Accepted: 27 June 2017
DOI: 10.1002/ajim.22750

RESEARCH ARTICLE

WILEY AMERICAN JOURNAL OF INDUSTRIAL MEDICINE

Mortality in asbestos cement workers in Pavia, Italy: A cohort study

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Funding information
Italian Ministry of Health

Background: The aim of this study was to describe the mortality of a cohort of asbestos-cement workers in the largest plant in the most industrialized Italian region (Lombardy).

Methods: A cohort study was carried out on 1818 subjects, corresponding to 47 536.1 person-years of observation. Standardized mortality ratios (SMRs) were computed for the major causes of death.

Results: Increased SMRs were observed for pleural, peritoneal and lung cancers, and for asbestosis (SMR 26.73, 95% Confidence Interval (CI) 20.99-33.55; 9.15, 95%CI 5.00-15.34; 1.48, 95%CI 1.27-1.72; and 368.05, 95%CI 214.40-589.29, respectively). No excess in mortality for laryngeal cancer was observed (SMR 0.70, 95%CI 0.30-1.39). An increased mortality for ovarian cancer (SMR 3.64, 95%CI 0.99-9.33) was observed, although it was not statistically significant. Among men, mortality for pleural malignant mesothelioma was observed to be related to the duration of exposure, though not to latency.

Conclusions: The results of this study are generally consistent with present knowledge. Conversely, our results do not support the hypothesis that pleural malignant mesothelioma risk indefinitely increases after exposure, suggesting instead that the alternative hypothesis of a risk plateau or decrease after a time since first exposure of more than 40 years is more consistent with the observed data.

KEYWORDS
asbestos, asbestos-cement, cohort study, duration of exposure, time since first exposure

1 | INTRODUCTION

Italy was one of the most important countries involved in the extraction, importation and use of asbestos fibers until Law 257/1992 banned these activities. From the end of the Second World War to 1992, approximately 3 748 550 tons of raw asbestos were used, with a peak between 1976 and 1980 of about 160 000 tons/year.[1] As a result of this large consumption, high incidence and mortality rates for asbestos-related diseases were observed in Italy, in particular for malignant mesotheliomas.[2–5] Lombardy is the most populated and industrialized Italian region, with 10 million inhabitants (one-sixth of the Italian population) and dramatically high incidence rates of mesothelioma. These rates rose to 4.7 per 100 000 person-years among men and 2.5 per 100 000 person-years among women during the period 2000-2012,[6] compared to an estimated background incidence rate in populations not exposed to asbestos of 1-2 cases per million person-years.[7,8]

In such a worrisome context, the province of Pavia holds the negative record for the highest incidence rates of malignant mesothelioma for both men (8.7 per 100 000 person-years) and women (5.3 per 100 000 person-years.[6] According to the data provided by the Lombardy Region Mesothelioma Registry (ie, the

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regional section of the Italian National Mesothelioma Registry—ReNaM), the town of Broni ranked first in the malignant mesothelioma incidence rate for both genders (57 cases, incidence rate 100.0 per 100 000 person-years and 44 cases, 68.4 per 100 000 person-years, for men and women, respectively).[6] As well as environmental and para-occupational exposures, the presence of Italy's second largest asbestos-cement plant, the Fibronit factory, which manufactured asbestos-cement products from 1932 to 1992 and employed around 3500 workers, provided the main source of asbestos exposure.

The aim of this study is to provide the updated mortality of workers in this asbestos-cement factory, with a special focus on some time-related variables such as latency and duration.

2 | MATERIALS AND METHODS

2.1 | Plant characteristics

The plant in Broni (Pavia, Italy) started to produce cement in 1919, and since 1932 the manufacturing was converted to asbestos cement products. About 8000 tons per year of asbestos cement products were manufactured until the 1960s, when production rose to 100 000 tons/year. In 1993, production was permanently stopped due to a law-enforced ban on the production, import, export and use of asbestos in new products, as well as the commerce of such products (Law 257/1992). The residual production of cement was continued until 1997. The premises were not reclaimed when the factory was closed.

Until the 1970s, seven different production lines were present in the plant, allowing for the manufacturing of tubes, sheets, chimneys, pipes, and other special products in asbestos cement. During this period, all mixing procedures were manual. Two more production lines were subsequently added, and from the early 1980s the plant was improved with a close-circuit mixer to prepare all the asbestos cement blends. Local ventilation units were installed to aspirate and filter the dust. The plant consisted of two principal buildings divided into different connecting rooms (some of them also in the basement).

During the 1970s, the period of maximum production, the mean number of workers was about 1300, including both men and women.

The standard asbestos cement blend was made up of Portland cement 325, chrysotile and crocidolite asbestos, while amosite fibers were used only as an additive. Considering the dry weight of the final products, the asbestos percentage could vary from 10 to 15% for sheets to 30% for tubes.

No data on environmental monitoring are available before 1981, after which interventions were made to improve working conditions. From 1981-1990, seven different campaigns to monitor fibers were carried out by independent entities (the University of Pavia, the Local Health Unit). No value exceeding the threshold limit value (2 fibers/cc) was detected in 1981-1983 or in 1984, when measurements had also been carried out separately for different types of asbestos fibers (threshold limit values 0,5 fibers/cc, 2 fibers/cc e 0,2 fibers/cc for amosite, chrysotile and crocidolite, respectively). In 1990, only 7 in 44 samples showed values exceeding 0.4 fibers/cc. However, in 1988, during a breakdown of the sack shredder, concentrations over 10 000 fibers/cc and 2000 fibers/cc were measured for chrysotile and amosite, respectively.

Crocidolite was used until the mid-1980s, but it was not present at the plant after 1987. The use of amosite was stopped in 1990, while chrysotile was used until the Italian asbestos ban (1993).

2.2 | Cohort description

The cohort was established by identifying workers from the company registries, which recorded for each worker, personal data and occupational period(s) (date of hiring and date of cessation) at the plant. No information was available on job title and tasks.

From 1932-1992, 3,452 workers were employed at the plant, 2,739 (79.3%) men, and 713 (20.7%) women. After a preliminary evaluation, and because of the difficulty in obtaining information on vital status for remote time periods, the cohort was restricted to workers already employed on January, 1, 1950, or hired thereafter (n = 2,012). Moreover, given that cause-specific incidence ratios for the general population in Lombardy were available from 1970, the follow-up period considered for statistical analyses was limited to January 1, 1970-December 31, 2014 (end of follow-up). One hundred and eighty-four subjects were lost at follow up or died before January 1, 1970. Workers hired after December 31, 1992 (n = 8), or with an impossible hiring or retirement age (n = 2), were also excluded from the analyses. Thus, our cohort included a total number of 1818 subjects, 1663 (91.5%) men and 155 (8.5%) women, corresponding to 47 536.1 person-years of observation.

