An Update of a Mortality Study of Talc Miners and Millers in Italy

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Background While talc containing asbestiform fibers is considered a human carcinogen, only limited animal and human data are available on non-asbestiform talc. To provide further evaluation on the issue, we updated the analysis of an Italian cohort of talc miners and millers in Val Chisone; talc found here is free from asbestiform fibers.

Methods The cohort was comprised of 1,795 men who had worked for at least 1 year in the mine and/or in the factory between 1946 and 1995. Vital status and death certificates were obtained from registration offices in the municipality of death or of birth. Employment, termination of employment, and detailed job history were obtained from personnel records at the plant.

Results No excess was found for total cancer mortality, nor mortality for lung cancer. No case of mesothelioma was reported. There was a significant excess mortality from non-neoplastic respiratory diseases (SMR 228.2, 95% CI 190.2–271.5). Mortality excess for non-neoplastic respiratory diseases was mainly due to silicosis.

Conclusions This study provides additional support for an association between talc in mining and milling and non-neoplastic respiratory diseases, while showing no significant excess risk for lung cancer and mesothelioma. The results also provide additional information of interest to evaluate the potential association between silica and lung cancer. Am. J. Ind. Med. 44:63–69, 2003. © 2003 Wiley-Liss, Inc.

KEY WORDS: cohort mortality study; talc; silica; miners and millers; mesothelioma; lung cancer _____



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INTRODUCTION

Talc is a silicate with a lamellar structure that can be contaminated with other minerals including asbestiform fibers. That is the reason why a former definition was "fibrous talc."

While talc containing asbestiform fibers is considered a human carcinogen [IARC, 1997], only limited animal and human data are available on the potential carcinogenic effect of non-asbestiform talc.

Lung cancer and pleural mesothelioma have been the main sites considered in occupational cohort studies of non-asbestiform talc. Of these, three showed no excess risk. A historical cohort study of 1992 talc miners and millers in Italy followed between 1946 and 1974 showed a standardized mortality ratio (SMR) of 47 among miners and 66 among millers for lung cancer, and no cases of pleural mesothelioma

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[Rubino et al., 1976, 1979]. A study of 392 workers from Vermont, US [Selevan et al., 1979] and one of 389 workers from Norway [Wergeland et al., 1990] found no excess risk for millers, but some excess for miners, which may however be related to radon exposure. A study of 2,055 pottery workers from the US, in contrast, showed an excess lung cancer mortality (relative risk (RR): 2.5) among workers exposed to non-fibrous talc plus silica [Thomas and Stewart, 1987].

To provide further evaluation on the issue, we updated the analysis of the Italian cohort of talc miners and millers in Val Chisone, Turin [Rubino et al., 1976, 1979], in which the talc was free from asbestiform fibers [Verdel et al., 1983; Parkes, 1994]. The large size of the cohort and the uniquely long follow-up allow separate analyses by job title, besides detailed considerations of latency and other time factors. The presence of data on exposure levels between 1946 and 1975 [Rubino et al., 1976] and between 1990 and 1995 allow further considerations.

SUBJECTS AND METHODS

The cohort was comprised of 1,974 men who had worked for at least 1 year in the mine and/or in the factory between 1946 and 1995. After exclusion of 179 men with no follow-up information, the analyses were based on 1,795 subjects (90.9% of the total).

Dates of birth, employment and termination of employment, the last known address and detailed job history were obtained from personnel records at the plant. No information was available on smoking habits. Death certificates were obtained from registration offices in the municipality of death.

Further verification of vital status was obtained from registries of current residence.

For the present analysis, the follow-up began 1 January 1946 and ended at 31 December 1995. A total of 880 deaths and 50,701 man-years were documented.

DATA ANALYSIS

The expected number of deaths from all causes, selected cancer sites and other selected non-neoplastic conditions were computed using national and regional death rates for each 5 year calendar period and age group. Regional rates were provided by the Regional Cancer Register of Piedmont for the period 1970–95, and national death rates were used before 1970. Rates for the early 1950s were applied to the period 1946–49. No regional rates for cancers of the oral cavity and esophagus and for suicides were available; national rates were also used after 1970.

We computed SMRs (SMR = observed/expected \times 100) and the corresponding 95% confidence intervals (CI) [Breslow and Day, 1987]. We also computed observed and expected numbers by year of first employment, duration of employment, and type of job (miners and millers). Miners

(n = 1,244) were all men who worked in the mine only, or with mixed exposure in the mine and in the plant. The job category defined as "millers" comprised millers and other workers of the plant only (n = 551).

