Mortality in the cohort of talc miners and millers from Val Chisone, Northern Italy: 74 years of follow-up

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Abstract

Objective
To update the analysis of mortality of a cohort of talc miners and millers in Northern Italy.

Methods
We analyzed overall mortality and mortality from specific causes of death during 1946–2020 of 1749 male workers in a talc mine where asbestos was not detected (1184 miners and 565 millers) employed during 1946–1995.

Results
The overall standardized mortality ratio (SMR) was 1.21 (95 % confidence interval [CI] 1.14–1.28); no deaths were observed from pleural cancer. Mortality from lung cancer was not increased (SMR = 1.02 95 % CI 0.82–1.27), while mortality from pneumoconiosis was (SMR 9.55; 95 % CI 7.43–12.08), especially among miners (SMR 12.74; 95 % CI 9.79–16.31). There was a trend in risk of pneumoconiosis with increasing duration of employment in the overall cohort, and the SMR for 25+ years of employment was 15.12 (95 % CI 10.89–20.43).

Conclusions
This uniquely long-term follow up confirms the results of previous analyses, namely the lack of association between exposure to talc with no detectable level of asbestos and lung cancer and mesothelioma. Increased mortality from pneumoconiosis among miners is related to past exposure to silica.

Highlights

- Silica exposure caused pneumoconiosis in talc miners.
- Talc exposure did not increase lung cancer or mesothelioma risk.
- Asbestos-non detected cancer is not carcinogenic.

Keywords: Pneumoconiosis; Lung cancer; Mesothelioma; Talc; Mortality.

1. Introduction

Talc is a natural lamellar structured silicate, widely used in industrial and commercial products as well as for cosmetic and therapeutic purposes. Talc containing asbestos (''fibrous talc") was classified by the International Agency for Research on Cancer (IARC) (International Agency for, 1997; International Agency for, 2010) as a group 1 agent (carcinogenic to humans) while talc with no detectable level of asbestos was classified as a group 3 agent (unclassifiable as to carcinogenicity in humans). Talc use in the perineal area was classified as a group 2B agent (possibly carcinogenic to humans) based on limited evidence of ovarian carcinogenicity.

Other possible carcinogenic effects of talc have been discussed in the literature. A systematic review (Chang et al., 2020) showed a positive association between occupational talc exposure and risk of stomach cancer; however, the association with talc with no detectable level of asbestos was not significant.

Concerning possible carcinogenic effects on the lung and pleura, several studies of workers exposed to talc with no detectable level of asbestos reported no cases of mesothelioma and no excess risk of lung cancer (Wild, 2006; Rubino et al., 1976; Selevan et al., 1979; Wergeland et al., 1990; Wild et al., 2002). Mesothelioma cases have been reported in workers of talc contaminated with asbestos, and a meta-SMR of fourteen cohort studies, including cohorts of workers exposed to asbestos-contaminated talc, was 1.45 (95 % CI: 1.22–1.72) for lung cancer among subjects exposed to talc (Chang et al., 2017). Subgroup analysis for asbestos contamination showed no difference in lung cancer risk between subjects exposed to talc with and without asbestos ($p = 0.9$). Other authors observed occasional excesses of lung cancer risk among miners, not paralleled by comparable results in millers, attributed to co-exposure to radon decay products (Wergeland et al., 1990) or crystalline silica (Thomas and Stewart, 1987).

We aimed at providing additional evidence regarding risk of cancer and non-malignant diseases among miners and millers exposed to talc with no detectable level of asbestos by conducting an updated mortality follow-up of a cohort from Val Chisone, Northern Italy, that has been previously studied (Rubino et al., 1976, 1979; Coggiola et al., 2003; Pira et al., 2017a).

2. Methods

The cohort comprised men employed for at least one month in the mine or the mill between 1946 and 1995. Information on date of birth, date of first employment, date of last employment, last known address and detailed job history were obtained from personnel records at the plant. Miners worked in the mine, either exclusively or in combination with other departments; while millers worked in the mill or in other settings, but not in the mine. In a sample of 200 workers collected in 1993 during a routine medical surveillance the prevalence of current smoking was 47 % among miners and 44 % among millers, and in a 2010 survey of 102 workers the prevalence was 51 % (52 smokers) (Pira et al., 2017a).