The Registrar's Offices of the town of residence were accessed to obtain the information on vital status, according to a procedure tested in past cohort studies in Italy.[9] The causes of death for decedents after 1985 were provided by the Local Health Authorities or the Regional Registries of Causes of Death. For earlier deaths, the cause was provided by the Registrar Office of the municipality where the deaths occurred.

The underlying cause of death was coded according to the International Classification of Disease, 8th, 9th, and 10th Revisions, according to the date of death.

The study was submitted to the University of Eastern Piedmont Ethical Review Board (Authorization CE 112/13, July 12, 2013).

2.3 | Statistical analysis

Statistical analyses for the present report were based on person-years and standardized mortality ratios (SMRs; ie, the ratio of observed to expected deaths using indirect standardization) method.[10] Workers in the cohort contributed until their most recent date of observation. Duration of exposure was computed by summing up the duration of all employment periods in the cohort. Latency was computed from the date of first employment.

Reference rates were age-, period-, sex-, region-, and cause-specific. Mortality rates were used for the Lombardy region, where the plant was located. The set of rates was prepared by the National

Institute of Health based on mortality and population figures provided by the National Institute of Statistics—ISTAT (Rome, Italy), which were available from 1970 on.[11] Correspondingly, analyses were restricted to person-years and events occurring after January 1, 1970. Therefore, deaths and person-years before 1970 were excluded from the analyses presented here.

We computed SMRs for the major causes of death, including accidents, and violence. We included the causes of death associated with asbestos, following an IARC evaluation[12]: namely, pleural and peritoneal malignant neoplasm and cancers of the lung, larynx, and ovary. Moreover, we also carried out statistical analyses for other cancer sites of interest, such as the gastro-intestinal tract, and for asbestosis. Causes connected to the healthy worker effect,[10] in particular, respiratory and cardiovascular diseases, were also included. The list of causes was decided a priori. Supplementary Table SI presents the ICD codes for the nosologic categories considered in the analyses.

Statistical significance was set at 5%; however, alpha errors (*P*-value) at 1% or lower were highlighted. Confidence intervals were computed according to the Poisson distribution of observed deaths,[10] at the 95% confidence value (95%CI).

Calculations were performed using OCMAP PLUS v 3.10 (University of Pittsburgh, PA) and SAS version 9.2 (Cary, NC).

3 | RESULTS

A total number of 1818 workers were included in this cohort study, 1663 (91.5%) male and 155 (8.5%) female. At the end of the follow up, 460 (25.3%) workers were still living, 1338 (73.6%) were deceased, and 20 (1.1%), 17 men and 3 women, were lost to follow up. Causes of death were traced for 1142 (85.4%) decedents.

The vast majority of male workers (76.9%) was first exposed before 1970, while the beginning of exposure after 1959 was exceptional among women (1.9%). In both genders, first exposure was before 40 years of age for the large majority (76.1% and 89.0% for male and female, respectively). About 44% of women started their work before 20 years of age. Length of employment (duration) was greater than 10 years for the majority of workers in both genders, although the frequency of short durations (>5 years) was not negligible, especially among male workers. The time since first exposure (latency) was 30 years or greater for the majority of male (73.2%) and for almost all (94.8%) female workers (Table 1).

Table 2 shows the mortality figures (observed and expected deaths, and SMRs with 95%CI) by gender. Overall mortality and mortality for all malignancies significantly increased both for men ($P < 0.01$) and women ($P < 0.01$ and $P < 0.05$ for all deaths and all cases of malignant neoplasm, respectively). Malignant tumors of respiratory organs significantly increased ($P < 0.01$) in both genders, with a remarkable result among women. Moreover, an elevated increase in mortality ($P < 0.01$) for pleural cancer was observed in both sexes. Within the cohort described in this study, 74 deaths for malignancies of the pleura have been observed. A significant increase in lung cancer mortality was observed among men ($P < 0.01$) and women, based on six cases ($P < 0.05$). In both sexes, a strong increase in mortality was observed for peritoneal cancer. It should be noted that four cases of ovary cancer were observed, with a threefold increase in mortality, although the threshold of statistical significance was not reached. No other cancers showed a significant increase in mortality, while lip, oral cavity, and pharynx cancers and pancreatic cancer showed a SMR lower than 1 ($P < 0.05$).

Our study traced 17 men who died from asbestosis, while in the general population almost no cases of this pneumoconiosis are expected.

Mortality was significantly lower than expected cardiovascular diseases ($P < 0.01$), ischemic heart diseases in particular ($P < 0.01$). Respiratory diseases showed borderline results, with a slight non-significant increase in mortality. Of interest is the increase in mortality for digestive diseases, mainly represented by cirrhosis, whose SMR showed a significant increase ($P < 0.01$). The number of deaths with poorly specified causes also exceeded the expected number ($P < 0.01$).

Table 3 shows mortality figures by time since first exposure (latency) for selected cancers and other diseases of particular a priori interest. All causes mortality showed an increase by time since first exposure in both genders, although in male workers the trend is more linear. Similarly, the mortality due to malignancies increased with time since first exposure ($P = 0.0003$), as did the mortality due to cancers of respiratory organs ($P = 0.0002$), lung cancer ($P = 0.027$), and peritoneal cancer ($P = 0.013$). A non-linear trend by time since first exposure was observed for asbestosis, and, more interestingly, for pleural cancer, in which mortality among men did not show a statistically significant trend ($P = 0.187$) with time since first exposure. Conversely, among women an inverse trend regarding time since first exposure was observed ($P = 0.011$), although this was based only on eight cases. These points are dealt with in depth in the discussion section.

Table 4 shows mortality figures for duration of exposure. The mortality for pleural ($P = 0.0004$) and peritoneal ($P = 0.033$) cancers increased with duration of exposure. This time variable was not related to overall mortality, while the mortality for all malignancies and for respiratory organ cancers increased with duration of exposure, both for the cohort as a whole and for male workers (whole cohort: $P = 0.034$ and $P = 0.012$, respectively; male workers: $P = 0.036$ and $P = 0.02$, respectively). Among asbestos-related diseases, asbestosis, and lung cancer seemed unrelated to duration.