RESULTS

Table I gives observed and expected death and the corresponding SMR for all causes of death, selected cancer sites and other major non-neoplastic causes of death. Total mortality was significantly higher than expected (880 observed vs. 735 expected, SMR 119.7, 95% CI 111.9–127.9).

There was no excess mortality for all cancers (185 observed, 186.5 expected, SMR 99.2, 95% CI 85.4–114.5). No deaths were seen from pleural or peritoneal mesotheliomas, and there was no excess deaths from lung cancer (44 observed, 46.9 expected, SMR 93.8, 95% CI 68.1–125.9).

A significant excess mortality was found from oral cavity cancer (31 observed vs. 6 expected, SMR 514.4, 95% CI 349.4–730.1) and esophageal cancer (10 observed,

TABLE I. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946—1995

| | OBS | EXP | SMR | 95% CI | | |
|----------------------------|-----|-------|-------|--------|--------|--|
| All causes | 880 | 735 | 119.7 | 111.9 | 127.9 | |
| All cancers | 185 | 186.5 | 99.2 | 85.4 | 114.5 | |
| Oral cavity | 31 | 6 | 514.4 | 349.4 | 730.1 | |
| Esophagus | 10 | 4.7 | 212.9 | 101.9 | 391.6 | |
| Stomach | 31 | 26.8 | 115.5 | 78.5 | 164 | |
| Intestines | 13 | 19.9 | 65.4 | 34.8 | 111.8 | |
| Liver and gall bladder | 10 | 8.6 | 116.6 | 55.8 | 214.5 | |
| Pancreas | 7 | 6.2 | 112.7 | 45.2 | 232.3 | |
| Peritoneum | 0 | 0.9 | 0 | 0 | 393.8 | |
| Larynx | 8 | 7 | 115 | 49.5 | 226.7 | |
| Lung | 44 | 46.9 | 93.8 | 68.1 | 125.9 | |
| Pleura | 0 | 1.8 | 0 | 0 | 206.9 | |
| Connectival sarcoma | 1 | 0.2 | 469 | 6.1 | 2609.3 | |
| Skin | 3 | 1.6 | 183.1 | 36.8 | 535 | |
| Prostate | 6 | 10.5 | 57.3 | 20.9 | 124.7 | |
| Bladder | 1 | 8.7 | 11.5 | 0.2 | 64 | |
| Kidney | 1 | 2.9 | 33.9 | 0.4 | 188.9 | |
| Non Hodgkin lymphomas | 2 | 2.9 | 69.7 | 7.8 | 251.8 | |
| Hodgkin's disease | 0 | 1.8 | 0 | 0 | 204.7 | |
| Leukemia | 5 | 7 | 71.7 | 23.1 | 167.4 | |
| Diabetes | 5 | 11.0 | 45.3 | 14.6 | 105.8 | |
| Cardiovascular diseases | 288 | 309.2 | 93.2 | 82.7 | 104.6 | |
| Ischemic heart disease | 88 | 101.6 | 86.6 | 69.5 | 106.7 | |
| Cerebrovascular disease | 60 | 90.2 | 66.5 | 50.8 | 85.7 | |
| Respiratory tract diseases | 127 | 55.7 | 228.2 | 190.2 | 271.5 | |
| Digestive tract diseases | 79 | 55.5 | 142.2 | 112.6 | 177.3 | |
| Cirrhosis | 55 | 31.2 | 176.3 | 132.8 | 229.4 | |
| Injuries | 49 | 49.2 | 99.6 | 73.7 | 131.7 | |

4.7 expected, SMR 212.9, 95% CI 101.9–391.6). There was a non-significant excess mortality from stomach cancer (31 observed, 26.8 expected, SMR 115.5, 95% CI 78.5–164).

With reference to non-neoplastic causes of death, there was a significant excess mortality from respiratory tract diseases (127 observed, 55.7 expected, SMR 228.2, 95% CI 190.2–271.5), from digestive tract diseases (79 observed, 55.5 expected, SMR 142.2, 95% CI 112.6–177.3), and from liver cirrhosis (55 observed, 31.2 expected, SMR 176.3, 95% CI 132.8–229.4). Mortality excess for non-neoplastic respiratory diseases was mainly due to silicosis (62 deaths). In fact, excluding silicosis from deaths for non-malignant respiratory disease, the SMR was 116.6 (95% CI 97.1–138.5). The SMR was 93.2 for cardiovascular disease, 86.6 for ischemic heart disease, 66.5 for cerebrovascular disease. For 62 subjects, the cause of death was unknown or undefined.