The follow-up for mortality started one month after beginning of employment and was conducted by contacting the municipality of residence; death certificates were obtained from the same source and causes of death were coded according to the version of the International Classification of Diseases used at the time of death. The follow-up was truncated when cohort members reached the age of 85 years. For the present analysis the follow-up began on January 1, 1946 or date of first employment, whichever occurred later, and ended on date of last contact, date of death, 85th birthday, or January 31, 2020, whichever occurred earlier.

The analysis was performed on 1749 subjects (1184 miners and 565 millers). The initial database comprised 1822 subjects, We excluded 37 women, and 29 men who ceased work before February 1946, because they did not meet the inclusion criteria. Seven additional subjects were excluded because of inconsistencies between date of last employment and date of death. The number of subjects included in the present analysis ($n = 1749$) is higher than the one in a previous report from

this cohort (n = 1722) (Pira et al., 2017a), because missing values for a few subjects were retrieved. Furthermore, we imputed the missing dates of last employment for two subjects using the cohort's median duration of employment (25 years) and missing dates of death for five subjects (set at 75 years of age).

Miners were exposed to talc, silica, mining gases and radon, and, since 1991, to diesel engine emission, while millers were exposed to talc and silica, as potential contaminant of talc. Diesel engine emissions comprise gases (SO_2, NO_x) and particulate matters, which entail exposure to polycyclic aromatic hydrocarbons (PAHs). In the previous follow up (Pira et al., 2017a) we reported data on environmental measurements of respirable dust, talc and silica for millers during the period 1974–1981 and between 2003 and 2014 for millers and miners. Since 1991 periodical air monitoring of diesel emissions had shown exposure levels lower than threshold limit values (TLVs) for gases and, for PAH, close to 1 ng/m^3, i.e., a level considered acceptable for general population. Underground radon exposure levels, available since 1991, were below 300 Bq/m^3.

The number of expected deaths from all causes, and selected causes was computed using male national and regional death rates for each 5 years calendar period and age group. Regional rates were used for the period 1970–2020, and national death rates for the period 1950–1969. Rates were not available for the period 1946–1949, for which 1950–1954 national rates were used. For the period 2015–2020 rates for 2015–2017 were used. No regional rates were available for cancers of the oral cavity and esophagus up to 1999, and national rates were used instead for these causes. We computed standardized mortality ratios (SMRs) as ratios of observed and expected deaths, and the corresponding 95 % confidence intervals (CIs) were calculated using the exact Poisson distribution for up to 10 observed deaths, and Byar's formula for 10 or more. (Breslow and Day, 1987). We also computed SMRs by year of first employment, duration of employment, and department (miners and millers). Trends in the SMRs were tested using Poisson regression, and the heterogeneity between exposure subgroups (e.g., miners vs. millers) was examined through a χ^2 test (Breslow and Day, 1987).

2.1. Measurement of talc samples

Talc product (massive material) were collected by the contractor from the row material, directly extracted from the mine, before any cleaning and processing technique. Samples arrived in the laboratory of the University of Turin with the request for the qualitative analysis (presence or absence of asbestos fibers) for fibrous content and not for quantitative analysis (Table 4). The overall weight of the product brought each time to the laboratory was 500 g.

The samples from the overall product were collected and prepared for the analysis according to the method indicated by the Ministerial Decree n° 6/9/94, Attachment 1 paragraph B (2B, 3B, 4B, 5B) (Decreto Ministeriale del, 1994).

Analysis were conducted with an Electron Microscope (SEM) model Hitachi TM3000 equipped with SWIFTED 3000 microanalysis with Sprite XY motorized stage and with a COXEM Mod EM30AXPlus compact transportable scanning electron microscope equipped with Ametek Edax model Element microanalysis with 30 sqmm window in Silicon Nitride.

We analyzed 3 portions for every sample and the final result is represented by the arithmetic average of the 3 portions. For the identification of the different asbestos fibers we used the standard reference material NIST, 1866a Bulk Asbestos Common.

The sensitivity can be estimated, considering a Poisson distribution of the fibres, by the following formula:

$$N.fibers(ff\ /\ mg)\ \frac{4*A}{Nc*a*P}$$

Where.

Nc = number of microscope fields observed

a = area of every microscope field.