Table 5 shows mortality figures for time since first exposure and duration of exposure, using the same time classes showed in Tables 3 and 4 and limiting the analysis to male workers. Results were presented only for some cancers of a priori interest and for asbestosis. The mortality for all malignancies and for lung cancer seemed to increase with an increase in time since first exposure within the same class of duration of exposure; however, in the 0-9 and 20-29-years classes of duration, SMRs for workers deceased 40 or more years since first exposure are generally lower than those for workers deceased 30-39

TABLE 1 Cohort study of asbestos-cement workers in Broni (Pavia)

	Male		Female		All	
	N	%	N	%	N	%
Follow up state						
Alive	441	26.5	19	12.2	460	25.3
Deceased[a]	1205	72.5	133	85.8	1338	73.6
Lost at follow-up	17	1.0	3	2.0	20	1.1
Total	1663	100.0	155	100.0	1818	100.0
Year of first exposure						
<1940	220	13.2	57	36.8	277	15.2
1940-1949	197	11.8	60	38.7	257	14.1
1950-1959	296	17.8	35	22.6	331	18.2
1960-1969	566	34.0	0	0	566	31.1
1970-1979	176	10.6	0	0	176	9.7
1980-1989	180	10.8	3	1.9	183	10.1
1990-1992	28	1.7	0	0	28	1.5
Age at first exposure (years)						
<20	138	8.3	69	44.5	207	11.4
20-29	604	36.3	42	27.1	646	35.5
30-39	524	31.5	27	17.4	551	30.3
40-49	325	19.5	14	9.0	339	18.6
50-59	71	4.3	3	1.9	74	4.1
60+	1	0.1	0	0	1	0.1
Exposure duration (years)						
0-4	386	23.2	12	7.7	398	21.9
5-9	246	14.8	19	12.3	265	14.6
10-19	492	29.6	49	31.6	541	29.8
20-29	387	23.3	49	31.6	436	24.0
30+	152	9.1	26	16.8	178	9.8
Time since first exposure[b] (years)						
0-9	34	2.0	0	0	34	1.9
10-19	111	6.7	2	1.3	113	6.2
20-29	300	18.0	6	3.9	306	16.8
30-39	451	27.1	20	12.9	471	25.9
40+	767	46.1	127	81.9	894	49.2

Cohort description and follow-up results.
[a]196 (14.6%) causes of death unknown: 178 male and 18 female.
[b]Latency.

years since first exposure. Considering the 0-19-years duration class, the mortality for peritoneal cancer was seen to increase both considering latency within the same duration class and vice-versa. Despite the fact that SMRs for 10-19 years of latency are based on small numbers, the same figure was not observed for pleural cancer, for which mortality increased with increasing duration of exposure within the same class of time since first exposure, but did not show a linear trend that increased with latency, given the class of duration.

4 | DISCUSSION

The study presented here contributes to the description of mortality of a group of workers heavily exposed to asbestos during the past decades in a single asbestos cement factory located in Broni (Pavia, Italy), providing an update of a previous cohort study.[13] Asbestos cement manufacturing was one of the most important industrial branches using asbestos throughout the past decades in Italy, attaining a country-wide

TABLE 2 Cohort study of asbestos-cement workers in Broni (Pavia)

	Male				Female				All			
Cause of Death	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**
All	1205	1043.40	1.15**	1.09-1.22	133	94.04	1.41**	1.18-1.68	1338	1137.44	1.18**	1.11-1.24
Malignant Neoplasms (MN)	457	370.75	1.23**	1.12-1.35	36	25.18	1.43*	1.00-1.98	493	395.92	1.24**	1.14-1.36
MN lip, oral cavity, and pharynx	3	11.18	0.27**	0.05-0.78	1	0.22	4.47	0.11-24.91	4	11.40	0.35*	0.10-0.89
MN digestive organs (incl peritoneum)	128	137.05	0.93	0.78-1.11	9	10.48	0.86	0.39-1.63	137	147.53	0.93	0.78-1.10
MN esophagus	7	9.68	0.72	0.29-1.49	1	0.24	4.16	0.10-23.16	8	9.92	0.81	0.35-1.59
MN stomach	35	39.20	0.89	0.62-1.24	0	2.75	-	-	35	41.96	0.83	0.58-1.16
MN small intestine	1	0.68	1.48	0.04-8.23	0	0.05	-	-	1	0.73	1.37	0.03-7.64
MN colon	25	22.33	1.12	0.72-1.65	1	2.13	0.47	0.01-2.62	26	24.46	1.06	0.69-1.56
MN rectum	6	9.87	0.61	0.22-1.32	0	0.82	-	-	6	10.69	0.56	0.21-1.22
MN of liver and intrahepatic bile ducts	28	28.89	0.97	0.64-1.40	4	1.54	2.59	0.71-6.64	32	30.43	1.05	0.72-1.48
MN pancreas	7	15.80	0.44*	0.18-0.91	1	1.52	0.66	0.02-3.67	8	17.31	0.46*	0.20-0.91
MN peritoneum	12	1.34	8.95**	4.62-15.63	2	0.19	10.53*	1.27-38.04	14	1.53	9.15**	5.00-15.34
MN respiratory organs	237	127.04	1.86**	1.64-2.12	14	2.37	5.91**	3.23-9.91	251	129.41	1.94**	1.71-2.19
MN larynx	8	11.29	0.71	0.31-1.40	0	0.07	-	-	8	11.36	0.70	0.30-1.39
MN lung	163	111.86	1.46**	1.24-1.70	6	2.09	2.87*	1.05-6.25	169	113.94	1.48**	1.27-1.72
MN pleura	66	2.61	25.28**	19.55-32.16	8	0.16	50.68**	21.88-99.86	74	2.77	26.73**	20.99-33.55
MN uterus	-	-	-	-	2	1.28	1.56	0.19-5.63	2	1.28	1.56	0.19-5.62
MN ovary	-	-	-	-	4	1.10	3.64	0.99-9.33	4	1.10	3.64	0.99-9.33
MN testicle	0	0.38	-	-	-	-	-	-	0	0.38	-	-
MN prostate	22	22.23	0.99	0.62-1.50	-	-	-	-	22	22.23	0.99	0.62-1.50
MN bladder	16	14.35	1.12	0.64-1.81	0	0.41	-	-	16	14.76	1.08	0.62-1.76
MN kidney	6	8.46	0.71	0.26-1.54	0	0.46	-	-	6	8.92	0.67	0.25-1.46
MN eye and nervous system	6	5.67	1.06	0.39-2.30	0	0.47	-	-	6	6.14	0.98	0.36-2.13
Leukemia and lymphoma	28	22.58	1.24	0.82-1.79	3	2.01	1.49	0.31-4.37	31	24.58	1.26	0.86-1.79
MN unspecified site	4	9.41	0.42	0.12-1.09	1	0.78	1.28	0.03-7.10	5	10.19	0.49	0.16-1.14
Psychiatric diseases	12	7.75	1.55	0.80-2.70	1	1.27	0.79	0.02-4.39	13	9.02	1.44	0.77-2.46
Neurological diseases	12	20.04	0.60	0.31-1.05	6	2.46	2.44	0.89-5.30	18	22.51	0.80	0.47-1.26
Cardiovascular diseases	310	391.50	0.79**	0.71-0.89	53	44.00	1.20	0.90-1.58	363	435.50	0.83**	0.75-0.92
Ischemic heart diseases	101	164.74	0.61**	0.50-0.75	8	13.18	0.61	0.26-1.20	109	177.92	0.61**	0.50-0.74
Respiratory diseases	81	74.72	1.08	0.86-1.35	5	5.14	0.97	0.32-2.27	86	79.87	1.08	0.86-1.33

