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ORIGINAL ARTICLES AND REVIEWS

Mortality in an Italian cohort of former asbestos cement workers

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Abstract

Background. A pooled study on Italian asbestos cement plant cohorts observed mortality risk for asbestos-related diseases. This study analysed the mortality of workers cohort of an asbestos cement plant in Syracuse, Italy.

Methods. Workers' vital status and causes of death, during 1970-2018, were identified in regional health databases. Standardized mortality ratios (SMRs) by sex and temporal variables were calculated.

Results. Of the 900 cohort's subjects (636 men, 259 women, 5 unknown sex), for 867 the vital ascertainment was possible: 505 died during study period. All-cause mortality is similarly to the expected among men and lower among women. Pleural and lung malignant neoplasms (MN) exceeded in men (SMR=27.1, SMR=1.95), retroperitoneal and peritoneal MN in both sexes, no cases of larynx MN were observed. Mortality excess for ovarian MN (SMR=1.5) and asbestosis in both sexes (men: SMR=431.9, women: SMR=116.6) were found.

Conclusions. Exceeding mortality from asbestos-related diseases, particularly in men was highlighted.

Key words

- asbestos
- occupational exposure
- crocidolite
- mesothelioma
- lung neoplasms

INTRODUCTION

Exposure to asbestos (a group of naturally occurring fibrous minerals) causes malignant neoplasms, as confirmed by the International Agency for Research on Cancer (IARC), in its update on the health effects of asbestos. Asbestos has been recognized as a human carcinogen (Group 1), causing malignant mesothelioma and lung, larynx and ovarian cancers with sufficient evidence. For malignant neoplasms of the pharynx, stomach and colorectum, IARC found limited evidence (Group 2A) [1]. Asbestos exposure also causes asbestosis, a fibrotic disease affecting the lung parenchyma, and benign pleural effusions, pleural plaques, diffuse pleural fibrosis, and rounded atelectasis.

Commercial use of asbestos began in the second half of the 19th century. Modern industry began in Italy and the United Kingdom after 1860, and was augmented by the exploitation of extensive chrysotile asbestos deposits in Quebec, Canada, in the 1880s. Due to its tensile and heat-resistant properties, asbestos has been widely used in a wide range of industries. In 1972, asbestos consumption in the United States was prevalent in the following industries: construction (42%); friction materials, felts, packaging, and gaskets (20%); floor tiles (11%); paper (9%); insulation and textiles (3%); and other uses (15%) [2].

In 1997 worldwide, global consumption began to decline to a stable level of about 2 million tons of asbestos per year [3]. Robust ecological correlations have been demonstrated between the incidence of malignant pleural mesothelioma in a country and the per capita amount of asbestos imported (or consumed) in that country, 40 years earlier, due to the latency period [4]. Italy was a major European producer and importer of raw asbestos until the 1992 ban [5] as part of a restriction on asbestos use in Western Europe and North America.

In Italy, national asbestos consumption gradually increased to 132,358 tons in 1970, peaking at 180,528 tons in 1980, and then declined [6]. The largest use was in asbestos cement production, followed by thermal insulation in ship and rail car construction. The asbestos cement industry used 85 percent of the asbestos produced or imported to European countries [7]. It employed a large number of workers: asbestos cement workers in Italy were estimated at 9,000 in

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1979 and 5,000 in 1987, active in a large number of plants [8, 9].

According to the European database on exposure to carcinogens (CAREX), the estimated number of Italian workers exposed to asbestos was 352,691 in 1990-1993; in an update referring to 2000-2003, the number dropped to 76,100 [8].

The most recent report of the Italian mesothelioma registry (Registro nazionale dei mesoteliomi, ReNaM) documented 27,356 incident cases of malignant mesothelioma from 1993-2015, mainly due to occupational exposure; domestic and environmental cases were also reported [10].

A study of the Italian pool of 43 cohorts of asbestos-exposed workers (42 occupational cohorts and one of workers' wives) showed excesses in mortality from asbestos-related diseases [11]. In August 2019, a pooled study of Italian cohorts of workers in asbestos cement companies (12,578 workers, 10,275 men and 2,303 women) observed an increased risk of mortality from asbestos-related diseases: asbestosis and malignant neoplasms of pleura, peritoneum, lung, and ovary [12].