P = Total weight of the sample on the filter.
The minimum detectable concentration is the concentration for which the average number of asbestos fibers on the observed filter area (n * a) is sufficiently high to allow for a 95 % probability level the lower confidence limit of ≥1 fiber. Considering a 95 % probability level the medium number of fibers should be at least 4 (confidence interval on Poisson's ditribution = 1-10). According to the method the medium level of 4 fibers correspond to a concentration of 1.2×10^4 fibres/mg. The limits of detection for our analysis (based on our field area and the sample weight anlyzed) was calculated accordingly:

$$N.fibers(ff/mg)\ \frac{4*379.9mm^2}{2.54mm^2*0.1mg} = 569(ff/mg)$$

3. Results

The cohort comprised 1749 men (64,349.38 person-years) employed in the mine or the mill between 1946 and 1995. At the end of the follow-up, 321 subjects (18.35 %) were alive, 1346 subjects (76.69 %) were deceased, 90 of whom from an unknown cause, and 82 subjects (4.68 %) were lost to follow-up. The age at death of 172 deceased subjects was older than 85: these subjects were excluded from the mortality analysis.
Results of the mortality follow-up are reported in Table 1. Mortality from all causes was higher than expected (SMR 1.21, 95 % CI 1.14–1.28) while there was no excess of mortality from all cancers (SMR 1.01, 95 % CI 0.89–1.12). No deaths were observed from pleural cancer (2.8 expected deaths); two deaths were observed from peritoneal cancer. After a detailed review of the medical records, we ascertained that the specific causes of the two deaths from peritoneal cancer were one peritoneal carcinomatosis and one retroperitoneal tumor. There were no deaths from either pleural or peritoneal cancer among the subjects deceased after the 85th birthday, who were excluded from the analysis.
On average, the SMR for lung cancer was 1.02 (95 % CI 0.82–1.27). An excess mortality was noticed for oral and pharyngeal cancer (SMR 3.65, 95 % CI 2.52–5.10) and esophageal cancer (SMR 1.91, 95 % CI 1.04–3.21). Increased mortality from non-neoplastic respiratory diseases (SMR 2.09, 95 % CI 1.77–2.45) was also observed mainly due to mortality from pneumoconiosis (SMR 9.58, 95 % CI 7.43–12.08, based on 69 observed deaths). The SMR for non-malignant respiratory diseases, after excluding deaths from pneumoconiosis, was 0.85 (95 % CI 0.68–1.06). The SMR for liver cirrhosis was 1.88 (95 % CI 1.46–2.39), that for cardiovascular diseases was 0.76 (95 % CI 0.62–0.92), and that for cerebrovascular diseases was 0.71 (95 % CI 0.56–0.89).
Results of the mortality analysis for miners and millers are presented in Table 2. Results for all the causes of deaths included in the analysis were consistent in the two groups of workers, with the exception of pneumoconiosis and non malignant respiratory diseases, for which the excess was more marked among miners (SMR 12.75; 95 % CI 9.80–16.31, SMR 2.69; 95 % CI 2.24–3.21) than millers (SMR 2.63; 95 % CI 0.96–5.73, SMR 1.06; 95 % CI 0.71–1.53, p for heterogeneity < 0.0001 for both causes of death).
Results of mortality by duration of employment are presented in Table 3. A trend with duration of employment was not observed for non-neoplastic respiratory diseases (p = 0.23); pneumoconiosis was positively associated with duration of employment (p < 0.0001), while esophageal cancer was negatively associated with it (p = 0.044).

4. Discussion

This updated mortality analysis of a cohort of Italian miners and millers of talc with no detectable level of asbestos confirms the results of previous analyses (Table 5) (Rubino et al., 1976; Coggiola et al., 2003; Pira et al., 2017a). No association between exposure to talc with no detectable level of