(Continues)

TABLE 2 (Continued)

Cause of Death	Male				Female				All			
	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
Digestive diseases	82	66.08	1.24	0.99-1.54	4	4.41	0.91	0.25-2.32	86	70.49	1.22	0.98-1.51
Cirrhosis	63	40.85	1.54**	1.18-1.97	3	1.76	1.70	0.35-4.98	66	42.61	1.55**	1.20-1.97
Genitourinary diseases	11	14.57	0.75	0.38-1.35	3	1.34	2.23	0.46-6.52	14	15.92	0.88	0.48-1.48
Pneumoconioses	23	2.67	8.62**	5.46-12.93	0	0.01	-	-	23	2.68	8.58**	5.44-12.87
Asbestosis	17	0.05	372.33**	216.89-596.15	0	0.00	-	-	17	0.05	368.05**	214.40-589.29
Accidents and violence	22	39.05	0.56**	0.35-0.85	2	2.78	0.72	0.09-2.60	24	41.83	0.57**	0.37-0.85
Poorly specified causes	14	6.05	2.31**	1.27-3.88	2	1.17	1.70	0.21-6.15	16	7.22	2.22**	1.27-3.60

Overall results. Number of observed and expected deaths and Standardized Mortality Ratios (SMR) with 95% Confidence Intervals (95% CI).
$^{*}P < 0.05$; $^{**}P < 0.01$.

production of 120 000 tons/years of asbestos-cement pipes and 700 000 tons/year of other asbestos-cement goods, with a total workforce of about 5 000 people during the 1980s.[14]

Follow-up results were satisfactory, as only 1.1% of cohort members were lost to follow-up (including untraced migrants abroad) and the causes of death were known for 85.4% of decedents. The decision to restrict our analyses to 1970 onwards depends on the availability of reference mortality rates[11] and not on the quality of cohort data. Only 155 female workers were included in this study, preventing it from carrying out a meaningful analysis in such a subgroup for some of the time variables and causes of death considered here. Despite this, it should be emphasized that eight cases of pleural cancer, two of peritoneal cancer, six of lung cancer, and four of ovarian cancer were observed among women. The total amount of deaths from malignant neoplasms among female workers was 36.

Our study is consistent with current knowledge on asbestos exposure.[12] We observed increased mortality for all causes, all malignancies, lung cancer, pleural and peritoneal mesothelioma, and asbestosis. Ovarian cancer mortality showed an increase, though not statistically significant, due to small numbers (four cases, SMR = 3.64, 95%CI 0.99-9.33). This cohort study failed to observe an increase in mortality for laryngeal cancer and for tumors of the digestive tract in both genders. These results are also consistent with previous findings among the same cohort.[13]

The analyses, using time-dependent variables, of the occurrence of pleural and peritoneal neoplasms, as well as of lung cancer and other asbestos-related diseases, are one of the major aims that led to the updating of this cohort.

SMRs increased with the duration of employment for pleural and peritoneal neoplasms in men, while in women small numbers prevented us from drawing firm conclusions. While SMRs for asbestosis were dramatically elevated, asbestosis showed no clear trend with duration of employment. For lung cancer, no trend was present regarding duration of employment among men ($P = 0.24$), whereas in women no specific trend was apparent, given that only six cases were observed.

Duration of employment is generally considered as a modest indicator of exposure severity. Nevertheless, in this cohort, duration of employment could be considered as the only available proxy of exposure intensity, due to the lack of information on individual exposure severity. It is worth noting that duration of exposure is a very weak indicator of exposure severity, also given the fact that asbestosis was observed to have an irregular exposure-response relationship with duration in our study.

The work environment was not split into different, well-separated rooms, and thus a quite homogeneous exposure level could be assumed. Moreover, it was impossible to calculate for each worker the cumulative dose of exposure due to the lack of data regarding personal exposures to asbestos fibers. However, different studies have pointed out that duration is an independent determinant of malignant mesothelioma occurrence,[1] and thus analyses carried out using this time variable can be meaningful and useful.

TABLE 3 Cohort study of asbestos-cement workers in Broni (Pavia)

