Cancer Science
The official journal of the Japanese Cancer Association

Cause-specific mortality in a Chinese chrysotile textile worker cohort

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(Received September 21, 2012/Revised October 27, 2012/Accepted October 30, 2012/Accepted manuscript online November 3, 2012/Article first published online December 12, 2012)

Chrysotile asbestos has continued to be mined and used in China, but its health effects on exposed workers have not been well documented. This study was conducted to give a complete picture about cause-specific mortality in Chinese asbestos workers. A cohort of 586 males and 279 females from a chrysotile textile factory were prospectively followed for 37 years. Their vital status was identified, and the date and underlying cause of death were verified from death registry. Cause-specific standardized mortality ratios by gender were computed with nationwide gender- and cause-specific mortality rates as reference. Male workers were 11 years older, and had 6 years longer exposure duration than females; 79% in males and 1% in females smoked. In males, the mortality rate of all cancers doubled; both larynx and lung cancer were four-fold, and mesothelioma was 33-fold. In females, there was slightly excess mortality from lung cancer and all cancers, and significant increase in mesothelioma and ovarian cancer. Other significantly increased mortality was seen from cancers of thymus, small intestine and penis in males, and cancers of bone and bladder in females. In addition to asbestosis, mortality from pulmonary heart disease was significantly elevated in both genders. The data confirmed significantly excess mortality from mesothelioma in either gender, lung and larynx cancers in males, and ovarian cancer in females. A gender difference in mortality from lung cancer and all cancers could be mainly due to the discrepancies in age, exposure duration and smoking between the male and female workers. (*Cancer Sci* 2013; 104: 245–249)

Asbestos, a naturally occurring fibrous mineral, is an important cause of human disease, which may cause asbestosis, a progressive, debilitating fibrotic disease of the lungs, lung cancer, mesothelioma, and laryngeal cancer, and may cause ovarian, gastrointestinal cancers and other cancers.[1,2] Although 52 countries have banned production and use of all types of asbestos,[3] there remain about 125 million people in the world who are currently exposed to asbestos in their working environment; more than 107 000 people die each year from asbestos-related lung cancer and asbestosis.[4] Chrysotile asbestos has been intensively mined, imported and used in many developing countries. Thus, the topic of occupational exposure to asbestos and its related adverse health outcomes remains interesting, though not new to the scientific community, policy makers and the general public.[5] Overall, an increasing amount of evidence for chrysotile related lung cancer and mesothelioma in relation to asbestos has been accumulated.[6–10]

In China, production and use of chrysotile asbestos has continued, and over 100 000 workers are estimated to be currently exposed to asbestos occupationally. However, asbestos-related diseases, in particular, asbestos-related cancers, have been understudied. Although asbestos-related lung cancer has been defined officially as occupational disease since the 1980s, national data of the incidence/prevalence or mortality of lung cancer and other malignant diseases among asbestos workers are lacking. There have been several individual studies that addressed the risks of lung cancer and mesothelioma in either asbestos textile workers[11–13] or asbestos miners in China.[14] We recently reported excess mortality from lung cancer and nonmalignant respiratory diseases in male workers from a chrysotile textile manufacturing factory, who were prospectively followed for 37 years.[10] The risks for lung cancer and respiratory disease deaths in the asbestos workers were over threefold that in the unexposed controls. We also observed an exposure-dependent mode with asbestos exposure level and lung cancer mortality in both smokers and nonsmokers. In the current analysis, we computed all cause mortality, including both malignant and non-malignant outcomes, in these workers and female workers from the same factory. The latter was never reported before. The aim of the analysis is to provide a complete picture of the cause-specific deaths observed in this cohort, and to make a comparison of the mortality rates between the males and females.

Materials and Methods

The cohort was established on 1 January 1972 in an asbestos textile factory in China, where only chrysotile was used since 1958 to manufacture asbestos textiles, friction and rubber materials, and construction materials, such as asbestos cement and tiles. The factory did not hire females until 1970. The concentrations of dust and fibers measured at different workshops periodically were generally far higher than the Chinese national standards.[12] A more recent measurement conducted in 2002 indicated that the asbestos fiber concentrations in air samples were 18 f/cm^3 in the raw material section, and 6 f/cm^3 in the textile section; the fiber concentrations in personal samples were 6 and 8 f/cm^3 in the two sections, respectively.[10] Analysis of available chrysotile samples by X-ray diffraction and transmission electron microscopy indicated a very low level of tremolite contamination.[12] The cohort, consisting of 586 males and 279 females, who had been hired by the factory for at least 1 year at the beginning of 1972, was prospectively followed through the end of December, 2008. About 30% of the males worked in the raw material and textile sections, 22% as maintenance, 28% in rubber and cement sections, and 20% in administration or real service. In females, 9% were in raw materials, 9% in rubber and cement, 16% in administration or real service, and the remaining 68% in the textile section. Only nine men and two women got lost in the end of follow-up, leaving a follow-up rate of nearly 99% in both genders.