asbestos and cancers of the lung, pleura or peritoneum was found. Our cohort does not include female workers. Therefore, our study is not informative as of possible association between talc exposure and risk of ovarian cancer. Mortality from pneumoconiosis was increased, in particular in miners; mortality from several alcohol-related conditions was also increased in the cohort.
Rubino and colleagues (Rubino et al., 1976) reported dust levels in this mine from 1946 to 1976, and showed a progressive decrease for total respirable dust exposure among miners (from a range 100–1000 million particles per cubic foot [mmpcf] before 1955 to less than 10 mmpcf between 1960 and 1975). They estimated higher exposure to silica among miners, owing to drilling and other operations in footwall rocks with high content of quartz (Coggiola et al., 2003). In the case of millers, dust comprises almost exclusively talc.
The issue of a possible contamination with asbestos of talc from Val Chisone was discussed in previous reports of this cohort (Rubino et al., 1976, 1979), and elsewhere (Pira et al., 2017b). Asbestos or asbestiform fibers were not detected in the talc mined and processed in Val Chisone (Rubino et al., 1976, 1979; Pooley, 1973; Verdel et al., 1983; Parkes, 1994). Some recent allegations of possible contamination by asbestos (Gordon et al., 2014; Finkelstein, 2017, 2019) were not supported by empirical evidence (Pira et al., 2017b; Geyer, 2019). The results of the analyses of additional samples collected between 2017 and 2020 confirm that talc from Val Chisone is pure talc with no detectable level of asbestos (Table 4).
Throughout the follow-up of this cohort there were no deaths from pleural cancer or peritoneal mesothelioma, nor an excess mortality from lung cancer in either miners or millers. These data confirm that exposure to talc with no detectable level of asbestos is not associated with risk of these diseases. In the present analysis almost 20 % of the subjects, contributing 11,596 person-years of observation, had been followed for more than 40 years since first employment, providing evidence against the hypothesis that the lack of deaths from mesothelioma can be attributed to an insufficiently long latency.
Data on tobacco smoking in this cohort were obtained from two surveys of limited groups of workers conducted in 1993 and 2000 during health surveillance; in both surveys the prevalence of current smokers was similar to that of men in Italy in the same period (Pagano et al., 1996). Therefore, these data do not support the hypothesis of a substantially lower prevalence of smoking in this cohort compared to the reference population, which might mask an increased risk of lung cancer. This conclusion is reinforced by the lack of increase in mortality from chronic obstructive pulmonary disease, another condition strongly associated with tobacco smoking.
The excess mortality from oral and pharyngeal cancer (SMR 3.65, 95 % CI 2.52–5.10) and esophageal cancer (SMR 1.91, 95 % CI 1.04–3.21) and from liver cirrhosis (SMR 1.88, 95 % CI 1.46–2.39) confirms the results of earlier reports of this cohort (Rubino et al., 1976; Coggiola et al., 2003; Pira et al., 2017a), and is likely related to increased alcohol consumption (Boffetta and Hashibe, 2006). The inverse association between esophageal cancer mortality and duration of employment might be due to chance, or subsequent to competing mortality from alcohol-related diseases. The excess mortality from non-malignant respiratory diseases is predominantly due to the high number of deaths from pneumoconiosis.
Crystalline silica is classified as human carcinogen (International Agency for, 1997), but the presence of an excess lung cancer risk in the absence of confirmed silicosis remains open to discussion (Pelucchi et al., 2006; Poinen-Rughooputh et al., 2016; Erren et al., 2011; Kurihara and Wada, 2004). The data of our study support the hypothesis that exposure level required to exert a carcinogenic effect are higher than those required for silicosis development, since we observed a high number of deaths from silicosis (69 observed vs. 2.6 expected), in the absence of an excess risk for lung cancer. It is possible that the excess risk of lung cancer observed in cohorts of silicosis patients (Leung et al., 2012; Hnizdo et al., 1993) is related to higher exposure levels than those required to cause silicosis, typically in the range of 0.1 mg/m^3 (Morfeld et al., 2013). Consequently occupational exposure limit values able to prevent silicosis would also prevent an excess risk of lung cancer, as it has been proposed by the Scientific Committee on Occupational Exposure Limit Values of the European

Commission (Scientific Committee on O, 2003). Deaths from pneumoconiosis observed among miners from this cohort and, to a lesser extent, among millers are therefore attributable to high silica exposure in the past, when rock drilling activities were frequent and technical prevention means had not yet been introduced (Rubino et al., 1976). It should be also noted that no deaths from pneumoconiosis were observed among workers first employed after 1969, and no new cases of silicosis were observed during medical surveillance since 1991 (M. Coggiola, personal communication).