	Male				Female				All			
Cause of death	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**
All												
<10 years	27	26.34	1.02	0.67-1.49	0	0.08	-	-	27	26.42	1.02	0.67-1.49
10-19 years	105	98.62	1.06	0.87-1.29	2	0.37	5.43	0.66-19.60	107	98.98	1.08	0.89-1.31
20-29 years	216	189.17	1.14	1.00-1.30	6	5.31	1.13	0.41-2.46	222	194.48	1.14	1.00-1.30
30-39 years	305	269.63	1.13*	1.01-1.27	16	16.72	0.96	0.55-1.55	321	286.35	1.12*	1.00-1.25
40+ years	552	459.65	1.20**	1.10-1.31	109	71.56	1.52**	1.25-1.84	661	531.21	1.24**	1.15-1.34
p for trend			0.179				0.333				0.064	
Malignant Neoplasms (MN)												
<10 years	3	8.85	0.34	0.07-0.99	0	0.05	-	-	3	8.90	0.34*	0.07-0.98
10-19 years	33	36.92	0.89	0.61-1.26	1	0.16	6.16	0.15-34.30	34	37.09	0.92	0.63-1.28
20-29 years	76	75.29	1.01	0.80-1.26	2	1.73	1.16	0.14-4.18	78	77.02	1.01	0.80-1.26
30-39 years	144	101.95	1.41**	1.19-1.66	6	4.80	1.25	0.46-2.72	150	106.75	1.40**	1.19-1.65
40+ years	201	147.72	1.36**	1.18-1.56	27	18.44	1.46	0.96-2.13	228	166.17	1.37**	1.20-1.56
pfor trend			0.0003				0.956				0.0003	
MN peritoneum												
<10 years	0	0.04	-	-	0	0.00	-	-	0	0.04	-	-
10-19 years	0	0.16	-	-	0	0.00	-	-	0	0.16	-	-
20-29 years	1	0.28	3.57	0.09-19.90	0	0.01	-	-	1	0.29	3.40	0.08-18.97
30-39 years	3	0.41	7.35*	1.52-21.49	0	0.03	-	-	3	0.44	6.77*	1.40-19.79
40+ years	8	0.45	17.66**	7.62-34.79	2	0.14	14.33*	1.73-51.78	10	0.59	16.87**	8.09-31.03
p for trend			0.015				0.482				0.013	
MN respiratory organs												
<10 years	2	3.47	0.58	0.07-2.08	0	0.00	-	-	2	3.48	0.58	0.07-2.08
10-19 years	22	14.58	1.51	0.95-2.28	1	0.01	77.29**	1.93-430.63	23	14.59	1.58	1.00-2.36
20-29 years	34	28.50	1.19	0.83-1.67	2	0.13	15.51*	1.88-56.04	36	28.62	1.26	0.88-1.74
30-39 years	76	35.44	2.14**	1.69-2.68	2	0.38	5.31	0.64-19.18	78	35.82	2.18**	1.72-2.72
40+ years	103	45.06	2.29**	1.87-2.77	9	1.85	4.87**	2.23-9.25	112	46.90	2.39**	1.97-2.87
p for trend			0.0003				0.020				0.0002	
MN larynx												
<10 years	0	0.46	-	-	0	0.00	-	-	0	0.46	-	-

(Continues)

TABLE 3 (Continued)

	Male				Female				All			
Cause of death	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
10-19 years	2	1.75	1.14	0.14-4.12	0	0.00	-	-	2	1.75	1.14	0.14-4.12
20-29 years	2	2.87	0.70	0.08-2.52	0	0.01	-	-	2	2.87	0.70	0.08-2.51
30-39 years	1	2.99	0.33	0.008-1.86	0	0.02	-	-	1	3.01	0.33	0.01-1.85
40+ years	3	3.22	0.93	0.19-2.72	0	0.05	-	-	3	3.27	0.92	0.19-2.68
p for trend			0.949				-				0.963	
MN lung												
<10 years	2	2.91	0.69	0.08-2.48	0	0.00	-	-	2	2.92	0.68	0.08-2.48
10-19 years	13	12.46	1.04	0.56-1.78	1	0.01	89.60*	2.24-499.23	14	12.47	1.12	0.61-1.88
20-29 years	30	24.87	1.21	0.81-1.72	0	0.11	-	-	30	24.98	1.20	0.81-1.71
30-39 years	52	31.39	1.66**	1.24-2.17	0	0.33	-	-	52	31.71	1.64**	1.22-2.15
40+ years	66	40.23	1.64**	1.27-2.09	5	1.63	3.06	0.99-7.14	71	41.87	1.70**	1.32-2.14
p for trend			0.031				0.350				0.027	
MN pleura												
<10 years	0	0.04	-	-	0	0.00	-	-	0	0.04	-	-
10-19 years	7	0.18	39.31**	15.80-81.00	0	0.00	-	-	7	0.18	39.14**	15.73-80.64
20-29 years	2	0.46	4.38	0.53-15.80	2	0.01	301.59**	36.49-1089.50	4	0.46	8.62**	2.35-22.08
30-39 years	23	0.72	32.14**	20.37-48.22	2	0.02	98.60**	11.93-356.18	25	0.74	33.97**	21.98-50.15
40+ years	34	1.22	27.87**	19.30-38.94	4	0.13	30.79**	8.39-78.84	38	1.35	28.15**	19.92-38.64
p for trend			0.187				0.011				0.298	
Cardiovascular diseases												
<10 years	7	7.44	0.94	0.38-1.94	0	0.02	-	-	7	7.46	0.94	0.38-1.93
10-19 years	24	32.25	0.74	0.48-1.11	1	0.11	9.29	0.23-51.74	25	32.36	0.77	0.50-1.14
20-29 years	54	66.19	0.82	0.61-1.06	1	2.32	0.43	0.01-2.40	55	68.51	0.80	0.60-1.04
30-39 years	67	101.35	0.66**	0.51-0.84	4	7.92	0.50	0.14-1.29	71	109.27	0.65**	0.51-0.82
40+ years	158	184.27	0.86	0.73-1.00	47	33.64	1.40*	1.03-1.86	205	217.91	0.94	0.82-1.08
p for trend			0.585				0.115				0.173	
Respiratory diseases												
<10 years	1	0.97	1.03	0.03-5.75	0	0.00	-	-	1	0.97	1.03	0.03-5.74
10-19 years	3	4.57	0.66	0.13-1.92	0	0.01	-	-	3	4.58	0.66	0.13-1.91
20-29 years	10	10.47	0.96	0.46-1.76	0	0.25	-	-	10	10.72	0.93	0.45-1.72

(Continues)

TABLE 3 (Continued)

	Male				Female				All			
Cause of death	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**
30-39 years	16	18.24	0.88	0.50-1.42	1	0.84	1.18	0.03-6.60	17	19.09	0.89	0.52-1.43
40+ years	51	40.47	1.26	0.94-1.66	4	4.04	0.99	0.27-2.54	55	44.51	1.24	0.93-1.61
p for trend			0.160				0.787				0.164	
Asbestosis												
<10 years	0	0.00	-	-	0	0.00	-	-	0	0.00	-	-
10-19 years	1	0.00	378.70**	9.47-2110.13	0	0.00	-	-	1	0.00	377.53**	9.44-2103.59
20-29 years	1	0.01	175.32*	4.38-976.89	0	0.00	-	-	1	0.01	174.64*	4.37-973.12
30-39 years	5	0.01	445.87**	144.73-1040.48	0	0.00	-	-	5	0.01	442.10**	143.51-1031.68
40+ years	10	0.03	390.34**	187.17-717.84	0	0.00	-	-	10	0.03	384.25**	184.25-706.64
p for trend			0.952				-				0.952	
Digestive diseases												
<10 years	5	3.15	1.59	0.51-3.70	0	0.01	-	-	5	3.16	1.58	0.51-3.70
10-19 years	8	10.64	0.75	0.32-1.48	0	0.03	-	-	8	10.67	0.75	0.32-1.48
20-29 years	18	15.15	1.19	0.70-1.88	0	0.32	-	-	18	15.47	1.16	0.69-1.84
30-39 years	22	16.44	1.34	0.84-2.03	2	0.87	2.30	0.28-8.30	24	17.31	1.39	0.89-2.06
40+ years	29	20.70	1.40	0.94-2.01	2	3.19	0.63	0.08-2.27	31	23.88	1.30	0.88-1.84
p for trend			0.306				0.699				0.405	
Accidents and violence												
<10 years	1	3.14	0.32	0.01-1.77	0	0.01	-	-	1	3.14	0.32	0.01-1.77
10-19 years	3	6.42	0.47	0.10-1.37	0	0.02	-	-	3	6.44	0.47	0.10-1.36
20-29 years	5	8.07	0.62	0.20-1.44	0	0.17	-	-	5	8.24	0.61	0.20-1.42
30-39 years	6	8.57	0.70	0.26-1.52	0	0.52	-	-	6	9.09	0.66	0.24-1.44
40+ years	7	12.85	0.55	0.22-1.12	2	2.07	0.97	0.12-3.50	9	14.92	0.60	0.28-1.14
p for trend			0.643				0.460				0.536	