The excess mortality from cancers of the oral cavity and esophagus, digestive tract disease, and liver cirrhosis was similar for miners and millers. Conversely the excess in all causes mortality and particularly respiratory tract diseases were confined to miners only.

Table II gives corresponding stratified analysis for miners and millers.

The excess risk for miners is attributable to silicosis (58 silicosis observed in miners compared to 4 in millers). No increase in mortality from lung cancer was seen in miners or millers.

Table III shows mortality by duration of exposure. For lung cancer, no significant increase in mortality was found in the four duration levels (less than 10 years—SMR 135.8, between 10 and 19 years—SMR 66.7, between 20 and 29 years—SMR 94.1, over 30 years—SMR 73.2). For oral cavity cancer, the SMR was significantly elevated in the exposure category under 20 years and over 30 years, and for esophageal cancer a significant SMR was seen in the group between 10 and 19 years of exposure, in the absence, however, of any trend in risk with duration. The excess in

TABLE II. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946—1995 by Job Category

| | | | Miners | | Millers | | | | | | | |
|----------------------------|-----|-------|--------|--------|---------|-----|-------|-------|-------|--------|--|--|
| | OBS | EXP | SMR | 95% CI | | OBS | EXP | SMR | 95 | % CI | | |
| All causes | 590 | 466.8 | 126.4 | 116.4 | 137 | 290 | 268.3 | 108.1 | 96 | 121.3 | | |
| All cancers | 130 | 120.6 | 107.8 | 90.1 | 128 | 55 | 65.6 | 83.4 | 62.8 | 108.6 | | |
| Oral cavity | 24 | 3.9 | 611.8 | 391.8 | 910.3 | 7 | 2.1 | 332.7 | 133.3 | 685.6 | | |
| Esophagus | 7 | 3 | 231.9 | 92.9 | 477.8 | 3 | 1.7 | 178.8 | 35.9 | 522.5 | | |
| Stomach | 20 | 16.8 | 119.2 | 72.8 | 184.1 | 11 | 10.1 | 109.4 | 54.5 | 195.7 | | |
| Intestines | 11 | 12.9 | 85.5 | 42.6 | 152.9 | 2 | 7 | 28.5 | 3.2 | 102.8 | | |
| Liver and gall bladder | 4 | 5.4 | 73.7 | 19.8 | 188.6 | 6 | 3.1 | 190.8 | 68.7 | 415.3 | | |
| Pancreas | 4 | 4.1 | 98.7 | 26.5 | 252.6 | 3 | 2.2 | 139.2 | 28 | 406.7 | | |
| Peritoneum | 0 | 0.6 | 0 | 0 | 599.6 | 0 | 0.3 | 0 | 0 | 1147.1 | | |
| Larynx | 7 | 4.5 | 154.1 | 61.7 | 317.6 | 1 | 2.4 | 41.4 | 0.5 | 230.6 | | |
| Lung | 33 | 30.9 | 106.7 | 73.4 | 149.9 | 11 | 16 | 68.8 | 34.3 | 123 | | |
| Pleura | 0 | 1.2 | 0 | 0 | 312 | 0 | 0.6 | 0 | 0 | 614.6 | | |
| Connectival sarcoma | 1 | 0.1 | 699.2 | 9.1 | 3890.3 | 0 | 0.1 | 0 | 0 | 5224.2 | | |
| Skin | 2 | 1.1 | 188.2 | 21.1 | 679.4 | 1 | 0.6 | 173.8 | 2.3 | 966.7 | | |
| Prostate | 3 | 6.5 | 46 | 9.2 | 134.4 | 3 | 4 | 75.3 | 15.1 | 220.1 | | |
| Bladder | 0 | 5.6 | 0 | 0 | 65.9 | 1 | 3.1 | 31.9 | 0.4 | 177.5 | | |
| Kidney | 1 | 2.2 | 46.3 | 0.6 | 257.7 | 0 | 1.1 | 0 | 0 | 327.2 | | |
| Non Hodgkin lymphomas | 0 | 1.9 | 0 | 0 | 192.9 | 2 | 1 | 206.9 | 23.2 | 747.1 | | |
| Hodgkin's disease | 0 | 1.2 | 0 | 0 | 302.6 | 0 | 0.6 | 0 | 0 | 632.8 | | |
| Leukemias | 4 | 4.6 | 87.8 | 23.6 | 224.7 | 1 | 2.4 | 41.4 | 0.5 | 230.5 | | |
| Diabetes | 2 | 7 | 28.7 | 3.2 | 103.5 | 3 | 4.1 | 74 | 14.9 | 216.2 | | |
| Cardiovascular diseases | 177 | 192.8 | 91.8 | 78.8 | 106.4 | 111 | 116.4 | 95.4 | 78.5 | 114.9 | | |
| Ischemic heart disease | 56 | 64.7 | 86.5 | 65.3 | 112.3 | 32 | 36.9 | 86.8 | 59.4 | 122.6 | | |
| Cerebral vasculopathy | 42 | 55.5 | 75.7 | 55.5 | 102.3 | 18 | 34.7 | 51.9 | 30.7 | 82 | | |
| Respiratory tract diseases | 105 | 34.4 | 305.2 | 249.6 | 369.5 | 22 | 21.3 | 103.5 | 64.8 | 156.7 | | |
| Digestive tract diseases | 50 | 36 | 138.9 | 103.1 | 183.1 | 29 | 19.5 | 148.4 | 99.4 | 213.2 | | |
| Cirrhosis | 37 | 20.5 | 180.3 | 127 | 248.6 | 18 | 10.7 | 168.4 | 99.8 | 266.2 | | |
| Injuries | 34 | 33.2 | 102.4 | 70.9 | 143.1 | 15 | 16 | 93.8 | 52.5 | 154.7 | | |