Both studies did not include the Syracuse-Eternit cohort [11, 12], due to the lack of available data at the beginning of the studies. This study analyzed, for the first time, mortality data from the cohort of former asbestos cement workers from the Eternit plant located in the municipality of Syracuse, Italy.

Established in the early 1950s, the Syracuse plant went into full production of asbestos cement products in 1955. It was finally closed in 1991, a year before asbestos was banned in Italy [5]. A detailed description of the production cycle can be found in the *Supplementary Material section available online*.

The cohort was reconstructed using information received in January 2013 from the Turin Public Prosecutor's Office as part of an investigation. On that occasion, the Istituto Superiore di Sanità, ISS (Italian National Institute of Health) had provided the Prosecutor's Office with a technical report with an analysis of mortality for specific diseases, for the period from 1/1/1970 to 12/09/2012, calculating the standardized mortality ratios (SMRs) for all causes, malignant tumours of the trachea, bronchus and lung, pleural, peritoneal, and unspecified mesothelioma, malignant tumours of the ovary, and asbestosis (unpublished data).

To the Authors' knowledge, there has been only one previous study related to this plant, an epidemiological survey presented in 1991 in Siena, Italy, at an international conference [13]. Carried out in 1990 by the Local Health Unit 26 of Syracuse, the study found that among 358 Eternit workers with at least 5 years of employment, the prevalence of asbestosis recognized by the National Institute for Insurance against Accidents at Work (Istituto Nazionale Assicurazione contro gli Infortuni sul Lavoro, INAIL) was 12.29%, with an increasing trend depending on the duration of exposure.

This study aims to assess broadly, and not only for asbestos-related diseases, the mortality of workers employed during the company's years of operation.

This study was carried out within the framework of the "Organic intervention plan in areas at environmental risk in Sicily", promoted by the Sicily Regional Health Department, Italy.

The protocol was submitted and approved by Ethical Review Board of Messina Medicine University, Italy.

MATERIALS AND METHODS

Mortality for a wide spectrum of causes was analysed in a 49 year-period (1/1/1970-31/12/2018). Causes of death were selected consistently with the study of pooled 21 cohorts of asbestos cement workers in Italy [12]. The analyses' restriction from 1970 onwards was related to the availability of reference mortality rates [14].

As the Italian National Institute for Health (ISS) technical consultancy had analysed data up to 12/09/2012, an update was necessary: vital status, and causes of death up to 31/12/2018 were ascertained through a record linkage between workers' identification data and health information routinely collected and coded for administrative purpose (Cause of Death Register, Syracuse Provincial Health, ReNCaM-ASP), operated by the Health Authority of the Sicilian Region - Department for Health Activities and Epidemiological Observatory (DASOE), in charge of these information flows. The regional law n. 2 (08/02/2007), such as the national law of 03/03/2017, established the mortality data collection system for the purpose of health surveillance as a public health tool.

After collection, data were pseudonymized, shared with the ISS, and integrated with dataset already available.

Two expert researchers (AZ, CB) double-blindly coded causes of death according to the International Classification of Disease (ICD), 8th, 9th, and 10th revisions, taking into account the date of death. ICD 10th revision in Italy has been used since 2003.

They discussed the reasons for their choices in case of discrepancies, in order to reach an agreement.

To analyse the data for the entire period, it was necessary to examine the codes of the selected causes in the three revisions of ICD, which were then reported in *Supplementary Material* (*Table S1 available online*). Following this step, a variable with specific values for each cause was created for each row of the table. Considering that before 2003, when the 10th revision ICD came into use in Italy, a specific code for malignant mesotheliomas was not available, the analyses were performed for all malignant neoplasms of pleura, including also malignant pleural mesotheliomas.

To calculate the reference regional mortality rates, we used the ISS mortality database, which is in turn based on the Italian National Institute of Statistics (Istituto Nazionale di Statistica, Istat) population data, stratified by sex, five-year age classes and calendar period.

Statistical analysis

Person-years at risk (PYs) were computed from date of employment or 01/01/1970, which ever was most recent, and stopped at 31/12/2018 (the more recent data available at the beginning of the present investigation)

or date of death, which ever occurred earlier. Time since the first exposure (TSFE) was calculated from the beginning date of first employment.