Number of observed and expected deaths and Standardized Mortality Ratios (SMR) with 95% Confidence Intervals (95% CI), by time since first exposure (latency).
*$P < 0.05$; **$P < 0.01$.

TABLE 4 Cohort study of asbestos-cement workers in Broni (Pavia)

	Male				Female				All			
Cause of death	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**	**Obs**	**Exp**	**SMR**	**95%CI**
All Duration												
<10 years	357	305.19	1.17**	1.05-1.30	25	14.58	1.71*	1.11-2.53	382	319.77	1.20**	1.08-1.32
10-19 years	396	351.02	1.13*	1.02-1.24	46	42.31	1.09	0.80-1.45	442	393.32	1.12*	1.02-1.23
20-29 years	318	280.55	1.13*	1.01-1.27	44	25.24	1.74**	1.27-2.34	362	305.79	1.18**	1.06-1.31
30+ years	134	106.64	1.26*	1.05-1.49	18	11.91	1.51	0.90-2.39	152	118.56	1.28**	1.09-1.50
p for trend			0.740				0.544				0.542	
Malignant Neoplasms (MN)												
<10 years	128	112.95	1.13	0.94-1.35	7	4.66	1.50	0.60-3.09	135	117.61	1.15	0.96-1.36
10-19 years	141	122.89	1.15	0.97-1.35	12	9.42	1.27	0.66-2.23	153	132.31	1.16	0.98-1.35
20-29 years	134	99.42	1.35**	1.13-1.60	11	7.15	1.54	0.77-2.75	145	106.57	1.36**	1.15-1.60
30+ years	54	35.50	1.52**	1.14-1.98	6	3.95	1.52	0.56-3.31	60	39.44	1.52**	1.16-1.96
p for trend			0.036				0.843				0.034	
MN respiratory organs												
<10 years	65	39.20	1.66**	1.28-2.11	3	0.47	6.38*	1.32-18.65	68	39.67	1.71**	1.33-2.17
10-19 years	3	1.86	1.61	0.33-4.71	5	0.80	6.22**	2.02-14.52	72	42.96	1.68**	1.31-2.11
20-29 years	73	33.79	2.16**	1.69-2.72	5	0.67	7.43**	2.41-17.34	78	34.47	2.26**	1.79-2.82
30+ years	32	11.89	2.69**	1.84-3.80	1	0.42	2.36	0.06-13.16	33	12.32	2.68**	1.84-3.76
p for trend			0.020				0.562				0.012	
MN larynx												
<10 years	2	3.39	0.59	0.07-2.13	0	0.01	-	-	2	3.41	0.59	0.07-2.12
10-19 years	5	3.86	1.29	0.42-3.02	0	0.03	-	-	5	3.89	1.28	0.42-3.00
20-29 years	1	2.92	0.34	0.01-1.91	0	0.02	-	-	1	2.94	0.34	0.01-1.90
30+ years	0	1.12	-	-	0	0.01	-	-	0	1.13	-	-
p for trend			0.409				-				0.408	
MN lung												
<10 years	50	34.53	1.45*	1.07-1.91	2	0.41	4.82	0.58-17.41	52	34.94	1.49**	1.11-1.95
10-19 years	45	37.04	1.21	0.89-1.63	2	0.70	2.84	0.34-10.26	47	37.75	1.24	0.92-1.66
20-29 years	48	29.85	1.61**	1.19-2.13	1	0.59	1.68	0.04-9.39	49	30.44	1.61**	1.19-2.13
30+ years	20	10.44	1.92*	1.17-2.96	1	0.38	2.66	0.07-14.82	21	10.81	1.94**	1.20-2.97
p for trend			0.242				0.486				0.278	

(Continues)

TABLE 4 (Continued)

	Male				Female				All			
Cause of death	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
MN pleura												
<10 years	13	0.87	15.02**	8.00-25.68	1	0.03	31.14	0.78-173.49	14	0.90	15.59**	8.52-26.16
10-19 years	17	0.83	20.55**	11.97-32.90	3	0.05	57.01**	11.76-166.61	20	0.88	22.73**	13.89-35.11
20-29 years	24	0.70	34.15**	21.88-50.82	4	0.04	91.11**	24.83-233.29	28	0.75	37.50**	24.92-54.20
30+ years	12	0.22	55.76**	28.81-97.40	0	0.03	-	-	12	0.24	49.09**	25.37-85.75
p for trend			0.0003				0.800				0.0004	
MN peritoneum												
<10 years	2	0.42	4.73	0.57-17.08	0	0.03	-	-	2	0.46	4.37	0.53-15.78
10-19 years	2	0.45	4.49	0.54-16.23	0	0.07	-	-	2	0.51	3.89	0.47-14.04
20-29 years	7	0.35	19.96**	8.02-41.13	1	0.06	17.92	0.45-99.83	8	0.41	19.68**	8.50-38.78
30+ years	1	0.12	8.19	0.20-45.66	1	0.03	33.27	0.83-185.40	2	0.15	13.15*	1.59-47.51
p for trend			0.100				0.122				0.033	
Cardiovascular diseases												
<10 years	94	107.70	0.87	0.70-1.07	9	6.11	1.47	0.67-2.79	103	113.81	0.90	0.74-1.10
10-19 years	111	133.47	0.83	0.68-1.00	18	21.83	0.82	0.49-1.30	129	155.30	0.83*	0.69-0.99
20-29 years	76	107.78	0.70**	0.56-0.88	19	11.37	1.67*	1.01-2.61	95	119.15	0.80*	0.64-0.97
30+ years	29	42.55	0.68*	0.46-0.98	7	4.69	1.49	0.60-3.08	36	47.24	0.76	0.53-1.05
p for trend			0.107				0.300				0.292	
Respiratory diseases												
<10 years	16	19.95	0.80	0.46-1.30	0	0.70	-	-	16	20.65	0.77	0.44-1.26
10-19 years	31	25.53	1.21	0.82-1.72	3	2.52	1.19	0.24-3.48	34	28.05	1.21	0.84-1.69
20-29 years	24	20.68	1.16	0.74-1.73	1	1.34	0.75	0.02-4.17	25	22.02	1.13	0.73-1.68
30+ years	10	8.56	1.17	0.56-2.15	1	0.58	1.71	0.04-9.55	11	9.14	1.20	0.60-2.15
p for trend			0.323				0.512				0.272	
Asbestosis												
<10 years	2	0.01	140.89**	17.05-508.97	0	0.00	-	-	2	0.01	139.94**	16.93-505.55
10-19 years	9	0.01	602.34**	275.40-1143.44	0	0.00	-	-	9	0.02	593.62**	271.42-1126.89
20-29 years	5	0.01	398.46**	129.34-929.84	0	0.00	-	-	5	0.01	394.36**	128.01-920.28
30+ years	1	0.00	251.77**	6.29-1402.89	0	0.00	-	-	1	0.00	246.40**	6.16-1372.95
p for trend			0.137				-				0.086	