TABLE III. Total Mortality and Selected Causes of Death in a Cohort of Talc Miners and Millers in Val Chisone, Italy, 1946—1995 by Duration of Exposure

| | <10 years (n = 519) | | | | 10 – 19 years (n = 421) | | | | 20–29 years (n = 504) | | | | \geq 30 years (n $=$ 351) | | | |
|----------------------------|---------------------|-------|-------|--------|-------------------------|-------|-------|--------|-----------------------|-------|-------|--------|-----------------------------|--------|-------|---------|
| | OBS | SMR | 95 | % IC | OBS | SMR | 95 | % IC | OBS | SMR | 95 | % IC | OBS | SMR | 95 | % IC |
| All causes | 212 | 134.7 | 117.2 | 154.1 | 221 | 138.2 | 120.6 | 157.7 | 300 | 112.6 | 100.2 | 126.1 | 147 | 97.2 | 82.1 | 114.2 |
| All cancers | 47 | 113.6 | 83.4 | 151.1 | 50 | 130.6 | 96.9 | 172.2 | 53 | 80.7 | 60.4 | 105.5 | 35 | 85 | 59.2 | 118.3 |
| Oral cavity | 10 | 713.5 | 341.6 | 1312.2 | 11 | 846.6 | 422.0 | 1514.9 | 5 | 244 | 78.6 | 569.4 | 5 | 391.6 | 126.2 | 913.8 |
| Esophagus | 2 | 198.6 | 22.3 | 717.1 | 4 | 399.1 | 107.4 | 1021.9 | 4 | 241.3 | 64.9 | 617.7 | 0 | 0 | 0 | 356.3 |
| Stomach | 4 | 77.3 | 20.8 | 197.9 | 9 | 141.7 | 64.7 | 269.1 | 10 | 101.2 | 48.4 | 186.1 | 8 | 147.4 | 63.5 | 290.5 |
| Intestines | 3 | 70.1 | 14.1 | 204.9 | 4 | 110.0 | 29.6 | 281.6 | 3 | 41.4 | 8.3 | 120.9 | 3 | 63.5 | 12.8 | 185.5 |
| Liver and gall bladder | 2 | 110.4 | 12.4 | 398.7 | 5 | 247.7 | 79.8 | 578.1 | 2 | 66.7 | 7.5 | 240.7 | 1 | 57.3 | 0.7 | 319 |
| Pancreas | 0 | 0 | 0 | 258.0 | 3 | 245.0 | 49.2 | 715.8 | 0 | 0 | 0 | 1170.6 | 0 | 0 | 0 | 1899.3 |
| Peritoneum | 0 | 0 | 0 | 1598.4 | 0 | 0 | 0 | 1875.2 | 2 | 93.4 | 10.5 | 337.1 | 2 | 140.8 | 15.8 | 508.3 |
| Larynx | 2 | 126.6 | 14.2 | 457.1 | 0 | 0 | 0 | 256.3 | 5 | 207.3 | 66.8 | 483.8 | 1 | 65.3 | 0.9 | 363.2 |
| Lung | 15 | 135.8 | 75.9 | 223.9 | 6 | 66.7 | 24.4 | 145.3 | 15 | 94.1 | 52.6 | 155.2 | 8 | 73.2 | 31.5 | 144.2 |
| Pleura | 0 | 0 | 0 | 857.6 | 0 | 0 | 0 | 1195.2 | 0 | 0 | 0 | 600.7 | 0 | 0 | 0 | 858.4 |
| Skin | 0 | 0 | 0 | 902.1 | 2 | 545.8 | 61.3 | 1970.7 | 1 | 183.3 | 2.4 | 1019.7 | 0 | 0 | 0 | 1147.6 |
| Connectival sarcoma | 0 | 0 | 0 | 6222.6 | 0 | 0 | 0 | 8646.7 | 0 | 0 | 0 | 5460 | 1 | 2238.1 | 29.3 | 12452.4 |
| Prostate | 0 | 0 | 0 | 199.8 | 1 | 50.7 | 0.7 | 281.8 | 2 | 47.9 | 5.4 | 173 | 3 | 119 | 23.9 | 347.6 |
