excess mortality from pleural cancer in this mature cohort of asbestos (predominantly chrysotile) miners and millers.
- No significantly increased mortality from lung cancer was apparent, nor an association with indicators of asbestos exposure.
- The study strengthens the evidence of an association between chrysotile mining and pleural cancer, and provides no supporting evidence for a similar association with lung cancer.

Abstract

Objectives: To investigate the long-term mortality of a cohort of Italian asbestos miners.

Methods: The cohort included 1,056 men employed in a chrysotile mine between 1930 and 1990, who were followed up during 1946-2014, for a total of 37,471 person-years of observation. Expected deaths and standardized mortality ratios (SMRs) were computed using national and local (after 1980, when available) reference.

Results: A total of 294 (27.8%) subjects were alive and the end of follow-up, 722 (68.4%) were dead and 40 (3.8%) were lost to follow-up. The SMR for overall mortality was 1.35 (95% confidence interval [CI] 1.25-1.45). The SMR for pleural cancer, based on seven observed deaths, was 5.54 (95% CI 2.22-11.4), and related to time since first exposure, but not to duration of employment, cumulative exposure or time since last exposure. The SMR for lung cancer was 1.16 (95% CI 0.87-1.52; 53 observed deaths), with no excess among workers with cumulative exposure below 100 fiber/mL-years (SMR 0.82; 95% CI 0.44-1.40).

Conclusions: The update of the follow-up of this cohort confirmed an increased mortality from pleural cancer mortality in miners exposed to chrysotile, and a lack of significant increase in lung cancer mortality.

Key words

Asbestos; chrysotile; mining; pleural cancer; lung cancer

Introduction

The Balangero mine was the largest open-air asbestos mine in Europe. It was located in the foothills of the Alps, in Northwestern Italy. It started operation in 1916 and the production increased until an yearly average of 130,000- 160,000 tons of chrysotile asbestos in 1970s. The mine closed in 1990, shortly before the 1992 ban on the mining, marketing and use of all types of asbestos, including chrysotile, in Italy. The mortality of the cohort of asbestos workers in this mine was reported in 1979 (1) and updated in 1990 (2) and 2009 (3).

We continued to follow-up the mortality experience of this work force, which numbered over 1,000 men, 68% of whom are now deceased. Compared to the previous report (3), this report comprises 29% more expected deaths, 18% more observed lung cancer deaths and 75% more observed pleural cancer deaths; in addition, we provide information on the role of various time-related factors related to asbestos exposure in contributing to the mortality of this uniquely mature cohort of asbestos miners.

Materials and Methods

The initial cohort included 1,182 men: After excluding contract workers, those who were employed for less than one year, those with inconsistencies in the data, and those known to have died before 1946, a total of 1,056 men (for a total of 37,471 person-years of observation) employed in the Balangero mine for at least 1 year between 1930 and 1989 were included in the analysis.

Information on date and place of birth and period of hire and of last employment was obtained from the personnel records of the mine. Since no data were available about the employment history after December 31st 1987, we hypothesized that subjects still working on that date remained employed until 1990 when production ceased, unless deceased in that period.

Details of jobs hold by cohort members were obtained from factory records and co-workers. Jobs were classified as mining, crushing, waste dumping, screening and fiber separation, bagging and storage, and maintenance. For each worker, cumulative exposure was calculated by summing across all jobs the products of estimated exposure and duration of employment in that job.

Fiber counts at the plant were first carried out in 1969. In order to categorize jobs by dust exposure levels before 1969, exposure circumstances occurring between 1946 and 1969 were simulated at the plant. Factory files were examined for information on daily production, equipment used, characteristics of the job and number of hours worked per day, and workers employed since 1935 helped to reconstruct the appropriate conditions.

Weights were introduced to make comparable simulated and measured data: for example, many of the more dusty operations, such as drilling, had a duration of only 1-2 hours in a typical working day; on the other hand, working shifts were longer in the past (up to 48 hours per week until 1963). Simulated and measured fiber levels were reported in a previous publication (1): for example, mean concentration in drilling were 37±10 fiber/mL up to 1950 and 5±1 fiber/mL in 1971-1976.

Cumulative exposure was calculated for each worker by summing the exposure level for each year of employment in the specific job category, and expressed as fiber/mL-years. For 38 workers for whom no details on job history were available, and for maintenance workers the mean value of all jobs was used.

Data on prevalence of tobacco smoking was obtained for 171 members of cohorts (14.5% of the total) from medical records compiled between 1970 and 1979 (median year, 1971).