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doi: 10.1111/cas.12060

In addition to detailed information on workers' occupational history and personal data that were collected from either personnel records or individual contacts,[10] workers' vital status was verified by using a combination of active follow-up and record linkages to death certificates kept in the factory. Personnel records including workers' addresses and vital status information were well kept in the factory. For those deceased, the date and underlying cause of death were retrieved and verified from hospitals and a local death registry. All causes of deaths were coded according to the Tenth Revision of the International Classification of Diseases (ICD-10). There were nine deaths in men and one death in women with unknown cause of death. The study was approved by the Research Ethics Committee of the Chinese University of Hong Kong.

The data analysis was centered on computing cause-specific standardized mortality ratios (SMRs) by gender. The expected number of deaths was calculated based on person years multiplied by the Chinese nationwide gender- and cause-specific mortality rates adjusted for 5-year age groups. Person years were accrued from the date of entry into the cohort until the date of death or the end of follow-up. Mortality rates from three available national censuses during 1973–1975,[15] 1990–1992[16] and 2004–2005[17] were used as reference mortality, which corresponded to three calendar periods, i.e. 1972–1981, 1982–1995 and 1996–2008, respectively. National mortality rates of pneumoconiosis were used to calculate SMRs for asbestosis due to unavailability of a mortality rate for asbestosis in the general population. SMR for mesothelioma was estimated based on the third national survey (2004–2005) because this type of cancer was not coded until the application of ICD-10. Ninety five percent confidence intervals (95% CI) of SMRs were estimated based on an assumption of a Poisson distribution for the observed deaths.[18] All data analyses were carried out with the Statistical Package for the Social Sciences Software version 16.0 for Windows and EXCEL 2007.

Results

Table 1 gives the main characteristics of the cohort by gender. The follow-up observation generated 17 508 person years in males and, 9 967 person years in females. Male workers were 40 years old when entering in the cohort (at entry), on average, as opposed to 29 years old in females. Correspondingly, males had employment duration of 6 years longer than did females either at entry or in total. The majority of males (79%) smoked, whereas only three females (1%) did; 127 males (22%) and 23 females (8%) were diagnosed as having asbestosis. Overall, 259 deaths (44%) in males and 26 deaths (9%) in females were identified over the period of observation.

Table 1. Basic data of males and females in asbestos textile worker cohort, China, 1972–2008

	Males (n = 586)	Females (n = 279)
Total person-years of follow up	17 508	9967
Year of birth, median (P25, P75)	1930 (1922, 1944)	1946 (1936, 1950)
Age at entry, mean (SD)	39.8 (11.9)	28.8 (8.6)
Employment years at entry, mean (SD)	10.8 (6.7)	4.6 (4.4)
Total employment years, mean (SD)	25.5 (8.4)	19.4 (9.3)
Ever-smoking, n (%)	460 (78.5)	3 (1.1)
Asbestosis, n (%)	127 (21.7)	23 (8.2)
Vital status, n (%)		
Alive	318 (54.3)	251 (90.0)
Deceased	259 (44.2)	26 (9.3)
Lost	9 (1.5)	2 (0.7)

SD, standard deviation.

Table 2 shows the observed and expected numbers of deaths and SMRs from all sites of malignant disease. In males, there were 96 deaths from all cancers, leading to twofold mortality that in the national level (SMR 2.09; 95% CI 1.71–2.55). Significantly excess mortality was observed from cancer of small intestine, larynx, lung cancer (including tracheal and bronchial cancer), mesothelioma, thymus cancer and penis. Mortality from either larynx or lung cancer was over four-fold and that from mesothelioma and cancers of thymus and penis were 31–59-fold, as opposed to the excepted, although the calculations were based on only one or two cases in most of these cancers. In addition, there was elevated mortality from leukemia and kidney cancer, and slightly increased mortality from cancer of prostate, esophagus, liver and bile duct. In females, 10 deaths from different forms of cancer were observed, leading to a slightly excess mortality rate (SMR 1.34; 0.73, 2.46). There were two deaths from lung cancer, with a slight increase in the mortality. Meanwhile, one death from mesothelioma (peritoneum), cancer of bone, ovary, bladder, respectively, was observed, leading to significantly excess mortality from these cancers. Mortality from stomach and uterus cancers was also increased.