| Bladder | 1 | 57.3 | 0.7 | 318.6 | 0 | 0 | 0 | 227.4 | 0 | 0 | 0 | 112.7 | 0 | 0 | 0 | 175.9 |
| Kidney | 0 | 0 | 0 | 461.5 | 0 | 0 | 0 | 571.8 | 1 | 91.3 | 1.2 | 507.8 | 0 | 0 | 0 | 490.5 |
| Non Hodgkin lymphomas | 0 | 0 | 0 | 475.4 | 1 | 161.3 | 2.1 | 897.2 | 1 | 109.6 | 1.4 | 609.6 | 0 | 0 | 0 | 651.2 |
| Hodgkin's disease | 0 | 0 | 0 | 632.6 | 0 | 0 | 0 | 771.9 | 0 | 0 | 0 | 728.1 | 0 | 0 | 0 | 1572.6 |
| Leukemias | 3 | 175.9 | 35.4 | 514.0 | 1 | 69.6 | 0.9 | 387.0 | 0 | 0 | 0 | 153.5 | 1 | 69.6 | 0.9 | 387 |
| Diabetes | 1 | 46.1 | 0.6 | 256.8 | 1 | 45.6 | 0.6 | 253.7 | 3 | 72.5 | 14.6 | 211.7 | 0 | 0 | 0 | 145 |
| Cardiovascular diseases | 66 | 113.4 | 87.7 | 144.3 | 70 | 107.1 | 83.5 | 135.3 | 108 | 91 | 74.6 | 109.9 | 44 | 65.7 | 47.8 | 88.2 |
| Cerebral vasculopathy | 11 | 69.2 | 34.5 | 123.9 | 13 | 68.6 | 36.5 | 117.3 | 24 | 67.5 | 43.2 | 100.4 | 12 | 60.7 | 31.3 | 106.1 |
| Respiratory tract diseases | 23 | 225.3 | 142.7 | 338.0 | 27 | 223.3 | 147.1 | 324.9 | 53 | 246 | 184.3 | 321.8 | 24 | 203.1 | 130.1 | 302.2 |
| Digestive tract diseases | 18 | 139.0 | 82.4 | 219.8 | 22 | 174.7 | 109.4 | 264.4 | 22 | 114.3 | 71.6 | 173 | 17 | 158.2 | 92.1 | 253.3 |
| Cirrhosis | 13 | 173.6 | 92.4 | 296.9 | 17 | 250.1 | 145.6 | 400.4 | 15 | 140.6 | 78.7 | 232 | 10 | 159.9 | 76.6 | 294.1 |
| Injuries | 18 | 110.6 | 65.5 | 174.8 | 14 | 115.9 | 63.3 | 194.4 | 11 | 79.1 | 39.4 | 141.5 | 6 | 86.7 | 31.7 | 188.8 |
| Suicide | 2 | 88.4 | 9.9 | 319.2 | 6 | 324.8 | 118.6 | 706.9 | 2 | 93.8 | 10.5 | 338.6 | 2 | 182.2 | 20.5 | 657.9 |

mortality from non-neoplastic respiratory disease was increased in subsequent duration exposure groups, again in the absence of a clear trend of increasing risk with duration. Moreover, there was no consistent duration-risk relation when the analysis was restricted to miners only.

The duration of exposure for total mortality and selected causes of death is considered in Table IV for miners only. The SMR for the longest category (>20 years) were 112.8 for all causes, 91.6 for all cancers, 323.2 for oral cancer, 173.6 for esophageal cancers, 95.9 for lung cancer, and 322.9 for non-neoplastic respiratory diseases. A direct trend in risk with exposure was observed only for non-neoplastic respiratory diseases.