(Continues)

TABLE 4 (Continued)

Cause of death	Male				Female				All			
	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
Digestive diseases												
<10 years	28	19.99	1.40	0.93-2.02	0	0.74	-	-	28	20.73	1.35	0.90-1.95
10-19 years	28	22.76	1.23	0.82-1.78	0	1.81	-	-	28	24.57	1.14	0.76-1.65
20-29 years	16	16.69	0.96	0.55-1.56	3	1.25	2.41	0.50-7.04	19	17.94	1.06	0.64-1.65
30+ years	10	6.63	1.51	0.72-2.77	1	0.62	1.62	0.04-9.03	11	7.25	1.52	0.76-2.71
p for trend			0.618				0.065				0.886	
Accidents and violence												
<10 years	10	13.79	0.72	0.35-1.33	1	0.43	2.31	0.06-12.86	11	14.22	0.77	0.39-1.38
10-19 years	6	12.79	0.47	0.17-1.02	0	1.27	-	-	6	14.06	0.43*	0.16-0.93
20-29 years	2	9.14	0.22*	0.03-0.79	0	0.74	-	-	2	9.88	0.20**	0.02-0.73
30+ years	4	3.34	1.20	0.33-3.07	1	0.33	3.00	0.07-16.75	5	3.67	1.36	0.44-3.18
p for trend			0.800				0.810				0.878	

Number of observed and expected deaths and Standardized Mortality Ratios (SMR) with 95% Confidence Intervals (95% CI), by duration of exposure in years.

$^*P < 0.05$; $^{**}P < 0.01$.

Early cohort and case-control studies predicted malignant mesothelioma risk would increase according to a power of time since first exposure.[15,16] More recently, Berry,[17] based on observations extended beyond 40 years after the first exposure, hypothesized that incidence after the initial increase has a downward long-time trend, which could be modeled by a negative exponential term becoming dominant at time since first exposure of 40 years or more. The early studies[15] did not explore such long latencies because of the time limits of the epidemiological observations they were based on. Berry's hypothesis was tested in previous studies,[18–20] which invariably concluded against the hypothesis of an indefinite increase in incidence and were consistent with the alternative hypothesis of a long-term downward flex. Moreover, two of those studies[18,20] observed that pleural and peritoneal malignant mesothelioma showed a different behavior, with the downward flex observed only for pleural malignant mesotheliomas. Other studies also reported a downward incidence trend after latencies of 30 years or longer.[21–24]

Regarding this issue, our trend results are affected by the lack of pleural mesothelioma cases in the 20-29 years-of-time-since-first-exposure class, although a decrease of SMRs is present in the 40+ years class compared to the previous one (30-39 years). The analyses stratified by duration showed a decline in mortality due to pleural neoplasm in the longest classes of latency for all classes of duration, except the 10-19-years class (Table 5). On the other hand, the risk of peritoneal neoplasm increased through the entire observation time for men. Our results for peritoneal neoplasm are similar to those presented by Reid et al,[20] who observed a continuing increase of risk, while the British Asbestos Survey[21] observed a flex in mortality after 50 years of time since first exposure.

In conclusion, our results do not support the hypothesis that pleural malignant mesothelioma risk indefinitely increases after exposure, suggesting instead that the alternative hypothesis of a risk plateau or decrease after a time since first exposure of more than 40 years is more consistent with the observed data.

Small numbers of observed deaths among women prevented us from drawing conclusions based on analyses of this subgroup regarding time-dependent variables. Moreover, conclusions on ovarian cancer are strongly limited due to small numbers of exposed women, and we are aware that a misclassification with peritoneal mesothelioma is a possible issue. A pathologic review of ovarian cancer cases could not be made based on the available data, given that we accessed only the death certificates provided to the Italian Institute of Statistics (ISTAT). Furthermore, no strong difference between the SMR for peritoneal cancer among men and women was observed, suggesting that probably no severe misclassification of ovarian cancers is present.

Deaths from cardiovascular diseases were fewer than expected, suggesting the presence of a healthy worker effect and excluding marked differences in smoking habits between the cohort and the general population. Moreover, the SMR for digestive diseases increased, though it did not achieve statistical significance. This result

TABLE 5 Cohort study of asbestos-cement workers in Broni (Pavia)