Lung cancer mortality in workers with or without asbestosis was calculated. There was no lung cancer death observed in female workers with asbestosis. In males, lung cancer deaths accounted for 17% (22/127) in those with asbestosis, and only for 7% (31/450) in those without asbestosis. Furthermore, mortality from lung cancer and all cancers by smoking was also analyzed in males. The mortality rate of lung cancer in smokers was 10% (47/452), which was double that (5%, 6/125) in nonsmokers. The rate of all cancers was 18% (79/452) in smokers and 14% (17/125) in nonsmokers.

Table 3 displays observed and expected deaths and SMRs from non-malignant diseases. Thirty-seven men and three women died from asbestosis, accounting for a major cause of deaths in respiratory diseases. Mortality from pulmonary heart disease was significantly increased in either gender, with 13 times in men and eight times in women than expected. Besides, deaths from diabetes mellitus were significantly increased in females and from accidents (including injury and poisoning) in males. When deaths from all causes were combined, mortality was significantly increased in males (SMR 1.31; 95% CI, 1.16–1.48), but not in females.

Discussion

Since the 1970s, International Agency for Research on Cancer (IARC) has classified all types of asbestos as carcinogenic agents of larynx, lung, mesothelioma and ovary cancers with sufficient evidence in humans and of colorectum, pharynx and stomach cancers with limited evidence.[19, 20] We estimated cause-specific SMRs in both male and female asbestos workers, and confirmed significantly excess mortality from mesothelioma in either gender, lung and larynx cancers in the males, and ovary cancer in the females. There were 53 deaths from lung cancer, and two deaths from larynx and mesothelioma, respectively, in male workers. The deaths from lung cancer and mesothelioma (one pleural and one peritoneal) were reported previously.[10,12] SMR from either larynx cancer or lung cancer was fourfold and that from mesothelioma was 33-fold that expected. SMR from mesothelioma was 166.7 and ovarian cancer 7.7 in the females, although that was based on only one death.

These observed results, overall, were consistent with other studies observed from chrysotile exposed workers in different countries. In a follow-up study of chrysotile textile workers in

doi: 10.1111/cas.12060

Table 2. Standardized mortality ratios (SMRs) for all sites of cancer in asbestos textile worker cohort, China, 1972–2008

Cause of death (ICD-10)	Males (n = 577)		Females (n = 277)	
	Obs/Exp	SMR (95% CI)	Obs/Exp	SMR (95% CI)
All cancers	96/45.96	2.09 (1.71, 2.55)†	10/7.47	1.34 (0.73, 2.46)
Digestive system				
Esophagus (C15)	7/5.59	1.25 (0.61, 2.59)	0/0.39	
Stomach (C16)	3/6.98	0.43 (0.15, 1.27)	2/1.04	1.92 (0.53, 7.01)
Liver and bile duct (C22)	15/11.21	1.34 (0.81, 2.21)	0/1.02	
Small intestine (C17)	1/0.11	9.09 (1.60, 51.50)†	0/0.02	
Colon and rectum (C18–20)	3/2.80	1.07 (0.36, 3.15)	0/0.45	
Respiratory system				
Larynx (C32)	2/0.47	4.26 (1.17, 15.52)†	0/0.02	
Nasopharynx (C11)	1/0.98	1.02 (0.18, 5.78)	0/0.12	
Trachea, bronchus and lung (C33–34)	53/13.00	4.08 (3.12, 5.33)†	2/1.62	1.23 (0.34, 4.50)
Bone cancer (C40–41)	0/0.61		1/0.11	9.09 (1.06, 51.50)†
Mesothelioma‡(C45)	2/0.06	33.33 (9.14, 121.55)†	1/0.006	166.67 (29.42, 944.18)†
Thymus (C75)	1/0.02	58.82 (10.38, 333.24)†	0/0.006	
Lymph sarcoma (C81)	2/0.87	2.30 (0.63, 8.38)	0/0.35	
Leukemia (C91)	1/1.05	0.95 (0.17, 5.40)	0/0.63	
Male genital organs (C60–63)				
Penis (C60)	1/0.03	31.25 (5.52, 177.03)†	–	
Prostate (C61)	1/0.59	1.69 (0.30, 9.60)	–	
Female genital organs(C51–58)				
Breast (C51)	–		1/0.78	1.28 (0.23, 7.26)
Ovary (C56)	–		1/0.13	7.69 (1.36, 43.58)†
Uterus (C55)	–		1/0.33	3.03 (0.53, 17.17)
Urinary organs (C64–68)				
Kidney (C64)	1/0.33	3.03 (0.53, 17.17)	0/0.12	
Bladder cancer (C67)	0/0.07		1/0.04	25.0 (4.41, 141.63)†
Brain (C70)	1/1.16	0.86 (0.15, 4.88)	0/0.42	
Unspecific site of cancer	1	–	–	