Table V considers the role of time since first exposure (latency) for the same causes of deaths. For the longest latency level, the SMR was 111.1 for all causes, 92.1 for all cancers, 481.7 for oral cancer, 69.1 for esophageal cancer, 90.8 for lung cancer, and 242.4 for non-neoplastic respiratory diseases. Again a direct trend in risk with time from first

exposure was observed only for non-neoplastic respiratory diseases.

DISCUSSION

In this cohort, there was an excess total mortality due chiefly to non-neoplastic respiratory diseases (mainly classified as silicosis), liver cirrosis, other digestive tract diseases, and suicides. Furthermore, a non-negligible number of deaths (7%) was for unknown cause. Consequently, assuming a non-differential distribution, the SMR for various causes of deaths may also be somewhat underestimated. The potential error due to the use of national rates is in contrast small, since rates for Piedmont were similar to national ones for most diseases considered [Cislaghi et al., 1986].

Our study found no relation between occupational exposure to non-asbestiform talc and risk of mesothelioma and lung cancer. This finding was common to both millers and miners. Miners were also exposed to quartz, radon, and to

| | <10 years | | | | | 10-20 | 0 years | | >20 years | | | | |
|----------------------------|-----------|-------|-------|--------|------|-------|---------|--------|-----------|-------|-------|-------|------|
| All causes | OBS | OBS | SMR | 95 | % CI | OBS | SMR | 95 | % CI | OBS | SMR | 95 | % CI |
| | 144 | 145.4 | 122.6 | 171.2 | 150 | 142.4 | 120.5 | 167.1 | 296 | 112.8 | 100.3 | 126.4 | |
| All cancers | 37 | 136.6 | 96.2 | 188.3 | 30 | 121.4 | 81.9 | 173.3 | 63 | 91.6 | 70.3 | 117.1 | |
| Oral cavity | 9 | 967.2 | 441.3 | 1836.2 | 8 | 967.6 | 416.6 | 1906.7 | 7 | 323.2 | 129.5 | 666.0 | |
| Esophagus | 2 | 306.7 | 34.4 | 1107.4 | 2 | 313.3 | 35.2 | 1131.1 | 3 | 173.6 | 34.9 | 507.1 | |
| Stomach | 2 | 63.9 | 7.2 | 230.6 | 5 | 123.0 | 39.6 | 287.1 | 13 | 135.7 | 72.2 | 232.0 | |
| Intestines | 3 | 106.9 | 21.5 | 312.5 | 4 | 166.9 | 44.9 | 427.4 | 4 | 52.2 | 14.0 | 133.6 | |
| Larynx | 2 | 190.8 | 21.4 | 689.0 | 0 | 0 | 0 | 402.2 | 5 | 193.7 | 62.4 | 452.0 | |
| Lung | 11 | 147.0 | 73.3 | 263.0 | 5 | 87.5 | 28.2 | 204.1 | 17 | 95.9 | 55.9 | 153.6 | |
| Cardiovascular diseases | 43 | 123.6 | 89.4 | 166.5 | 45 | 104.1 | 75.9 | 139.3 | 89 | 77.5 | 62.3 | 95.4 | |
| Cerebral vasculopathy | 7 | 75.9 | 30.4 | 156.5 | 10 | 79.7 | 38.2 | 146.6 | 25 | 74.1 | 48.0 | 109.4 | |
| Respiratory tract diseases | 17 | 284.8 | 165.8 | 455.9 | 22 | 275.1 | 172.4 | 416.6 | 66 | 322.9 | 249.7 | 410.9 | |
| Digestive tract diseases | 11 | 130.5 | 65.0 | 233.4 | 15 | 182.6 | 102.1 | 301.3 | 24 | 124.0 | 79.4 | 184.5 | |
| Cirrhosis | 9 | 179.6 | 81.9 | 340.9 | 12 | 274.0 | 141.4 | 478.7 | 16 | 143.8 | 82.2 | 233.6 | |
| Injuries | 12 | 106.2 | 54.8 | 185.5 | 11 | 134.0 | 66.8 | 239.8 | 11 | 80.3 | 40.1 | 143.8 | |
| Suicide | 1 | 64.2 | 0.8 | 357.0 | 5 | 407.6 | 131.4 | 951.2 | 3 | 140.5 | 28.2 | 410.6 | |

TABLE IV. Total Mortality and Selected Causes of Death by Duration of Exposure for Miners Only

diesel exaust (this last exposure was confined to a short period of time, since 1991). Our results strengthen previous findings on the absence of a major role of non-asbestiform talc in inducing mesothelioma and lung cancer [Rubino et al., 1976, 1979; Leophonte, 1983; Rubino, 1983; Wergeland et al., 1990]. A recent study by Wild et al. [2002] is consistent with our results, since the authors did not find any lung cancer excess mortality from talc exposure.