PYs and standardized mortality ratios (SMRs) for the whole study period were calculated, by sex, five-year age classes (15-19 to 95+), calendar period duration of employment (sum of all working periods) and TSFE; moreover, PYs were computed by age at hiring.

The SMRs, with the corresponding 95% confidence intervals (CIs), were computed under the assumption that the observations were distributed according to a Poisson distribution and the ratios were estimated respect to the regional figures. The data were processed according to the European Union General Data Protection Regulation (https://gdpr-info.eu/) and the analyses were performed using software STATA 11 (StataCorp. *Stata statistical software: release 11*. College Station, TX: StataCorp LP; 2009).

RESULTS

The cohort was constituted of 900 subjects (636 men, 259 women, 5 sex unknown). Vital status ascertainment at 31/12/2018 was possible for 867 subjects (96.3%), among which 505 subjects resulted died (392 men, 113 women). Thirty-three subjects (3.6% of the entire cohort), 29 males and 4 females, were excluded from the analysis, due to the unknown vital status or insufficient information on duration of working activity: ten deceased before 01/01/1970, the beginning of follow-up period, six subjects had the same date of hiring and exit from the industry or only one day of employment; for seventeen we were unable to determine the vital status at the end of the follow-up period.

Finally, the analyses included 867 subjects for which it was possible to calculate, among other things, age at hiring and at the end of follow-up, and TSFE; the analyses by duration of the working activity were performed for 830 ex-workers, for whom this information was available.

The person-years (PYs) for men and women were respectively 22,213.6 and 11,009.4. *Table 1* shows the distribution of PYs at risk, by period- and age-class and by sex (A: men; B: women); *Table 2* reports details on the PYs by TSFE and employment duration.

The causes of death investigated are presented in *Table S1 available online* as *Supplementary Material*: mortality for all causes and for all malignant tumours, for groups and single malignant neoplasms, for benign diseases of apparatuses and systems were explored.

Mortality for all causes did not diverge from the expected among men (*Table 3*) and was lower than the expected among women. Statistically significant excess of mortality for all malignant causes was observed among men, and lower than the expected among women (not statistically significant).

With regard to the asbestos related diseases, malignant tumours of the pleura (proxy for pleural mesothelioma) were in excess in men, and no cases were found among women: 16 cases were observed (SMR 27.06, 95% CI 16.58-44.17), starting from a working duration

Table 1
Person-years at risk, computed from the beginning of follow-up, by calendar period- and age-class, among men (A) and women (B)

(A) MEN

Age-class	Calendar period									
	1970-1974	1975-1979	1980-1984	1985-1986	1990-1994	1995-1999	2000-2004	2005-2009	2010-2014	2015-2018
≤ 15	7.702943	5.281314	0.069815							
20-24	47.6256	40.73169	18.22519	0.069815	4.861054					
25-29	169.3018	87.94798	96.10335	20.68173	19.51266	5.460643				
30-34	365.4572	203.9035	123.0041	108.0452	28.25941	22.03149	5.460643			
35-39	505.6277	377.8056	222.5599	125.3888	108.0452	28.25941	22.03149	5.460643		
40-44	511.4627	508.9836	390.6188	223.9781	125.3888	108.0452	28.25941	22.03149	5.460643	
45-49	399.603	524.9008	512.2444	385.7858	220.0876	125.3888	108.0452	28.25941	22.03149	5.460643
50-54	344.3025	402.3498	524.3854	497.4709	381.4298	215.1834	125.3888	108.0452	28.25941	18.63244
55-59	144.5736	344.9562	403.6988	501.9179	480.3224	378.6468	200.5715	123.3621	106.9172	23.15195
60-64	93.0835	133.5305	330.2464	391.4634	480.4148	466.204	357.373	191.3326	109.5537	88.6167
65-69	46.75565	90.54415	122.2669	315.9357	364.3682	418.6626	430.603	324.23	172.7734	81.77892
70-74	14.6653	43.90418	76.72485	104.4983	287.0062	313.9514	343.7817	370.0048	275.3847	131.9699
75-79	5.988364	7.743326	29.30048	57.64476	70.17728	219.8275	252.9767	286.6715	294.7611	195.1875
80-84		3.982204	2.971937	21.74196	33.94114	44.72964	157.1047	184.1355	226.0253	200.538
85-89			3.982204	0.247091	6.901437	23.57358	23.08624	108.8029	135.6208	109.6653
90-94						1.030801	6.912389	6.92334	42.12115	70.36961
95+									0.952772	21.76249