Among other exposures of miners in this cohort are radon and diesel engine exhaust. Use of diesel engines started in 1991. Although the number of miners with sufficiently long latency is not large, the results provide no support to the hypothesis of a risk of lung cancer from diesel exhaust exposure in this cohort of underground non-metal miners. Radon exposure levels were consistently below 300 Bq/m^3.

Strengths of our study include the large size of the cohort, the uniquely long follow-up that allows separate analyses by job title, detailed considerations of latency and other time-related factors, the presence of data on exposure levels in the early period of operation of the plant (Rubino et al., 1976), that are consistent with the new sampling data, and the availability of some data on smoking prevalence. Limitations include the lack of individual exposure data, the lack of detailed information on potential confounders (e.g., alcohol drinking), the lack of validation of causes of death, and of information on morbidity. The relatively large proportions of subjects lost to follow-up (4.7 %) and of deceased subjects with unknown cause of death (6.7 %) are additional limitations.

In conclusion, we confirmed previous results on lack of an association between exposure to talc with no detectable level of asbestos and lung cancer and malignant mesothelioma. Mortality from non-malignant respiratory diseases was increased in these workers, which can likely be attributed to past exposure to silica. The absence of a parallel excess mortality from lung cancer does not support the hypothesis of an association between silica exposure and the development of lung cancer, in the absence of silicosis (Leung et al., 2012).

Credit author statament

Design of the study: CC, EP, MC, PB. Collection of data: CC, NF, AG. Statistical analysis: CLV, EN.First draft of the manuscript: CC, PB. Critical review of the manuscript: MC, NF, AG, CLV, EN.
Approval of the manuscript: All authors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table 1. Standardized mortality ratio for selected causes among miners and millers exposed to talc with no detectable level of asbestos.

Cause of deaths	ICD	Obs	Exp	SMR (95 % CI)
All causes	1–999	1174	969.6	1.21 (1.14–1.28)
All cancers	140–239	304	303.5	1.00 (0.89–1.12)
Oral & pharyngeal cancer	140–149	34	9.3	3.65 (2.53–5.10)
Esopageal cancer	150	14	7.3	1.92 (1.05–3.22)
Stomach cancer	151	37	32.0	1.15 (0.81–1.59)
Colorectal cancer	152-154, 159.0	31	32.6	0.95 (0.65–1.35)
Liver cancer	155	18	13.4	1.34 (0.80–2.12)
Pancreas cancer	157	11	11.9	0.93 (0.46–1.66)
Peritoneal cancer	158	2	1.4	1.43 (0.17–5.15)
Laryngeal cancer	161	8	8.7	0.92 (0.40–1.81)
Lung cancer	162	85	83.0	1.02 (0.82–1.27)
Pleural cancer	163	0	2.8	–
Prostate cancer	185	15	18.8	0.80 (0.45–1.32)
Bladder cancer	188	3	13.3	0.23 (0.05–0.66)
Kidney cancer	189	5	6.2	0.80 (0.26–1.87)
Brain & CNS cancer	191–192	5	7.1	0.70 (0.23–1.64)
LHN	200–208	13	20.2	0.64 (0.34–1.10)
Lymphoma	200–202	4	8.1	0.49 (0.13–1.27)
Mieloma	204–208	0	3.5	–
Leukemia	410–414	9	8.7	1.04 (0.47–1.97)
Ischemic heart disease	430–438	105	138.6	0.76 (0.62–0.92)
Cerebrovascular disease	490–496	74	104.5	0.71 (0.56–0.89)
Non neoplastic respiratory diseases	460–519	152	72.5	2.10 (1.78–2.46)
COPD	500–508	40	43.3	0.92 (0.66–1.26)
Pneumoconiosis	460-496, 510-519	69	7.2	9.55 (7.43–12.1)
Liver cirrhosis	571	68	36.1	1.88 (1.46–2.39)
External causes	800–999	62	56.3	1.10 (0.84–1.41)

CI, confidence interval; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; Exp, expected deaths; ICD-IX, International Classification of Diseases, 9th version; LHN, lymphohematopoetic neoplasms; Obs, observed deaths; SMR, standardized mortality ratio.

Table 2. Standardized mortality ratio for selected causes stratified by department of employment[a].