Exp, expected number of deaths; Obs, observed number of deaths. †95% CI does not include unity. ‡Mesothelioma mortality was computed based on the third national survey (2004–2005).

Table 3. Standardized mortality ratios (SMRs) for non-malignant diseases in asbestos textile worker cohort, China, 1972–2008

Cause of death (ICD-10)c	Males (n = 577)		Females (n = 277)	
	Obs/Exp	SMR (95% CI)	Obs/Exp	SMR (95% CI)
Respiratory diseases				
Asbestosis (J66)	37/0.37	100.00 (72.55, 137.83)†	3/0.038	78.95 (26.85, 232.14)†
Others (Pneumonia, abscess) (J18, J44)	5/6.67	0.75 (0.32, 1.75)	2/1.33	1.50 (0.41, 5.48)
Lung tuberculosis (A19)	4/2.21	1.81 (0.70, 4.65)	0/0.91	
Digestive diseases (K25–27)	3/1.62	1.85 (0.63, 5.45)	0/0.78	
Cirrhosis and other chronic liver diseases (K72–74)	5/4.27	1.17 (0.50, 2.74)	0/1.55	
Diseases of heart				
Pulmonary heart disease (I26)	36/2.75	13.09 (9.46, 18.12)†	2/0.24	8.33 (2.29, 30.39)†
Other diseases of the heart (I11, I09, I25, I50)	15/17.34	0.87 (0.52, 1.43)	3/2.95	1.02 (0.35, 2.99)
Cerebrovascular diseases (I62–63)	22/22.50	0.98 (0.65, 1.48)	1/3.51	0.28 (0.05, 1.61)
Diabetes mellitus (E10–14)	3/3.16	0.95 (0.32, 2.79)	3/0.80	3.75 (1.28, 11.03)†
Nervous system disorders (G00)	3/1.16	2.59 (0.88, 7.60)	0/0.86	
Accidents (V71–72, Y17–18, T50, T97)	21/13.50	1.56 (1.02, 2.38)†	1/3.21	0.31 (0.05, 1.76)
Unknown cause‡	9	–	1	–
All causes§	259/197.27	1.31 (1.16, 1.48)†	26/31.57	0.82 (0.56, 1.21)

Exp, expected number of deaths; Obs, observed number of deaths. †95% CI does not include unity. ‡Includes deaths with a missing cause, SMR not reported. §Including deaths from both malignant and nonmalignant diseases.

South Carolina,[6] SMR from all cancers were significantly elevated in males, and slightly increased in females, while significantly excess SMR for lung cancer was observed in both males and females. There were three cases of mesothelioma in the South Carolina worker cohort, all in males. Mortality from larynx in both males and females was over twofold that expected, though not significantly. No ovarian cancer was reported specifically. In a Quebec cohort study,[21] increased mortality was observed from lung cancer (SMR 1.40), larynx (SMR 1.3) and stomach (SMR 1.17), but neither confidence interval nor P-value was provided in that study. Apart from these cancers, we also observed significantly increased mortality from cancers of

thymus, small intestine and penis in the males, and cancer of bone and bladder in the females, but all were based on one case. Two deaths from stomach cancer were found in the females, resulting in nearly doubled mortality that expected. There was no increased SMR from colorectal cancer in either gender.