Continues

Table 1
Continued

	(B) WOMEN									
Age-class	**Calendar period class**									
	1970-1974	**1975-1979**	**1980-1984**	**1985-1986**	**1990-1994**	**1995-1999**	**2000-2004**	**2005-2009**	**2010-2014**	**2015-2018**
≤ 15	1.089665	2.431211								
20-24	9.802875	6.138261	5.728953	3.976044	3.78987					
25-29	58.07803	19.21424	9.71937	6.557837	5.381246	3.78987				
30-34	314.9274	65.07734	23.42779	9.71937	6.557837	5.381246	3.78987			
35-39	373.1472	318.4045	68.73785	23.42779	9.71937	6.557837	5.381246	3.78987		
40-44	242.0698	374.36	316.5229	68.73785	23.42779	9.71937	6.557837	5.381246	3.78987	
45-49	147.3635	242.0698	371.2957	313.9322	68.73785	23.42779	9.71937	6.557837	5.381246	3.78987
50-54	71.13142	146.5654	236.3039	368.1567	313.9322	68.73785	23.42779	9.71937	6.557837	4.203285
55-59	18.24709	68.51335	140.4736	228.7071	358.7625	313.9322	68.73785	23.42779	9.71937	5.493498
60-64	4.100616	16.70773	66.93635	134.7611	218.8522	351.3546	308.9076	68.73785	23.42779	7.681725
65-69		4.100616	16.70773	65.27447	132.0787	214.1253	331.5784	290.4997	68.73785	20.56605
70-74			4.100616	16.70773	56.21013	124.6674	194.1889	302.4983	268.5044	62.32854
75-79				4.100616	14.90486	52.04517	105.2539	169.7385	265.6516	213.5715
80-84					1.002738	4.954141	46.26831	92.72348	134.1198	175.3628
85-89						0.926078	0.748118	35.07461	66.59274	77.08282
90-94									22.18207	40.05818
95+										11.32307

Table 2
Person-years (PYs) distribution by sex, time since the first exposure (TSFE) and duration of employment

Sex	**PYs**
Men	22,213.6
Women	11,009.4
Total	33,222.9
TSFE	
<10	12.2
10-19	125.0
20-29	987.3
30-39	3,447.3
40-49	8,683.0
50-59	9,718.3
≥60	10,249.8
Duration of employment	
<10	20,057.2
10-19	7,798.5
20-29	3,153.1
≥30	2,214.1

lower than 10 years, TSFE from 20-29 years, and age at hiring lower than 20 years (*Table 4*).

Statistically significant excesses for retroperitoneal and peritoneal malignant tumours were found in both sexes (men 2 cases, SMR 4.39, 95% CI 1.10-17.54; women 2 cases, SMR 8.96, 95% CI 2.24-5.82). Cases begin to appear from a working life lower than 10 years, TSFE from 40-49 years, and age at hiring less than 20 years (*Table 4*).

No cases of malignant tumour of the larynx were found in both sexes.

In men, there was a statistically significant excess for lung cancer (40 cases, SMR 1.95, 95% CI 1.43-2.66). For these cases, the minimum values for working duration, TSFE and age at recruitment were less than 10 years, in the 10-19 years class, and less than 20 years, respectively (*Table 4*).

In women there is a higher risk than expected for ovarian malignant tumours (3 cases, SMR 1.48, 95% CI 0.48-4.59), not statistically significant.

Cases of malignant stomach cancer were lower than expected in men and higher in women, both not statistically significant (men 4 cases, SMR 0.65, 95% CI 0.24-1.73; women 4 cases, SMR 1.42, 95% CI 0.53-3.78).

Among men there were a statistically significant excess of malignant neoplasms of the rectum (7 cases, SMR 2.66, 95% CI 1.27-5.59) and a higher risk for malignant neoplasms of colon, not statistically significant (11 cases, SMR 1.40, 95% CI 0.78-2.73). Reduced risks for both malignancies were observed among women, not statistically significant.