	Miners			**Millers**			**p-value[b]**
Cause of deaths	**Obs**	**Exp**	**SMR (95 % CI)**	**Obs**	**Exp**	**SMR (95 % CI)**	Empty Cell
All causes	789	629.1	1.25 (1.17–1.34)	385	340.5	1.13 (1.02–1.25)	0.10
All cancers	205	201.1	1.02 (0.88–1.17)	99	102.4	0.97 (0.79–1.18)	0.71
Oral & pharyngeal cancer	25	6.2	4.06 (2.62–5.99)	9	3.1	2.86 (1.31–5.43)	0.47
Esophageal cancer	11	4.8	2.30 (1.14–4.11)	3	2.5	1.20 (0.25–3.49)	0.46
Lung cancer	56	55.7	1.01 (0.76–1.31)	29	27.3	1.06 (0.71–1.52)	0.91
Ischemic heart disease	64	89.1	0.72 (0.55–0.92)	41	49.5	0.83 (0.59–1.12)	0.54
Cerebrovascular disease	47	65.5	0.72 (0.53–0.95)	27	39.0	0.69 (0.46–1.01)	0.98
Non-neoplastic respiratory diseases	124	46.1	2.69 (2.24–3.21)	28	26.4	1.06 (0.71–1.53)	<0.0001
Pneumoconiosis	63	4.9	12.75 (9.80–16.31)	6	2.3	2.63 (0.96–5.73)	<0.0001
Liver cirrhosis	46	23.6	1.95 (1.43–2.60)	22	12.5	1.76 (1.10–2.66)	0.78

CI, confidence interval.
Exp, expected deaths.
Obs, observed deaths.
SMR, standardized mortality ratio.
[a]See text for definition of department of employment.
[b]p-value of test for heterogeneity between departments.

Table 3. Standardized mortality ratio for selected causes stratified by duration of employment.

Cause of deaths	Duration of employment						p-value[a]
	<15 years		15–24 years		25+ years		
	Obs	SMR (95 % CI)	Obs	SMR (95 % CI)	Obs	SMR (95 % CI)	
All causes	430	1.27 (1.15–1.40)	331	1.21 (1.08–1.35)	413	1.15 (1.05–1.27)	0.17
All cancers	116	1.06 (0.88–1.28)	72	0.91 (0.71–1.15)	116	1.01 (0.83–1.21)	0.67
Oral & pharyngeal cancer	15	4.44 (2.48–7.32)	6	2.42 (0.89–5.27)	13	3.76 (2.00–6.44)	0.65
Esophageal cancer	8	3.14 (1.35–6.18)	4	2.04 (0.55–5.21)	2	0.72 (0.09–2.59)	0.044
Lung cancer	31	1.03 (0.70–1.46)	18	0.87 (0.52–1.38)	36	1.12 (0.78–1.55)	0.72
Ischemic heart disease	41	0.89 (0.64–1.21)	28	0.69 (0.46–1.00)	36	0.69 (0.48–0.96)	0.26
Cerebrovascular disease	25	0.77 (0.50–1.14)	15	0.47 (0.26–0.78)	34	0.84 (0.58–1.17)	0.65
Non-neoplastic respiratory diseases	42	1.79 (1.29–2.42)	47	2.19 (1.61–2.91)	63	2.29 (1.76–2.92)	0.23
Pneumoconiosis	11	4.19 (2.09–7.50)	16	8.78 (5.02–14.3)	42	15.1 (10.9–20.4)	<0.0001
Liver cirrhosis	22	1.75 (1.10–2.65)	28	2.70 (1.79–3.90)	18	1.37 (0.81–2.17)	0.47

CI, confidence interval.
Obs, observed deaths.
SMR, standardized mortality ratio.
[a]p-value of test for linear trend.

Table 4. Results of analysis of talc samples collected between 2017 and 2020[a].