Cause of death	Duration															
	0-9 years				10-19 years				20-29 years				30+ years			
Latency	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
All																
<10 years	26	26.33	0.99	0.64-1.45												
10-19 years	53	46.06	1.15	0.86-1.50	52	52.55	0.99	0.74-1.30								
20-29 years	96	73.79	1.30*	1.05-1.59	81	75.52	1.07	0.85-1.33	39	39.86	0.98	0.70-1.34				
30-39 years	83	68.81	1.21	0.96-1.50	115	107.28	1.07	0.89-1.29	87	78.42	1.11	0.89-1.37	20	15.11	1.32	0.81-2.04
40+ years	99	90.19	1.10	0.89-1.34	147	115.66	1.27**	1.07-1.49	192	162.26	1.18*	1.02-1.36	114	91.53	1.24*	1.03-1.50
Malignant Neoplasms (MN)																
<10 years	3	8.85	0.34*	0.07-0.99												
10-19 years	18	17.64	1.02	0.60-1.61	15	19.28	0.78	0.43-1.28								
20-29 years	32	28.03	1.14	0.78-1.61	31	30.60	1.01	0.69-1.44	13	16.66	0.78	0.41-1.33				
30-39 years	35	26.63	1.31	0.92-1.83	48	38.28	1.25	0.92-1.66	48	31.17	1.54**	1.14-2.04	13	5.86	2.22*	1.18-3.79
40+ years	40	31.79	1.26	0.90-1.71	47	34.72	1.35	1.00-1.80	73	51.58	1.41**	1.11-1.78	41	29.63	1.38	0.99-1.88
MN lung																
<10 years	2	2.91	0.69	0.08-2.48												
10-19 years	7	5.80	1.21	0.48-2.49	6	6.65	0.90	0.33-1.96								
20-29 years	10	8.65	1.15	0.55-2.12	12	10.21	1.17	0.61-2.05	8	6.00	1.33	0.58-2.63				
30-39 years	17	8.14	2.09**	1.22-3.34	10	11.15	0.90	0.43-1.65	20	10.08	1.98**	1.21-3.06	5	2.01	2.49	0.81-5.80
40+ years	14	9.02	1.55	0.85-2.60	17	9.02	1.88*	1.10-3.02	20	13.77	1.45	0.89-2.24	15	8.43	1.78	1.00-2.94
MN pleura																
<10 years	0	0.04	-	-												
10-19 years	3	0.10	30.11**	6.21-88.00	4	0.08	51.01**	13.90-130.60								
20-29 years	1	0.20	5.03	0.13-28.03	0	0.18	-	-	1	0.08	12.35	0.31-68.82				
30-39 years	4	0.21	18.78**	5.12-48.10	5	0.28	18.07**	5.87-42.17	10	0.20	50.43**	24.18-92.74	4	0.03	144.27**	39.31-369.4
40+ years	5	0.31	15.90**	5.16-37.11	8	0.29	27.14**	11.72-53.47	13	0.42	30.70**	16.35-52.50	8	0.19	42.67**	18.42-84.1
MN peritoneum																
<10 years	0	0.04	-	-												
10-19 years	0	0.07	-	-	0	0.08	-	-								

(Continues)

TABLE 5 (Continued)

Cause of death	Duration															
	0-9 years				10-19 years				20-29 years				30+ years			
Latency	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI	Obs	Exp	SMR	95%CI
20-29 years	1	0.11	9.42	0.23-52.47	0	0.11	-	-	0	0.06	-	-				
30-39 years	0	0.10	-	-	1	0.15	6.67	0.17-37.19	2	0.13	15.54*	1.88-56.13	0	0.03	-	-
40+ years	1	0.10	10.29	0.26-57.35	1	0.10	9.92	0.25-55.25	5	0.16	31.50**	10.22-73.51	1	0.10	10.38	0.26-57.83
Asbestosis																
<10 years	0	0.00	-	-												
10-19 years	0	0.00	-	-	1	0.00	740.90**	18.52-4128.32								
20-29 years	0	0.00	-	-	1	0.00	502.29**	12.56-2798.73	0	0.00	-	-				
30-39 years	1	0.00	307.51**	7.69-1713.46	4	0.01	792.72**	216.02-2029.77	0	0.00	-	-	0	0.00	-	-
40+ years	1	0.01	155.38*	3.88-865.76	3	0.01	457.64**	94.43-1337.37	5	0.01	554.26**	179.91-1293.41	1	0.00	277.28**	6.93-1545.0

Number of observed and expected deaths and Standardized Mortality Ratios (SMR) with 95% Confidence Intervals (95% CI), by time since first exposure in years and duration. Male only.

$^{*}P < 0.05$; $^{**}P < 0.$

is mainly driven by cirrhosis ($P < 0.01$), possibly due to high alcohol consumption in an area with high volumes of wine production, although other alcohol-related pathologies did not show any significant increase.

As in the previous study,[13] exposure could not be assessed in this study on an individual basis because of the lack of individual data on jobs and work activities of cohort members.

5 | CONCLUSIONS

The results of this study are consistent with the existing knowledge regarding asbestos-related diseases, as well as with previous findings[13] for the same cohort. Despite asbestos being considered a risk factor for laryngeal cancer,[12] no increase in mortality was observed for this neoplasm in our cohort, and the small number of employed women prevents us from achieving statistical significance for the observed increase in ovarian cancer.

Mortality for peritoneal mesothelioma and for lung cancer increased with an increase in time since first exposure (latency). Mortality for pleural mesothelioma did not follow the same pattern; in fact, there was a decrease in both genders after 40 years since first exposure. By contrast, mortality for pleural mesothelioma increased monotonically with an increase in duration of exposure. This observation may suggest the presence of a mechanism of asbestos clearance from the lung, which deserves further study to better understand the role of such clearance in the onset of pleural mesothelioma.

AUTHORS' CONTRIBUTIONS

EO: conception and design of the work; interpretation of data for the work; drafting the work; final approval of the version to be published. DF: conception and design of the work; acquisition, analysis, and interpretation of data for the work; final approval of the version to be published. ST: conception and design of the work; acquisition, analysis, and interpretation of data for the work; final approval of the version to be published. CM: Conception and design of the work; interpretation of data for the work; critical revision and final approval of the version to be published.

ACKNOWLEDGMENTS

Authors thank Lucia Miglio for the update of the follow up and Dr. Silvano Andorno for the coding of causes of death. The provision of mortality statistics was carried out in the frame of Asbestos Project: Research line n° 1-2, University of Eastern Piedmont, Novara (Italy); Research line n° 4, Central Institute of Health, Rome (Italy).

FUNDING

Grant sponsor: Italian Ministry of Health—Asbestos project; Grant not numbered.

ETHICS APPROVAL AND INFORMED CONSENT

The study was reviewed and approved by the University of Eastern Piedmont Ethical Review Board (Authorization CE 112/13, July 12th, 2013).

DISCLOSURE (AUTHORS)

The authors declare no conflicts of interest.

DISCLOSURE BY AJIM EDITOR OF RECORD

Rodney Ehrlich declares that he has no competing or conflicts of interest in the review and publication decision regarding this article.

DISCLAIMER

None.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Oddone E, Ferrante D, Tunesi S, Magnani C. Mortality in asbestos cement workers in Pavia, Italy: A cohort study. *Am J Ind Med*. 2017;60:852–866. https://doi.org/10.1002/ajim.22750