Regarding pneumoconiosis, 13 cases were observed, entirely attributable to asbestosis (men 11 cases, SMR 431.92, 95% CI 239.20-779.91; women 2 cases, SMR 116.57, 95% CI 29, 15-466.10) (*Table 3*). Cases began to appear from a working life of less than 10 years, TSFE from 20-29 years, and age at hiring between 20-29 years (*Table 4*).

Table 3
Causes of death, by sex. Observed (OBS) and expected cases (EXP), standardized mortality ratios (SMRs) and their 95% confidence intervals (95% CIs); regional reference population (1970-2018)

	Men			Women		
Cause of death	**OBS**	**EXP**	**SMR (95% CIs)**	**OBS**	**EXP**	**SMR (95% CIs)**
All causes	392	383.87	1.02 (0.92-1.13)	113	181.77	0.62 (0.52-0.75)
Malignant neoplasms (MN)	142	98.10	1.45 (1.23-1.71)	37	49.84	0.74 (0.54-1.02)
MN of the lip, oral cavity, and pharynx	2	1.45	1.38 (0.35-5.52)	0	0.72	
MN digestive organs (peritoneum included)	41	33.21	1.23 (0.91-1.68)	18	16.61	1.08 (0.68-1.72)
MN of the stomach	4	6.14	0.65 (0.24-1.73)	4	2.82	1.42 (0.53-3.78)
MN of the small intestine	0	0.15		0	0.08	
MN of the colon	11	7.85	1.40 (0.78-2.53)	4	4.16	0.96 (0.36-2.56)
MN of the rectum	7	2.63	2.66 (1.27-5.59)	0	1.26	
MN of the liver and intrahepatic bile ducts	10	7.36	1.36 (0.73-2.52)	6	3.60	1.67 (0.75-3.71)
MN of the retroperitoneum and peritoneum	2	0.46	4.39 (1.10-17.54)	2	0.22	8.96 (2.24-35.82)
MN of the respiratory organs	57	22.85	2.50 (1.93-3.24)	0	12.04	
MN of the larynx	0	1.42		0	0.69	
MN of the lungs	40	20.47	1.95 (1.43-2.66)	0	10.86	
MN of the pleura	16	0.59	27.06 (16.58-44.17)	0	0.32	
MN of the uterus				5	1.18	4.24 (1.77-10.19)
MN of the ovaries				3	2.03	1.48 (0.48-4.59)
MN of the prostate	11	6.62	1.66 (0.92-3.00)			
MN of the bladder	8	4.58	1.75 (0.87-3.49)	0	2.31	
MN of the kidney, ureter, and other unspecified urinary organs	6	1.63	3.69 (1.66-8.21)	0	0.90	
MN unspecified sites	6	2.55	2.36 (1.06-5.25)	1	1.33	0.75 (0.11-5.34)
Laeukaemias and lymphomas	8	7.85	1.02 (0.51-2.04)	1	4.09	0.24 (0.03-1.73)
Psychiatric diseases	4	5.45	0.73 (0.28-1.96)	2	2.95	0.68 (0.17-2.71)
Neurological diseases	11	9.46	1.16 (0.64-2.10)	4	5.11	0.78 (0.29-2.09)
Cardiovascular diseases	128	163.63	0.78 (0.66-0.93)	40	73.03	0.55 (0.40-0.75)
Respiratory diseases	33	27.77	1.19 (0.85-1.67)	8	12.75	0.63 (0.31-1.26)
Chronic and obstructive respiratory diseases	17	17.29	0.98 (0.61-1.58)	5	7.93	0.63 (0.26-1.52)
Pneumoconiosis	11	0.46	23.96 (13.27-43.27)	2	0.21	9.39 (2.35-37.55)
Asbestosis	11	0.03	431.92 (239.20-779.91)	2	0.02	116.57 (29.15-466.10)
Digestive diseases	17	17.86	0.95 (0.59-1.53)	5	8.17	0.61 (0.25-1.47)
Genitourinary diseases	11	7.95	1.38 (0.77-2.50)	2	3.80	0.53 (0.13-2.10)
Poorly specified causes	24	8.56	2.81(1.88-4.19)	7	3.72	1.88 (0.90-3.94)
Accident and violence	4	12.76	0.31 (0.12-0.84)	3	6.17	0.49 (0.16-1.51)

Malignant neoplasms of the kidney and unspecified malignant neoplasms were statistically significantly in excess among men. Risk of diseases of the circulatory system was statistically significantly reduced in both sexes.