For the purpose of this analysis, cohort members contributed person-time of observation starting one year after first employment at the mine or in 1946 for those first employed earlier and present in 1946, and ending at death, date of last contact for those lost to follow-up, 85th birthday, or December 31st 2014. We excluded deaths and person-years above the 85th birthday, because this is an open category, and because of lower validity of causes of death in this age group. The cohort had been previously followed up to the end of 2003 for mortality (3); we extended the follow-up to 2014 by ascertaining vital status and cause of death, including contributory causes for deaths that occurred after 1988, from population registers and municipal registration offices, and collecting death certificates from local health authorities. The causes of death were coded according to the Ninth Revision of the International Classification of Diseases (ICD-9) (4).

The expected numbers of deaths from selected cancers and other relevant causes were computed using age- and calendar-year specific (5-yr categories) male death rates from the whole country before 1981 and for the Piedmont Region, where the mine was located, from 1981 onward (regional rates were not available before 1981). National mortality rates were available since 1955 from the National Institute of Statistics (ISTAT) and the World Health Organization (WHO); we applied the 1955-1959 rates to the period 1946-54; this choice might have led to an underestimate of expected deaths of causes which showed an increased rate during this period, such as lung cancer. However, given the small numbers of deaths in that period, the impact on the final results is unlikely to be relevant. In addition, mortality rates were not available for years 2004-2005, and from 2011 onwards. Therefore, we applied rates for 2001-2003 to the period 2000-2004, and rates for 2006-2010 to the period 2005-2014. We applied the version of the ICD in use at the time of death, and reported the results according to ICD-9 for consistency with previous reports (3).

We computed standardized mortality ratios (SMR) as the ratio of observed and expected numbers of deaths. For selected causes of death, we also computed the SMRs according to several indices of exposure, according to categories chosen a priori. The Poisson distribution was used to compute the confidence intervals (CI) for up to 10 observed deaths, and the normal approximation for >10 observed deaths (5). The Poisson trend statistic was used to detect trends in the SMRs (5). In the case of lung cancer mortality, we performed an internal analysis based on Poisson regression models to compute mortality rate ratios (MRR), and the corresponding 95% CI, according to

duration of exposure, age at first exposure and time since first exposure (5). To assess the influence of the assumption that workers employed in 1987 remained employed until 1990, we conducted a sensitivity analysis in which employment histories were truncated on December 31sr, 1987.

Results

At the end of the follow-up 294 (27.8%) subjects were alive and 722 (68.4%) had died; for six of them (0.8%) the cause of death was not available. A total of 40 (3.8%) subjects either emigrated or were lost to follow-up. Overall, the 1,056 men in the cohort contributed a total of 37,963 person-years of observation.

Table 1 gives the observed and expected numbers of deaths from selected causes, and the corresponding SMRs. We observed an excess overall mortality, based on 722 observed and 533.4 expected deaths (SMR 1.35, 95% CI 1.25-1.45). Mortality from all cancers was close to expectation (176 observed vs. 165.3 expected deaths, SMR 1.07, 95% CI 0.91-1.23). The SMR for pleural cancer was 5.54 (95% CI 2.22-11.4), based on 7 observed deaths. With reference to lung cancer mortality, the SMR was 1.16 (95% CI 0.87-1.52), based on 53 observed versus 45.5 expected deaths. Only one case of peritoneal cancer was detected, resulting in an SMR of 1.09 (95% CI 0.03-6.08).

The SMRs for cancers in organs of the upper aerodigestive tract were increased, without however reaching statistical significance (oral cavity and pharynx, 1.35; 95% CI 0.54-2.77; esophagus, 1.23; 95% CI 0.40-2.87; larynx, 1.58; 95% CI 0.68-3.11). Results for mortality from other cancers were unremarkable. Considering other major causes of death, we observed 62 deaths from liver cirrhosis (21.2 expected, SMR 2.92; 95% CI 2.24-3.74) and 58 from accidents and violence (33.1 expected, SMR 1.75; 95% CI 1.33-2.26). Mortality from ischemic heart diseases (SMR 0.89; 95% CI 0.69-1.12), cerebrovascular diseases (SMR 0.82; 95% CI 0.60-1.09) and chronic obstructive pulmonary diseases (SMR 1.02; CI 0.65-1.51) was close to expectation.

Table 2 provides details on the number of deaths from selected causes in the different follow-ups of this cohort. No separate results on pleural cancer have been reported in the first study. The first survey showed a significant excess for laryngeal cancer, but no additional deaths from laryngeal cancer occurred after the second follow-up.