The results support therefore that excess mortality from mesothelioma and lung cancer can be attributed to asbestiform fibers contained in talc exposure [Kleinfeld et al., 1974; Brown, 1979; Vianna, 1981].

A significant excess mortality from non-malignant respiratory diseases was found in miners only. This observation had already been made by Rubino et al. [1976, 1979] in previous follow-up of the same cohort, and was attributed to the high frequency of silicosis as a cause of death in this cohort. This can be explained by the mixed exposure (including a certain amount of inhalable silica particles) that took place in the past, when rock drilling activity was frequent and technical prevention means had not yet been introduced. Before 1950, dry drilling was still in use and forced ventilation system (FVS) had yet to come; since 1950 wet drilling was introduced and more widely applied in the following years, FVS was introduced between 1958 and 1959 and completed in 1963. Therefore the exposure levels of total respirable dust have been progressively decreasing from 1950 to 1995 (from 100 to 1000 MPPCF—million particles per cubic foot before 1955 to less than 10 MPPCF between 1960 and 1975 [Rubino et al., 1976]). In the last years, exposure levels to talc dusts were monitored and the values in the mine were between 0.5 and 2.5 mg/m³, mean 1.1 mg/m³ for respirable fraction and 0.3–2.0 mg/m³, mean 1.0 mg/m³ for talc alone. There was a remarkable difference in the amount of free silica in air dust, respectively, in mines and mills and within the mine jobs between drilling and other operations. This was mainly due to the high content of quartz in footwall rocks, as opposed to the absence of free silica in talc minerals. In spite of such an exposure to silica particles, no excess lung cancer was observed in this cohort.

Together with other recent reports, including experimental and epidemiological data evaluations [Chan et al., 2000; Hessel et al., 2000; Soutar et al., 2000; Carta et al., 2001; Cocco et al., 2001], the present study provides additional information of interest to further evaluate the association between silica and lung cancer [IARC, 1997; Steenland et al., 2001].

Combined exposure to talc and asbestos has been associated to gastric cancer risk in one German study of 11,633 rubber workers, with a significant RR of 2.3 [Straif et al., 2000]. The RR for lung cancer was 1.7. However we did not find any significant excess mortality for those cancers.

The significant excess mortality from oral cavity and esophageal cancers is likely due to alcohol consumption and cigarette smoking [La Vecchia et al., 1986; Franceschi et al., 1990]. Elevated alcohol drinking in this cohort is also suggested by the excess mortality from liver cirrosis [Corrao et al., 1998].

CONCLUSIONS

In conclusion, no association was found between exposure to talc containing no asbestos fibers and lung cancer or pleural mesothelioma. An excess mortality from alcohol

TABLE V. Total Mortality and Selected Causes of Death by Time Since First Exposure (Latency) for Miners and Millers