DISCUSSION

The results of this study contribute to filling a knowledge gap regarding the studied cohort, which, as previously mentioned, had not been the subject of publications in scientific journals.

Data relating to the completeness of the vital status ascertainment (867 subjects, 96.3% of the cohort), and the subjects excluded from the analysis (33 subjects, 3.6% of the cohort), are one point of strength of the study. Another one is represented by the length of follow-up (49 years).

The observed results relating to all-cause mortality, chronic respiratory and circulatory diseases could in part be influenced by the presence of the healthy worker's effect, the phenomenon observed in occupational health studies where employed individuals tend to exhibit a lower morbidity and mortality compared to the general population [15].

Table 4
Mortality for malignant neoplasms (MN) of the pleura, retroperitoneum and peritoneum, lung and asbestosis, by duration of employment, age at hiring and time since the first exposure (TSFE). Two sexes combined

	Duration of employment				Age at hiring				TSFE			
	Years	OBS	EXP	SMR (95% CIs)	Years	OBS	EXP	SMR (95% CIs)	Years	OBS	EXP	SMR (95% CIs)
MN of the pleura	<10	7	0.55	12.80 (6.10-26.84)	<20	4	0.17	22.88 (8.59-60.96)	<10	0	0.00	
	10-19	4	0.23	17.67 (6.63-47.07)	20-29	7	0.40	17.72 (8.45-37.16)	10-19	0	0.00	
	20-29	3	0.09	32.46 (10.47-100.63)	30-39	4	0.26	15.10 (5.67-40.24)	20-29	1	0.01	90.36 (12.73-641.45)
	≥30	2	0.05	41.59 (10.40-166.30)	40-49	1	0.06	15.86 (2.23-112.61)	30-39	7	0.06	120.50 (57.45-252.76)
	-	-	-	-	50-59	0	0.01		40-49	6	0.18	32.62 (14.66-72.62)
	-	-	-	-	≥60	0	0.00		50-59	2	0.30	6.64 (1.66-26.56)
	-	-	-	-	-	-	-		≥60	0	0.36	
MN of the retroperitoneum and peritoneum	<10	2	0.40	5.04 (1.26-20.16)	<20	3	0.12	25.36 (8.18-78.62)	<10	0	0.00	
	10-19	1	0.17	5.76 (0.81-40.86)	20-29	0	0.29		10-19	0	0.00	
	20-29	0	0.07		30-39	1	0.20	5.08 (0.72-36.08)	20-29	0	0.01	
	≥30	1	0.03	28.63 (4.03-203.26)	40-49	0	0.06		30-39	0	0.06	
	-	-	-	-	50-59	0	0.01		40-49	2	0.16	12.41 (3.11-49.63)
	-	-	-	-	≥60	0	0.00		50-59	2	0.21	9.40 (2.35-37.59)
	-	-	-	-	-	-	-	-	≥60	0	0.23	
MN of the lungs	<10	21	18.31	1.15 (0.75-1.76)	<20	4	5.02	0.80 (0.30-2.12)	<10	0	0.01	
	10-19	9	7.84	1.15 (0.60-2.21)	20-29	22	14.41	1.53 (1.01-2.32)	10-19	2	0.05	41.46 (10.37-165.79)
	20-29	7	3.56	1.97 (0.94-4.13)	30-39	8	9.27	0.86 (0.43-1.73)	20-29	4	0.43	9.21 (3.45-24.53)
	≥30	3	1.63	1.85 (0.60-5.72)	40-49	6	2.12	2.83 (1.27-6.31)	30-39	9	2.12	4.25 (2.21-8.17)
					50-59	0	0.49		40-49	18	6.49	2.77 (1.75-4.40)
					≥60	0	0.03		50-59	7	10.31	0.68 (0.32-1.42)
					-	-	-		≥60	0	11.93	
Asbestosis	<10	3	0.03	115.23 (37.17-357.29)	<20	0	0.01		<10	0	0	
	10-19	4	0.01	399.21 (149.83-1,063.65)	20-29	10	0.02	475.09 (255.63-882.99)	10-19	0	0	
	20-29	4	0	950.32 (356.67-2,532.03)	30-39	3	0.01	263.17 (84.88-815.97)	20-29	1	0	7,387.30 (1,040.60-52,442.80)
	≥30	2	0	846.86 (211.80-3,386.12)	40-49	0	0.00		30-39	1	0	1,122.20 (158.10-7,966.50)
					50-59	0	0.00		40-49	5	0	1,075.60 (447.70-2,584.10)
					≥60				50-59	6	0.01	406.50 (182.60-904.90
									≥60	0	0.02	