Collection date	Analysis date	Sample ID	Extern denomination	Results	Method
January 01, 2017	August 08, 2018	I-3205	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
January 01, 2017	August 08, 2018	I-3206	Talco Extra A	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
January 01, 2017	August 08, 2018	I-3207	Talco Prever M10	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
February 01, 2017	August 07, 2018	I-2424	Talco Steasilck 5CI	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
February 01, 2017	August 07, 2018	I-2426	Talco Extra D	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
April 01, 2017	September 12, 2017	H-3197	Talco Luzenac Pharma	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
July 01, 2017	August 07, 2018	I-2427	Talco Extra 5/0 DEC	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
July 01, 2017	August 08, 2018	I-3203	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
July 01, 2017	August 08, 2018	I-3204	Talco Extra D	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
August 01, 2017	August 07, 2018	I-2423	Talco Extra A	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
September 01, 2017	August 07, 2018	I-2425	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
September 01, 2017	July 17, 2018	I-1411	Talco Extra 510	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
October 01, 2017	July 17, 2018	I-1412	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
November 01, 2017	July 17, 2018	I-1413	Talco Steasilck 5CI	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
January 01, 2018	July 17, 2018	I-1414	Talco Extra A	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
January 01, 2018	July 17, 2018	I-1415	Talco Extra 510	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
March 01, 2018	August 07, 2018	I-2422	Talco Extra A/S	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
May 01, 2018	August 08, 2018	I-3202	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994

Collection date	Analysis date	Sample ID	Extern denomination	Results	Method
September 01, 2018	December 07, 2018	I-5453	Talco Extra A/S	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
September 01, 2018	December 07, 2018	I-5452	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
April 01, 2019	September 06, 2019	L-2471	Talco Luzenac Pharma	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
April 01, 2019	September 06, 2019	L-2472	Talco Extra 5/0	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
April 01, 2019	September 06, 2019	L-2473	Talco Extra A/S	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
July 01, 2020	September 01, 2020	M-2121	Talco Luzenac Pharma	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994
July 01, 2020	September 01, 2020	M-2122	Talco Extra DM30	No asbestos fibers detected	SEM + EDAX - All. 1B, D.M. September 06, 1994

[a]See text for details on collection and analytical methods.

Table 5. Standardized mortality ratios for selected causes in subsequent follow-ups of the cohort, by department (Rubino et al., 1976; Coggiola et al., 2003; Pira et al., 2017a).

	Follow-up to 1974 (Rubino et al., 1976)		**Follow-up to 1995 (Coggiola et al., 2003)**		**Follow-up to 2013 (Pira et al., 2017a)**		**Follow-up to 2020[a]**	
Cause of deaths	**Miners**	**Millers**	**Miners**	**Millers**	**Miners**	**Millers**	**Miners**	**Millers**
All cancers	0.77 (0.64–0.96)	0.92 (0.66–1.24)	1.08 (0.90–1.28)	0.83 (0.63–1.09)	1.10 (0.95–1.27)	0.93 (0.74–1.16)	1.02 (0.88–1.17)	0.97 (0.79–1.18)
Oral & pharyngeal cancer	–	–	6.12 (3.92–9.10)	3.33 (1.33–6.86)	4.53 (2.93–6.69)	2.47 (0.99–5.09)	4.06 (2.62–5.99)	2.86 (1.31–5.43)
Esophageal cancer	1.25 (0.7–2.07)	1.35 (0.54–2.77)	2.32 (0.93–4.78)	1.79 (0.36–5.23)	2.55 (1.27–4.57)	1.32 (0.27–3.86)	2.30 (1.14–4.11)	1.20 (0.25–3.49)
Lung cancer	0.46 (0.21–0.87)	0.62 (0.16–1.57)	1.07 (0.73–1.50)	0.69 (0.34–1.23)	1.07 (0.80–1.40)	0.96 (0.61–1.44)	1.01 (0.76–1.31)	1.06 (0.71–1.52)
Non-neoplastic respiratory diseases	–	–	3.05 (2.50–3.69)	1.03 (0.65–1.57)	2.94 (2.44–3.52)	1.13 (0.74–1.64)	2.69 (2.24–3.21)	1.06 (0.71–1.53)
Pneumoconiosis	2.01 (1.53–2.57)	1.43 (0.29–4.17)	–	–	38.7 (29.7–49.5)	6.23 (2.29–13.6)	12.7 (9.80–16.31	2.63 (0.96–5.73)
Liver cirrhosis	–	–	1.80 (1.27–2.49)	1.68 (1.00–2.66)	1.86 (1.34–2.53)	1.87 (1.17–2.84)	1.95 (1.43–2.60)	1.76 (1.10–2.66)

[a]This report 95 % confidence intervals in parentheses Results with $p < 0.05$ are reported in bold.