| | <20 years | | | | | 20-3 | 0 years | | >30 years | | | | |
|----------------------------|-----------|-------|-------|--------|-----|-------|---------|--------|-----------|-------|-------|--------|--|
| | OBS | SMR | 95 | % CI | OBS | SMR | 95 | % CI | OBS | SMR | 95 | 5% CI | |
| All causes | 154 | 129.6 | 109.9 | 151.7 | 215 | 137.7 | 119.9 | 157.4 | 511 | 111.1 | 101.7 | 121.1 | |
| All cancers | 29 | 112.2 | 75.1 | 161.2 | 46 | 111.4 | 81.5 | 148.6 | 110 | 92.1 | 75.7 | 111.0 | |
| Oral cavity | 7 | 741.1 | 296.9 | 1526.9 | 7 | 450.7 | 180.6 | 928.6 | 17 | 481.7 | 280.4 | 771.3 | |
| Esophagus | 2 | 304.6 | 34.2 | 1099.8 | 6 | 521.0 | 190.3 | 1134.1 | 2 | 69.2 | 7.8 | 250.0 | |
| Stomach | 3 | 61.7 | 12.4 | 180.2 | 8 | 117.0 | 50.4 | 230.6 | 20 | 132.1 | 80.7 | 204.1 | |
| Intestines | 2 | 118.9 | 13.3 | 429.2 | 2 | 57.4 | 6.4 | 207.2 | 9 | 61.1 | 27.9 | 116.0 | |
| Liver and gall bladder | 3 | 190.6 | 38.3 | 557.0 | 3 | 136.1 | 27.4 | 397.8 | 4 | 83.4 | 22.4 | 213.5 | |
| Pancreas | 2 | 277.9 | 31.2 | 1003.4 | 1 | 75.9 | 1.0 | 422.5 | 4 | 95.9 | 25.8 | 245.5 | |
| Peritoneum | 0 | 0 | 0 | 2153.3 | 0 | 0 | 0 | 1647.3 | 0 | 0 | 0 | 681.1 | |
| Larynx | 1 | 96.0 | 1.3 | 533.9 | 2 | 114.5 | 12.9 | 413.3 | 5 | 120.0 | 38.7 | 280.1 | |
| Lung | 6 | 107.6 | 39.3 | 234.2 | 10 | 95.2 | 45.6 | 175.2 | 28 | 90.8 | 60.3 | 131.2 | |
| Pleura | 0 | 0 | 0 | 2325.3 | 0 | 0 | 0 | 1085.7 | 0 | 0 | 0 | 287.3 | |
| Skin | 0 | 0 | 0 | 1190.2 | 0 | 0 | 0 | 937.5 | 3 | 319.5 | 64.2 | 933.6 | |
| Connectival sarcoma | 0 | 0 | 0 | 1048.5 | 0 | 0 | 0 | 8013.8 | 1 | 754.9 | 9.9 | 4200.0 | |
| Prostate | 0 | 0 | 0 | 691.1 | 0 | 0 | 0 | 229.9 | 6 | 71.6 | 26.1 | 155.9 | |
| Bladder | 0 | 0 | 0 | 501.1 | 0 | 0 | 0 | 231.5 | 1 | 15.7 | 0.2 | 87.2 | |
| Kidney | 0 | 0 | 0 | 906.7 | 0 | 0 | 0 | 522.9 | 1 | 46.0 | 0.6 | 256.0 | |
| Non Hodgkin lymphomas | 1 | 167.9 | 2.2 | 934.3 | 0 | 0 | 0 | 573.5 | 1 | 61.3 | 0.8 | 340.8 | |
| Hodgkin's disease | 0 | 0 | 0 | 493.7 | 0 | 0 | 0 | 768.8 | 0 | 0 | 0 | 641.2 | |
| Leukemias | 0 | 0 | 0 | 285.7 | 2 | 138.8 | 15.6 | 501.2 | 3 | 70.7 | 14.2 | 206.4 | |
| Diabetes | 1 | 91.1 | 1.2 | 506.7 | 0 | 0 | 0 | 170.6 | 4 | 51.4 | 13.8 | 131.6 | |
| Cardiovascular diseases | 32 | 90.5 | 61.9 | 127.8 | 72 | 117.6 | 92.0 | 148.1 | 184 | 86.6 | 74.5 | 100.0 | |
| Cerebral vasculopathy | 7 | 78.9 | 31.6 | 162.6 | 15 | 87.1 | 48.7 | 143.6 | 38 | 59.3 | 42.0 | 81.4 | |
| Respiratory tract diseases | 11 | 147.6 | 73.4 | 263.6 | 26 | 234.8 | 153.4 | 344.1 | 90 | 242.4 | 194.9 | 298.0 | |
| Digestive tract diseases | 16 | 136.0 | 77.7 | 220.9 | 26 | 182.7 | 119.3 | 267.7 | 37 | 125.2 | 88.2 | 172.6 | |
| Cirrhosis | 11 | 180.8 | 90.1 | 323.5 | 23 | 265.8 | 168.4 | 398.8 | 21 | 127.5 | 78.9 | 195.0 | |
| Injuries | 25 | 134.6 | 87.1 | 198.6 | 8 | 70.1 | 30.2 | 138.1 | 16 | 83.3 | 47.6 | 135.3 | |
| Suicide | 6 | 233.6 | 85.3 | 508.5 | 2 | 107.8 | 12.1 | 389.2 | 4 | 137.2 | 36.9 | 351.3 | |

related cancers and from other non-malignant disease relative to alcohol was found. Mortality from non-malignant respiratory diseases was increased only in miners, and this excess can be attributed to a mixed exposure to quartz in past years. Furthermore our mortality data from silicosis in miners, in the absence of an excess mortality from lung cancer, do not support the hypothesis of an association between silica exposure, silicosis, and the development of lung cancer.

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