Table 3 presents the number of deaths and the corresponding SMRs from selected causes, according to selected measures of asbestos exposure. No trend in SMRs was found for pleural cancer mortality according to duration of employment, cumulative exposure and any other measure of exposure considered. All pleural cancer deaths occurred 30 or more years since first exposure,

and five of them 40 or more years since first exposure. Four of the deceased workers experienced 20 or more years of employment. There was however no significant duration-risk relationship. Mortality from pleural cancer remained elevated 30 or more years after cessation of exposure. Cumulative asbestos exposure and other time-related factors considered did not show a clear pattern of risk with mortality from pleural cancer. In particular, the SMR for pleural cancer among workers with cumulative exposure below 100 fiber/mL-years was 5.84 (95% CI 1.20-17.1). The SMR for lung cancer was 0.82 (95% CI 0.44-1.40) among workers with cumulative exposure below 100 fiber/mL-years. A separate analysis of workers with cumulative exposure below 25 fiber/mL-years resulted in a SMR equal to 2.40 (95% CI 0.49-7.01, 3 deaths).

Results of the Poisson regression analysis on lung cancer mortality are reported in Table 4. This internal analysis showed no significant trend for any of the exposure variables considered. The sensitivity analysis in which the employment history of workers employed on December 31st, 1987 was truncated on that date produced results very clos to those of the main analysis (not shown in detail).

The analysis of laryngeal cancer was limited by small numbers. Out of eight workers who died from this cause, seven were first employed before 1946, and a trend was suggested according to duration of exposure and cumulative exposure (Table 3). SMRs for ischemic heart disease did not show an association with indicators of exposure, although there was a trend of increasing SMR according to period of first employment (Table 3).

Among other cases of death at increased mortality are "ill-defined descriptions and complications of heart disease" (62 deaths; no reference rates available), asbestosis (24 deaths) and tuberculosis (16 deaths).

The prevalence of tobacco smoking in the 1970s was 42.9%, 65.5%, 54.8%, 75.0%, and 37.5% in the age groups 25-24, 35-44, 45-54, 55-64, and 65-74, respectively.

Discussion

The present update of mortality in a cohort of asbestos miners from Italy confirmed the increased risk of pleural mesothelioma, which persisted more than 30 years after cessation of exposure, and the lack of a significant excess of risk of lung cancer and other neoplasms, notably laryngeal cancer, which was elevated in a previous report (1-3). The study is not informative with respect to peritoneal mesothelioma. Thus, the update of this cohort of asbestos chrysotile miners provides additional quantitative evidence on the role of chrysotile on mesothelioma risk (6).

There is anecdotal evidence that crocidolite was occasionally present at the Balangero mine for material testing and mixture preparation (7). Piolatto et al. (2) reported that the examination of several samples of chrysotile from the mine ruled out the presence of contamination with amphiboles at detectable concentrations and that a new fibrous silicate, named balangeroite, was characterized (0.2-0.5 % of the total mass samples of asbestos commercialized from the Balangero mine). Balangeroite fibers dimensions are similar to those of amphiboles, and in some studies this fiber appears to be even more durable than crocidolite (8-10). We previously considered a possible role of balangeroite and of amphibole fibers used in the plant, as explanation for the increased mortality from pleural cancer (1-3).

In the first analysis of this cohort no deaths from pleural cancer were reported (1), and two deaths were observed in the second follow-up. This did not allow carrying out in depth analyses (2). In the third analysis, four deaths from pleural cancer and one from peritoneal cancer were reported (3) (Table 2). Pleural cancer deaths occurred among cohort members with high cumulative exposure, which is compatible with an effect of level of exposure (11), although no linear trend in risk was evident, and the small number of deaths did not allow allowance for latency and other relevant risk determinants. In the present update, deaths from pleural cancer were also observed among workers with low cumulative fiber exposure, and, while applying due caution in the interpretation of the results because of the small number of deaths from pleural cancer, a role of cumulative dose was no longer apparent. The small number of deaths from pleural cancer also reduced the ability to disentangle the effect of various indicators of asbestos exposure, e.g., through a multivariate internal analysis. Our results confirmed the need for long latency in order to detect the full effect of asbestos exposure on mesothelioma risk: all deaths from pleural and peritoneal cancer in this cohort were observed 30 or more years from first exposure, with no suggestion of a decline in risk after cessation of exposure (12, 13).