There was an obvious gender difference in mortality from all cancers and lung cancer observed in the cohort. Significantly increased SMR from all cancers was seen in males, but not in females. Furthermore, the females had a slightly elevated SMR (1.23) from lung cancer, in contrast to the males that had fourfold SMR that expected. A different distribution in workshops/departments or job titles between the genders did not seem to be an explanation for the discrepancy in cancer mortality between genders. The majority of the females worked in either textile or raw material sections where asbestos dust or fiber concentrations were higher than other sections.[10,12] Nevertheless, there were several other possible explanations. First of all, their ages were significantly different: the females were 11 years younger than the males when they entered the cohort. At the end of follow-up, the males reached an average 77 years old, whereas the females were 66 years old. It was not surprising that more deaths from cancers occurred in an older age group. It would be reasonable to expect that more deaths than expected from cancers, as well as other diseases, would be observed in the females during the next 10 years or so. The second explanation is the different exposure duration between the genders. The males had average exposures of 11 years when entering the cohort, and 26 years in total, compared to the females who had nearly 5 years when entering the cohort and 19 years in total. Exposure duration was found to be a significant determinant for mortality from lung cancer and all cancers in our previous analyses.[10,12] Besides, only males were employed during the first 10 years after the factory started to operate. A dust control procedure in the factory was not implemented until the 1970s. Although asbestos dust/fiber concentrations always exceeded the national occupational standards, they were generally decreased over time. Therefore, workers (male workers) employed in the early years in the factory were likely to be exposed to a higher level of asbestos than those hired later on, due to higher dust /fiber concentrations and poorer working conditions in the early years. Another important factor for explaining the gender difference in cancer mortality, especially lung cancer mortality, is smoking. There was a big difference in smoking status between the genders: most of the males (79%) were smokers, while only a few females (1%) smoked. The male smokers had a doubled rate of lung cancer, compared to the nonsmokers. It was not beyond the expectation that more deaths from lung cancer were observed in the males, given the interactive effect of smoking and asbestos exposure on lung cancer observed in the male asbestos workers[10] and chrysotile asbestos miners.[14] On the other hand, the prevalence of smoking was about 60% in males and 3–5% in females in the general population of China. It is possible that the estimated SMR for lung cancer has been overestimated in the males and somewhat underestimated in the females by using the mortality data of the general population as reference, because of different proportions of smokers from these workers. In addition, the data indicated that more lung cancer deaths occurred in workers with asbestosis than those without.

In terms of mortality from nonmalignant diseases, there were 37 males and three females who died of asbestosis-related conditions. Altogether, 127 males and 23 females in the cohort were diagnosed as having asbestosis according to the Chinese radiographic diagnosis criteria, with prevalences of 22% and 8%, respectively. Again, the gender difference in the prevalence of asbestosis may be explained by discrepancies in age, exposure duration, and a higher level of exposure by the males in the early years. In addition, 36 deaths in the males and two deaths in the females were coded as pulmonary heart disease, leading to significantly increased SMR in either gender. There was no excess mortality from cerebrovascular disease in either males or females in this study, although some studies reported a higher mortality rate in asbestos workers. In South Carolina chrysotile textile workers, significantly increased SMR from cerebrovascular disease was observed in males, but not in females.[6] A recent mortality study among British asbestos workers also reported statistically significant excess mortality from the disease in both men and women, which were associated with asbestos exposure and birth cohort.[22] However, no increase in SMR (1.06) from the disease was found in the Quebec miner cohort.[21] These indicated no consistent evidence regarding the association between cerebrovascular disease and asbestos exposure.

In summary, we estimated cause-specific SMRs in the Chinese male and female asbestos textile workers who were exposed to only chrysotile and confirmed significantly excess mortality from mesothelioma in either gender, lung cancers and larynx in the males, and ovary cancer in females, although the case number in some cancers was limited. In addition to asbestosis, mortality from pulmonary heart disease was significantly increased in either males or females. A gender difference in mortality from lung cancer and all cancers observed in this cohort could be mainly explained by the discrepancies in age, exposure duration and smoking between the male and female workers.

Acknowledgments

This study was funded by the Pneumoconiosis Compensation Fund Board, Hong Kong SAR, China. The authors wish to thank Professors Mianzhen Wang and Zhiming Wang and Dr Du Lili for participating in data collection and all workers in the asbestos factory for their cooperation.

Disclosure Statement

The authors have no conflict of interest.

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doi: 10.1111/cas.12060

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