OBS: number of observed subjects; EXP: number of expected subjects; SMR: standardized mortality ratio; CIs: confidence intervals.

In men, statistically significant excesses related to mortality are observed for all malignant tumours, and for several specific malignant diseases. Female population shows a different pattern, and a statistically significant reduced all-causes mortality.

For asbestos-related malignancies, several statistically significant excesses are observed in men (malignant tumours of the pleura, retroperitoneum and peritoneum, lung, rectum). These findings support evidence of prior exposure to asbestos fibres. A no significant increased risk for colon cancer is also present in men.

Among women, statistically significant excesses are observed for retroperitoneal and peritoneal malignancies. Non-statistically significant increased risk is observed for malignancies of the ovary and stomach. No cases of pleural, lung, and rectal malignancies are documented in women.

Cases of laryngeal cancer are absent in both sexes.

Mortality from asbestosis is in excess, statistically significant in both sexes, representing a clue of high exposure. Considering the low mortality rate of this pathology, it is reasonable to hypothesize that the total (alive and deceased) cases of asbestosis were higher. Our results show malignant tumours of the pleura starting after 20 to 29 years since the first exposure (TSFE), retroperitoneal and peritoneal malignant tumours after 40 to 49 years, and lung tumours after 10 to19 years. Asbestosis starts to appear after 20 to 29 years of TSFE. These figures are in agreement with the results reported by Luberto *et al.*, in the pooled analyses of Italian asbestos cement plant workers [12].

Another important point of discussion is the use of malignant neoplasm of the pleura code as a proxy for malignant mesothelioma of the pleura. It is well known that in similar situations, especially when data from death certificates are used, overestimation of the true cases of malignant mesothelioma of the pleura can occur. However, a good correspondence between mesothelioma and malignant neoplasm of pleura has been observed in Italy [16, 17] and this proxy has been used in our country for mesothelioma mortality surveillance [18].

Regarding double-blind coding of causes of death, the two researchers showed agreement in 85% of cases. Discussing the remaining ones, they reached a complete agreement.

The lack of information on job qualification and exposure levels prevented comparisons between subgroups of ex-workers to evaluate the role of different levels of asbestos exposure. Moreover, the risk estimates of asbestos-related diseases recognizing other risk factors besides asbestos, such as lung and ovary cancers and smoking habits, were not controlled for confounding factors due to unavailability of information. However, the presence of asbestos-related diseases (asbestosis, peritoneal and retroperitoneal pathologies, although it is not possible to exclude misclassification phenomena for the latter) documents an exposure that cannot be underestimated. In favour of an important exposure there is also the description of the working cycle, described in the *Supplementary Material available online*.

The figure relating to lung cancer may indicate, also, a different smoking habit between the two sexes. In both sexes there is a statistically significant defect in cardiovascular diseases, and a not significant reduction in the risk of chronic and obstructive pulmonary diseases (COPD): these two groups of diseases are of interest, being cigarette smoking a common risk factor [19]. The healthy worker's effect, previously mentioned, and a reduced smoking habit could underlie these results, with varying, unanalyzable impact.

CONCLUSIONS

The present study shows excesses of mortality from asbestos-related causes in the investigated cohort of asbestos cement plant workers, particularly in men. Despite some limitations of the study, high asbestos exposure levels in workplace could be confirmed. These results could contribute to update the estimates of the health impact of occupational asbestos exposure in Italy and in the world and to draw up suitable public health interventions, including social security and welfare, at local level.

Conflict of interest statement

The Authors declare that there are no conflicts of interest.

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