Our analysis confirmed results of previous analyses of this cohort (3) of a lack of substantive increased mortality from lung cancer in this cohort; in particular, no increase in risk was observed in the group of workers with a cumulative dose of less than 100 fiber/mL-years. Our study has 90% statistical power to detect a SMR of 2.0 for lung cancer among workers with less than 100 fiber/mL-years cumulative exposure (5). On the other hand, the power of the analysis on lung cancer risk among workers with less than 25 fiber/mL-year was low.

Asbestos exposure has been associated with a few other cancers, but the available evidence is not consistent (14-17). This study confirmed previous follow-ups that did not support an association with stomach and colorectal cancers. No new cases of laryngeal cancer were observed in the current update of the follow-up; the SMR for this cause of death remains elevated, although the excess is lower than in earlier analyses (Table 2). The increased mortality from this cause detected in the first analysis (1) may have been due to random fluctuation.

Results of the mortality analysis of this cohort are persistently consistent with an higher mortality from cancers related to alcohol drinking (oral cavity, esophagus) and other alcohol related causes (liver cirrhosis, accidents and violence), although the mortality excess from these causes appears to have become less pronounced in previous follow-ups (Table 2), likely reflecting improved social and health conditions in these workers over time. Drinking habits of the area could also have played an important role in determining the increased overall mortality of this cohort, which cannot be explained only by cancer mortality.

Among the strengths of this study research are the very long follow-up, the low proportion of subjects lost-to-follow-up, and the relatively large number of lung cancer deaths, which allow detailed dose-response analysis according to chrysotile exposure.

A limitation of this study, common to other occupational cohort studies, is related to the potential confounding role of tobacco smoking, occupational exposures outside the mine, and alcohol drinking. We retrieved data on tobacco smoking for 14.5% of cohort members: the prevalence of smoking was comparable to that of the general male population (18). Our study lacks information on other confounders, but these are unlikely negative confounders for lung cancer however, occupational exposure to asbestos in other jobs might have contributed to the excess mortality from pleural cancer; a possible role of alcohol as confounder is discussed above. In order to address the

problem that environmental measurements were available only since 1969, simulated data were generated for the earlier period. These values have considerable limitations: they represent mean values for large job categories, and could not consider specific circumstance (e.g., weather conditions), which might have affected exposure levels. Reliance on death certificates is an additional limitation of this study.

The Balangero mine was an open-air quarry: it is unlikely however that this characteristics resulted in important environmental contamination (and therefore non-occupational exposure to the workers in this cohort, many of whom lived in the same area), because the proportion of asbestos in the residual material that was dismissed from the mill was in the order of 0.3%.

As discussed in a previous analysis of this cohort (3), reliance on death certification for outcome assessment could result in low sensitivity and specificity in the diagnosis of mesothelioma, potentially leading to bias in the SMR in both directions. In addition, detailed analysis of mortality from pleural and peritoneal cancers suffered from limited statistical power from small number of deaths.

In conclusion, the extended follow-up of this cohort of asbestos (primarily chrysotile) miners confirmed the presence of an increased mortality from pleural cancer, and the lack of a significantly increased mortality from lung cancer. This may be explained by the relatively low exposure level experienced by these workers, although other explanations, such as exclusion of highly exposed (contract) workers, competitive mortality from other causes of death such as non-neoplastic pulmonary diseases asbestosis, healthy worker effect (though absent in this cohort for total mortality, and small and non significant for cardiovascular mortality), and differences in smoking habits relative to the general population, cannot be excluded. The cohort also experienced an increased mortality from causes linked to excessive alcohol drinking.

Contributorship

EP, CR, CLV and PB designed the study. EP and CR established the cohort. EP, CR and CLV were involved in previous analyses of this cohort. FD acquired the additional mortality data. CP contributed to the statistical analysis. PB and EP drafted the manuscript. All authors reviewed and approved the manuscript.

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Competing interests

EP and CR reported personal fees for the defense from several law firms, outside the submitted work. CLV reported personal fees from expert opinion for the court and the defense in asbestos litigation, excluding mining and manufacturing, outside the submitted work. PB reported personal fees from expert witness for the defense in asbestos-related litigation, outside the submitted work. FD and CP reported no competing interests.

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Table 1. Standardised mortality ratios for selected causes (asbestos miners in Balangero, Italy 1946-2014).

Cause of death	ICD-9	O	E	SMR (95% CI)
Neoplastic causes				
Oral cavity/pharynx	140-149	7	5.2	1.35 (0.54-2.77)
Esophagus	150	5	4.1	1.23 (0.40-2.87)
Stomach	151	18	18.4	0.98 (0.58-1.55)
Colorectal	152-154,159.0	14	16.8	0.83 (0.45-1.40)
Liver	155	5	7.7	0.65 (0.21-1.51)
Pancreas	157	3	6.2	0.48 (0.10-1.41)
Peritoneum	158	1	0.9	1.09 (0.03-6.08)
Larynx	161	8	5.1	1.58 (0.68-3.11)
Lung	162	53	45.5	1.16 (0.87-1.52)
Pleura	163	7	1.3	5.54 (2.22-11.41)
Prostate	185	9	9.8	0.91 (0.42-1.74)
Bladder	188	8	7.1	1.12 (0.48-2.21)
Kidney	189	2	3.2	0.62 (0.07-2.23)
Brain and CNS	191-192	4	3.9	1.02 (0.28-2.62)
Lymphatic and hematopoietic	200-208	11	10.7	1.03 (0.51-1.83)
All cancers	140-239	176	165.2	1.07 (0.91-1.23)
Non-neoplastic causes				
Ischemic heart diseases	410-414	69	77.9	0.89 (0.69-1.12)
Cerebrovascular diseases	430-438	47	57.4	0.82 (0.60-1.09)
Chronic obstructive pulmonary diseases	490-496	24	23.6	1.02 (0.65-1.51)
Liver cirrhosis	571	62	21.2	2.92 (2.24-3.74)
Accidents and violence	800-999	58	33.1	1.75 (1.33-2.26)
All causes	1-999	722	533.4	1.35 (1.26-1.46)

ICD-9, International Classification of Diseases, 9th revision (4); CI, confidence interval; E, expected deaths; O, observed deaths; SMR, standardized mortality ratio

Deaths and person-years beyond age 85 were excluded

Table 2. Observed and expected deaths from selected causes in subsequent mortality follow-ups (asbestos miners in Balangero, Italy).

Cause of death	Rubino et al.1979 (1)			Piolatto et al.1990 (2)			Pira et al 2009 (3)			Current analysis		
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI
Laryngeal cancer	6	3.16	1.16-6.89	8	2.67	1.15-5.26	8	1.82	0.78-3.59	8	1.58	0.68-3.11
Lung cancer	11	1.06*	0.53-1.89	22	1.11	0.69-1.67	45	1.27	0.93-1.70	53	1.16	0.87-1.52
Pleural cancer	NA	NA	NA	2	6.67	0.81-24.07	4	4.67	1.27-11.96	7	5.54	2.22-11.41
Peritoneal cancer	NA	NA	NA	NA	NA	NA	1	1.38	0.02-7.67	1	1.09	0.03-6.08
All cancers	50	1.06	0.79-1.40	82	1.08	0.86-1.34	142	1.12	0.95-1.33	176	1.07	0.91-1.23
Ischemic heart diseases	NA	NA	NA	37	0.81	0.57-1.11	59	0.93	0.71-1.20	69	0.89	0.69-1.12
Liver cirrhosis	31	3.13	2.13-4.45	45	2.94	2.14-3.94	57	2.94	2.23-3.81	62	2.92	2.24-3.74
Accidents and violence	45	2.60	1.90-3.48	47	1.94	1.43-2.58	54	1.88	1.41-2.45	58	1.75	1.33-2.26
All causes	332	1.55	1.39-1.72	427	1.49	1.35-1.64	590	1.43	1.32-1.55	722	1.35	1.26-1.46

CI, confidence interval; NA, not available; O, observed deaths; SMR, standardized mortality ratio

* including pleural cancer

Table 3. Standardised mortality ratios from selected causes according to indicators of asbestos exposure (asbestos miners in Balangero, Italy, 1946-2014).

	Laryngeal cancer			Lung cancer			Pleural cancer			Ischemic heart disease			Person-years
	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	O	SMR	95% CI	
Duration of exposure (years)													
<10	2	0.95	0.11-3.43	17	0.95	0.55-1.53	3	6.42	1.32-18.75	27	0.81	0.54-1.18	18,561
10-19	1	1.00	0.02-5.55	15	1.66	0.93-2.73	0	0	-	17	1.05	0.61-1.68	9813
20-29	4	3.19	0.87-8.16	11	0.95	0.47-1.70	2	6.10	0.74-22.04	20	1.08	0.66-1.67	6714
≥30	1	1.41	0.04-7.88	10	1.43	0.68-2.62	2	9.97	1.21-35.98	5	0.50	0.16-1.17	2382
p for linear trend			0.32			0.54			0.59			0.86	
Age at first exposure (years)													
<25	1	0.52	0.01-2.87	24	1.21	0.78-1.80	4	6.63	1.80-17.0	26	0.99	0.65-1.45	18,533
25-34	5	2.30	0.74-5.35	19	0.98	0.59-1.54	3	5.57	1.15-16.3	28	0.86	0.57-1.25	14,413
≥35	2	2.11	0.25-7.61	10	1.57	0.75-2.88	0	0	-	15	0.78	0.44-1.29	4524
p for linear trend			0.21			0.75			0.44			0.45	
Years since first exposure													
<20	2	3.71	0.45-13.4	5	1.64	0.53-3.82	0	0	-	5	0.58	0.19-1.36	15,969
20-29	2	1.91	0.23-6.89	7	0.98	0.39-2.03	0	0	-	18	1.21	0.72-1.92	8783
30-39	2	1.31	0.16-4.72	11	0.85	0.42-1.52	2	5.93	0.72-21.4	17	0.79	0.46-1.26	6957
≥40	2	1.02	0.12-3.70	30	1.34	0.90-1.91	5	6.73	2.18-15.7	29	0.88	0.59-1.27	5762
p for linear trend			0.19			0.74			0.32			0.98	
Years since last exposure													
During exposure	1	1.68	0.04-9.34	2	0.55	0.07-1.99	1	16.85	0.43-93.9	7	0.90	0.36-1.86	12,840
1-9	3	3.35	0.69-9.77	12	1.80	0.93-3.14	1	6.75	0.17-37.6	12	1.03	0.53-1.80	7588
10-29	3	1.36	0.28-3.97	22	1.06	0.66-1.60	2	3.32	0.40-12.0	30	0.83	0.56-1.18	12,611
≥30	1	0.73	0.02-4.06	17	1.18	0.69-1.89	3	6.59	1.36-19.3	20	0.90	0.55-1.39	4431
p for linear trend			0.29			0.95			0.64			0.83	

Period at first exposure													
Before 1946	7	2.10	0.84-4.33	28	1.09	0.72-1.57	5	8.31	2.69-19.4	40	0.73	0.52-1.00	18,931
1946-1959	1	1.10	0.03-6.16	12	1.45	0.75-2.53	1	4.46	0.11-24.8	14	1.13	0.62-1.89	6380
1960 or later	0	0	-	13	1.13	0.60-1.93	1	2.28	0.06-12.7	15	1.36	0.76-2.25	12,160
			0.15			0.80			0.19			0.03	
Cumulative dust exposure (fibre/mL--years)													
<100	1	0.65	0.02-3.61	13	0.82	0.44-1.40	3	5.84	1.20-17.1	24	1.06	0.68-1.57	14,830
100-<400	2	1.30	0.16-4.70	20	1.46	0.89-2.26	1	2.76	0.07-15.4	21	0.89	0.55-1.35	10,956
≥400	5	2.51	0.81-5.85	20	1.25	0.76-1.93	3	7.72	1.59-22.6	24	0.76	0.49-1.13	11,685
p for linear trend			0.16			0.26			0.76			0.26	

O, observed deaths; SMR, standardized mortality ratio
Deaths and person-years beyond age 85 were excluded

Table 4. Mortality rate ratios from lung cancer according to selected indicators of asbestos exposure (asbestos miners in Balangero, Italy, 1946-2014).

	MRR	95% CI
Duration of exposure (years)		
<10	1.00	Ref.
10-19	1.73	0.81-3.70
20-29	1.05	0.48-2.31
30+	1.48	0.64-3.42
p for linear trend		0.50
Time since first exposure (years)		
<20	1.00	Ref.
20-29	0.78	0.21-2.86
30-39	0.83	0.18-3.79
40+	1.89	0.30-11.81
p for linear trend		0.31
Time since last exposure (years)		
During exposure	1.00	Ref.
1-9	2.97	0.60-14.69
10-29	1.63	0.32-8.24
≥30	2.12	0.38-11.78
p for linear trend		0.93
Cumulative dust exposure (fibre/mL--years)		
<100	1.00	Ref.
100-<400	1.84	0.91-3.71
≥400	1.54	0.76-3.10
p for linear trend		0.26

MRR, mortality rate ratio
CI, confidence interval
Ref, reference category
Deaths and person-years beyond age 85 were excluded
Regression models included age (time-varying), period at first exposure (except the analysis of cumulative dust exposure), and age at first exposure.